Introduction to Evidence Based Medicine

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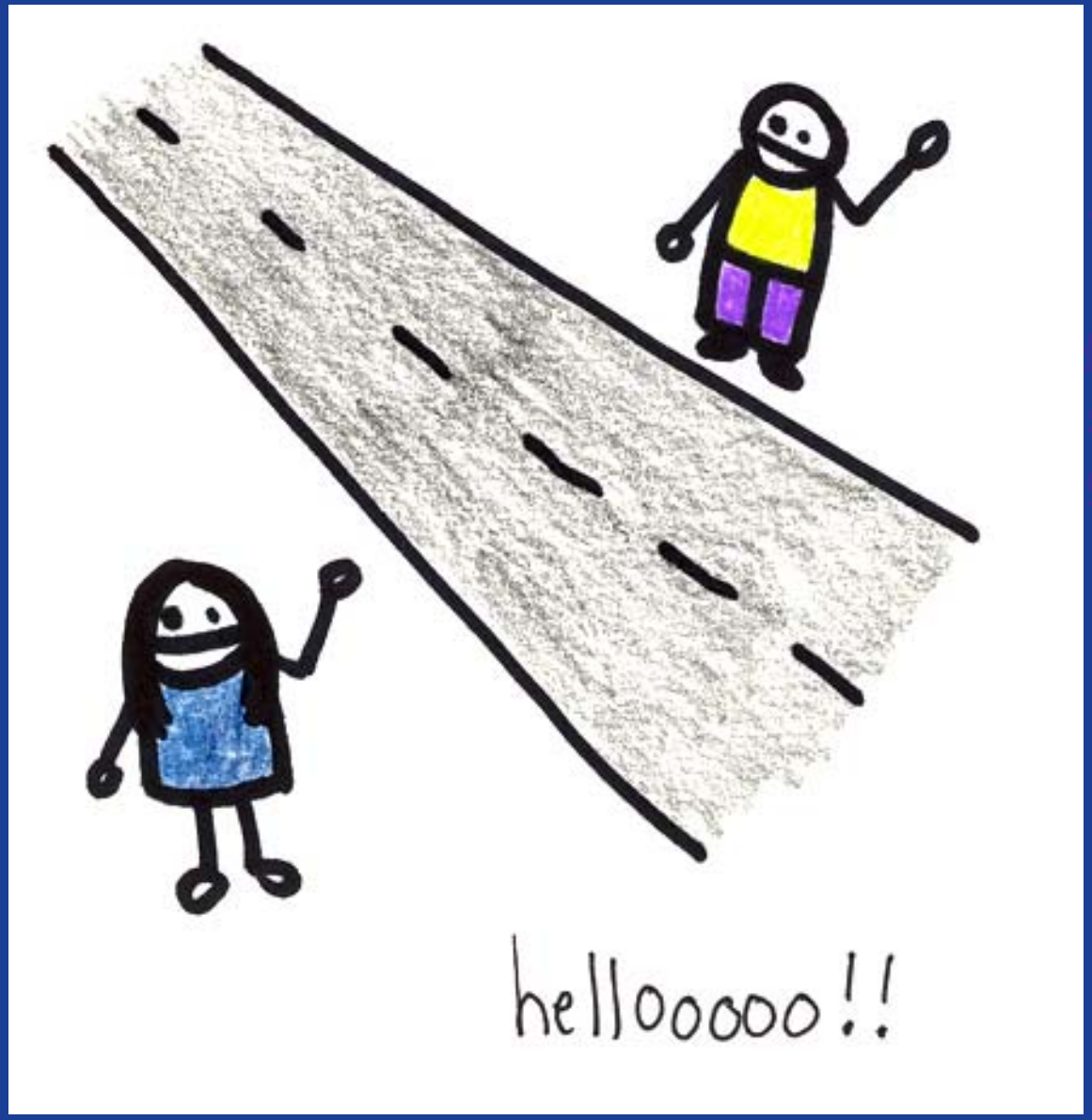

hellooooo!!

What I want to cover

- Why we try and use evidence in medicine
- A few key principles
- Why it is difficult
- One or two things that might help

Task 1

Imagine you are about to buy a new car.

Talk to the people around you about what you would like the new car to have – colour, size, and so on.

You have 3 minutes.

Task 2

What do you understand by evidence based medicine?

Talk to the people around you.

You have 6 minutes.

"Evidence based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research.

Sackett, D.L. et al. Evidence based medicine: what it is and what it isn't. BMJ 1996; 312: 71-72

Increased expertise [includes]… especially more effective and efficient diagnosis and…more thoughtful identification and compassionate use of individual patients' predicaments, rights, and preferences in making clinical decisions.

Sackett D, et al. BMJ 1996;312:71-2

Task 3

Why have health care systems and health care professions adopted “evidence based medicine” as an important element of modern practice?

Talk to the people around you.

You have 6 minutes.

Making the right choices

- Diagnosis
  - What are the most likely diagnoses? AND…..
  - What serious but rare diagnoses do I need to rule out (if I can)?
- Management
  - What is the best treatment for this condition in this patient?

Consultation 1

- 26 year old woman.
- Dysuria and frequency 24 hours, nocturia x 4, ?haematuria
- Sexually active, not pregnant

Diagnosis? UTI

Rx: Trimethoprim

Why would you choose trimethoprim (or your usual antibiotic)?

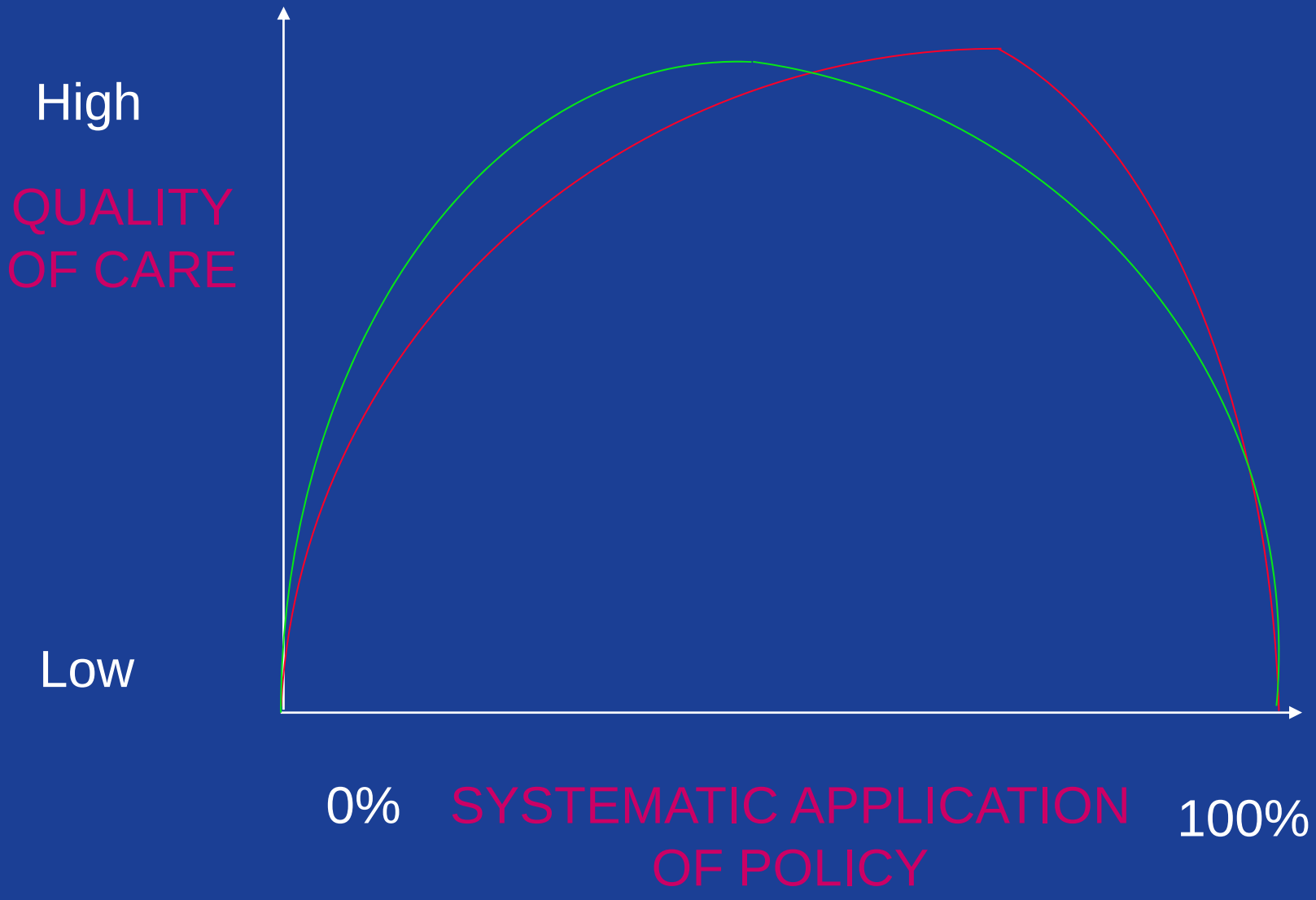
EFFECTIVE *Benificence*	SAFE *Non-malfeasance*
COST *Justice*	PATIENT FACTORS *Patient autonomy*

From: What constitutes good prescribing?
Barber N. BMJ 1995; 310: 923-925

Consultation 2

Aspirin reduces the chances of a further heart attack by……..how much?

1. What is the quality of care likely to be for patients after a heart attack when prescribers have no consistency in whether they prescribe aspirin or not? Low or high?
2. What is the quality of care likely to be for patients after a heart attack when prescribers have greater consistency in their prescribing of aspirin? Getting better or getting worse?
3. What is the quality of care likely to be for patients after a heart attack when prescribers achieve 100% of patients getting aspirin? The best we can achieve?


High
QUALITY OF CARE
Low
0%
SYSTEMATIC APPLICATION OF POLICY
100%

A bit more on costs

Maynard A. Lancet 1997; 349: 126-128

- Budget for drugs for treating condition X is €120,000 a month

- Medicine A cures 50% of people
- It costs €10 a month.
- So for the budget we can treat 12,000 people and cure 6,000.

- Medicine B cures 60% of people
  - A 20% increase in those cured
  - If you treat 100 people with B rather than A, then 10 more are cured
- It costs €30 a month.

- So by using the ‘better’ medicine B, for the same budget we can only treat 4,000 people and cure 2,400 of them.

Do you want to cure 6,000 people or 2,400???

- Where does the information on ***effectiveness*** come from?
- Where does the information on ***safety*** come from?

A hierarchy of evidence

- (MA of several, similar, large well designed randomised controlled trial (RCTs))
- Large well designed RCT
- Meta analysis of smaller RCTs
- Case control and cohort studies
- (Case reports and case series)
- Consensus from expert panels
- I think

So what would a well conducted RCT look like?

matters

How does the size of the study affect the result?

Counsell CE, et al. BMJ 1994; 309: 1677-1681
[Bandolier Nov 2002]

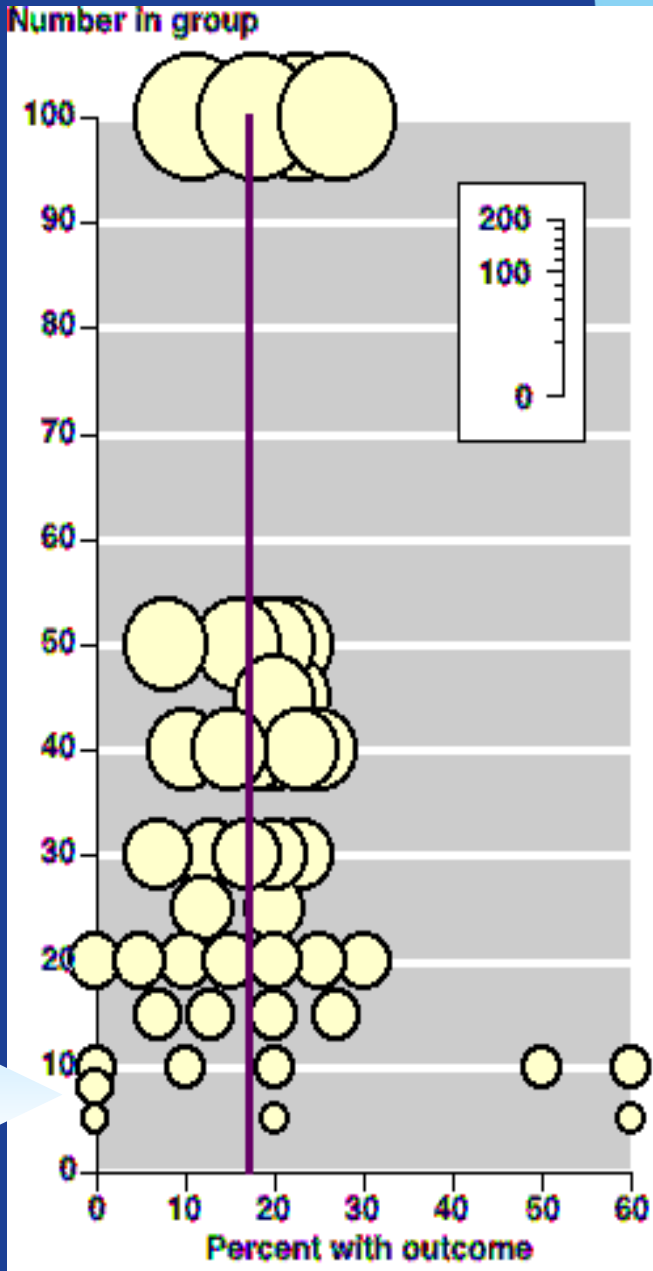
- Investigators used a dice to simulate outcomes in a trial
- 'Treatment' arm vs. control arm
- Roll of a dice = outcome in the trial:
  - 1-5 survival
  - 6 = death
- Did for 'treatment' group then repeated for control group
- Number of times the dice was rolled varied from 5 to 100.

More consistency in results

Results according to number of times the dice was rolled:

- Variation in ‘outcome’ was largest in the ‘smallest’ studies
- i.e the chance of a spurious result decreased with increasing numbers included in the trial

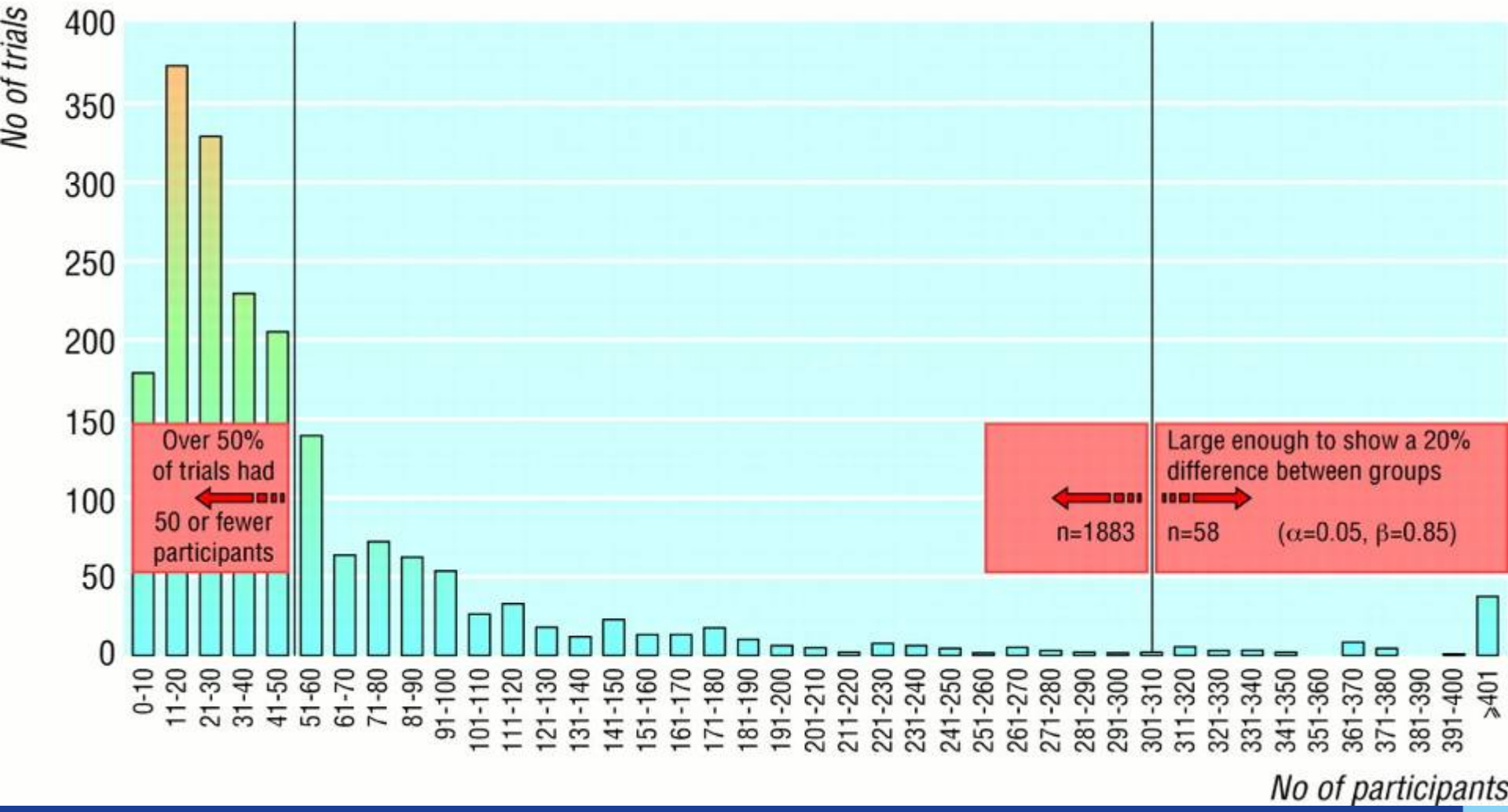
Wide variation in results



The evidence for the management of schizophrenia

Thornley B, et al. BMJ 1998; 317: 1181-1184

Size of trials (n=1941; 59 studies did not report study size)



Sub-group analyses – caveat emptor

ISIS 2 trial:

- 17,187 patients, 417 hospitals up to 24 hours after MI.
- Randomised to either streptokinase, aspirin or placebo in 2x2 factorial design
- Streptokinase alone and aspirin alone each produced a highly significant reduction in 5-week vascular mortality: ARR 2,8%, together ARR vs double placebo 5.2%.
- To try and allay concerns re benefit:safety ratio in subgroups, *the Lancet* pushed for subgroup analyses.
- The authors agreed – but with the proviso that they should analyse by astrological star signs and that this should appear first in the table of subgroup results.
- The result?

Gemini and Libra: aspirin of no benefit.

All other star signs: aspirin strongly beneficial

Outcomes matter

When **you measure matters**

Jüni P, et al. BMJ 2002; 324: 1287-1288

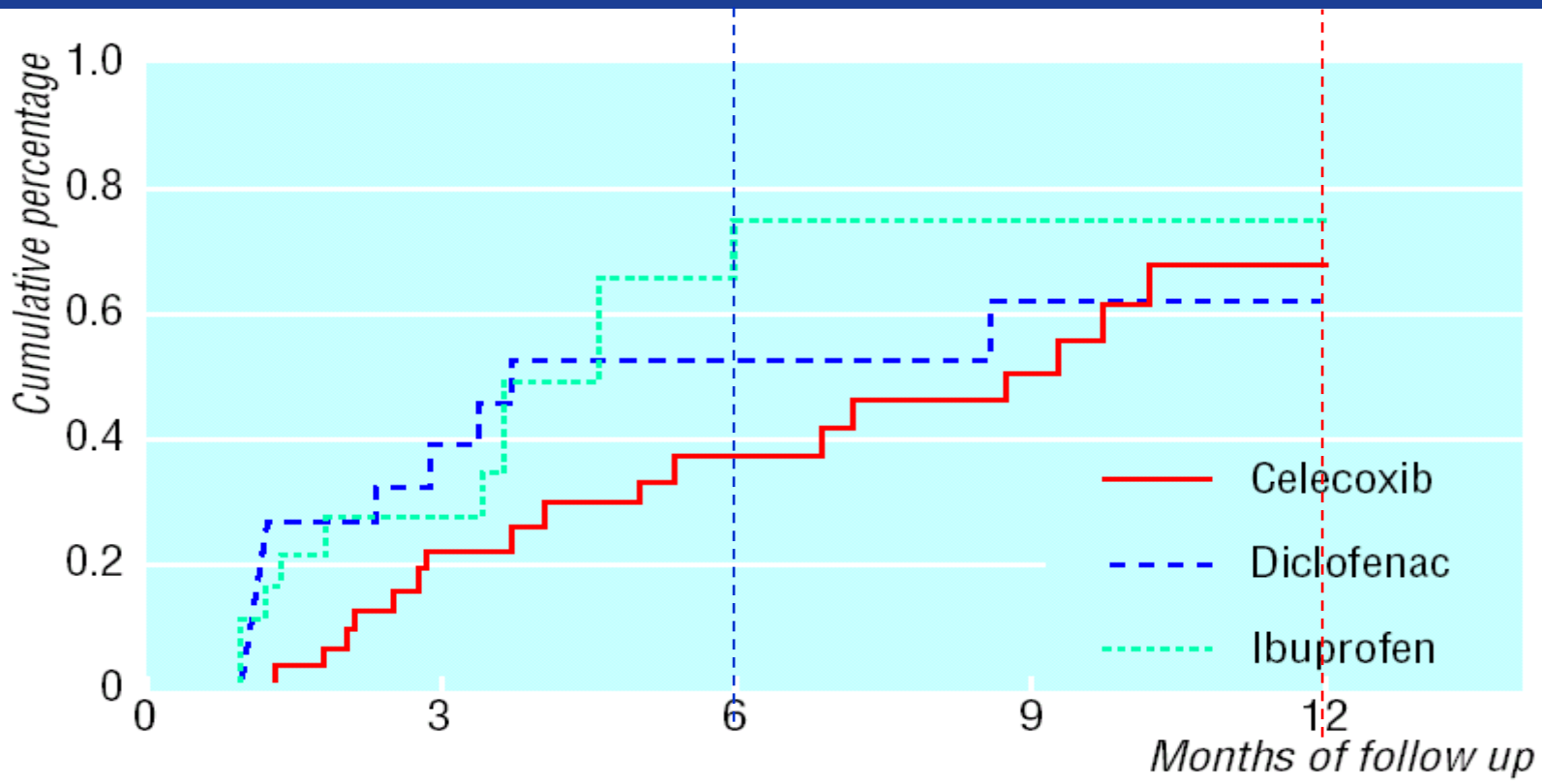


Fig 2 Kaplan-Meier estimates for ulcer complications according to traditional definition. Results are truncated after 12 months, no ulcer complications occurred after this period. Adapted from Lu 2001.[7]

What you measure matters – POOs and DOOs

Patient Oriented Outcomes:

- Reduces heart attacks and strokes
- Reduces diabetic foot ulcers
- Reduces night time awakenings

Disease Oriented Outcomes:

- Reduces Blood pressure
- Improves HBA1c
- Improves PEF

Like with like **comparisons matter**
Meloxicam vs ……

MELISSA 1998

- 9,323 pts with OA, 28 days
- Meloxicam 7.5mg vs. diclofenac-SR 100mg
- Fewer GI adverse events with meloxicam - 13% vs. 19% (p<0.001) but no diff. in PUBs (5 cases vs. 7)
- Efficacy favoured diclofenac (NS)
- More drop-outs due to lack of efficacy with meloxicam (80 vs.49, p<0.01)

SELECT 1998

- 9,286 (8,656) pts with exacerbations OA, 28 days
- Meloxicam 7.5mg vs. piroxicam 20mg
- GI events - 10% vs. 15% (p<0.001)
- PUBs - 9 vs. 17 (NS)
- Drop-outs:
  - total - 350 vs. 382
  - lack of efficacy - 75 vs. 68
  - ADRs - 265 vs. 314
- Equally effective

Task 4

- Do you see evidence being used routinely by all clinicians in your hospital?

Task 5

- Why don’t you see evidence being used routinely?

EFFECTS OF CLOPIDOGREL IN ADDITION TO ASPIRIN IN PATIENTS WITH ACUTE CORONARY SYNDROMES WITHOUT ST-SEGMENT ELEVATION

THE CLOPIDOGREL IN UNSTABLE ANGINA TO PREVENT RECURRENT EVENTS TRIAL INVESTIGATORS*

The primary outcome – a composite of death from CV causes, nonfatal MI or stroke – occurred in 9.3% of the patients in the clopidogrel group and 11.4% of the patients in the placebo group (RR 0.80, 95% CI 0.72 to 0.90; P<0.001)

For the first primary outcome, what was the:-

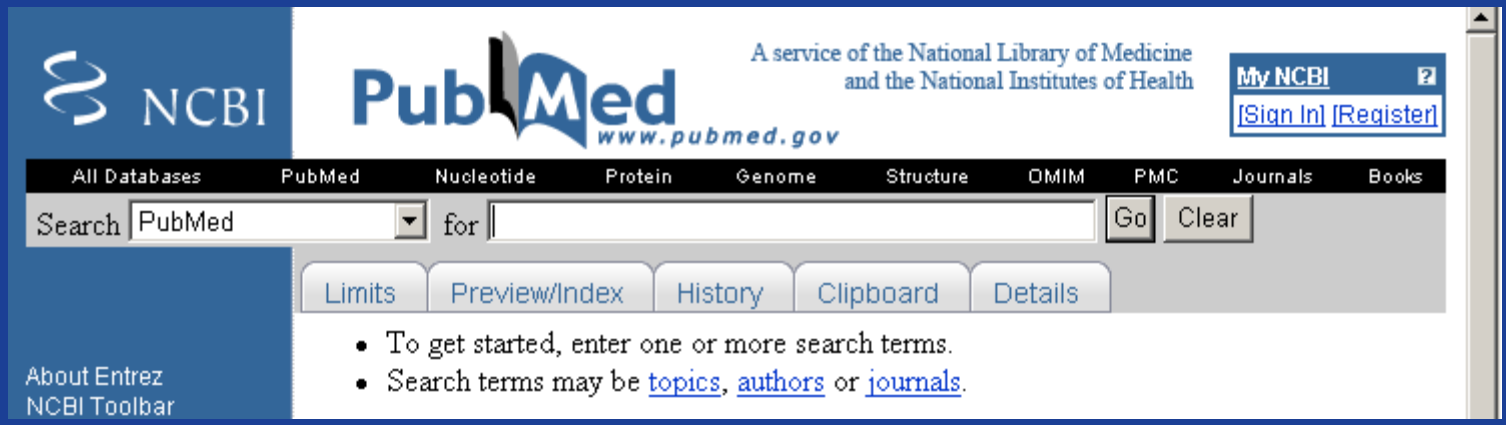
1. Absolute risk reduction (ARR)
2. Relative risk reduction (RRR)
3. Number needed to treat (NNT)

How would you explain these benefits to a patient?

N Engl J Med 2001; 345: 494-502.

"We surveyed one acute medical take in our hospital. In a relatively quiet take, we saw 18 patients with a total of 44 diagnoses. The guidelines that the on call physician should have read remembered and applied correctly for those conditions came to 3679 pages. This number included only NICE, the Royal Colleges and major societies from the last 3 years. If it takes 2 min to read each page, the physician on call will have to spend 122h reading to keep abreast of the guidelines" (for one 24h on-call period).

Allen D, Harkins KJ. Lancet 2005; 365: 1768



- There are 1500 pages indexed in Medline each day.

Prof Sir JA Muir Gray
Best Current Evidence Strategy.
March 2006

(So which ones will you choose to read?)

Abstracts lie (lots)

Pitkin RM, et al JAMA 1999; 281: 1110-1111

- Random samples from 44 articles and their abstracts from Annals, BMJ, Lancet, JAMA, NEJM (12 months from July 1996), and 44 articles CMAJ (15months from July 1996) were compared with the original articles
- 19% of abstracts contained statements that were inconsistent with the full article
- 11% of abstracts contained statements that were not present in the full article

20% of RCTs don’t report all outcomes

Chan A-W, Altman DG. BMJ 2005; 330: 753-756

- 519 RCTs in 553 publications were examined for incompletely reported outcomes per trial. Original authors were surveyed (response rate 69%).
- 32% denied the existence of unreported outcomes when there was evidence to the contrary in their publications.
- On average, 20% of outcomes measured in RCTs were incompletely reported.

Reading journals

Evidence-based treatment for my patient

Recognise lack of certainty

1. Formulate question

2. Efficiently track down best available evidence

3. Critically review the validity and usefulness of the evidence

4. Implement changes in clinical practice

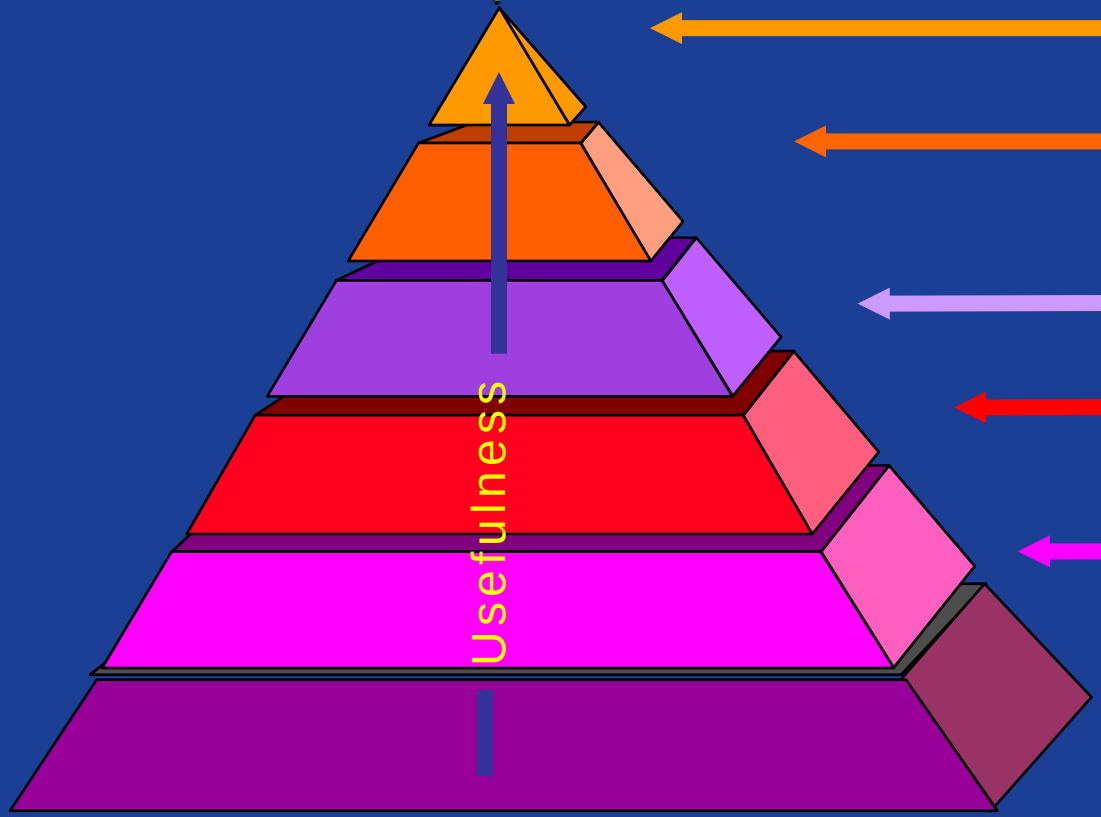
5. Evaluate performance

- If you ask doctors, they say they need information about once a week. But if you debrief them, they raise about 2 questions for every three patients Covell DG et al. Ann Intern Med 1985 103: 596–599
- Many potential questions are not recognised by general practitioners (over confidence?, failure to recognise uncertainty?) Barrie AR et al. BMJ 1997; 315: 1512–1515
- Answers to most questions are not immediately pursued. Ely JW et al. BMJ 1999; 31: 358-361
- Doctors spent an average of less than 2 minutes pursuing an answer, and they used readily available print and human resources. Only two questions (out of over 1100) led to a formal literature search. Ely JW et al. BMJ 1999; 31: 358-361

Reading journals and critical appraisal can (largely) be replaced by using brief summaries of evidence from trusted sources

Finding the ‘best answer’, first time

Essential Evidence Plus, NHS Evidence(?), self-assembly



Cochrane Library
NICE, SIGN

Clinical Evidence
NPC & NPCi
CKS

EBM DTB Bandolier

“Ivy League” journals

Textbooks

Medline,
Google scholar

- Foraging
- Hot synching

Summary

- EBM is important
- There are many obstacles to its use
- Find high quality summaries of evidence produced by the public sector
- Some new skills are usually required to understand a summary of evidence
- Then you have to be able to communicate those results to a colleague or patient