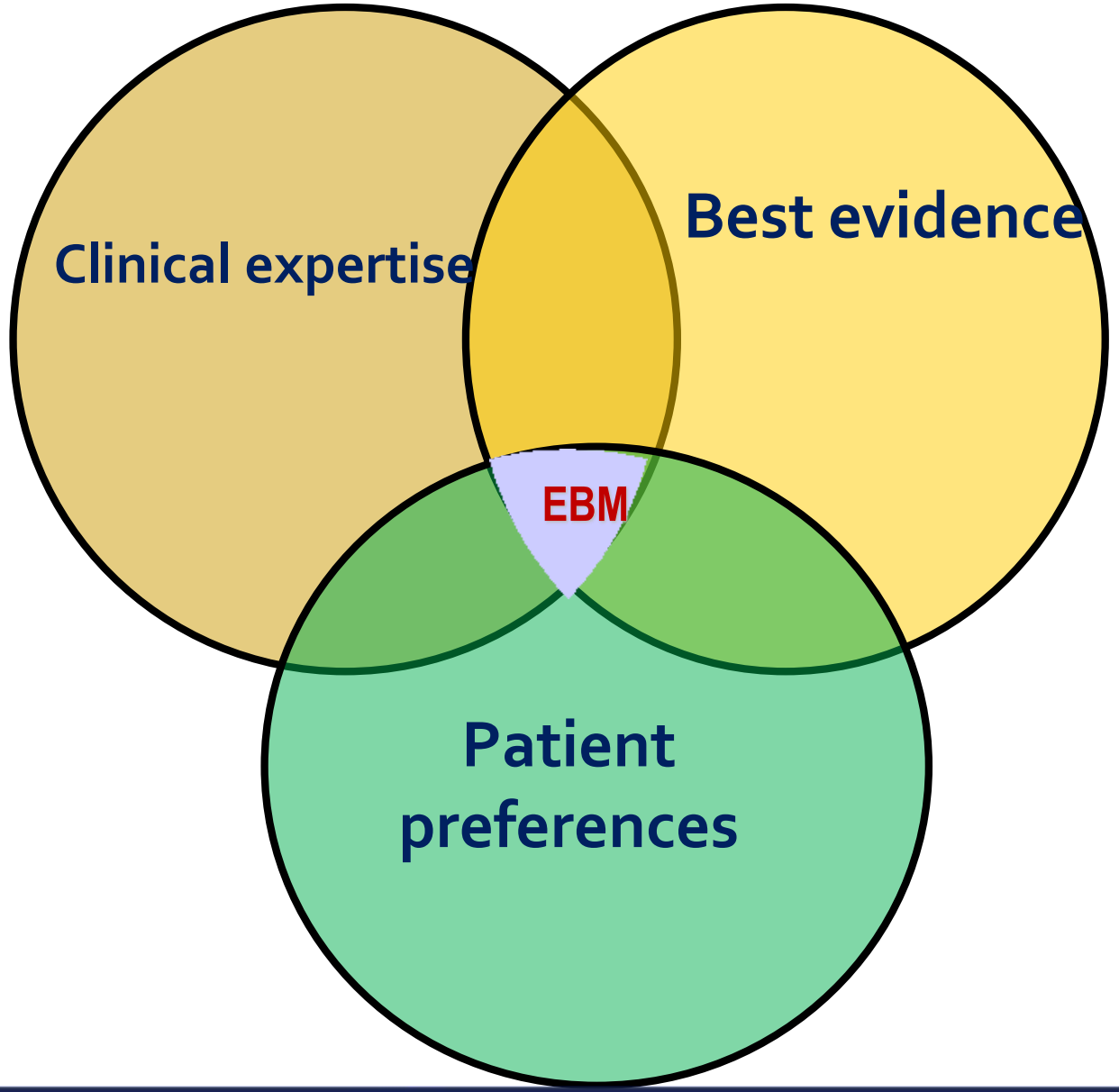
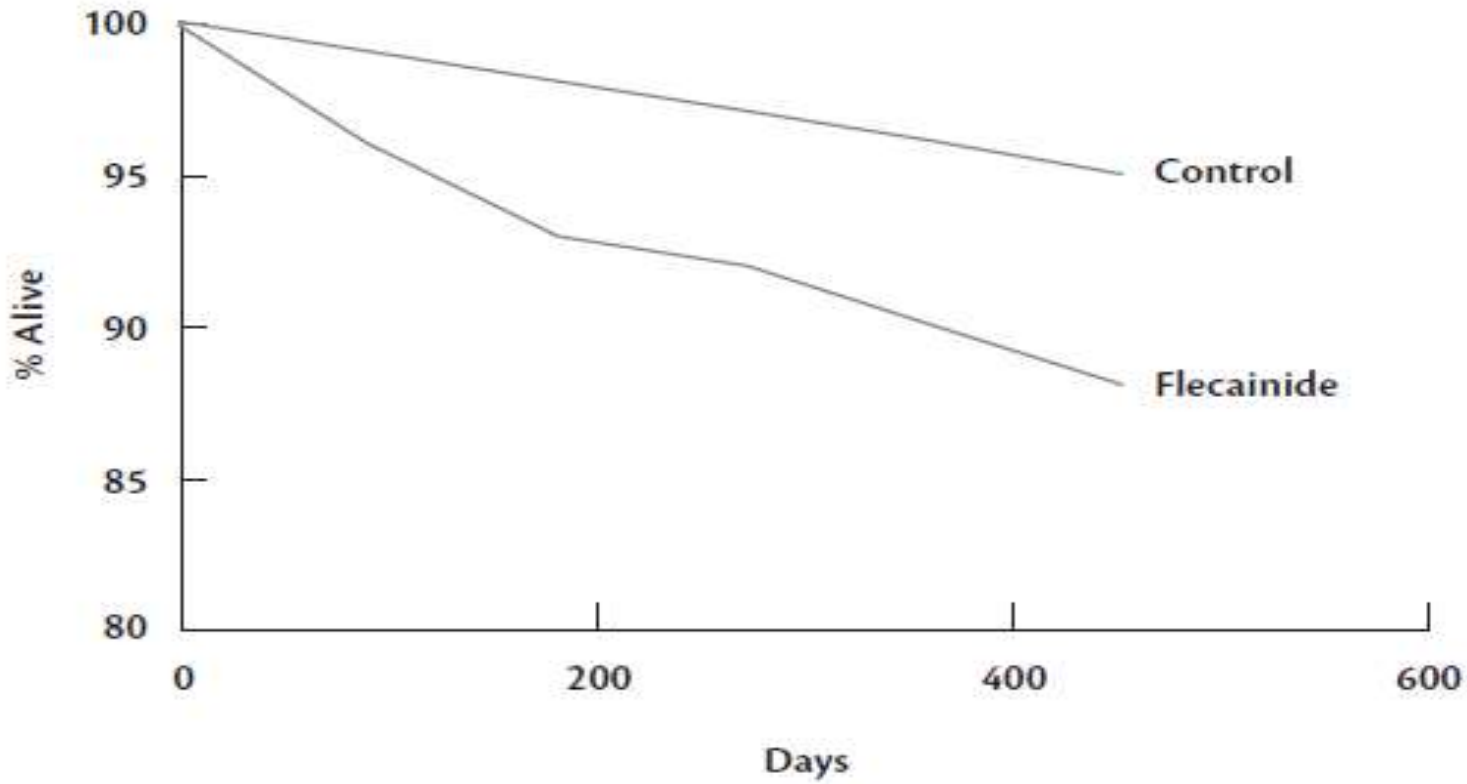
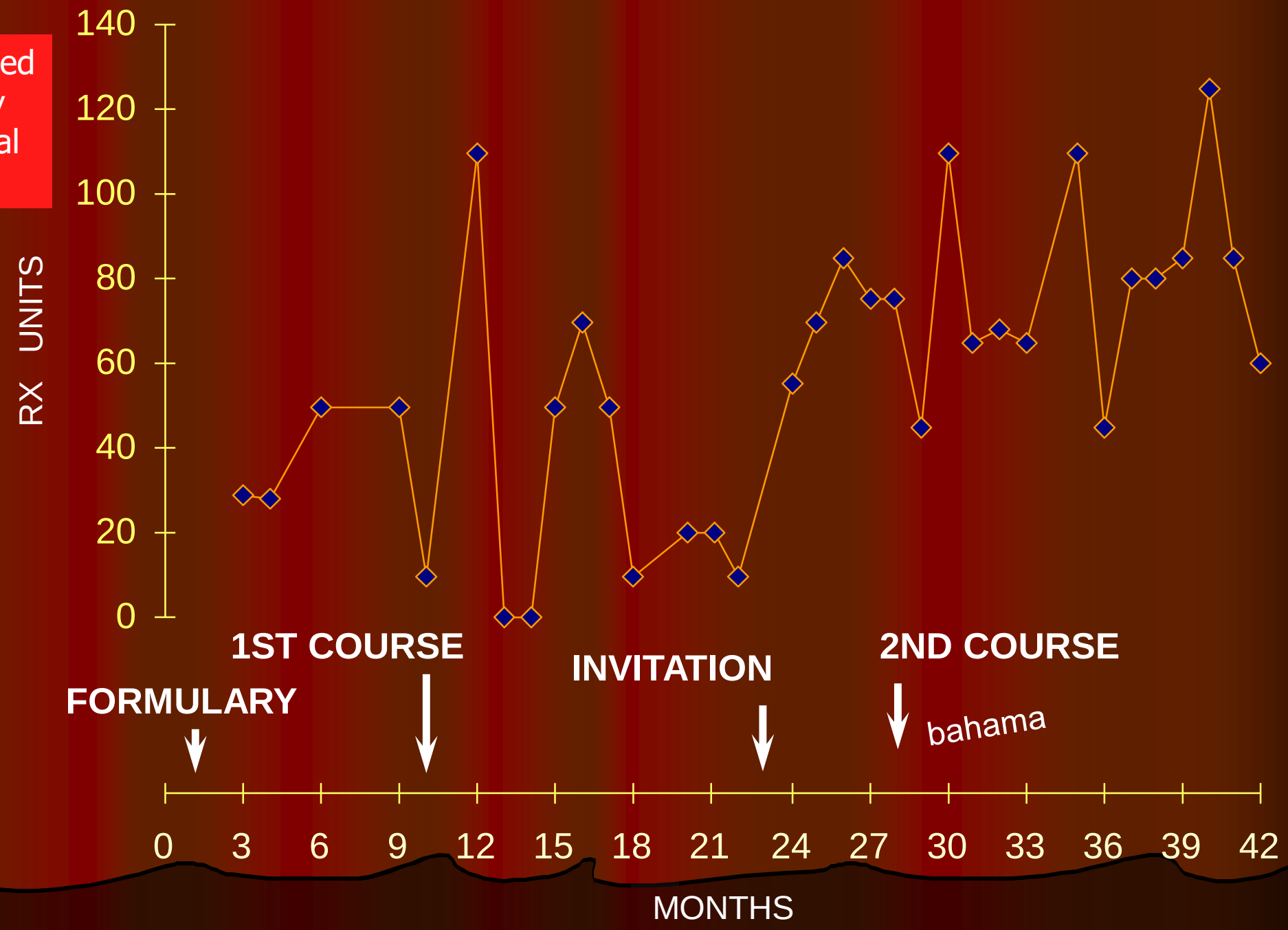
- **Evidence-based medicine (EBM)—asking clear, relevant clinical questions, finding appropriate studies, critically appraising the literature, and implementing changes in practice behavior**


Clinical expertise
Best evidence
EBM
Patient preferences

Cardiac arrhythmia suppression trial



Not to be fooled nor bribed by pharmaceutical companies



Confounding factors

- If a study demonstrates that men who drink more alcohol have increased risk to develop lung cancer
- This is not a causal relationship:
  Drinking alcohol is **confounder** to risk factor & outcome
  Men who drink more also smoke more

The main point

- **is to be critical**.

EBM

- **the use of mathematical estimates of the risk of benefit and harm , derived from high –quality research to inform clinical decision – making in the management of individual patient**

Dr Sydney Burwell

Dean of Harvard Medical School

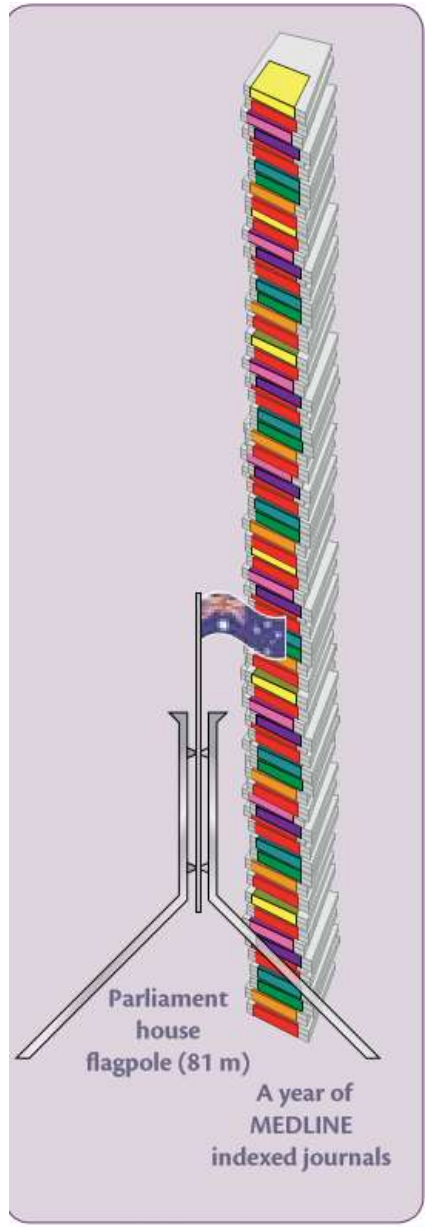
1935-1949

"Half of what you are taught as medical students will in10 years have been shown to be wrong. And the trouble is, none of your teachers knows which half."

I am here because?

- I wanted 3 days of work
- Formulate an answerable questions

scientist is inundated with more papers than he or she can ever hope to read


Parliament
house
flagpole (81 m)
A year of
MEDLINE
indexed journals

High quality/relevant data

Pearls

If not valid → No value

If not relevant → No value

- How can diligent physicians narrow the gap between their current behaviors and best practices?

What's the "E" in EBM?

The best evidence is

the evidence most likely to provide an unbiased view of the truth.

Bias is difference between study results & truth

- It has been recognized that providing evidence from clinical research is a necessity, but **not sufficient**, condition for the provision of optimal care

Being fair and open minded ; not dismissing anything without examination ,and not accepting anything without examination either

Patient’s centered

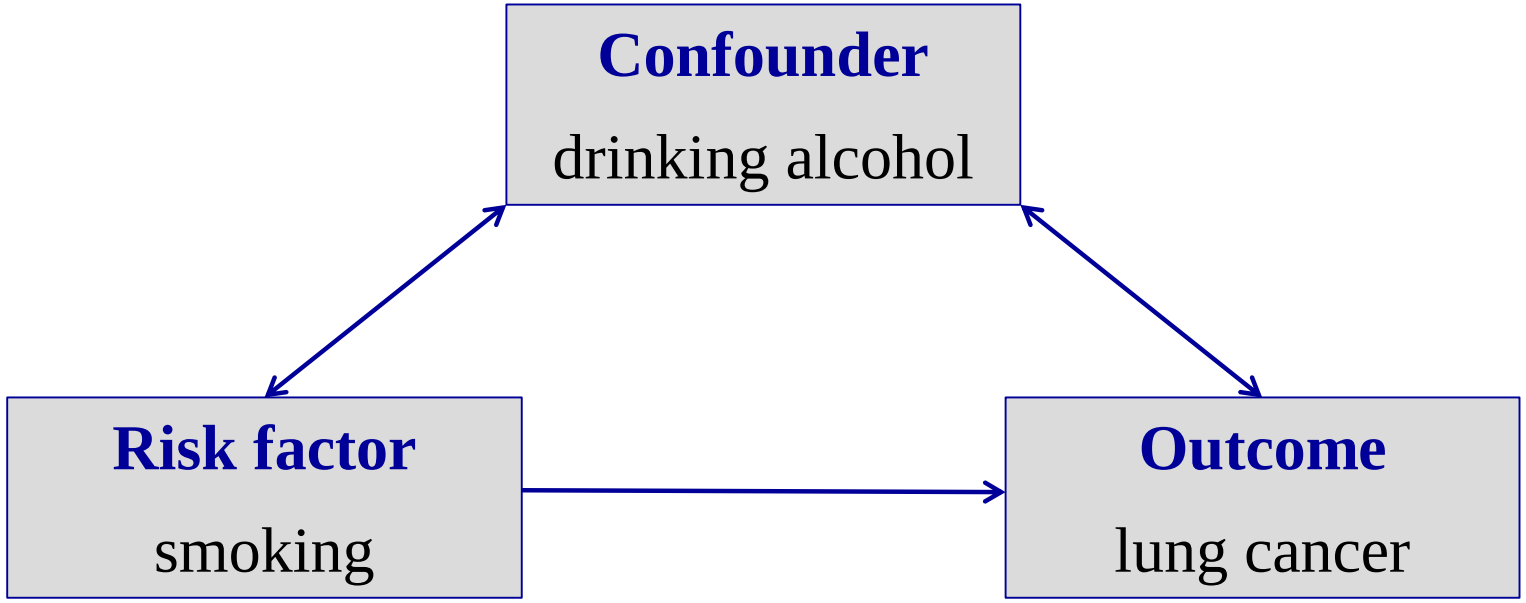
Well according to these tests you’re feeling much better! Maybe you just don’t know it yet...

To be an intelligent reader of the medical literature

Confounding factor

systematic error due to influence of a third variable

Association of smoking & lung cancer



Drinking more alcohol is confounder to:

risk factor (smoking) & outcome (lung cancer)

Glasser SP. Essentials of clinical research. Springer , 1st Edition, 2008.

The message is clear :

All evidence , all information **is not** necessarily equivalent

Keep sharp eye out for the believability of **whatever** information we find **wherever** we find it

Judgmental& Forming judgment

Judgmental

- involves attaching an emotional value of good or evil, *generally harsh one* ,to a persons , place, or idea.

Forming judgment

- forming an opinion , or evaluating the truth or falsehood of a claim , based upon discernment , logic and comparison.

- Since: CT is
  -not forming emotional attachments to your opinions,
  -being fair,
  -looking simply for the truth
  (not for good or evil)

It is hard but worth it

rationalizing

- **Start with conclusion**

- finding the evidence for it

C. Thinker

- Start with evidence

- arriving to conclusion

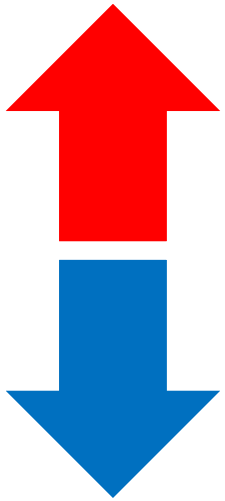
- Start examining everything given to you
- Decide the merits of what is given based on clear and critical thinking and use that as a basis for your actions or opinions

- Do what you decide is the right thing for you to do

- To be persuasive we must be believable;
  to be believable we must be credible;
  to be credible we must be truthful.
- (Edward R. Murrow)

Appraising validity

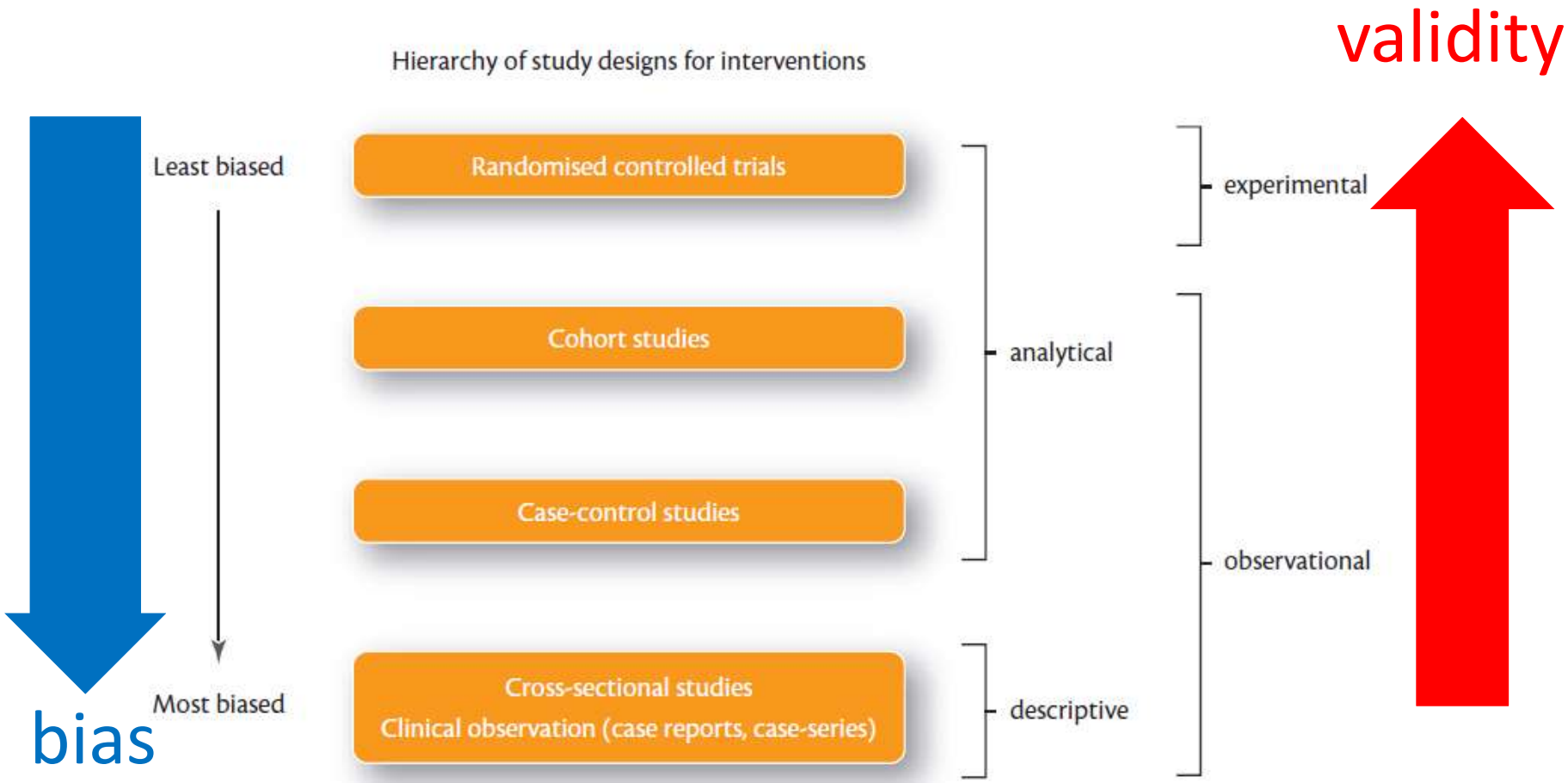
Validity refers to how close we think study results are to the truth.



validity

bias

Hierarchy of evidence

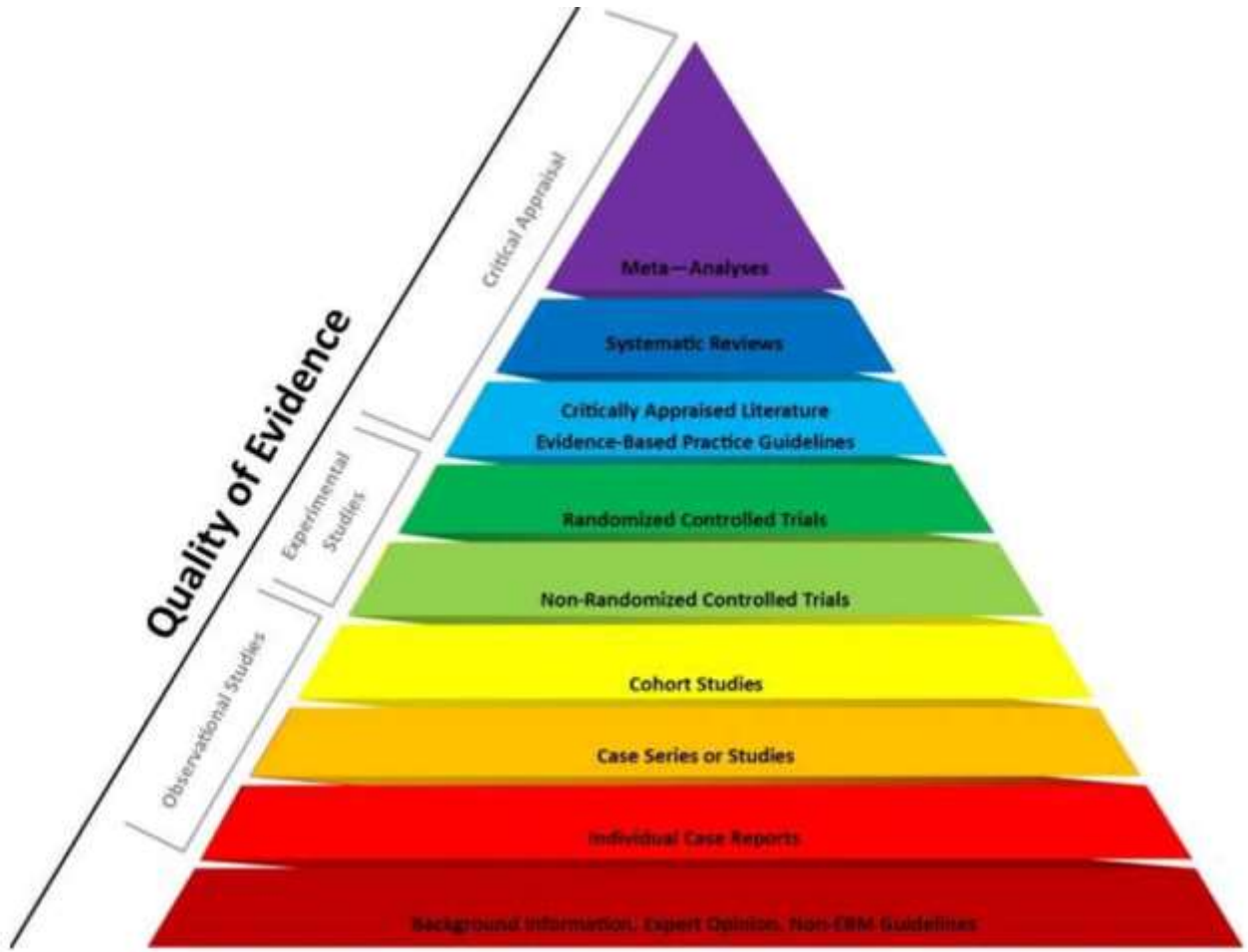


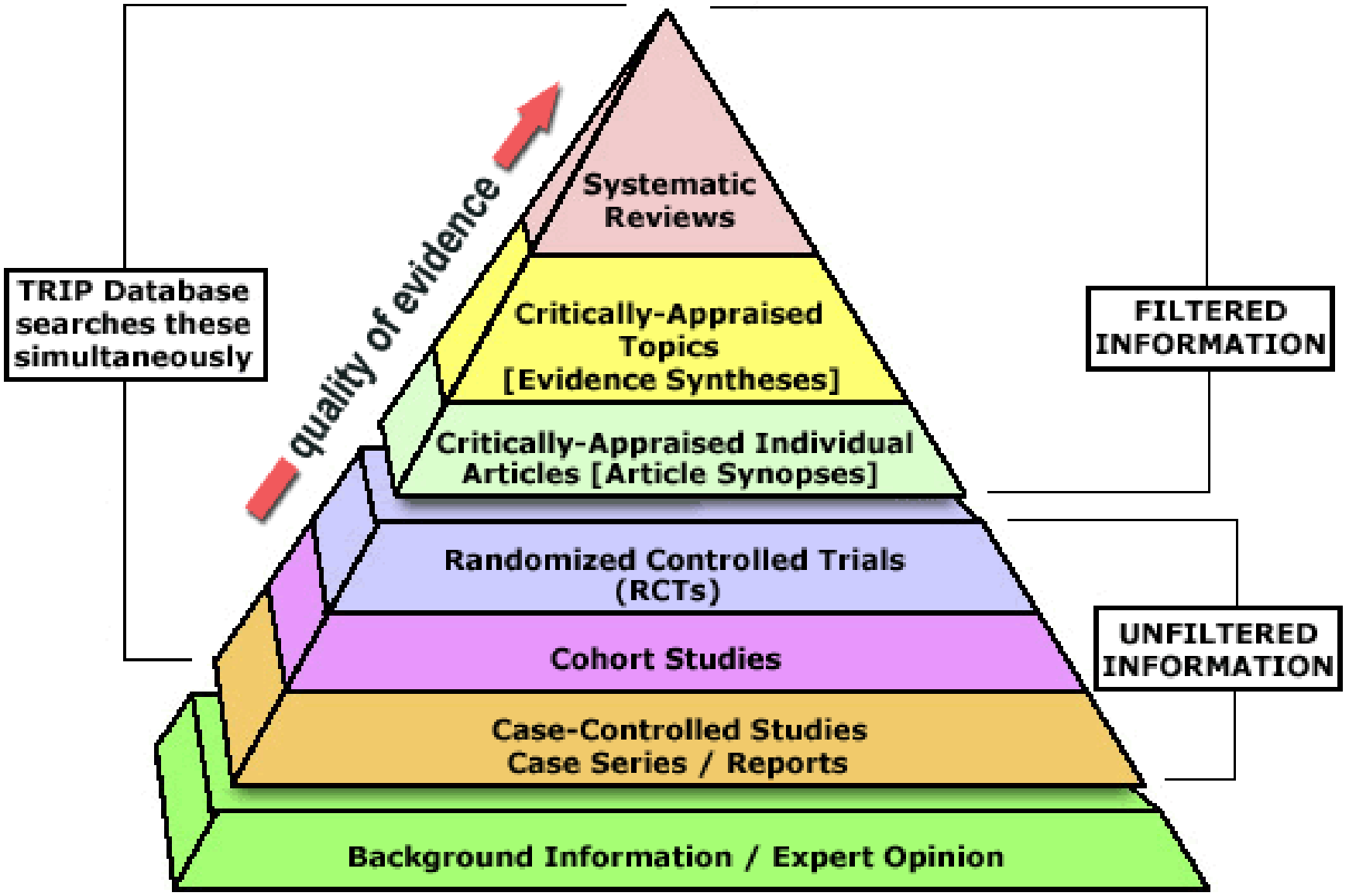
“Hierarchy of evidence “

Levels upon Levels of evidence

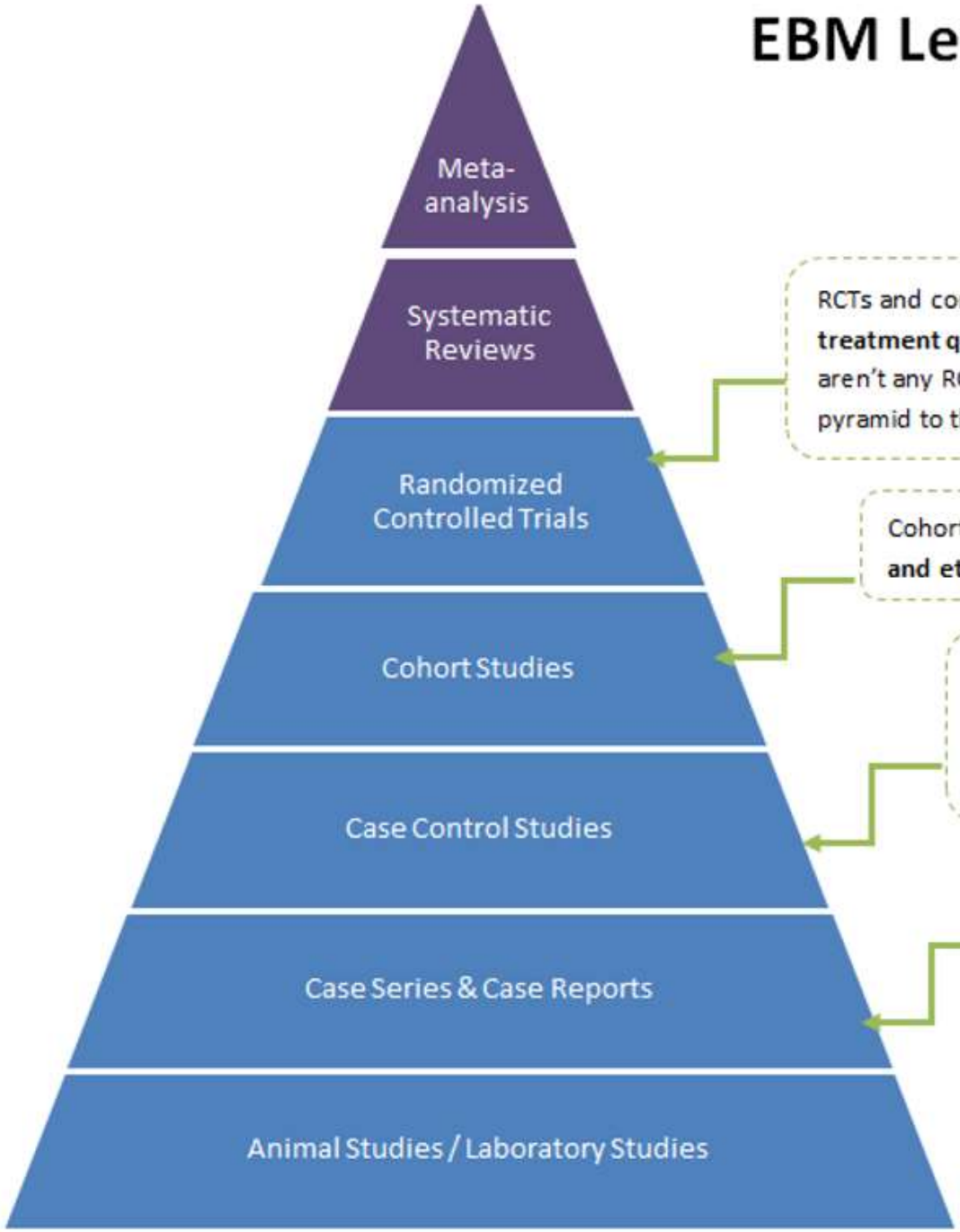
EBM can (amongst other things!)

- Help you make clinical decisions
- Share decision making with patients
- Provide better diagnostic reasoning
- Understanding benefits versus harms
- Allow you to practice more safely


Quality of Evidence
Critical Appraisal
Experimental Studies
Observational Studies
Meta—Analyses
Systematic Reviews
Critically Appraised Literature
Evidence-Based Practice Guidelines
Randomized Controlled Trials
Non-Randomized Controlled Trials
Cohort Studies
Case Series or Studies
Individual Case Reports
Background Information, Expert Opinion, Non-EBM Guidelines



EBM Levels of Evidence Pyramid



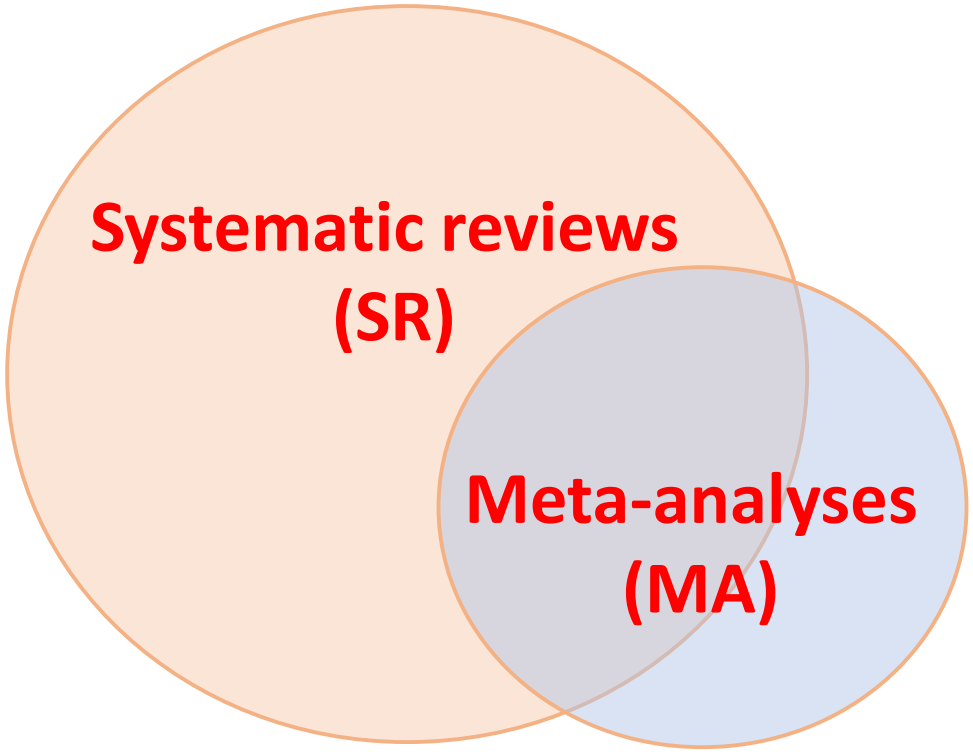
RCTs and controlled clinical trials help to answer **treatment questions and diagnosis questions.** If there aren't any RCTs or controlled clinical trials, move down the pyramid to the next best option.

Cohort Studies help to answer **prognosis questions and etiology/harm questions.**

When you cannot find a cohort study to answer your **prognosis** or **etiology/ harm question**, look for a Case Control Study.

When you cannot find a cohort study or a case control study to answer your **prognosis** or **etiology / harm question**, look for a Case Series or Case Report.

Systematic review & meta-analysis



MA may, or may not, include a SR

Egger M et all. Systematic reviews in health care: Meta-analysis in context. BMJ Publishing Group, London, 2nd edition, 2001.

Type of Question	Suggested best type of Study
Therapy	RCT > Cohort > Case control > Case Series
Diagnosis	RCT > Cohort
Prognosis	Cohort > Case Control > Case Series
Etiology	Cohort > Case Control > Case Series

Question type & study design

Question	*Study Design*
Prevalence	*Cross-sectional study*
Diagnosis	*Cross-sectional study*
Etiology & risk factors	*Cohort or case-control*
Incidence & prognosis	*Cohort study*
Intervention	*RCT*

In each case, SR of all available studies better than individual study

Identifying the Best Study

Question Type	Best Type of Study
Therapy	Systematic Review / RCT
Diagnosis	Systematic Review / RCT
Etiology	Systematic Review / Cohort
Prognosis	Systematic Review / Cohort

Level of Evidence

Ia	• Evidence obtained from at least one properly designed randomized, controlled trial.
Ib	• Evidence obtained from at least one randomized controlled trial
IIa	• Evidence obtained from at least one well designed controlled study without randomization
IIb	• Evidence obtained from at least one other type of well designed quasi experimental study
III	• Evidence obtained from well designed non experimental studies, such as comparative studies, correlational studies, and case studies
IV	• Evidence obtained from expert committee reports or opinions

Grade of Recommendation

Grade A	• There is good evidence to support the recommendation, either for or against.
Grade B	• There is fair evidence to support the recommendation, either for or against.
Grade C	• There is insufficient evidence to support the recommendation, either for or against.

The practice of EBM requires:

- Asking
- Acquiring
- Appraising
- Applying

later assessing the impact

Process of EBP

Patient dilemma

Ask

Acquire

Appraise

Hierarchy of evidence

Apply

Act & Assess

Principles of evidence-based practice

Evidence alone does not decide – combine with other knowledge and values

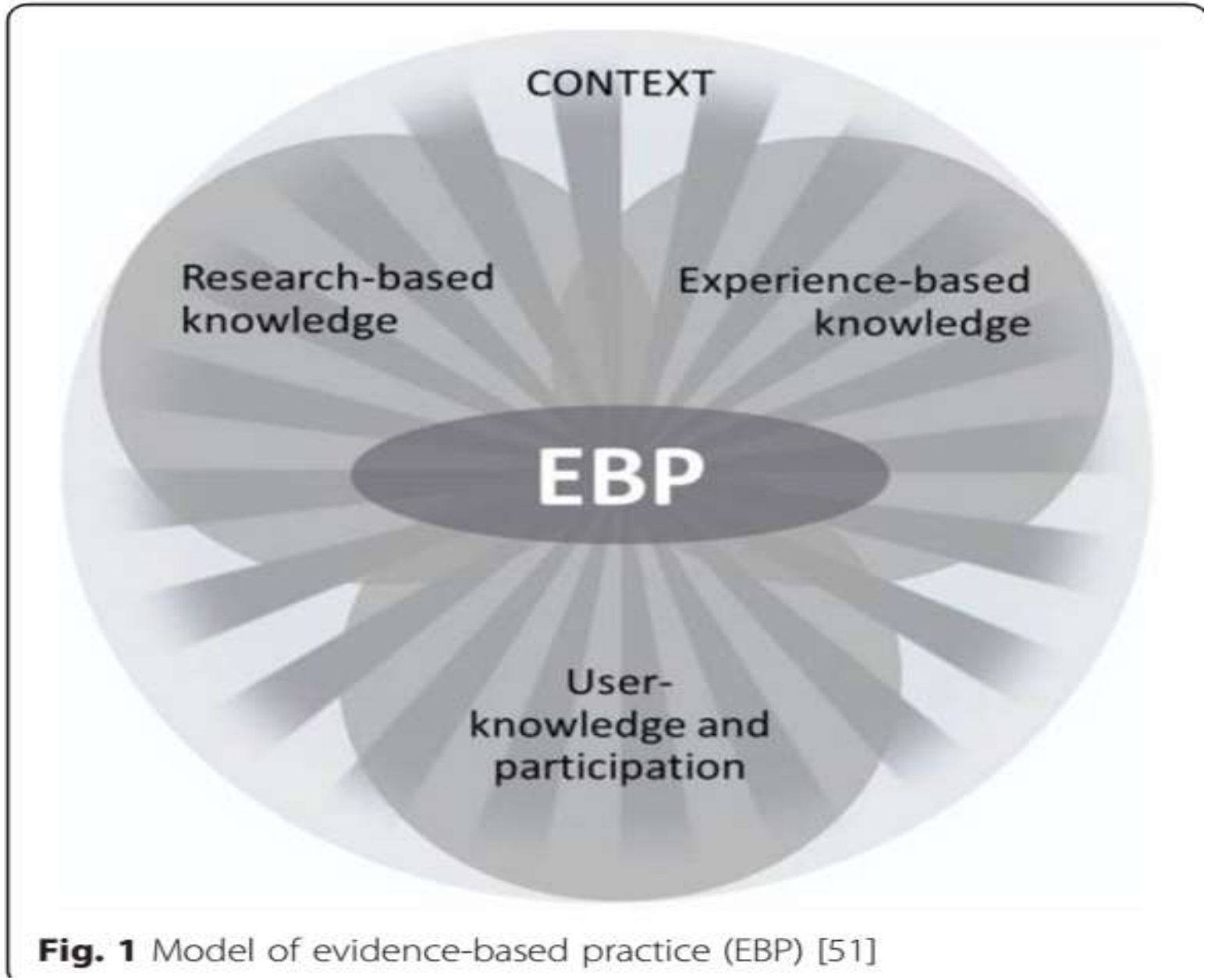
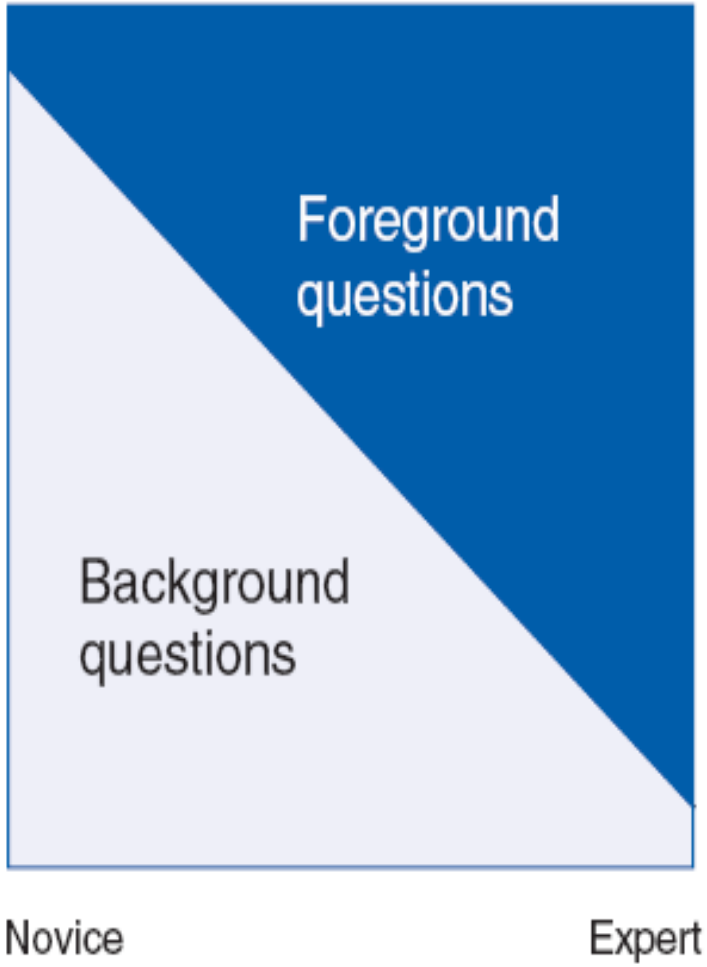


Fig. 1 Model of evidence-based practice (EBP) [51]

Types of Clinical Questions

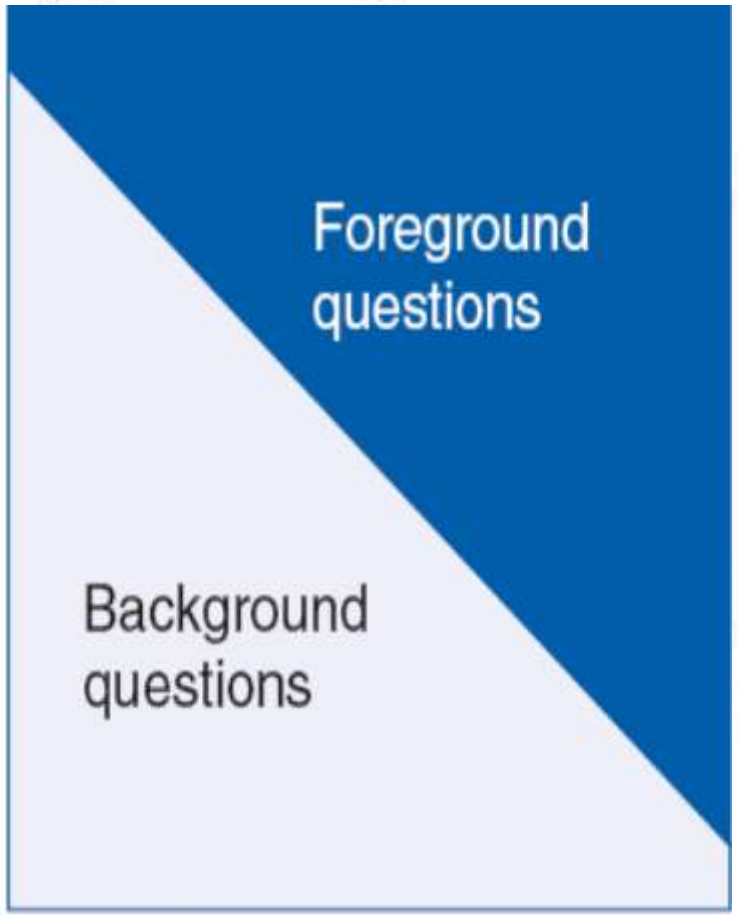
Background	Foreground
General knowledge	Specific Questions
Ask who, what, when, where, why	PICO

Background and Foreground Questions



Experience of doctor

Types of questions



- More general
- Whole condition, symptoms, signs
- Pathophysiology
- Textbooks/online

- Specific clinical decisions
- Primary/pre assessed studies
- Patient centred
- Diagnosis, prognosis, management of disease

‘Background’ Questions

- **About the disorder, test, treatment, etc.**

2 components:

a. Root* + Verb: “What causes …”

b. Condition: “… Ebola?”

- *** Who, What, Where, When, Why, How**

‘Foreground’ Questions

- **About patient care decisions and actions**

4 (or 3) components:

a. Patient, problem, or population

b. Intervention, exposure, or maneuver

c. Comparison (if relevant)

d. Clinical Outcomes (including time horizon)

Box 1.1 Well-built clinical questions

"Background" questions

Ask for general knowledge about a condition, test, or treatment
Have two essential components:

1. A question root (who, what, where, when, how, why) and a verb.
2. A disorder, test, treatment, or other aspect of health care.

Examples:

"How does heart failure cause pleural effusions?"
"What causes swine flu?"

"Foreground" questions

Ask for specific knowledge to inform clinical decisions or actions
Have four essential components:

1. P: Patient, population, predicament, or problem.
2. I: Intervention, exposure, test, or other agent.
3. C: Comparison intervention, exposure, test, and so on, if relevant.
4. O: Outcomes of clinical importance, including time, when relevant.

Example:

"In adults with heart failure and reduced systolic function, would adding the implantation of an electronic resynchronization device to standard therapy reduce morbidity or mortality enough over 3 to 5 years to be worth the potential additional harmful effects and costs?"

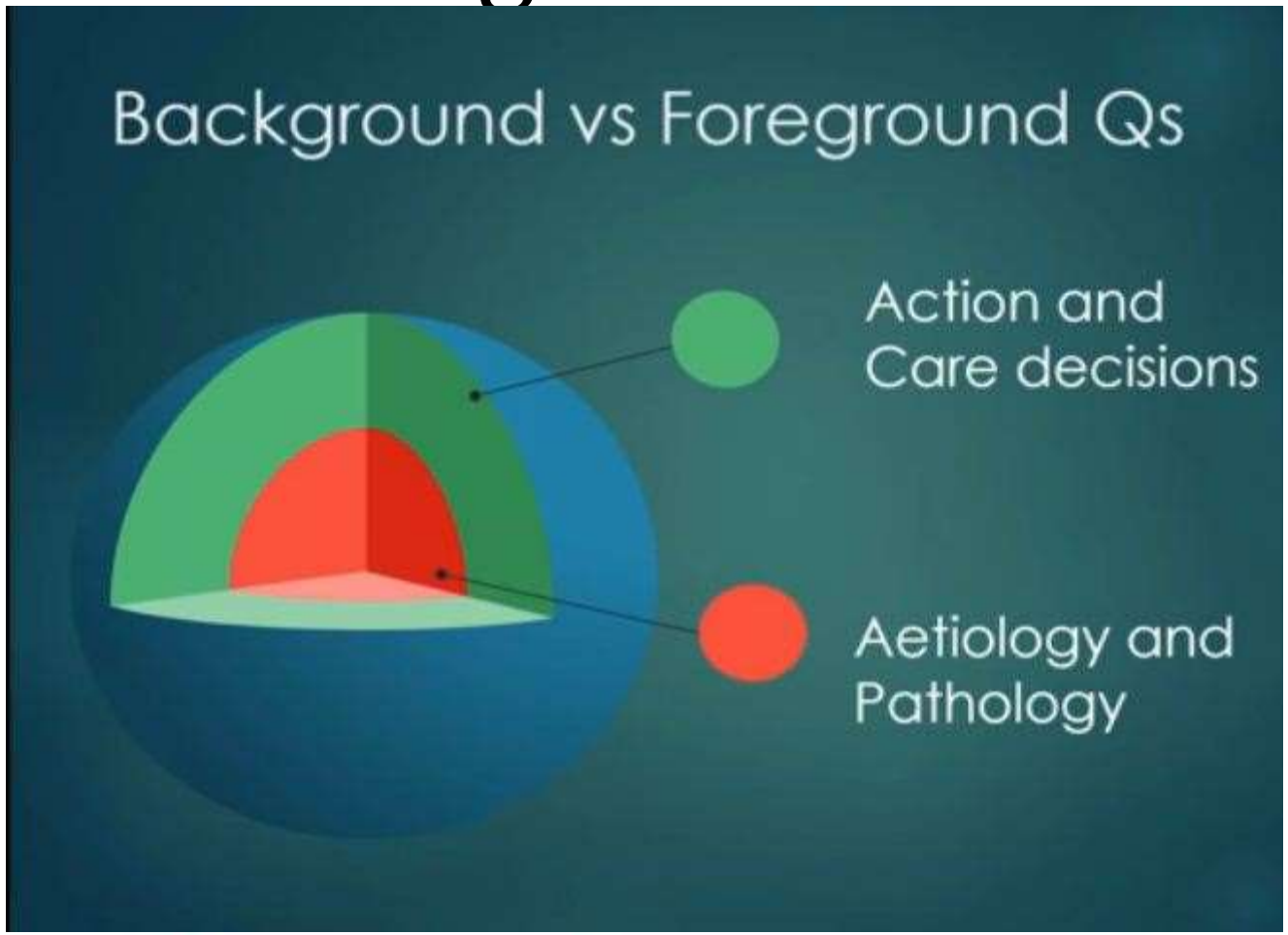
Does this intervention help?

For every 100 people with Bell's palsy at 3 months

83 in the corticosteroid group will have recovered facial function &
64 in the placebo group will have recovered facial function

- Risk difference = 19%
- Relative Risk Reduction = 23%
- Number Needed to Treat = 6
- Natural Frequency 19 per 100

Background & Foreground

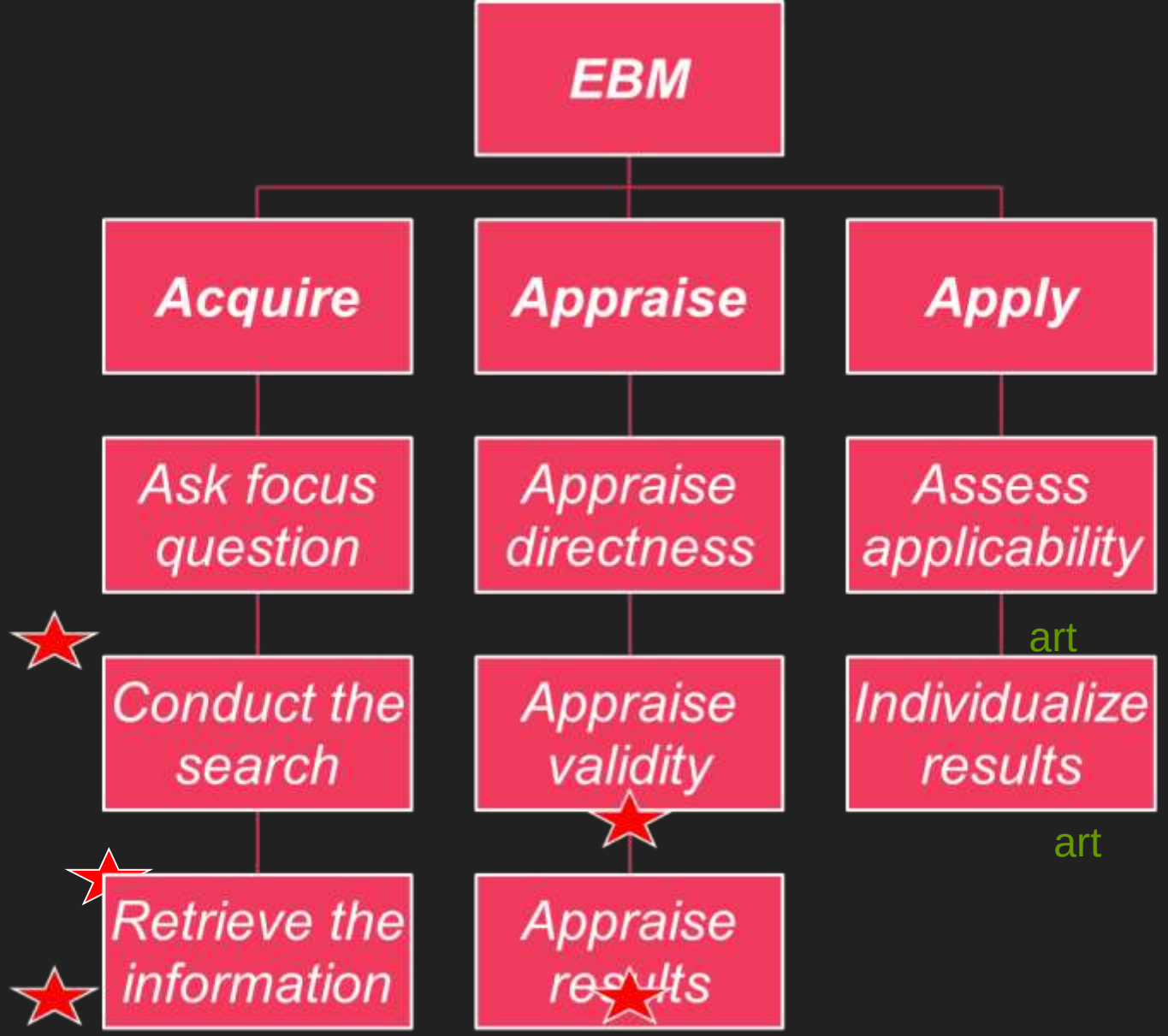


Experience with Condition

The practice of EBM requires:

- Asking
- Acquiring
- Appraising
- Applying

later assessing the impact


EBM
Acquire
Appraise
Apply
Ask focus question
Appraise directness
Assess applicability
Conduct the search
Appraise validity
Individualize results
Retrieve the information
Appraise results
art
art

We tend to receive knowledge passively at many stages of education

Programmed instruction was introduced in 1954 by B. F. Skinner of Harvard and much of
the system is based on his theory of the nature of learning, which is based on the principles of
small steps, self-pacing, and immediate feedback (Skinner, 1954). Programmed instruction
enables learners to work individually, calling for active participation of the learner .

Evolving EBM

- Early EBM: (“teach them to read it and they will come”)
- Current EBM: Push diffusion
  (“read it for them and send it to them”)

Synthesised sources : Systems , summaries and syntheses

Very High level of evidence

Relatively new

Translate research into practice

Inform Clinician and patient decision making

Synthesised sources : Systems , summaries and syntheses

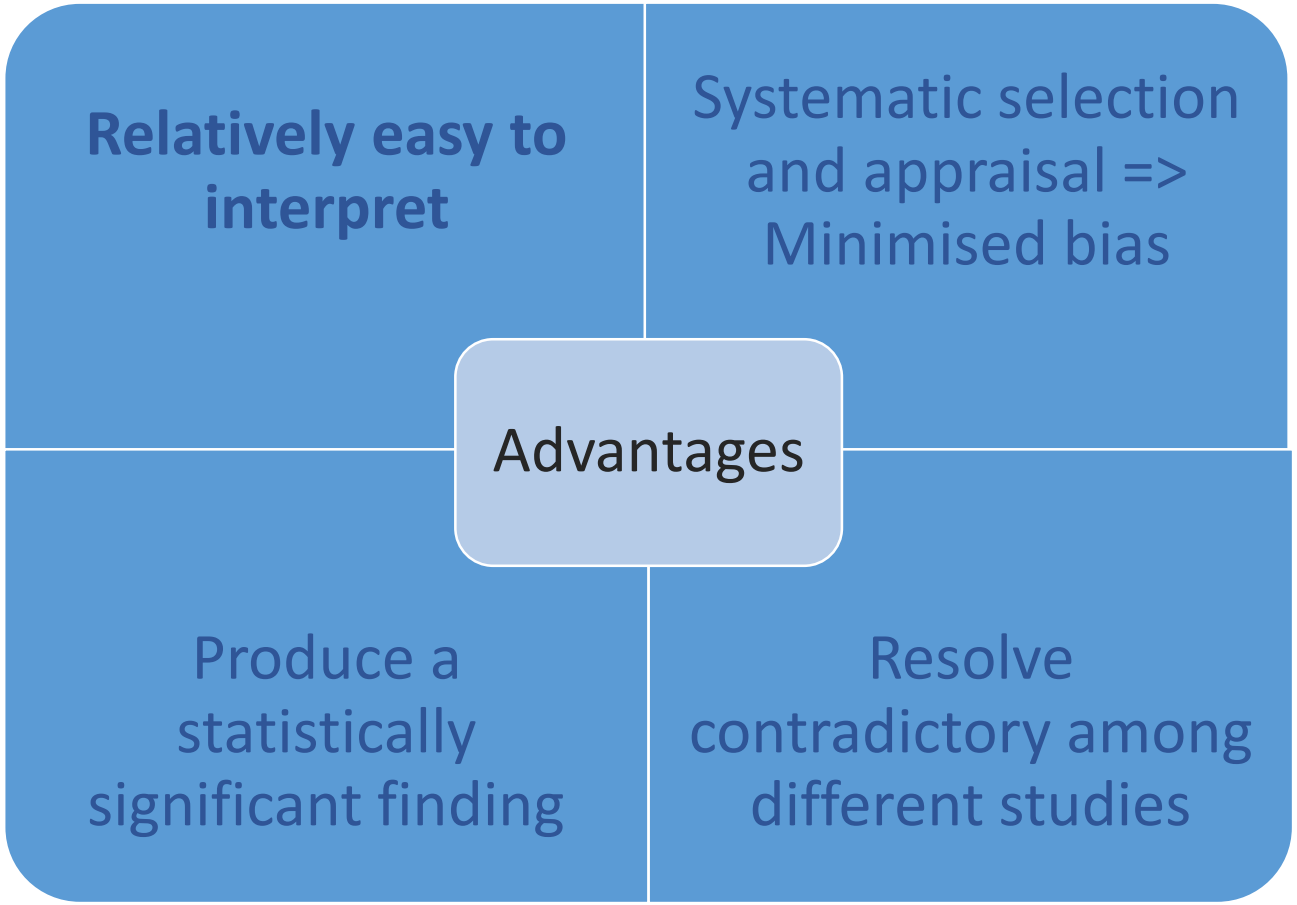
Point of care

Like electronic textbooks or detailed clinical handbooks

BUT

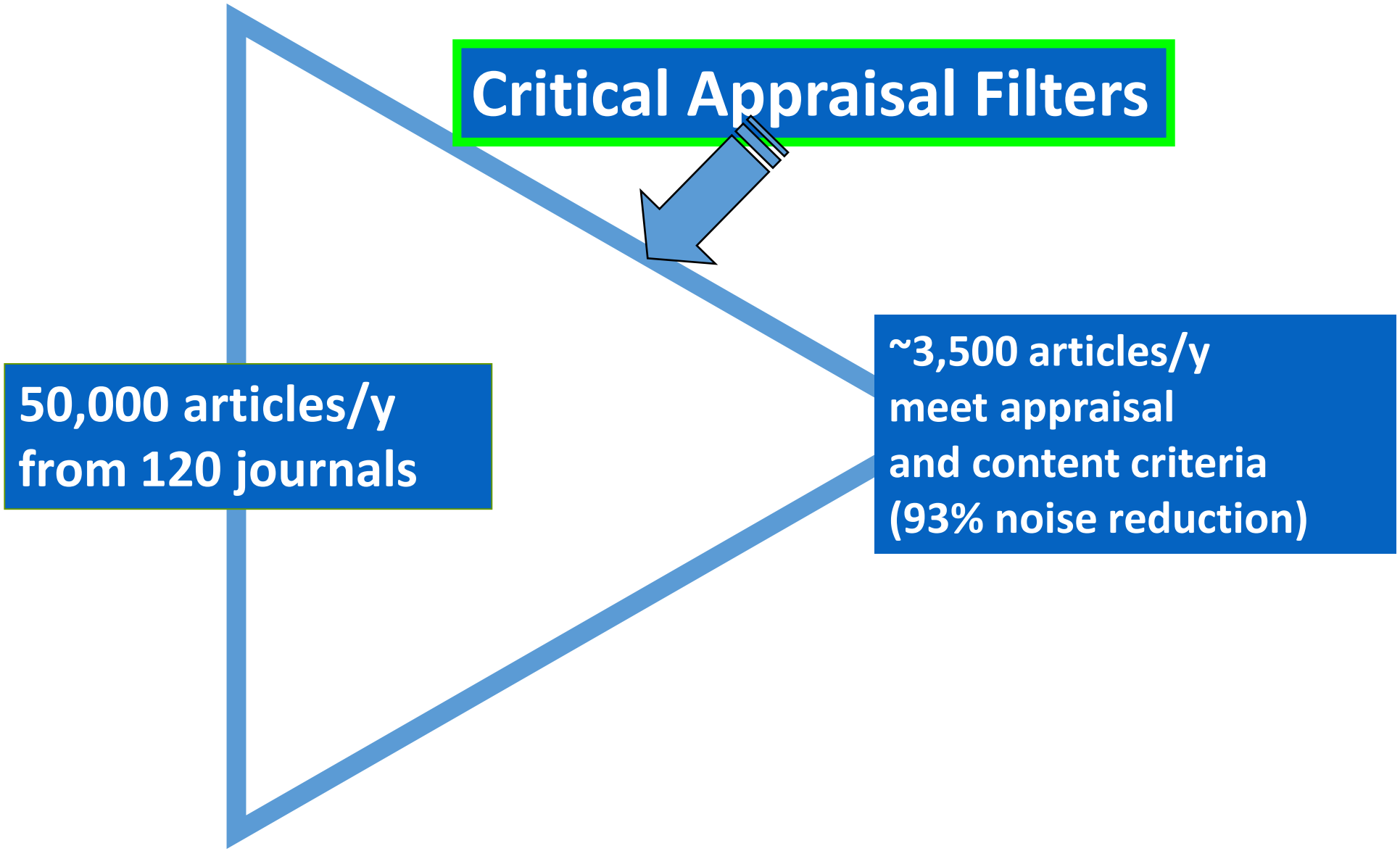
- Explicity **evidence based**
- Continuously **updated**
- Designed to be **user friendly**

Synthesised sources : Systems , summaries and syntheses

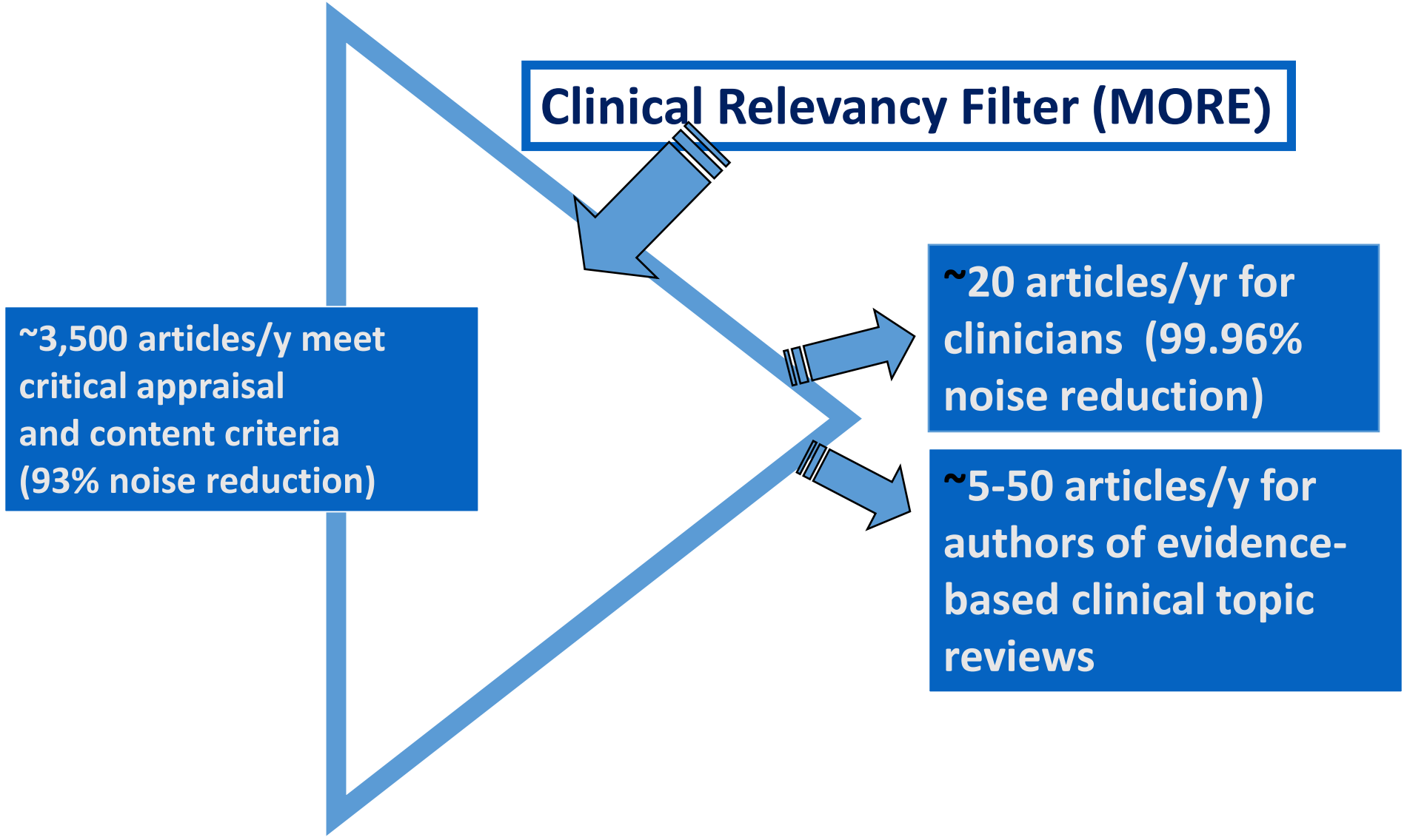


Save time and exersion

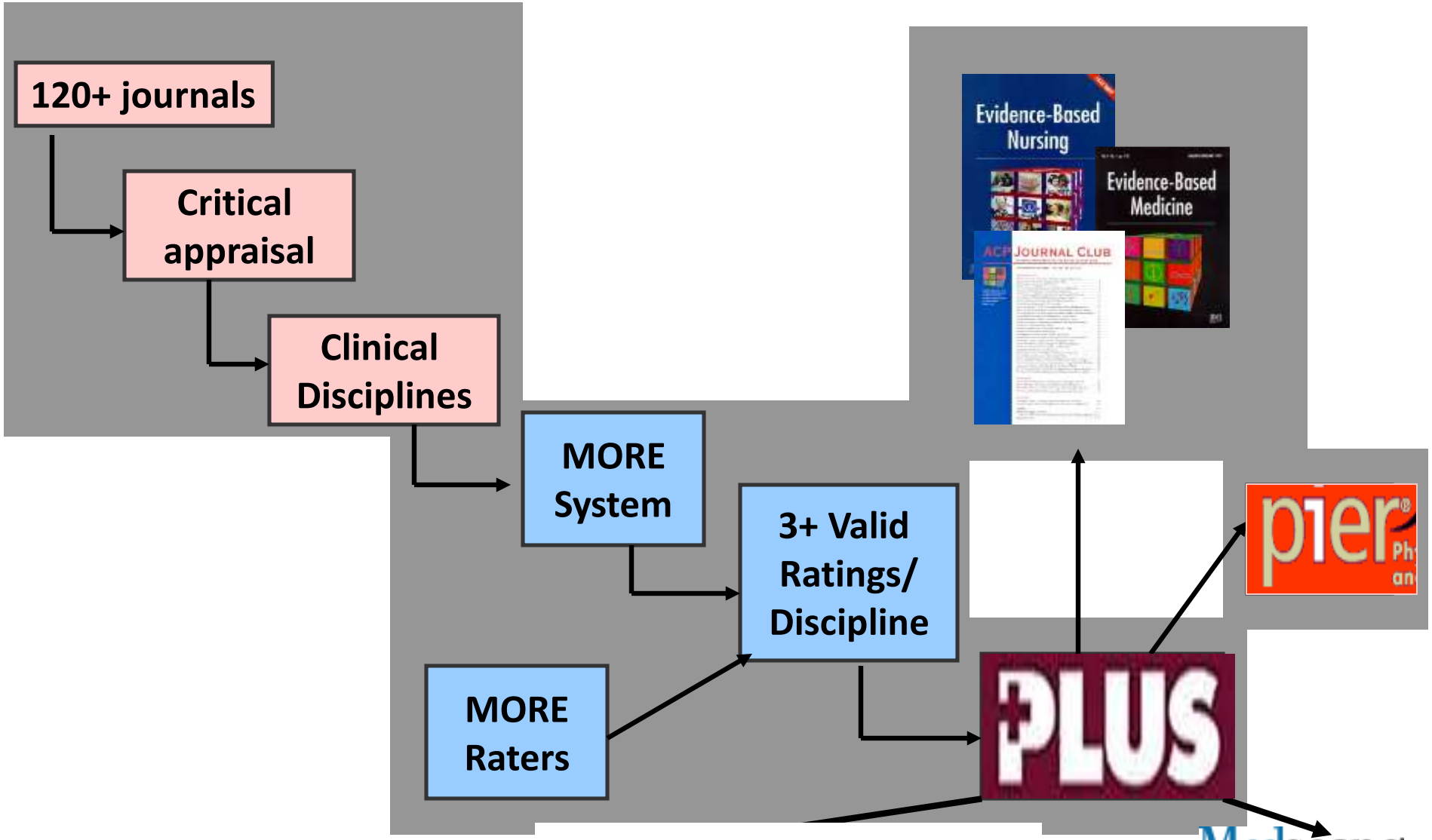
Evidence-Based Journals



McMaster PLUS Project



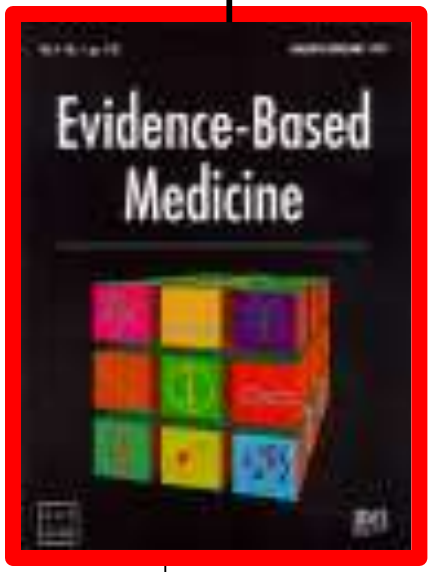
McMaster PLUS "Refinery" and Products

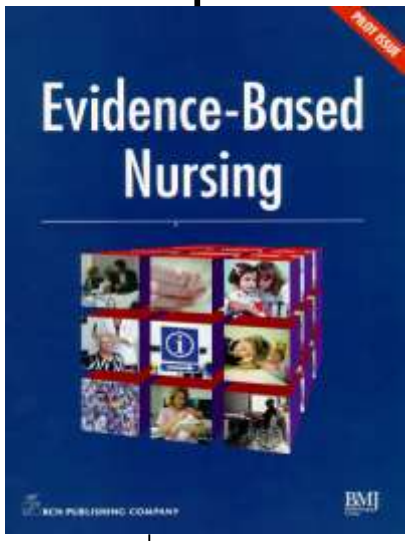


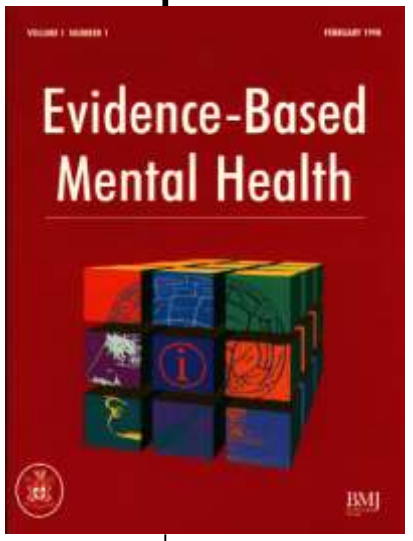
Using

- searches are restricted to evidence resources that have already undergone critical appraisal by others, such as evidence summaries

EBM JOURNALS

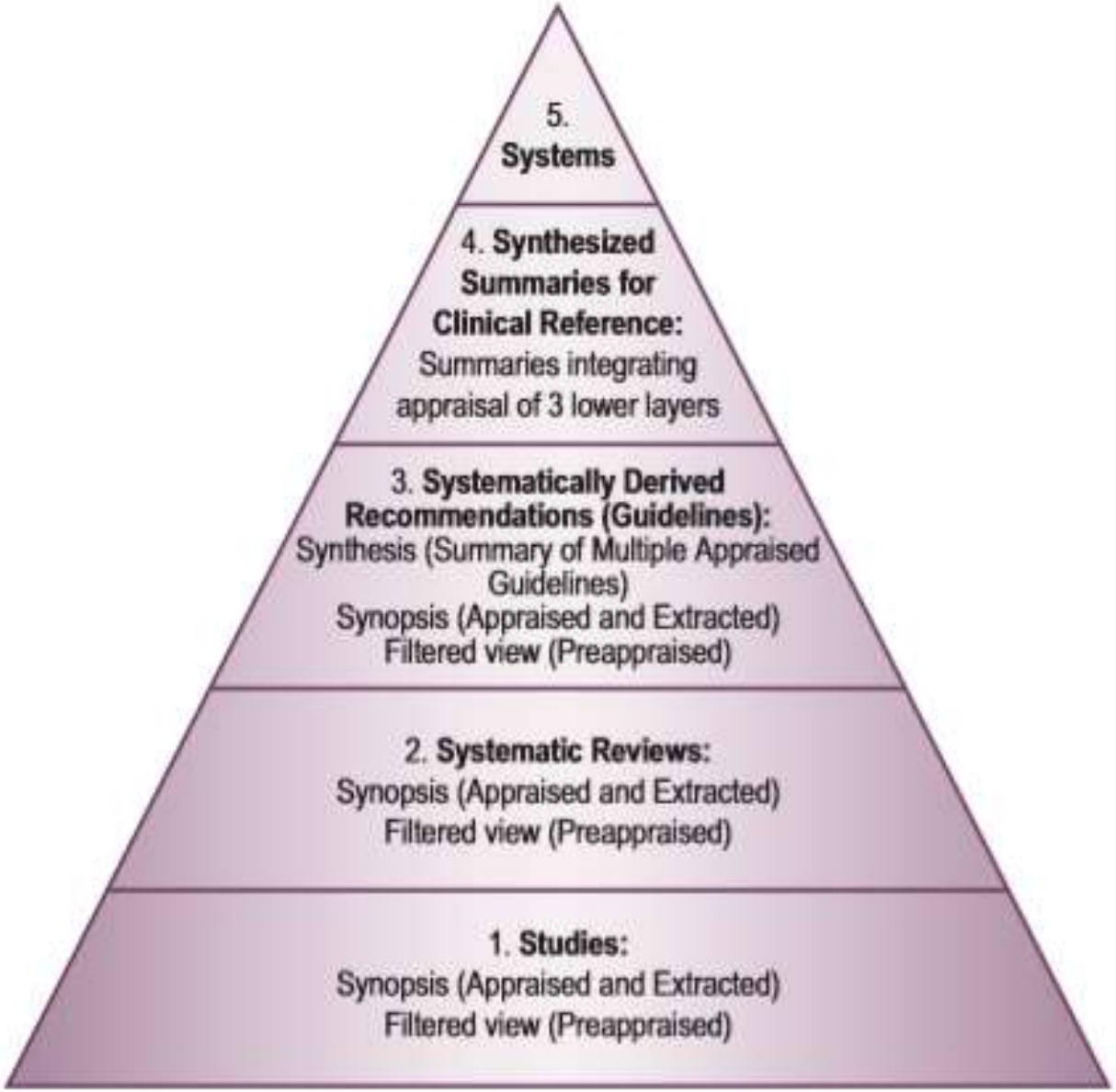




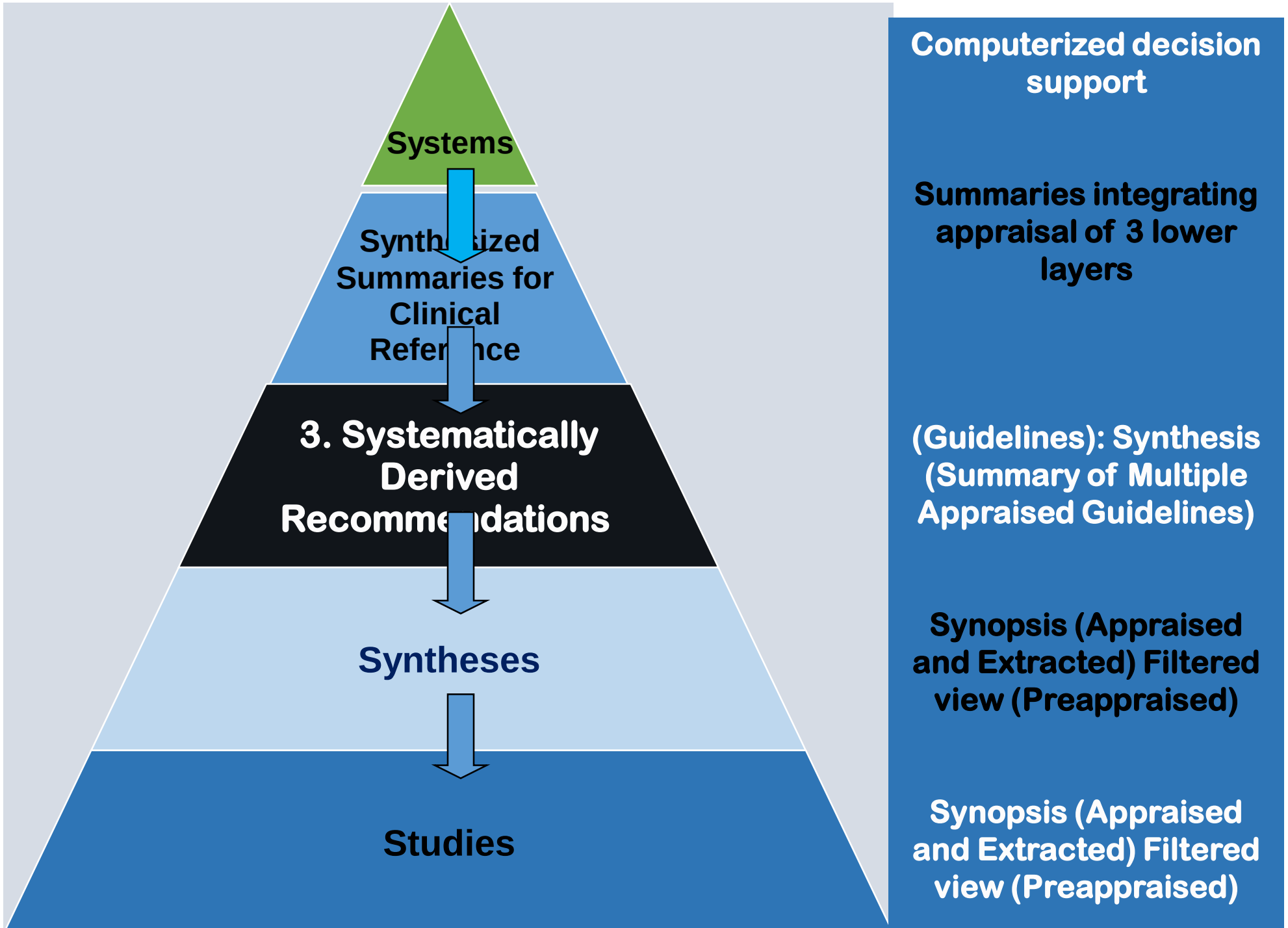


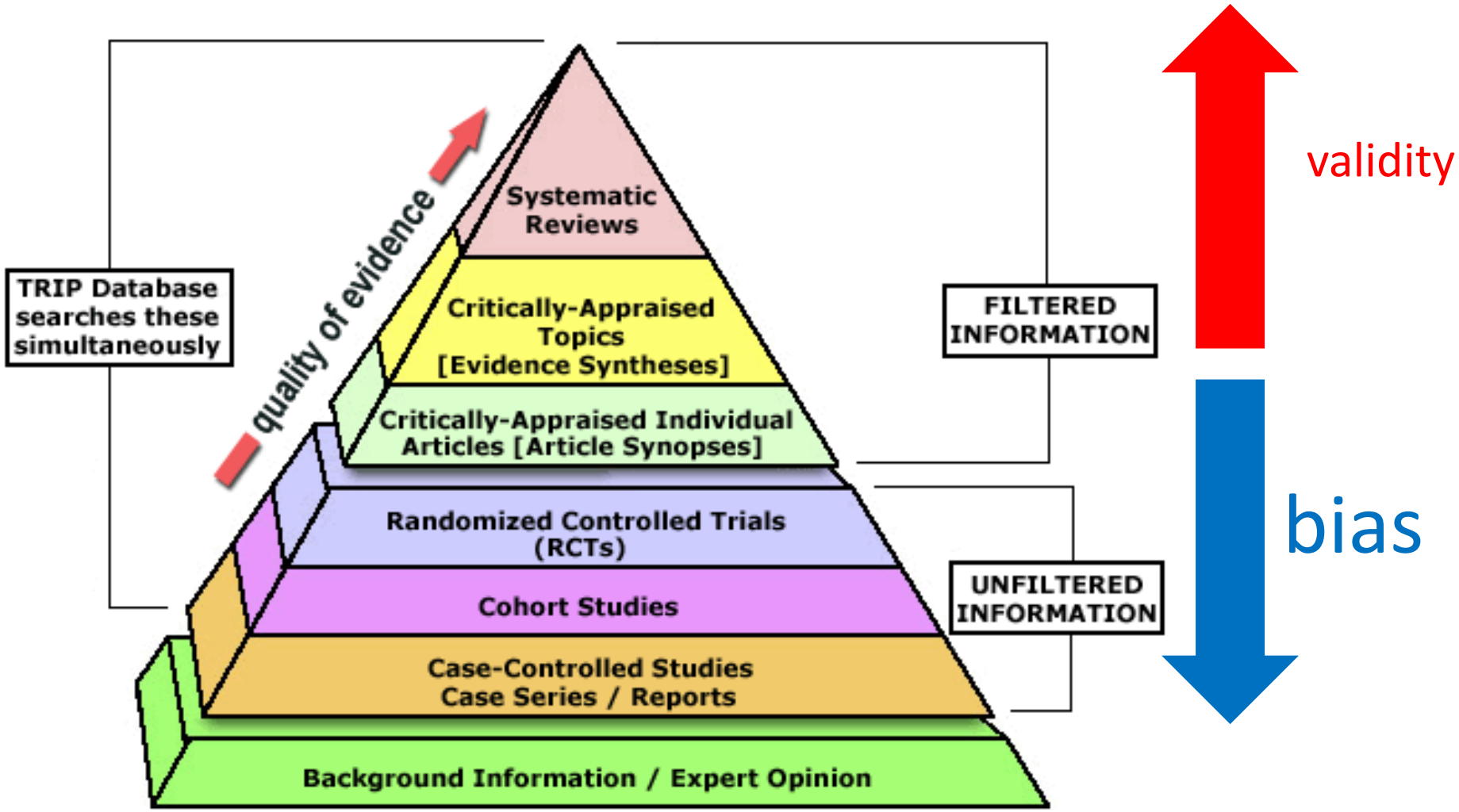
American College of Physicians

BMJ Publishing Group



Evidence-Based Health Care Pyramid 5.0 for finding preappraised evidence and guidance. (From Alper BS, Haynes RB. EBHC pyramid 5.0 for accessing preappraised evidence and guidance.


Systems
Synthesized Summaries for Clinical Reference
3. Systematically Derived Recommendations
Syntheses
Studies
Computerized decision support
Summaries integrating appraisal of 3 lower layers
(Guidelines): Synthesis (Summary of Multiple Appraised Guidelines)
Synopsis (Appraised and Extracted) Filtered view (Preappraised)
Synopsis (Appraised and Extracted) Filtered view (Preappraised)




Systematic review
Cohort studies
Ideas opinions
Randomized controlled trials
Case series, Case reports

Modes:

- Doing
- Using

- Not everyone needs to do everything

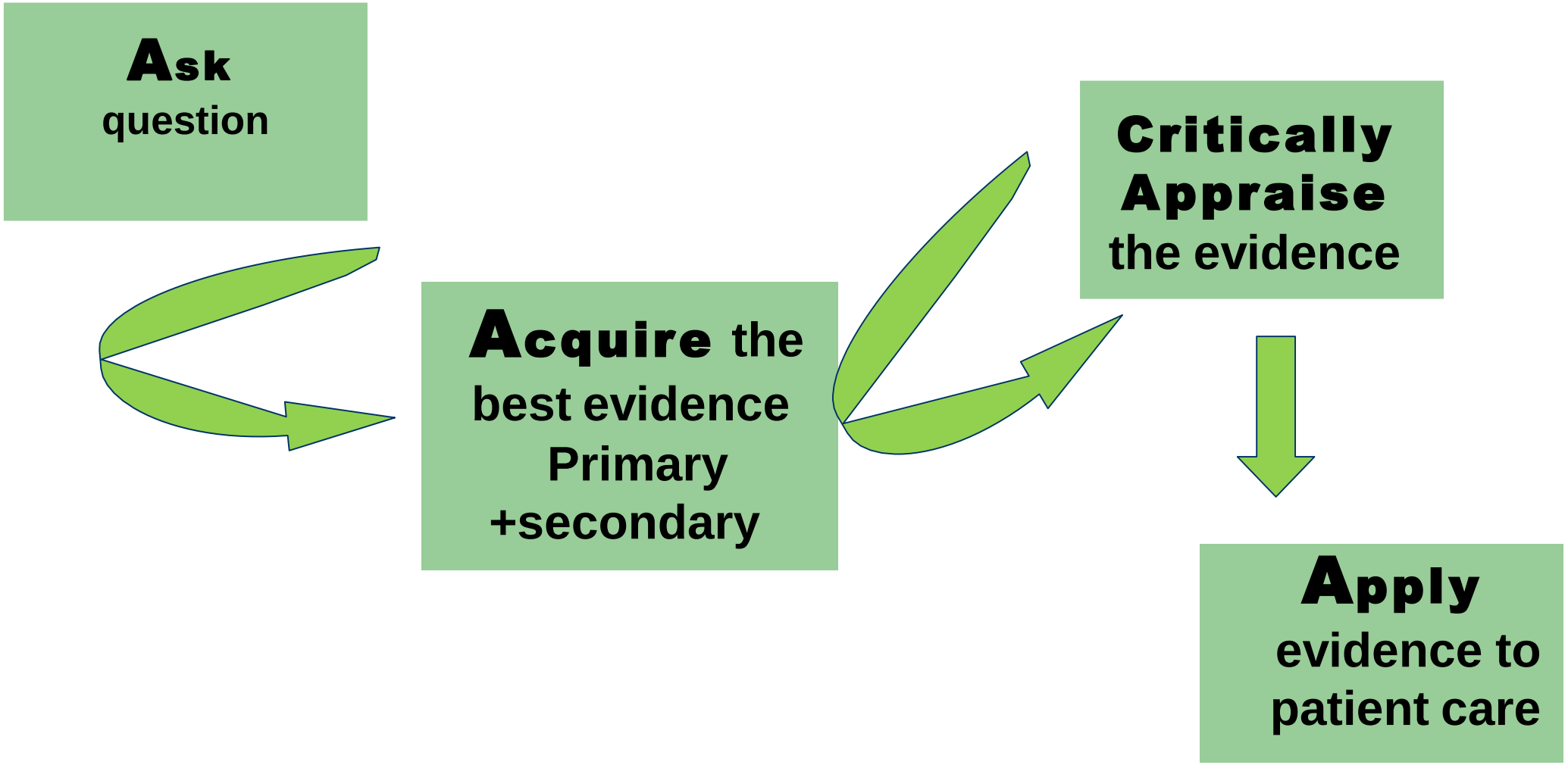
doing

- in which at least the first four steps above are completed

clinicians can incorporate evidence into their practices in three ways

- “Doing” mode (1-4)
- “Using” mode(skipping Step 3)
- “Replicating” (mode) abandoning at least Steps 2 and 3)

practice EBM -doing mode



Using

- searches are restricted to evidence resources that have already undergone critical appraisal by others, such as evidence summaries

practice EBM -Using mode

Ask PICO question

Acquire the best evidence secondary

Apply evidence to patient care

Fortunately

- New resources to assist doctors are available and the pace of innovation is rapid

FORMULATE AN ANSWERABLE QUESTIONS

- Primary care physicians identify 2.4 clinical questions for every 10 encounters (Barrie and Ward, 1997),
  but they spend less than 15 minutes on average with each patient

PICO

P	I	C	O
Population Patient Problem	Intervention Or Exposure	Comparison	Outcome
Who are the patients? What is the problem?	What do we do to them? What are they exposed to?	What do we compare the intervention with?	What happens? What is the outcome?

Rx Educational Prescription

Patient's Name

Learner:

3-part Clinical Question

Target Disorder:

Intervention (+/- comparison):

Outcome:

Date and place to be filled:

“What should I do about this problem?”

“What are the types of problems?”

“What causes the problem?”

“How common is the problem?”

“Does this person have the condition or problem?”

“Who will get worse ?”

Background:

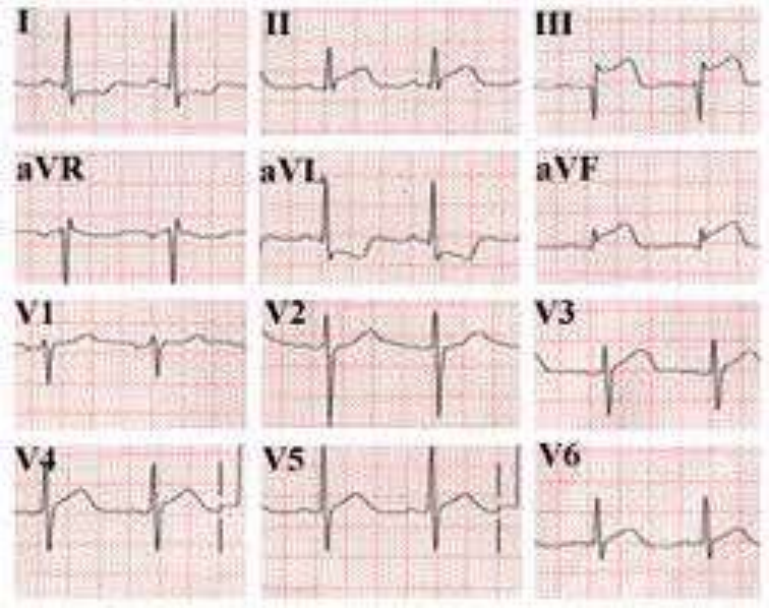
Patient presenting with MI

1. What are the symptoms and signs of someone presenting with MI?

1. What are the diagnostic tests for MI?

1. What are the causes of MI?

1. What are the treatments of MI?



Patient presenting with MI

Foreground’ Questions

About actual patient care decisions and actions

For treatment
4 (or 3) components:

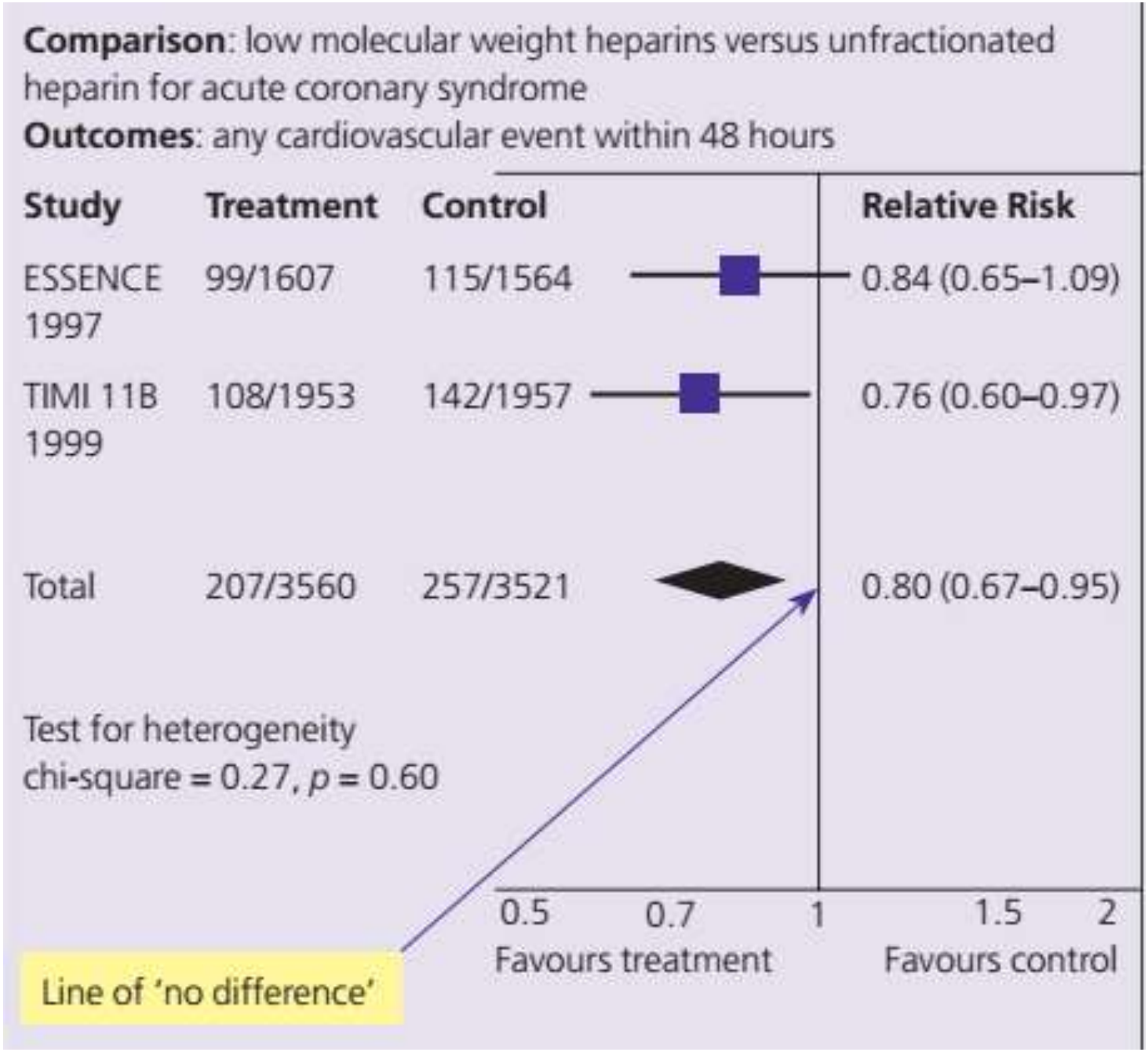
In Patients with a MI
Does (I) cholesterol lowering therapy
Compared to placebo
reduce mortality (O)

Patient presenting with MI (7 types of questions)

1. How common is the problem	Prevalence
2. Is early detection worthwhile	Screening
3. Is the diagnostic test accurate	Diagnosis
4. What will happen if we do nothing	Prognosis
5. Does this intervention help	**Treatment**
6. What are the common harms of an intervention	
7. What are the rare harms of an intervention	

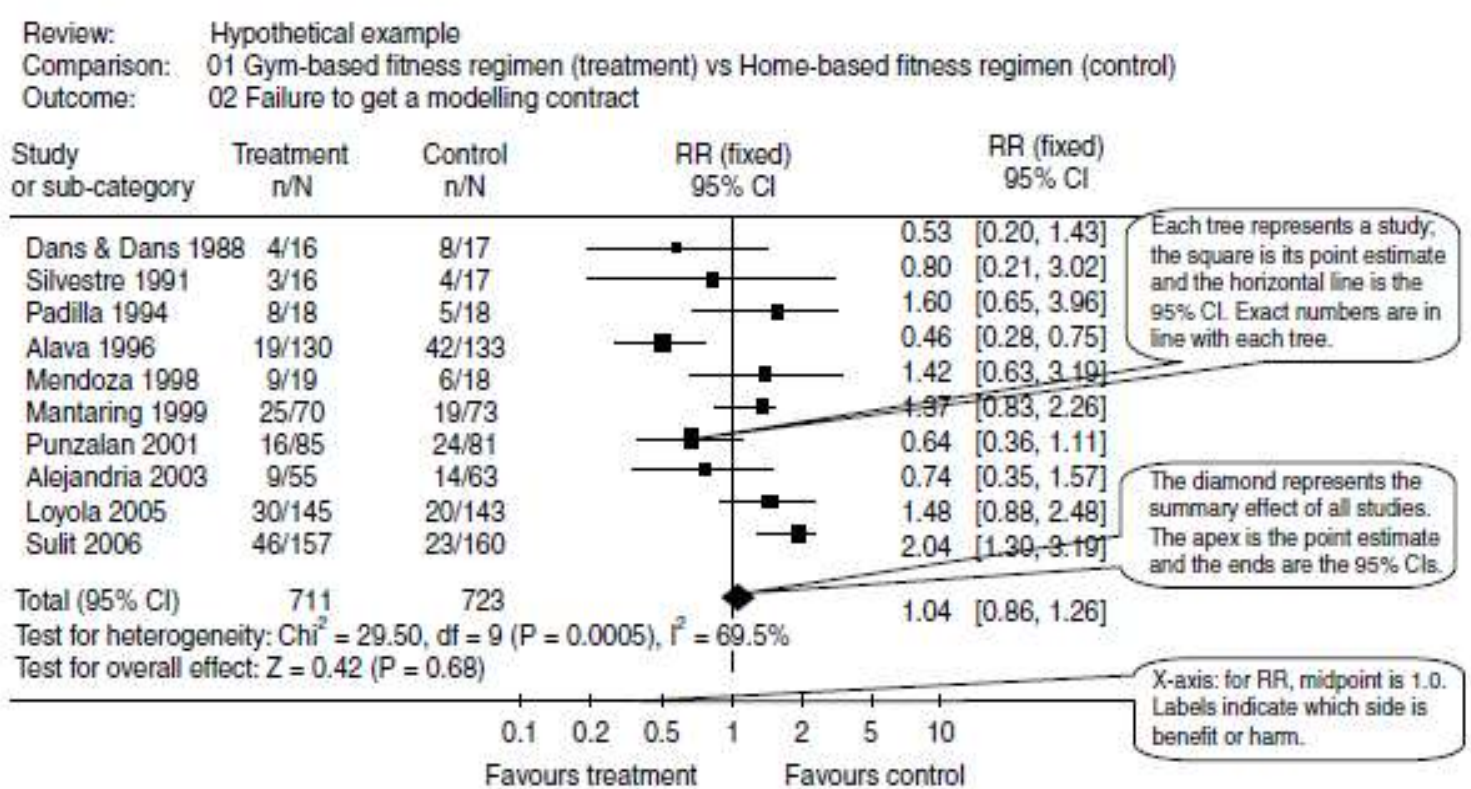
Comparison: low molecular weight heparins versus unfractionated heparin for acute coronary syndrome

Outcomes: any cardiovascular event within 48 hours



Notes: A forest plot can tell us:

1. how many studies the review included: just count the number of trees!
2. which studies are the largest: the bigger the square in the middle, the bigger the study.
3. which studies had more outcome events: these have the narrowest 95% CI.
4. which studies showed statistically significant benefit (entire line is to the left of 1.0).
5. which studies showed statistically significant harm (entire line is to the right of 1.0).
6. which studies were inconclusive (line straddles 1.0 and extends far into either side).
7. which studies were inconclusive but showed a trend towards benefit (line is on the left, and barely touches 1.0).
8. which studies were inconclusive but showed a trend towards harm (line is on the right, and barely touches 1.0).
9. which studies show that the therapies are equal (line straddles 1.0 and doesn't go far to either side).
10. whether there are important differences (heterogeneity) between studies: if the lines hardly overlap, we should worry.



- we’ve all learned that teachers and examinations do not reward us for showing our ignorance and being ready and willing to learn.

Odds Ratios and Relative Risk

Case-control studies

Odds of exposure in the case group divided by the odds of exposure in the control group

Cohort and RCT's

Ratio of the odds of disease in the exposed vs. the unexposed

Relative Risk

	Outcome +	Outcome -
Exposure +	a	b
Exposure -	c	d

$$RR = \frac{a/(a+b)}{c/(c+d)}$$

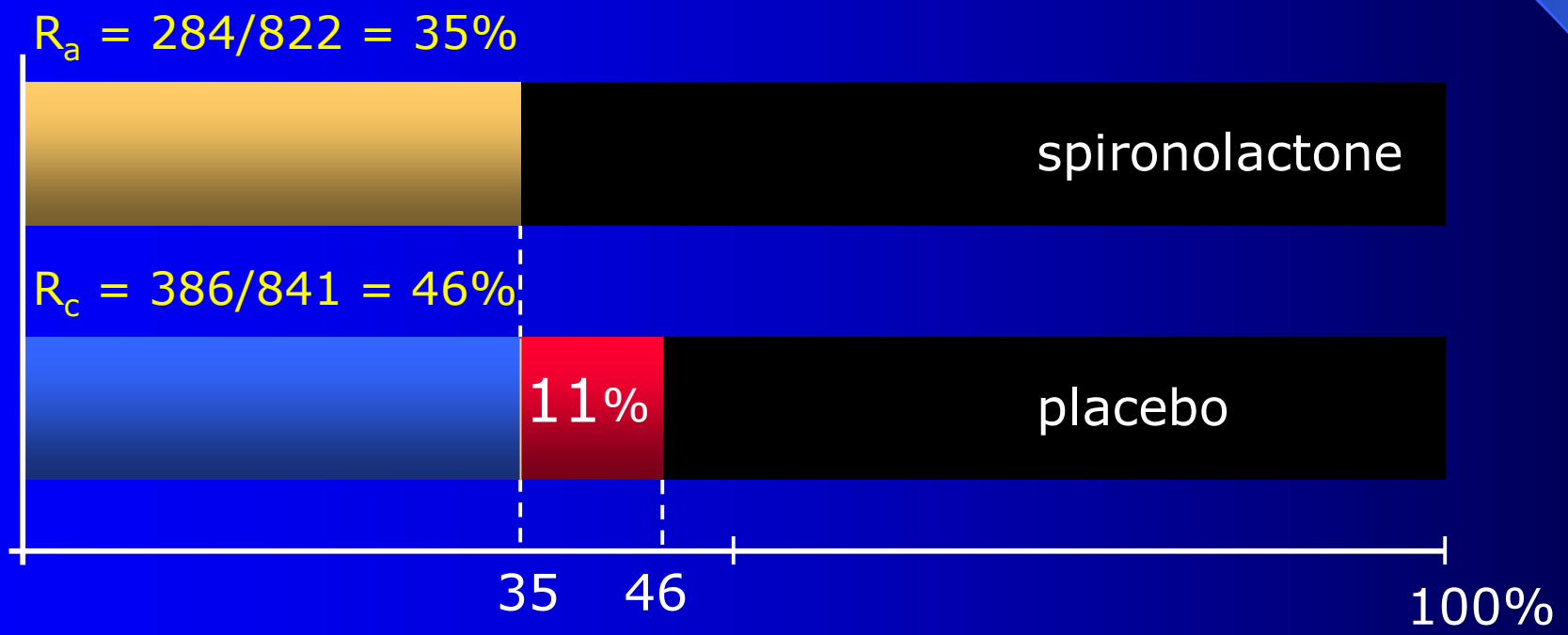
$$OR = \frac{a/c}{b/d}$$

Train the Trainers

Spironolactone in CHF (RALES)

NEJM 1999; 341: 709

- ماهو الفرق المطلق في الخطر بين المجموعتين؟



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Exposure	Outcome +	Outcome -
+	a	b
-	c	d

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Train the Trainers

Odds Ratios and Relative Risk

Exposure	Outcome +	Outcome -
+	93	12
-	73	28

$$RR = \frac{93/105}{73/101} = 1.23 \qquad OR = \frac{93/73}{12/28} = 2.97$$

Odds Ratios and Relative Risk

		Outcome +	Outcome -
Exposure	+	93	1200
	-	73	2800

$$RR = \frac{93/1295}{73/2873} = 2.83 \quad OR = \frac{93/73}{1200/2800} = 2.97$$

Train the

odds ratio.

- The association between exposure (i.e., HRT) and outcome (i.e., CHD) in a case-control study is typically summarized by a statistical measure called
- *odds ratio*.

odds ratio

- An odds ratio is an estimation of the true relative risk for the outcome in question.

RR – Relative Risk

- **Definition:**
- A measure of the strength of association based on prospective studies (cohort studies).

The relative risk (RR) :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

How to calculate the RR

	interesting outcome		
	present	absent	
Exposed	a	b	
Not exposed	c	d	
Total	a+c	b+d	a+b+c+d

$$RR = [\ a/(\ a+b\ )\ ]\ /\ [\ c/(\ c+d\ )\ ]$$

Absolute Risk Reduction

- (ARR) refers to the decrease of a bad event as a result of the intervention
- [ARR = EER-CER]

Relative Risk Reduction (RRR)

- is the *proportional reduction in risk between the rates of events in the control group and the*
- experimental group.
- Relative Risk Reduction is often a larger number than the ARR and
- therefore may tend to exaggerate the difference
- [RRR = EER - CER/CER].

- An RR of 1.0 indicates no difference applicable

NNT

- it is the number of patients that a clinician would have to treat with the experimental treatment to achieve one additional patient with a favorable outcome

- [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

Control event rate (CER)

Absolute risk reduction (ARR)

Experimental event rate (EER)

Risk ratio, or relative risk (RR)

- The ratio of risk in the treated group (EER) to the risk in the control group (CER). This is used in randomized trials and cohort studies and is calculated as EER/CER.

- RRR is the most commonly reported summary measure of treatment effect
- To truly understand the effectiveness of the treatment we should consider the absolute risk reduction ”ARR” and “NNT

Relative versus Absolute measures of treatment effect

- Relative measures
  - RRR
  - RR
- Absolute measure
  - ARR
  - NNT

	Control	Experimental	Total
Event	a	b	a + b
No Event	c	d	c + d
Total	a+c	b+d	
Event rate	Control event rate CER = a/(a + c)	Experimental event rate EER = b/(b + d)	
Relative risk	EER/CER		
Absolute risk reduction	CER – EER		
Relative risk reduction	$\frac{(CER - EER)}{CER}$		

	active	control
improved	80	20
N	100	100

$$\text{Relative Risk (RR)} = (Imp_{act}/N_{act}) / (Imp_{con}/N_{con})$$

$$\text{Relative Risk Reduction (RRR)} = (1-RR) / 100$$

$$\text{Absolute Risk (AR)} = (Imp_{act}/N_{act}) - (Imp_{con}/N_{con})$$

$$\text{Number Needed to Treat (NNT)} = 1/AR$$

RR = 4; AR = 0.6; NNT = 1.7 (best 1.25)

“2 by 2” table in qualitative data

hypertension in smokers

Exposure (smoking)	**Disease** (hypertension)		**Total**
	Hypertension	**No hypertension**	
Smokers	a	b	a + b
Non-smokers	c	d	c + d
Total	a + c	b + d	a + b + c + d

“2 by 2 table” in qualitative data

Exposure (smoking)	**Disease** (hypertension)		**Total**
	Hypertension	**No hypertension**	
Smokers	120	280	400
Non-smokers	30	570	600
Total	150	850	1000

Risk of HTA in smokers:	a/(a + b) = 120/400 = 0.3
Risk of HTA in non-smokers:	c/(c + d) = 30/600 = 0.05
Relative Risk (**RR**):	0.3/0.05 = **6**

Odds of HTA in smokers	a/b = 120/280 = 0.43
Odds of HTA in non-smokers	c/d = 30/570 = 0.053
Odds Ratio (**OR**):	(a/b) / (c/d) = 0.43/0.053 = **8.11**

Number Needed to Treat (NNT):

An NNT is just one part of the information required in making a purchasing decision

RR	ARR	RRR	Meaning
<1	> 0	> 0	Less events in experimental group
1	0	0	No difference between the groups
>1	< 0	< 0	More events in experimental group

Interpretation of RR & OR

RR or OR should be accompanied by their CIs

RR or OR > 1

Increased likelihood of outcome in exposed group

RR or OR < 1

Decreased likelihood of outcome in exposed group

RR or OR = 1

No outcome difference between exposed & control groups

CI: confidence interval – RR: relative risk – OR: odds ratio

ARR is a more clinically relevant measure to use than the RR or RRR. This is because relative measures 'factor out' the baseline risk, so that small differences in risk can seem significant when compared to a small baseline risk.

Know your background

Numbers needed to treat (NNTS)

The Number of people who have to be treated for ONE to benefit

Number-needed-to-treat (NNT)

	Controls	Actives
Number of patient	N_{con}	N_{act}
Improved = Clinical end point	Imp_{con}	Imp_{act}

$$NNT = \frac{1}{\frac{IMP\ act}{N\ act} - \frac{IMP\ con}{N\ con}}$$

Number-needed-to-treat (NNT)

NNT is treatment specific -takes into account the event rate in controls:

- may be a placebo effect
- may be the effect of another treatment

$$NNT = \frac{1}{\frac{100}{100} - \frac{0}{100}}$$

Number needed to treat (NNT)

Number needed to treat is the most useful measure of benefit, as it tells you the absolute number of patients who need to be treated to prevent one bad outcome. It is the inverse of the ARR:

$$NNT = 1/ARR$$