Evidence Based Medicine at time of crisis

By

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Outline

- *What is EBM*
- *How to acquire the evidence*
- *Appraise the evidence*
- *GRADE*
- *Challenges of EBM during medical crisis*

Evidence Based Medicine

- “ the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients”

Why do we need evidence?

- Resources should be allocated to things that are **EFFECTIVE**
- The only way of judging effectiveness is **EVIDENCE**

Why do we need evidence?

- **Move towards:**

  EVIDENCE-BASED MEDICINE

- **Move away from:**

  EMINENCE- BASED MEDICINE

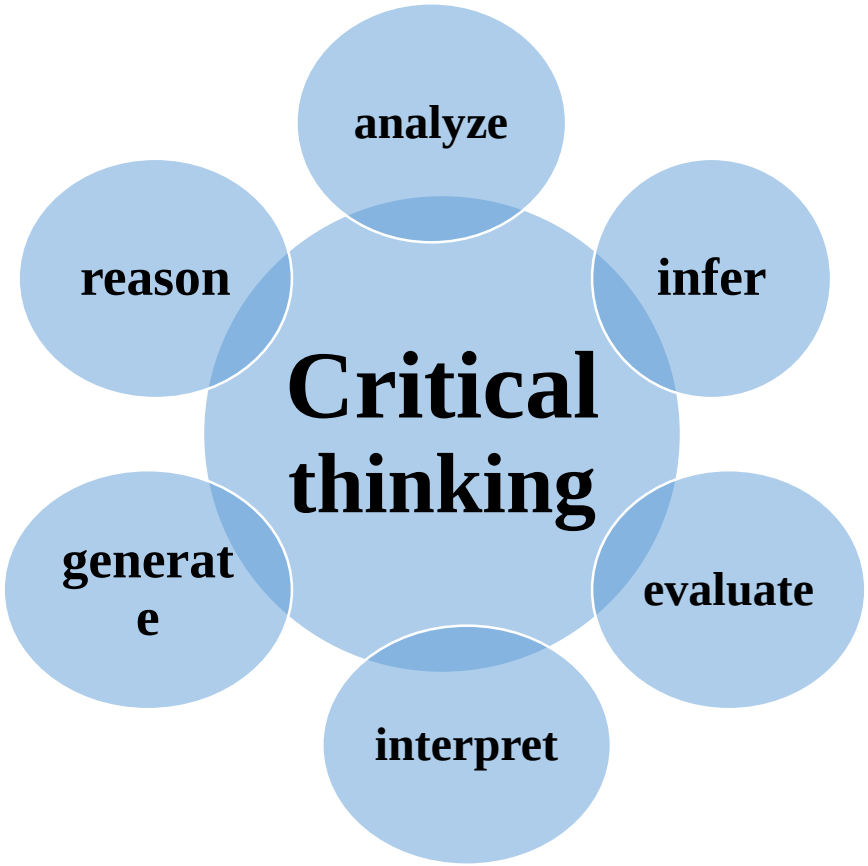
EMINENCE-BASED MEDICINE?

It refers to a clinical decision that is made by relying purely on the opinion of a **medical** specialist or any prominent health professionals rather than relying on critical appraisal of scientific evidence available

- The first EBM principle is that some health claims are more trustworthy than others

What we really, really want is

Evidence-informed medicine


analyze
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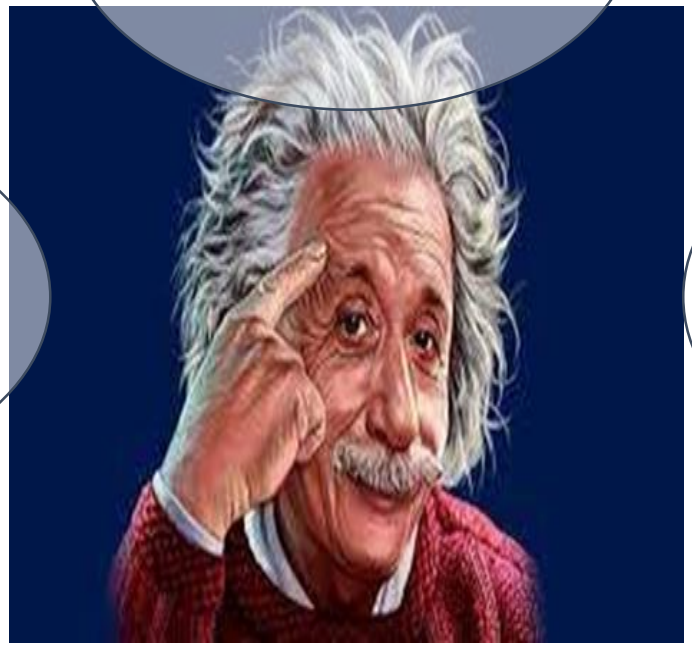
How

What



Why

Critical thinking

When

Who

Evidence-based medicine

5 steps

1. Converting information needs into answerable questions
2. Finding the best evidence with which to answer question
3. Critically appraising evidence for validity and usefulness
4. Applying the results in clinical practice
5. Evaluating performance

What is an answerable question? - step 1

- Should contain the following components:
  - **P** = participants or population or problem
  - **I** = interventions
  - **C** = comparisons
  - **O** = outcomes
  - **S** = study design

Finding evidence – step 2

- What are ‘good’ sources of evidence?
- Think about sources of evidence that you have used – were they useful?
- What makes a ‘good’ source of evidence?

Finding evidence - step 2

- Can search many of these sources simultaneously using:
  - TRIP
  - PubMed
  - Embase
  - Dynamed
  - Cochrane
  - Google scholar

Appraising evidence - step 3

- **Validity -** closeness to the truth, *i.e.* do we believe it?
- **Usefulness -** clinical applicability, *i.e.* is it important?

Using efficacy data from clinical trials to estimate

Clinical Effectiveness

equator network

Enhancing the QUAlity and Transparency Of health Research

EQUATOR resources in German | Portuguese | Spanish

Your one-stop-shop for writing and publishing high-impact health research

find reporting guidelines | improve your writing | join our courses | run your own training course | enhance your peer review | implement guidelines

Library for health research reporting

The Library contains a comprehensive searchable database of reporting guidelines and also links to other resources relevant to research reporting.

- Search for reporting guidelines
- Not sure which reporting guideline to use?
- Reporting guidelines under development
- Visit the library for more resources

Reporting guidelines for main study types

Randomised trials	CONSORT	Extensions
Observational studies	STROBE	Extensions
Systematic reviews	PRISMA	Extensions
Study protocols	SPIRIT	PRISMA-P
Diagnostic/prognostic studies	STARD	TRIPOD
Case reports	CARE	Extensions
Clinical practice guidelines	AGREE	RIGHT
Qualitative research	SRQR	COREQ
Animal pre-clinical studies	ARRIVE	
Quality improvement studies	SQUIRE	
Economic evaluations	CHEERS	

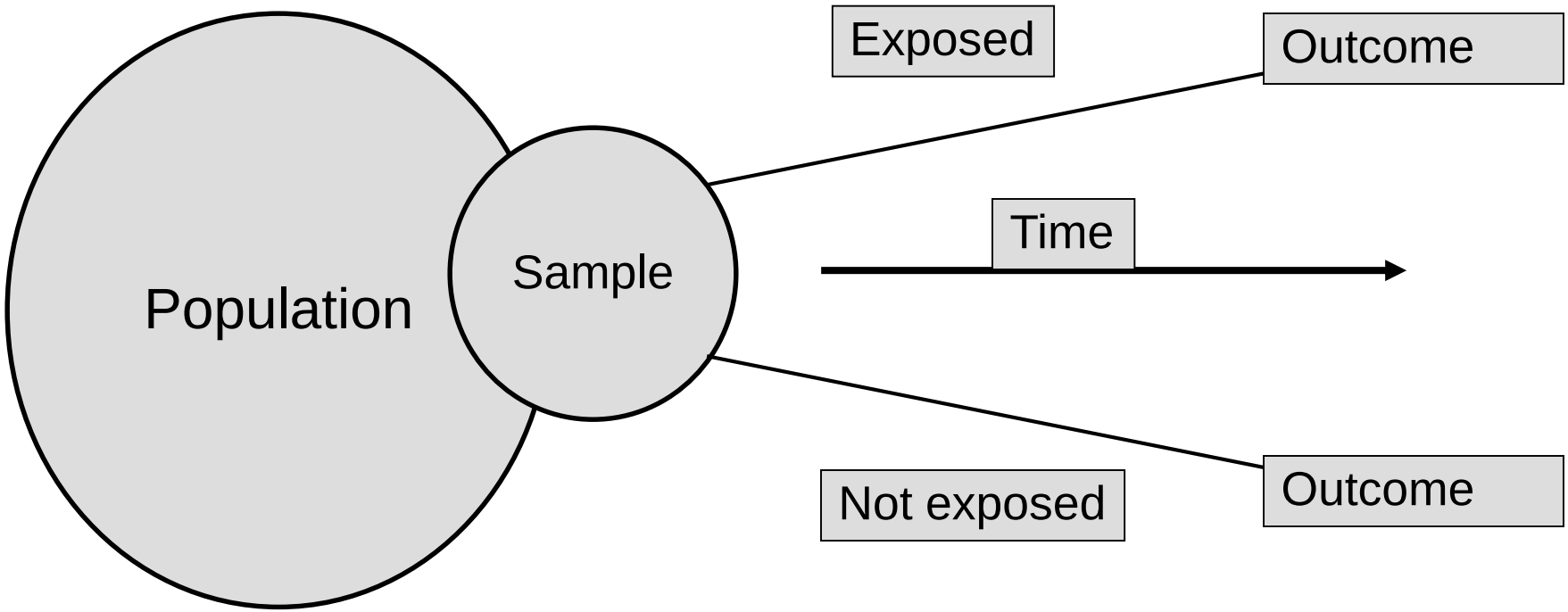
CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	
	2b	Specific objectives or hypotheses	
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	
Participants	4a	Eligibility criteria for participants	
	4b	Settings and locations where the data were collected	
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	
	6b	Any changes to trial outcomes after the trial commenced, with reasons	
Sample size	7a	How sample size was determined	
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	

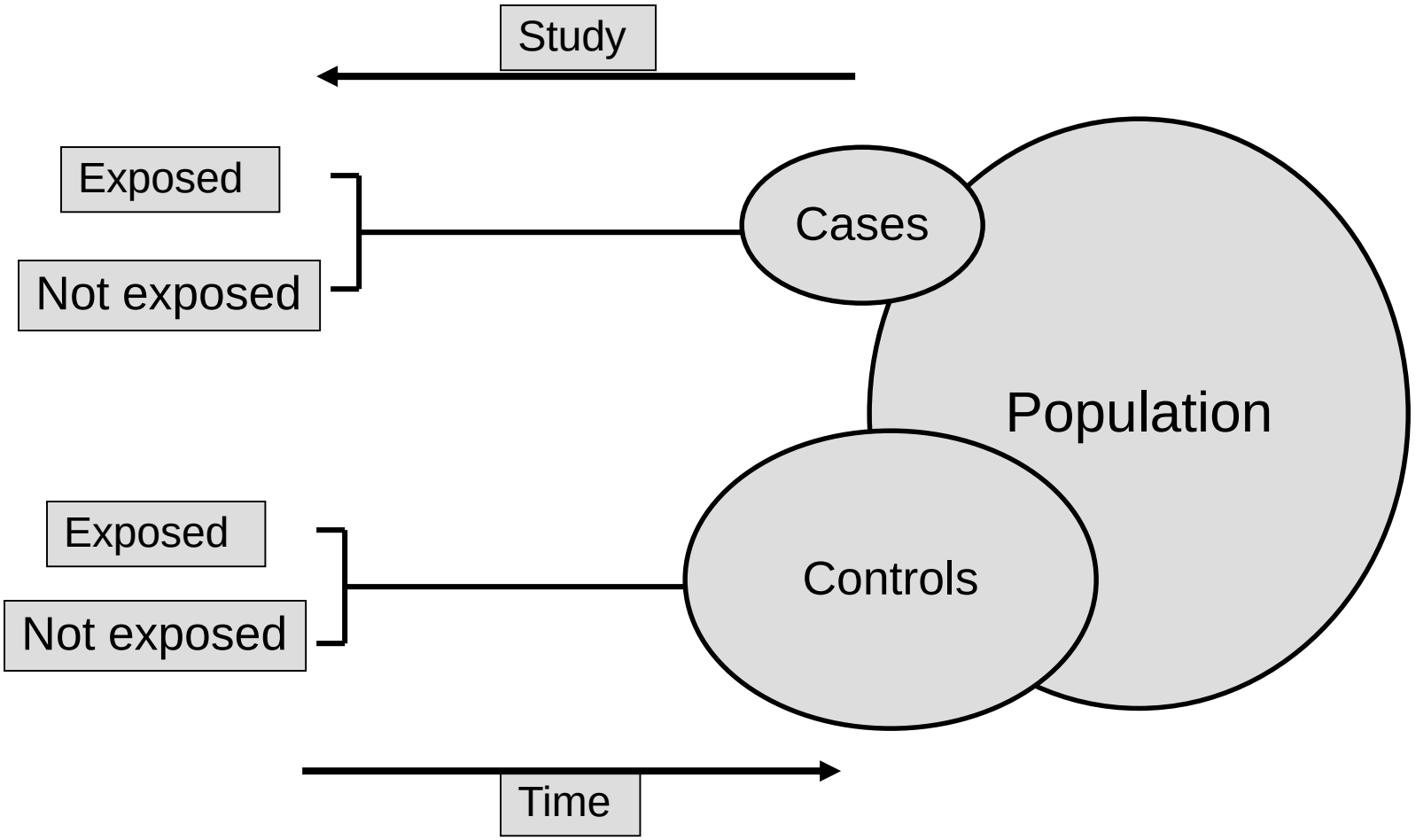
Summary of PRISMA guidelines.

Title	**Identification of the report as a systematic review, meta-analysis, or both.**
Abstract	Structured Summary: background; objectives; eligibility criteria; results; limitations; conclusions; systematic review registration number.
Introduction	-Description of the rationale for the review -Provision of a defined statement of questions being concentrated on with regard to participants, interventions, comparisons, outcomes, and study design (PICOS).
Methods	-Specification of study eligibility criteria -Description of all information sources -Presentation of full electronic search strategy -State the process for selecting studies -Description of the method of data extraction from reports and methods used for assessing risk of bias of individual studies in addition to methods of handling data and combining results of studies.
Results	Provision of full details of: -Study selection. -Study characteristics (e.g., study size, PICOS, follow-up period) -Risk of bias within studies. -Results of each meta-analysis done, including confidence intervals and measures of consistency. -Methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression).
Discussion	-Summary of the main findings including the strength of evidence for each main outcome. -Discussion of limitations at study and outcome level. -Provision of a general concluded interpretation of the results in the context of other evidence.
Funding	Source and role of funders.

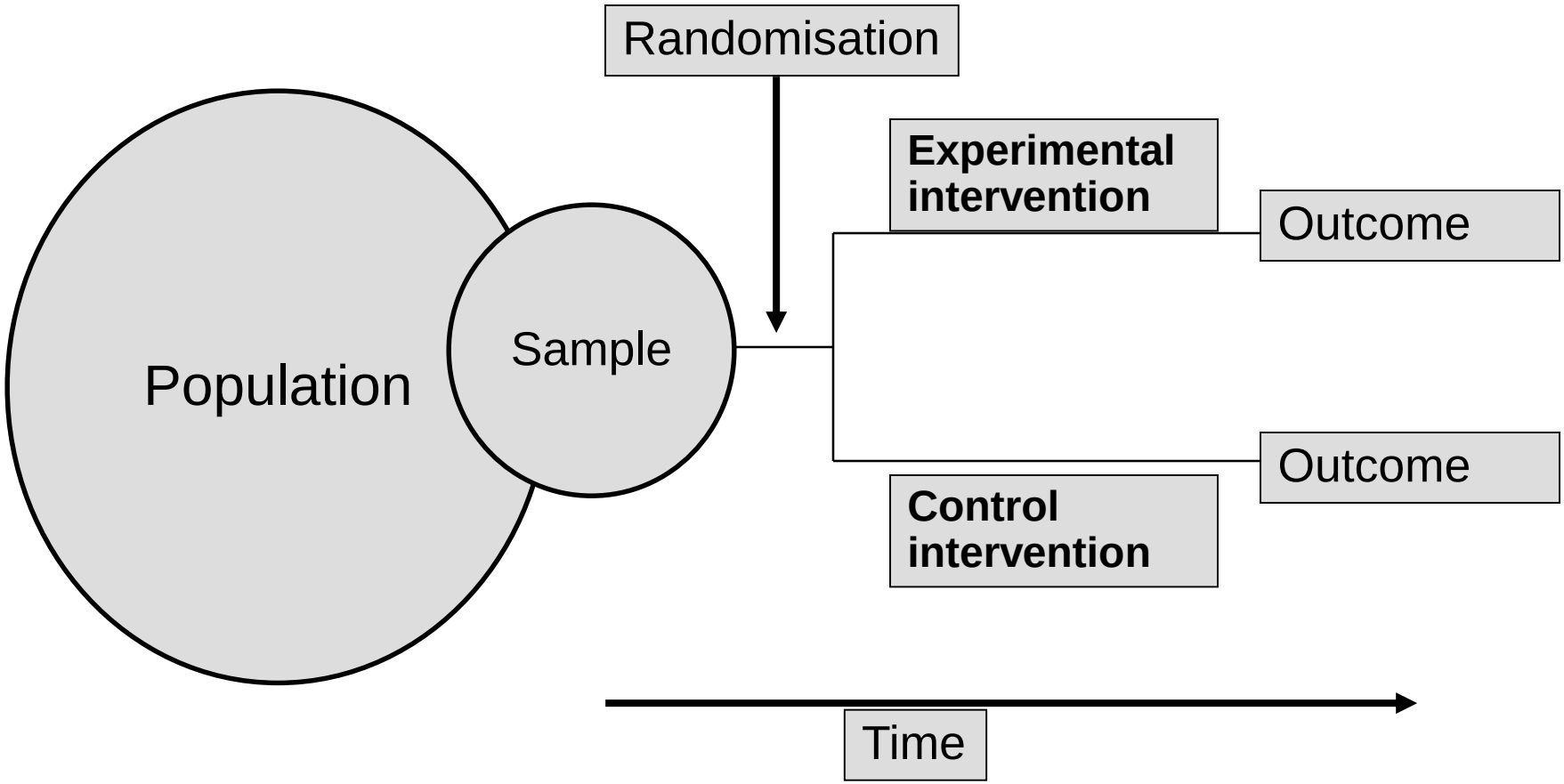
Cohort study



Case control study



Randomised, controlled trial



Applying results to local practice - step 4

- Local policies
- Guideline development
- Implementing clinical effectiveness and clinical governance agendas

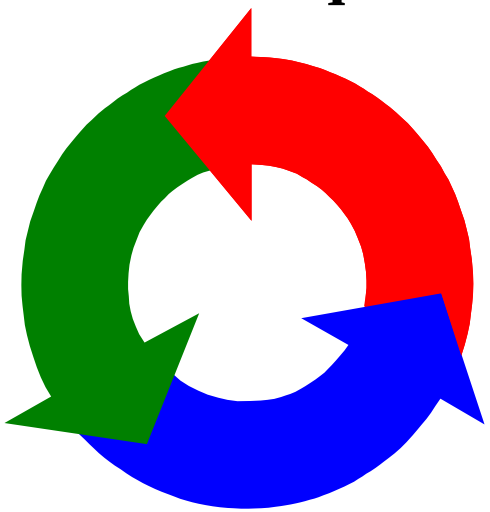
Evaluating performance - step 5

- Clinical audit!

Evidence based medicine

Formulate question

Efficiently track Down best Available Evidence



Evaluate Performance

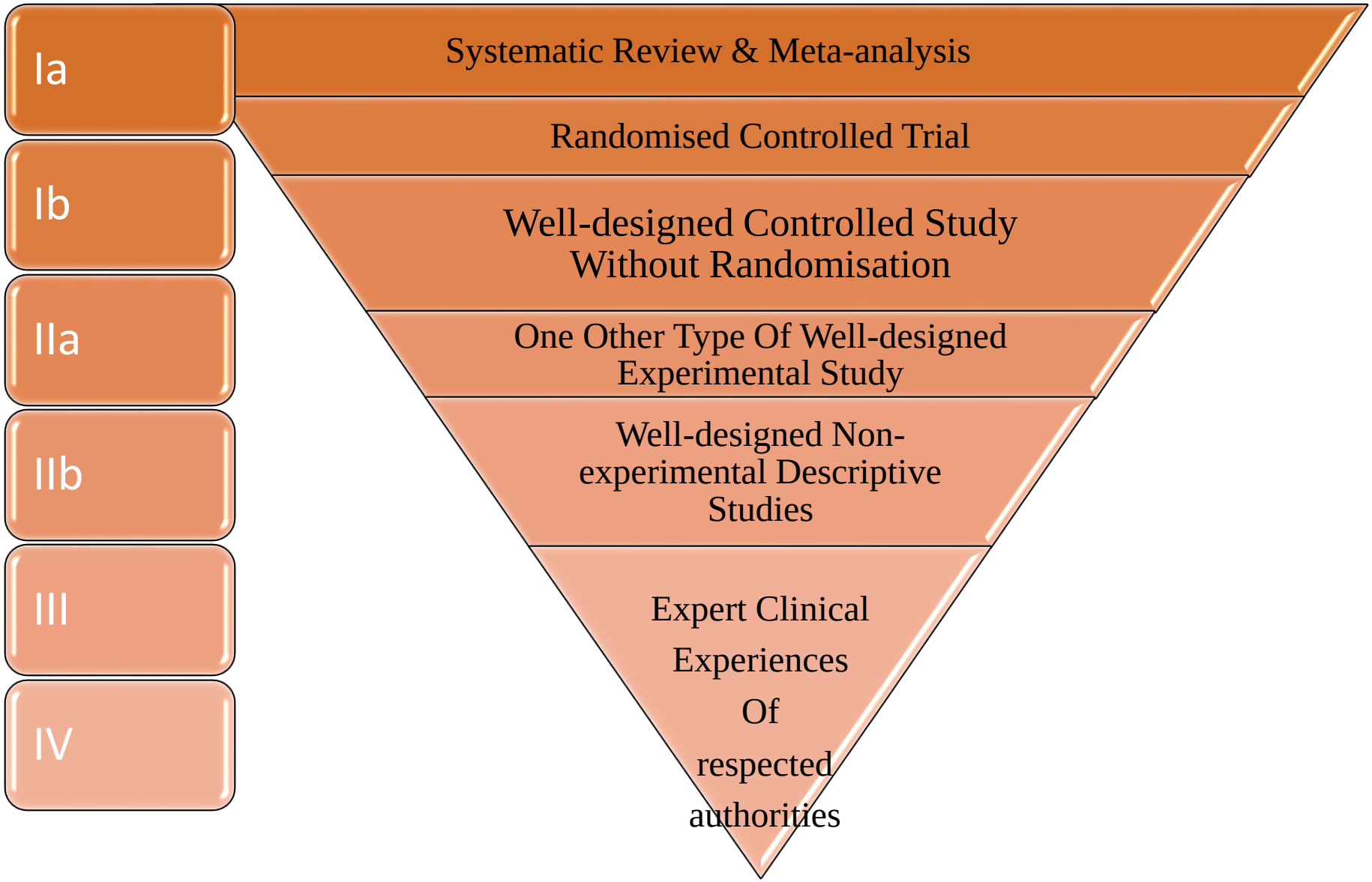
Implement Changes In clinical Practice

Critically review the Validity and usefulness Of the evidence

- Should policy or practice change as a result of the evidence contained certain body of evidence?
- Are the likely benefits worth the potential harms and costs?

Hierarchy of evidence

(used in NICE Guidelines)



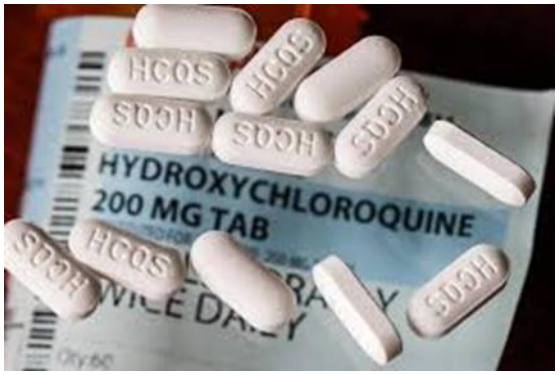
Grading of Recommendations Assessment, Development and Evaluation

- System (and common language) that
  - was developed and updated by GRADE Working Group
  - Endorsed by large number of organisations
  - expresses degree of confidence one can place in **quality of evidence** and **strength of recommendation**

- System for assessing quality of evidence of a body of evidence based on
  - study design
  - criteria for downgrading/upgrading

GRADE Working Group (2004); Guyatt et al (2008)

In response to COVID-19, people are interested in recommendations regarding issues such as use of masks, hand hygein, social distance or of drugs such as **hydroxychloroquine**.



implementing interventions based on high-quality evidence of substantial effectiveness will result in net benefit

whereas adopting interventions based on very low quality runs a high risk of net harm.

Thus, foresight generally dictates not implementing interventions when only very-low-quality evidence exists

Example:

- Based on in vitro data that the antimalarial **hydroxychloroquine** possesses antiviral activity against SARSeCoV-2, many physicians started using this drug for treatment and prophylaxis against COVID19.
- Possibly motivated by fear, and the resultant feeling that we must do something, this rush to judgment is, for a number of reasons, very likely to do net harm

A second key EBM principle incorporated in the GRADE system is that evidence is necessary but not sufficient for management recommendations and associated decision-making

Rating quality of evidence

GRADE quality of evidence

Definition: The degree of confidence in an estimate of effect.

High (++++)	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate (+++)	We are moderately confident in the effect estimate: The true effect is **likely to be close** to the estimate of the effect, but there is a possibility that it is substantially different.
Low (++)	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low (+)	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of the effect.

Determinants of quality of evidence

Study design:

- Bodies of RCTs start as high
- All other study designs start as low

Upgrading/downgrading criteria:

- Five factors can decrease quality of evidence
- Three factors can increase quality of evidence

RCTs versus observational study designs usually run through assessment separately

Determinants of quality of evidence (2)

Quality	Study design	Lower quality if:	Higher quality if:
High (++++)	Randomised controlled trials	Risk of bias (-1, -2) Inconsistency (-1, -2) Indirectness (-1, -2) Imprecision (-1, -2) Publication bias (-1, -2)	Large effect (+1, +2) Dose-response (+1) Direction of residual confounding and biases (+1)
Moderate (+++)			
Low (++)	Observational studies		
Very low (+)	Case reports, expert opinion, modelling		

The GRADE approach recognizes the impact of potential errors, and the likelihood of those errors

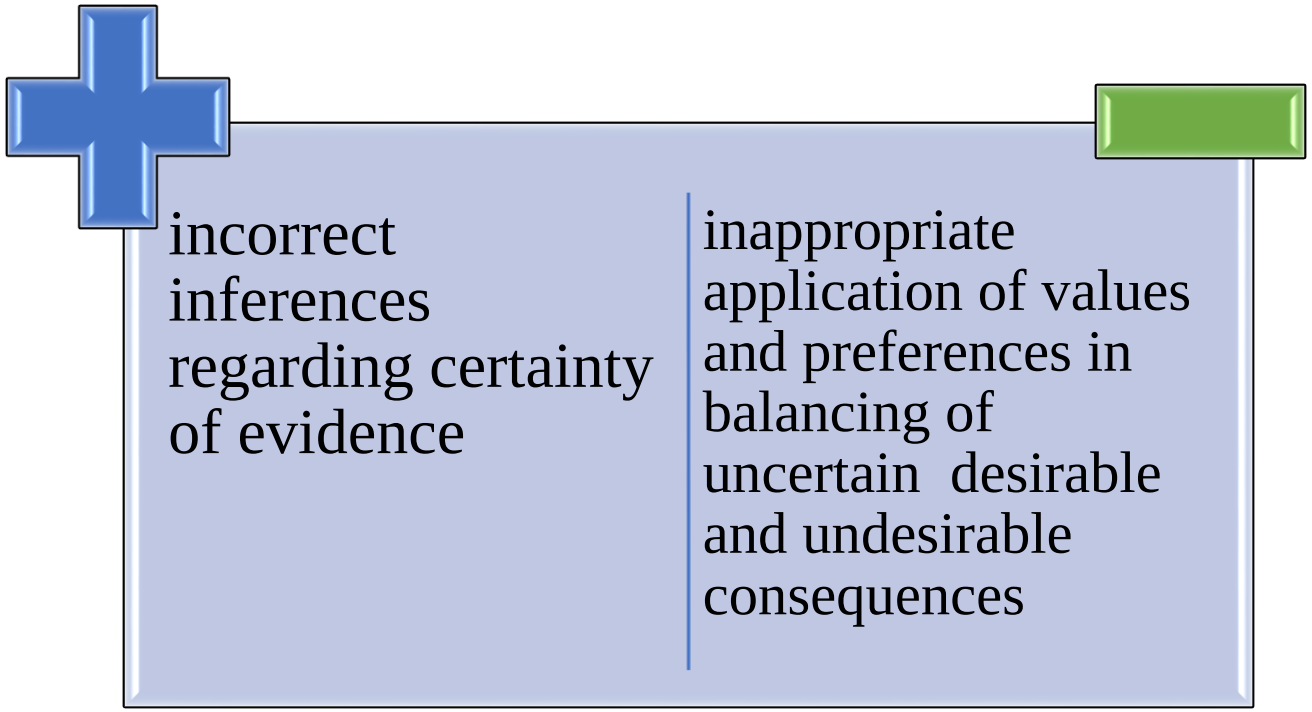
- How will we feel if we fail to give a drug such as hydroxychloroquine and it turns out to be beneficial?
- How will we feel if it turns out to be useless, or serious adverse effects, or drug resistance
- People who need the drug for proven indications suffer because of its unavailability?

Another example:

- Until recently, there was little evidence for wearing a mask in open spaces, but given low level of harms associated with doing so (as long as the consequences do not include unavailability of masks in situations in which their use is more important), encouraging use may be reasonable.
- By contrast, locking down whole societies comes with grievous economic consequences.
- But how would we feel if lockdowns are in fact beneficial, and failure to implement results in tens, perhaps hundreds of thousands, of unnecessary deaths?

Application of EBM and associated GRADE principles can reduce the likelihood of such errors.

Failure to use these principles will result in two sets of errors:



Appropriate application of EBM and GRADE is never more important than in times of health crisis affecting millions of people worldwide

Grading strength of a recommendation

GRADE strength of recommendation

Definition: The degree of confidence that desirable effects of adherence to a recommendation outweigh undesirable effects.

- **Strong recommendation:**

  The panel is confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects.

- **Weak/ conditional/ discretionary** recommendation:

  The panel concludes that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, but is not confident.

Strength of recommendations used in NICE Guidelines

Grade A At least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation (evidence levels 1a and 1b)

Grade B Well conducted clinical studies but no randomised clinical trials on the topic of the recommendation (evidence levels Iia, IIb, III)

Grade C Expert committee reports or opinions and/or clinical experience of respected authorities. This grading indicates that directly applicable clinical studies are absent (evidence level IV)

Low quality of evidence, strong recommendation?

- Clear distinction between
  - quality of evidence, driven by confidence in body of evidence
  - strength of recommendation, driven by confidence in body of evidence plus other considerations

- All combinations possible, e.g.:
  - High quality of evidence -> weak recommendation
  - Very low quality of evidence -> strong recommendation

- **Paradigmatic situations** for strong recommendations in the absence of high-quality evidence (Alexander et al. 2016)

These are some of the criticisms you will sometimes hear about evidenced based medicine

EBM is NOT

- "Cookbook" medicine
- Rigid adherence to clinical guidelines
- Managed care
- Cost-cutting measures A rigorously systematic way to:
- Evaluate the strength of available evidence

BUT is

A rigorously systematic way to:

• Evaluate the strength of available evidence

• Evaluate the appropriateness of available evidence for a particular clinical situation

• A way to avoid waste by considering both the efficacy and effectiveness of a particular intervention in a particular clinical setting.


Thank you

REFERENCES

- CASP Tool
- www.phru.nhs.uk/casp/resourcescasp.htm

- Additional Reading

- Montori V et al Users' guide to detecting misleading claims in clinical research reports BMJ 2004; 329: 1093-1096
- Greenhalgh T. How to read a paper: Getting your bearings (deciding what a paper is about). BMJ 1997; 315: 243-246
- Greenhalgh T. How to read a paper: Assessing the methodological quality of published papers. BMJ 1997; 315: 305-308
- Guyatt GH, *et al*. Users' Guides to the Medical Literature: II. How to use an article about therapy or prevention. A. Are the results of the study valid? JAMA 1993; 270: 2598-2601
- Guyatt GH, *et al*. Users' Guides to the Medical Literature: II. How to use an article about therapy or prevention. B. What are the results and will they help me in caring for my patients? JAMA 1994; 271: 59-63

REFERENCES cont.

Statistics for the non-statistician

I: Different types of data need different statistical tests

Greenhalgh T *BMJ* 1997; 315: 364-6

II: “Significant” relations and their pitfalls

Greenhalgh T *BMJ* 1997; 315: 422-5

Statistics in small doses- a series of articles available on UKMI web-site (http://www.ukmi.nhs.uk/activities/Research/default.asp?pageRef=27)