CIRS and Evidence Based Medicine (EBM)

As the name suggests, evidence-based medicine (EBM), is about finding evidence and using that evidence to make clinical decisions. Being able to read, understand and analyze research studies is a critically important skill every clinician treating patients hands on, needs to have. I can vividly recall during my advanced clinical doctorate, EBM and critical analysis was the bane of existence for almost every student. Students were failing this course constantly. Our professor requested two of us students to help him tutor the entire class of 24 doctoral candidates and we did. It was a truly monumental task. Doctoral candidates were unable to assign variables, had no clue about independent and dependent or outcome variables and hadn't the foggiest idea how to calculate effect size of a therapeutic intervention, look at confidence intervals, sample size, bias within, the area under the bell curve, parametric versus non-parametric statistical analysis method etc. I ended up tutoring doctoral, and post-doctoral students for the subsequent 7 years and it was a rewarding experience to have practitioners no longer go straight to the results section and attempt to replicate the intervention in their practice just because the effectiveness was said to be a high number like 85%. They now realized that even the simple fact of looking at the sample size could help them understand the validity and the power of the study design and thus the true effect size of the intervention being touted as the next miracle cure.

Having studied the works of world-renowned EBM writers like Guyatt, Rennie, Sackett Straus, Portney and Watkins, and the pioneering efforts of McMaster University has been an amazing educational journey. It is important to cultivate a healthy skepticism towards the application of diagnostic, therapeutic and prognostic technologies, research studies, and newly developed interventions in the day to day management of patients.

This outlook requires a formulation of and a clear delineation of the relevant question, a thorough search of available medical literature, a critical appraisal of the evidence and finally its applicability to the clinical situation of the patient. Textbooks that usually take years into publication are the weakest/lowest level of evidence whereas systematic reviews, meta analyses, double blind Randomized controlled trials (RCTs), single blind RCTs, Cohort studies and so on are the higher forms of evidence that one should look for in the right order of hierarchy.

When faced with a clinical question, patient values are the foremost importance. Once the patient and the clinician are willing to collaborate then the next step is to formulate what is called as a **PICO question** for the problem/dilemma at hand

P patient problem

I Intervention under consideration

C comparison with other available options

O what is the outcome we're interested in for our patient

A thorough investigation of medical literature based on the guidelines highlighted above is the next step.

There are two fundamental principles of EBM that Ive learned about are:

1) Evidence by itself isn't sufficient to make an informed clinical decision. An educated clinician must always take into account other important factors like finances, risks versus benefit and patient values and preferences into consideration.
2) EBM provides us with a hierarchy of guidance to clinical decision making. Potential evidence and applicability of the same is an acquired skill. Looking at various aspects of a study like bias, sample size, inclusion and exclusion criteria, statistical methods used, confidence intervals etc plays an important part in decision making.

Several organizations have developed grading systems for assessing the quality of evidence. For example, in 1989 the U.S. Preventive Services Task Force (USPSTF) put forth the following:[61]

> **Level I**: Evidence obtained from at least one properly designed randomized controlled trial.
>
> **Level II-1**: Evidence obtained from well-designed controlled trials without randomization.
>
> **Level II-2**: Evidence obtained from well-designed cohort studies or case-control studies, preferably from more than one center or research group.
>
> **Level II-3**: Evidence obtained from multiple time series designs with or without the intervention. Dramatic results in uncontrolled trials might also be regarded as this type of evidence.
>
> **Level III**: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Important questions to have in mind before arriving at a clinical decision:

1) Were the study patients similar to my patient and to what extent? One needs to see if the primary database the investigators drew their sample from is readily similar to the patient you have.

2) Was the duration of follow up short term or fairly adequate for the condition being studied
3) What was the effect size?
4) What was the magnitude of the risk if any.
5) Is the intervention duplicable in my clinical setting
6) Does my patient agree with all of the above and my final conclusion

With the information above, Its relatively easy to calculate the number needed to treat, the absolute risk reduction and the effect size of a therapeutic intervention to make a truly informed clinical course of action. As is evident, EBM is the gold standard in clinical practice and should be meticulously used with our patients especially since patients with CIRS have already been suffering for years and are possibly comorbid with several other conditions.

MCID: The Minimal Clinically Important Difference

Bottom Line: We need some method to make judgments about whether improvements reported in intervention studies represent meaningful, clinically important changes. Comparing the observed effect size to the MCID provides us with that method.

Jaeschke et. al.[1] define the minimal clinically important difference (MCID) as "…the smallest change score associated with a patient's perception of a change in health status."

Whenever we find evidence for the efficacy of therapy, we will want to know not only whether the treatment group fared better than the control (or placebo, or comparison treatment) group, but we want to know whether the degree of difference in outcome is large enough to be important. That is, we want to know whether the effect size (difference between groups) is non-trivial: big enough to care about; big enough to make a functional difference; big enough to be worth paying for. We make this judgment by comparing the observed effect size to the MCID.

Having said that, the term "effect size" can be used to mean different things by different authors (sorry, it's the nature of statistics and research in general). Still, it's not too hard to sort out.

- Effect size as most commonly used in the EBP framework is the magnitude of the between-group difference at the end-point of the study. The end-point can be defined as right after the treatment is over or at the end of the follow-up period.

- For <u>continuous scale outcomes</u> this difference is in raw units of the dependent variable and is a simple subtraction: mean of Group 1 minus mean of Group 2. This assumes that the mean scores on the dependent variables were about the same in both groups at baseline. One variation on this you sometimes see is that authors might compute a

mean "change score" and report it as a percentage for each group (i.e., Group 1 improved 30% from baseline while Group 2 improved only 5% -- here the effect size would be 30% - 5% = 25%). For dichotomous scale outcomes the between-group difference is expressed as ARR, RRR, & NNT.

- Effect size can also be computed for the within-group effect. This is also in simple units of the dependent variable and is simple subtraction: mean (end-of-treatment) minus mean (baseline).

- The effect size index is a unitless quantity suggested by Cohen and reviewed on pp. 705-706 of P&W. The arithmetic here isn't hard either. It's just the difference (mean 1 minus mean 2) divided by the SD. So if Group 1 has a mean of 100, Group 2 has a mean of 90, and the SD is about 20 for both groups, the effect size is 0.50, or about half a SD ((x1-x2)/SD) = (100-90)/20) = 0.50). Cohen suggests that values of 0.20, 0.50, and 0.80 reflect small, medium, and large effect sizes, respectively. Just to make this hard, many writers use the terms "effect size" and "effect size index" interchangeably (unfortunate, in my view). Note that even P&W do this on pp. 705-706.

- Other authors besides Cohen have suggested alternate effect size indices: eta squared, partial eta squared, & omega squared. Omega squared generalizes to the population, whereas Cohen's effect size index applies to the sample only. Proponents of omega squared suggest that 0.01 is a small effect size index, 0.06 is medium, and 0.15 is large.

So how do you use these effect sizes to make a judgment about clinical meaningfulness? This is where we must decide what a reasonable value is for the MCID, and compare that MCID to the effect size.

Values for MCIDs can come from 3 places:

- If you know the outcome scales well and use them often, you may have your own expert opinion for how many units on a scale is meaningful (lesser units of difference being trivial). An example of this is 5 degrees or less being trivial (or attributable to measurement error only) for joint ROM using a universal goniometer. So you may consider the MCID to be >5 degrees for joint ROM (depending on the joint, etc.).

- You may find published values that some authors have used to declare their beliefs of that the MCID should be for a certain outcome scale. For example, Deyle et al. quote Barr et al. (developers of the WOMAC scale) on p. 179 as saying that changes of 20% or

more are clinically important for the WOMAC; others suggest a MCID of 12% for the WOMAC.

- MCIDs established for minimally important within-group differences (improvements from baseline) are commonly also used for MCIDs when evaluating between-group effect sizes at the study's end point. You may be able to find articles publishing values for MCIDs on various scales using the following search string in PubMed: "minimal clinically meaningful difference AND [enter scale name here]". I've sometimes had good results with the same search string using Google.

- If you strike out with the two options above, you can always convert the raw continuous scale effect sizes to percent differences, and use your clinical intuition about what percent might be clinically meaningful. For example, you can probably judge whether you feel that a person's ability to walk 20% farther than another person in a given time might be important (enough to make the difference in traversing a crosswalk before the light turns red, etc.). This same intuitive method is usually what you'll need to apply to dichotomous outcomes: is a RRR of 2% clinical meaningful? 5%? 10%? 20%? Ask yourself these questions in the context of the particular "event" (bad outcome) under consideration; the value at which you stop saying "no" and first say "yes" is your MCID.

Dr Shoemaker is an inspiration in the field of EBM as well. His entire body of work is meticulously evidence based and provides us clinicians mentoring with him with readily applicable, critically appraised and clinically applied methodology based on objective data and findings from thousands of patients. Dr Scott McMahon also has a large body of evidence-based research in the field of CIRS.

Jodie A. Dashore
Director
www.bionexushealth.com

References

Sacket, DL; Richardson, WS (1997) Evidence-Based medicine: How to Practice and Teach EBM. Edinburgh: Churchill Livingston

Burns P.B., Rohrich R.J., Chung K.C. The levels of evidence and their role in evidence-based medicine. Plast Reconstr Surg. 2011;128(1):305–310.

Evidence-Based Medicine Working Group (November 1992). "Evidence-based medicine. A new approach to teaching the practice of medicine" JAMA. **268** (17): 2420

Sackett DL, Rosenberg WMC, Muir Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. BMJ 1996;312:71.

Jaeschke R, Singer J, Guyatt GH. Measurement of health status: ascertaining the minimal clinically important difference. Control Clin Trials 1989;10:407-15.

Portney LG, Watkins MP. Foundations of Clinical Research: Applications to Practice. 2nd ed. Upper Saddle River, NJ: Prentice-Hall Inc, 2000.

Deyle GD, Henderson NE, Matekel RL, Ryder MG, Garber MB, Allison SC. Effectiveness of manual physical therapy and exercise in osteoarthritis of the knee. A randomized, controlled trial. Annals of Internal Medicine. 2000 Feb 1;132(3):173-81.