Evidence Based Practice

Part 1: Locating the Evidence
Part 2: Critical Appraisal of the Evidence

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Learning Outcomes (Part 1)

Tracking Down the Evidence

- Formulate an answerable clinical question about the **effects of therapy.**
- Know what databases are appropriate to use for searching for high quality evidence about effects of physiotherapy interventions.

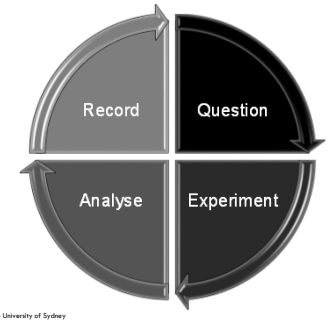
Let's start with an examples

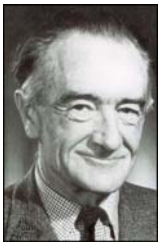
Have you heard of anything about this new treatment?

What is the Top Global Challenge in Healthcare?

- To provide evidence based, cost-effective quality care that will improve practice and patient outcome.
- Only 20% of what healthcare providers do is based on evidence – 80% is not (Gary, et al., 2002)
- Only 55% of time patients get the evidence based recommended course of treatment (IOM, 2001)
- It takes 15-20 years to get evidence into practice!

The Foundations of Evidence Based Practice



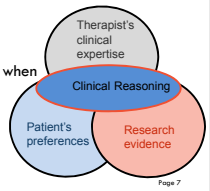


Professor Archibald Leman Cochrane, (1909-1988)

What is Evidence Based Physiotherapy?

Evidence-based practice is clinical practice informed by :

- External evidence (scientific evidence): relevant, high-quality research including systematic reviews, randomised clinical trials, best practice, and clinical practice guidelines that support a change in clinical practice
- Internal evidence: Practice-generated knowledge or healthcare provider expertise
- Patient/client:
  - Preferences: What does the patient really want when given several options
  - Perspectives and values: Quality of life
- Context



Evidence Based Practice (EBP)

EBP encompasses evaluating evidence about:

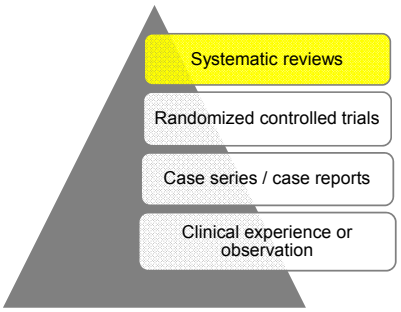
Which is the most effective treatment for this patient?
Is this therapy effective?
Effects of interventions

What can I tell this patient about the likely prognosis?
Prognosis

How certain am I about my patient's diagnosis?
Diagnosis

Cost-effectiveness
Experiences and attitudes – qualitative

Sources of evidence



Evidence Based Practice (EBP); Steps to Take

Step 1: Ask Answerable Questions

Specify:

- The **p**atient or problem to be treated
- The **i**ntervention of interest
- The **c**omparison therapy
- The **o**utcomes of interest

"pico"

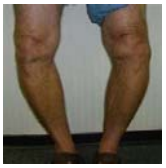
Possible Comparisons - examples

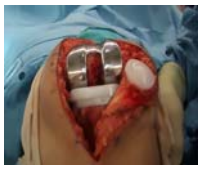
Rx A v Rx B Exercise v ultrasound	• Which of these two Rxs is more effective?
Rx A v No Rx Exercise v no exercise	• Is Rx A more effective than no Rx A?
Rx A v Rx A + Rx B Exercise v exercise +ultrasound	• Is there a benefit of adding Rx B to Rx A?

Sackett et al (2000). *Evidence-Based Medicine.* London: BMJ Books.

Asking Answerable Clinical Questions - example

Knee replacement surgery





Continuous Passive Motion (CPM) Machine

Asking answerable clinical questions: an example

Does the addition of CPM *(intervention of interest)*

following knee replacement surgery *(patient/problem)*

improve range of motion and function *(outcome)*

more than exercise alone *(comparison therapy)*?

Q: what sort of comparison is this?

Step 2. Tracking Down The Evidence

Ask answerable questions

Efficiently locate the best evidence

Critically appraise the evidence

Apply the results to patients

Evaluate the results

Databases for Physiotherapy Evidence

- **MEDLINE** – largest database of medical literature. Fair coverage of physiotherapy journals.
- **EMBASE** - Nearly as big as Medline; better coverage of physiotherapy journals.
- **AMED** – Allied Health; Complementary Medicine
- **CINAHL** - Smaller database; indexes most physiotherapy journals.
- **OVID** – Numerous databases including Medline, AMED, EBM reviews..

ALL REQUIRE SUBSCRIPTION

Note: slides 13-20 are provided for review purposes. During the lecture you will be instructed how to search the data-bases and we will not go through these slides. But you can use them in the future to guide you.

Database: PubMed

PubMed is a free database (mostly Medline) from the US National Library of Medicine; > 21 million citations; links to abstracts ± full text

http://www.ncbi.nlm.nih.gov/pubmed and see 'Clinical Queries'

Try the PubMed online tutorials

Database: Cochrane Collaboration

- Free access for every person in Australia with a computer for another 5 years (NHMRC, August 2012)

http://www.cochrane.org

- **Most useful for systematic reviews** (Cochrane Database of Systematic Reviews)
- Free full text of reviews, protocols etc
- Cochrane reviews all very high quality
- Cover most areas of health care

PEDro

- PEDro is the Physiotherapy Evidence Database
- PEDro is a free database of over 21,000 randomised trials, systematic reviews and clinical practice guidelines in physiotherapy.
- For each trial, review or guideline, PEDro provides the citation details, the abstract and a link to the full text, where possible.
- All trials on PEDro are independently assessed for quality (0-10 scale)
- It is freely available on the web at **http://www.pedro.org.au/**

Search Terms

- Determine your search terms (key elements; synonyms; alternative terms)
  "osteoarthritis, knee"[MeSH Terms] OR knee osteoarthritis[Text Word]
- MeSH Database: Medical Subject Headings is the US National Library of Medicine's controlled vocabulary thesaurus
- Many terms entered by searchers are automatically mapped to MeSH descriptors to facilitate retrieval of relevant information
- Try the MeSH tutorials on PubMed at http://www.ncbi.nlm.nih.gov/mesh

Search Terms

- How will you combine search terms? AND / OR
  - AND (linking PICO): knee osteoarthritis AND exercise AND pain
  - OR (synonyms): exercise OR physical activity OR strengthening

Result? Too limiting vs unmanageable….help from Librarian

- Wild Cards: truncations
  - A wildcard is a symbol that is used to find multiple word endings e.g. arthr$ osteoarth* exer* random*
  - Different databases use different methods for truncating
    - PEDro: no symbol
    - Medline: $
    - PubMed: *

Getting Full-Text Copies of Papers

- Usually NOT available through PubMed OR PEDro
- **You need to use your student access to University of Sydney library electronic databases OR catalogue**
- Some journals have free access (e.g. British Medical Journal)
- Cochrane Systematic Reviews free
- Join APA for free access to a number of journals

Consolidation

1. Familiarise yourself with the PEDro, Ovid and PubMed websites – read their online tutorials and check out the links.
2. Try using PEDro to find an RCT or systematic review that provides an answer to the clinical question you formulated today

Step 3. Critically Appraise the Evidence

Learning Outcomes (Part 2)

Critical Appraisal (Therapy)

- A: Can I believe this clinical trial?
  - Critically evaluate the **internal validity** ("believability") of clinical trials
  - Understand possible sources of bias in clinical trials and how these are minimized in high quality studies.
- B: What is this trial telling me?
- Critically evaluate the external validity ("applicability") of clinical trials
- Identify and where possible, obtain estimates of the size of a treatment's effects (with 95% confidence intervals).
- Use a tree plot or forest plot to conclude whether a therapy has a clinically worthwhile effect.

A: Can I believe this clinical trial?

- If a randomised clinical trial is published in a peer-reviewed scientific journal, it must be believable, right?

Sadly…NO!

- You need to be able to differentiate trials of high and low quality (bias)

Low quality trials tend to over-inflate treatment effects.

But… no clinical trial is perfect!

To be useful, trials need only be ***good enough*** for clinical decision-making

Sources of Bias

1. Were subjects randomly allocated to groups?


2. Was there adequate allocation concealment?

3. Was there adequate follow-up of study participants?


4. Were assessors and subjects blinded to allocation group?


Internal Validity: 1st and 2nd Criteria

There are two components to rigorous randomisation:

1. Generation of a **truly random** sequence
2. Implementation ensuring **allocation concealment**

What if allocation is not concealed?

Quasi randomisation

Not random. Including allocation by the person's date of birth, by the day of the week or month of the year, or just allocating every alternate person. These methods of allocation are relatively easy to manipulate, introducing **selection bias**

Why Randomise Subjects?

To ensure that groups are relatively balanced (comparable) in terms of factors that might influence outcome, both **known** and **unknown**.

Then, any difference between groups after Rx should be due to..... THE INTERVENTION

Internal Validity: 3rd Criterion

1. Were subjects randomly allocated to groups?
2. Was there adequate allocation concealment
3. Was there adequate **follow-up**?
4. Were assessors and subjects blinded to allocation group?

Some loss to follow-up is inevitable in most trials

Loss to Follow-up

Note: Participants can withdraw from study treatment, but still attend follow-up outcomes assessments (encouraged to do so!)

- Calculate loss to follow-up (study attrition):
  Examine flow diagrams, text, tables
- Was drop-out even from each allocation group?
- Were the reasons for drop-out explained?
  - Participants may drop out of the treatment group due to **side effects, ineffectiveness** or poor feasibility of the intervention.
  - Participants may drop out of control group as wish to seek treatment, or simply 'unhappy' with allocation, loss of interest in study as doing well now

Why is Adequate Follow-up Important?

- Reduce possibility of **attrition bias**
- **Attrition bias** caused by systematic (non-random) differences between **allocation groups (treatment, control)** in loss to follow-up or exclusions of **participants** from the results of a study.

What is Adequate Follow-up?

- No set criteria
- Depends on follow-up period (e.g. 4 weeks vs 3 years)
- Usually >15-20% drop-out of concern, particularly if 'unbalanced' between treatment-control groups (this is arbitrary threshold).
- Higher loss, up to even 30%, may be unavoidable for long-term trials

Do you know what is the longest research follow-up time in history??

Internal Validity: 4th Criterion

1. Were subjects randomly allocated to groups?
   Look for mention of randomisation in title, abstract or methods
2. Was there adequate allocation concealment?
   Who/how was the randomisation carried out?
3. Was there adequate follow-up?
   Calculate loss to follow-up from the number of subjects randomised and the number with missing outcomes data.

4. Were assessors and subjects **blinded** to group allocation?
   Look for evidence of blinding in title, abstract or methods

Blinding

- Blinding (masking): being unaware of group allocation
- Who needs to be blinded?
  - Patients
  - Therapists
  - Outcome assessors
  - Data analysts, e.g. statisticians

Minimise risk of biased results

Why is Blinding Important?

- Subject blinding controls for:
  - placebo effects (? part of a treatment?)
  - polite patients reporting as 'expected' ("Hawthorne" effect)
- Assessor blinding controls for:
  - measurement bias (even with "objective measures" of physical performance)

Can I Believe Results Of This Clinical Trial?

Review the 4 criteria (reducing bias):

1. Were subjects randomly allocated to groups?
2. Was there adequate allocation concealment?
3. Was there adequate follow-up?
4. Were assessors and subjects blinded?

- 'Yes' to all 4 questions - reasonably strong basis to trust the results
- 'No' - weigh up the seriousness of the threats to validity to decide how believable that study's findings are.

Overall judgement about clinical trials

- After evaluating how well these 4 criteria are met, you need to make an overall judgement about the validity of the study, identifying serious threats to validity.
- E.g. 1: *"This study has high validity as the subject allocation was randomised and concealed, patients and assessors were blinded and there was minimal (8%) loss to follow-up."*
- E.g. 2: *"This study has low validity as quasi-randomisation was used, blinding was not discussed and there was large (28%) loss to follow-up. These features may bias the results and hence constitute serious threats to validity."*

Learning Outcomes Revisited

Critical Appraisal (Therapy)

A: Can I believe this clinical trial?

- Critically evaluate the **internal validity** ("believability") of clinical trials
- Understand possible sources of bias in clinical trials and how these are minimized in high quality studies.

B: What is this trial telling me?

- Critically evaluate the external validity ("applicability") of clinical trials
- Identify and where possible, obtain estimates of the **size of a treatment's effects** (with 95% confidence intervals).
- Use a **tree plot** or forest plot to conclude whether a therapy has a clinically worthwhile effect.

Quantifying outcomes

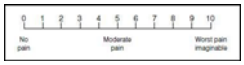
There are two common ways that the results of interventions are reported:

1. **Statistical significance (p-value)**
   - Signifies whether differences between groups are greater than may occur by chance alone
   - Conventionally p<0.05 is threshold…i.e. less than 5% chance
   - HOWEVER, p value does not signify whether the effects are large enough to be clinically worthwhile (*influence of sample size*)
2. **The size of the treatment effect**
   - MOST useful: reveals *how much* good, *on average,* the treatment provides

There is no **"one"** treatment effect

Metrics of treatment effect

1. **Continuous level data**
   - Pain VAS Scale *(score from 0 to 10 cm)*
   - Roland Morris Disability Questionnaire *(score from 0-24)*
   - Walking velocity *(metres per sec)*



2. **Dichotomous data** ("yes/no")
   - Injured / Not injured
   - Return to sport / Don't return to sport
   - Able to drive/Not able to drive

Determining the Size of Treatment Effects

Example:

Treatment Group N = 40 • Mean FSS = 21.4 • SD = 18.8

Control Group N = 38 • Mean FSS = 30.6 • SD = 16.8

Effect Size: 30.6 – 21.4 = 9.2

$$95\%\ \text{CI} \cong \text{difference between means} \pm \frac{3 \times SD_{average}}{\sqrt{n_{average}}}$$

$= 9.2 \pm (3 \times 17.8) / \sqrt{39}$

$= 9.2 \pm 53.4 / 6.2 = 9.2 \pm 8.6$

The treatment effect is: 31 mm (95% CI 0.6 to 17.8)

i.e., This study found a treatment effect of 9.2 reduction in the score of FSS (0-63 scale); 95% confident the 'true' treatment effect lies between reduction of 0.6 to 17.8 in the FSS score

Tree plots

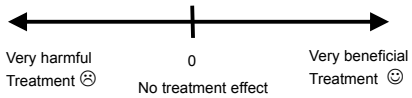
Use tree plots to help you work out if the treatment is likely to be clinically worthwhile or not.

To construct a tree plot, you need:

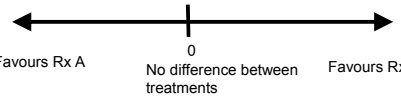
1. Point estimate average effect size
2. 95% CI around that estimate
3. "Smallest clinically worthwhile effect" of that treatment.

Tree Plot – Rx effectiveness

1. Treatment vs no treatment



2. Treatment A vs Treatment B



Smallest clinically worthwhile effect (SCWE)

- The SCWE is a ***subjective judgement***, based on your understanding of patient's preferences and weighing up benefits, costs ($ and time) and safety of the treatment, prognosis with no treatment etc.
- It is a matter of clinical judgement.
- A reasonable **estimate** you can use is 15% score improvement above that achieved by the control group
- An individual patient's value can range from 5% to 50%....depending on their preferences and circumstances…

Determining the Size of Treatment Effects

Example:

Treatment Group N = 40	• Mean FSS = 21.4 • SD = 18.8	Effect Size: 30.6 – 21.4 = 9.2
Control Group N = 38	• Mean FSS = 30.6 • SD = 16.8	

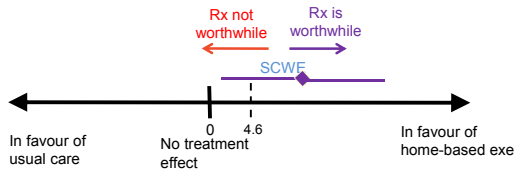
The treatment effect is: 31 mm (95% CI 0.6 to 17.8)

SCWE after 12 weeks of home-based exercise?

(15 % x 30.5 control group ≈ 4.6)

Tree Plot

Reduction in FSS



The treatment effect is: 9.2 (95% CI 0.6 to 17.8)

Estimates of therapy effectiveness

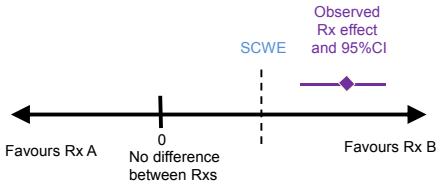
Once you have estimated the treatment effect size, its 95% CI and the smallest clinically worthwhile effect, you can conclude whether the study provides:

Poor/Moderate/Strong evidence (believability) of…..

A. Certainty of a clinically worthwhile effect
B. Certainty of no clinically worthwhile effect.
C. Uncertainty of a clinically worthwhile effect
D. Uncertainty of no clinically worthwhile effect

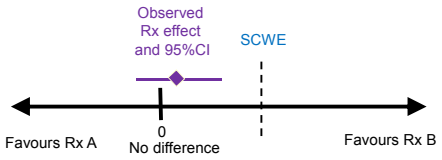
Estimates of therapy effectiveness

A. Certainty of a clinically worthwhile effect



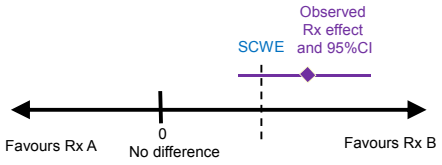
Estimates of therapy effectiveness

B. Certainty of no clinically worthwhile effect (RxB);



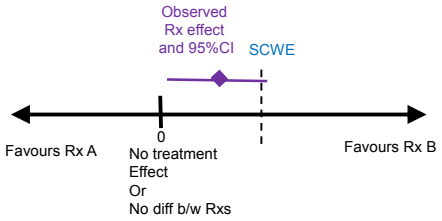
Estimates of therapy effectiveness

C. Uncertainty of a clinically worthwhile effect (Rx B)



Estimates of therapy effectiveness

D. Uncertainty of no clinically worthwhile effect



Determining the size of treatment effects

II. Dichotomous data

For dichotomous outcomes, the treatment effect is reported in terms of RISK of a (usually) poor outcome.

Absolute risk reduction (ARR) is the difference in risk between the intervention and the control groups.

ARR = risk $_c$ – risk $_i$

Determining the size of treatment effects

II. Dichotomous data

Example (Olsen et al 1997)

Research question (PICO)
Does chest physiotherapy Rx reduce the risk of respiratory complications after abdominal surgery? (vs no therapy)

Outcome: respiratory complication (yes/no)

Herbert et al (2011) p.107-114

Absolute risk reduction (ARR)

ARR = risk $_c$ – risk $_i$

- Controls: 52 of 192 pts had respiratory complications,
  - so **risk $_c$** = 27% ((52 /192) X 100)
- Rx group: 10 of 172 pts had respiratory complications,
  - so **risk $_i$** = 6% ((10 / 172) X 100)

ARR = Difference in risk
= 27% - 6%
= 21%

Determining the 95% CIs of ARR

For ARR: 95% CI ≅ difference in risk +/- 100*/ $\sqrt{n_{av}}$

Formula for dichotomous outcomes

* If risk expressed as a %; if expressed as a fraction or decimal use 1

95% CI ≅ (27% - 6%) +/- 100/ √182 (.27-.06) +/- 1/ √182
95% CI ≅ 21% +/- 7% .21 +/- .07

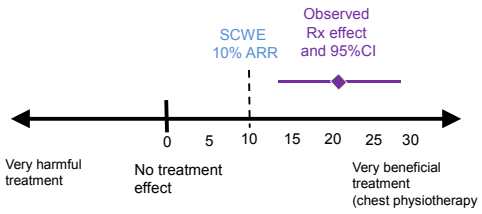
Best estimate of ARR: 21% (95% CI 14% to 28%)

Herbert RD. 2. Dichotomous outcomes (Blackboard)

Determining the size of treatment effects

II. Dichotomous data

Tree Plot of ARR (respiratory complications) with 95% CI



Overall conclusions

This is a *high quality, believable study* that provides strong evidence of certainty of a clinically worthwhile benefit for chest physiotherapy in terms of reducing the risk of respiratory complications for patients undergoing abdominal surgery.

This study provides moderate evidence (unexplained high loss to follow-up) of uncertainty of no clinically worthwhile benefit of adding manual therapy to strengthening exercise, compared to strengthening exercise alone, for reducing pain among patients with chronic knee pain due to osteoarthritis.

…….

Recommended Text

Herbert, RD et al (2011). *Practical Evidence-Based Physiotherapy*. Oxford: Elsevier.