Module 3: Finding the evidence: pre-appraised literature

Now that we have developed a usable base search query from our PICO, we are ready to find the evidence by searching the literature databases. As you proceed, keep in mind the hierarchy of study types.

To review: at the bottom are the observational studies that generally report anecdotal events. In etiology, causation, and harm scenarios, the cohort study is the best single study to use.

Our scenario involves a therapeutic intervention, so we should be searching for controlled trials, in particular the RCT, which provided the strongest empirical evidence of all the study types.

Atop the hierarchy are the systematic reviews which, of course, provide the strongest evidence, because their conclusions are based on several studies on a single topic.

Let's spend a few minutes discussing the review or "pre-appraised" literature. There are several types of reviews published in the literature, most are not systematic but present a discussion, or narrative, of the literature on a narrow or broad topic without drawing a conclusion.

Systematic reviews, on the other hand, address a specific clinical question and include an explicit (reproducible) literature search methodology. In addition, a systematic review draws conclusions about the quality of evidence found and, if possible, answers a specific clinical question.

A Meta-analysis is a type of systematic review that also examines a number of valid studies on a topic and combines the results using accepted statistical methodology as if they were from one large study. Many small studies do not have enough subjects to yield statistically significant results, whereas meta analyses pool the data of smaller studies to increase the statistical significance. Because of this, the meta analysis sits perched atop the evidence hierarchy.

Be aware, however, that systematic reviews are being created and published at a staggering rate. Over 15,000 reviews were published in the medical literature in 2009 alone. As a result, readers need to be vigilant about assessing their quality.

There are some excellent sources to find pre-assessed systematic reviews, where one can leave the job and time and effort of appraising the quality of the review to the experts and editors.

In the previous tutorial we have discussed one of the best places to look for top-notch reviews: the *Cochrane Database of Systematic Reviews*, which includes roughly 5000 reviews created by the Cochrane Collaboration.

Your search for good pre-appraised systematic reviews should not stop here. Here are some more resources that might be useful:

The *Database of Abstracts of Reviews of Effects*, also known as DARE, is a free resource that actually reviews systematic reviews found in the published literature (yes, reviews reviews). Editors of DARE scan

60 or so clinical journals and a handful of databases for high impact systematic reviews, and provide a structured abstracts with commentary about the quality of the review.

Here is a section of a DARE review relevant to our St Johns Wort scenario. Note how the commentary is focuses on the quality of the review.

Another good source for pre-appraised reviews is the *ACP Journal Club Database*. Similar to DARE, editors of the ACP Journal Club Database scrutinize a number of clinical journals (over 100) for reviews and important single studies that warrant the attention of clinicians. However, ACP does not offer much about the quality of review, but instead provides commentary about how a particular study or review adds to what is known about the particular clinical topic. Let's look at a section of an ACP Journal Club Review and note how it differs in tone and content from the DARE review.

BMJ's Clinical Evidence is one more place to look for pre-appraised reviews. This product contains a collection of systematic reviews on interventions for over 260 medical conditions. Each review describes the best available evidence from other systematic reviews, RCTs, and observational studies.

A Clinical Evidence review provides an excellent overview of a condition. In our case: **Depression in adults: drug and physical treatments**, with a list of potential interventions for the condition. We can click on an intervention of interest to get to a full review. Note how the review includes a summary of the intervention as well as sections on the benefits, harms, and a BMJ Clinical Evidence commentary. You may also be interested in the "updates" tab for new studies and reviews that have not yet been incorporated in this review.

If one is not able to find relevant reviews for a clinical question in these sources, there are several resources that can be utilized to find systematic reviews published in the health literature. Keep in mind that these reviews are not pre-appraised, so the burden is on the reader to assess quality. The best and largest resource for finding reviews is, of course, *PubMed*. You should all be well versed on how to enter a search query into PubMed and limit the results to systematic reviews.

There are several other sources for reviews out there. Here are two you may or may not know about:

International Pharmaceutical Abstracts or IPA includes 30 years coverage of the world pharmacy literature; plus, related health, medical, and cosmetic journals, and state pharmacy journals. IPA is unique in its coverage-no other resource provides this. The numerous references to alternative and herbal medicine are an example of this unique coverage and it good for our scenario.

TRIP (or *Turning Research into Practice*) is a free evidence-based database that allows the simultaneous searching of multiple sites. TRIP filters search results into both secondary literature (ebm sysnopses, systematic reviews, guidelines, etc.) and primary literature categories.

If you do uncover relevant reviews from PubMed or some of these other sources, as I mentioned, you need to spend a few moments appraising them. Here are some of the questions you might want to pose to assist in your assessment

- Does the review focus on one specific clinical question?
- Does the review include an explicit literature search?
- What types of studies were included? Were certain studies excluded? Why?
- Was there some form of critical appraisal performed? Were the inclusion, exclusion criteria explicit and applied?
- Were the interventions similar among the included studies?
- Were findings appropriately combined?

Even though this looks like a lot of work, authors of systematic reviews are often aware that readers will ask such questions and will, therefore, design reviews in ways that answer these questions. Let's look at an example:

Here is a meta-analysis from the *British Journal of Psychiatry* uncovered in the results of our PubMed search.

We can quickly assess this publication by skimming the review for answers to our questions.

Here is a section discussing the singular purpose of the review.

This section outlines how the studies were uncovered and specifics of the literature search.

Other sections inform us as to the studies types included and with the total number of trials and total participants and interventions used in the studies. Many reviews also add a helpful visual representation of the studies included and excluded.

A final section uses a nice forest plot to display the findings from each study.

Few would argue that utilizing the pre-appraised systematic review literature to answer a clinical question is most effective. However, keep in mind a few caveats about relying solely on the review literature:

- There are still many interventions not covered by systematic reviews. You will no doubt have clinical questions that are not answered by a review found in the literature.
- Systematic reviews are never really current. Since it take at the very least 6 months (sometimes years) to create a good systematic review, it is often the case that important, potentially significant, single studies have been more recently published.

You have completed Module 3