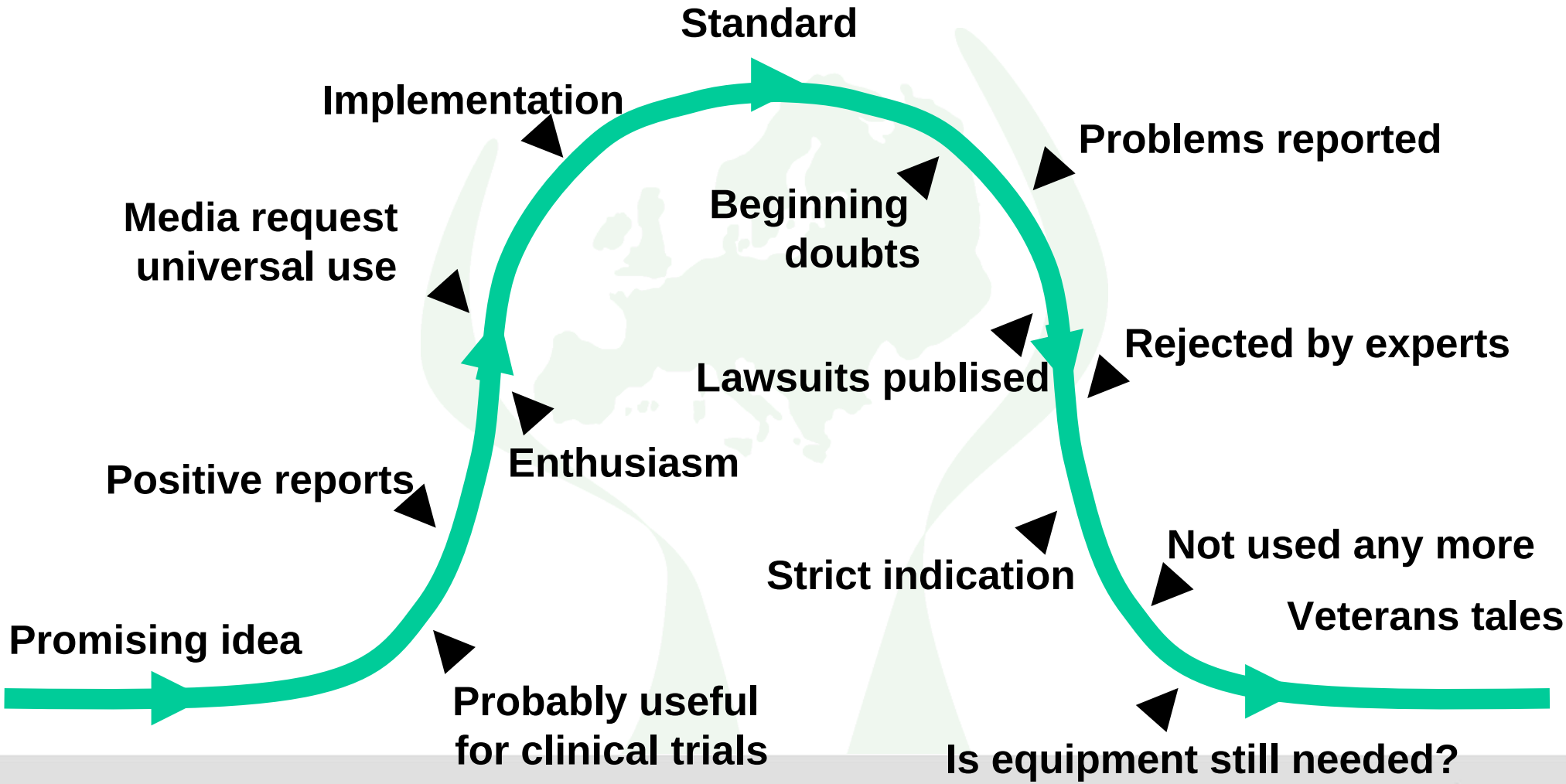
Evidence-based medicine

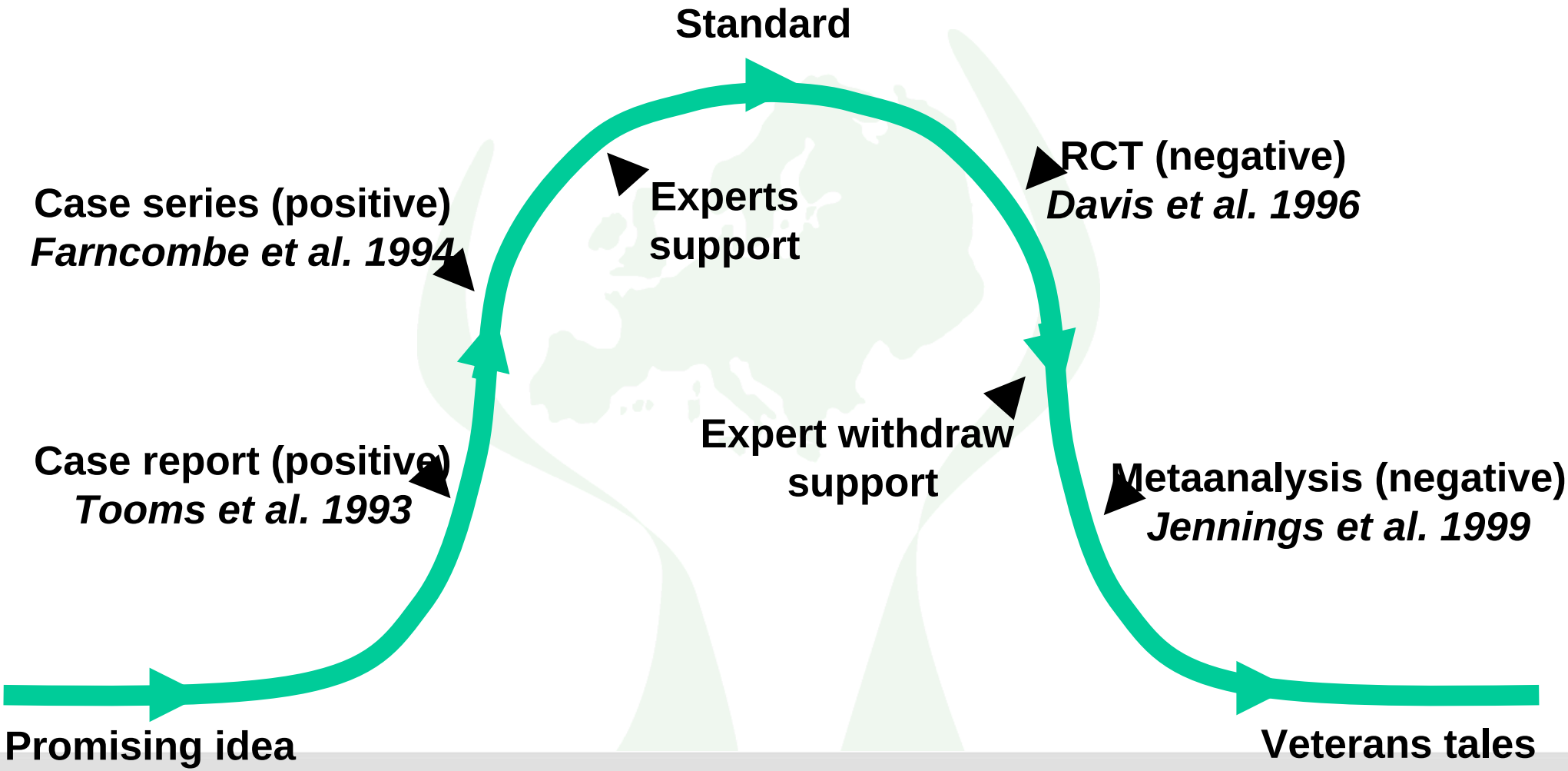
We have to consent on a treatment regimen. Please draw a straw.

Scott's Parabola
Rise and fall of a new method



Scott, BMJ 323 (2001) 1477

Scott's Parabola: nebulized morphine



Controlled trials

Open	Patient and physician know treatment group
Single-blind	Patient does not know physician knows
(Observer blinded)	Patient does not know Physician knows Observer does not know
Double-blind	Patient does not know Physician does not know
Triple-blind	Patient does not know what he gets Nurse does not know what she hands out Physician does not know what he does

Journal of Irreproducable Results, New York 1983, p. 96

Grading the evidence

CEBM	SIGN	GRADE
1 RCT 2 cohort studies 3 case control studies 4 case series 5 expert opinion	1 meta-analysis 2 case control, cohort studies 3 case reports, series 4 expert opinion	High: Randomised trial Low: Observational study Very low: Any other evidence
A consistent level 1 B consistent level 2 / 3 or extrapolated from L1 C level 4 or extrapolated from L 2 / 3 D level 5 evidence or inconsistent results	A meta-analysis, sys.rev., or RCT (1 ++) B level 2 ++ or extrapolated 1+/1++ C level 2 + or extrapolated 2 ++ D level 3 / 4 or extrapolated from 2 +	Do it, Don't do it Probably do it. Probably don't do it:

EAPC guidelines on opioids

C Morphine is the opioid of first choice for moderate to severe cancer pain.

A Hydromorphon or oxycodone, if available in an immediate release and a modified release form for oral application, are an effective alternative to oral morphine.

B Transdermal fentanyl is an effective alternative to oral morphine, though it should be restricted to patients with stable dose requirements.

Hanks et al. Br J Cancer 84 (2001) 587-93

Cancer pain guidelines

⇧⇧ For some weak opioids such as codeine or tramadol research evidence from cancer pain together with the evidence from non-cancer pain can be taken as proof of efficacy.

Drug Commission of the German Medical Board 2007

Cancer pain guidelines

⇧⇧ **For strong opioids such as morphine, oxycodone, hydromorphon, buprenorphine or fentanyl clinical trials have been published, that can be used as proof of efficacy, even though in most trials other analgesics and not placebo have been used as comparators. This evidence is supported with clinical trials (placebo-controlled in some cases) in non-cancer pain.**

Drug Commission of the German Medical Board 2007

Cancer pain guidelines

⇧⇧ **Results of several comparative trials demonstrate comparable efficacy and tolerability of oral slow release application forms of morphine and other potent opioids with immediate release**

Drug Commission of the German Medical Board 2007

Cancer pain guidelines

⇧⇧ For fentanyl and buprenorphine patches results from placebo-controlled trials in chronic pain, some of it in cancer pain, are available. Not all trials could demonstrate superiority of the transdermal system against a sometimes high placebo rate.

⇧ For oral transmucosal fentanyl citrate several trials have described effective relief of breakthrough pain compared to placebo as well as to morphine.

Drug Commission of the German Medical Board 2007

Cochrane reviews

++ Opioids for dyspnea in terminal disease
Jennings et al. 2001, 18 studies:
oral, parenteral significant effect,
not with nebulized opioids

++ Hydromorphon for acute and chronic pain
Quigley 2001, 43 studies:
little difference morphine to hydromorphine
metaanalysis not possible

www.cochrane.de

Cochrane review: oral morphine

- 54 trials
- 19 trials compared morphine to other opioids
- Insufficient comparable data for metaanalysis, no NNT
- Most trials recruited < 100 patients

Wiffen P, McQuay H, Cochrane Database 2007

More questions than answers

- Systematic literature review 1966 - 2001

• „More questions than answers“ [TI, AB]	163
„More answers than questions“ [TI, AB]	3
• „Need more research“ [TI, AB]	162
„Need less research“ [TI, AB]	1

- Is scientific research really helpful?

David A, BMJ 323 (2001) 1462

Cochrane reviews: fatigue

- Minton et al, Cochrane Database 2007:
  - *Patients with clinical diagnosis of cancer*
  - *Assessing drug therapy for the management of CRF*
  - *Compared to placebo or usual care*
  - *Only RCTs*
- Radbruch et al, Cochrane Protocol 2007:
  - *Palliative care*
  - *Pharmacological treatment with fatigue (asthenia) as primary outcome (not erythropoetin)*
  - *Only RCTs*

Rating the quality of studies

- Randomized study? +1
  - method of randomization described and appropriate (f.e. table of random numbers, computer generated) +1
  - method of randomization inappropriate # (f.2. allocated alternately by birth date / hospital no.) -1
- Double blind study?:
  - Method of blinding described and appropriate? (f.e. identical placebo) +1
  - Method of blinding inappropriate (f.e. comparing placebo tablet with injection) -1
- Withdrawals and dropouts described? +1

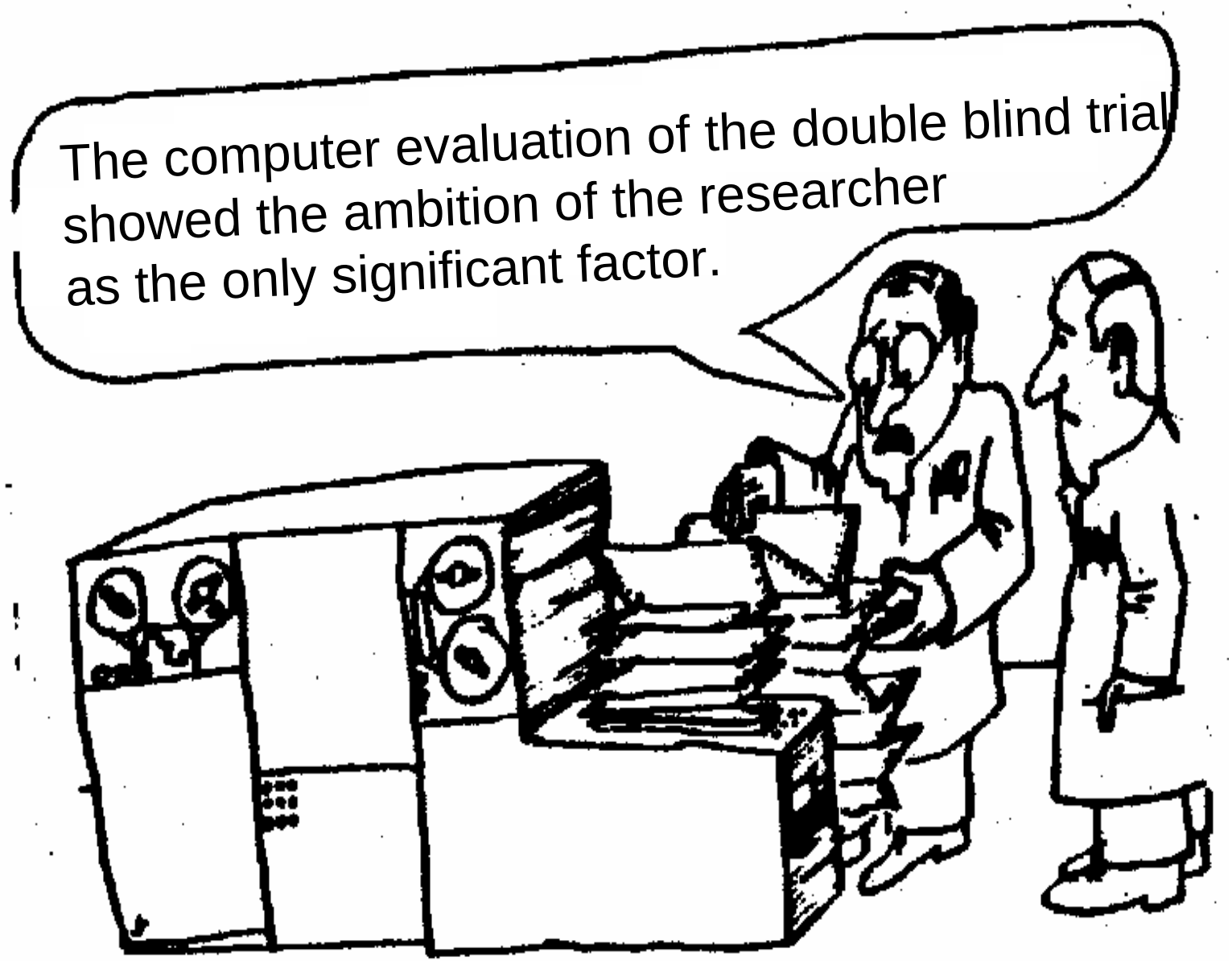
Jadad et al. Control Clin Trials 17 (1996) 1-12

Rating the quality of studies

- Trial population
- Study size
- Comparator (placebo, active placebo, gold standard)
- Placebo techniques (f.e. hidden injections)
- Potential sources of bias

Dangers in inadequate use of reviews

- Clinicans confuse absence of evidence with evidence of absence
- Health care organizations do not reimburse if efficacy is not proven
- Trial methodology adapted to EBM, not to setting of palliative care (placebo as comparator instead of gold standard)
- Systematic reviews take up research resources that are not available for clinical trials.


The computer evaluation of the double blind trial showed the ambition of the researcher as the only significant factor.

Aristotle: What is probable?

what all or most people

or the wise deem true,

or among the wise again

either all or most

or the most well known and renowned.

Aristotle, Topik, First book