**Session 8 - Evidence Based Medicine**

Welcome to the session on Evidence Based Medicine (EBM) which is designed to provide an introduction to the topic. You will be introduced to different types of studies that you can gather evidence from, with an emphasis on randomized controlled trials (RCT) and systematic reviews (SR) and an introduction to meta-analysis. You will also watch a video by Maureen Dobbins to improve your understanding of meta-analyses. With tools presented in this session you will have an opportunity to evaluate clinical literature systematically and scientifically, focusing on randomized controlled trials and on systematic reviews. Evidence Based Medicine is useful in decision making for selection of medicines for standard treatment guidelines and essential medicines lists.

**Session Contents:**

Session 5 will cover the following topics:

1. Introduction to Evidence Based Medicine
2. Obtaining high quality evidence
3. Presenting the evidence
4. Critical appraisal of an article
5. Session Summary
6. References and further reading

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| **Learning Outcomes**By the end of this session, you should be able to:* Apply the concept of evidence based decision making
* Apply the concept of evidence based medicine
* Assess whether a study design is most appropriate to answer the research question investigated
* Evaluate the quality the chosen study design
* Understand the importance of critically evaluating clinical medicine literature
* Appraise a journal article to see if it contains all key components that allow drawing the conclusion stated in the article
* Evaluate if strengths, weaknesses and/or biases of the study design are considered in the journal article reporting on the study
* Interpret key results of a clinical study
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**Readings**

Cook, D*. et al* (2011). Dalteparin versus unfractionated heparin in critically ill patients. *New England Journal of Medicine* 2011; 364:1305-14. Masachusetts Medical Society.

Available at: http://[RCT Paper\_Daltepari\_vs\_unfractionatedHEP.pdf](file:///C%3A%5CUsers%5CUser%5CDocuments%5CSoPH%5CMedicines%20Modules%5CRMU%5CSession%208%5CRCT%20Paper_Dalterpari_vs_unfactionatedHEP.pdf)

Darlenski, R. B., Neykov, N. V., Vlahov, V. D., & Tsankov, N. K. (2010). Evidence-based medicine: Facts and controversies. *Clinics in dermatology*, 28(5), 553-557. Available at <http://derm.hsl.washington.edu/wp-content/uploads/2010/12/ebm.pdf>

Monami, M., Lemanna, C., Marchionni, N. & Mannucci, E. (2007). Comparison of different drugs as add-on treatments to metformin in type 2 diabetes: a meta-analysis. *Diabetes Research and Clinical Practice*. (2008) 79: 196-203. Elsevier. Available at: http://[SR Paper\_Monami et al\_metformin.pdf](file:///C%3A%5CUsers%5CUser%5CDocuments%5CSoPH%5CMedicines%20Modules%5CRMU%5CSession%208%5CSR%20Paper_Monami%20et%20al%20-%20Metformin.pdf)

**Other Resources:**

Video on ‘forest plots’ by Maureen Dobbins:

<https://www.youtube.com/watch?v=KvtEuaKzq5A>

**1 INTRODUCTION**

What is evidence based medicine?



The concept of Evidence Based Medicine (EBM) dates from the middle of the 19th century in France. In 1990 Dr Gordon Guyatt from McMaster University in Canada first coined the term EBM and defined it as “the process of integrating individual clinical expertise with the best available external clinical evidence from systematic research” (Sur, R. *et al.* 2011, p 1). To get an overview of EBM and its origin, we suggest you read this article, “[Evidence-based medicine: Facts and controversies”](http://derm.hsl.washington.edu/wp-content/uploads/2010/12/ebm.pdf) available at:

 <http://derm.hsl.washington.edu/wp-content/uploads/2010/12/ebm.pdf>

Sackett, *et al* (1996) defined evidence based medicine as “the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients” (Sackett, D.L. 1996, p71). One can further define EBM as the process of systematically reviewing, appraising and using clinical research findings integrated with patient values and clinical expertise to aid the delivery of optimum clinical care to patients (as shown by Figure 1 below).



**Figure 1: The triad of Evidence Based Medicine. Source: Florida State University, College of Medicine**.

<http://community.cochrane.org/about-us/evidence-based-health-care/>

Retrieved 27.02.15

**2 OBTAINING HIGH QUALITY EVIDENCE**

Conceptually, evidence starts simply with what is observed. Every individual observation is an isolated piece of evidence. To generate evidence of high quality, it is important to compile, organize, and evaluate those individual observations in a systematic way. The McMaster model of EBM states 5 key steps that one can follow to obtain high quality evidence. These are:

1. Asking the right question;
2. Accessing the relevant evidence;
3. Appraising the evidence for validity and clinical importance;
4. Applying the evidence to patient care to see if it is feasible and acceptable;
5. Assessing clinical practice regularly.

We will now look at each step in turn and give more information on how the step is performed.

**2.1**. **Asking the right question**

For you to access the best evidence regarding a particular situation or problem, you need to have a clear understanding of the question you want to address. To make sure that the question is clear, you can use the conventional way of formulating a clinical question using the PICO elements:

P: the patient *population*;

I: the *intervention* (medicine, condition, risk or test) you are interested in;

C: the *comparative* medicine/intervention or group;

O: the *outcome* of interest

*Example 1*:

Question: *Does zinc improve symptoms for the common cold?* Do you think this question is clear? I would argue that it is not. Let us therefore use the PICO elements as defined above to help refine our question:

P: children below the age of 5

I: zinc syrup

C: no treatment

O: alleviation of the common cold symptoms.

New question: *In children residing in the Cape Metropole below the age of 5, does the use of zinc syrup versus no treatment alleviate symptoms of the common cold during the winter season?*

When formulating your question it is important to fully describe the patient population e.g. in the above example the initial question did not state whether the question was addressing the problem in children or adults, while the second question clarifies the population for us. You can see from the new question that the population has been described in more detail in that the person (children under 5 years), place (Cape Metropole), and time (winter season) have all been specified.

**NB**: the patient population could also be a *problem* for some questions; the intervention could also be an *issue*; not all questions will have a comparator; and ALL questions will have an outcome. The intervention is mainly used for experimental studies; while in observational studies it will either be an issue or an “exposure” (which may also be referred to as the risk factor/variable).

***Activity 1: Formulate a clinical question using the PICO elements.***

*Think of a clinical question related to medicines use relevant to your situation, and use the PICO elements to analyse whether the question is specific enough. Adjust the question accordingly if it is not. You will be asked to comment on your question and the process of designing it, in the Discussion Forum.*

**2.2**. **Accessing the relevant evidence**

Once you have formulated your clinical question, you need to then find relevant literature (commonly known as clinical evidence) to answer your question. Remember that this literature must be recent and up to date. There are a number of sources that you could search to access clinical evidence. These are:

1. Bibliographic databases
* The Cochrane Central Register of Controlled Trials (CENTRAL)
* PubMed (To access the MEDLINE database)
* Embase
* National and regional databases e.g. African Index Medicus
* Subject specific databases
* Citation Indexes
* Grey literature database
1. Journals and other non-bibliographic database sources
* Full text journals available electronically.
* Hand-searching
* Conference abstracts or proceedings.

Clinical evidence that you will obtain from these sources will be in the form of reports and articles. These articles and reports provide information on studies with different study designs which have different qualities of evidence.

**2.2.1 Study designs**

A study design is basically the manner in which a research study is conducted. Study designs can be experimental or observational, and the quality of evidence produced by the study design is highly dependent on the manner in which the study was conducted. Let us now differentiate between experimental and observational studies as well as the units of analysis for these studies (Figure 2). In experimental studies, researchers are testing an intervention i.e. researchers will give the intervention to participants to test if it works; while in observational studies researchers do not actively intervene but merely “observe” what is already happening or what happened in the past.

Analytic Study

Descriptive Study

*(Individuals)*

Community Randomized Trial

*(Communities)*

Randomized Controlled Trial

*(Individuals)*

Ecological Study

*(Groups)*

* Cohort Study
* Case controlled Study
* Cross sectional Study

*(Individuals)*

Experimental Study

Observational Study

Type of Study

**Figure 2: Study designs and their units of analysis.**

\*\* Unit of analysis: the study design will answer the question of interest for *individual* participants, or *communities*, or *groups*. \*\*

We use study designs to answer different kinds of questions.

For instance if it is a:

* *Treatment* question - ideally we would use a *randomized controlled trial*.
* *Diagnostic* question - ideally we would use a *cross sectional study*.
* Question *assessing risk -* we would use a *cohort study* (prospective or retrospective) OR a *case control study*.

We will now look at the key features for all study designs using the illustration below:

Exposure Assigned?

 Yes No

Experimental Study Observational Study

*Random Allocation?* *Comparison Group?*

Yes No Yes No

RCT Non-RCT Analytic Study Descriptive Study

 Cross Sectional Study

 Direction of Enquiry

*Exposure to Outcome Outcome to Exposure Exposure & Outcome*

 *same time*

Cohort Study Case Control Study Cross Sectional Study

**Figure 3: Key features of study designs**

Figure 3 gives an overview of how we decide which study design is most appropriate to answer a clinical question. As stated earlier, in experimental studies we test an intervention (which some writers will also refer to as an exposure). In observational studies we do not intervene or subject our participants to a certain exposure, we basically observe what is there, taking into consideration the timing of the study and the exposure status.

We will now give a brief overview of the different study designs that can be used to collect evidence. We will commence with the studies that collect primary data, starting with the ones providing the strongest evidence, up to those providing very weak evidence. Then we will discuss systematic reviews which compile primary data from several studies with similar study designs; and data may then be pooled into a meta-analysis. The systematic review with or without meta-analysis will produce secondary data.

On the following pages we will discuss each study design. The different study designs report their findings using certain statistical measures.

1. **Randomized Controlled Trials**

A randomized controlled trial (RCT) is the “gold standard” of research designs. In a basic RCT participants are randomly selected (i.e. have an equal chance of being in either group) into two groups. The one group receives the intervention (*treatment group*), and the other group does not (*placebo/control group*). For an example, in cases where a new medicine is being tested, the treatment group will receive the new medicine, while the placebo group receives the existing standard of care. Some researchers may refer to the groups as study arms. Treatment given to participants in the two groups is concealed (*allocation concealment*) such that participants will not know which study arm they were allocated to. The random selection of participants and allocation concealment minimize bias to a great extent, hence rendering RCTs the “gold standard” of research designs as it is difficult to minimize bias in the other study designs.

Participants are then followed up in time in a similar manner (both treatment and placebo group), with controlled procedures, to see if the intervention will have an effect. In this way we are then certain that whatever outcome (e.g. improvement in symptoms) observed in the treatment group at the end of the follow up period is due to the treatment given.

To analyse (measure the relationship between intervention and outcome) RCTs we use *risk ratios*.

1. **Cohort Studies**

These studies are also called “follow-up” OR “longitudinal studies” OR “incidence studies”. With this type of study we start with a group of participants who do not have the outcome of interest but are at risk of developing it. Cohort studies thus measure incidence (new people who develop the disease/outcome). Participants must have the same exposure status for them to qualify to be in a cohort. Hence for this study design participants are recruited according to their exposure status. Cohort studies can be:

* Prospective: participants without the outcome are selected now, and followed up to see if they develop it. *For an example, a group of women aged 18 years and above with no signs/symptoms of breast cancer are recruited into a study. These women are followed for 5 years, at the end of which they are examined for breast cancer*.
* Retrospective: the group of participants is recruited now but followed back in time to see if they were exposed for them to have the outcome. For this kind of study we can conduct a patients’ record review.
* Concurrent: the group of participants was assembled in the past, some follow-up took place in the past, and some is taking place into the future. This type of cohort design is useful for short exposures with long term outcomes.

To measure the outcome (analysis) in cohort studies we use *incidence rates*, and *risk ratios*. A risk ratio is often the ratio of two incidence rates.

1. **Case control studies**

Case control studies are retrospective in nature (i.e. we are looking at people who have the outcome/disease to ascertain what they were exposed to), meaning that the direction of enquiry is from the present to the past. We therefore select a group of participants with the disease (cases), and a group of participants without the disease (controls). The controls must be similar to the cases in all aspects (e.g. age, sex, economic status) except that they must not have the disease of interest.

This study design is good for rare diseases; and participants are selected according to disease status (as opposed to cohort studies where participants are recruited according to the exposure status). To analyze case control studies we use *odds ratios*.

1. **Cross sectional studies**

Cross sectional studies are also referred to “prevalence studies” OR “cross sectional surveys”. In this design, the relationship between an exposure and disease in a population is measured at one point in time (“snapshot”). Hence, this design reports the number of people with the disease in that population at that particular time when the study is conducted. The relationship between exposure and outcome is reported using *prevalence ratios*.

1. **Case series**

A case series is an observational descriptive study that follows a group of patients who have a similar diagnosis or who are undergoing the same procedure over a certain period of time. This design does not test a relationship between exposure and outcome, but is very useful in generating a hypothesis that can be further explored with more rigorous study designs.

1. **Case reports**

A case report is a detailed report of an individual patient’s symptoms, diagnosis, treatment, and follow up. It does not generate any evidence as it does not test the relationship between exposure and outcome, but information gathered from a case report can generate a hypothesis.

1. **Systematic Reviews and Meta-analyses**

Laxmaiah *et al* (2009, p 930) define a systematic review as a study design that “attempts to collate all empirical evidence that fits pre-specified eligibility criteria in order to answer a specific research question”. As is the case for a randomised controlled trial the design of the review will be submitted in a protocol before the systematic search and analysis of scientific literature happens, specifying all steps listed below.

As stated earlier systematic reviews generate high quality evidence that can be applied in the management and care for individual patients. Systematic reviews are generated by bringing together a group of studies investigating the same problem or research question to collate information found by individual studies. Thus you can have a systematic review of several randomized controlled studies (in many cases these generate the highest quality of evidence), of several cohort studies, of case control studies, or a combination of studies with different study design. Generally systematic reviews are not common for other types of studies (case series, case reports) because there is less sense in pooling these data and often such studies generate weak evidence on their own.

Listed below are the key steps each systematic review has to go through:

* A clearly stated set of objectives with predefined eligibility criteria;
* An explicit reproducible methodology:
	1. research question,
	2. search terms to use,
	3. search strategy,
	4. who will search,
	5. on which databases will the searches be done,
	6. the analysis that will be carried out with the results of the searches,
	7. biases that will be investigated and reported on.
* A systematic search that attempts to identify all studies that will meet the eligibility criteria;
* An assessment of the validity of the results of included studies;
* A systematic presentation, and synthesis of the characteristics of findings of the included studies.

This step by step approach used for systematic reviews is similar to the approach we would use to search and appraise evidence to answer a clinical question or evaluate a new medicine.

*When it is possible to pool comparable data* of several studies in a systematic review, a**meta-analysis**can be undertaken. A meta-analysis is the use of statistical methods to summarize the results of independent studies included in a systematic review (Liberati, Alessandro 2009). Because the sample size of study subjects of several studies will be larger than that of each individual study, meta-analyses provide more precise estimates of treatment effect, and allow a better judgment if a treatment effect has – or has not occurred by chance. They not only provide information on the significance of the treatment effect but go further to give information on the magnitude (how strong) and direction (positive or negative) of the effect. The direction and magnitude of the treatment effect is reported visually through a *forest plot*. To get a better understanding of forest plots, watch the [video by Maureen Dobbins](https://www.youtube.com/watch?v=KvtEuaKzq5A), a scientific director at the National Collaborating Centre for Methods and Tools. [www.youtube.com/watch?v=KvtEuaKzq5A](file:///C%3A%5CUsers%5CUser%5CDocuments%5CSoPH%5CMedicines%20Modules%5CRMU%5CSession%208%5Cwww.youtube.com%5Cwatch%3Fv%3DKvtEuaKzq5A)

Listed below are reasons for us to conduct meta-analyses:

* To increase power
* To improve precision
* To answer questions not posed by individual studies
* To settle controversies arising from apparently conflicting studies, or to generate new hypothesis.

**NB:** *Since systematic reviews and meta-analyses generate the highest quality of evidence, they are therefore used in evaluating medicines to select optimal treatments*.

**2.3 Appraising the evidence for validity and clinical importance**

When evaluating scientific evidence we look at **three main aspects**:

- **methodological** quality (what are the strength or weaknesses of the study design, are there any biases linked to the design or how the study was rolled out)

- **reporting** quality (is the data correctly interpreted, are missing data addressed, did analyses happen in a scientifically sound way?)

- the size of the **effect** and its significance for the entire population

**2.3.1 Quality of the evidence**

Having looked at the study designs, let us now look at the quality of clinical evidence generated by these studies. Figure 4 illustrates the different levels of evidence generated by different types of study designs.



**Figure 4:** **Hierarchy of evidence in clinical studies**

<http://boneandspine.com/what-is-hierarchy-of-evidence/>

From Figure 4 we can deduce that background information or expert opinions generate weak evidence, while systematic reviews and meta-analyses present the best evidence that we can confidently apply in caring for our patients.

An observation on a single event can constitute weak evidence (case report); while a more organized compilation of several observed events (case series) can constitute a higher level of evidence. An observation to evaluate the effects of an exposure and outcome at the same time (“snapshot” of events) also generates evidence which is still weak. An even more organized way to evaluate an event or an intervention is to give an intervention or exposure to participants, especially in a randomized controlled trial (RCT), and follow them over time to see if they develop the outcome. A systematic review provides even higher quality evidence by systematically grouping together and synthesizing the results of multiple large, well-conducted randomized controlled trials. Furthermore, a group of systematic reviews can generate a meta-analysis which is the highest level of evidence.

Thus, the more systematic the approach taken to gather and organize evidence, the higher the quality of the evidence. All studies allow a certain level of evidence as long as each aspect is looked into ranging from the individual anecdote up to the meta-analysis in systematic reviews of large, well conducted randomized controlled trials.

**2.3.2 Validity**

For purposes of this module we will mainly concentrate on randomized controlled trials as our clinical study, though the issues discussed in this section generally apply to all study types. So, let us discuss information that we need to be aware of to help us decide whether we can trust the results generated by a study.

The main issue that we will consider is the study **validity**. The validity of a clinical study is defined as the degree to which one can draw a conclusion about the effects of an intervention/medicine from a study. To determine the validity we need to take into account the *study methods*, *how representative of the target population the sample is*, as well as the *nature of the population from which the sample was drawn.* Study validity can be broken down into two components:

1. Internal validity: which is the extent to which a study reflects the truth, aside errors made during the sampling process. Internal validity is determined by the degree to which bias has been reduced through rigorous methods used in the study. Listed below are factors that could affect internal validity:
2. Confounding – mixing of effects of risk factors (exposure and another risk factor) in the occurrence of the disease (outcome).
3. Systematic error – deviation of results from the truth due to systematic flaws in the conduct of the study (***bias***).
4. Random error – deviation of results from the truth due to chance.
5. External validity: this is also referred to as the generalizability of study findings. It is the extent to which the results obtained from the study sample apply to the population from which the sample was drawn.

**2.3.3 Bias**

Let us now discuss the term bias further to get more understanding of what it is and how it can affect findings/results from a clinical study. Biasis a systematic error in a clinical study that results in an incorrect estimation of the association between an intervention/medicine and the disease (outcome). The reliability of results of a clinical study depends on the extent to which potential sources of bias have been avoided. Bias ultimately leads to underestimation or overestimation of the true treatment effect.

Bias can be introduced at various stages during the conduct of a clinical study:

1. During selection of participants

*-Selection bias*: systematic differences between the baseline characteristics of the groups (treatment and control group) that are compared.

1. During the conduct of the study

-*Performance bias*: systematic difference between the groups in the care that is provided.

-*Attrition bias*: systematic difference between groups in withdrawals from a study.

-*Information bias*: systematic difference in the way data on exposure or outcome is obtained from various groups.

-*Detection bias*: Systematic difference between groups in how outcomes are determined.

1. Reporting study findings

-*reporting bias*: systematic differences between reported and unreported findings.

If we read through the study and the researchers report how they controlled for bias, confounding, random error etc. and we are convinced that these were reduced to a great extent; we can conclude that the results are valid.

**2.4 Applying the evidence to patient care to see if it is feasible and acceptable**

Having looked at the first 3 steps to be followed in obtaining high quality evidence, we will now look at how we can decide whether to trust the results of a study and apply them in caring for our patients. For us to trust the results we need to answer three main questions: what are the results (effect size); do the study results apply to the population (making inferences); and how can we apply the results to patient care?

1. *What are the results? (The effect size)*

For us to answer this question we need to know the size of our treatment effect (measure of the relationship between exposure and outcome). We tend to use RR in RCTs and cohort studies; and OR in case control studies. Note that we will not go into detail calculating these measures. We are just showing the formulae to help you understand article results that report on the measures. To get a better understanding of RR and OR we suggest you read this [biostatistics document](https://www.biostat.wisc.edu/~kendzior/STAT541/lc4.short.pdf) attached.

For randomized controlled trials we use the relative risk (which will ultimately be reported in a systematic review if that particular RCT is included) to measure the effect size.

The **Relative Risk** **(RR)** represents the probability of something happening (i.e. risk) e.g. death, hip fracture with the intervention studied as compared to without the intervention. It is the probability that a member of an exposed group will develop a disease relative to the probability that a member of an unexposed group will develop that same disease*.*

RR = P (disease|exposed)

 P (disease|unexposed)

*\*\*RR ≈ 1 ⇒ association between exposure and disease unlikely to exist.*

*RR > 1 ⇒ increased risk of disease among those that have been exposed.*

*RR < 1 ⇒ decreased risk of disease among those that have been exposed.\*\**

Below are other risk measures that can also be used and reported in RCTS:

* 1. Relative Risk Reduction (RRR)

The proportional reduction in rates of events between experimental and control groups.

RRR = ([event rate control - event rate treatment] / event rate control) x 100

* 1. Absolute Risk Reduction (ARR)

The difference between the probabilities of an event in experimental group and control groups.

ARR = CER- EER

**Table 1: Summary of risk and risk reduction results**.

|  |  |  |  |
| --- | --- | --- | --- |
| Measure | Equal Effect Between treatment and Placebo group | Improved Benefit (favours treatment) | Decreased Benefit |
| RR | 1 | <1 | >1 |
| RRR | 0 | >0 | <0 |
| ARR | 0 | >0 | <0 |

* 1. Number Needed to Treat (NNT)

In a study that compares treatment with a comparison, the number needed to treat is the number of patients that need to be treated to prevent one additional bad outcome (e.g. stroke, death etc.). To calculate NNT, you need to know the absolute risk reduction (ARR) as NNT is the inverse of ARR:

NNT = 1 / ARR

*NB: ARR = CER (Control Event Rate) – EER (Experimental Event Rate).*

*NNTs are always rounded up to the nearest whole number.*

A second measure of effect size which can be reported is the **odds ratio (OR).** The OR is the odds of disease among exposed individuals divided by the odds of disease among unexposed i.e. is the number who participants who experience events to the number of participants who have non-events.

OR = P(disease|exposed)/(1 − P(disease|exposed)) i.e. odds in experimental group

 P(disease|unexposed)/(1 − P(disease|unexposed))i.e. odds in control group

*b. Do the results from the study sample apply to the population? (Making inferences)*

Once the effect has been measured we need to then determine how precise that effect is; and for this we use ***confidence intervals***. We also need to determine if the result is due to chance or if it is statistically significant (***p*-value**). Before we go into detail about these issues let us first look at why we need to do this for our clinical study by introducing the concept of testing a hypothesis.

In a clinical study (RCT) there is a hypothesis to be tested. We are interested in knowing whether the medicine of interest is superior or safer or otherwise different from another comparative medicine or placebo. The null hypothesis (H0) will therefore say that *there is no difference between the medicine of interest and a comparative medicine or placebo.* To reach a decision on whether to reject the null hypothesis or not we take into consideration *p*-values and confidence intervals. A *p*-value is the probability of rejecting the null hypothesis when that hypothesis is actually true. *p*-values of less than 0.05 (1 chance in 20) are used by convention to show that the results of the study are not the result of chance (i.e. the result is statistically significant). The *p*-value on its own only judges statistical significance of a result but does not tell you anything more on clinical significance; hence we also use the 95% confidence interval (CI) to provide an estimation of the effect size that allows you to judge the clinical significance. The 95% CI is a range of values within which lies the *measure of effect* with 95% probability.

Since it is not possible to include all members of the target population in a study, we draw a sample from the population. Results from this sample must however be inferred to represent what the result would have been if all members of the population were in the study. The 95% CI can therefore be defined as follows: if the same study (i.e. same sample size, from the same population, using exactly the same methodology) was to be repeated a hundred times, 95% of similarly constructed confidence intervals will contain true *population* (note the population and NOT sample) value. In simple terms we can define the 95% CI as: “We are 95% sure that the CI (range) contains the true value of the *measure of effect* in the population”. [http://www.statsdirect.com/help/default.htm#basics/confidence\_interval.htm Accessed 5Mar15](http://www.statsdirect.com/help/default.htm#basics/confidence_interval.htm]. Accessed 5Mar15).

*If the CI includes* the point of no difference between medicine of interest and placebo/comparative treatment (i.e. RR = 1), we do not reject the null hypothesis. However, if *the CI does not include 1*, we reject the null hypothesis and conclude that there is a difference between medicine of interest and placebo/comparative treatment. For clinical studies, the larger the sample size, the smaller the CI, and the more confident we are that these results are reliable.

*C. How can we apply the results to patient care?*

In deciding whether we can apply the results in caring for patients in our settings we need to ask ourselves the following questions:

* Were the study patients similar to my patients?
* Were all patient–important outcomes considered?
* Are the likely treatment benefits worth the potential harm and costs?

If the answer is “yes” to all questions, and we agree with the results (as discussed in I above) we may then confidently apply the results.

**2.5 Assessing clinical practice regularly.**

This is now the final step in obtaining high quality evidence. Having done the previous steps we need to frequently check if we are following guidelines in caring for our patients. This helps in identifying areas of care that can be improved and as well identifying gaps in knowledge that can be filled.

This step is particularly relevant to the use of medicines as treatment protocols, including standard treatment guidelines, change overtime as new treatments and medicines become available.

**3 PRESENTING THE EVIDENCE**

As mentioned earlier, research studies are generally reported as scientific journal articles; and all articles are generally structured using following important components:

* Abstract – summary of the study
* Introduction – background information on what the study is about as well as literature on similar studies that have already been done.
* Methods – how the study was conducted.
* Results – findings of the study.
* Discussion – what the findings mean and whether these findings are in line with existing literature.
* Conclusions – summary of findings.
* References – literature used in writing the article
* Acknowledgements – sources of help e.g. funding during the conduct of the study.

**4 CRITICAL APPRAISAL OF AN ARTICLE**

We critically appraise articles by systematically evaluating them for effectiveness, efficacy, and validity. We do this appraisal in order to answer these questions:

1. Does this study address a clear and focused question?
2. Were valid methods used in addressing this question?
3. Are the study results valid?
4. Are the study results important?
5. Can these results be applied to my population or patient?

There are tools available for critically appraising articles of all types of study designs, and you will use two to appraise two study designs (RCT appraisal sheet and SR appraisal sheet). You can find these under course resources.

***Activity 2 – Critically appraise an RCT article***

*In this activity you will use standardized tools for a randomized controlled trial (RCT) to critically appraise an RCT article. You can choose between two options, (a)* ***or*** *(b) for this activity. Send your answers to the session convenor via File Sharing and you will be given feedback.*

*a) Read the paper by Cook et al, (2011), and use the RCT critical appraisal tool to decide if the study and article are of good quality.*

***or***

*b) Read the systematic review by Monami et al, (2008), and use the SR critical appraisal tool to decide if the systematic review and article are of good quality.*

**5 SESSION SUMMARY**

This session has introduced you to EBM which is an important component of decision making with regard to selecting medicines to be included/excluded from guidelines (STGs), formularies and medicines lists (EML) to help improve rational use of medicines. The critical appraisal skills you have practiced in this session form key aspects of PTCs (to be covered in subsequent sessions).

**6 REFERENCES AND FURTHER READING**

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