Grey literature: An important resource in systematic reviews

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Gray literature: An important resource in systematic reviews

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Abstract

Systematic reviews aide the analysis and dissemination of evidence, using rigorous and transparent methods to generate empirically attained answers to focused research questions. Identifying all evidence relevant to the research questions is an essential component, and challenge, of systematic reviews. Gray literature, or evidence not published in commercial publications, can make important contributions to a systematic review. Gray literature can include academic papers, including theses and dissertations, research and committee reports, government reports, conference papers, and ongoing research, among others. It may provide data not found within commercially published literature, providing an important forum for disseminating studies with null or negative results that might not otherwise be disseminated. Gray literature may thusly reduce publication bias, increase reviews' comprehensiveness and timeliness, and foster a balanced picture of available evidence.

Gray literature's diverse formats and audiences can present a significant challenge in a systematic search for evidence. However, the benefits of including gray literature may far outweigh the cost in time and resource needed to search for it, and it is important for it to be included in a systematic review or review of evidence. A carefully thought out gray literature search strategy may be an invaluable component of a systematic review. This narrative review provides guidance about the benefits of including gray literature in a systematic review, and sources for searching through gray literature. An illustrative example of a search for evidence within gray literature sources is presented to highlight the potential contributions of such a search to a systematic review. Benefits and challenges of gray literature search methods are discussed, and recommendations made.

KEYWORDS

gray literature, evidence, publication bias, search, systematic review

1 | BACKGROUND

Systematic reviews are important tools in the analysis and dissemination of evidence and provide guidance for clinical decision-making.[1–4] Systematic reviews generate empirically attained answers to focused research questions, providing "the most reliable and comprehensive statement about what works."[5] Using rigorous and transparent methods in order to minimize bias, researchers identify, critically appraise, and synthesize all relevant, available evidence, whether quantitative or qualitative, making evidence more accessible to decision-makers and guiding practice.[4,6] Locating and identifying all studies relevant to the primary research questions is an essential component, and challenge, of systematic reviews, and a comprehensive search for evidence across multiple sources is vital for systematic reviews to avoid missing significant evidence.[1,3,6–12] An important issue to be addressed in a systematic review is whether evidence from gray literature should be included and how it should be searched for.[11–13] This narrative review provides guidance about the benefits of including gray literature in a systematic review, and sources for searching through gray literature. Benefits and challenges of gray literature search methods are discussed, and recommendations made. An illustrative example of a search for evidence within gray literature sources is presented to highlight the potential contributions of such a search to a systematic review.

2 | GRAY LITERATURE

Gray literature is defined as: "that which is produced on all levels of government, academics, business and industry in print and electronic formats, but which is not controlled by commercial publishers."[11,14,15] Types of gray literature can include academic papers, including theses and dissertations, research and committee reports, government

reports, conference papers, and ongoing research, among others. As a result of its wide range of formats and scopes, gray literature is often a rich source of evidence used in systematic reviews and meta-analysis. Helmer found that 26% to 41% of the evidence found in some systematic reviews is found in gray literature, with 33.6% of the findings of one gray search consisting of randomized controlled trials.[16] Other gray literature, such as conference abstracts and proceedings make up approximately 10% of studies cited in Cochrane Reviews.[17] McCauley et al. found that 33% of meta-analyses reviewed included gray literature, accounting for 4.5% to 75% of studies in the meta-analyses.[18]

3 | BENEFITS OF SEARCHING FOR AND INCLUDING GRAY LITERATURE

Gray literature can make important contributions to a systematic review.[2,11,13,19,20] It can provide data not found within commercially published literature, reducing publication bias and facilitating a more balanced view of the evidence.[12,18,19] Much research is unpublished or not disseminated through peer-reviewed, commercial media.[14] Up to half of all clinical trials maybe unreported.[21] Long manuscript submission processes and difficulty getting studies with inconclusive or nonsignificant data published may discourage some researchers from publishing data, creating a "file-drawer" effect.[12,16,22] The lag time between article acceptance and publication in many scholarly journals ranges from 2 to 11 months and rejection rates range from 31% to 88% for submitted manuscripts.[23]

Gray literature also provides an important forum for disseminating studies that might otherwise not be disseminated, such as those with null or negative results.[18,19] As a result, including gray literature in meta-analyses may help minimize the effects of publication bias.[11,15,18] Publication bias refers to the propensity for only studies reporting positive findings to be published, and may skew the results of the meta-analysis and systematic review.[6,24,25] As gray literature may describe neutral or negative results, including it with commercially published research may provide a more balanced understanding of the evidence and a more accurate effect sizes.[12,13,15,18,19,25] Reviews of meta-analyses have found published trials report greater treatment effects than those found in gray literature. Removing gray literature from some meta-analyses results in 15% larger estimates of treatment effects, less precise effect-size estimates and more significant results.[12,13,18] As a result, excluding unpublished studies may compromise the validity and reliability of meta-analyses and the specificity of systematic reviews.[18,19,25]

4 | SOURCES FOR GRAY LITERATURE SEARCHING

Based on these factors, it is important to search through gray literature and include "gray" evidence in systematic reviews and meta-analyses. However, gray literature's diverse formats and intended audiences can present a significant challenge in a systematic search for evidence.[11,20,26] In order to address the challenge of searching in gray literature, a "gray search" plan can incorporate various search strategies. Three such strategies are: searches in gray literature databases, searches in clinical trial registers, and searches in conference proceedings. Although other methods are also possible, such as web searches (ex, with Google or Google Scholar [GS]), these methods are chosen for their sensitivity, potential for increased specificity, and labor intensity. An important consideration in designing a systematic review search strategy is maximizing search sensitivity and precision while keeping the search results manageable.[6,27] A search's sensitivity refers to its comprehensiveness. A search strategy should be sensitive, so important evidence is not missed, but too much comprehensiveness may produce a flood of results and reduce the search precision, retrieving more potentially nonrelevant articles.[6,27] The search should be specific, reducing the volume of nonrelevant results so that it must be sorted through those meet the review's criteria. Sensitivity is necessary for completeness and specificity is needed for manageability.

Gray literature databases allow the user to search for gray literature from various sources, simultaneously. A rapidly growing amount of gray literature, and medical research more generally, has led to increased need for systematized searches in comprehensive databases.[28] Although several databases including gray literature exist, a few will be presented in this paper, and a more comprehensive, annotated list of gray literature databases to be used for this review can be found in Appendix I. An example of a systematic review question, and a sample search for evidence from within gray literature databases, will be presented later in this paper.

Databases that can be searched for gray literature include OpenGrey, WONDER, and SCOPUS, among others (see Appendix I). Searches on online gray literature oriented databases and search engines, such as OpenGrey, CPI, and Proquest Digital Dissertations, yield predominantly gray literature references.[11] OpenGrey (www.opengrey.com) allows open access to over 700,000 bibliographical references from gray literature, including doctoral dissertations, papers from conferences, research publications, and other kinds of gray literature.[29] Wonder (https://wonder.cdc.gov), or Wide-ranging Online Data for Epidemiologic Research, is the online, public health resource and information database of the United States Centers for Disease Control and Prevention (CDC), allowing access to a wide range of public health data from scientific, academic, and government sources.[30] Scopus (https://www.elsevier.com/solutions/scopus), by Elsevier, is a large abstract and citation database for peer-reviewed literature, ranging from scientific journals research papers to conference proceedings.[31] It includes over 7.2 million papers from over 88,800 global conferences, peer-reviewed papers, and proceedings and patents from the United States, United Kingdom, Europe, Japan, and the World Intellectual Property Organization.[31]

Clinical trials can be searched in ClinicalTrials.gov, the U.S. National Institutes of Health's registry of world-wide clinical trials supported federally and privately.[32] Additionally, searches can be undertaken with other online databases such as Zetoc and Proquest's Digital Dissertations and Conference Papers Index (CPI). Zetoc (http://zetoc.jisc.ac.uk) is a research database accessing over 30,000 journals and 52 million citations, including conference papers and

proceedings, accessed through the British Library's electronic table of contents. It allows for searches to be performed in conference materials and journals, separately, or in combination. CPI, via Proquest(http://www.proquest.com/products-services/cpi-set-c.html), allows searches for papers and poster presentations in conference programs, abstracts, and published proceedings, providing citations and bibliographic information for papers and poster sessions from scientific meetings around the world.[33]

Another strategy that can be used to find evidence within gray literature is handsearching through conference proceedings and abstracts. Searching of conference proceedings is an effective method for finding evidence in gray literature.[11,12,34] In one study, only 47% of conference presentations went on to be published in commercial publications.[34,35] Conferences can be selected by title or subject, such as "The American Society of Neurorehabilitation." Alternately, searchers can match researchers with relevant published papers to conferences they have presented at, then search through those conference's proceedings for other evidence that might not be published elsewhere.

Authors of conference papers and presentations and other gray literature sources can be contacted for further, specific information about their work.[36] They may also be able to provide reference to other data or materials presented elsewhere, or not yet published. Although this targeted correspondence may provide useful information, others correspondence may be of less utility. Corresponding with experts in the topic being investigated, or in the field, and asking them to identify unpublished data or ongoing research they may be aware of has been suggested as an alternate way to find gray evidence. While this method could potentially produce useful evidence, it is time-consuming and offers no guarantee of obtaining relevant information.[11,15,20,34] In previous studies, such correspondence was sent repeatedly to experts, adding little new information to the reviews.[11,26,37] Given the time constraints typically faced in conducting a systematic review, this option may not return sufficient results for the amount of time needed.

An alternate strategy that can be used to find gray literature is web searching with commonly used search engines such as Google.com and GS. Although this search method is easily accessible and familiar to many, the low specificity, sensitivity, and large likelihood of finding material already found elsewhere reduce its effectiveness.[11] Controlled vocabulary searching, collecting related words and index terms together under a single word, is not possible in Google or GS, which use free-text searches.[37–39] This requires users to specify possible related terms, increasing search complexity. Reproducibility, important in systematic reviews, is also a concern with Google and GS searches.[11] Google filters results based on geographic location and search words previously entered, creating slightly different results based on location and search history.[37–39] Google's "PageRank" function orders results by popularity. As a result, results from gray literature may rank lowly in search results, making them hard to find, or the ranking may change while the review is taking place, making it less likely the results are reproducible and consistent.[34,40] The very large yields possible with Google searches may exceed the reviewers' ability to sort and evaluate them within the review's time constraints. Limiting the search by language or other constraints to reduce the number of results might risk not identifying relevant references and bias the results of the review.[20]

An alternative web-search method that may provide additional, more specific results is Mednar (http://mednar.com/mednar/desktop/en/search.html). Mednar is a free, medically focused, deep-web search engine. Deep-web search engines search web pages whose contents are not indexed for any reason, and not therefore searched, by standard search engines.[41] Mednar searches multiple databases in real time, retrieving relevant information from public and deep web resources, returning the most relevant results based on the search terms.[42]

These examples illustrate how gray literature searches can provide valuable evidence and background information for systematic reviews.

5 | A SAMPLE GRAY LITERATURE SEARCH

An example of a systematic search for evidence that can be enriched with gray literature searching is presented to illustrate the utility of gray literature searching and these resources. A review topic was chosen at random from the table of contents of published articles in the *Journal of Neurotrauma*, a journal available to the author at the time this article was written.[43] As a result, search for evidence from gray literature on the prevalence and effects of growth hormone (GH) deficiency after traumatic brain injury (TBI) on patient outcomes is presented as such an example. The following brief summary provides context for this illustrative example. GH deficiency is a condition associated with TBI, but systematic review is needed to clarify the state of the evidence and help form consensus about its effect on outcomes for individuals with TBI. In 2010, the U.S. Centers for Disease Control estimated that TBI led to 2.5 million emergency room visits, hospitalizations, and deaths and was the leading cause of death and disability among young adults in the United States.[44,45] Recent studies have suggested GH deficiency and hypopituitarism may affect 15% to 40% of people after TBI and are associated with depression, decreased cognitive function and reduced quality of life.[45,46] GH plays an important role in mental function and GH replacement therapy may lead to significant improvements in quality of life, physical capacity, and cognition after TBI.[47] Despite increasing interest, consensus on the role of GH deficiency after TBI or its effect on patient outcomes is lacking. A systematic reviewer seeking to review evidence for the prevalence and influence of GH deficiency after TBI may find that searching gray literature may contribute valuable evidence in that review.

A PubMed search (all fields) with mesh terms and keywords related to "TBI and GH," restricted to humans, produced 168 results, at the time of the writing of this paper (see Appendix II). An exploratory search for additional material published within gray literature and not already found in the PubMed search included a search in ClnicalTrials.gov, with search terms "TBI and GH." This produced 15 results, including three completed and five active trials. One example, "anterior pituitary hormone replacement in TBI," is a double-blind, placebo-controlled trial of GH replacement therapy in adults with TBI.[48] The study has been completed and presented in conferences

but not yet published in a peer-reviewed journal. The study examines the effect of GH replacement therapy on physical and neuropsychological function in TBI patients with documented abnormalities in GH, providing detailed outcome measures, eligibility criteria, interventions and contact information, and potentially enriching the evidence base for the systematic review. This, and other results from the search, may ultimately lead to data that might otherwise have been missed by the systematic review, help quantify and define the "state of the evidence" of the topic of the systematic review, or allow the reviewer to contact study authors, who may be able to refer the reviewer to other investigators or works not yet published in commercial literature.

Similar exploratory searches with terms "TBI" and "GH" on OpenGrey found three doctoral theses exploring GH deficiency after TBI, not duplicated in the PubMed search, and further enriching the scope of evidence for the review. Abstracts, a detailed summary of study procedures and authors' contact information, are provided on OpenGrey, making it possible to contact the authors for more information. Searches with alternate terms for TBI and GH, such as "anterior pituitary hormone" or "somatotropin," for example, can be used to find more results.

To further illustrate the potential benefit of gray literature searching for this sample systematic review question, a search for conference paper related materials was conducted on Zetoc, with search terms "TBI, GH." This revealed 15 records at the time of the writing of this article. Included in these is "Rehabilitation and hypopituitarism after traumatic brain injury," by Masel.[49] This was presented at the "International Symposium on Growth Hormone and Growth Factors in Endocrinology and Metabolism," in Prague, Czech Republic, in April 2003. This presentation and its conference proceedings review literature and examine the epidemiology, symptomology, evaluation, and rehabilitation of GH deficiency and hypothyroidism after TBI. Another conference paper found, "Growth Hormone Deficiency after Traumatic Brain Injury in Adults: When to Test and How to Treat?" by Kelestimur, was presented and can be found in the proceedings of the first "Merck Serono growth hormone symposium; New challenges in growth hormone therapy" in Frankfurt, Germany, in 2008.[50]

Such papers could provide valuable information, from noncommercially published data to identify ongoing research, trends within the review topic, or data not yet commercially published that may further inform a systematic review examining GH deficiency in TBI.

Additional, exploratory handsearching of proceedings for conferences or associations identified in conference materials searches may provide further works that may help to enrich the review's findings. For example, handsearching the proceedings of the American Society of Neurorehabilitation's, 2015 Annual Meeting, revealed: "Prevalence of Growth Hormone Deficiency in Chronic Traumatic Brain Injury (TBI), Kreber et al."[51] Such a presentation may yield valuable insight into the state of evidence or research activity within the topic covered by the review question. Conference paper and presentation abstracts and presenters' contact information are available in the society's digital archives. This source of gray evidence may yield clinical context or data that were unpublished in commercial publications.

6 | CHALLENGES OF SEARCHING FOR GRAY LITERATURE

Gray literature has its drawbacks. It can be time-consuming to find, as searches may be required in multiple search engines, or in multiple sites if handsearching is taking place, and there may be a considerable volume or results found.[28] This may be ameliorated imposing some constraint, such as date range or language constraints, on the search in order to limit the scope of the search. It is also possible to miss significant evidence from within gray literature, as it is varied intended audiences and purposes can make it difficult to access it, or duplicate evidence that was later published in commercial publications.[28] There is no accepted, gold standard method for conducting rigorous, gray literature searches, and little specific guidance available for performing gray literature searches.[12,15,20]

Other features of gray literature may provide methodological challenges to the researcher seeking to include it in a systematic review. Gray literature may often not be formatted to meet the page limits and citation requirement of academic or commercial journals, adding potential variability to the kind of documents that must be identified and examined by the researcher.[19,28] A lack of consistent title and indexing information, and potential variability among gray literature abstracts, may contribute to the difficulties associated with gray literature searching. Particularly when gray literature is found on web-based platforms, the dynamic nature of website domains and addresses and the geographic, location-based features of popular search engines may reduce the reproducibility of gray literature searches.[42,46–49] Documents and links to them may also become unavailable after the initial search has taken place. As gray literature it is not published in commercial, peer-reviewed publications, there may be temptation to excluding gray literature completely from review or not utilize information found in gray literature in clinical or academic decision-making. Publication in peer-reviewed journals is sometimes considered an essential indicator of quality lacking in gray literature.[13] Despite this, some gray literature, such as theses and dissertations, are rigorously reviewed and may be of high quality.[15] Conference presentations are often peer-reviewed before acceptance.[11] Critical review of published research may equally find variability its quality, suggesting that the peer-review process may not be an adequate indicator of research quality on its own.[12,13,15] Gray literature that does not include peer-review or rigorous, independent scientific review, such as from some trade or commercial publications, etc., may produce significant challenges for the systematic reviewer. However, bias and confounding factors may not be adequately addressed in evidence produced for, or found in, such sources, and a lack of scientific rigor may lead to methodological issues that may significantly reduce the validity of the results.

7 | RECOMMENDATIONS

Despite the potential challenges involved in searching for evidence in gray literature, it is important for gray literature to be included in a systematic review, given its potential to provide a balanced view of the evidence.[2,11,18] Including gray literature in a researcher's search

strategy may increase the comprehensiveness of the search.[52] Including evidence from a wide range of sources in a systematic review may enrich the review's findings and reduce the possibility of publication bias. Gray literature may also help provide a sense of context for the question being examined, especially when a lack of consensus about the research question, or the setting or context of the intervention (or subject examined) may affect its outcome, or there is a paucity of available evidence in commercial publications.[19] As there is sometimes a long lag time between the submission and publication of evidence, gray literature may also help ensure the most current picture of what is happening within a body of evidence or area of practice at the time of the review.[15] The benefits of including gray literature may far outweigh the cost in time and resource needed to search for it. Given these benefits, a carefully thought out gray-literature search strategy, incorporating some of the search strategies described in this paper, may be an invaluable component of a systematic review.

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REFERENCES

1. Mulrow CD. Systematic reviews: Rationale for systematic reviews. *BMJ*. 1994;309:597–599.
2. Higgins JPT, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]*. The Cochrane Collaboration, 2011. Available from http://handbook.cochrane.org.
3. da Costa BR, Juni P. Systematic reviews and meta-analyses of randomized trials: principles and pitfalls. *Eur Heart J*. 2014;35:3336–3345.
4. Oxman AD, Cook DJ, Guyatt GH, et al. Users guide to medical literature: Vi. How to use an overview. *JAMA*. 1994;272:1367–1371.
5. van der Knaap LM, Leeuw FL, Bogaerts S, Nijssen LTJ. Combining Campbell standards and the realist evaluation approach: the best of two worlds? *Am J Eval*. 2008;29:48–57.
6. Centre for Reviews and Dissemination U of Y. Systematic reviews: CRD's guidance for undertaking reviews in health care. Centre for Reviews and Dissemination, University of York, 2008. https://gate2.library.lse.ac.uk/login?url=http://onlinelibrary.wiley.com/doi/10.1046/j.1365-2524.2003.00433.x/abstract%5Cnhttp://zw4gk5cr3l.search.serialssolutions.com?sid=CentralSearch:null&genre=article&atitle=Scoping+the+field&volume=11&issue=4&title=Hea (accessed August 18, 2016).
7. Royle P, Bain L, Waugh N. Systematic reviews of epidemiology in diabetes: finding the evidence. *BMC Med Res Methodol*. 2005;5:2.
8. Avenell A. Lessons for search strategies from a systematic review, in The Cochrane Library, of nutritional supplementation trials in patients. *Am J Clin Nutr*. 2001;73: 505–510.
9. Farquhar C, Vail A. Pitfalls in systematic reviews. *Curr Opin Obstet Gynecol*. 2006;18:433–439.
10. Lemeshow AR, Blum RE, Berlin JA, Stoto MA, Colditz GA. Searching one or two databases was insufficient for meta-analysis of observational studies. *J Clin Epidemiol*. 2005;58:867–873.
11. Mahood Q, van Eerd D, Irvin E. Searching for grey literature for systematic reviews: challenges and benefits. *Res Synth Methods*. 2014;5:221–234.
12. Conn VS, Valentine JC, Cooper HM, Rantz MJ. Grey literature in meta-analyses. *Nurs Res*. 2003;52:256–261.
13. Hopewell S, McDonald S, Clarke M, Egger M. Grey literature in meta-analyses of randomized trials of health care interventions. *Cochrane Database Syst Rev*. 2007;MR000010, https://doi.org/10.1002/14651858.MR000010.pub3.
14. Pappas C, Williams I. Grey literature: its emerging importance. *J Hosp Librariansh*. 2011;11:228–234.
15. Bellefontaine SP, Lee CM. Between black and white: examining grey literature in meta-analyses of psychological research. *J Child Fam Stud*. 2014;23:1378–1388.
16. Helmer D. How do various fugitive literature searching methods impact the comprehensiveness of literature uncovered for systematic review? How do various fugitive literature searching methods impact the comprehensive. 4th International Conference on Grey Literature, Washington, USA, 1999.
17. Mallet S, Hopewell S, Clarke M. The use of grey literature in the first 1000 Cochrane reviews. 4th Symposium on Systematic Reviews: Pushing the Boundaries, Oxford, UK, July 2–4, 2002. http://www.mrw.interscience.wiley.com/cochrane/clcmr/articles/CMR-4005/frame.html (accessed August 18, 2016).
18. McAuley L, Pham B, Tugwell P, Moher D. Does the inclusion of grey literature influence estimates of intervention effectiveness reported in meta-analyses? *Lancet*. 2000;356:1228–1231.
19. Benzies KM, Premji S, Hayden KA, Serrett K. State-of-the-evidence reviews: advantages and challenges of including grey literature. *Worldviews Evid-Based Nurs*. 2006;3:55–61.
20. Giustini D, Thompson D. Finding the hard to finds: Searching for grey literature. *The University of British Columbia*, 2006. http://blogs.ubc.ca/dean/files/2009/02/greylit_manual_may111.pdf (accessed August 20, 2016).
21. Riveros C, Dechartres A, Perrodeau E, Haneef R, Boutron I, Ravaud P. Timing and completeness of trial results posted at ClinicalTrials.gov and published in journals. *PLoS Med*. 2013;10:1–12.
22. Dickersin K. The existence of publication bias and risk factors for its occurrence. *JAMA*. 1990;263:1385–1389.
23. Floyd RG, Cooley KM, Arnett JE, Fagan TK, Mercer SH, Hingle C. An overview and analysis of journal operations, journal publication patterns, and journal impact in school psychology and related fields. *J School Psychol*. 2011;49:617–647.
24. Easterbrook P, Gopalan R, Berlin J, Matthews D. Publication bias in clinical research. *Lancet*. 1991;337:867–872.
25. Dickersin K. How important is publication bias? A synthesis of available data. *AIDS Educ Prev*. 1997;9:15–21.
26. Haig A, Dozier M. BEME guide no. 3: systematic searching for evidence in medical education-part 2: constructing searches. *Med Teach*. 2003;25:463–484.
27. Wilczynski NL, Haynes RB. EMBASE search strategies achieved high sensitivity and specificity for retrieving methodologically sound systematic reviews. *J Clin Epidemiol*. 2007;60:29–33.
28. Adams RJ, Smart P, Huff AS. Shades of grey: guidelines for working with the grey literature in systematic reviews for management and organizational studies. *Int J Manage Rev*. 2016: 1–23. https://doi.org/10.1111/ijmr.12102.
29. INIST-CNRS. OpenGrey. System for Information on Grey Literature in Europe. https://http://www.opengrey.eu (accessed August 19, 2016).
30. Massengale LN. Cdc wonder. *Choice Curr Rev Acad Libr*. 2008;45:1979.

31. Elsevier. Scopus. SCOPUS. 2016. https://www.elsevier.com/solutions/scopus. Cited November 27, 2016.
32. U.S. National Institutes of Health. ClinicalTrials.gov. ClnicalTrials.gov. https://clinicaltrials.gov (accessed August 17, 2016).
33. ProQuest. Conference Papers Index-Proquest. http://www.proquest.com/products-services/cpi-set-c.html (accessed August 19, 2016).
34. Balshem H, Stevens A, Ansari M, et al. Finding grey literature evidence and assessing for outcome and analysis reporting biases when comparing medical interventions: AHRQ and the Effective Health Care Program. *Methods Guid Comp Eff Rev*. 2013;1–41.
35. Van Royen P, Sandholzer H, Griffiths F, et al. Are presentations of abstracts at EGPRN meetings followed by publication? *Eur J Gen Pract*. 2010;16:100–105.
36. Shekelle PG, Morton SC, Suttorp MJ, Buscemi N, Friesen C. Challenges in systematic reviews of complementary and alternative medicine topics. *Ann Intern Med*. 2005;142:1042–1047.
37. Kirkham JJ, Dwan KM, Altman DG, et al. The impact of outcome reporting bias in randomised controlled trials on a cohort of systematic reviews. *BMJ*. 2010;340:c365.
38. Jamali HR, Asadi S. Google and the scholar: the role of Google in scientists' information-seeking behaviour. *Online Inf Rev*. 2010;34:282–294.
39. Kousha K, Thelwall M. Google Scholar citations and google Web/URL citations: a multi-discipline exploratory analysis. *J Am Soc Inf Sci Technol*. 2007;58:1055–1065.
40. Franceschet M. PageRank. *Commun ACM*. 2011;54:92–101.
41. Hamilton N. The mechanics of a deep net metasearch engine. Proceedings of the 12th International World Wide Web Conference. 2003. http://scholar.google.com/scholar?hl=en&btnG=Search&q=intitle:The+Mechanics+of+a+Deep+Net+Metasearch+Engine#0 (accessed August 27, 2016).
42. Mednar. Mednar. http://mednar.com/mednar/desktop/en/search.html. Cited January 1, 2016. (accessed November 27, 2016).
43. Kreber LA, Griesbach GS, Ashley MJ. Detection of growth hormone deficiency in adults with chronic traumatic brain injury. *J Neurotrauma*. 2016;33:1607–1613.
44. Centers for Disease Control and Prevention. Report to Congress on Traumatic Brain Injury in the United States: Epidemiology and Rehabilitation. National Center for Injury Prevention and Control; Division of Unintentional Injury Prevention, Atlanta, GA, 2015.
45. Schneider HJ, Kreitschmann-Andermahr I, Ghigo E, Stalla GK, Agha A. Hypothalamopituitary dysfunction following traumatic brain injury and aneurysmal subarachnoid hemorrhage: a systematic review. *JAMA*. 2007;298:1429–1438.
46. Gardner CJ, Mattsson AF, Daousi C, Korbonits M, Koltowska-Haggstrom M, Cuthbertson DJ. GH deficiency after traumatic brain injury: improvement in quality of life with GH therapy: analysis of the KIMS database. *Eur J Endocrinol*. 2015;172:371–381.
47. Powner DJ, Boccalandro C, Alp MS, Vollmer DG. Endocrine failure after traumatic brain injury in adults. *Neurocrit Care*. 2006;5:61–70.
48. Urban RJ. Anterior Pituitary Hormone Replacement in Traumatic Brain Injury, Galveston, Texas, 2016. https://clinicaltrials.gov/ct2/show/0NCT00957671?term=traumatic+brain+injury+AND+growth+hormone&rank=1 (accessed August 19, 2016).
49. Masel BE. Rehabilitation and hypopituitarism after traumatic brain injury. *Growth Horm IGF Res*. 2004;14:S108–113.
50. Kelestimur F. Growth hormone deficiency after traumatic brain injury in adults: when to test and how to treat? *Pediatr Endocrinol Rev*. 2009;6:534–539.
51. Lefaivre BC. *American Society of Neurorehabilitation and Translational and Computational Motor Control Annual Meeting*, Carmichael ST, editor, Chicago, IL; 2015.
52. Cook AM, Finlay IG, Edwards AGK, et al. Efficiency of searching the grey literature in palliative care. *J Pain Symptom Manage*. 2001;22:797–801.

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APPENDIX I: RESOURCES FOR SEARCHING FOR GRAY LITERATURE, ANNOTATED

1 Grey Literature Databases and Search Engines

1.1 Grey Matters: A Practical Search Tool for Evidence-Based Medicine

https://www.cadth.ca/resources/finding-evidence/grey-matters

Online resource for gray literature searching revised and updated, using the Canadian Agency for Drugs and Technologies in Health (CADTH) free online Resource for gray literature searching, "Grey matters." Includes links to Canadian and international health technology assessment agencies, regulatory industries, and clinical trial registries. (Download Word document, "Grey Matters: a practical tool for searching health-related grey literature," which contains hyperlinks to global gray literature resources.

1.2 GreyNet, currently available via INSIT through OpenSIGLE

opensigle.inist.fr (formerly, http://www.greynet.org)

INIST, the Institute for Scientific and Technical Information, in France, maintains OpenSIGLE, providing access to all GreyNet records, and data from EAGLE (European Association for Grey Literature Exploitation).

1.3 Grey Literature Report

http://www.greylit.org/home

The New York Academy of Medicine Library's gray literature collection, allowing full-text, keyword searching, and subject searching for gray literature. Gray Literature resources are cataloged and indexed with MeSH.

1.4 The Healthcare Management Information Consortium (HMIC) database

http://www.ovid.com/site/catalog/databases/99.jsp

Searches in records of the Library and Information Services Department of the Department of Health (DH) in England, and the King's Fund and Library Service (an independent health charity that works to develop and improve management of health and social care services Information). Includes gray literature from a variety of health and community care–related areas.

1.5 The National Technical Information Service (NTIS)

www.ntis.gov/

Provides access to the results of both US and non-US government-sponsored research and can provide the full text of the technical report for most of the results retrieved. NTIS is free on the Internet.

1.6 OpenGrey

http://www.opengrey.eu

System for Information on Grey Literature in Europe: Allows open access to over 700,000 bibliographical references of gray literature (paper) produced in Europe and allows users to export records and locate the documents. Includes technical or research reports, doctoral dissertations, some conference papers, some official publications, and other types of gray literature.

1.7 PsycEXTRA

www.apa.org/psycextra/

A companion database to PsycINFO in psychology, behavioral science, and health. It includes references from newsletters, magazines, newspapers, technical and annual reports, government reports, and consumer brochures. It includes abstracts and citations plus full text for a major portion of the records.

1.8 Scopus

https://www.elsevier.com/solutions/scopus

By Elsevier, Scopus is the largest abstract and citation database of peer-reviewed literature: scientific journals, books, and conference proceedings. It includes over 7.2 million conference papers from over 88,800 worldwide events, peer-reviewed papers, and proceedings and patents from the United States, United Kingdom, Europe, Japan, and the World Intellectual Property Organization.

1.9 Web of Science

http://ipscience.thomsonreuters.com/product/web-of-science/

(log in for institutional users-Shibboleth, Athens…. http://login.webofknowledge.com/)

World's leading citation databases. It covers over 12,000 of the highest impact journals worldwide, including Open Access journals and over 150,000 conference proceedings. Coverage in the sciences, social sciences, arts, and humanities, with coverage to 1900.

1.10 Wonder

https://wonder.cdc.gov

Wonder, or Wide-ranging Online Data for Epidemiologic Research, is the online, public health resource and information database of the United States Centers for Disease Control and Prevention (CDC), providing access to a wide array of public health data from scientific, academic, and government sources.

1.11 Zetoc

http://zetoc.jisc.ac.uk

Research database accessing over 30,000 journals and 52 million citations, including conference papers and proceedings, accessed through the British Library's electronic table of contents.

2 Clinical Trials

2.1 ClinicalTrials.gov A service of the U.S. National Institutes of Health

https://clinicaltrials.gov

ClinicalTrials.gov is a registry of federally and privately supported clinical trials conducted in the United States and around the world.

2.2 Cochrane Central Register of Controlled Trials

http://onlinelibrary.wiley.com/cochranelibrary/search?searchRow.searchOptions.searchProducts=clinicalTrialsDoi.

A source of clinical trials and handsearching results from the Cochrane Collaboration.

2.3 World Health Organization (WHO) International Clinical Trials Registry Platform

http://apps.who.int/trialsearch/

The Clinical Trials Search Portal provides access to a central database containing the trial registration data sets provided by global registries. It also provides links to the full original records.

3 Conference Papers

3.1 Conference Alerts

http://www.conferencealerts.com/faq

Conference Alerts, containing information from academic conferences worldwide. The database is searchable by city, country, date, and keyword.

3.2 Conference Papers Index, via Proquest

http://www.proquest.com/products-services/cpi-set-c.html

Conference Papers searches through citations for scientific papers and poster presentations presented at major scientific meetings around the world, including final programs, abstracts, and published proceedings. Records include ordering information for reprints and other conference publications, and author and title information for specific papers.

3.3 Digital dissertations

Index to Scientific and Technical Proceedings, via Web of Science

http://ipscience.thomsonreuters.com/product/web-of-science/

BIOSIS Previews, via Web of Knowledge.

3.4 Zetoc

http://zetoc.jisc.ac.uk

Comprehensive research database, accessing over 30,000 journals and more than 52 million article citations and conference papers through the British Library's electronic table of contents.

4 Dissertations, Theses, and Academic Papers

4.1 OpenGrey

http://www.opengrey.eu

System for Information on Gray Literature in Europe: Allows open access to over 700,000 bibliographical references of gray literature (paper) produced in Europe and allows users to export records and

locate the documents. Includes technical or research reports, doctoral dissertations, some conference papers, some official publications, and other types of gray literature.

4.2 ProQuest Dissertation & Theses Global (PQDT Global)

http://www.proquest.com/products-services/cpi-set-c.html

Searches dissertations and theses via a single access point to explore an extensive, trusted collection of 3.8 million graduate works, with 1.7 million in full text. Designated as an official offsite repository for the U.S. Library of Congress, PQDT Global offers comprehensive historic and ongoing coverage for North American works and significant and growing international coverage from a multiyear program of expanding partnerships with international universities and national associations. We offer effective and efficient results on our curated content platform with expert metadata that reduces noise in search results. Direct access to full text and other ProQuest and e-book subscriptions advance the research process.

4.3 WorldCatDissertations

http://www.worldcat.org

A database of all dissertations and theses available in WorldCat, a catalog of books and other materials available in libraries worldwide. Available without a subscription at worldcat.org. More information also available at http://www.oclc.org/en-US/worldcat.html

5 Web Searches

5.1 Google Scholar

https://scholar.google.com

5.2 Mednar

http://mednar.com/mednar/desktop/en/search.html

Mednar is a free, medically focused deep web search engine. Deep web search engines search web pages whose contents are not indexed for any reason, and not therefore searched, by standard search engines. Mednar searches multiple databases in real time, retrieving relevant information from public and deep web resources, returning the most relevant results based on the search terms.

6 Other Resources

6.1 The Grey Literature Report

http://www.greylit.org/about

The report is a bimonthly publication of the New York Academy of Medicine, alerting readers to new gray literature publications in health services research and selected urban health topics.

6.2 University of Michigan Library, Grey Literature Overview

http://guides.lib.umich.edu/greyliterature

Provides an overview of gray literature, sources for finding it, organized by topic of interest, and type of literature.

6.3 National Institutes of Health (NIH), Office of Research Management, Systematic Reviews: The Literature Search: Gray Literature

http://nihlibrary.campusguides.com/c.php?g=38332&p=244522

NIH Library support for systematic reviews, specifically gray literature searching, including search and documentation methods, search engines, support, and resources.

APPENDIX II: PUBMED SEARCH STRATEGY

PubMed search strategy: (“brain injuries, traumatic”[MeSH Terms] OR (“brain”[All Fields] AND “injuries”[All Fields] AND “traumatic”[All Fields]) OR “traumatic brain injuries”[All Fields] OR (“traumatic”[All Fields] AND “brain”[All Fields] AND “injury”[All Fields]) OR “traumatic brain injury”[All Fields]) AND (“growth hormone”[MeSH Terms] OR (“growth”[All Fields] AND “hormone”[All Fields]) OR “growth hormone”[All Fields])

Results: 227

Filter: Humans: 186 results