Primary Care Team

Critical Appraisal Skills, Therapeutic

Done By: Abdulaziz Alshamlan

From slides | Doctor's Notes | Team's Notes | From the book | Important

431 Teams

WHAT IS EBM ?

The conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients.

DAVID SACKETT

The "integration of the best research evidence with clinical expertise and patient values to make clinical decisions

Five steps in EBM:

1. Formulate an answerable question

2. Track down the best evidence

3. Critically appraise the evidence for:

. Relevance

. Validity

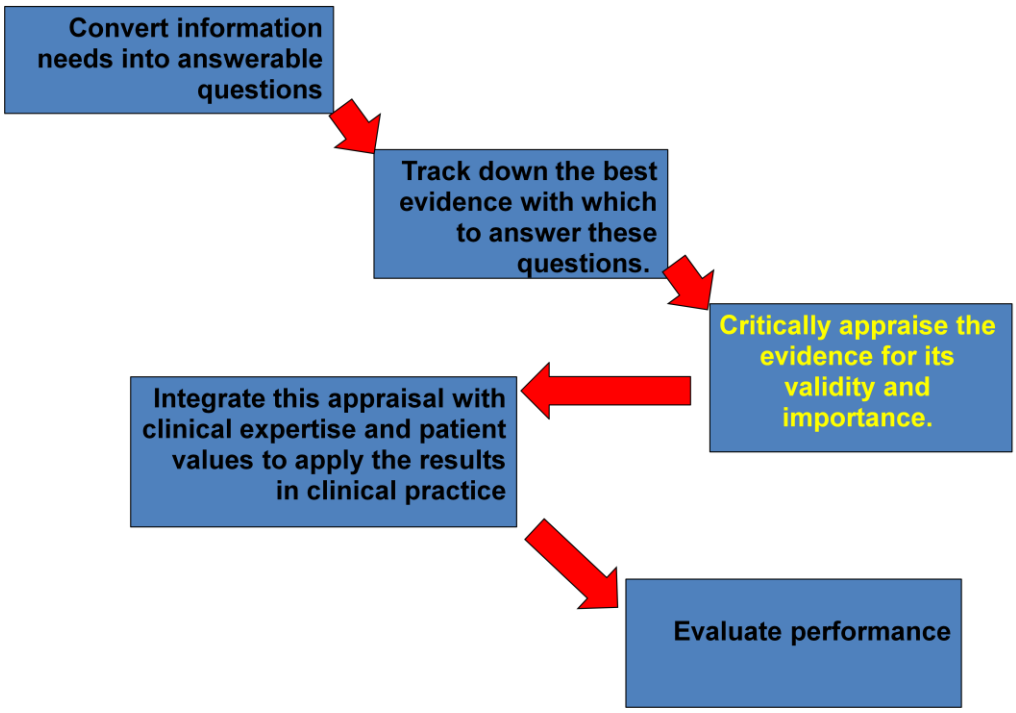
. Impact (size of the benefit)

. Applicability

4. Integrate with clinical expertise and patient values

5. Evaluate our effectiveness and efficiency

. keep a record; improve the process



WHAT STUDY DESIGN ?

TYPES OF STUDY:

. EXPERIMENTAL **. NONEXPERIMENTAL**

THERAPUETIC STUDY:

WHAT STUDY DESIGN ?
CLINICAL TRIAL.

What does make the clinical trial distinctive ?

It has : 1. Intervention. 2. Comparison.

USEFULNESS OF MEDICAL INFORMATION:

USEFEULNESS = RELEVANCE X VALIDITY

WORK

DISEASE ORIENTED EVIDENCE THAT MATTERS

(DOES)

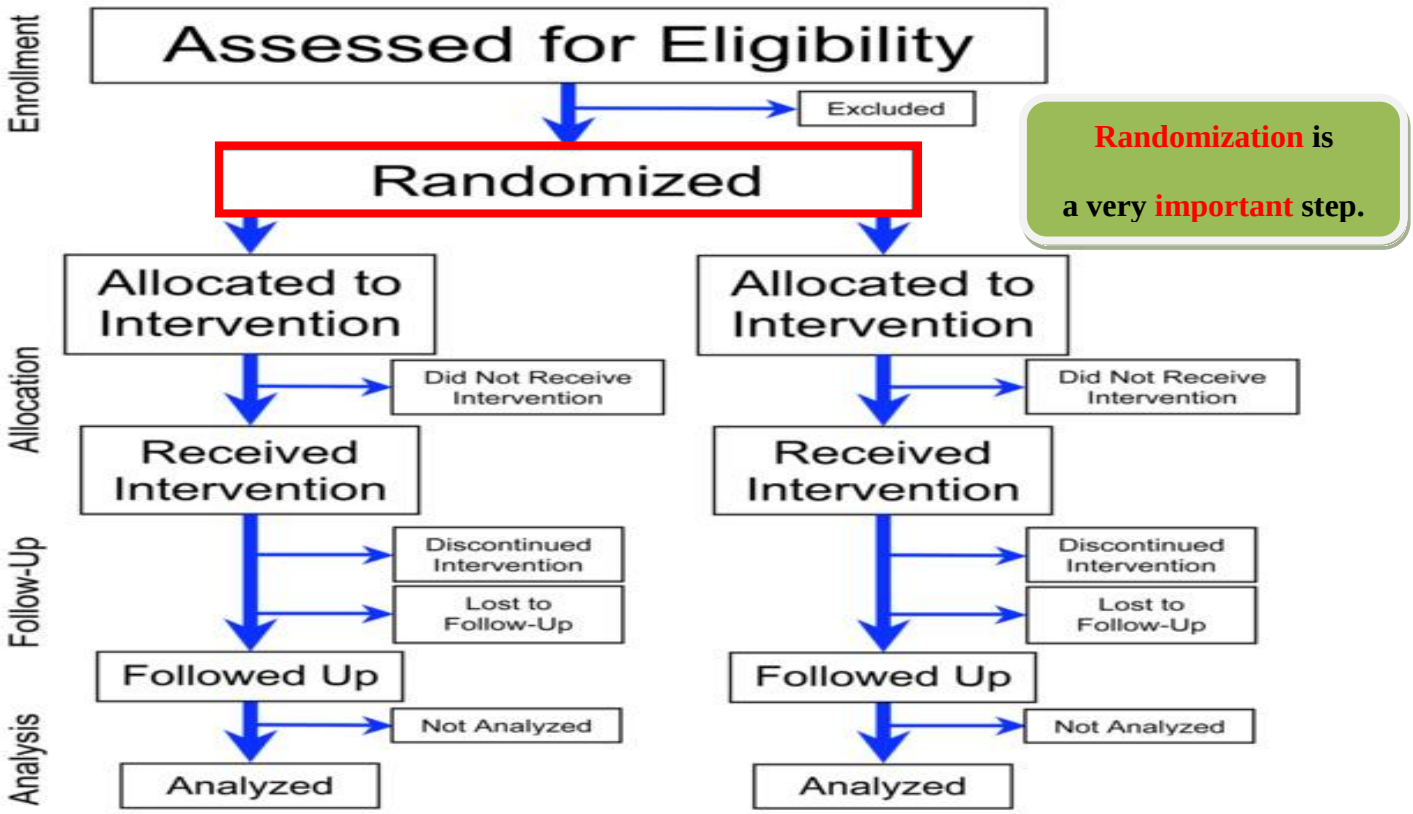
PATIENT ORIENTED EVIDENCE THAT MATTERS

(POEMS)

DOEs----------→ POEM

Drug A lowers cholesterol	Drug A decreases cardiovascular mortality/morbidity	Decreases overall mortality
PSA screening detects prostate cancer most of the time and at an early stage	PSA screening decreases mortality	PSA screening improves quality of life
Corticosteroid use decreases neutrophil chemotaxis in patients with asthma	Corticosteroid use decreases admissions, length of hospital stay, and symptoms of acute asthma	Corticosteroid use decreases asthma-related mortality
Tight control of type 1 diabetes mellitus can keep fasting blood glucose <140mg/dl	Tight control of type 1 diabetes can decrease microvascular complications	Tight control of type 1 diabetes can decrease mortality and improve quality of life

THE ANATOMY OF CLINICAL TRIAL



Randomization is a very important step.

This is an example of Randomization.

Figure 1. Profile of the Estrogen Plus Progestin Component of the Women's Health Initiative

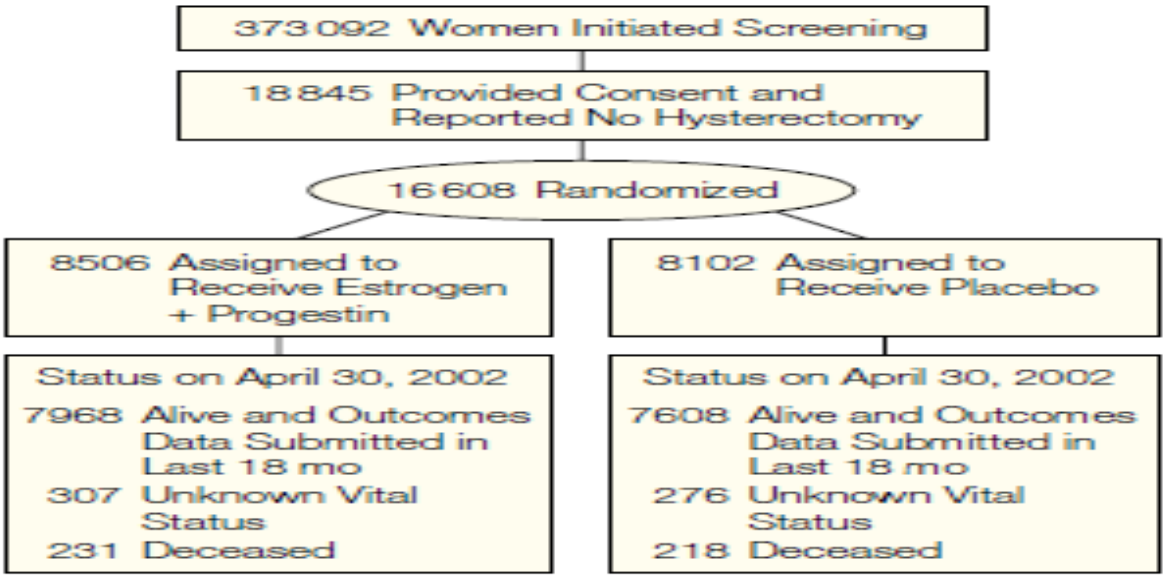
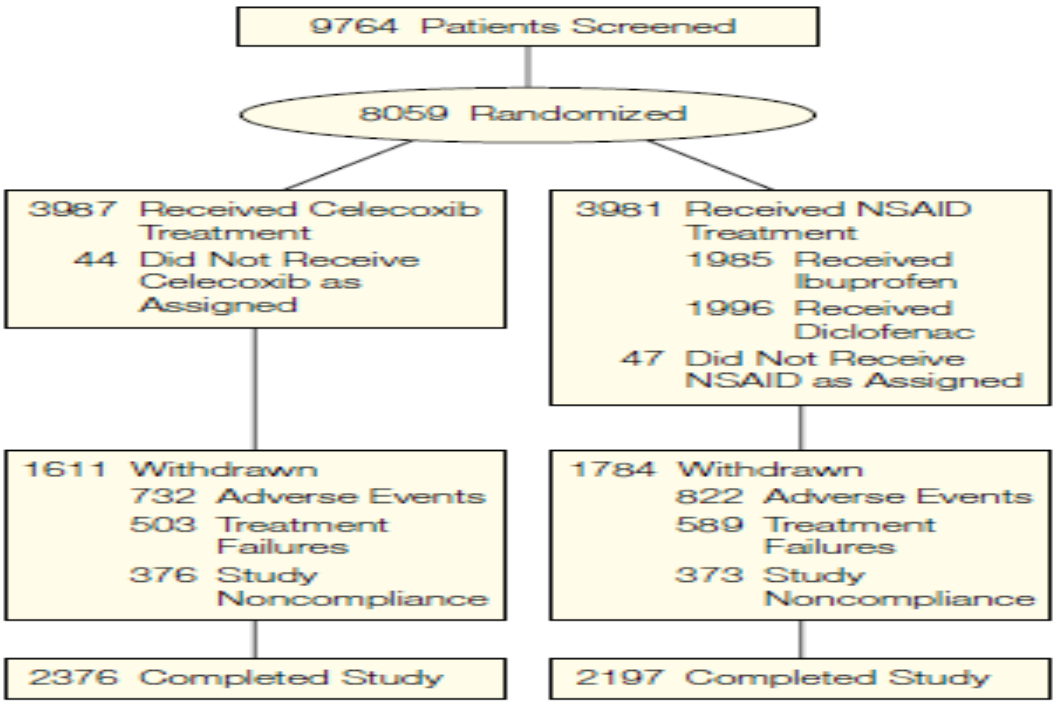


Figure 1. Flowchart of Patient Disposition at 6 Months



Menerba® Phase 3 Advanced Clinical Trial Design

PI: Wulf Utian, M.D., Ph.D. D.Sc.
Founder and President Emeritus of the North American Menopause Society (NAMS)

40 U.S. Clinical Sites Approved and Trained

Eligibility:

- Postmenopausal women ages 40-65
- ≥ 7 moderate to severe hot flashes/day

Randomization:

1200 patients to 12 weeks of treatment

- 400 Participants 5g/day
- 400 Participants 15 g/day
- 400 Participants Placebo

Primary Endpoint:

Change in frequency of moderate to severe hot flashes at 12 weeks

77 Participants Assessed for Eligibility

0 excluded from randomization

77 Participants Randomly Assigned to Condition.

ePREP Condition n = 38	Placebo/Control Condition n = 39
Number completed assessments:	Number of completed assessments:
Baseline: 6males 29 females (All 38 received intervention, but data for 3 participants was not recorded due to computer error)	Baseline: 12 males 22 females (All 39 received intervention, but data for 5 participants was not recorded due to computer error)
8wk: 8 males 27 females	8wk: 11 males 20 females
10 month: 7 males 24 females Reason for drop outs: Did not respond to our multiple attempts to contact	10month: 10 males 16 females Reason for drop outs: Did not respond to our multiple attempts to contact
38 included in analysis	39 included in analysis

A CHECKLIST FOR APPRAISING RANDOMIZED CONTROLLED TRIALS:

1. Was the objective of the trial sufficiently described?

2. Was a satisfactory statement given of the diagnostic criteria for entry to the trial?

3. Were concurrent controls used (as opposed to historical controls)?

4. Were the treatments well defined?

5. Was random allocation to treatments used?

6. Was the potential degree of blindness used?

7. Was there a satisfactory statement of criteria for outcome measures? Was a primary outcome measure identified?

8. Were the outcome measures appropriate?

9. Was a pre-study calculation of required sample size reported?

10. Was the duration of post-treatment follow-up stated?

11. Were the treatment and control groups comparable in relevant measures?

12. Were a high proportion of the subjects followed up?

13. Were the drop-outs described by treatment and control groups?

14. Were the side-effects of treatment reported?

15. How were the ethical issues dealt with?

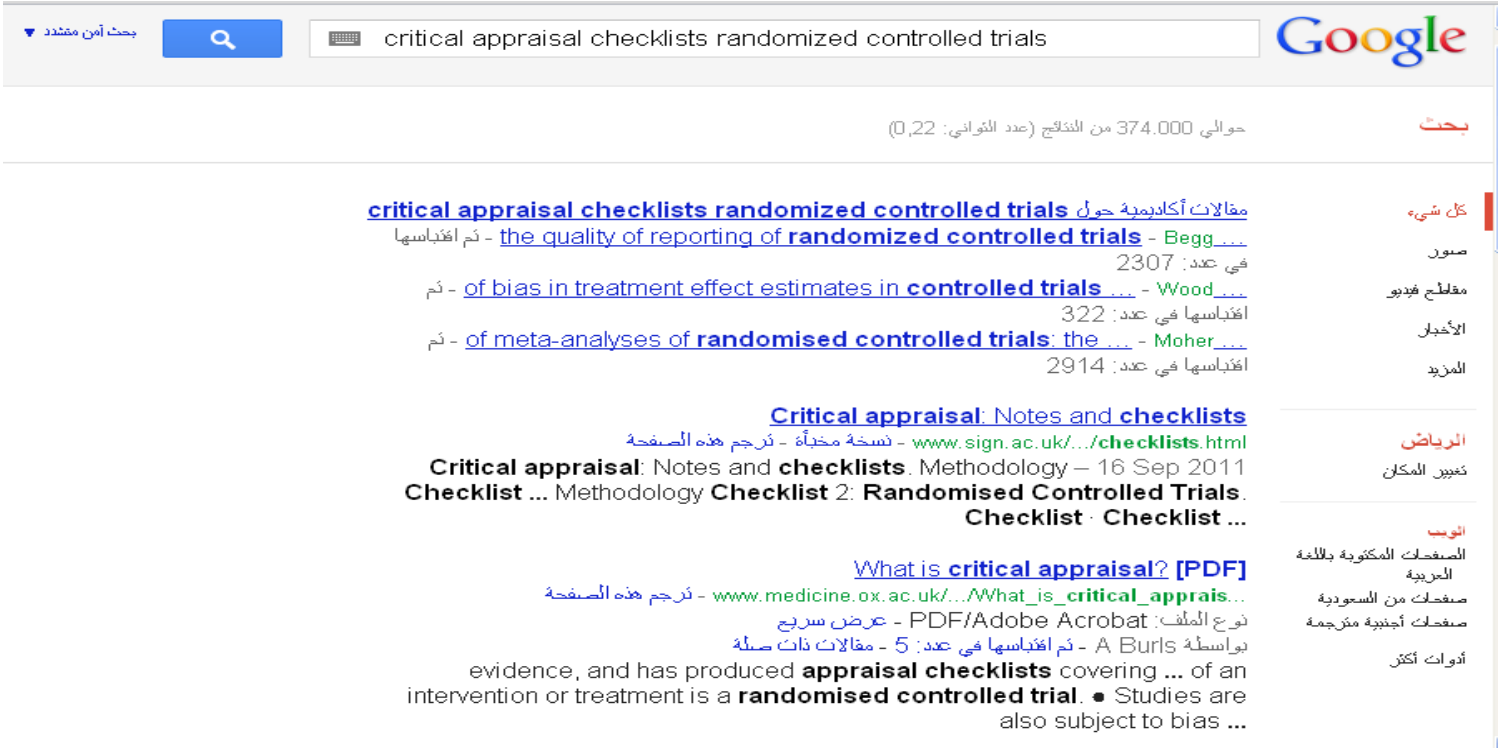
16. Was there a statement adequately describing or referencing all statistical procedures used?

17. What tests were used to compare the outcome in test and control patients?

18. Were 95% confidence intervals given for the main results?

19. Were any additional analyses done to see whether baseline characteristics (prognostic factors) influenced the outcomes observed?

20. Were the conclusions drawn from the statistical analyses justified?



WHAT DO WE LOOK FOR?

. VALIDITY

. IMPORTANCE

. APPLICATION

VALIDITY :

Are the results of this single preventive or therapeutic trial valid?

Was the assignment of patients to treatments randomised? **Was the randomisation list concealed?**
Was follow-up of patients sufficiently long and complete?
Were all patients analysed in the groups to which they were randomised?
Were patients and clinicians kept "blind" to treatment?
Were the groups treated equally, apart from the experimental treatment?
Were the groups similar at the start of the trial?

Was the assignment of patients to treatments randomised?

Was the randomisation list concealed?

Ensuring Allocation Concealment :

BEST – most valid technique

Central computer randomization

DOUBTFUL

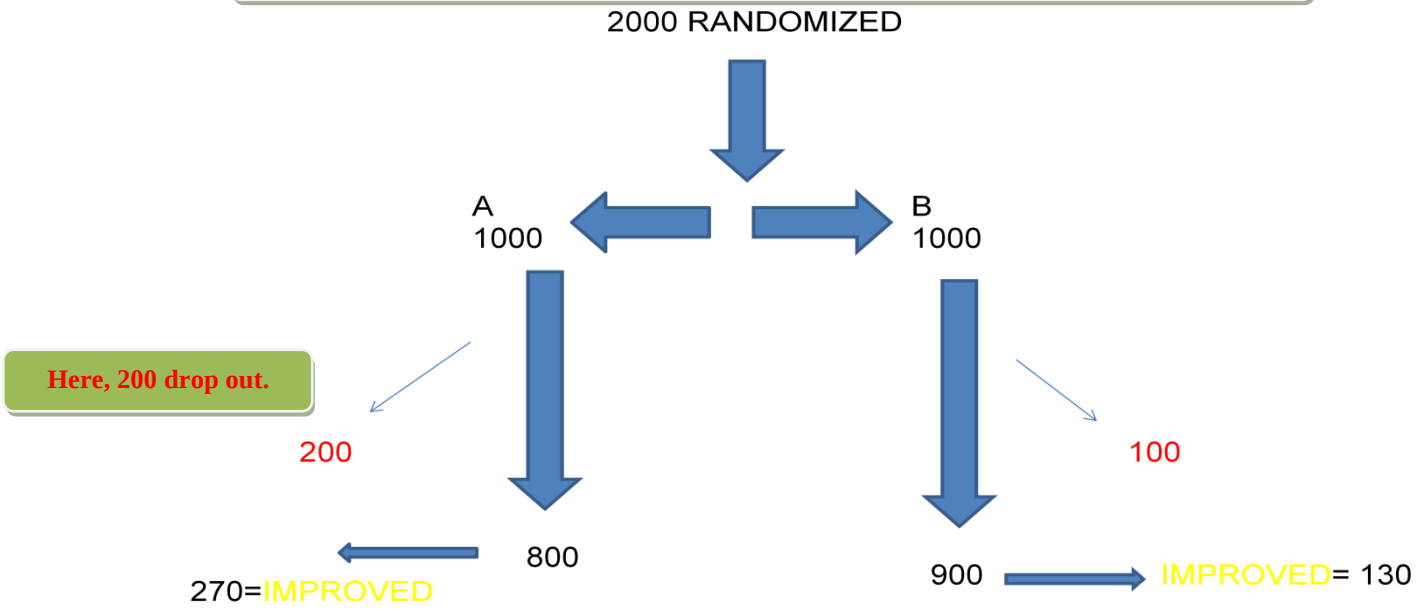
Envelopes, etc

NOT RANDOMIZED

Date of birth, alternate days, etc

Was follow-up of patients sufficiently long and complete?

When 20% of the participants or above drop out, that will affect the validity of the study.



EER= 270/? **270/ the total**

CER=130/? **270/1000**

We do that because it is better to find underestimation than overestimation

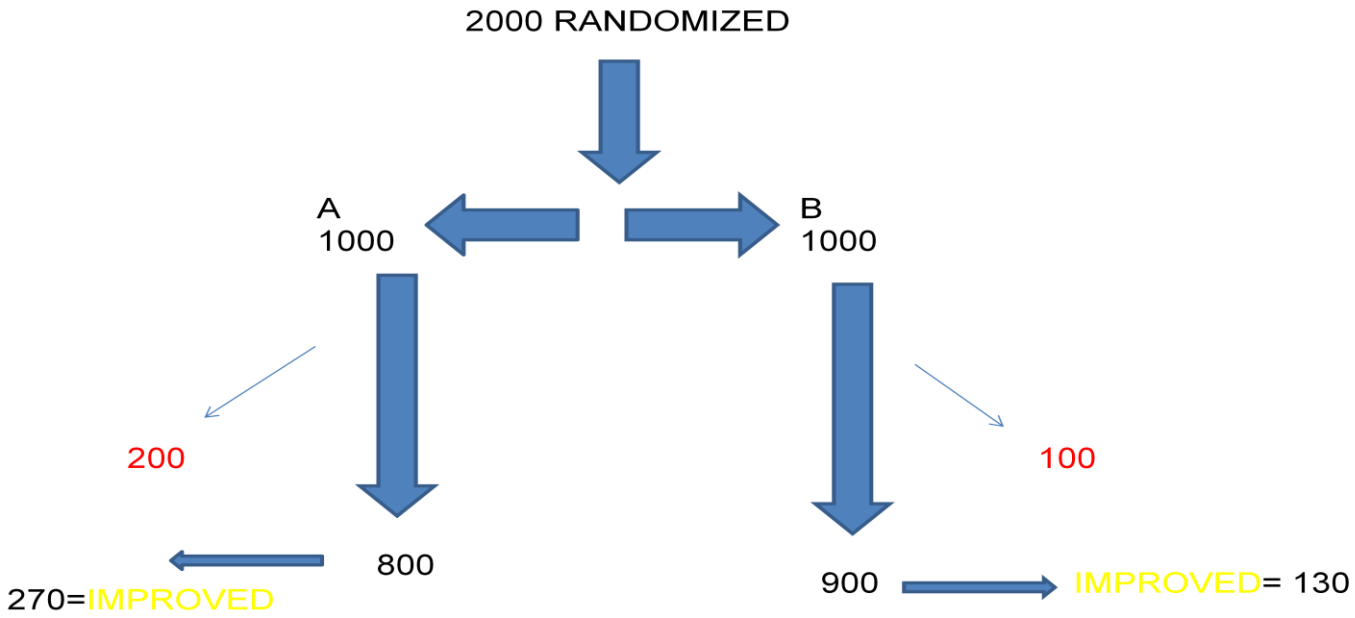
Losses-to-follow-up
How many is too many?

"5-and-20 rule of thumb"

. 5% probably leads to little bias

. >20% poses serious threats to validity

Were all patients analysed in the groups to which they were randomised?



EER= 270/?
CER=130/?

Intention-to-Treat Principle :

Maintaining the randomization

Principle:

Once a patient is randomized, s/he should be analyzed in the group randomized to - even if they discontinue, never receive treatment, or crossover.

Exception: If patient is found on BLIND reassessment to be ineligible based on pre-randomization criteria.

Were patients and clinicians kept "blind" to treatment?

Measurement Bias -
minimizing differential error

Figure 1: The authors: double blinded versus single blinded

Figure 2: The authors blinded and masked

Blinding – Who?

Participants?

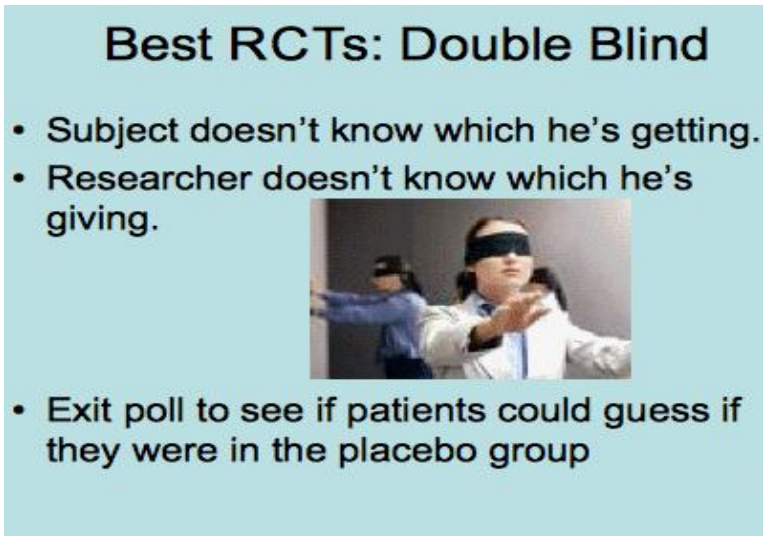
Investigators?

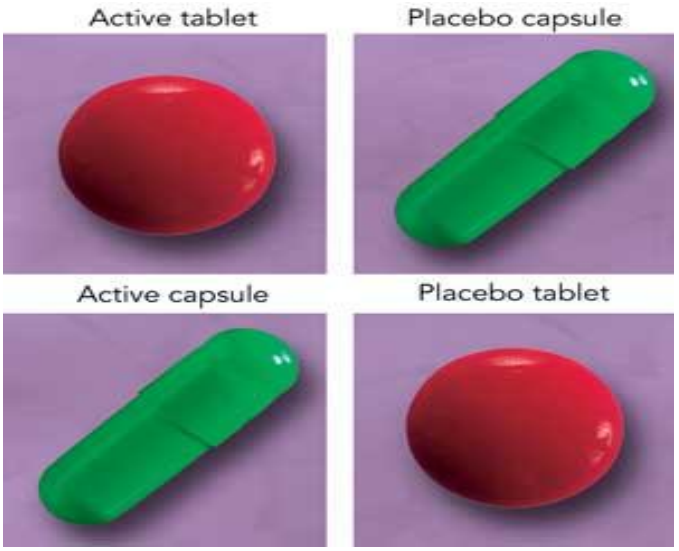
Outcome assessors?

Analysts?

Most important to use "blinded" outcome assessors when outcome is not objective!

Papers should report WHO was blinded and HOW it was done





Were the groups treated equally, apart from the experimental treatment?

Were the groups similar at the start of the trial?

IMPORTANCE

MEASURES OF ASSOCIATION

Definition :

. Number Needed to Treat (NNT):

. Number of persons who would have to receive an intervention for 1 to benefit.

NNT=1/ARR

NNTs from Controlled Trials

	CER%	EER%	ARR%	NNT
Population: hypertensive 60-year-olds Therapy: oral diuretics Outcome: stroke over 5 years	2.9	1.9	1	100
Population: myocardial infarction Therapy: ß-blockers Outcome: death over 2 years	9.8	7.3	2.5	40
Population: acute myocardial infarction Therapy: streptokinase (thrombolytic) Outcome: death over 5 weeks	12	9.2	2.8	36

OUTCOME :

INTEREVENTION	+VE	-VE	TOTAL
DRUG A	24	17	41
DRUG B	13	27	40
TOTAL			

EER= Drug A : 24/41=0.585

CER= Drug B : 13/40=0.325

ARR=EER-CEER= 0.585-0.325= 0.26

NNT=1/ARR=1/0.26=3.8

You can get the interpretation with the next example

outcome	TEGASEROD	PLACEBO	TOTAL
+ve	327	279	
-ve			
	767	752	

EER= 327/767= 42.6%=0.43

CER=279/752= 37.1%=0.37

ARR=0.43-0.37=0.06

NNT=1/0.06= 16

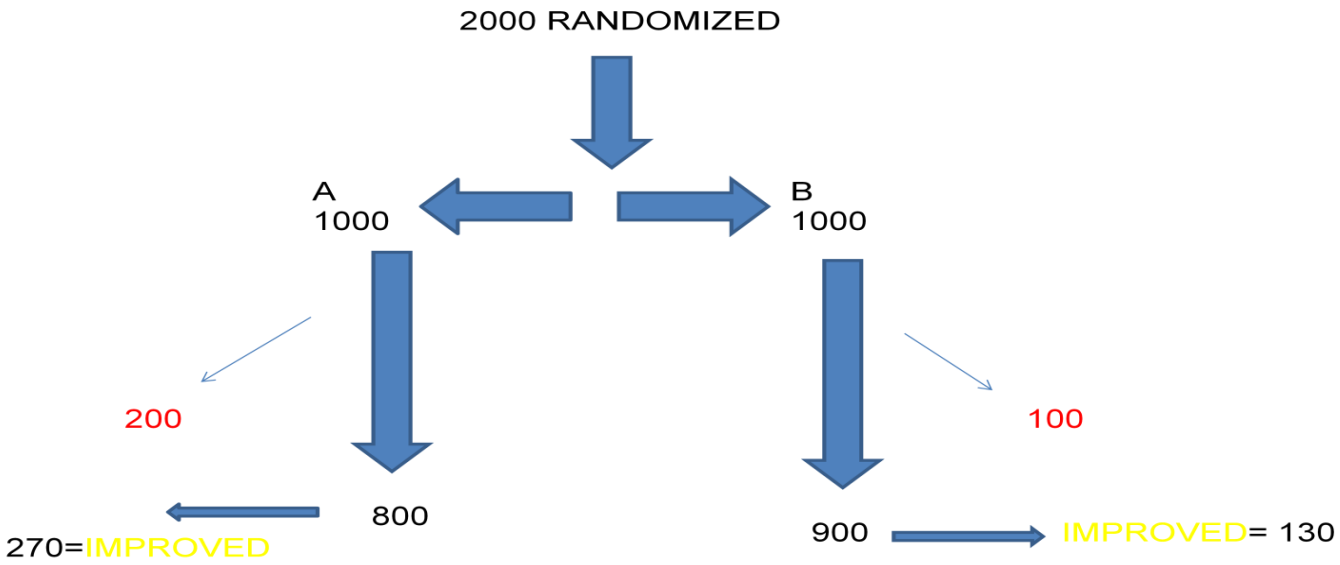
WE NEED TO TREAT 16 PATIENT WITH IBS WITH TEGESROD(FOR 12 WEEKS) TO GET SGA RELIEF OF SYMPTOMS IN ONE PATIENT

Occurrence of diabetic neuropathy at 5 years among insulin-dependent diabetics in the DCCT trial		Relative risk reduction (RRR)	Absolute risk reduction (ARR)	Number needed to treat (NNT)
CER	EER	(CER-EER)/CER	CER-EER	1/ARR

CER= CONTROL EVENT RATE **ARR= RELATIVE RISK REDUCTION**

EER= EXPERIMENTAL EVENT RATE

ARR=ABSOLUTE RISK REDUCTION **NNT= NUMBER NEED TO TREAT**



EER= 270/?

CER=130/?

EER=270/800 = 33%= 0.33

CER= 130/900=14 %=0.14

ARR= 0.33-0.14= 0.19

NNT=1/0.19= 5.2=6

EER=270/1000=27%=0.27

CEER=130/1000= 13%=0.13

ARR=0.27-0.13=0.14

NNT=1/0.14=7

EER= 77/1000= 7.7%=0.077

CER=23/1000=2.3%=0.023

ARR=0.077-0.023= 0.054

NNT=1/0.054=18.5=19

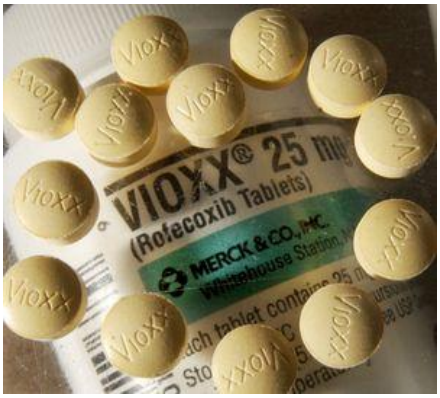
EER=77/800=9.6%=0.096

CER=23/900=2.5%=0.025

ARR=0.096-0.025=0.071

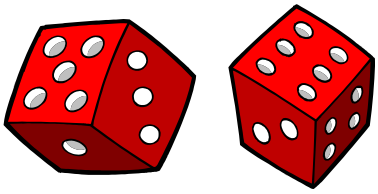
NNT=1/0.071=14

NUMBER NEED TO HARM(NNH)



WHAEN THE OUTCOME IS UNFAVOURABLE

We use NUMBER NEED TO HARM (NNH) when the active drug is worse than placebo.



Confidence Intervals (Estimation) - in DVT study

Incidence of DVT

Stocking group - 0

No Stocking group - 0.12

Risk difference = 0.12 - 0 = 0.12

(95% CI, 0.058 - 0.20)

The true value could be as low as 0.058 or as high as 0.20 - *but is probably closer to 0.12*

Since the CI does not include the 'no effect' value of '0' → the result is statistically significant

APPLICABILITY

CAN I APPLY THESE VALID, IMPORTANT RESULTS TO MY PATIENT?

Do these results apply to my patient?

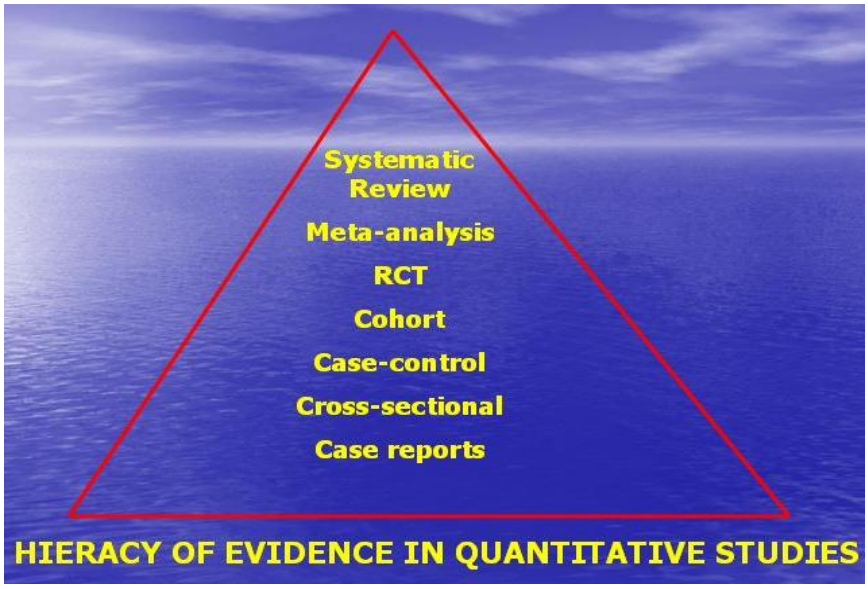
- IS OUR PATIENT SO DIFFERENT?

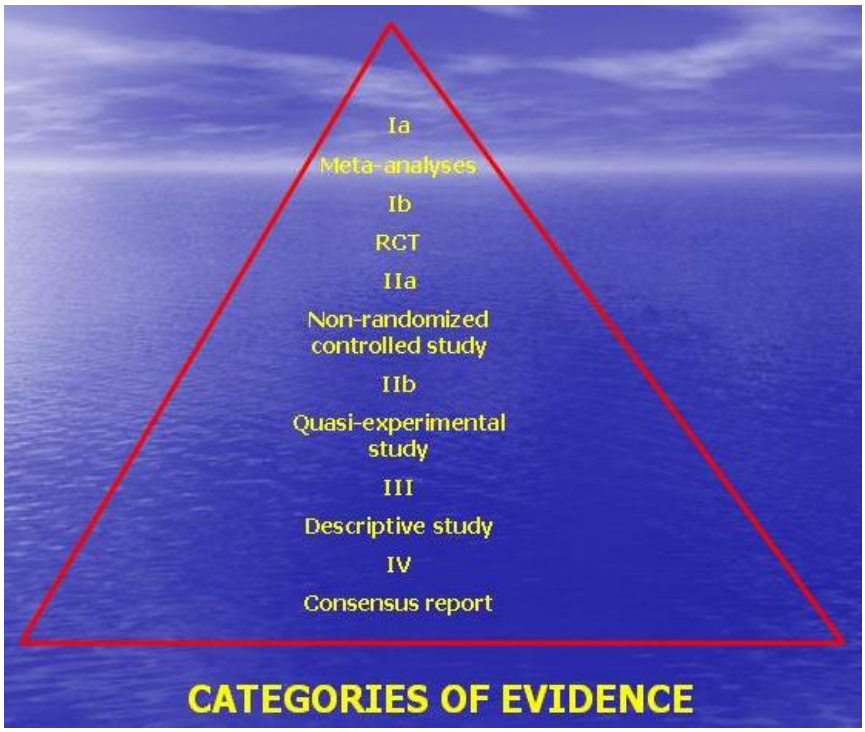
- IS THE TREATMENT FEASIBLE?

- POTENTIAL BENEFITS AND HARMS

Are my patient's values and preferences satisfied by the intervention offered?

PYRAMID OF EVIDENCE





MCQs:

1. Which one of the following is a step of EBM ?

A. Formulate an answerable question

B. Track down the best evidence

C. Critically appraise the evidence for

D. All of the above

2. Which one of the following is an element of Critically appraise the evidence?

A. Validity

B. Impact (size of the benefit)

C. Applicability

D. All of the above

3. Which type of study design is best used in therapeutic study ?

A. Case control

B. Clinical trial

C. Cross sectional

D. Cohort study

4. What is the most important step in clinical trial ?

A. Randomization

B. Following up

C. Analysis

D. Allocation

5. Which one of the following percentages will affect the validity of the study when the participants drop out ?

A. 5% or more.

B. 10% or more.

C. 15% or more.

D. 20% or more.

Answers :

1. D

2. D

3. B

4. A

5. D