Are MEDLINE Searches Sufficient for Systematic Reviews and Meta-analyses of the Diagnostic Accuracy of Depression Screening Tools? A Review of Meta-analyses

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Running Head: Searching MEDLINE for Meta-analyses of Depression Screening Tools

Abstract

Objective: Database searches for studies of diagnostic test accuracy are notoriously difficult to filter, highly resource-intensive, and a potential barrier to quality evidence synthesis. We examined published meta-analyses of depression screening tool accuracy to evaluate the (1) proportion of included primary studies found in any online database in the original meta-analyses that were indexed in MEDLINE; (2) the proportion of patients from MEDLINE-indexed studies; and (3) the proportion of depression cases from studies indexed in MEDLINE.

Methods: MEDLINE and PsycINFO were searched from January 1, 2005 through October 31, 2014 for meta-analyses in any language on the accuracy of depression screening tools.

Results: We identified 16 eligible meta-analyses that included 398 primary study citations, which had been identified via an online database in the original meta-analyses, including 257 unique citations and 234 unique patient samples. The 234 unique patient samples included 69,957 total patients and 11,867 depression cases. Of these, 220 samples (94%) were from studies indexed in MEDLINE, including 97% of all patients and 96% of all depression cases. When applying a peer-reviewed search strategy in MEDLINE, 91% of all samples, 96% of patients and 95% of depression cases were retrieved. Results were similar for total and unique citations.

Conclusions: Restricting searches to MEDLINE may capture almost all eligible studies, patients and depression cases. Although not examined in the present study, MEDLINE may not be indexed as quickly as other databases. Thus, MEDLINE searches should be complemented by date-limited searches of other databases for recent citations.

Keywords: Depression screening; diagnostic test accuracy; meta-analyses; search strategies; MEDLINE

INTRODUCTION

Meta-analyses of diagnostic test accuracy (DTA) quantitatively synthesize results of individual diagnostic accuracy studies and provide information about the quality of primary studies (1). One key component that determines the quality of a meta-analysis is the degree to which database searches are sufficiently comprehensive to ensure that all relevant studies are identified for inclusion (2).

The process of gathering relevant literature and identifying publications that fit inclusion criteria can be time-consuming and costly. Searching for DTA studies is even more complex and resource-intensive than other study designs, including randomized controlled trials, and may be a barrier to conducting quality systematic reviews and meta-analyses (3). Thus, finding a balance between having a manageable number of citations from databases to evaluate, while being as complete as possible is an important consideration (1). Search strategies are typically designed with the goal of finding all available references that can help answer a research question (4). However, failing to find all studies does not necessarily influence summary estimates meaningfully (1). A recent study, for instance, reported that restricting searches for DTA studies to only MEDLINE did not influence summary estimates of meta-analyses reviewed (5). That is, across published meta-analyses, it was the case that there were few eligible studies listed in databases other than MEDLINE, the studies that were listed in non-MEDLINE databases generated similar results to those in MEDLINE, or studies in non-MEDLINE databases included samples of too few patients to influence meta-analysis results.

Systematic reviews and meta-analyses of the diagnostic test accuracy of depression screening tools can often involve scrutinizing very large numbers of citations from searched databases (6, 7). No research, however, has evaluated the proportion of studies on depression

screening tools that would be identified if only MEDLINE were searched. Thus, the objectives of this study were to evaluate meta-analyses on the diagnostic accuracy of depression screening tools to determine (1) the proportion of included primary studies found in any online database in original meta-analyses that were indexed in MEDLINE; (2) the proportion of patients from primary studies found in any database that were from studies indexed in MEDLINE; and (3) the proportion of cases of depression from primary studies found in any database that were from studies indexed in MEDLINE.

METHODS

Identification of Meta-Analyses on the Diagnostic Accuracy of Depression Screening Tools

We searched MEDLINE and PsycINFO (both on the OvidSP platform) from January 1, 2005 through October 31, 2014 for meta-analyses in any language on the diagnostic accuracy of depression screening tools. A peer reviewed search strategy originally designed to identify primary studies on the diagnostic accuracy of depression screening tools was used (8), and adapted by a librarian to restrict the results to meta-analyses. The complete search strategy for MEDLINE can be found in Appendix A. The strategy was adapted by the librarian for PsycINFO.

We included publications of meta-analyses, but not systematic reviews without meta-analyses, in order to focus only on relatively commonly used screening tools, which are more likely to be included in systematic reviews with meta-analyses. Eligible publications had to include one or more meta-analyses that: (1) included a documented systematic review of the literature using at least one electronic database; (2) statistically combined results from ≥ 2 primary studies; and (3) reported measures of diagnostic accuracy (e.g., sensitivity, specificity,

diagnostic odds ratio) of one or more depression screening tools compared to a reference standard diagnosis of depression based on a clinical interview or validated diagnostic interview. We excluded meta-analyses of only measurement properties other than diagnostic accuracy (e.g., general validity, reliability). Publications that included meta-analyses of diagnostic accuracy and other measurement characteristics were included, but only results related to diagnostic accuracy were extracted. Similarly, publications that included meta-analyses of the diagnostic accuracy of screening tools for depression and for other disorders, such as anxiety disorders, were included, but only results for screening for depression were reviewed.

Search results were initially downloaded into the citation management database RefWorks (RefWorks, RefWorks-COS, Bethesda, MD, USA) and transferred into the systematic review program DistillerSR (Evidence Partners, Ottawa, Canada). DistillerSR was used to identify duplicate citations and to track results of the review process. Two investigators independently reviewed citations for eligibility. If either reviewer deemed a meta-analysis potentially eligible based on a review of the title and abstract, we carried out a full text review of the article. Any disagreement between reviewers after full-text evaluation was resolved by consensus after consultation with an independent third reviewer.

Data Extraction

Meta-analyses. One investigator independently extracted data from each included meta-analysis publication into a standardized database. Data extraction was checked by a second reviewer and any disagreements were resolved by consensus. For each meta-analysis publication, we extracted author, year of publication, journal, and journal impact factor for 2014. Some publications included results from more than one meta-analysis. In these publications, for each meta-analysis, separately, we extracted the name of the screening tool(s) evaluated, patients or

setting, the number of primary depression screening accuracy studies from which data were meta-analyzed, and the number of unique patient samples from those studies.

Primary Studies. For each primary study included in the meta-analyses we reviewed, we extracted the screening tool(s) evaluated, study population, the number of patients included in analyses, the number of depression cases included in analyses, and whether or not the primary study was from a publication indexed in MEDLINE. We did this by means of a known-item search, using the OvidSP platform. We conducted this search based on information in the full reference (title, author, year of publication, or other metadata) that was extracted from each primary study. For each primary study found in MEDLINE, we recorded its PubMed identification number. In addition, for all studies listed in MEDLINE, we checked whether the study would be retrieved using a previously published peer-reviewed search (9). All data were extracted by one reviewer and validated by a second reviewer. Discrepancies were resolved by consensus.

For any primary studies not found in MEDLINE, we searched a core set of electronic databases in the health sciences (PsycINFO, Scopus, EMBASE, Web of Science, and CINAHL) using a similar approach to attempt to find the study. If the primary study was not indexed in any of these core databases, we then searched all additional databases that were searched in the original meta-analysis to determine the source database. If publications were still not found, Google Scholar was searched in an attempt to locate the database where the primary study was indexed. We recorded the database where the studies were located. If not located in any of our core databases or the original meta-analysis databases, we concluded that the study was not retrievable from the databases and had been identified via other methods in the original meta-analyses.

Of primary studies included in each included meta-analysis, we only extracted data for primary studies that compared a depression screening tool to a clinical interview or validated diagnostic interview to diagnose depression. We excluded from consideration primary studies where a depression screening tool was compared to a score on a rating scale (e.g. Hamilton Rating Scale for Depression), but not a diagnosis of depression, even if these were included in the meta-analyses.

When there were multiple publications from the same patient sample listed in a meta-analysis, we extracted data for each publication separately since a purpose of the present study was to ascertain the degree to which a MEDLINE search alone would identify all potentially relevant publications. However, we also identified publications that reported on the same or overlapping patient samples so that we could also calculate the proportion of unique samples, patients, and depression cases that could have been found in MEDLINE.

If the number of depression cases for a primary study was not reported in the meta-analysis, we extracted the largest number of depression cases available from the primary study. For instance, if the primary study reported both number of major depression cases and number of patients with any depressive disorder, we extracted the larger number.

Comprehensiveness of Searches of Meta-analyses

To assess the comprehensiveness of the search used for each included meta-analysis, we identified (1) the number of electronic databases searched and the names of each database included with the platform used; (2) whether additional methods (e.g., reference lists of other reviews, reference lists of included primary studies, expert contacts, known-author searches, manual journal searches, forward citation searches of included primary studies, domain specific conference abstracts) were used and, if any, which were used (see Appendix B); (3) the years

covered by the search; and (4) whether the search included a search filter, and if so, which one(s). We evaluated each component of search comprehensiveness individually, but did not attempt to generate a sum score for search comprehensiveness since there is no evidence of the validity of any method for summing components of search conduct and reporting. In addition, for each meta-analysis, we determined if the full, reproducible MEDLINE search strategy was provided in the text, an appendix, or as a supplemental online file.

Data Analysis

For each meta-analysis and for all meta-analyses combined, we determined the number and proportion of included primary studies that could be retrieved through MEDLINE. In addition, of primary studies found within an online database we evaluated the proportion of total patients and the proportion of total cases of depression that were included in studies found in MEDLINE. Further, we determined the proportion of unique citations and unique patient samples that could be retrieved through MEDLINE. Studies not found within a core database or a database that the meta-analyses authors searched were excluded from totals since the purpose of our study was to compare the effectiveness of MEDLINE versus all relevant databases but not to compare to other methods, such as author queries or reference lists.

RESULTS

Search Results

The electronic database search yielded 1321 unique titles and abstracts for review. Of these, 1296 were excluded after title and abstract review because they did not report results from a meta-analysis or because the study was not related to the diagnostic accuracy of a depression screening tool. Of the 25 articles that underwent full-text review, 9 were excluded, resulting in 16 eligible meta-analyses (6, 7, 10-23) (see Figure 1). Of these, all 16 were identified by

searching MEDLINE, whereas only 11 were identified by searching PsycINFO. Characteristics of selected meta-analyses are shown in Table 1. The 16 meta-analysis publications included between 4 and 107 primary studies and were published in 13 different journals with impact factors ranging from 2.3 to 6.8.

Figure 1 Flow Diagram of Selection of Meta-Analyses of the Diagnostic Accuracy of Depression Screening Tool

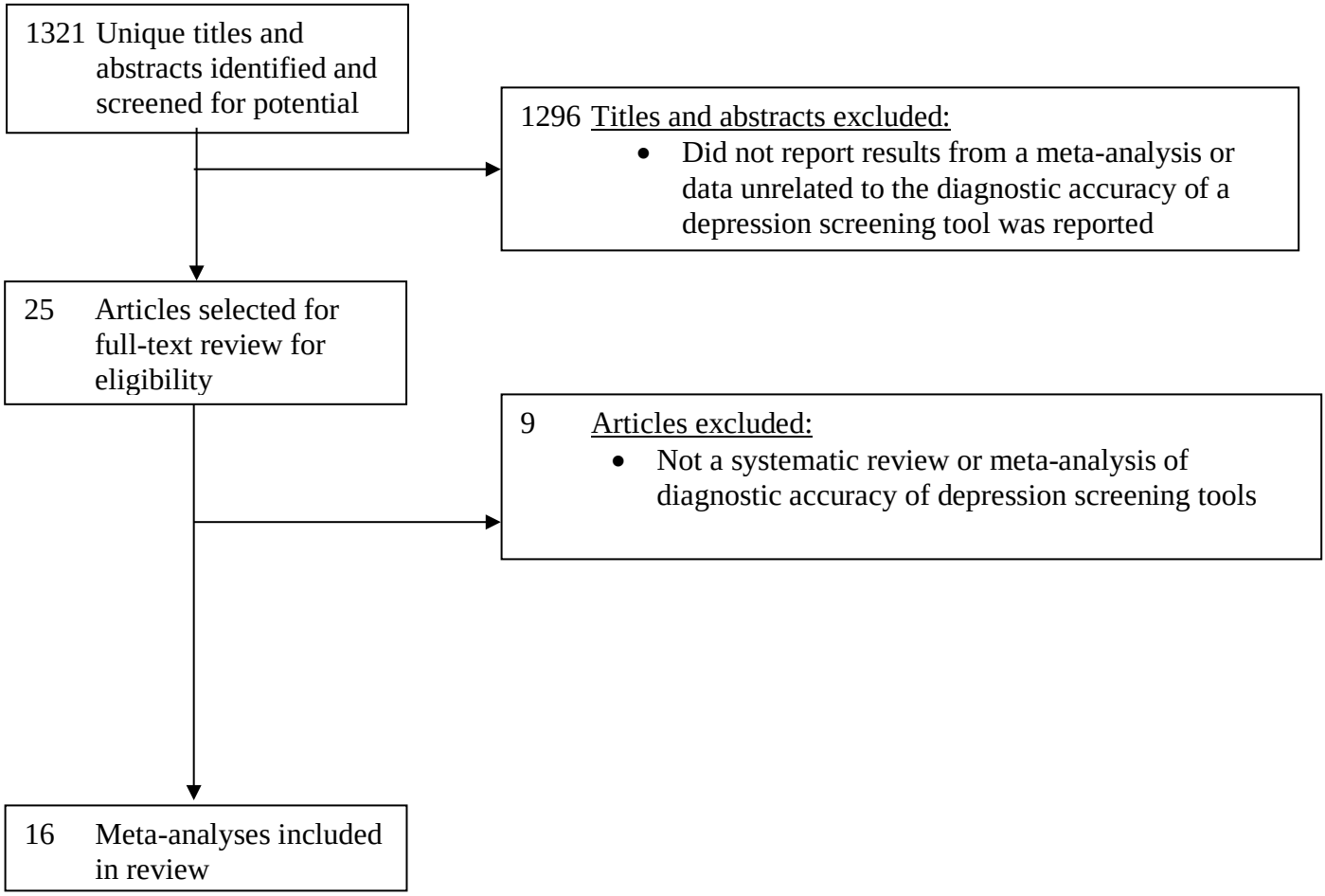


Table 1 Characteristics of Included Meta-Analyses

First Author, Year of Publication	Journal (2014 Impact Factor)	Focus of Meta-Analysis	Number of Studies Indexed in PubMed	% of Total Studies in Meta-Analysis	Number of Patients in Studies in PubMed	% of Total Patients in Meta-Analysis	Number of Depression Cases in Studies in PubMed	% of Total Depression Cases in Meta-Analysis
Meader, 2014	J Neurol Neurosurg Psychiatry (6.8)	Screening tools in poststroke patients	20	100	2542	100	663	100
Tsai, 2014	JAIDS (4.6)	Screening tools in HIV-positive adults in Africa	4	100	1502	100	200	100
Tsai, 2013	PLoS One (3.2)	Screening tools in pregnancy or postpartum in Africa	10	91	1984	97	353	95
Manea, 2012	CMAJ (6.0)	PHQ-9 in any setting	16	89	6472	97	875	96
Mitchell, 2012	J Affect Disord (3.4)	Screening tools in cancer patients	29	97	4842	96	869	98
Meader, 2011	Br J Gen Pract (2.3)	Screening tools in patients with chronic physical health problems	103	96	18246	97	4232	95
Vodermaier, 2011	Support Care Cancer (2.5)	HADS in cancer patients	13	93	2348	93	465	97
Brennan, 2010	J Psychosom Res (2.7)	HADS in any setting	22	92	4071	96	778	95
Mitchell, 2010a	Am J Geriatr Psychiatry (4.2)	GDS in older patients	30	83	3650	91	929	89
Mitchell,	J Affect Disord	HADS in cancer and	10	100	1950	100	430	100

2010b	(3.4)	palliative settings						
Mitchell, 2010c	J Affect Disord (3.4)	GDS in older primary care patients	13	100	3554	100	676	100
Hewitt, 2009	Health Technol Assess (5.0)	Screening tools in women in pregnancy or postpartum	56	93	13029	96	2134	97
Mitchell, 2008	Br J Cancer (4.8)	One and two-question screening tools in cancer and palliative care	9	100	1405	100	251	100
Gilbody, 2007	J Gen Intern Med (3.4)	PHQ in medical settings	18	100	5413	100	852	100
Mitchell, 2007	Br J Gen Pract (2.3)	Ultra-short screening tools in primary care	12	100	21195	100	2757	100
Wittkampf, 2007	Gen Hosp Psychiatry (2.6)	PHQ in any setting	10	83	5186	99	659	99
Total			375/398	94	97398/99767	98	17123/17680	97

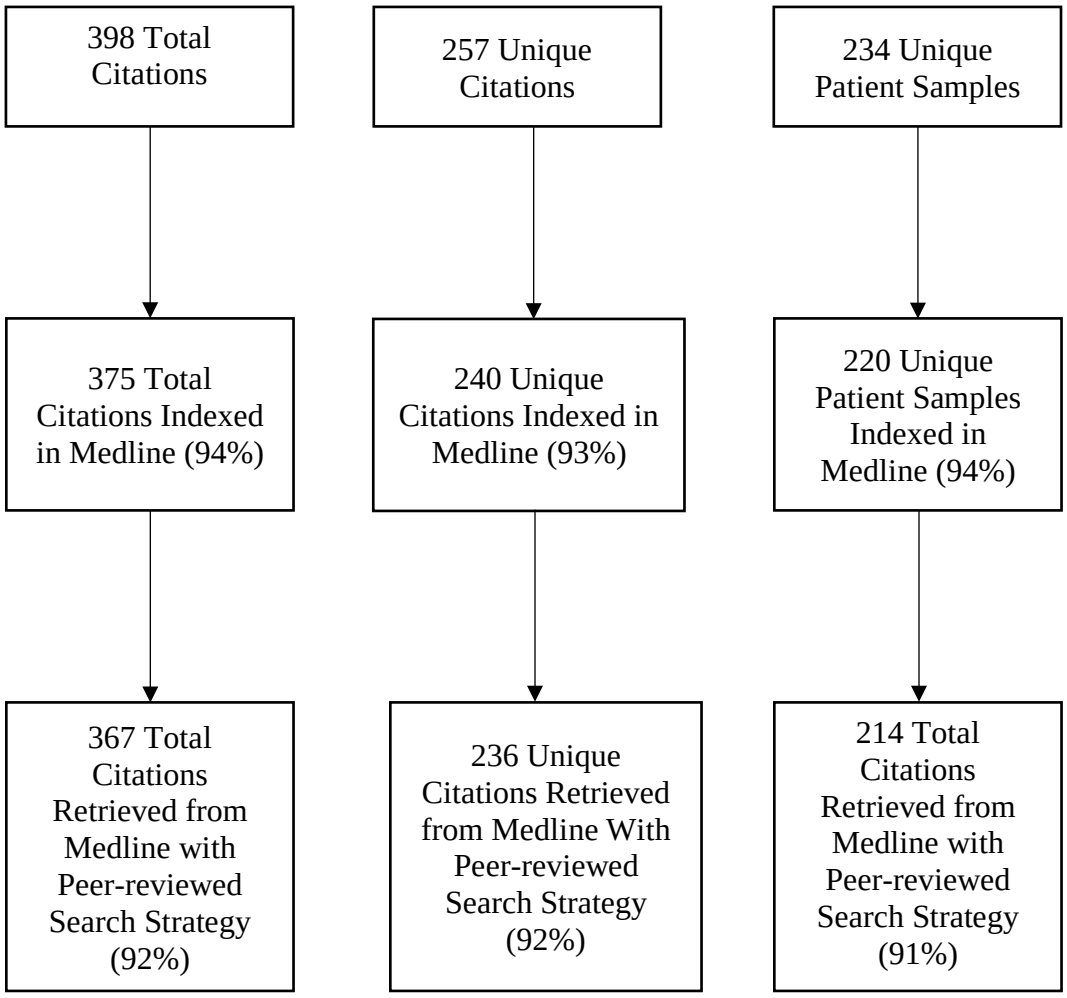
GDS= Geriatric Depression Scale; HADS= Hospital Anxiety and Depression Scale; PHQ= Patient Health Questionnaire.
Note: Individual study results are presented in Appendix D.

Primary Studies Indexed in MEDLINE

The 16 meta-analysis publications listed a total of 418 citations of primary studies. Of the 418 citations listed in one or more meta-analysis, we excluded 12 because they were citations to studies that used a rating scale (e.g., Hamilton Depression Rating Scale) rather than a self-report screening tool as the index test or because they used a rating scale as the reference standard (see Appendix C for list of excluded studies). Of the remaining 406 citations, we were able to retrieve 398 (98%) from one or more of the databases used in the original meta-analysis where it was included. Thus, there were 8 citations (2%) that were not found in the databases used in the original meta-analyses, and we concluded that they were identified by the meta-analysis authors via alternative, non-database methods (e.g., reference lists of included studies, consultation with experts; see Appendix D). Of the 398 total citations of primary studies in the 16 meta-analyses that were identified in the original meta-analyses through database searches, there were 257 unique citations and 234 unique patient samples after duplicate citations included in more than one meta-analysis and that reported results from the same primary study sample were removed (see Figure 2).

Of the 398 total citations found in any online database in the 16 meta-analyses, 375 citations (94%) were indexed in MEDLINE. Within these 398 citations, there were a total of 99,767 patients screened and interviewed, and 97,398 (98%) of these patients were from one of the 375 publications indexed in MEDLINE. Further, there were a total of 17,680 cases of depression in the 398 citations, and 17,123 (97%) were from the 375 studies indexed in MEDLINE. Of the 398 total citations, 367 (92%) were retrieved using our peer reviewed search strategy for MEDLINE, including 96,399 (97%) of total patients and 16,936 (96%) of total depression cases.

Figure 2. Flow Diagram of Total Citations, Unique Citations and Unique Patient Samples in 16 Included Meta-Analyses.



Of the 257 unique citations in the 16 meta-analyses, 240 (93%) were indexed in MEDLINE. Within these 257 unique citations there were a total of 75,167 patients screened and interviewed, and 72,350 (96%) of these patients were from one of the 240 citations indexed in MEDLINE. There were a total of 12,590 depression cases, and 11,972 (95%) were from the 240 studies indexed in MEDLINE. Of the 257 unique citations, 236 (92%) were retrieved from the peer-reviewed search of MEDLINE, including 67,381 (90%) of total patients and 11,220 (89%) of total depression cases.

In the 234 unique patient samples from online databases in the 16 meta-analyses, there were a total of 69,957 patients and 11,867 depression cases. Out of these, 220 patient samples (94%) were in an article indexed in MEDLINE. These included 68,196 (97%) of total patients and 11,386 (96%) of total depression cases. Of the 234 unique patient samples, 214 (91%) were found in a peer-reviewed MEDLINE, including 67,381 (96%) of total patients and 11,220 (95%) of total depression cases.

Of the 14 unique patient samples not found in MEDLINE-indexed studies, only 2 studies (N total = 165; N cases = 43), which were retrieved from African Journals Online and Proquest Dissertations and Theses, were not found in our core set of databases. The majority of the 12 unique patient samples found in databases other than MEDLINE were indexed in Scopus (n=10; 71%), PsycINFO (n=9; 64%), and/or EMBASE (n=7; 50%) (see Appendix D).

In each meta-analysis, at least 91% of total patients and 89% of depression cases were from studies indexed in MEDLINE. In 7 of the 16 meta-analyses, all primary studies, patients screened and interviewed, and depression cases were available in MEDLINE with a median of 97% of primary studies, 97% of total patients and 98% of depression cases. When only studies in

MEDLINE that were identified with a peer-reviewed search were considered, this accounted for 91% of all primary studies, 98% of total patients, and 97% of depression cases.

Comprehensiveness of the Meta-Analyses Searches

The 16 meta-analyses searched an average of 5 bibliographic databases. All meta-analyses searched MEDLINE and at least one other bibliographic database, up to a maximum of 14 additional databases searched (see Table 1). Most meta-analyses (94%) also used additional methods to identify eligible studies, with searching reference lists of included primary studies being employed most often (56%), followed by inquiries to expert contacts (38%), forward citation of included primary studies (38%), manual journal searches (19%) and domain-specific conference abstracts (13%). Each search covered a large range of years with most meta-analyses searching from database inception until approximately a year prior to the meta-analysis publication date. Search filters were not used in any of the meta-analyses search strategies. Only 4 out of the 16 meta-analyses (25%), however, included a fully reproducible MEDLINE search strategy in the text, an appendix or as a supplemental online file (6, 15, 19, 20).

Table 2. Bibliographic Databases Searched in Meta-Analyses.

First Author, Year	Number of Bibliographic Databases Searched	Names of Bibliographic Databases Searched
Meader, 2014	7	MEDLINE CENTRAL CINAHL EMBASE Health Management Information Consortium PsycINFO Web of Science
Tsai, 2014	5	MEDLINE CINAHL EMBASE PsycINFO WHO African Index Medicus
Tsai, 2013	5	MEDLINE CINAHL EMBASE PsycINFO WHO African Index Medicus
Manea, 2012	3	MEDLINE EMBASE PsycINFO
Mitchell, 2012	7	MEDLINE CENTRAL CINAHL EMBASE Health Management Information Consortium PsycINFO Web of Science
Meader, 2011	7	MEDLINE CENTRAL CINAHL EMBASE Health Management Information Consortium PsycINFO Web of Science
Vodermaier, 2011	3	MEDLINE EMBASE PsycINFO
		MEDLINE Allied and Complementary Medicine

Brennan, 2010	6	Database British Nursing Index CINAHL EMBASE PsycINFO
Mitchell, 2010	2	MEDLINE EMBASE
Mitchell, 2010b	3	MEDLINE EMBASE PsycINFO
Mitchell, 2010c	2	MEDLINE EMBASE
Hewitt, 2009	15	MEDLINE CENTRAL CINAHL Cochrane Database of Systematic Reviews DARE Dissertation Abstracts EMBASE HSRProj Inside Conferences LILACS Maternity and Infant Care National Research Register Archive (NRR) PsycINFO ReFeR (Research Findings Electronic Register) Web of Science ("SSCI")
Mitchell, 2008	4	MEDLINE CINAHL EMBASE PsycINFO
Gilbody, 2007	4	MEDLINE CINAHL EMBASE PsycINFO
Mitchell, 2007	4	MEDLINE CINAHL EMBASE PsycINFO
Wittkampf, 2007	3	MEDLINE EMBASE PsycINFO

DISCUSSION

The main finding of this study was that 94% of 398 primary studies on the diagnostic accuracy of depression screening tools that could be located from an online database were indexed in MEDLINE. These studies accounted for 98% of the total patients and 97% of depression cases that were from studies retrievable via any online database. When considering unique citations only, 93% of 257 unique citations were in MEDLINE, including 96% of total patients and 95% of depression cases. Of 234 unique patient samples, 94% were found in an article in MEDLINE, as were 97% of total patients and 96% of depression cases. Not all articles indexed in MEDLINE would necessarily be found in searches. When considering unique patient samples, we found that a peer-reviewed MEDLINE search successfully accounted for 91% of all samples, 98% of unique patients, and 97% of unique depression cases.

Our findings were consistent with those of a 2014 study that examined diagnostic test accuracy systematic reviews, which were indexed in MEDLINE between 2006 and 2011 (5). To be included, meta-analyses had to be published in a journal with an impact factor of $\geq$4, had to have conducted extensive searches, and had to include primary studies that were published in both MEDLINE and non-MEDLINE databases. The 10 systematic reviews, which included 15 separate meta-analyses, covered a range of diagnostic tests (e.g. pelvic ultrasonography for ectopic pregnancy, anti-citrullinated peptide antibodies for rheumatoid arthritis, serum galactomannan ELISA for invasive aspergillosis). One of the included studies was a study of depression screening accuracy that was also included in the present study (11). In re-analyses of the original meta-analyses, the relative diagnostic odds ratio did not change when only studies found in MEDLINE were included instead of all studies in the original meta-analyses (relative diagnostic odds ratio = 1.04, 95% confidence interval 0.95 to 1.15). Furthermore, overall sensitivity and specificity

changed less than 1% when results from all meta-analyses were pooled. This is consistent with the results of our study in that we found that 98% of all patients and 97% of cases in primary diagnostic accuracy studies of depression screening tools could be found in studies indexed in MEDLINE.

The findings of the present study have important implications for future systematic reviews and meta-analyses of the diagnostic accuracy of depression screening tools. Searching and screening relevant literature to identify publications that fit eligibility for a systematic review or meta-analysis can be burdensome. Our findings suggest that when conducting a meta-analysis of the diagnostic test accuracy of depression screening tools, searching fewer databases in addition to MEDLINE will result in substantively less literature to screen and will likely not result in a large portion of studies, patients, or depression cases being missed. Decreasing the number of databases searched may be one way to reduce resources and increase the capacity for systematic reviews and meta-analyses. We found that when employing a reasonable search strategy, a high proportion of primary studies of diagnostic test accuracy of depression screening that are indexed in MEDLINE can be identified. The majority of studies not found within MEDLINE were located in Scopus (71%), PsycINFO (64%), and/or EMBASE (50%).

There are limitations to consider in interpreting the results of our study. First, we did not re-analyze meta-analyses, although the small number of missed studies and patients suggest that it is highly unlikely that accuracy results would have changed meaningfully due to missing studies. Second, our search was undertaken over a year ago. Nonetheless, results were robust, and it is not likely that this would change by including meta-analyses published in the last year. Third, we retrospectively reviewed existing meta-analyses, which is not the same as conducting a “live” systematic review and meta-analysis. There is some evidence that MEDLINE may not index as

rapidly as other databases (24, 25), which would not have influenced our results as only published meta-analyses were examined, but would influence the ability of meta-analysis authors to identify recent primary studies. This possibility needs further study and should be taken into consideration if researchers do limit their database searching. For instance, authors might consider searching only MEDLINE, but including other databases for the most recent year. Finally, we were unable to examine whether the search strategies used by authors in each meta-analysis did, in fact, identify the articles indexed in MEDLINE as most included meta-analyses did not provide reproducible search strategies. Nonetheless, when we applied a reasonable, peer-reviewed search strategy, almost all studies available in MEDLINE were retrieved.

In conclusion, the present study found that restricting a search of diagnostic test accuracy for depression screening tools to only MEDLINE database identified 94% of unique studies available in online databases, as well as 98% of unique participants and 97% of unique depression cases, even though the meta-analyses we reviewed searched 5 databases on average. Our results suggest that it may be appropriate for researchers to rely on MEDLINE in certain circumstances and that supplementing a MEDLINE search with other databases for recently published evidence would likely identify the majority of studies, total patients and depression cases from studies of the accuracy of depression screening tools.

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CONFLICTS OF INTEREST

All authors have completed the Unified Competing Interest form at http://www.icmje.org/coi_disclosure.pdf and declare that no authors have any conflict of interest disclosures for the past 3-year reporting period.

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