HEALTH TECHNOLOGY ASSESSMENT

WHERE DO YOU FIND INFORMATION FOR HEALTH TECHNOLOGY ASSESSMENT (HTA)?

MODULE 2

Workshop Manual
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WELCOME

Welcome to the **second** module of six in a series on Health Technology Assessment (HTA). The primary objective of this second module and workshop is to provide you with an overview of where you can find information for Health Technology Assessment (HTA).

We hope that the fundamentals presented in this module will not only assist you in your own search for information for Health Technology Assessment, but also provide you with the tools required to critically evaluate research in a sound, objective, and appropriate manner.

We look forward to sharing this experience with you and your colleagues. Your feedback and comments on both the module and workshop will be greatly appreciated! Please send comments to the Office of Surgical Research at osr@ucalgary.ca

Prepared by:

Elizabeth Oddone Paolucci

Tyrone Donnon

Paule Poulin

The HTA Education Team Members,

Paule Poulin, PhD
Office of Surgical Research, Associate Director, Calgary Health Region

Tyrone Donnon, PhD
Medical Education & Research Unit, Assistant Professor, Faculty of Medicine

Elizabeth Oddone Paolucci, PhD
Medical Education & Research Unit, Educational Consultant

Norm Schachar, MD, FRCSC
Office of Surgical Education, Director, Department of Surgery

Anita Jenkins, RN, BN, MN
Office of Surgical Education, Education Coordinator, Department of Surgery

David Sigalet, MD, PhD., FRCSC
Office of Surgical Research, Director, Department of Surgery

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Based on the statement above, no conflict of interest exists with the author(s) and/or external reviewers of the second module.

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TABLE OF CONTENTS

1.0 OBJECTIVES

The primary goals of this HTA module are:

1. Assist clinicians in obtaining relevant information for HTA.
2. Review the terminology associated with various types of research reviews.
3. Identify sources of research evidence and where it can be found.
4. Discuss what critical appraisal skills are and how they should best be employed.
5. Determine types of bias in types of research evidence.
6. Evaluate the limitations and challenges to finding information for HTA.

By the end of this HTA module, participants will be able to:

1. Distinguish between various types of review procedures (e.g., narrative, meta-analysis, HTA) and their accompanying strengths and limitations.
2. Identify relevant sources of information for HTA, as well as how to navigate within these databases.
3. Understand the fundamentals in conducting a critical appraisal of the empirical research.
4. Identify ways to overcome the limitations and challenges to finding information for HTA.

2.0 INTRODUCTION

There is growing awareness that not everything that is technically possible is useful for bringing about improvements in individual or collective health (The Pan American Health Organization, 1998). Consequently, health technology and its management are leading priorities for policy makers, decision-makers and academic researchers.

One of the challenges facing today's health care professionals is the difficulty in keeping current with the proliferation of medical literature and in being able to critically assess the wide variety of evidence. It has been stated that the pace of health technology development is outpacing the health systems' ability to effectively operationalize it (Health Technology Assessment Task Group, 2004). This is compounded by the fact that the circle of those who "need to know" how effective and efficacious a particular technology is, has been widened and diversified. For example, now HTA publications need to be understood by a wide audience including lawmakers, officials, health administrators, researchers, biomedical engineers, managers of the pharmaceutical industries and medical equipment, and patients and families. In addition, there has been a transition from an assessment based mainly on the needs of Health Technology producers to one that gives priority to the individual and collective needs of Health Technology users (The Pan American Health Organization, 1998). To fulfill these differing needs, HTA reports comes in a wide variety of formats. Some can provide very rapid responses to urgent requests for information (for example, AHFMR QwikNotes) while others include more comprehensive, systematic, peer-reviewed assessments (for example, CCOHTA Technology Reports).

The purpose of HTA is to promote change rather than to accumulate knowledge simply for knowledge sake (The Pan American Health Organization, 1998). HTA is not a speculative or purely academic discipline, but rather a systematic interdisciplinary process with the objective of effecting change. Since HTA is grounded in the available basic and applied research (The Pan American Health Organization, 1998), successful HTA requires assembling relevant evidence. For very new technologies, this information may be sparse and difficult to find; for many technologies it can be profuse, scattered and of widely varying quality. The type of technology and the properties or impacts of interest should be incorporated into a systematic search strategy of appropriate information resources.

In this module we will: 1) explore how information can be accumulated by examining different types of research evidence; 2) identify some of the major sources of research evidence; 3) review some of the skills required for critical appraisal, 4) determine major types of bias involved in the gathering of evidence, and 5) evaluate some of the major limitations and challenges to finding relevant information for HTA.

3.0 TYPES OF RESEARCH REVIEWS

In any area, it is not unusual for studies to give unclear, confusing, and even contradictory results. Looked at individually, each study may offer little insight into effectiveness of a particular health technology. So, the hope is that when taken together, a clearer and more consistent picture will emerge (Davies & Crombie, 2003). The method commonly used to assess a technology is to consolidate the best available empirical evidence.

Reviews have become an increasingly important means by which research results are collected, sorted, appraised, and summarized (JBIEBNM, 2001). There is a range of approaches to reviewing research literature. Information reviewed can be both primary (content in originals works) and secondary (content in systematic review, files, and by databases) (The Pan American Health Organization, 1998). However, before examining these sources of information, it is important to discuss the main types of reviews available and the ways information can be synthesized.

3.1 TRADITIONAL NARRATIVE REVIEW

Narrative reviews are both widespread and influential. The majority of reviews are narrative and have always been a part of the medical literature. Respected peer leaders and experts in their field, have sought to collate existing knowledge and publicize these summaries (Davies & Crombie, 2003). Traditional narrative reviews are generally comprehensive, cover a wide range of issues within a topic, and tend to contain non-technical idiomatic language (Collins & Fauser, 2005). Therefore, they tend to be most appropriate for describing the history or development of a problem and its management. According to Cook, Mulrow, and Haynes (1997), narrative reviews may be the choice of review when the goal is to describe cutting-edge developments, especially if research is scant or preliminary, or if studies are very limited by flawed design or execution. Narrative reviews can draw analogies and can conceptually integrate two independent fields of research.

While most useful for obtaining a broad perspective on a topic, narrative reviews are less useful in furnishing quantitative answers to specific clinical questions (Cook, Mulrow, & Haynes, 1997). The connection between clinical recommendations and evidence in narrative reviews is often tenuous, incomplete, or based on a biased citation of studies. Narrative reviews typically do not inform the reader as to how decisions were made regarding relevance and validity of studies included in the review. Thus, there is an absence of transparency and reproducibility in traditional narrative reviews.

Traditional narrative attempts at synthesis of information have not always been as rigorous as might have been hoped. Narrative reviewers rarely begin with an open mind as to the likely recommendations. Those involved in developing a review may well have started it or were commissioned to write a review precisely because of their accumulated experience and professional opinions (Davies & Crombie, 2003). However, if strong prior beliefs are held, then a dispassionate review of evidence will be difficult to achieve. At worst, a reviewer may simply build a case in support of their personal beliefs, selectively citing appropriate studies

along the way (Davies & Crombie, 2003). Thus, it was from the inadequacies of traditional reviews that the need for a more rigorous systematic approach emerged.

3.2 QUALITATIVE SYSTEMATIC REVIEW

Qualitative systematic reviews are summaries of all past research on a topic of interest. They utilize the same principles and rigor that is expected of primary research (JBIEBNM, 2001). Systematic reviews involve summarizing large bodies of evidence and help to explain differences among studies on the same question. They are scientific investigations with pre-planned methods and an assembly of original studies as their "subjects" (Cook, Mulrow, & Haynes, 1997). Systematic reviews synthesize the results of multiple primary investigations by using strategies that limit bias and random error. These strategies include a comprehensive search of all potentially relevant articles and the use of explicit reproducible criteria in the selection of articles for review. Primary research designs and study characteristics are appraised, data are synthesized, and results are interpreted. It is the use of these explicit and rigorous methods that distinguish systematic reviews from the traditional reviews of the literature (JBIEBNM, 2000).

A well-conducted systematic review is invaluable for practitioners. Unlike single studies that are unable to provide definitive answers to clinical questions, systematic reviews can help practitioners solve specific clinical problems. By critically examining primary studies, systematic reviews can also improve our understanding of inconsistencies among diverse pieces of research evidence. High quality systematic reviews can define the boundaries of what is known and what is not known (Cook, Mulrow, & Haynes, 1997). Of course, the quality of a review (i.e., its worth), depends on the extent to which scientific review methods were used to minimize the risk of error and bias.

Developing a systematic review requires the following steps: (1) defining an appropriate question; (2) searching both the published and unpublished literature; (3) employing two independent reviewers to assess the studies for eligibility for inclusion, study quality and reported findings; (4) combining the results to produce a "bottom line" on the clinical effectiveness of the intervention; and (5) placing the findings in context by addressing issues such as the quality and hetereogeneity of the included studies, the likely impact of bias and chance, and the applicability of the findings (Davies & Crombie, 2003; Khan, ter Riet, Glanville, Sowden, & Kleijnen, 2001).

When formulating policy recommendations in medicine, the need for a synthesis of information to evaluate effectiveness and costs is irrefutable. The systematic review attempts to reduce reviewer bias through the use of objective, reproducible criteria to select relevant individual publications and assess their validity. Thus, the systematic review involves explicit, transparent methods which are clearly stated, and reproducible by others (Collins & Fauser, 2005). However, quantitative systematic reviews take things one-step further. The chief difference between systematic qualitative review and a systematic quantitative review (or meta-analysis) is that a qualitative review explains differences only between studies, while a quantitative review provides a pooled result and does not tell the difference between individual studies.

3.3 QUANTITATIVE SYSTEMATIC REVIEW OR META-ANALYSIS

Quantitative systematic reviews (also known as meta-analysis) employ statistical methods to combine the results of two or more primary studies. The goal is to improve generalizations and arrive at conclusions not possible by reviewing individual studies alone. Meta-analysis is distinguished from systematic review in that statistical methodologies are applied to derive more objective conclusions than those that typify by narrative and systematic reviews.

Meta-analysis provides a framework for a systematic review, in that similar measures from comparable studies are listed systematically, and the measures of the effect of an intervention are combined. Synthesis of results from different studies is achieved by converting individual results to a common scale or measure and applying standard statistical analysis procedures. Meta-analysis is useful when many studies address the same issue, as it provides the means by which to statistically combine the results. It is also useful when studies are too small and so lack the power to detect treatment effects, as combining studies increases the sample size and therefore the power (JBIEBNM, 2000). Therefore, meta-analysis attempts at "reconstructing a larger" clinical trial by statistically combing similar results from small trials thereby increasing the power to detect treatment effects.

Meta-analysis involves the application of statistical procedures to a collection of studies. While a traditional researcher collects data from multiple participants, a meta-analyst uses each study as one data point. The procedure of meta-analysis is a rigorous alternative to the narrative review and is an objective statistical procedure above systematic review alone. The methods are standardized and the analyses are widely recognized and used. A meta-analysis is not merely another study to be added to the pile of individual pieces of research. It is more powerful and conclusive than any individual or group of studies, and is considered a breakthrough which has propelled the health sciences beyond the exploratory domain of narrative reviews and single studies and beyond the explanation of differences between studies as described in systematic reviews. The result is a comprehensive, statistical statement of the learning to date in a specific area of study (Lipsey & Wilson, 1995; Lytton, 1994; Wolf, 1986).

Proponents and opponents of the meta-analysis approach have engaged in an academic debate regarding its strengths and limitations. The primary strengths of meta-analysis include: the ability to accumulate knowledge through quantitative summaries and to effectively add to the extant body of knowledge; the identification of systematic sources of differences in results; the building of theory and development of new hypotheses; and the promotion of efficiency in program research design in times of scarce research resources (Farley & Lehman, 1986). Meta-analyses are useful both substantively and for the design of future research.

The cited limitations of meta-analysis include: retrievability bias or file drawer problem; threats to "inter-coder" reliability resulting from reliance on printed documents; heterogeneity

of variance, methods, and samples; inclusion of poorly designed and conducted research; lumping together of non-independent data; and over-reliance on single values and correlational data. Although some of these limitations can be addressed, others remain and should be recognized as limitations to the procedure. For instance, meta-analysis is not used when studies are different in terms of their population, intervention or how outcomes were measured. When treatments evaluated in the individual studies are different, combining these results to obtain an average of the treatment effect will be meaningless. Similarly, there is little point in combining studies if they measured different outcomes or used different populations. When the findings of individual studies differ significantly they should not be combined in a meta-analysis. This is because combining widely differing results to produce an average effect would fail to represent the great variation in the outcomes (JBIEBNM, 2000).

Still, meta-analysis as a statistical and scientific tool has grown immensely in popularity over the last decade as a way to systematically present new research results in the proper context, given all previous related work. By using methods of meta-analysis, researchers may decrease bias and increase the precision of their treatment effects, thus reducing the probability of type-I and type II errors and, in the process, making the acceptance of new treatments more timely (JBIEBNM, 2000).

Meta-analysis, decision analysis, and cost-effectiveness analysis are the cornerstones of evidence-based medicine. These related quantitative methods have become essential tools in the formulation of clinical and public policy based on the synthesis of evidence. All three methods are taught with increasing frequency in medical schools and schools of public health and in health policy courses at the undergraduate and graduate level (JBIEBNM, 2000).

3.4 HEALTH TECHNOLOGY ASSESSMENT (HTA)

Multiple definitions of Health Technology Assessment (HTA) exist, thereby making it difficult to present one clear and comprehensive definition. Some define HTA by its methods, some treat it as research, and others focus on whatever it is that those who assess technologies do (AETMIS & ISTAHC, 2001). Nonetheless, what is clear is that HTA is more than simply a type of "review" and it is quickly becoming the keystone of evidence-based practice (NCCHTA, 2003).

HTA is a bridge between the world of research and the world of decision-making, particularly policy-making (Battista & Hodge, 1999). At its most effective, HTA not only connects the world of the scientific and technical with that of policy-making, but it also helps reduce obstacles to improving both decision-making and health (Battista & Hodge, 1999). HTA is related to research due to its methods, as well as to planning, administration, and management due to its focus on decision-making (DIHTA, 2001). HTA involves the systematic evaluation of scientific evidence about the properties and impacts of health care technologies, in order to provide information on the safety, effectiveness, economic, and social implications of these technologies. HTA encompasses treatments, operations, health promotion, disease prevention, rehabilitation, and long-term care (Eldar, 2002; NCCHTA, 2003). Moreover, HTA addresses the performance of providers as they care for individuals

and communities; and does not only focus on the technical component of care, but also on its interpersonal aspect (Eldar, 2002).

It is important to recognize that HTA is not simply more research. While HTA links the realm of research and policy- and decision-making, HTA also highlights the crucial importance of maintaining a certain distance between them – policy- and decision-making must be informed but not limited by the scientific tendency to reductionism, and scientific inquiry and synthesis of its results must proceed without interference from but informed by the needs of the policy-making process. Effective health technology assessment requires some form of mutual agreement about the role of technical information and that of research evidence (Battista & Hodge, 1999).

Unlike health-related research, HTA seeks to produce and communicate the contribution of scientific inquiry to policy and clinical decision-making, rather than the interests of an individual scientist (Battista & Hodge, 1999). Another difference between HTA and research is that HTA incorporates the medical, social, ethical, and economic implications of the diffusion and use of health technology (Ritchie, 2004). It is this integration of the efforts of multiple disciplines that defines the strength and character of HTA (Battista & Hodge, 1999). Distinct from research, the methods employed to conduct a HTA are more varied and are driven by the relevance of the results to improve decision-making. HTA can involve the synthesis of information, examination of databases, and/or the generation of primary data (Battista & Hodge, 1999). HTA methodology draws upon a variety of analytical, evaluative and planning techniques. Among these are systems analysis, cost-benefit analysis, consensus methods (e.g., Delphi method), engineering feasibility studies, clinical trials, market research, technological forecasting, systematic reviews, and others (Goodman, 1998). Finally, while research findings are often reported in publications of like-minded readers, HTA results are actively disseminated to different target audiences with the goal of impacting the decision-making process (Battista & Hodge, 1999). It is important to mention that HTA reports are not yet available on pub-med and must be searched within specific HTA agency databases.

The tendency has been to define HTA too broadly or in ways that make it seem the same as research. Defining HTA as research in general misses the importance of HTA's linkage to decision-making. A more operational definition of HTA is the following: "Health technology assessment is policy-relevant research focused on both the short- and long-term effects of using health technologies. This involves examining not only the health effects, technical performance, and financial costs of a particular technology or group of interventions, but also other factors – organizational, social, cultural, legal and ethical that affect the use of a technology or may be affected by technology use" (AETMIS & ISTAHC, 2001).

4.0 SOURCES OF RESEARCH EVIDENCE AND HTA

As already stated, the volume of literature is now too large for any professional to stay continually updated. However, the need for evidence to support clinical practice has never been greater (JBIEBNM, 2001). Information needed to undertake any form of HTA is found in a multitude of databases ranging from those primarily focused on primary research data like (e.g., Medline, EMBASE, CINHAL…), to those specializing in secondary research data to formulate systematic reviews and meta-analysis (e.g., the Cochrane library…) and other research-based literature (e.g., Trial registries, grey literature, researcher and manufacturers…)

So where does one to begin to look for information amongst the mountainous sources of evidence? In the following sections, we will discuss where one can begin with a search for evidence-based sources. Although the following represent the main sources of research evidence, this list is by no means exhaustive.

4.1 "HTA ON THE NET: A GUIDE TO INTERNET RESOURCES"

The Health Technology Assessment unit at the Alberta Heritage Foundation for Medical Research (AHFMR) has compiled a list of frequently used, helpful, and relevant websites from affiliate organizations, government, and related research centres both locally and internationally. The AHFMR guide focuses in Internet sites, particularly those that may be useful for people involved in health care in Alberta, Canada, but health technology assessments will also incorporate data from other sources.

The URL to the publication "Health Technology Assessment on the Net: A Guide to Internet Resources: is:
http://www.ahfmr.ab.ca/download.php/5c1545296c8a70e3854f5dcf934773a6

and the accompanying bookmark file is:
http://www.ahfmr.ab.ca/download.php/2930c5fb6dc06f0ecfc0ad5389419592

Listed below, are brief summaries of some of the frequently used databases.

4.2 ELECTRONIC DATABASES

The ability to access databases by computer has revolutionized the transmission and access of information. There are numerous advantages to searching an electronic database over a print index. For instance, searching an electronic database does not limit you to searching under just one subject heading at a time, but rather enables you to search words or phrases in several different fields. Moreover, with electronic databases, one can search several years of research at once, as well as limiting or expanding a search by things like date, type of publication, and language.

Depending on which database is being used, there are different features that can vary the sensitivity and specificity of the search. They can be used alone or in combination with each

other (Jones-Harris, 2003). To facilitate your searching, it is important to be aware of how indexers classify and index systematic reviews and meta-analyses. The indexers at the National Library of Medicine recognize meta-analyses and index them using Medical Subject Heading (MeSH) and publication type (pt). However, they do not recognize systematic reviews as different from traditional review articles (Hunt & McKibbon, 1997).

In an attempt to classify various sources of information, in the following sections we discuss two types of electronic database resources. The first includes general and specific health and medical databases, while the second is organized within the Cochrane Library.

PRIMARY RESEARCH DATABASES

4.2.1 GENERAL AND SPECIFIC HEALTH AND MEDICAL DATABASES

These selected health and medical databases are searchable via OVID, Silverplatter, Knowledge Finder, and Dialog Corporation (Khan, ter Riet, Glanville, Sowden, & Kleijnen, 2001).

MEDLINE

Medical Literature Analysis and Retrieval System Online. Compiled by the National Center for Biotechnology Information (NCBI) of the American National Library of Medicine (NLM), MEDLINE is a comprehensive literature database of life sciences and biomedical information. It covers the fields of medicine, nursing, dentistry, veterinary medicine, and the health care system. In addition, MEDLINE covers nearly all of the literature in biology and biochemistry, and fields with no direct medical connection (e.g., molecular evolution). MEDLINE is available on the internet and searchable via PubMed and NLM's Entrez. The database contains more than 16 million records from nearly 5,000 publications from the late 1940s to present, and new citations are added daily. Most records are from English-language sources (Khan, ter Riet, Glanville, Sowden, & Kleijnen, 2001; http://en.wikipedia.org/wiki/Medline).

To most effectively utilize MEDLINE, it is recommended that users obtain some training. There are tutorials on using the PubMed interface which explain the ways to get the best out of the site. MEDLINE uses Medical Subject Headings (MeSH) for information retrieval. The key skill lies in framing the correct search string. Because of the size and complexity of MEDLINE, searching this database for systematic reviews requires careful planning and an understanding of the terms and phrases used to describe systematic reviews (which form the basis of your search strategy). They include the adjectives "quantitative", "methodological", and "systematic" to describe either "reviews" or "overviews". Another phrase, less commonly used is "review articles with a methods section." (Hunt & McKibbon, 1997).

EMBASE

EMBASE is the electronic version of Excerpta Medica and is also known as the European MEDLINE. It is a comprehensive bibliographic database that covers the worldwide literature on biomedical and pharmaceutical fields

(http://info.cas.org/ONLINE/DBSS/embasess.html; Khan, ter Riet, Glanville, Sowden, & Kleijnen, 2001). This database has a strong European content and little overlap with MEDLINE in terms of the journals covered. New publications are included more quickly in EMBASE than in MEDLINE. The EMBASE database places special emphasis on physical and occupational therapy, biology, drug research, psychiatry, health policy, and alternative medicine. The database is produced in the Netherlands by Elsevier B.V., the world's largest publisher of scientific information. Although librarians can often provide EMBASE searches, user costs are higher than those for MEDLINE, and few clinicians outside Europe have ready access to it (Hunt & McKibbon, 1997). The EMBASE database is fully accessible from the University Medical Library.

CINAHL

Cumulative Index to Nursing and Allied Health Literature database. Records of literature on all aspects of nursing and allied health disciplines (Khan, ter Riet, Glanville, Sowden, & Kleijnen, 2001). It covers research from 1982 to present, and articles from about 1200 journals, dissertations, standards of professional practice, book chapters, research instruments, and AV materials are indexed (http://www.uic.edu/depts/lib/lhsu/resources/cinahl_tutorial.shtml).

CINAHL purportedly covers some physical therapy journals that are not indexed in other databases such as MEDLINE. New citations are usually added to CINAHL 4 to 10 weeks after publication (http://www.ptjournal.org/PTJournal/March2002/Mar02_EiP.cfm). In addition to providing abstracts for most articles, CINAHL also provides access to the full-text version of some articles. Access to these full-text articles is helpful because certain journals may not be directly available in institution's medical library. Access to CINAHL, however, is not free to the public. For a fee, CINAHL can be accessed through the publisher's Web site (www.cinahl.com). Also, many college or health professional libraries provide access directly to CINAHL or enable the user to access CINAHL through another vendor (http://www.ptjournal.org/PTJournal/March2002/Mar02_EiP.cfm).

PsycLIT

Published by the American Psychological Association (APA), this international database contains records of research in psychology and related behavioral and social sciences (Khan, ter Riet, Glanville, Sowden, & Kleijnen, 2001). PsycLIT contains over 730,000 psychology records from nearly 50 countries dating from 1887 to the present. Over 12,000 entries are added quarterly from journal articles, books, and book chapters (http://www.rose-net.co.ir/products/PRODUCTS1/EBSCO/PsycLIT.htm).

SYSTEMATIC REVIEWS DATABASES

While most major medical journals publish systematic reviews, this can help keep clinicians up-to-date. However, few systematic reviews are published in each issue. As a result,

reading journals is not necessarily a high-yield source of systematic reviews for clinical problem solving (Hunt & McKibbon, 1997). A better source of systematic reviews are the following databases.

4.2.2 THE COCHRANE LIBRARY

The Cochrane Library is a collection of databases in medicine and other healthcare specialties that has evolved to help prepare, maintain, and disseminate the results of systematic reviews of health care interventions. It is the first large-scale, multidisciplinary product of this collaboration (Cook, Mulrow, & Haynes, 1997).

At its core is a database of systematic reviews and meta-analyses which summarise and interpret the results of high-quality medical research. The Cochrane Library aims to make the results of well-conducted controlled trials readily available. It is a key resource in evidence-based medicine. Most of the material in the Cochrane Library takes one of three formats: systematic review, randomised controlled trial, or economic evaluation.

The Cochrane library is made up of eight databases, all of which can be accessed in one interface (Hunt & McKibbon, 1997; http://www.ion.ucl.ac.uk/library/cochrane_guide.html). The databases are:

(1) Cochrane Database of Systematic Reviews (CDSR),
(2) Database of Abstracts of Reviews of Effects (DARE),
(3) Cochrane Central Register of Controlled Trials (CENTRAL),
(4) Cochrane Database of Methodology Reviews (CDMR),
(5) Cochrane Methodology Register (CMR),
(6) Health Technology Assessment Database (HTA),
(7) NHS Economic Evaluation Database (NHS EED), and
(8) About the Cochrane Collaboration.

When you search, you search all of them at the same time so you do not have to decide which to search. However, your results are presented database by database, enabling you to know what is in each database so that you can go directly to the one that is most likely to have the information you need.

(1) CDSR. The systematic reviews cover many areas of health care (including consumer concerns) and are often more thorough reports of systematic reviews that have been published elsewhere in limited form. The Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE) are the sections of the Library that are most useful to clinicians interested in identifying systematic reviews (Hunt & McKibbon, 1997). Specifically, the CDSR database gives details about systematic reviews and offers the chance to access full-text reviews. When looking at the results, there is the option to limit one's search to reviews or protocols. Reviews are full-text systematic reviews and protocols are reviews that are currently being written. These are indicated by a 'p' or an 'r' next to the record.

(2) DARE. Another database that gives you information about systematic reviews is the Database of Abstracts of Reviews of Effects (DARE). This database not only informs about systematic reviews that are featured in other places (e.g., journals), assessments analyse the quality of the review methodology employed as well. Therefore, results in this database take the form of summaries of systematic reviews and the material contained within DARE is critically appraised. The critical appraisal comes in the form of a CRD commentary (Centre for Reviews and Dissemination), so when you're browsing the record, you can go directly to the CRD commentary to get the appraisal of the review.

(3) CENTRAL. If a systematic review has not been written that answers your query, you may wish to use primary research material. The Cochrane Central Register of Controlled Trials (CENTRAL) electronic database contains bibliographic references to randomised controlled trials, the Medical Editors Trials Amnesty and notification of unpublished trials with contact details. A randomised controlled trial (RCT) is considered to be the gold standard of primary research. One thing to keep in mind with CENTRAL is that the material it contains has not been critically appraised, thereby leaving the job of critical appraisal of the information to the reader.

(4) CDMR. The Cochrane Database of Methodology Reviews consists of ongoing and completed methodology reviews published by the Cochrane Collaboration.

(5) CMR. The Cochrane Methodology Register houses information about the process of conducting reviews and trials.

(6) HTA. The Health Technology Assessment Database presents health technology assessments and ongoing projects, including systematic reviews and primary research.

(7) NHS EED. The NHS Economic Evaluation Database (NHS EED) is a database that looks at how much interventions cost. Therefore, it reports economic evaluations of healthcare interventions with critical abstracts (Khan, ter Riet, Glanville, Sowden, & Kleijnen, 2001). An economic evaluation looks not just at how effective an intervention is, but how cost-effective it is. The material in this database is critically appraised.

(8) Cochrane Collaboration. Finally, the database About the Cochrane Collaboration, simply contains contact details for the various Cochrane entitites (http://www.ion.ucl.ac.uk/library/cochrane_guide.html).

The Cochrane Library is a quick and valuable resource for locating systematic reviews, but it has some limitations. Although the number of reviews is increasing as more systematic reviews are published, it still is rather modest in size. Moreover, since Cochrane is an international organization, care must be taken when applying the results of reviews done outside the UK. Finally, like some of the other databases, even

though attempts have been made to improve this, searching the Cochrane Library can be difficult, especially when complex search strategies are used.

4.2.3 THE CENTRE FOR REVIEWS AND DISSEMINATION

The Centre for Reviews and Dissemination (CRD) was established in January 1994 to provide the NHS with important information on the effectiveness of treatments and the delivery and organization of health care. The CRD undertakes reviews of research about the effects of interventions used in health and social care, as well as maintains various databases, provides an enquiry service, and disseminates results of research to NHS decision makers (http://www.york.ac.uk/inst/crd/).

CRD helps to promote the use of research-based knowledge by offering:

- Rigorous and systematic reviews of research on selected topics
- Reviews which map the research literature
- Three databases (DARE, NHS EED, and the HTA Database)
- "Hitting Headlines"
- Publications like CRD Reports, *Effective Health Care*, and *Effectiveness Matters*
- Dissemination service
- Information and enquiry service

As indicated on its website, CRD works closely with a number of other health, social research and information organizations, as well as with international networks such as the Cochrane and Campbell Collaborations. It is a member of the International Network of Agencies for Health Technology Assessment (INAHTA) and the Guidelines International Network (G-I-N). Moreover, CRD has undertaken work for a number of different agencies including the National Institute for Clinical Excellence (NICE), the Home Office, the Social Care Institute for Excellence (SCIE), the Economic and Social Research Council (ESRC), the Health Technology Assessment Programme (HTA) and the Service Delivery & Organisation Programme (SDO).

4.3 BEST EVIDENCE

A resource called Best Evidence, produced by the American College of Physicians, can be used to efficiently identify systematic reviews on clinical topics of interest to internists. Best Evidence is the electronic version of both *ACP Journal Club* and *Evidence-Based Medicine* (Hunt & McKibbon, 1997). These publications contain structured abstracts of and expert commentary on high-quality, clinically important studies from more than 75 medical journals. Since each article must meet certain minimum methodologic quality standards, articles abstracted in Best Evidence are likely to be valid and relevant to patient care.

To be included in Best Evidence, review articles must address a specific clinical question and describe how potentially relevant primary studies were identified and either included or excluded. All review articles in Best Evidence are systematic reviews rather than narrative reviews, with most of them containing the terms "meta-analysis" or "review" in their short title (Hunt & McKibbon, 1997).

4.4 RESEARCH REGISTERS

Research registers record ongoing research, some of which may never be formally published. Unbiased study retrieval can only be guaranteed in those few areas where prospective comprehensive research registers are maintained. There are many national (e.g., National Research Register), local, and specialist registers which record research. Research funders also record the research that they fund. A selected list of some key indexes and registers is available from the CRD website. In addition, research registers can be identified from Internet searching (e.g., metaRegister of Controlled Trials provided by Current Controlled Trials), contacting specialists in the field of interest and contacting funders and specialist information services (Khan, ter Riet, Glanville, Sowden, & Kleijnen, 2001).

4.4.1 THE NATIONAL ELECTRONIC LIBRARY FOR HEALTH (NELH)

http://www.le.ac.uk/li/lgh/library/training/nelh.htm

The National Electronic Library for Health is a project initiated by NHS Information Authority with the aim of providing users with easy access to best current knowledge and improving health and healthcare, clinical practice and patient choice. It is a web based information resource for NHS staff, patients, and the public. The role of NeLH is to provide health care professionals with the knowledge to support health care related decisions. The NeLH policy is to complement and supplement NHS libraries that provide books, journals, and access to databases such as MEDLINE or CINAHL. The three types of information found on NeLH with some examples of the available database resources within each are:

(2) Knowledge

- CLIP Database
- Commission for Health Improvement (CHI)
- Health Care Needs Assessment
- Maternity (MIDIRS)
- National Patient Safety Agency
- National Service Frameworks Zones
- NeLH Guidelines Finder
- NHS Modernisation Agency
- NICE Guidance
- NICE Guidelines
- NICE Audit Principles
- NeLH Care Pathways Database
- Care Pathways Know-How Zone
- Patient Group Directions (Approved Group Protocols) Library

(3) Know-how

- Anatomy
- Bandolier
- OMNI Reviewed Internet Resources
- The British National Formulary
- Clinical Evidence
- The Cochrane Library
- DIPEx
- Evidence Based on Call
- HTA Publications
- Medline/Pubmed
- NHS Economic Evaluation Database
- DARE
- Effectiveness Health Care Bulletins
- Research Findings Register
- ZETOC

(4) Resources

- Virtual Branch Libraries (specialized information in cancer, child health, communicable diseases, etc.)
- Professional Portals (information on frameworks and guidelines, evidence based materials, reviewed internet resources, etc.)
- Reference Section (information on anatomy, coronary heart disease zone, etc.)

4.4.2 NATIONAL RESEARCH REGISTER (NRR)

(http://www.nrr.nhs.uk/; *http://www.update-software.com/national/nrrframe.html*)

The National Research Register is a register of ongoing and recently completed research projects funded by, or of interest to, the United Kingdom's National Health Service. Approximately 350 research organizations in England, Scotland and Wales contribute to the NRR. The Register evolved out of a pilot project in 1998. The current Register includes some of the projects from the early 1990s as well as projects that were ongoing from early 2000 onwards. New records are added and existing records are updated every three months to a growing list of records. Projects are automatically classified as "ongoing" or "complete" based on whether their end dates fall after a cut-off date or not.

4.5 HAND SEARCHING, GREY LITERATURE AND CONFERENCE PROCEEDINGS

Hand Searching: There is always a risk that relevant publications may be overlooked in electronic searching due to inaccurate or incomplete indexing in the databases, and weaknesses in the search strategy. Consequently, it is good practice to hand-search journals to identify articles that may have been missed in the first "sweep" of one's search of databases and reference lists. Important results may have been published in reports, technical reports, discussion papers or other formats that are not indexed in the major databases. Scanning the reference lists of publications (primary studies and reviews) found through the database searches may identify further studies for consideration. Hand-searching can also assist researchers in identifying very recent publications which may not yet be cited in other publications or included on the electronic databases (Khan, ter Riet, Glanville, Sowden, & Kleijnen, 2001).

Grey Literature: In our world of instantaneous communication where, many of the barriers to information flow have been eliminated, a form of information called "grey literature" is gaining greater importance. According to Weintraub (2000), "grey literature refers to publications issued by government, academia, business, and industry, in both print and electronic formats, but not controlled by commercial publishing interests, and where publishing is not the primary business activity of the organization. Scientific grey literature comprises newsletters, reports, working papers, theses, government documents, bulletins, fact sheets, conference proceedings and other publications distributed free, available by subscription, or for sale" (http://library.brooklyn.cuny.edu/access/greyliter.htm). Grey literature is available in print format, but is also available in electronic format via the world wide web, CD-ROM, or other electronic gateways.

A website called Grey Net: Grey Literature Network Service assists students, librarians, publishers, and researchers in the study, use, and production of grey literature. A peer-reviewed journal entitled the *International Journal on Grey Literature* was launched to serve as a forum for discussions of all aspects of grey literature and its applications for academics and practitioners. Unfortunately, after four issues, it ceased publication (http://library.brooklyn.cuny.edu/access/greyliter.htm). Comprehensive identification of grey literature is hard to achieve, but some of it is indexed on databases such as:

- System for Information on Grey Literature (SIGLE),
- National Technical Information Service (NTIS),
- The Health Management Information Consortium CD-ROM, and
- British National Bibliography for Report Literature.

The libraries of specialist research centers, research organizations, and professional societies may provide additionally useful sources of grey literature. Dissertations and theses can also be routes into obtaining otherwise unpublished research and are recorded in databases such as CINAHL and Dissertation Abstracts (Khan, ter Riet, Glanville, Sowden, & Kleijnen, 2001).

Conference Proceedings: Finally, conference proceedings can also provide information on research in progress, as well as completed research. These are recorded in several databases including:

- The Index to Scientific and Technical Proceedings (available to the UK academic community via ISI Web of Science),
- The Conference Papers Index, and
- In Library Catalogues.

Conference Papers (Index)
Conference Papers Index is the print equivalent to Conference Papers, which provides citations to papers and poster sessions presented at major scientific meetings around the world. Subject emphasis since 1995 has been in the life sciences, environmental sciences and the aquatic sciences, while older material also covers physics, engineering and materials science (http://www.csa.com/factsheets/cpi-set-c.php; Khan, ter Riet, Glanville, Sowden, & Kleijnen, 2001). Information is derived from final programs, abstracts booklets and published proceedings, as well as from questionnaire responses. Records include complete ordering information to obtain preprints, abstracts, proceedings and other publications derived from the conference, together with title and author information needed to track the specific papers (http://www.csa.com/factsheets/cpi-set-c.php).

The abstracts in conference proceedings may present limited information and there may be differences between data presented in abstracts and final reports. Thus, Khan et al. (2001) recommend acquiring reports of the studies presented at conferences from the authors, before any of the data are included in a systematic review.

4.6 RESEARCHERS AND MANUFACTURERS

Until now, we have presented information that can be accessed either electronically or in paper print form. However, another valuable source of evidence can come from one's personal contact with experts in the field. These experts may be other investigators who have worked in the particular area of interest or they may be manufacturers of the health technology you are interested in. In either case, conducting information interviews with these professionals may provide you with leads, new directions, and even simply corroboration of what you have already uncovered or know to be true.

After a thorough and systematic search has been conducted, a list of studies that meet the inclusion criteria should be sent to the subject experts. It is a useful practice to ensure reference lists are scrutinized for completeness, and that information be provided on any ongoing research that could be considered for inclusion in the review. The success of these contacts relies on the goodwill of the researchers and subject experts contacted and the time available to them (Khan, ter Riet, Glanville, Sowden, & Kleijnen, 2001). However, the resulting benefits from networking in this manner may be immeasurable.

It is also important to contact relevant companies and manufacturers who may be willing to release results that have not already been published. For instance, many trials of pharmaceutical products are conducted or supported by companies who have details "on file" in a private database. Access to this information may be of great benefit to many stakeholders. In fact, there has been a movement urging companies to make these data more readily accessible and some pharmaceutical companies are including records of their ongoing and completed trials on the CCTR, the metaRegister of Controlled Trials, and on their own web pages (Khan, ter Riet, Glanville, Sowden, & Kleijnen, 2001).

4.7 THE INTERNET

The Internet may be a useful source of information about completed and ongoing research particularly that which has not been formally published. However, searching the Internet can be a major undertaking. Many of the general search engines do not allow sophisticated multi-line searching and as a result, searches may produce thousands of web sites to assess (Khan, ter Riet, Glanville, Sowden, & Kleijnen, 2001). In addition to the list below, refer to "Module 1: What is HTA?" for a comprehensive list of the international, national and provincial websites for a variety of HTA publications.

However, it is possible to search the internet in a systematic way using meta-search engines. For instance one could employ:

- Meta-search engines such as Copernic and Dogpile
- Gateways to sites with search engines such as NSABP Medical Search Engines or MedNets
- General purpose search engines which have a medical focus such as Northern Light
- Gateway services to evaluated sites such as OMNI

4.7.1 EVIDENCE BASED MEDICINE WEBSITES

In addition to the resources already presented, one could also explore evidence based medicine websites on the internet, such as:

- **Centre for Evidence-Based Medicine**
  - http://www.cebm.utoronto.ca/
  - The goal of this website is to help develop, disseminate, and evaluate resources that can be used to practice and teach EBM for undergraduate, postgraduate and continuing education for health care professionals from a variety of clinical disciplines.This site also serves as a support for the book entitled, Evidence-based Medicine: How to practice and teach EBM by David

L. Sackett, Sharon E. Straus, W. Scott Richardson, William Rosenberg, and R. Brian Haynes.

- **Centre for Evidence Based Mental Health**
  - http://www.cebmh.com/
  - Focused on advances in treatment, diagnosis, aetiology, prognosis, continuing education, economic evaluation and qualitative research in mental health.

- **British Association of Plastic Surgeons (BAPS) Evidence Based Plastic Surgery**
  - http://www.baps.co.uk/about_cat/Home/1/about_cat.htm
  - The Association was founded in 1946 with the objects of relieving sickness and protecting and preserving Public Health by the promotion and development of Plastic Surgery. The aim of the Association is to advance education in the field of Plastic Surgery.

- **TRIP Database**
  - http://www.update-software.com/trip/
  - ***TRIP database*** has been seen as the premier information server for health care information since it started in 1997 providing access to all the top health care publications relevant to clinical practice in one place. All the best evidence-based publications are searched monthly by experts and indexed fully before being presented in an easy-to-use format with access to full-text articles, medical images, patient leaflets and more.

- **Effective Health Care**
  - http://effectivehealthcare.ahrq.gov/
  - The AHRQ Effective Health Care Program has three approaches to research on the comparative effectiveness of different treatments and clinical practices: (1) Review and **synthesize knowledge**. The Evidence-based Practice Centers systematically review published and unpublished scientific evidence; (2) Promote and **generate knowledge**. The DEcIDE Research Network studies new scientific evidence and analytic tools in an accelerated and practical format; and (3) Compile the findings and **translate knowledge**. The Clinical Decisions and Communications Science Center compiles the research results into a variety of useful formats for stakeholders.

- **BMJ – Topic Collections**
  - http://bmj.bmjjournals.com/collections/
  - UK site which contains all articles published in the British Medical Journal since January 1998 listed in contents categories. Contains many original papers, research findings, reviews and debate on a wide variety of medical conditions.

- **NHS Centre for Reviews and Dissemination**
  - http://www.york.ac.uk/inst/crd/
  - UK site that provides details of various reviews of areas of clinical practice and their effectiveness. The majority of the CRD's dissemination activity involves raising awareness of messages from research and aims to provide important information in an easily accessible form.

5.0 CRITICAL APPRAISAL SKILLS

As we have seen, to gather information for Health Technology Assessment reports often requires critical appraisal skills used in developing systematic reviews, in particular quantitative systematic reviews (i.e., meta-analysis) which are a powerful and useful way to assemble evidence. However, the amount of information available to sort through is vast and ongoing. As researchers and clinicians, we must decide how to make sense of the evidence that has been greatly accumulated over time. With this responsibility in hand, we must not be blinded by the illusions we may possess of science. For instance, it is important to recognize that just because a review has been conducted employing systematic review methods does not guarantee that its results are credible. Regardless of the source, all systematic reviews (like all types of research evidence) require critical appraisal to determine their validity and to establish whether and how they will be useful in practice (Hunt & McKibbon, 1997). The strength of inference we can draw from a review depends on the review methods employed. Assessment of the validity of a review article requires evaluation of each step in the review process before consideration of the results and how they might apply to the specific situation of interest (Hunt & McKibbon, 1997).

For instance, we may come across sources of information that have already undergone some form of appraisal. Critically Appraised Topics (CATs) and Best Evidence Topics (BETs) are considered preappraised. CATs are a standardized, one-page summary of the critically appraised evidence from an article related to a given clinical topic. BETs are a modification of CATs and were developed to allow emergency physicians rapid access to best current evidence on a wide range of clinical topics. According to Jones-Harris (2003), studies are retrieved through an explicit search, and those that provide the highest available levels of evidence are critically appraised in order to determine a clinical bottom line. Before determining these sources as definitive, we need to explore the procedures used to synthesize the information. Thus, since CATs are often based on single investigations rather than systematic reviews, they may not be representative of the entire body of evidence and they may become obsolete as soon as newer, better evidence becomes available. Furthermore, individual CATs can be inaccurate if they were produced without undergoing the peer-review process first.

The main point here is that not all systematic reviews are rigorous and unbiased. As with any type of research, caution must be exercised before accepting the veracity of any systematic review (Davies & Crombie, 2003). Therefore, it is critical to evaluate any review or primary form of research. In order to do this, consumers of research need to learn the skills for assessing the quality and credibility of the information they access (whether it is found in a scientific journal or on an internet website).

In the following sections we will discuss some important questions that can be used to guide a critical appraisal of research information. This is further demonstrated by the material in

Appendices 11.1, 11.2, and 11.3, respectively, where we present a checklist useful for engaging in a critical appraisal of a primary study, components of a critical appraisal tool, and a model for the critical appraisal of a systematic review.

5.1 STEPS IN CONDUCTING A CRITICAL APPRAISAL OF THE RESEARCH

5.1.1 WHAT IS THE REVIEW'S OBJECTIVE?

Regardless of whether it is a primary research study or a systematic type review, a clearly defined research question (or HTA question) should be indicated. A focused question provides the study or review with direction and it defines the area of interest. Typically the question should address the population of interest and condition, the intervention, a comparison or control, and the outcome measure that is to be used to determine effectiveness (JBIEBNM, 2000). Having a focus clearly stated, permits the investigator and the reader to seek an answer from the available research.

5.1.2 WHAT SOURCES WERE SEARCHED TO IDENTIFY PRIMARY STUDIES?

As we have already seen, given the vast amount of information available, it is not difficult to possibly overlook important or relevant studies in a literature search. Confidence in the results of a review is greater when we are certain that no relevant and high-quality studies, either published or unpublished, have been missed. According to Hunt and McKibbon (1997), a comprehensive search for unpublished work may be important in some situations (for example, evaluation of new technologies, an area in which much of the data may not be published) if the data are amenable to the same careful assessment of quality as the published work.

While resource constraints may limit an investigator or reviewer's search strategies, it is possible that researcher error is responsible for producing biased results. Assessing the comprehensiveness of the search obviously requires that the authors of reviews explicitly report their methods. Unfortunately, some authors fail to completely describe the databases they use to gather relevant information. Others rely on a single database for the synthesis of current knowledge or inadequately describe the search semantics (Rupert & Colonvega, 2002). In the absence of detailed descriptions of the methods employed by researchers, the fundamental principles of replicability and verifiability that serve to distinguish science from other disciplines are substantially undermined.

5.1.3 WHAT WERE THE INCLUSION CRITERIA AND HOW WERE THEY APPLIED?

The inclusion criteria operationalises the review question, putting it into a practical format. It is used to help the researcher decide which studies should be included in the review and which ones should not. As it is developed and documented prior to the commencement of the review, it helps reduce the risk bias introduced by the investigator during the selection process (JBIEBNM, 2000). The inclusion criteria explicitly limit and document the focus and nature of the review. Therefore, the main

question to ask when appraising the inclusion criteria of a systematic review is: were the inclusion criteria used to select articles appropriate?

5.1.4 WHAT CRITERIA WERE USED TO ASSESS THE QUALITY OF PRIMARY STUDIES AND HOW WERE THEY APPLIED?

Was the validity of the included studies assessed? Although the conclusions we derive from a systematic review depend in large part on the rigor of the review methods, they obviously also depend on the quality of the included studies. The appropriate criteria for this assessment of quality depend on the type of studies included in the review.

According to Hunt and McKibbon (1997), if the systematic review deals with treatment, it is important to ascertain whether the trials were randomized; whether the randomization process was concealed from patients or investigators; whether patients, caregivers, or persons assessing outcome were blinded to the treatment allocation; and the extent to which follow-up was complete. For systematic reviews that address questions of harm, the most important considerations include documentation of the similarity of the comparison groups and the methods used to establish that patients had the exposure and outcome of interest. Duration of follow-up is also important if a cohort design was used (Hunt & McKibbon, 1997).

Assessing the validity of research means determining whether the methods used during the study can be trusted to provide a genuine, accurate account of the technology being evaluated (JBIEBNM, 2000). By excluding lesser quality studies from a systematic quantitative review, it is presumed that the risk of error and bias in the findings of the review will be lessened.

5.1.5 HOW WERE THE DATA EXTRACTED FROM THE PRIMARY STUDIES?

Were the assessments of studies reproducible? Even when explicit criteria are used to include studies in a review and evaluate their methodologic quality, the judgment of the reviewers' is still required (Hunt & McKibbon, 1997). If the authors did each of the review steps independently and in duplicate and then reported their level of agreement, we can assess how open to judgment each of these steps was.

5.1.6 HOW WERE THE DATA SYNTHESIZED?

As we have seen, the objective of a systematic review is to summarize the results from different studies to obtain an overall evaluation of the effectiveness of an intervention or treatment (JBIEBNM, 2000). Synthesizing the results of studies (whether qualitative or quantitative) requires assessing the similarity of the studies to each other. This means that the patients, exposures or interventions, outcomes, and other features of study design must be considered. Pooling the results of several studies is not appropriate if the studies differ in a clinically important fashion with regard to any of these design elements. This is because combining widely differing results to produce an average effect would fail to represent the great variation in the outcomes.

If after an initial assessment, it appears that all the studies are similar, then it is important to evaluate whether the results of the studies are in fact similar. If studies have different findings, pooling results often suggests that the trials may have differed in some important way, more than initially seemed to be the case (Hunt & McKibbon, 1997). Then the sources of the differences become the appropriate focus of interest.

So important questions at this stage are: how were the studies combined and were the findings combined appropriately? In a meta-analysis, one of the ways we can determine whether the included results of trials are similar is by graphing the size of the treatment effect and its confidence interval from each trial (Hunt & McKibbon, 1997). If the magnitude or direction of the effect sizes differs greatly among studies, and the confidence intervals do not substantially overlap, one could call into question the appropriateness of pooling the results.

An alternative approach is to use a statistical test to ascertain whether the study results differ more than would be expected by chance alone. If the studies combined measure approximately the same effect and any differences that occur do so because of chance, then one concludes statistically nonsignificant results (usually reported as $P > 0.05$). A significant test result means that the difference in results among the individual studies is not likely to have been caused by chance. This calls into question whether it is appropriate to pool the results; it may also suggest that a priori subgroup analyses may be appropriate (Hunt & McKibbon, 1997). However, when the results of large trials are pooled, the test for homogeneity may indicate that statistically significant (but perhaps clinically unimportant) differences exist in the results). In this situation, it may still be reasonable to pool the results statistically.

5.1.7 WHAT ARE THE OVERALL RESULTS AND HOW PRECISE ARE THEY?

We can further ask "will the results help in caring for patients?" Determining this involves asking several questions: Can I apply the results to my patients? Did the results consider all the clinically important outcomes? Are the benefits worth any associated risks or costs? It is important to consider the patients in the individual studies and to ascertain whether your patient is similar with regard to age, comorbid conditions, or other risk factors (such as smoking and family history). Does he or she have a comparable baseline risk for the outcome of interest, or is the risk higher or lower in a meaningful way? A systematic review that finds that a new treatment delays death but that does not address any of the potential adverse events associated with use of the treatment may prompt us to seek additional information from other sources or to refer back to some of the more detailed original articles. We would want to discuss these issues with our patient (or we may choose not to offer the intervention in the first place) (Hunt & McKibbon, 1997).

6.0 TYPES OF BIAS

Although investigators and reviewers alike should employ methods that try to avoid bias altogether, the reality is that all studies likely possess bias, and a post-hoc evaluation of it is difficult and often impossible (Khan, ter Riet, Glanville, Sowden, & Kleijnen, 2001). Still, we know that it is not the mere presence of flaws that vitiates the findings. Even flawed studies may carry important information. The reader must exercise judgment in assessing whether individual flaws undermine the findings to such an extent that the conclusions are no longer adequately supported (Davies & Crombie, 2003).

Bias can be introduced at numerous points throughout the research or review process. In the proceeding sections we report four main types of bias that may threaten the internal and external validity of research evidence.

6.1 SELECTION BIAS

In general, selection bias refers to the error of distorting a statistical analysis due to the methodology of how the samples are collected. For instance, the sample selection may involve pre- or post-selecting samples in such a way that may preferentially include or exclude certain kinds of results. Selection bias is closely related to sample bias (i.e., a deliberate or unconscious manipulation bias is introduced in the sampling technique), publication or reporting bias (i.e., distortion produced by not publishing uninteresting, usually negative results, or results that go against the experimenter's prejudices or expectations), and confirmation bias (i.e., distortion produced by experiments that are designed to seek confirmatory evidence instead of trying to disprove the hypothesis).

At the primary study level, selection bias can be avoided through the use of experimental techniques. For example, both subjects and investigators may be made unaware of which group (i.e., treatment or control group), subjects are being randomly assigned to. The use of randomization and blinding means this part of the study is free from any influence of people or bias that may be injected into the research process (JBIEBNM, 2000; Khan, ter Riet, Glanville, Sowden, & Kleijnen, 2001).

In a systematic review, selection bias refers to what types of studies have been included in the analysis (or the ones that have been unknowingly excluded). Researchers introduce bias into the process of information synthesis by exclusion of references for various reasons. One way bias is introduced is through language. There is a tendency to restrict the literature search to a single database like MEDLINE, which already has a documented language bias, and then further restrict the MEDLINE articles to only those written in English. Hence, a large pool of possible pertinent information from other countries may be ignored (Rupert & Colonvega, 2002).

Another way bias is introduced in a systematic review is through the search and documentation procedures of the reviewer. Researchers may inadequately describe the

literature search semantics they employed; omit a description of the medical subject heading terms, subheadings, check tags, and keywords employed in the search; not include a description of the semantic logic utilized or the Boolean expression. Consequently, the semantic relationships used with the search terms can profoundly affect the types of medical research sources retrieved.

To improve quality information, some strategies of searching have been designed to eliminate or minimize the possible database bias. Furthermore, it can be very helpful to avoid these forms of selection bias by setting very clear inclusion criteria, apriori, as well as creating a team of expert consultants to appraise the strategies used in the systematic review or primary research.

6.2 PERFORMANCE BIAS

In a primary research investigation, performance bias refers to the systematic differences that may arise in the care provided to the participants in the comparison group versus those in the intervention group. For instance, if patients know they are in the control group, they may be more likely to use other forms of care, while patients who know they are in the intervention group may experience placebo effects. It is also possible that those interacting with the study participants may treat them different depending on what group they are in. Therefore, like selection bias, blinding of study participants (both the recipients and providers of care) is used to protect against performance bias (JBIEBNM, 2000; Khan, ter Riet, Glanville, Sowden, & Kleijnen, 2001).

6.3 ATTRITION BIAS (EXCLUSION BIAS)

Attrition bias refers to the systematic differences between the comparison groups in the loss of participants from the study. It is also known as exclusion bias. Because of inadequacies in reporting how losses of participants (e.g. withdrawals, dropouts, protocol deviations) are handled, authors should be cautious about implicit accounts of follow-up (http://www.cochrane.dk/cochrane/handbook/6_assessment_of_study_quality/6_5_attrition_bias.htm). The approach to handling losses has great potential for biasing the results and reporting inadequacies cloud this problem. However, generally, inclusion of such participants in the analysis (in combination with a sensitivity analysis) protects against this bias (Khan, ter Riet, Glanville, Sowden, & Kleijnen, 2001).

6.4 MEASUREMENT BIAS (DETECTION BIAS, ASCERTAINMENT BIAS)

Measurement bias exists when a researcher fails to control for the effects of data collection and measurement. Most clinical research is highly vulnerable to measurement bias because many measures used are not as valid or precise as we would like them to be. Once again, an effective way to avoid measurement bias (also known as detection or ascertainment bias) is to employ randomization and blinding techniques to study participants.

Bias due to the selective reporting of results is a different, but equally relevant form of bias in outcome assessment. This problem is frequently encountered by reviewers conducting

quantitative integrations of the research (i.e., meta-analysis). In some cases, studies are excluded from a meta-analysis simply because original researchers did not accurately report in enough detail, their statistical results. In this case, this source of bias could be taken to suggest the need for better reporting and efforts by authors to obtain missing data.

6.5 USERS' GUIDES TO EVIDENCE-BASED PRACTICE

http://www.cche.net/usersguides/main.asp

The following is the complete set of Users' Guides, originally published as a series in the *Journal of the American Medical Association* (*JAMA*). The Centre for Health Evidence (CHE) continues to maintain the full text pre-publication version of this series on behalf of the Evidence-Based Medicine Working Group. See the Disclaimer and Copyright for more information.
The individual articles are listed below and can be viewed in their entirety by clicking on their titles.
Please note that all tools formerly associated with the Guides below - including calculators, worksheets, and additional educational materials - have been removed. These features have been enhanced and re-introduced in a new interactive website, http://www.usersguides.org. Access to the site is available by subscription through JAMA.

6.5.1 BACKGROUND

- Evidence-Based Medicine: A New Approach to Teaching the Practice of Medicine [text only]
- Why Users' Guides? [text only]
- How to Get Started [text only]

6.5.2 PRIMARY STUDIES

- Therapy or Prevention [text only]
- Harm [text only]
- Diagnosis [text only]
- Prognosis [text only]

6.5.3 INTEGRATIVE STUDIES

- Overview [text only]

- Screening [text only]
- Clinical Decision Analysis [text only]
- Computer-Based Clinical Decision Support System [text only]
- Clinical Practice Guideline [text only]
- Surrogate Endpoints [text only]
- Health Care Recommendations [text only]
- Class Effect [text only]
- Variations in the Outcomes of Health Services [text only]
- Integrating Research Evidence [text only]
- Clinical Utilization Review [text only]
- Electronic Health Information Resources [text only]
- Health-Related Quality of Life Measurements [text only]
- Clinical Prediction Rules [text only]
- Economic Analysis [text only]
- Qualitative Research [text only]
- Applicability of Clinical Trials Results [text only]
- Clinical Manifestations of Disease [text only]
- Disease Probability for Differential Diagnosis [text only]
- Applying the Users' Guides [text only]
- Treatment Recommendation [text only]

6.5.4 DISCLAIMER AND COPYRIGHT

- Disclaimer & Copyright for the Users' Guides to Evidence-Based Practice

7.0 LIMITATIONS AND CHALLENGES TO FINDING INFORMATION FOR HTA

Health Technology Assessment (HTA) is a term widely understood in international academic circles to mean the secondary research activity of collecting primary research data about a given health technology and normalizing it for policy input (Health Technology Assessment Task Group, 2004). HTAs are expected to provide unbiased information to policy-makers on a technology's:

1. Clinical effectiveness,
2. Impact to providers,
3. Service improvements to patients, and
4. Economic impact.

However, many concerns related to current HTA products and services have been raised. Some of the cited limitations are:

1. HTA reports take too long to develop delaying important policy decisions impacting patient care.
2. HTA reports often report that insufficient primary research exists to cull together a complete report.
3. HTA reports use technical language that is difficult for policy-makers to understand.
4. The number of people completing HTA reports is inadequate compared to the amount of technology diffusing into the health systems.
5. HTAs do not effectively address policy issues common to all federal, provinicial, and territorial jurisdictions (Health Technology Assessment Task Group, 2004).

Traditional HTA focuses on providing evidence to support policy decisions to operationalize a technology. A wider spectrum of evidence is required commensurate with the true broad nature of policy development (Health Technology Assessment Task Group, 2004). Traditional HTA pulls together research evidence including clinical effectiveness, service improvements to patients, impact to providers, and economic impact. Unfortunately, the wide range of policy development processes means a "one size fits all" traditional HTA fails to fully meet the needs of many policy-makers. This is referred to "the gap" between policy-makers and HTA researchers, namely the inability of HTA to provide a full contextual application of research to different health systems (Health Technology Assessment Task Group, 2004). Thus, while systematic reviews and critical appraisal skills are of primary importance to HTA, they are not always needed when rapid information is needed.

8.0 SUMMARY

Timely, useful evidence from the biomedical literature needs to be an integral component of clinical decision-making. For instance, if one medical intervention has been demonstrated more effective than another, then health professionals and patients should have this information available to them. According to Cook, Mulrow, and Haynes (1997), the worldwide effort to develop new tests and treatments, and to determine their usefulness, has never been stronger, and patients and their families expect physicians to be at the forefront of the knowledge that results from this effort.

Systematic reviews represent the best chance that most practitioners will have to understand and accurately apply the key signals arising from the robust and increasingly productive search for solutions to medical problems. A properly conducted systematic review faithfully summarizes the evidence from all relevant studies on the topic of interest, and it does so concisely and transparently (Cook, Mulrow, & Haynes, 1997). However, to merely have access to the information available is no longer sufficient. Instead, the individual equipped with the knowledge of how to search and evaluate the existing knowledge, is likely the more empowered critical consumer of health technology information.

8.1 REVIEW OF MODULE OBJECTIVES

The second module presented information on how to find information for HTA. Specifically, there was a discussion of: various research review procedures, sources of research evidence, ways to access information sources, and the critical skills involved in appropriately assessing the research evidence accumulated on any particular topic of interest. The module concluded with an evaluation of the types of research bias to be on the look-out for, as well as possible limitations and challenges one may encounter when searching for information for HTA.

By the end of this module, participants should now be able to:

1. Distinguish between various types of review procedures (e.g., narrative, meta-analysis, HTA) and their accompanying strengths and limitations.
2. Identify relevant sources of information for HTA, as well as how to navigate within these databases.
3. Understand the fundamentals in conducting a critical appraisal of the empirical research.
4. Identify ways to overcome the limitations and challenges to finding information for HTA.

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10.0 APPENDICES

10.1 CRITICAL APPRAISAL CHECKLIST FOR A SYSTEMATIC REVIEW

CRITICAL APPRAISAL CHECKLIST FOR
A SYSTEMATIC REVIEW.

Study Design: Systematic Review, with or without Meta-analysis

Adapted from:

Critical Appraisal Skills Programme (CASP), Public Health Resource Unit, Institute of Health Science, Oxford.

Oxman AD, Cook DJ, Guyatt GH. Users' guides to the medical literature. VI. How to use an overview. *JAMA* 1994; 272:1367-1371.

Dept. of General Practice
University of Glasgow.

DOES THIS REVIEW ADDRESS A CLEAR QUESTION?

1. Did the review address a clearly focussed issue? Was there enough information on: • The population studied • The intervention given • The outcomes considered	**Yes**	**Can't tell**	**No**
2. Did the authors look for the appropriate sort of papers? The 'best sort of studies' would • Address the review's question • Have an appropriate study design			

ARE THE RESULTS OF THIS REVIEW VALID?

3. Do you think the important, relevant studies were included? Look for • Which bibliographic databases were used • Follow up from reference lists • Personal contact with experts • Search for unpublished as well as published studies • Search for non-English language studies	**Yes**	**Can't tell**	**No**
4. Did the review's authors do enough to assess the quality of the included studies? The authors need to consider the rigour of the studies they have identified. Lack of rigour may affect the studies results.			
5. If the results of the review have been combined, was it reasonable to do so? Consider whether • The results were similar from study to study • The results of all the included studies are clearly displayed • The results of the different studies are similar • The reasons for any variations are discussed			

WHAT ARE THE RESULTS?

6. What is the overall result of the review? Consider • If you are clear about the reviews 'bottom line' results • What these are (numerically if appropriate) • How were the results expressed (NNT, odds ratio, etc)	
7. How precise are the results? Are the results presented with confidence intervals?	

WILL THE RESULTS HELP LOCALLY?

	Yes	Can't tell	No
8. Can the results be applied to the local population? Consider whether • The patients covered by the review could be sufficiently different from your population to cause concern • Your local setting is likely to differ much from that of the review			
9. Were all important outcomes considered?			
10. Are the benefits worth the harms and costs? Even if this is not addressed by the review, what do you think?			

JARGON BUSTER.

Systematic review	A review in which evidence on a topic or research question has been systematically identified, appraised and summarised according to predetermined criteria. Systematic reviews may incorporate meta-analysis, but don't have to.
Meta-analysis	A statistical technique. Summarises the results of several studies into a single estimate, giving more weight to larger studies.
Publication bias	When only studies with positive results are published, not the neutral or negative studies. If only published studies are included in a systematic review, it may overestimate the effect of the treatment or intervention.
Number Needed to Treat (NNT)	The number of patients who needed to be treated to prevent the occurrence of one adverse event (e.g. complication, death) or promote the occurrence of one beneficial event (e.g. cessation of smoking).
Odds	A ratio. It is the odds (or chance) of an event occurring.
Odds ratio	The ratio of two odds. Used as measure of a treatment's effectiveness. If OR = 1.0, then the effect of the experimental treatment is no different from that of the control treatment. If the OR is >1.0 (or <1.0), then the experimental treatment effect is greater than (or less than) the control treatment. **N.B.** The effect being measured may be good (e.g. stopping smoking) or bad (death).

Dept. of General Practice
University of Glasgow.

Taken from: http://www.gla.ac.uk/departments/generalpractice/systematic_review.PDF

10.2 COMPONENTS OF CRITICAL APPRAISAL TOOLS

Table 1: Components of Critical Appraisal Tools

Based on published systematic review checklists, the following are the most common questions addressed during the critical appraising of a review [2-7].

Focus	Specific Questions
Question	Is the specific purpose of the review stated? Is the review question clearly and explicitly stated?
Literature Search	Were comprehensive search methods used to locate studies? Was a thorough search done of appropriate databases and were other potentially important sources explored?
Study Selection	How were studies selected? Are the inclusion criteria reported?
Critical Appraisal	Was the validity of included studies assessed? Was the validity of studies assessed appropriately? Are the validity criteria reported?
Similarity of Groups and Treatments	Are treatments similar enough to combine? Were reasons for any differences between individual studies explored?
Data Synthesis	Were findings from individual studies combined appropriately? Are the methods used to combine studies reported?
Methods Documented	Are review methods clearly reported?
Summary of Findings	Is a summary of findings provided? Are specific directives for new research proposed? Were the conclusions supported by the reported data?

supplement 1, page 2, 2000

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10.3 CRITICAL APPRAISAL OF A SYSTEMATIC REVIEW

Table 2: Critical Appraisal of a Systematic Review

Review Question	Is the review question clearly and explicitly stated?
Search Strategy	Were comprehensive search methods used to locate studies? Was a thorough search done of appropriate databases, and were other potentially important sources explored?
Inclusion Criteria	How were studies selected?
Critical Appraisal	Was the validity of studies assessed appropriately?
Data Synthesis	How were the studies combined? Were findings combined appropriately?
Similarity of Studies	Were the populations of the different studies similar? Was the same intervention evaluated by the individual studies? Were the same outcomes used to determine the effectiveness of the intervention being evaluated? Were reasons for differences between studies explored?
Reporting of Findings	Are review methods clearly documented? Is the review question clearly and explicitly stated? Was the search strategy reported? Was the inclusion criteria reported? Was the criteria for appraising studies reported? Were the methods used to combine studies reported?
Conclusions & Recommendations	Is a summary of findings provided? Are specific directives for new research proposed? Were the recommendations supported by the reported data?

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