The principles of evidence-based medicine

By the end of this module you should be able to:

- Describe what evidence based medicine is
- Know where to find quality evidenced based medicine on the internet
- Be able to critically appraise a research paper

Doctors are now faced with an increasing body of information and a rapidly changing evidence base from which to guide their clinical decision making process. This can make it difficult to maintain up-to-date clinical practice and may result in heavy reliance on out-of-date undergraduate teaching, textbooks and anecdotal evidence from prior experiences. Evidence-based medicine is therefore a process of continued medical education which involves a systematic approach to finding, evaluating and implementing research findings as the basis for clinical decisions. It is about asking questions, finding and appraising the relevant data, and harnessing that information for everyday clinical practice[1].

Of course a doctor's expertise is still of great importance when making clinical decisions and should be combined with the principles of evidence-based medicine in order to provide optimum patient care and informed patient choice.

There are four steps in evidence based medicine[1]:

1. Formulate a clinical question
2. Search the literature for relevant clinical articles
3. Evaluate the evidence found
4. Implement useful findings into clinical practice

1. Formulate a clear clinical question from a patient's problem

   The question may relate to any aspect of patient care including diagnosis, prognosis and management. The scenario below is an example.

   A 32 year old lady is seen for her initial visit in the antenatal clinic at 16 weeks gestation in her 4th pregnancy. She has a poor obstetric history and all her pregnancies have been complicated by severe pre-eclampsia. In her first pregnancy she was delivered by cesarean section at 34 weeks due to pre-eclampsia and her son from that pregnancy is now 5 years of age and well. In her 2nd and 3rd pregnancies she was again delivered prematurely at 28 weeks and 27 weeks gestation respectively by cesarean section for fulminating pre-eclampsia, but unfortunately neither baby survived. Her sister also suffered from pre-eclampsia in her last 2 pregnancies and was given aspirin which she would now like you to prescribe her. You are unfamiliar with this topic.

   What kind of questions regarding the management of this lady with aspirin would you like to find out from the literature?

   Jot down some of your answers now.

   Does the use of aspirin reduce the risk of developing pre-eclampsia?
   Does the effect of aspirin differ if started before or after 20 weeks gestation?
   Does the effect of aspirin differ if high dose aspirin is used versus low dose?
   Does the use of aspirin in pregnancy result in increased risk of haemorrhage?
   Is there an increase in perinatal morbidity or mortality associated with its use?

   Now think about how you may go about finding the answer to these questions.

2. Search the literature for relevant clinical articles

   Unfortunately, although textbooks are an invaluable resource for updating and refreshing knowledge on a particular topic, they would have to be continually re-published in order to

include the most up-to-date information. Fortunately, wide access to the internet and improved computer literacy amongst doctors means that there is a wealth of information within reach.

Databases that can be used include:

- Medline
- Cochrane
- Knowledge finder
- Pubmed
- Embase

Once the references of relevant papers have been found, most of these databases will provide a link to the abstract of the paper and at times to the full text. Full texts can also be found as original paper copies in libraries.

3. Evaluate the evidence for its validity and usefulness

Once you have found a relevant research paper from your search, the next task is to be able to critically appraise the work that has been carried out. It is important to remember that not all research is valid, relevant or applicable to your own patient population. Therefore with the vast numbers of papers being published in journals each month, doctors must be able to pick out the most robust research and have the tools to be able to relate the results back to their own patients.

Here are some questions that you may want to ask yourself when appraising a research paper.

- Methodology:
  - What **type of study** is this?
  - If it is a randomised trial were the participants and/ or researchers **blinded**?
  - What is the main question (**outcome**) that this study is tying to answer?
  - Are there clearly-defined **selection criteria** for which patients were included and excluded?
  - Was the study adequately **controlled**?
  - Are there any obvious **biases** in the way the patients were selected or in the way that data was collected?
  - Have they clearly described every aspect of the methodology so that the study could be reproduced?

- Results:
  - Are all patients that were included into the start of the study accounted for?
  - Is there any missing data?
  - Were the groups comparable in all important aspects except for the variable being studied?
  - If not has this been accounted for?
  - Are there any obvious **confounding** influences?
  - Was the study large enough to make the results valid (See statistical tools- **power**)?
  - Was the study continued for long enough and was follow up complete enough to make the results credible?

- Discussion
  - Are the results discussed with reference to other important literature?
  - Do the discussion and conclusions speculate far beyond what has been shown in the study?

- Generalisability:

- The results of the study may not be generalisable to your patients even if the study had a sound methodology. For example a study showing benefit of an intervention in Swedish women aged 20-30 years may not be relevant to older women in Sub-Saharan Africa.

Now jot down some ideas of how you would design a trial to answer the first question from the previous example (Does the use of aspirin reduce the risk of developing pre-eclampsia?) using the important points above.

Here is a link of a paper published in the Lancet in 2007 regarding aspirin use and the risk of pre-eclampsia.

CLASP: a randomised trial of low-dose aspirin for the prevention and treatment of pre-eclampsia among 9364 pregnant women. CLASP (Collaborative Low-dose Aspirin Study in Pregnancy) Collaborative Group. Lancet. 343(8898):619-29, 1994.

How does your design compare to their methodology?

What are some of the good and bad points of this paper?

The Cochrane library contains reviews that analyse the results from many different trials in order to provide information on possible healthcare interventions. See a review by Duley *et al*. (2007)[2] for a review on the use of aspirin in preventing pre-eclampsia.

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4. Statistical tools required for critical appraisal:

- **Power**:
  - The power of a trial is determined using a mathematical calculation that tells us if the number of patients enrolled in the trial is sufficient to detect a difference between treatment arms. It estimates the ability of a trial to detect a statistically significant difference of a particular size between the treated and control groups.

- **Number needed to treat**
  - The number needed to treat (NNT) is an epidemiological measure used in assessing the effectiveness of a health-care intervention, typically a new treatment.
  - The NNT is the number of patients who need to be treated in order to prevent one additional bad outcome.
  - For example in the MAGPIE trial the NNT was 91. That is the same as saying 91 women need to be treated with magnesium sulphate to prevent one eclamptic fit.
  - It is defined as the inverse of the absolute risk reduction

- **Attributable risk**
    - Attributable risk is the disease rate in exposed persons minus that in unexposed persons.

- **Relative risk**
    - Relative risk (RR) is the risk of an event (or of developing a disease) relative to exposure. Relative risk is a ratio of the probability of the event occurring in the exposed group versus a non-exposed group.

$$RR = \frac{p_{\text{exposed}}}{p_{\text{non-exposed}}}$$

    - Relative risk is less relevant to making decisions in risk management than is attributable risk as it does not take into account the absolute risk of the condition.
    - For example, if given a choice between a doubling in their risk of developing pre-eclampsia or a doubling in their risk of developing acute fatty liver of pregnancy, most informed people would opt for the latter. The relative risk is the same (two), but the corresponding attributable risk is lower because acute fatty liver of pregnancy is a rarer disease.

- **Absolute risk**
    - Absolute risk is the chance of a person developing a specific disease over a specified time-period.
    - For example, let's say in a group of 20,000 women, 1,600 develop endometrial cancer over 50 years. The risk of any one individual getting this disease would be 1,600 divided by 20,000 or 0.08. That means that the absolute risk would be 8 percent or 8 in 100.

- **Odds ratio**
    - The odds ratio is a way of comparing whether the probability of a certain event is the same for two groups.
    - It is calculated by dividing the odds in the treated or exposed group by the odds in the control group.
    - An odds ratio of 1 implies that the event is equally likely in both groups. An odds ratio greater than one implies that the event is more likely in the first group. An odds ratio less than one implies that the event is less likely in the first group.
    - For example, on average 51 boys are born in every 100 births, so the odds of any randomly chosen delivery being that of a boy is:
    - Number of boys 51 / number of girls 49, or about 1.04.
    - We could also have calculated the same answer as the ratio of the baby being a boy (0.51) and it not being a boy (0.49).

5. Implement useful findings in clinical practice

Once the paper has been evaluated and has been deemed valid and relevant doctors can use this information in a number of ways:

- Use findings to directly alter a patient's care
- Develop team protocols and hospital guidelines.

- Use the evidence as a basis for audit.

A good way to ensure continued professional development in this way and to maintain evidence based practices in your department is to set up a journal club. A journal club is a group of individuals who meet regularly to critically evaluate recent articles in scientific literature. Each meeting is usually organized around a defined subject in basic or applied research.

Summary of learning points:

- Evidence based medicine is part of continued professional development and involves the systematic appraisal of research in order to improve our clinical practice.
- It needs to be combined with clinical experience and expertise and tailored to your individual patient.
- Results of research papers may be invalidated by poor methodology or statistical analysis and may be irrelevant to your patient population. Identifying good quality research relies on the ability to appropriately interpret their results and apply them appropriately.
- Journal clubs are a good way of keeping up-to-date and practicing critical appraisal skills.

References:

1. Evidence based medicine: an approach to clinical problem-solving. W Rosenberg et al. BMJ 1995;310:1122-1126

2. Duley L, Henderson-Smart DJ, Meher S, King JF. Antiplatelet agents for preventingpre-eclampsia and its complications. *Cochrane Database of Systematic Reviews* 2007, Issue 2. Art. No.: CD004659. DOI:10.1002/14651858.CD004659.pub2.

Useful website:

http://www.cebm.net/

Further Reading:

Heneghan C. and Badenoch D.:(2006) Evidence-Based Medicine Toolkit, 2nd Edition
Straus S.E. et al. (2005): Evidence-Based Medicine: How to Practice and Teach EBM. 3rd Edition
Evidence based medicine: what it is and what it isn't. D Sackett et al. BMJ 1996;312:71-72
Rose G, Barker DJP. Epidemiology for the uninitiated. 3rd ed. London: BMJ Books, 1993.
How to read a paper: getting your bearings (deciding what the paper is about). T Greenhalgh. BMJ 1997;315:243-246