Advancing PubMed? A comparison of 3rd-party PubMed/MEDLINE tools

INTRODUCTION

The first step of a systematic search is planning the search and in this step, systematic review authors can especially benefit from collaboration with librarians (Foster, 2015). Librarians' assistance surpasses general instruction in how the interface to the bibliographic database supports the methodological demands to the structure and scope of the search, the sensitivity of the search, bias and selection of articles. Our expertise in information and knowledge management facilitates critical appraisal activities. Rather than applying this expertise for our own professional practice, the medical librarian has the unique opportunity to inform the library users on the theoretical aspects of carrying out systematic searches and produce up-to-date critical appraisals of biomedical search software that are suggested as better ways of synthesizing medical evidence (Booth and Brice, 2004).

Since bio-medical researchers need to interpret an increasing quantity of data (Islamaj et al, 2009) and the publication rates of scientific articles are exploding, there are increasing demands on text mining technology to improve the relevance and precision of searches in the biomedical literature (Coccia, 2009). This demand has led to the development of third-party applications aiming to improve the efficiency of searching the millions of indexed papers (referred to as citations in the PubMed terminology) in PubMed (Keepanasseril 2014; Lu 2011: Connor, 2010). Medline data and NCBI Entrez Programming Utilities (the Global Query Cross-Database Search System that powers PubMed provided by the National Center for Biotechnology Information) are freely available for developers from academia and industry and allow the creative development of third-party tools complimentary to PubMed. These tools are designed to simplify the search modalities of PubMed, thus decreasing the problem of information overload and syntactic correctness in PubMed searches (Coccia, 2009). Ultimately, they aim to improve the specificity and sensitivity of exhaustive searches and ensure highly relevant replies to medical queries (Islamaj et al, 2009).

Keepanasseril (2014) and Lu et al (2011) present reviews of third party web tools to access, search and process Medline citations. These reviews presented 28 and 24 tools respectively, overlap 13, but do not test the functionality of these choosing instead to list the key features, technical developments and processing capabilities of each tool. In this paper, we compare the search functionality of third party web tools to PubMed, specifically in identifying, retrieving and exporting biomedical literature as part of a systematic search process.

The systematic search is a scientific methodology used to create medical systematic reviews. The method sets requirements to the process of the search. The search has to be exhaustive to capture all the available evidence so that conclusions based on the literature retrieved in the search are unbiased, it must be methodological, transparent, the rationale of the search defendable and importantly, the search must be reproducible so that it can be repeated and conclusions verified (Lefebvre et al, 2011). PubMed is traditionally the main database used for searching biomedical literature and constructing systematic reviews, but to search systematically requires the user learn how the interface works on par with an information professional (field descriptors, Boolean logic, combining search blocks, index terminologies, database structure, mapping and matching functionalities, filtering, limits, etc.). Hence developers of third party tools are keen to assist the novice user by simplifying the technicalities of the search and enhancing user-interactivity through advancing visualization and manipulation of results.

PubMed: contents

Available since 1996, PubMed includes over 25 million citations (time coverage 1946 to present) from the biomedical literature. It includes:

the Medline database,

in-process records of articles yet to be quality controlled and indexed with MeSH (Medical Subject Headings),

ahead-of-print citations that precede the article's final publication in a Medline indexed journal,

pre-1966 citations that have not yet been updated to current MeSH or Medline status

citations to full text articles in PMC (PubMed Central),

books on the NCBI Bookshelf and

manuscripts published by NIH-funded researchers (National Institutes of Health).

PubMed: search interface

PubMed supports block searches, Boolean logic, truncation, masking, and tagged field searches that limit the search to specific bibliographical fields indexed in the database. The search can be limited to methodological variables, e.g. date range, language, species or clinical study type and results filtered using several ranking and sorting parameters.

Results are displayed in a variety of formats: summary, abstract, Medline format (which is the tagged field format used to export citations into citation management programmes), XML and PMID list (PubMed's unique article identifier). Results can be sorted by reverse date order, first author, last author, journal, title or relevance.

Relevance is based on an algorithm that weights terms dependent on their frequency and position in the indexed document. The relevance of a document in a single word query is dependent on the number of times the word appears in all documents (global weight), in a specific document (local weight), the weight of the field the word appears in and the weight of the publication date. As user queries typically include more than a single word, the resulting weight is calculated as a sum of the weights of the individual words included in the document. In order to optimize performance, the list of documents in the result set is generated first using a Boolean bit-vector operation (NCBI, 2015, p.85).

PubMed also offers links to similar articles. Here, similarity is a vector score measured as the frequency of words documents have in common, adjusted for document length using a Poisson correction and again the weight of the field the term appears in, for example title words are weighted higher than abstract terms which are weighted higher than MeSH terms.

The search can be saved in the Search History so that search statements can be combined or re-run at a later date and results verified. Search results link to free full-text papers in PMC or to the publishing journal, however if the user is searching PubMed through a subscription service, links can be provided to journals and articles in this collection. Search results can be exported in different formats to a citation manager, CSV file, email, text, and more. Documentation of database contents and search tutorials are easily accessible and up-to-date.

PubMed: search functionality

From a search perspective, single words or phrases entered in the PubMed search box (that have not been tagged with field descriptors, quotation marks or asterisks) are matched in the order of Subjects (using MeSH Headings), Journals, Phrase List and Authors to several translation tables. When a match is found for a word or phrase in a translation table, the mapping process is complete and the word or phrase is searched according to the parameters set for this table. The search does not continue to the next translation table. If no match is found in any of the translation tables, PubMed breaks apart the phrases into individual words and repeats the automatic mapping process until a match is found. If there is no match, the individual words will be combined (ANDed) together and searched in all fields (Smith, 2004). If these words or phrases are tagged with field descriptors, the system modifies the search by removing the field tags and then searches each word in all fields (NCBI, 2015). The automatic mapping is powerful, translating for example "heart attack" into "myocardial infarction" and searches simultaneously for these synonyms. Thus importantly, the user can see this process at work in "Search Details" and can turn this mapping function off by either using search syntax or by editing the search directly in the query translation box, as turning the mapping off stops the automatic exploding of the terms and narrows the search.

METHOD

Selection of Third Party Tools

Third party tools identified in the reviews by Keepanasseril (2014) and Lu et al (2011) were selected and supplemented with tools identified through a PubMed search using the terms *PubMed AND (software[MeSH] OR "Systems Integration" [MeSH] OR "User-Computer Interface"[MeSH]) NOT (dental OR dentist* OR genetic OR protein OR drug) Limits year:2000-2015***.** The "similar articles" function was used on relevant citations to find related articles missed in the search. Seventy-six potentially relevant tools were identified.

We selected third party tools for assessment based on the following 4 criteria, summarized in Figure 1:

Tools were included if:

1. the tool searches the broad medical content offered by the PubMed/Medline database
2. the tool provides free access to searching the database. Tools requiring login but not payment are included.

Tools were excluded if:

the tool is limited to fit one bio-medical discipline.

The tool did not operate on online PubMed/Medline content.

[*INSERT FIGURE 1 HERE]*

Table 1 provides an overview of the 16 included tools included in the comparative assessment, Table 3 the 31 excluded tools while Table 4 presents 29 potentially relevant third party tools that we were unable to include in the analysis because these were either under construction, closed projects or dead-links.

[INSERT TABLE 1. MAIN FEATURES OF THE 16 THIRD PARTY TOOLS INCLUDED IN THE ASSESSMENT]

Comparison of Third Party Tools

Each tool was given an unique identifier and compared across 11 basic aspects that should be present in a robust and methodological search process, Table 2. These aspects support the search, manage the citations and document the search process (Lefebvre et al, 2011). Accordingly the tools are assessed:

1) on their ability to *support* a search structure that requires a subject search for a population and intervention together with methodological field codes, filters and limits. Further, the ability to combine concepts, synonyms and blocks of the search with Boolean operators is assessed.

2) on their ability to *manage* citations within the tool based on the interactivity the searcher has with the presented output, suggestions for related articles and links to a representation of the article. The ability to identify how many citations were retrieved in the search and the ability to export found citations to reference management tools for further analysis is assessed.

3) on their ability to *document* the search, specifically to save, edit and update the search.

Test Search

A search designed to fit the PubMed database, on a topic known to the authors, was run through each of the 16 third party tools and PubMed in December 2015 through January 2016. The search strategy is published in (Christensen et al, 2016), and is designed to fulfill the requirements of search according to the Cochrane Handbook for Systematic Reviews (Lefebvre et al, 2011). The search is available as an appendix via this link: http://tinyurl.com/h7nj4vu. Accordingly, we have a database of retrieved literature and a record of the literature deemed clinically relevant for this topic. Assessment of relevance was undertaken by medical physicians. Thus, this database is used as a benchmark to assess the specificity and sensitivity of the search using third party tools included in this study.

RESULTS

The purpose of each tool and the tool's main features are described in Table 1. The assessment across 11 basic aspects that support, document and manage the search process are reported in Table 2. Based on Table 1 and Table 2 we have the following observations of deploying the search and search interaction functionality of third party tools compared to a baseline performance in PubMed.

[INSERT TABLE 2: COMPARISON OF SEARCH FEATURES]

Supporting the search

Field codes, filters, limits and Boolean operators

The test search was adjusted when necessary to fit the specifications of each tool. Nine tools ran the PubMed search without adjustment, and were fully compatible with the pre-defined field codes, limits and Boolean operators (ID 1-3, 6, 7,10,11,14 and 16). A clinical approach to searching was provided by the PICO tool (ID 9) where blocks of the search were combined using Booelan logic under the aspects "medical condition" and

"intervention". The full search for the PICO tool is available in the electronic appendix link: http://tinyurl.com/h7nj4vu. Europe PMC (ID5) and PubVenn (ID15) required a simplified version of the search, limited to a combination of Mesh and keywords: *(peritoneum[MeSH Terms] OR peritoneum OR peritoneal) AND (ascites[MeSH Terms] OR ascites).* The two semantic tools askMedline (ID4) and askHermes (ID12) required the translation of the search to a plain language clinical question:*"What is currently the optimal type of tunneled catheter for treatment of recurrent ascites"* (cited from the original work of Christensen et al, 2016). Another semantic approach was the Medie tool (ID 13) which required definition of the verb, object and additional MeSH and keywords *(Verb: treat, stemming activated. Object: ascites, stemming activated. Additional keywords: abdomen* MeSH: ascites, ascitic fluid; peritoneal neoplasms; abdomen; paracentesis; catheters; drainage).*One tool was designed to support the search for major concepts only, and here the keyword *"ascites"* was run, (ID 8).

Options for filtering and limiting the citations to increase the specificity of the results were limited. Tools ID 1, 8, 11, 12 and 14 -16 do not provide filtering options to further modify the search. Tools ID 4, 5 and 7 offer filtering after language, document or study type, yet filtering by document type in PICO (ID 9) was problematic, as the filter could only be used to include document types and not exclude unwanted ones. PubReMiner provides the traditional filtering after year, journal, author, MeSH terms (ID 10), whereas MedlineRanker (ID2) and Medie (ID13) provide alternative filtering options that build on the Bayes-weighting scheme used in the presentation of citations. This gives the options to filter on a broad level according to subject, object or UMLS semantics, and on a narrow level using discriminative words in the citations title, abstract, method or conclusion. Go3R (ID6) presents a detailed ontology to limit the search and RefMed (ID3) allows the user to push relevance feedback to iteratively modify the results.

Managing the Search

Output

Results were presented as hyperlinked lists, similar to PubMed, with the same sorting options as in PubMed i.e. publication date, first/last author and journal, primarily ID 1, 3, and 16. In seven tools the citations were only displayed newest first (ID 4, 6-9 and 12). Other options included sorting citations after relevance using a word-weighting algorithm (ID 2). Visualization of the relation between citations as sociograms based on co-occurrence analysis was the preferred presentation in tools ID 14 and 15, these also provided standard list presentations similar to PubMed as well. PubReMiner and Medie presented the results in sortable tables, which the user can both sort the output in regards to a defined combination of year, journal, author, MeSH terms (ID 10), or subject, objects or UMLS definition (ID 13).

Related articles and links to article representation

Related articles were only suggested in ID 1, 6, 7, 9 and 11. To access the citation as full text or representation thereof, tools primarily sent the users over into the PubMed system (ID 1-7, 9, 12, 13 and 15). Tools (ID 8, 11, and 16) sent the user to the publisher or affiliated library collection whereas PubReMiner (ID10) and PubNet (ID14) did not hyperlink to a full-text representation of the citation itself but rather to a broader list of concepts related to the node or item identified in the tables or sociogram.

Number of citations on the result list

Each tool retrieved a different amount of citations ranging, where known, between a minimum of 226 and maximum of 5409 citations. Tools Anne O'Tate (ID 1) and Unbound Medline (ID16) produced the exact same amount and set of citations as the study control PubMed. Otherwise the number of citations varied even when the exact same search was implemented (ID 2, 3, 6, 7, 10, 11 and 14). Tools, ID 8, 12-14, do not report

the number of retrieved citations. PubMed returns by default 20 citations per page, but can be adjusted to include 5, 10, 50, 100 or 200 citations per page. Refmed (ID3) offers these same options and similarly Go3R (ID6) returns 20, 50 or 100 citations per page. Eight tools returned a fixed number of citations per page, either 10 citations (ID13), 20 to 30 citations (ID 1, 4, 5, 8, 9 and 11) or the first 1000 citations, where access to citations ranked after 1000 was not possible (ID 2). It was not possible in tools ID 7, 10, 15 and 16 to identify how many citations were returned on a page because the result pages were dynamic and continually added more citations towards the bottom of the page. For PubNet (ID14), which presented the results as a sociogram, the citations were, depicted as nodes and edges, hence this assessment is not applicable.

Exporting the citations

Export of search results was not available in tools ID 1, 4, 10-13, 15 and 16. However even though the remaining tools offer export, the functionality is limited. In three tools the citations could only be exported one at a time (ID 7, 9 and 14). Two tools directed the user to PubMed to export the results (ID 3 and 10). Tools ID 5, 6, and 8 offer bulk export in formats compatible with publically available reference managers while ID 2 limited export to PMIDs (the unique number assigned to each PubMed record) as a text file or discriminative words only as a table.

Documenting the Search

Saving the search and search history

Two out of 16 tools provided the option to save searches and/or view search history. These were PubVenn (ID15) and Europe PMC (ID5), though this function was not working at the time the study was undertaken.

DISCUSSION

The limitations in filtering and export functionality of third party tools meant that the intended analysis of the relevance of the retrieved citations compared to the PubMed study control was not viable. In tools that allowed the bulk export of citations, the records could either not be filtered (ID 8), or the filters did not work (ID5 and ID6), resulting in thousands of citations. Tools that provided innovative ranking and filtering options did produce a useable number of citations and it would have been interesting to compare the relevance of these citations to the PubMed set, yet the citations could not be exported or could only be exported one-by-one from the tool's interface (ID 1, 4, 7, 9, 11, 13, 15 and 16). Alternatively, tools directed the user to the PubMed system to export the citations one-be-one (ID 3, 10, 12, 14) or via a list of PMIDs (ID2), both reducing the flexible export options of PubMed and subsequently not supporting the user effectively.

The importance of the filter, save and export functions essential to a systematic search appears to be overlooked in the third party tools evaluated in this study. This could be because we are using the tools in systematic search context that they are not designed to support. For example, Anne O'Tate (ID 1) visualizes for the user the many facets the search encompasses by clustering MeSH pairs and important terms, resulting in an impression of the different facets that make up the set of retrieved citations. Likewise, Medie (ID13) and MedlineRanker (ID 2) highlight important terms in the presentation of search results while askMedline (ID 4) and PICO (ID 9) further enrich the result list by describing "the bottom line" of each citation[1] which can aid determing relevance. HubMed (ID7) meanwhile enriches the search results by identifying

[1] TBL (The Bottom Line) is the summarization of the conclusion section of journal abstracts, derived by applying computer algorithms, not by summarizations performed by humans. If an abstract has no conclusion section, TBL results are derived by using a word counting algorithm plus the last two sentences of the abstract.

discussions and actors within the subject area by linking to Twitter and Mendeley to find out if the citations have been picked up by news outlets, tweeted, or used on other social media and provides a demographic breakdown of who is mentioning these citations.
The primary aim of Medie (ID 13), PubNet (ID 14) and PubVenn (ID 15) is to further explore the collection of retrieved citations before returning to PubMed to improve the specificity and sensitivity of the search. These tools are beneficial as they give immediate, dynamic visual assessment of relationships between authors, topics and term hierarchies etc. in the bibliographic data, giving a strong starting point in evaluating and selecting literature to include in a systematic review, as discussed in Workman (2011).

Clearly, some tools are still experimental. Specific functionalities needing improvement include pushing feedback in RefMed (ID 3) which is intended to improve the relevance of the retrieved citation. In our study, the relevance function resulted in an increase in the results from 785 to 40,119 citations or an error message. In contrast, even though SLIM (ID 11) retrieved 560 citations, only the first 200 citations were displayed, likewise askMedline (ID4) only returned the first page of results leaving the other pages blank. askHermes presented innovative clustering of citations based on clinical methodologies e.g. survival days, insertion location and shunt type but did not return up-to-date citations, the newest citation being from 2012; Medie, Europe PMC and Go3R did not process Boolean logic correctly. We suspect terms are automatically ANDed together, OR irremittently ignored and the Boolean NOT is not recognized; Europe PMC also limits the number of characters in the search strategy to 1500 which restricts the methodological design of the search and further the parenthesis used to group blocks of the search had only a limited functionality. iPubMed, Europe PMC and Go3R each return thousands of citations and limiting the search was, respectively, not possible, because limits were based solely on document type, an confusingly extensive ontology and dubious implementation of Boolean logic.

CONCLUSION

The possibilities for search interfaces and systems that increase both the sensitivity and specificity of the search in an ever growing pool of biomedical literature has led to a demand to change PubMed to better serve its users. This in turn has led to a multitude of third party tools proposed as advancements to searching and collocating evidence indexed in PubMed. Only 16 of the 76 third party tools assessed in this study offer free literature searches in the same or enriched content as PubMed. In summary, the assessed tools limited rather than supported the specificity of the search through field codes, filtering, use of limits and Boolean logic. The searchers ability to manage the search was likewise restricted; especially the difficulty in exporting citations to reference managers was increased. Only 2 out of the 16 tools permitted the search to be saved and the history viewed, yet these functions were not working at the time we assessed the tools.

Therefore, we consider the PubMed interface still provides the superior tool to freely access and search systematically the biomedial literature stored in the PubMed/Medline database. However, even though we determine the 16 third party tools inferior to PubMed in supporting a systematic search methodology, when the bugs are fixed, we look forward to retesting their performance. The innovativeness of these tools has to be praised, and their endeavors to decrease the complexity of searching vast quantities of literature relevant. What needs to be done to make the third party tools efficient in a systematic search, is to improve their ability to support the search as a verifiable method where the innovative features are combined with the conditional steps in a search for evidence in the biomedical literature. As a baseline, the tools must effectively support the search, manage the retrieved citations and document the search.

[INSERT TABLE 3: EXCLUDED THIRD PARTY TOOLS]

[INSERT TABLE 4: POTENTIALLY RELEVANT THIRD PARTY TOOLS: SITES UNDER CONSTRUCTION, CLOSED PROJECTS OR DEADLINKS]

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Ranking interfaces			
MedlineRanker	Scores and relevance ranks citations by deducing automatically the most discriminative words in a test set of abstracts compared to a random selection based on a Naïve Bayes classifier.	Fontaine et al (2009)	http://cbdm-01.zdv.uni-mainz.de/~jfontain/cms/?page_id=4
RefMed	Relevant articles by ranking the articles according to a machine- learned relevance function, supports ad-hoc keyword queries and a multi-level relevance feedback in real time.	Yu et al (2010)	http://dm.postech.ac.kr/refmed/
Clustering interfaces			
Anne O'Tate	Displays multiple aspects of and relationships between found articles, according to pre-defined categories alone or as a combination e.g. "most important" words found in titles or abstracts; topics; journals; authors; publication years; and affiliations.	Smalheiser et al (2008)	http://arrowsmith.psych.uic.edu/cgi-bin/arrowsmith_uic/AnneOTate.cgi
Semantics and visualization interfaces			
askHERMES	Natural language query system to search PubMed that hierarchically clusters sentences as answers and a new sentence ranking function. Answers rather than document lists are presented to the user, organized by keywords.	Cao et al (2011),	http://www.AskHERMES.org
askMedline:	Developed by Plain language search tools for MEDLINE/PubMed. Allows free-text, natural language query.	Fontelo et al (2005).	http://askmedline.nlm.nih.gov/ask/ask.php
Medie	Ontology-based search that can be limited to specific types of sentences in the methods, results or PubMed annotation metadata, and allows the query verb to be replaced by any GENIA event ontology term.	Ohta et al (2006;2010)	http://www.nactem.ac.uk/tsujii/medie/
PubNet	Parses XML output of standard PubMed queries to create different kinds of network graphs using aiSee graph visualization software.	Douglas et al (2005),	http://pubnet.gersteinlab.org/
PubVenn:	Uses venn diagrams built on JavaScript and j jQuery to explore and visualize interactions between PubMed citations.	Sperr, (2015)	http://pubvenn.appspot.com/
Unbound MEDLINE	Traditional keyword search of PubMed/Medline with enriched display of related articles using common terms and "Grapherence" display.	Unbound Medicine.Inc (2012)	http://www.unboundmedicine.com/medline/
Improving search interface and research retrieval			
Europe PubMed (UKPMC)	5 million other relevant bio-medical resources such as patent records, research grants, clinical guidelines layered on top of PubMed content available through a single search.	The Europe PMC Consortium (2014)	http://europepmc.org/
Go3R:	Semantic search to avoid animal experiments that compares the terms and concepts of the search with the vocabulary used in the documents retrieved. Relevant terms in the documents are highlighted, related terms suggested and presented in tables.	Sauer et al (2009)	http://www.gopubmed.org/web/go3r/
HubMed:	Incorporates web services with PubMed searches to create and visualize clusters of related articles, export citation, receive daily, navigate links to related resources, retrieve data from formatted bibliography lists, and store annotated metadata..	Eaton (2006)	http://git.macropus.org/hubmed/
iPubMed:	Explores the entire MEDLINE collection using interactive and fuzzy algorithms to provide instant feedback and approximate searching.	Wang et al (2010)	http://ipubmed.ics.uci.edu/
PICO	Prompts searches using PICO elements of the question (patient problem, intervention, comparison and outcome), as well as patient age group, gender and publication type.	Schardt et al (2007)	http://pubmedhh.nlm.nih.gov/nlmd/pico/piconew.php
PubReMiner:	Generates frequency tables that shows the journals in which the search query is published the most, the authors which are most active in the field of the query, and the words that have been used most in the title and abstract of the articles, hyperlinks to PubMed.	Koster (2004)	http://hgserver2.amc.nl/cgi-bin/miner/miner2.cgi
SLIM	Interactive slider bars control limits, filters and MeSH terminologies in the search, developed with PHP and JavaScript.	Muin et al (2005)	https://pmi.nlm.nih.gov/slim/

Table 1. Main features of the 16 third party tools included in the assessment

		SUPPORT				MANAGE					DOCUMENT	
ID	TOOL	FIELD CODES	FILTER	LIMITS	BOOLEAN LOGIC	OUTPUT	RELATED ARTICLES	LINKS TO ARTICLE	NR. RESULTS	EXPORT	SEARCH HISTORY	SAVE SEARCH
0	*PubMed*	*yes*	*yes*	*yes*	*yes*	*list*	*yes*	*yes*	*560*	*bulk*	*yes*	*yes*
1	*Anne O'Tate*	yes	no	yes	yes	list	yes	via Pubmed	560	no	no	no
2	*MedlineRanker*	yes	yes	no	yes	list	no	via Pubmed	671	bulk	no	no
3	*RefMed*	yes	yes	no	yes	list	no	via Pubmed	785	via Pubmed	no	no
4	*askMedline*	no	yes	no	no	list	no	via Pubmed	397	no	no	no
5	*Europe PMC*	yes	yes	yes	yes	list	no	via Pubmed	5376	bulk	yes	yes
6	*Go3R*	yes	yes	yes	no	list	yes	via Pubmed	2763	bulk	no	no
7	*HubMed:*	yes	yes	no*	yes	list	yes	via Pubmed	801	singularly	no	no
8	*iPubMed:*	no	no	no	no	list	no	yes	?	bulk	no	no
9	*PICO*	no	no	no	yes	list	yes	via Pubmed	226	singularly	no	no
10	*PubReMiner*	yes	no	no*	yes	table	yes	yes	1146	via Pubmed	no	no
11	*SLIM*	yes	no	yes	yes	list	yes	yes	560	no	no	no
12	*askHERMES*	no	no	no	no	list	no	via Pubmed	?	via Pubmed	no	no
13	*Medie* †	no	yes	no	no	table	no	via Pubmed	?	no	no	no
14	*PubNet*	yes	no	no *	yes	list/ sociogram	no	yes	?	via Pubmed	no	no
15	*PubVenn:*	yes	no	no	yes	list/ venn diagram	no	via Pubmed	5409	no	yes	no
16	*UnBound Medline*	yes	no	yes	yes	list	no	yes	560	no	no	no

* accepts filters already in our search but no filter function on interface
† searched stopped after 4% of Medline searched

Table 2. Comparison of search functionalities across 11 aspects

TOOL	KEY FEATURE
Post-search tools	
BiolE	Extracting informative sentences from the biomedical literature from a corpus of literature that has already been found.
CiteGraph	Visualizes co-authorship networks from full-text biomedical articles. Access requested from developer but never given.
FASTA+/FACTA+:	Text analysis to find associated concepts.
MScanner	Uses input from PMIDs to produce term frequency tables.
PubGet	Displays PDFs directly in the search results, which links to credit card payments for the articles.
XploreMed	Uses abstracts from PubMed to cluster results.
Yale MeSH Analyzer	Presents a MeSH analysis grid of 20 retrieved articles and MeSH terms that can help identify the problems in your search strategy.
Specialty specific tools	
ALIBABA	Extracts associations between cells, diseases, drugs, proteins, species and tissues to visualize complex networks.
BITOLA	Used to generate potential explanations of the relationship between two entities based on literature corpus.
Chilibot	Identify genes and proteins in Medline sentences.
EBIMed	Co-occurrence analysis of Medline abstracts to retrieve citations and generate overview tables on proteins, Gene Ontology (GO) annotations, drugs and species used in the same biological context.
Evidentista	Evidence-based dentistry.
iHop Web Service	Identify genes and protiens in Medline sentences.
Info-pubmed	Searches for protein-protein interactions and gene-disease associations, also to identify the epidemiological connections of biomolecules.
PolySearch	Articles on diseases, tissues, cell compartments, gene/protein names, SNPs, mutations, drugs and metabolites.
POPLINE	Reproductive health literature.
PubAnatomy	Exploration tool for neurology literature.
Semedico	Articles on molecular biology. Under construction, could be expanding?
Whatizit	Semantic analysis of text to identify terms and then link them to the corresponding entries in gene, protein and bioinformatics.
Other tools	
Authority	Author name disambiguation tool.
BioMedLib (Relemed)	Payment required. Weights relationship between query words in the article to identify co-occurrence and rank articles based on this similarity metric.
BibliMed/BiblMed+	Search and viewing features simplify PubMed search interface. Requires payment for access to clinical and generic search filters.
Informer	Generates Email, SMS, RSS, and AvantGo alerts for Pubmed Queries.
MedlineTrend	Automated yearly statistics of PubMed results for any query.
MeSH on Demand	Uses NLMS Medical Text Indexer to identify mesh terms relevant to a text.
MedSum	Statistics summary tool.
Pubator	Annotation of PubMed citations.
PubCrawler	Checks and emails daily updates in MEDLINE to the pre-specified searches by the user.
PubPeer	Search for specific publications and join in the conversation about them.
Quetzal (Quertle)	Payment required for full functionality. Main concepts searched in the PubMed/Medline databases, results ranked based on linguistic phrase matching.
SemanticMedline	PubMed (up to 2012) in SQL form, that can be downloaded by users with a UMLS profile.

Table 3. Third party tools excluded from the study

TOOL	KEY FEATURE
Arrowsmith	Identifies relationships between terms to facilitate the discovery of plausible hypotheses, linking findings across specialties.
ClusterMED	Performs a PubMed search and organizes the results in a hierarchy based on MeSH terms.
eTBLAST	Text similarity search engine for PubMed.
Fable	Automated biomedical Literature Extraction that mines the biomedical literature for information about human genes and proteins.
G-Bean	Includes parallel document index creation, ontology-graph based query expansion using UMLS, MeSH, SNOMEDCT, CSP and AOD, a Personalized PageRank algorithm to compute concept relevance in this graph, Term Frequency - Inverse Document Frequency (TF-IDF) weighting scheme to re-rank the concepts, and retrieval and re-ranking of documents based on user's selection of articles from the search results.
GeneCite	Allows the users to integrate search results from PubMed with the sequence tagged database UniSTS and interpret biological significance, associations and links to literature.
GoPubMed	Now Go3R. Categorizes and defines citations based on term processing of abstracts according to the Gene Ontology (GO).
Hakia	Semantic search tool for PubMed.
HEALTH Geo-Junction	Retrieves, relevance ranks, contextualizes and visualizes abstracts from PubMed using locational, temporal and thematic components. Tag clouds visualize concepts, multi-view and space-time visualization explore cross connections in information.
LigerCat	Explores the biomedical literature by selecting terms within a "MeSH cloud" that is generated based on an initial query using journal, article, or gene data.
McSyBi	Hierarchically and non-hierarchically clusters citations based on titles, abstracts UMLS and MeSH terms using statistical and natural language processing methods.
MedEvi	Provides a single point of access to abstracts available through PubMed, PMC full-text articles, and an additional 5 million other relevant resources, such as patent records, research grants, and clinical guidelines.
Medkit	Increases the amount of PMIDs that can be downloaded and XML files that can be parsed using four modules; a querier, sampler fetcher and parser to improve text-mining.
MedMiner	Filters and organizes large amounts of textual and structured information returned from PubMed.
MEDrank	Generates concept graphs from biomedical text and then ranks the concepts within these graphs to identify the most important ones.
MedScan	Natural Language Processer to improve the PubMed search.
MiSearch	Search tool that ranks citations based on a statistical model for the likelihood that a user will choose to view them based on authorship, recency, term match, journal and PubMed indexing information.
PMinstant	Provides instant feedback as the query is being typed allowing users to dynamically modify or refine queries.
PubClust	'Unsupervised' Machine Learning method using a statistical clustering approach. Abstracts are linguistically preprocessed and classified using an agglomerative procedure to build a conceptual hierarchy and define intrinsic term dependency.
PubFinder	Based on selected abstracts, a list of discriminating words is automatically calculated and used to score all defined PubMed abstracts for their probability of belonging to the defined scientific topic.
PubFocus	Enriches queries with human factor-based bibliometric indicators of publication quality: journal impact factor and volume of forward references.
PubMed Assistant	Displays information about the citations, includes keyword highlighting, export to citation managers, clickable links to Google Scholar and other providers.
PubMed-EX	Marks up PubMed search results with additional text-mining information to help users focus on key terms and provides additional information on them.
PubMed Interact	Uses Entrez Programming Utilities to send search queries, retrieve results in XML format and display the citation list. Once the search results are loaded, dynamic HTML, DOM tree manipulation and Ajax scripting transforms the static page into an interactive application.
PubOnto	Enables the interactive exploration and filtering of search results through the use of multiple ontologies from the Open Biomedical Ontology.
PubViz	Displays structured publication data using a set of interactive visual representations working together, including timelines, bar charts for different publication types, word clouds to show co-authors as well as keywords, and a groupable list view.
PuReD-MCL	A graph-based PubMed document clustering methodology.
SimMed	Topically similar documents are clustered to support exploration by combining facet and similarity based browsing tools with links between clusters.
Twease	Searches abstracts in Medline, indexes words and provides features to expand the search.

Table 4. Potentially relevant third party tools, sites under construction, closed projects or dead links

Figure 1. Search flow diagram, after (Moher et al, 2010)