Drug Information Resources and Literature Retrieval

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An excerpt from ACCP's Pharmacotherapy Self-Assessment Program, 7th Ed., Science and Practice of Pharmacotherapy.

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Learning Objectives

1. Analyze the most appropriate drug information (DI) resources including primary, secondary, and tertiary sources for answering questions related to clinical practice.
2. Analyze the similarities and differences of secondary and tertiary information resources for specific types of drug or medical information.
3. Develop an appropriate search strategy for a given DI question that will result in high-quality literature retrieval.
4. Analyze evidence-based medicine resources and clinical guideline/trial resources used in the literature retrieval process.
5. Evaluate Web resources related to herbal products, product identification, and poisonings.
6. Develop strategies for accessing and searching quality Web-based resources.
7. Justify the use of valid and reliable Web resources by health care professionals and the general public.
8. Develop strategies for accessing information pertaining to adverse drug reactions and pharmacovigilance.

Self-Assessment Questions

Answers and explanations to these questions can be found at the end of this chapter.

1. A colleague tells you about a poster on the advantages and disadvantages of the Baxter IV pump specifically for pediatric patients in the Intensive Care Unit (ICU). The poster was presented at an annual national pharmacy meeting. Which one of the following sources would be best to find this poster?
   A. IDIS.
   B. IPA.
   C. MEDLINE.
   D. Ovid.

2. A physician requests a brief summary of a new antidepressant, vilazodone. The pharmacist answering this question has not heard of this drug. Which one of the following resources is best to consult for this information?
   A. MEDLINE, in-process
   B. IDIS
   C. PubMed
   D. IPA

3. A MEDLINE search using the MeSH terms for stroke and aspirin is conducted to find information on whether every woman over the age of 55 years should take low-dose aspirin for stroke prevention. In addition to this approach, which search strategy would best minimize the retrieval of erroneous data?
   A. Using the keyword word search of “aspirin AND stroke”.
   B. Using the subheading “therapeutic use”.
   C. Limiting the sex to “female”.
   D. Restricting the publication type to “review”.

4. Which mobile application for a personal digital assistant (PDA) or smart phone would most efficiently and effectively identity if simvastatin, benazepril, hydrochlorothiazide, and omeprazole will interact with clarithromycin?
   A. MobileMicromedex.
   B. Clinical Pharmacology OnHand.
   C. Epocrates.
   D. Lexi-Drugs.

5. A pharmacist is researching MEDLINE for the dose of gabapentin for treatment of spasticity in a 36-year-old woman newly diagnosed with multiple sclerosis. If using the MEDLINE terms “gabapentin” AND “spasticity,” which one of the following limit functions would best help narrow results and limit erroneous results?
   A. Human.
   B. English only.
   C. Human and English only.
   D. Clinical trials.

6. A medical resident has requested information on a recent news story regarding the depletion of magnesium by proton pump inhibitors. She requests more information as to the clinical presentation as well as the incidence of this depletion in patients. Which one of the following would be the best Internet source to find this information?
   A. *www.clinicaltrials.gov.*
   B. *www.fda.gov.*
   C. *www.mayoclinic.com.*
   D. *www.clinicalevidence.com.*

7. A 54-year-old woman has a 10-year history of relapsing, remitting multiple sclerosis. She has either not tolerated or failed all commercially available drug therapy options. The patient lives in rural Montana and has limited travel and medical resources. She is interested in trying to find a clinical trial that she might be eligible for that could provide some other therapeutic options. Which one of the following Web sites would provide her with the best options?
   A. WebMD.
   B. *www.clinicaltrials.gov.*
   C. *www.fda.gov.*
   D. *www.controlled-trials.com.*

Questions 8–11 pertain to the following case.

The Cochrane Library (Cochrane Database of Systematic Reviews) published a systematic review on the use of supplemental selenium in the prevention of cancer. The review was published in May of 2011 and included all pertinent clinical trials as of April 5, 2011. The review included 49 prospective observational studies and six randomized controlled trials (RCTs). In epidemiologic data, the review reported a reduced cancer incidence (odds ratio [OR] of 0.69 (95% confidence interval [CI] 0.53–0.91) and mortality (OR 0.55, 95% CI 0.36–0.83) with higher selenium exposure. The cancer risk reduction was more pronounced in men (incidence: OR 0.66, 95% CI 0.42–1.05) than in women (incidence: OR 0.90, 95% CI 0.45–1.77). The authors of the review stated that no reliable conclusions can be drawn regarding a causal relationship between low selenium exposure and an increased risk of cancer. They also summarized that the effect of selenium supplementation yielded inconsistent results in RCTs, and that to date there is no convincing evidence that selenium supplements can prevent cancer in men, women, or children. In addition, the results of the Nutritional Prevention of Cancer Trial (NPCT) and the Selenium and Vitamin E Cancer Prevention Trial (SELECT) raised concerns about possible harmful effects of selenium supplements.

8. A 47-year-old man has read recent information that selenium supplementation can decrease his risk of prostate cancer. His family history of prostate cancer includes his father, grandfather, and older brother, who all three developed prostate cancer in their 50s. The patient currently has a prostate-specific antigen test with his yearly physical, which includes a digital rectal examination of the prostate. He takes a daily multivitamin that contains 55 mcg of selenium. Based on the results of the Cochrane Review, which one of the following is the best advice for this patient?
   A. Continue the daily multivitamin that contains the RDA for selenium.
   B. Add an additional selenium supplement to the multivitamin to reach a daily dose of 200 mcg per day.
   C. Discontinue the daily multivitamin and increase his daily selenium to 400 mcg per day with nutritional milkshake supplements.
   D. Discontinue the current brand of multivitamin and find a supplement that does not contain selenium.

9. The conclusions of the Cochrane authors seem inconsistent with the OR reported for both cancer incidence as well as mortality. What is the best explanation as to why the reviews indicated that there is no reliable conclusion that can be drawn between selenium exposure and cancer risk?
   A. Odds ratios are an estimate of relative risk and the actual relative risks were not provided.
   B. The RCTs showed inconsistent results compared with the observational study designs; therefore, a causal relationships could not concluded.
   C. The CI showed wide variability and often included a value of one, thereby indicating that the data are weak.

D. The potential for sex bias in the observational studies created inconclusive results.

10. Both the NPCT and SELECT found possible harmful effects of selenium without additional reductions in cancer. The NPCT evaluated 200 mcg/day in prevention of non-melanoma skin cancers in light-skinned participants; the SELECT evaluated the use of selenium 200 mcg/day with or without vitamin E 400 international units/day in more than 35,000 men older than 55. The SELECT trial cohort included 15% African American males. These two RCTs illustrate a potential problem related to internal validity (methodology). Which one of the following was most important to consider when the Cochrane reviewers were evaluating the data?
    A. Variability in dose of selenium.
    B. Variability in sample size.
    C. Publication bias.
    D. Comparability or homogeneity of samples.

11. A student pharmacist is completing an Advance Practice Rotation and has been assigned the task of seeing if any additional studies have been published on selenium and cancers since the most recent Cochrane Review has been published. Which one of the following is the best resource for the student to use?
    A. PubMed.
    B. UpToDate.
    C. Google.
    D. *www.fda.gov.*

12. The health care advisory committee to an employee wellness program is contemplating adding vitamin D serum concentrations to its routine laboratory screening. The cost of adding this particular test is $12 per employee, which is a significant increase in overall expenditures. The vice president of human resources is asking the advisory committee to provide data or national guidelines that show the cost-benefit of this recommendation. Which one of the following would be the best reference source to start looking for national guidelines or standards?
    A. Google.
    B. WebMD.
    C. *www.controlled-trials.com.*
    D. *www.guideline.gov.*

13. A patient from the anticoagulation clinic has found a Web site that provides a comparison between dabigatran and warfarin for atrial fibrillation. The patient insists on switching to this new therapy because this Web site states that dabigatran is more effective than warfarin and does not require any blood work. When you inquire about the source of the information, the patient tells you that it is called "Dean's Stroke Musings." The patient has read several other Internet testimonials on treatment with dabigatran and how it has changed the writer's life. Which one of the following is the best advise to give this patient on the use of the Internet for patient information?
    A. Discourage them from using blogs and patient testimonials for advice.
    B. Caution them on opinion pieces and redirect them to search the web for other sites.
    C. Redirect them to WebMD to compare treatments for atrial fibrillation.
    D. Redirect them to better sites and provide them with some standard questions to help determine a high quality site.

Abbreviations

ADR	Adverse drug reaction
AHFS	American Hospital Formulary Service
CAM	Complementary and alternative medicine
CPG	Clinical practice guidelines
DI	Drug information
EBM	Evidence-based medicine
HCP	Health care professional
IDIS	Iowa Drug Information Service
IPA	International Pharmaceutical Abstracts
NLM	National Library of Medicine
PDA	Personal digital assistant
PSA	Prostate-specific antigen
RCT	Randomized controlled trial
REMS	Risk Evaluation and Mitigation Strategy
TCM	Traditional Chinese medicine

BPS Pharmacotherapy Specialty Examination Content Outline

This chapter covers the following sections of the Pharmacotherapy Specialty Examination Content Outline:

1. Domain II: Drug Information and Evidence-Based Medicine
    a. Task 1, Knowledge statements 2, 3
    b. Task 2, Knowledge statements 6,7

I. OVERVIEW OF DRUG INFORMATION RESOURCES

A. The efficient use of drug information (DI) is an important skill for all pharmacists to have regardless of their practice site. In all pharmacy settings, pharmacists are recognized as drug experts and as providers of DI. It is imperative, therefore, that pharmacists know how to provide accurate and complete responses to DI requests. Keeping current with DI resources is challenging for the clinician because of the vast amount and the variable quality of available resources. Technology has also brought DI to the patient's bedside. Pharmacists should know what DI resources are available and be able to use these sources effectively and efficiently. The chapter reviews the types of literature used in the synthesis and provision of DI.

B. Primary literature is the most up-to-date resource available to the clinician and consists of journal articles reporting original research, new ideas, or opinions. These resources are useful for research, education, and current awareness. Not all articles found in journals are considered primary literature; for example, review articles that summarize the literature are classified as tertiary resources.

C. Secondary resources include indexing and abstracting systems that organize and provide easy retrieval of primary resources. Indexing systems include the article citation, with or without access to the abstract; some include a link to the full-text article. Abstracting systems provide not only the citation but also the abstract and often a link to the full-text article. Examples of secondary resources include MEDLINE (through PubMed, EBSCO, Ovid), Academic Search Premier, Cochrane Database of Systematic Reviews, Iowa Drug Information Service (IDIS), International Pharmaceutical Abstracts (IPA), Embase/Excerpta Medica, Biosis Previews/Biological Abstracts, CancerLit, SedBase, Reactions, Clin-Alert, Current Contents, and Toxline. Proper training is required for efficient use of these resources.

D. Tertiary resources are sources that condense and summarize data from the primary literature. These include not only textbooks and compendia but also electronic databases (e.g., Micromedex, Lexicomp) and review articles. The best tertiary resources are written by experts in the field and are peer reviewed. If the tertiary resource is not current or comprehensive, a secondary resource should be consulted to locate primary literature on the topic. However, some questions can only be answered by using tertiary sources.

II. INTERNET SOURCES OF DI

There has been an explosion of information available on the Internet for both the health care professional and the consumer. An estimated 60 million U.S. adults use search engines daily basis to explore more than 1 trillion Web pages; studies suggest that about 60% of adults search for health-related information. According to some top Internet researchers, the public is unable to find the information they seek almost 50% of the time. The quality of the information that they do find is a separate concern.

Patients rely on the Internet for health and DI when they may not have access to a knowledgeable health care professional (HCP). Studies have shown that the younger population will use the Internet as one of their primary sources of DI. Older adults (60 years and older) prefer to talk to an HCP as their primary source of DI, but these patients will also access the Internet. Compared with an HCP, members of the public may have fewer skills to evaluate the validity of the DI that they receive from the Internet. The National Library of Medicine (NLM) has created a 16-minute video intended to help consumers distinguish a good Internet source of information (*www.nih.gov/MEDLINEplus/webevalu.html*). As the video points out, anyone can create an Internet site, and it is essential to determine the creator of the site, the creator's credibility, and the way to contact the organization who has ownership of the site.

As with any Internet source, pharmacists should evaluate the credibility, validity and reliability of the information. Health care professionals can rely on the same NLM concepts provided for consumers when searching the Internet. Many Internet services, either available free or for a paid subscription, can be invaluable sources of high-quality, evidence-based medicine. Many sites provide HCPs with fast results to DI questions and even access to professional journals. The skill of the researcher is essential in getting to the best information, and studies have documented that skill level can make a difference in the quality of the information obtained, whether from commercial sites or from free professional sites such as PubMed.

A. Search Engines

When searching for specific words or phrases, a search engine (e.g., Google, Yahoo!, Bing, AOL Search, Ask) is useful. Different search engines often produce different results for the same term; therefore, the use of more than one search engine can improve results. For searches that require broad or nonspecific terms, using an online subject director such as World Wide Web Virtual Library may help identify more appropriate terms. A free resource on Internet searching is available at *http://www.SearchingTheInternet.info/.*

The Internet does not replace the science of DI retrieval and evaluation. Internet searches retrieve data that still needs expert analysis and a critical eye to evaluate the evidence. A 2009 study found that search engines were vastly different and recommended against reliance on a single source. The study also found that search engines often show Wikipedia results at the top of the results list (referred to as the *visible area*). Wikipedia is not peer-reviewed and does not always provide valid and reliable information; its information should be viewed with skepticism and not relied upon as a major DI source. The study also revealed that the most valuable or highest quality references for a HCP are usually found in the *scroll area*, which requires you to scroll down to other pages to find significantly better results. Other studies have shown that both HCP and consumers do not typically take the time to look at the resources in the scroll area, and when they do, they often do not scroll more than two pages.

Another study evaluated the number of paid advertising sites that came up in the visible area after a search. Of the four sites evaluated, Google had the most sponsored links. The other sites evaluated were Yahoo!, MSN/Live, and Ask.com. However, Google had the best retrieval when looking at organic URLs (original Web site) versus a search engine or meta site. This study confirmed the need for good query or research skills when trying to find the best quality information on the Internet.

1. Boolean Logic

   Boolean logic is used in search engines such as Google, StatRef! MEDLINE, and AccessPharmacy. The use of Boolean operators *and*, *or*, and *not* can help narrow results in search strategies; some search engines automatically assume *and* as an operator. Use of two search terms and the operator *and* tells the engine to search for both terms. Articles that contain both of these search terms will be chosen. Two search terms and the operator *or* will tell the engine that one or both terms must appear within the record. If *not* is used, the engine will look for articles that do not contain the search term. Specific search engines may have different terms for NOT (e.g., Google uses a minus sign). In addition, most major search engines provide Advanced Search Operators that can be useful for searches on specific topics. The sites offer ways to restrict searches for a particular site or by a particular author or even by a particular link to another site. Look at sites for direction (e.g., Google Guide Quick Reference: Google Advanced Operators, Bing).

2. Advanced Search Keywords

   Metasearch engines (e.g., Dogpile, metaCrawlerdogpile, metacrawler, Search.com) allow the user to enter terms and search multiple search engines at one time. Some of these sites eliminate duplicate results and provide the user with a list ranked by relevancy. The caveat is that these search engines can miss valuable information on the Internet. The HCP will be most interested in specialty search engines specific to health care (e.g., Academic and Scholar Search Engines and Resources [*http://virtualprivatelibrary.blogspot.com/Scholar.pdf*], eHealth careBot [*www.ehealth carebot.com/*]).

3. MEDLINE MeSH Terms

Medical subject heading (MeSH) terms are a standardized vocabulary used for indexing articles in MEDLINE; familiarity with these terms is necessary for an efficient and effective search. The MeSH terms are organized within MEDLINE in a fashion referred to as a tree structure. This hierarchal system allows for either broad topic searches (e.g., cardiovascular disease) or more narrow searches (e.g., cardiac tamponade). Each MeSH term has its own subheading and subheadings also may have subheadings. When searching, a narrow subheading (e.g., congenital heart defects with a subheading of drug therapy) or a broad category (e.g., congenital heart defects) that will encompass several subheadings can be selected depending upon need. Such techniques help to search specific aspect or facet of the topic.

The multiple ways to search MEDLINE include by MeSH term, by keyword, by journal name, by author, and by title of article. The most efficient search will depend on the type of information is needed. Keywords are single terms that appear in the title, abstract, and MeSH terms of an article. The disadvantage of using keywords is that it may result in a search strategy that is too broad in scope and identifies irrelevant articles. When searching MEDLINE through Ovid or EBSCO, the engine will try to map keywords to a MeSH term; there may or may not be a suitable corresponding MeSH term. Keywords are typically used when no MeSH terms are available for a specific concept or when the MeSH term is not specific enough. For example, if a new drug has just been released but has not been assigned a MeSH term, a keyword search is the best approach to find articles on that particular drug.

B. Search Strategies

The most efficient search for a particular article often uses the article title or author name. Searching by journal name can locate a specific article or series of articles in one journal issue. When searching by journal name, the specific title as indexed by the National Library of Medicine (NLM) is required. Likewise, when searching by author name, the last name and first initial (or first and second initial) of the author are needed. A search by article title or author name can be performed with the single citation matcher available in PubMed.

The limit function in MEDLINE provides a means of filtering unwanted articles from a set of search results. The search parameters are limited according to the criteria the searcher selects. Examples of limits include language, human or animal species, gender, age group, review articles, latest updates, publication type, publication year, and local holdings.

C. Obtaining High-Quality DI (B)

Published articles provide helpful tips on how a busy practitioner can search a database such as MEDLINE and narrow the results to only high quality randomized controlled trials (RCTs). Researchers have found that the use of filters can provide clinicians with better searching strategies. The two most prominent filters being researched are content filters and validity filters.

Content filters are specific to the drug or disease state being searched and ensure that the clinician is searching the most appropriate content. For example, an advanced search in PubMed involving MeSH headings will show that if the search is for regional enteritis, "Crohn's disease" is a better content filter. In the IDIS system, the disease index would indicate that "enteritis, regional" would be the more appropriate term. Likewise, if searching for antibiotics for otitis media, the search term "antibiotics" would not be a good content filter because the databases are searched for just that term and not necessarily a specific type of antibiotic. PubMed and MEDLINE allow the researcher to explode terms like antibiotics to get better content results.

Validity filters are a means to narrow the search to only the highest-quality studies. Terms such as "randomized controlled trial" or "double-blind" can be used to eliminate studies of weaker methodology. In a recent study, pharmacy students provided with content and validity filters demonstrated improved searching abilities and identified more articles on evidence-based medicine (EBM) than students searching without these filters. For the busy practitioner, proper training on how to search secondary databases with the use of content and validity filters can produce DI answers in less time and with better-quality evidence.

Another consideration in searching the professional literature is that databases such as Google Scholar are not designed to be comprehensive; therefore, good-quality studies can easily be overlooked. The use of other, more reliable databases (e.g., MEDLINE, PubMed) is preferred for researching DI questions. A better role for Google Scholar would be in finding access to full-text articles once a proper search has been done using other databases or as a complement to other database searches. Google Scholar is also limited by its software and the algorithms that it uses to search for articles. Researchers have noted that some Google Scholar search results are questionable, and that the system is negatively influenced by typos and inaccuracies in the data. This continues to strengthen the need for checking more than one source when researching DI.

III. EVALUATING DI RESOURCES

A. Secondary DI Resources

Secondary sources provide a rapid method by which to search the primary literature. Today most secondary DI sources are electronic indexing systems that aid users in locating primary literature. These resources have detailed and user-friendly search engines that enable literature searches on a specific topic. The search engines employed are extensive and provide immediate results once the details of the system are learned. Not all secondary resources have the same collection of journals; therefore, it is important to explore several databases to achieve a comprehensive search. Data provided include the bibliographic citation, with some resources also displaying the article abstract and even a link to the full-text article. If the abstract is included, the system is referred to as an *abstracting system*; if not, the resource is an *indexing system*. Interpreting data presented only in abstract form is appealing but almost always inappropriate. A clinical decision should never be made from simply reading an abstract. The corresponding article should be reviewed and considered in the clinical decision-making process.

It is important to evaluate secondary resources. For example, there is a lag time between the time from article publication and the time to indexing into a secondary resource. With PubMed, the article is cataloged, indexed, and assigned biomedical terms. The indexing information and the article are then uploaded to the database and provided to the vendors of the database before finally becoming available to the user. The time involved in this process will vary among secondary resources; the user must keep in mind that a search may not produce the latest information on the search subject. Some secondary resources (e.g., PubMed) are able to access in-process records and provide this data.

The cost of secondary resources is typically based on the number of users granted access; therefore, they often require a library or institutional budget to finance. The ease of use varies among secondary resources. Each source uses a powerful search engine; these search engines may or may not use the same language, and there is no standardization of search terms across secondary resources. The user must become familiar with the structure and terminology of these databases to search effectively. Becoming proficient at search techniques also requires practice. Table 1 lists common secondary sources.

Table 1. Common Secondary DI Sources

Source	Search Language	Comments
MEDLINE	MeSH	Available through a variety of services: National Library of Medicine through PubMed *(www.ncbi.nlm.nih.gov/PubMed)* (free) Ovid *(www.ovid.com)* (commercial); allows search of more than one database at a time; offers other databases, such as those for dentistry and alternative health EBSCO *(www.ebscohost.com)*; allows search of more than one database at a time; offers other databases, such as those for dentistry and alternative health (commercial)
Excerpta Medica's Embase	Emtree: Contains 58,000 preferred terms (of which more than 28,000 are drugs and chemicals) and more than 240,000 synonyms (with over 150,000 drugs and chemicals) All MeSH terms are included Generic names as referenced by the FDA and European Medicines Agency (EMEA)	Contains more than 7500 titles from mostly peer-reviewed journals, including 2000 not in MEDLINE Includes 800 conference and 260,000 conference abstracts For more information, go to *www.embase.com*
IDIS (aka IOWA)	Uses United States Adopted Name (USAN) and the International Classification of Diseases (ICD) coding system Descriptors may differ from MeSH terms	Contains more than 200 peer-reviewed English-language medical and pharmaceutical journals Includes data back to 1966 Full-text articles available electronically from 1988 to present (articles from 1966 to 1988 on microfiche) For more information, go to *www.uiowa.edu/~idis/idistday.htm*
IPA	Descriptors may differ from MeSH terms	Contains information from more than 800 pharmacy and health-related journals published worldwide since 1970 Available through Ovid and EBSCO Concentrates on all aspects of drug development, pharmacy professional meetings, and state pharmacy journals including meeting abstracts For more information, go to *http://science.thomson-reuters.com*

DI = drug information; FDA = U.S. Food and Drug Administration; IDIS = Iowa Drug Information Service; IPA = International Pharmaceutical Abstracts; MeSH = Medical Subject Heading.

B. Tertiary DI Resources

Tertiary references often are the starting point to identify information because they typically provide a fairly complete overview of information on a specific topic. These references are convenient, easy-to-use, and familiar to most pharmacists. Their most significant limitation is the lag time for publication. Other limitations may include author bias, inaccurate information, or lack of author expertise. Therefore, it is important for readers to critically evaluate tertiary references. This chapter focuses on the online tertiary resources.

In evaluating tertiary literature, the important questions to ask include, "What are the qualifications of the evaluating author(s) and/or editor(s)?", "What is the timeliness of the information?", "Are the citations appropriate?", and "Is the publication free from potential bias?" Content should be considered as well. Some references have a general scope of coverage and others are more detailed, providing a specific focus on a topic. For tertiary references that provide a DI focus, the user should consider the type of drugs included in the reference (e.g., prescription only, over-the-counter, herbals) as well as the drug's country of origin.

The types of information reported should also be considered (e.g., U.S. Food and Drug Administration [FDA]-approved uses only or off-label uses as well). Organization of content is also an important. Several tertiary references provide excellent tables and figures that are easy to use and organize content in a concise manner. Users will often come to prefer one reference over another based on the organization of the information such as tables, appendices, or special sections. There are hundreds of tertiary references available and no pharmacy practice setting will provide access to them all. Hospitals, community pharmacies, clinics, and other practice settings will select references based on their particular needs, funding, patient populations, and the types of information commonly required.

Specific content titles of commonly used electronic tertiary databases are listed in Table 2. Common features of these databases are compared in Table 3.

Table 2. Content of Electronic Tertiary Resources

Clinical Pharmacology	Facts and Comparisons	Lexicomp	Micromedex
MedCounselor Sheets Drug Identifier Trissel's 2	Drug Facts and Comparisons Drug Interaction Facts Drug Interaction Facts: Herbal Supplements and Food MedFacts (patient information in English and Spanish) Comparative Efficacy Content The Review of Natural Products A to Z Drug Facts Nonprescription Drug Therapy Off-Label Drug Facts Trissel's 2 Cancer Chemotherapy Manual 5-Minute Clinical Consult ToxFacts Toxicology Treatment Guidelines Healthwise Patient Instructions The Formulary Monograph Service Martindale – The Complete Drug Reference	Pediatric Dosage Handbook DI Handbook Geriatric Dosage Handbook DI Handbook for Nursing, for Advanced Practice Nursing, for Oncology, for Psychiatry, for Anesthesiology & Critical Care Pharmacogenomics Handbook Series of handbooks for dentistry AHFS King's Guide to Parenteral Admixtures The Orange Book TOXNET (information on toxicology, carcinogenicity, and drugs in pregnancy and lactation)	POISINDEX IDENTIDEX Emergindex DRUG-REAX Trissel's 2 Martindale–The Complete Drug Reference Care Notes (formerly USP-DI vol. 2, Advice for the Patient) REPRORISK Material Safety Data Sheets (MSDS) Laboratory Advisor NeoFax Index Nominum

AHFS = American Hospital Formulary Service

Table 3. Features of Electronic Tertiary Databases

	Clinical Pharmacology	Facts and Comparisons eAnswers	Lexicomp	Micromedex
Drug identification[a]	Search by NDC number	Search by partial or complete NDC number		Comprehensive; 23,000 U.S. and foreign drugs
Drug interactions[b]	Drug-drug, duplications, drug-food, ethanol, laboratory, tobacco, caffeine	Drug-drug, drug-disease, duplications, allergy, drug-food, ethanol, laboratory, tobacco, pregnancy, lactation	Drug-drug, drug-laboratory, drug-food, allergy, herbal, pregnancy, OTC	Drug-drug, duplications, allergy, drug-food, ethanol, laboratory, tobacco, pregnancy, lactation
IV compatibility	Trissel's 2	Trissel's 2	King's Guide to Parenteral Admixtures	Trissel's 2
Laboratory information	Chart of normal laboratory values	Chart of normal laboratory values	Pertinent information in monographs Chart of normal laboratory values	Individual laboratory value monographs
Patient counseling materials	English and Spanish	Drug, oncology-specific administration, OTC administration techniques, disease-focused; English and Spanish	Drug, disease, and procedural information; 19 languages including English and Spanish	Drug, disease, and procedural; English, Spanish, and 13 other languages; customizable
Inert ingredients	Located in how supplied section	Located under product list	Not readily available	Through Tox and Drug Product Lookup
Teratogenicity information	Pertinent information in monographs	Uses Briggs' Drugs in Pregnancy and Lactation	Through TOXNET, Hazardous Substance database	Through REPRORISK
Breastfeeding information	Pertinent information in monographs	Uses Briggs' Drugs in Pregnancy and Lactation	Through TOXNET, LactMed	Through REPRORISK
Investigational drug monographs	Yes, readily referenced	Limited information	Limited	Yes, readily referenced
CAM information	Yes	Through review of Natural Products	Through Natural Products database	Yes; AltMedDex
FDA recalls	No	Weekly FDA news thread	Link to FDA	No
Drug shortages	No	Weekly FDA news thread	Link to ASHP	No
MSDS	No	No	No	Yes
Referencing	Comprehensive	Limited	Limited	Extensive
Available platforms	Web-based, PDA	Web-based, PDA, print	Web-based, PDA, print	Web-based, PDA
Cost[c]	Subscription required; 30-day free trial available; free access to students	Subscription required for basic and advanced packages	Subscription required for individual components; package prices available	Subscription required. Various package prices available

[a]Search solid dosage forms by color, shape, imprint, scoring; image available.

[b]Information provided within individual monographs.

[c]Subscriptions available to educational institutions free or at a nominal charge.

CAM = complementary and alternative medicine; FDA = U.S. Food and Drug Administration; IV = intravenous; MSDS = Material Safety Data Sheets; NDC = National Drug Code; OTC = over-the-counter; PDA = personal digital assistant.

1. Clinical Pharmacology
   This database offers a product comparison tool that can retrieve a list of products for a selected allergy or dietary restriction criteria (e.g., sugar free, alcohol free, latex free, sodium free, dye free). Most information is readily referenced with a link to PubMed citations, although some information, such as the adverse event reporting, is not referenced. Clinical Pharmacology also offers a drug comparison tool that easily generates information on product dosage forms, clinical attributes, and adverse events.
2. Facts and Comparisons eAnswers
   Facts and Comparisons eAnswers is the online version of the Facts & Comparisons textbook. Abbreviated DI is referenced, although not extensively. One great feature of this database is the comparison charts. A daily news update that includes FDA recalls is also a standard feature. Additionally, information on patient assistance programs, look-alike and sound-alike drugs, and a manufacturer index is provided.
3. Lexicomp
   Lexicomp is a point-of-service database providing comprehensive DI with over 1700 drug monographs. As of June 2011, Wolters Kluwer is acquiring Lexicomp to add these clinical references to their other holdings, including UpToDate. Other information found in Lexicomp includes current drug shortages, FDA recalls, dangerous drug abbreviations, therapeutically equivalent generic drugs (through the Orange Book, available at *www.accessdata.fda.gov/scripts/cder/ob/default.cfm*), and extemporaneous preparations (through the Pediatric Dosage Handbook found online in the Lexicomp series). References are not provided for all information; some references provided are not easily retrievable. Lexicomp is a good source to use when quick retrieval of easy-to-understand data is needed.
4. Micromedex
   Micromedex is a tertiary resource designed to provide information to the health care professional about clinical inquires. This resource, commonly used in the hospital or academic setting, provides a variety of information in the areas of DI, poison information, acute care medicine, and patient education. Information is provided as full-text and is referenced throughout.

   The DI is divided into two main sections: DRUGDEX and DrugPoints. DRUGDEX is a general tertiary resource. DrugPoint Summary (formerly known as USP-DI volume I) provides summary information on dosing, drug interactions, adverse effects, pregnancy warnings, indications, cautions, therapeutic classes, brand information. DRUGDEX provides evidence-based detailed DI that is gathered from primary literature and summarized by editorial specialists. Although Micromedex is a large database, the primary literature is readily referenced and easy to access. Therapeutic indications are given a graded evidence rating with usage recommendations. For the clinician, Micromedex offers comprehensive, easy-to-read, extensively referenced data on drugs. Micromedex now offers a drug interaction app through iTunes that allows an HCP to simultaneously enter 50 medications from a patient profile and search for interactions.
5. MD Consult/First Consult
   MD Consult is a large database that provides comprehensive medical information. MD Consult includes weekly summaries of journal articles, full-text reference books, practice guidelines, DI (through Gold Standard), information on what patients are reading in general literature, drug updates, daily medical news, customizable patient handouts, case of the week practice modules, medical images, clinical topic tours, and continuing education. First Consult, a part of MD Consult, provides information on over 700 medical topics as well as differential diagnoses and procedures. First Consult also offers an iPhone app that makes clinical medical information available for personal digital assistants (PDAs) and smart phones. Of note, MD Consult provides article summaries of top current interest journals as well as a really simple syndication (RSS) feed.

6. UpToDate
   UpToDate is an evidence-based, peer-reviewed reference that is available through the Web or by PDA. Content is generated by medical experts in their field and covers more than 16 different medical disciplines and 8300 topics. This database is geared toward prescribers, and all information includes summary documents of evidence-based medicine. UpToDate uses Lexicomp information as the source of point-of-service DI.
7. Electronic Textbook Databases
   There are numerous eTextbook collections available for purchase. These databases contain online textbooks in an electronic format. Large publishers such as McGraw-Hill and Wiley InterScience offer collections of their books in electronic format. These collections are often geared toward a specific subject area (e.g., pharmacy, medicine, nursing). Purchasing collections can be more cost effective than buying individual titles. An advantage of electronic texts is the availability for content to be updated in a timely fashion. A major disadvantage of these resources is their cost. The contents of two commonly used electronic textbook databases are listed in Box 1.

Box 1. Contents of Electronic Textbook Sources

AccessPharmacy
This multimedia database has 25 online textbooks. Case studies, laboratory tests, calculators, videos, and effectiveness statements are also available. Titles include Pharmacotherapy: A Pathophysiologic Approach, Goodman & Gilman's: The Pharmacological Basis of Therapeutics, Harrison's Principles of Internal Medicine, Drug Information: A Guide for Pharmacists, and Goldfrank's Toxicologic Emergencies. AccessPharmacy offers a review for the NAPLEX, Multistate Pharmacy Jurisprudence Examination (MPJE), and Top 200 drugs as well as patient cases. Searching may be done by keyword, curricular topic, or organ system.

STAT!Ref
STAT!Ref contains full-text versions of medical and pharmacy texts including AHFS, Mosby's Drug Consult, Rudolph's Pediatric, Basic and Clinical Pharmacolo-gy, and Stedman's Medical Dictionary. Subscription rates are à la carte or by col-lection. Collections are available for dentistry, mental health, nutrition and dietetics, pharmacology, and public health. Searching across all texts is available. In addition to popular texts, STAT!Ref offers a medical newsfeed as well as evidence alert feeds.

AHFS = American Hospital Formulary Service

8. Resources for Handheld Devices
   Many tertiary resources have applications for handheld devices like smart phones. All of these applications contain basic DI such as drug monographs, disease information, and drug interactions; however, they differ in cost and additional features such as drug identification, calculators, and laboratory information. For a list of features available for these electronic resources, see Table 3.

C. Web-Based Resources
   Qualified HCPs should be involved in establishing and reviewing sites. The pharmacist cannot control whether a consumer goes to the Internet for information but can provide patients with tools to help them glean high-quality information. Table 4 lists questions that a consumer should consider when searching for credible drug and health information. The pharmacist may also direct the consumer to the NLM video.

   Some Web sites have risk calculators for health and wellness (e.g., americanheart.org, mayoclinic.org, healthstatus.com). These sites may require personal information but usually do not request sensitive identification information such as Social Security numbers. These sites usually ask the user to set up a secure account and provide a privacy notice. Personal information should not be given to a site that does not have a privacy policy or when site security is in doubt.

Patients and HCPs alike should beware of sites that are blogs, micro blogs, social networks, social bookmarking sites, or collaborative harvesters. These sites are not usually high quality or valid providers of health and DI. To evaluate these sites, it is important to ask the questions found in Box 1. In general, sites that end in .gov, .edu, and .org may be more reliable; however, even these should be held to the same criteria as other sites. This continues to be an important area in which the pharmacist or other HCP can guide the health-care consumer.

Table 4. Questions Consumers Should Ask About Web-Based DI

Parameter	Questions
Source of information	What or who is the organization/person responsible for the site? Can you readily find this information on the Web site? Why has the organization/person created the site? What is the mission in providing this service?
Cost of access	Does the site want anything from you in return? If so, what and why is that necessary for gaining access to the information? Does the site want your personal information, and if it does, what will it do with that information? Who is paying or funding the site? Is there a site sponsor? Is the sponsorship readily available on the Web site and openly displayed for the public? Does the sponsor gain any benefit from your reading or accessing the site?
Quality of information	Is the information written and/or reviewed by health care experts with proven credentials? Where did the information on the site come from? Is it expert opinion, or is it based on studies—preferably studies that have high-quality evidence or at least studies that have been published in reputable journals (this can be difficult for consumers to ascertain and may require help from professionals)? What is the editorial policy of the site? Is the information current? When was the information last updated with new science?
Usability	Does the Web site provide information such as a site map, contact information, a mission/purpose statement, or the best way to use the site? Does the Web site make unbelievable claims or claim to be the answer to all questions or problems? Does it claim to be the only one to have true insight into the issues?

DI = drug information.

Information from the National Library of Medicine (www.nlm.nih.gov).

IV. ACCESSING QUALITY DI RESOURCES

A. Resources for the HCP

The sources of high-quality information for HCP have not changed much in the past 10 years. Most of the resources are familiar to practitioners and should be relied upon as the better venues for high-quality data. Studies show that subscription sources provide a faster means to get summarized answers, but these sources do not always contain all of the necessary primary literature. A study comparing the use of PubMed (a free resource) versus UpToDate (a subscription source) showed that medical residents spent less time searching for answers when using UpToDate; however, approximately one-fourth of the queries required additional searches in PubMedto fully answer the question. Table 5 lists some free-access Internet sites of value for the HCP interested in providing quality DI.

Table 5. Available Free Resources for Practitioners

Site	Features
PubMed (*www.ncbi.nlm.nih.gov*)	A compilation of more than 21 million articles from the biomedical literature that can be found in MEDLINE, online books, and life science journals. Many of these articles are linked to full-text references
Cochrane Library (*www.thecochranelibrary.com*)	Is more than 28,000 contributors writing systematic reviews dedicated to compiling up-to-date, accurate information about the effects of health care; serves as a leader in evidence-based medicine
Clinical Evidence (*www.clinicalevidence.com*)	An evidence-based medicine database that provides graded levels to help practitioners put evidence into practice. The focus is on medical practice in the hospital and in primary care
National Institute for Health & Clinical Excellence (*www.nice.org.uk*)	An independent organization in the United Kingdom that was started to provide responsible medical care with evidence-based medicine for promoting good health and preventing and treating ill health
National Cancer Institute (*www.cancer.gov*)	Provides unbiased information on the treatment of cancer including clinical trials, cancer statistics, research and funding, and patient information
U.S. Food and Drug Administration (FDA) (*www.fda.gov*)	A government site dedicated to protecting and promoting health by providing information on food, drugs, medical devices, vaccines, blood and biologics, animal and veterinary products, cosmetics, radiation-emitting products, and tobacco products. Provides both consumer and professional information. Allows anyone to submit problems identified with products as well as safety recalls
www.clinicaltrials.gov	Includes ongoing federal and privately supported U.S. and international clinical trials Available for both HCPs and patients Provides telephone numbers for contacting investigators currently enrolling for clinical trials Provides information to potential investigators
www.centerwatch.com[a]	Clinical trial research information for both practitioners and patients Very patient-friendly; provides several tools including education, publications, and resources Offers investigators help in recruiting patients for trials Web site is extensive, with transparent information, and provides the authors, the purpose, and history
apps.who.int/trialsearch/	This site is a portal for international clinical trials, but it is not a site for registering clinical trials. Some countries update their information weekly, whereas others provide monthly updates. Accuracy of the information depends on the countries submitting
www.controlled-trials.com/	This site allows searching, publishing, and registering of clinical trials. The search engine used covers seven databases including clinicaltrials.gov, five UK databases, and one international database. The site also has a journal location service (fee) for accessing published trials (BioMed Central)
www.cancer.gov/clinicaltrials	National Cancer Institute's search engine for locating more than 8000 cancer trials Provides patient education about clinical trials as well as recent results from completed trials
www.clinicalstudyresults.org/	A repository of completed trials, with the results provided in a user-friendly format for prescribers and patients. Not necessarily presented in a professional format that would allow drug literature evaluation Provides manufacturer clinical trial results and can be searched by country, manufacturer, drug, or disease state/diagnosis

[a]Site requires a fee for practitioners but is free to patients.

HCP = health care professional.

B. Resources for the Patient

The DISCERN tool *(www.discern.org.uk/discern_instrument.php)* was developed by researchers in the United Kingdom for patients to use when evaluating sources of information or in evaluating treatment options. This instrument is the first of its kind to help patients decide between various treatment options when they are provided with a wealth of or even conflicting information. Other quality resources that could be recommended to patients are listed in Table 6.

Table 6. Available Free Resources for Consumers

Site	Features
DailyMed *(www.dailymed.nlm.nih.gov)*	Provides high-quality information about marketed drugs, including FDA-approved labeling. Provides consumers with easy-to-read product labeling
Drugs A to Z *(www.drugs.com/drug_information.html)*	An easily searched database to look up drugs, both generic and brand name, to find consumer information that can help patients understand their medications including uses, risks, and benefits
Healthfinder *(www.healthfinder.gov)*	Links to 1500 organizations to search for health information that may be most applicable to a patient. Allows consumers to look at more than one site for a particular problem
Mayo Clinic *(www.mayoclinic.com/)*	High-quality health information written by professionals specifically for consumers. Provides a wealth of unbiased information for consumers
MedicineNet.com *(www.medicinenet.com/)*	An online health care publishing company that provides consumers with easy-to-read but in-depth medical information
MEDLINEPlus *(www.MEDLINEplus.gov)*	Consumer side of the NLM, allowing patients to link to articles and studies within the government database with user-friendly search terms
Merck Manual: Home Edition for Patients *(www.merck.com/mmhe/index.html)*	Provides consumers with disease-specific information that is written in consumer-friendly language
NetWellness *(www.netwellness.org/default.cfm)*	A consortium of three medical schools that provide high-quality health information and educational services to consumers written by health care professionals. Allows consumers to meet experts in different fields and ask them questions
WebMD *(www.webmd.com)*	Provides consumer health–related information written and edited by health care professionals. Allows users to create health accounts where health information can be securely scored as well as programs like vaccine trackers and food & fitness planners

NLM = National Library of Medicine.

Information from Medical Library Association (http://caphis.mlanet.org/consumer/generalhealth.html).

C. Clinical Trial Data

Current clinical trial data can be a useful tool for clinicians, researchers, and patients, and there are several resources available online (see Table 5). Clinicaltrials.gov is one of the most useful sites for the U.S. practitioner and has additional resources on international trials as well. Free and relatively easy to search, the site has clinical trial data that can be extremely valuable for the HCP who works in direct patient care, academia, or in research. Pharmacists can also find this site helpful when patients ask about ongoing clinical trials.

D. Evidence-Based Medicine Resources

Evidence-based medicine is a process for making disease management decisions by evaluating and rating the quality of studies. For the pharmacist, this means combining drug literature evaluation skills with the knowledge of clinical trial design to determine the usefulness and reliability of clinical trial results. The HCP can use EBM to decide whether a study has clinical merit that can be translated into patient care, or if flaws in the study design limit the study's clinical applicability. Available databases can assist HCPs in grading the evidence in the literature. However, drug literature evaluation skills are still required for the decision as to whether the evidence applies to the HCP's patients and practice site.

As in the use of traditional DI tertiary and secondary databases, it is necessary to search more than one EBM resource to get a complete picture. The Cochrane Database of Systematic Reviews is a collaboration of experts who review hundreds of studies about a topic in their specialty. Cochrane strives to include all known studies, as well as any meta-analyses or systematic reviews. The studies are evaluated using strict and consistent EBM criteria. The experts then write their own reviews, which are published in the database. The Cochrane review links all of the published studies that have been provided in the review to the reader. This allows the reader to look at any of the material on their own as well. Cochrane also notes the date that the topic was last reviewed as well as any new information. The Cochrane Library has several additional databases, including the Cochrane Central Register of Controlled Trials (a bibliography of more than 350,000 references to controlled trials) and the Cochrane Methodology Register (more than 9000 references to the types of research methods).

The Database of Abstracts of Reviews of Effectiveness, which is produced by the U.K.'s National Health Service, provides access to systematic reviews of the primary literature. Researchers trained in critical appraisal skills select only the highest quality reviews from published trials, then summarize the results and published them on the Web site. These reviews include trial outcomes and interventions, trial design strengths and weaknesses, and implications for clinical practice. Two other U.K. databases of EBM focus more on economic, social and ethical evaluations; these are the Health Technology Assessments database (*www.inahta.org/HTA/Database/*) and the Economic Evaluation Database (*www.york.ac.uk/inst/crd/*).

The American College of Physicians' ACP Journal Club evaluates recently published journal articles on their methodology and clinical relevance to practice. Specialists in the field critically evaluate recent articles, often pointing out where controversy exists between the study and previously published studies. However, the Journal Club does not provide a comprehensive EBM review of the other literature available on that topic.

There are other resources designed to reduce the amount of time the practitioner spends in finding answers to DI questions. The TRIP database (tripdatabase.com), which is free to clinicians, allows rapid searches for high-quality EBM articles. The TRIP database includes EBM synopses, EBM systematic reviews, U.S. published guidelines, core primary research, and extended primary research. The database will send alerts to a mobile device or e-mail when new information has been added in an area of interest.

UpToDate is a popular subscription service that can provide rapid answers to clinical questions. Described as a clinical decision support tool to help practitioners at the point-of-care, UpToDate is adding EBM into the database so clinicians can judge the level of evidence before implementing care. One study reported that physicians are able to retrieve information faster when using a service like UpToDate compared to database searches such as MEDLINE or PubMed. However, the study did point out that at least one-fifth of the physicians needed to search PubMed after looking up information in UpToDate to retrieve the primary literature before implementing therapy.

E. Clinical Practice Guideline Resources

As clinical practice guidelines (CPG) increase in both quality and quantity, it becomes more difficult to keep up on the latest guidelines. Table 7 lists some common resources to consider when looking for clinical guidelines.

Table 7. Resources for Locating Clinical Practice Guidelines

Site	Features
Guideline.gov *(www.guideline.gov)*	A national guideline clearinghouse of evidence-based guidelines. Has a large database of different guidelines from many professional organizations. Provides expert commentaries, guideline synthesis, guideline resources, annotated bibliographies, and comparative analysis of guidelines. Site is part of AHRQ (Agency for Healthcare Research and Quality)
National Institutes of Health *(www.nhlbi.nih.gov)*	Provides guidelines related to cardiovascular, pulmonary, and blood health. Provides interactive tools and resources. Provides current guidelines and reports as well as guidelines in progress. Also archives older guidelines for historical purposes
American College of Physicians *(www.acponline.org/clinical_information/guidelines/)*	Provides current clinical guidelines as part of the American College of Physicians Web site. This is a clearinghouse of clinically relevant guidelines
Open Clinical *(www.openclinical.org/guidelines.html)*	An international organization that has created a Web site to promote clinical decision support tools, clinical workflow, and advanced knowledge management technologies within patient care as well as clinical research. Provides tools and techniques for creating health care applications to improve quality, safety, and ethical standards

V. SPECIFIC DI RESOURCES

A. Resources on Complementary and Alternative Medicine

The field of complementary and alternative medicine (CAM) continues to expand. The standard references within this area of DI have not really changed over the years, but publishers continue to improve both the quantity and quality of the available information. A large number of newer Web-based resources are available (Table 8). It is difficult to keep up with all of the new products that come to the market from sources in the United States and around the world. These international references, which are available on the Web, may be a good way to identify new products that cannot be found in other references. The FDA Web site contains valuable information on product recalls or products that contain undeclared ingredients.

Standard resources for DI on natural/herbal products include the Natural Medicines Comprehensive Database (*www.naturaldatabase.com*), which provides a summary with an indicator of overall safety and efficacy for each product. Searching both brand and common names is easy, and references for the product information are provided. Furthermore, this reference indicates whether a specific product is U.S. Pharmacopeia (USP)-verified, an indicator of quality ingredients. The Natural Standard (*www.naturalstandard.com*), which provides monographs with summary tables of published literature, is a comprehensive source of graded evidence-based natural product information. The monographs also provide dosing and drug interaction information that can aid in the decision to use a natural product.

An optimal strategy is to consult multiple sources when evaluating the potential for herbal-drug interactions. In a pilot study of five patient files, the Natural Medicine Comprehensive Database and Natural Standard Database were compared in the ability to identify potential drug interactions between prescription medications and herbal therapies. The 21 different drugs in the files resulted in 2522 potential natural product and prescription medication drug interactions. However, each database was able to detect only about 50% of the potential interactions. There was also variability in the information provided, with only 205 of the interactions appearing in both databases.

The Review of Natural Products provides monographs for a large number of herbal products. Known for its very complete chemistry, pharmacology, and toxicology sections, this resource also references articles, including both human and animal studies. The Physician's Desk Reference for Herbal Medicines is useful for herbal products but does not offer information on other types of CAM. Each product is described in a monograph followed by references. This resource, which has information similar to those above, is often packaged with other Thomson DI publications.

Table 8. Select CAM Databases Available in English

Name (Web address)	**Topic Area**	**Content**
Sites with free access		
Acubriefs *(www.acubriefs.com)*	Acupuncture	24,000 citations
CAMbase *(www.cambase.de)*	CAM	80,000 citations
CAM on PubMed *(www.nlm.nih.gov/nccam/camonPubMed.html)*	CAM	462,000
Camlis *(www.cam.nhs.uk)*	CAM	EBM publications
Cards *(http://ods.od.nih.gov/research/cards_database.aspx)*	Dietary supplements	Research projects
Cochrane Collaboration CM Field *(www.compmed.umm.edu/cochrane.asp)*	CAM	EBM CAM reviews
Datadiwan *(www.datadiwan.de)*	CAM	6000 citations
Extract Database *(www.plant-medicine.com/grades/extract/main-menu.asp)*	Acupuncture	8000 citations
Hom-Inform *(hominform.soutron.com/)*	Homeopathy	24,000 citations
IBIDS *(ods.od.nih.gov/health_information/ibids.aspx)*	Dietary supplements	760,000 citations
Sites requiring subscription		
Amed *(www.ovid.com)*	CAM	227,000 citations
Arrcbase *(www.acupuncture.org.uk)*	Acupuncture	16,000 citations
China National Knowledge Infrastructure Database *(www.global.cnki.net/)*	TCM	> 1600 RCTs on TCM
HomBRex *(www.carstens-stiftung.org)*	Homeopathy	> 900 citations
Mantis *(www.healthindex.com/start.html)*	Osteopathy, chiropractic	280,000 citations
Napralert *(www.napralert.org/default.aspx)*	Herbal	150,000 records
TCMLARS *(www.cintcm.com/index.htm)*	TCM	73,000 citations
Wanfang Database *(www.wanfangdata.com/medical/intr.asp)*	TCM	300,000

CAM = complementary and alternative medicine; EBM = evidence-based medicine; RCT = randomized controlled trial; TCM = traditional Chinese medicine.

Information from Boehm K, Raak C, Vollmart HC, Ostermann T. An overview of 45 published database resources for complementary and alternative medicine. Health Info Libr J 2010;27:93–105.

B. Poison/Product Identification Resources

The area of poison/product identification is becoming more important for today's pharmacotherapy specialist. With prescription drug abuse now the third leading cause of drug abuse among teenagers, the pharmacist is increasingly called upon to help identify potential toxic medications as well as provide poison/toxicology information. In 2009, the Drug Abuse Warning Network reported that 4.6 million emergency department visits were drug-related, with 45.1% of these visits linked to misuse or abuse of legal and illegal drugs. In 2011, the White House Office of National Drug Control Policy reported that prescription drug abuse had doubled the number of persons visiting the emergency department in the past 5 years, and for the third year in a row prescription drug abuse surpassed illegal drug abuse. Therefore, it is imperative that the pharmacist be familiar with standard DI resources on overdose, poisoning, and toxicology.

An excellent resource for reviewing basic toxicology is Casarett & Doull's Toxicology: The Basic Science of Poisons. One of the most extensive references on the toxicologic effects of poisons and drugs, this textbook goes into great detail on the toxicity that occurs within every organ system and also discusses developmental toxicology, environmental toxicology, food toxicology, forensic toxicology, and occupational toxicology. Although it is not a good review for acute poisoning from prescription drug abuse, this text is valuable as a reference in the area of chronic exposure.

Another classic toxicology reference, Goldfrank's Toxicologic Emergencies, is written in a case study format. In-depth chapters provide information on various aspects of poisonings. A pocket-sized companion, Goldfrank's Manual of Toxicologic Emergencies, describes how to assess the patient and determine the best treatment option. The manual is a good resource for the pharmacist who might be called upon to provide clinical treatment recommendations for specific poisonings, or for the pharmacist in the emergency room or critical care areas who wants to improve their clinical poisoning knowledge base.

The Medical Toxicology Review: Pearls of Wisdom is an excellent and concise review of many drug-related overdoses. The book is organized in alphabetical order by the drug name or poisoning agent and provides concise bullet points that are critical for understanding the nature of the poisoning. Medical Toxicology is a clinically relevant reference that outlines the diagnosis and management of poisonings including those involving drugs. This textbook provides information on treating a patient with poisoning symptoms from an unknown cause. Because it also describes the toxicology of biological and chemical weapons, it is a good source of bioterrorism information for pharmacists.

Drug identification tools are a critical aspect of poisonings or drug abuse management. A number of well-known databases and textbooks can help the pharmacist, especially if the imprint codes are readily available. Micromedex with INDENTIDEX, mentioned previously, continues to be a gold standard in the area of poison and pill identification. Lexicomp provides imprint codes as well as tablet identification features with pictures. Clinical Pharmacology and Facts and Comparison's eFacts are other resources that have a tablet identification feature.

C. Adverse Drug Reactions/Pharmacovigilance Resources

1. New FDA Initiatives

The FDA has recognized that voluntary post-marketing evaluations of drug safety data have not been the most comprehensive method to identify serious adverse drug reactions. Recent drug-related adverse events such as spontaneous fractures with bisphosphonates and maternal heart problems in women taking terbutaline for preterm labor are two prime examples of the insufficiency of the voluntary reporting system. The FDA has developed new pharmacovigilance methods to improve the spontaneous reporting system (MedWatch program), and is working with private companies and academic researchers to develop and apply these newer monitoring and reporting techniques.

The FDA is using data mining as a new approach to more rapid identification of potential problems. Data mining is a statistical process that attempts to find an event, related to a drug, that is occurring at a higher-than-normal rate within the general population. Signal detection is the process of finding a higher-than-expected event rate. The FDA uses statistics and both Bayesian and non-Bayesian methods to identify these signals, then responds with an expert clinical review to determine if there is any validation to the signal. This data mining allows the FDA to look at multiple or unusual occurrences in a more timely fashion to see if further research or investigation is necessary. The FDA also offers an e-mail delivery service to send safety alerts to HCPs. Practitioners can subscribe to the MedWatch E-List on the FDA Web site. These new FDA initiatives are an important advance in the area of DI within the last few years. These changes make the FDA Web site a valuable resource in assessing early adverse reactions and drug interactions. Pharmacotherapy specialists should include this Web site in their routine surveillance of DI resources.

Under authority granted by the 2007 Food and Drug Administration Amendments Act, the FDA developed a required Risk Evaluation and Mitigation Strategy (REMS) for manufacturers. This program aims to ensure that the benefits of a drug or biological product outweigh the potential risks when the FDA deems that a product may have a risk profile that requires additional limitations. The manufacturer is required to put certain elements in place for the product; these can include a medication guide, elements to ensure safe use, implementation system, and a communication plan. The FDA Web site lists the REMS approvals, as well as instructions and guidance for manufacturers developing the required documents. The draft REMS guidance was posted in February 2011 (*www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM244570.pdf*); for pharmacists, a Web site is available listing the REMS drugs *(www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111350.htm).* The REMS program is so new that there has not been time to determine how helpful these guides will be to the pharmacotherapy specialist. Ongoing studies are assessing the impact of this program on drug use and safety.

Another area of concern is the boxed warning sometimes required by the FDA because of safety issues. Several secondary and tertiary references include these boxed warnings on package labeling as required by the FDA. A 2010 study looked specifically at the boxed warnings as listed in the drug interaction databases of Facts & Comparisons 4.0, MICROMEDEX DRUG-REAX, and Lexi-Interact. The study involved 11 drugs with boxed warnings related to contraindicated drug combinations. The authors concluded that additional studies need to be done to explore inconsistencies and suggest clinicians refer to multiple drug resources when evaluating the possibility of a serious drug-drug interaction.

In 2009, another study looked at five online resources and three online databases to evaluate their documentation of boxed warnings. The study showed that of the 416 marketed prescription drugs required to carry a boxed warning, only 135 (32%) were cited as such in all eight resources. Some resources provided information consistent with the boxed warning whereas others did not identify it as an interaction. The researchers indicated that the current registry of boxed warnings is lacking, which means that clinicians must check multiple sources to verify this type of information. The authors suggest that clinicians should subscribe to the MedWatch safety alerts that are sent to an HCP's e-mail account.

2. Adverse Drug Reaction Resources
   In researching adverse drug reactions (ADRs), most practitioners will use the standard tertiary references (e.g., MICROMEDEX, Lexicomp, Facts & Comparisons, Clinical Pharmacology). However, some other textbooks and databases are excellent resources in evaluating and searching for specific ADRs. One reference that critically reviews the international literature is Meyler's Side Effects of Drugs, which provides information on reported ADRs and their management. Side Effects of Drugs Annual: A Worldwide Yearly Survey of New Data and Trends in Adverse Reactions *(www.elsevier.com)* is another review of ADRs that is updated annually. A secondary source of ADR information is the database Reactions Weekly *(www.adisonline.com)*; this publication is updated weekly and is the most current ADR information available with minimal lag time. Reactions Weekly provides reports from journals, scientific meetings, press releases, news from regulatory agencies, and information from more than 80 World Health Organization International Drug Monitoring Programme participants. In addition to case reports, Reactions Weekly includes labeling changes, drug withdrawals caused by safety concerns, ADR research, and current issues in drug safety.

Conclusion

Drug information and drug literature evaluation skills are vital for the pharmacotherapy specialist. Pharmacists can take the lead in providing DI to other HCPs and to patients and their families. The field of DI continues to evolve with new and better references, new applications for electronic devices, and new sources on the Internet. The pharmacist's skills in drug literature evaluation and EBM are even more important today given the breadth of information overload. Pharmacists should acquire techniques to find high-quality information to maximize patient care.

Knowing all the various resources available to both HCPs and the public allows the pharmacist to suggest quality sources of information. Good drug literature evaluation skills can be a necessary filter to ensure that EBM is being disseminated. Pharmacists can use their DI skills to participate in developing practice guidelines and monographs as part of the patient care team. They can also serve in the role of verifying information from credible sources and advising the team when information may be of poor quality or from references that do not meet acceptable standards. Pharmacists must rely on the best practices related to DI to benefit patients and HCPs and ensure high-quality services.

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ANSWERS AND EXPLANATIONS TO SELF-ASSESSMENT QUESTIONS

1. Answer: B
IPA is the best answer because it contains information specific to pharmacy as well as information presented at a pharmacy scientific meeting. Since this question requires information specific to an IV pump, the best source would be one that contains information specific to pharmacy. Ovid (Answer D) is a platform for MEDLINE (Answer C) which contains primary medical literature. IOWA also contains information regarding the primary medical literature.

2. Answer: A
MEDLINE, in-process is the best answer because this source contains those records that are not yet indexed with Medical Subject Heading (MeSH) terms. Since the pharmacist has not heard of the drug and the physician states the drug is new, one can assume that any information contained in MEDLINE is new. IDIS, PubMed and IPA do not publish in-process papers and posts papers once publication occurs.

3. Answer: C
The best step to take to limit erroneous data is to limit the sex to female. This would limit the MeSH for aspirin AND stroke to only those studies that included females. Using the subheading "therapeutic use" (Answer B) would not limit the data as much as restricting the search to the female gender since the question was specific to information in women. A restriction to publication type of "review" (Answer D) may limit the search too much and cause one to miss pertinent articles. Using a keyword search provides too many hits that are irrelevant and is not time efficient (Answer A)

4. Answer: A
MobileMicromedex contains all features of the desk top version of Micromedex. The other mobile platforms for Clinical Pharmacology, Epocrates (Answer B), Epocrates (Answer C), and Lexi-Drugs (Answer D) are currently limited and do not contain a specific drug interaction tool.

5. Answer: C
Restricting the search to Human and English only will result in the most efficient search strategy. Articles to be reviewed are those written in the English language in which Human subjects were tested. To limit to only clinical trials (Answer D) could result in selection of animal data.

6. Answer: B
Answer B is correct because the FDA Web site is going to have the most current ADR information that is either being reported by manufacturers or is detected via the pharmacovigilance program. The FDA site is a good site as a clinician to have e-mail alerts sent when new ADRs are reported. *http://www.fda.gov/Drugs/DrugSafety/ucm245011.htm* Answer A, www.clinicaltrials.gov, is not the best answer because usually these ADRs are not reported through a clinical trial. Although clinicaltrials.gov does have safety trials and this would be a good source to look at later in your searching strategy but it is incorrect because it is not considered a first-line resource for this question. For the PPIs and magnesium, there are case series and observational studies published in the literature starting in 2006 so a Medline search would show results but none were clinical trials and a search of clinicaltrials.gov through June 2011 results no trials found. Answer C, www.mayoclinic.com, is incorrect because this site is meant for health care consumers versus information for the health care professional. Answer D, www.clinicalevidence.com, would be incorrect because clinicalevidence.com provides guidelines and does not have cutting edge safety data on the site.

7. Answer: B
Clinicaltrials.gov will provide the best resource to find clinical trials in the area of multiple sclerosis that might be available in the United States due to this patients travel and medical expenses. Clinicaltrials.gov does cover trials from other countries but it provides a means to search within the United States by city and/or state. It also provides information on what type of patients would be eligible for the trials. If she has failed on interferons then the patient would be able to identify those trials that are using interferons and know those would not be an option. Answer A, WebMD, would be incorrect because WebMD is not the best resource to find information on investigational trials around the country. It is better suited for consumer educational purposes. Answer C is incorrect because the FDA

Web site is not the best resource for finding clinical trials. Answer D is a choice that could be considered but is incorrect when compared to clinicaltrials.gov. Controlled-trials.com actually contains clinicaltrials.gov with other international registries. However, this site is much more complicated and harder to search. It does allow you to just search clinicaltrials.gov as an option. An internet search took 5 times longer to search clinicaltrials.gov compared to search clinicaltrials.gov through controlled-trials.com. Since this patient is looking for trials in the United States then clinicaltrials.gov makes more sense from an efficiency standpoint.

8. Answer: A

Answer A is correct because providing the RDA for selenium each day is consistent with the findings from the Cochrane review. The data suggests that there is no benefit when exceeding the RDA especially when patients are taking doses that exceed 200 mcg/ per day which is why Answers B and C would be incorrect. Based on the evidence from Cochrane and the SELECT trial, one could argue that this level of supplementation of selenium is putting them at an increased risk. Lippman SM, Klein EA, Goodman PJ, Lucia MS, Thompson IM, Ford LG, et al. Effect of selenium and vitamin E on risk of prostate cancer and other cancers: the Selenium and Vitamin E Cancer Prevention Trial (SELECT). *JAMA* 2009;301(1):39-51.

Answer D is incorrect because the data does not suggest that selenium has to be completely removed when it is given at the RDA levels.

9. Answer: B

Answer B is correct because RCTs are a stronger study methodology and are usually considered to be better evidence or higher quality evidence when compared to observational study designs. So when evidence is conflicting between RCTs and observational studies, the conclusions from a well-designed RCT are usually considered superior. An OR is an estimate of relative risk but relative risk is still a measure from an observational cohort study design and is still not considered superior to a well-designed RCT. So Answer A is not the best answer. Answer C is incorrect because this just describes a problem with the observational data which has some truth to it when looking at two of the CI within the results. However, this again is the data taken from the observational studies and not the RCTs. Answer D is incorrect because the observational studies did take into consideration the gender of the patients and controlled for this in the results that were given in the review.

10. Answer: D

Answer D is correct because the two studies are very different in the type of patients and the type of cancers that they are evaluating. Therefore, it is difficult to combine this data to determine overall effect of selenium on cancers. This is a concern when completing reviews such as done by Cochrane as well as when researchers are looking at combining studies from methodologies such as meta-analysis. The Cochrane review on selenium points this vary issue out in its limitations related to the methodology. Answer A is incorrect because in these two studies the dose of selenium was the same even though the SELECT study had a second group that received vitamin E. Answer B is incorrect because the difference in sample size is not a major factor in this type of review. Sample size differences can present challenges with other types of studies. The key is not so much the sample size difference but rather whether the outcome variables were powered. The powering of the outcome variable is critically no matter the sample size. Answer C is incorrect because both of these trials were published and the Cochrane review was unable to detect any publication bias from studies that had been completed but not reported. Both the SELECT and the NPCT have had multiple publications with both study design and substudy results.

11. Answer: A

Answer A is the best answer because this Cochrane Review was published in May 2011 and stated in the review that the studies were up-to-date through April 5, 2011. The student would know to search the literature from that point on. PubMed offers the best choice to look for the most recent studies since it offers the in process feature as it adds studies and publications to the database(. http://www.ncbi.nlm.nih.gov/pubmed/). Answer B is incorrect because UpToDate would not necessarily be updating the system to include recently published studies on all topics in the database in a timely fashion. There is no guarantee that this would be updated for selenium with the latest information. Answer C is incorrect because Google is not set up to search for the latest studies on a topic and it can be

difficult to search because it does not provide the same searching strategies and limits strategies that PubMed offers. Also, Google does not offer an in process option. Answer D is incorrect because the FDA web site is not designed to provide the latest publication on a specific topic especially this type of topic.

12. Answer: D

Answer D is correct because www.guideline.gov provides a comprehensive listing of national and even some local clinical guidelines. This is a difficult subject that does not always lend itself to development of quality guidelines and actually presents a difficult search strategy in answering the questions. However, the best starting place is to see what other guidelines have been published in this area. Answer A is incorrect because Google does not offer a good way to search guidelines in one place. The searching algorithms for Google are not the most efficient means to search this topic. Google may provide some additional information later in the search strategy but is not the best place to start. Answer B is incorrect because WebMD is a consumer web site that is not intended to provide guidelines to health care professionals. Answer C is incorrect because controlled-trials.com is not a good resource for looking for national guidelines but rather provides a good resource for identifying controlled clinical trials. It could be considered later in the search strategy if one was looking from clinical trials or even economic trials related to the use of vitamin D. Other databases are available that provide better searching strategies for economic studies than controlled-trials.com.

13. Answer: D

Answer D is correct because it redirects the consumer to look at better sites and also provides them some tools when searching the Internet for health-related information. It provides a platform for the pharmacist to interact with the consumer and help guide them to better health information. This also allows a dialogue with the patient about looking at testimonials and blogs without appearing too critical of their choice of Web sites. Answer A and B are incorrect because they are more critical in nature and do not really provide an opportunity for the pharmacist to educate the patient and provide them with alternatives. Answer C is incorrect because WebMD may have a good discussion of atrial fibrillation but this does not directly answer the consumer's question related to the comparison of the drugs and it does not open a dialogue with the HCP.