NICE National Institute for Health and Care Excellence

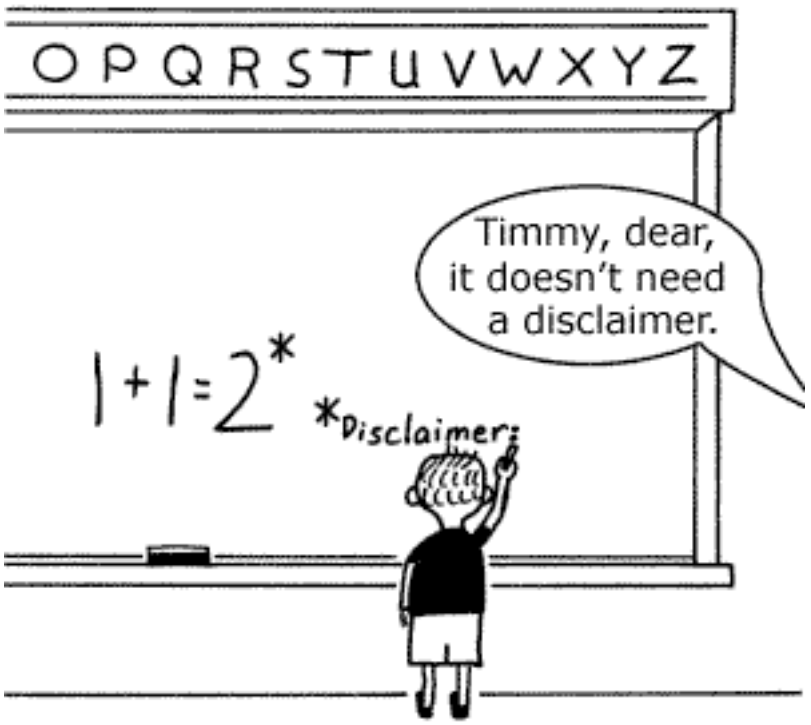
Systematic reviews: the policy makers dilemma

Sarah Garner, PhD BPharmMRPharm S
Associate Director R&D NICE

sarah.garner@nice.org.uk

Disclaimer

- I am an author and editor of systematic reviews and have been a Cochrane Editor for 8 years.
- The views are mine and not necessarily those of NICE.



Reducing ineffective practice: challenges in identifying low-value health care using Cochrane systematic reviews

Sarah Garner, Mary Docherty[1], John Somner[2], Tarang Sharma, Moni Choudhury, Mike Clarke[3], Peter Littlejohns[4]

National Institute for Health and Clinical Excellence, London; [1]Institute of Psychiatry, King's College London, London; [2]The Vision & Eye Research Unit, Anglia Ruskin University, Cambridge; [3]Queen's University Belfast, County Antrim, UK; [4]Division of Health and Social Research, King's College London, London, UK

Objectives: Despite international agreement that stopping low value practices will increase efficiency, identifying them is difficult and controversial. Opponents of centralized lists of low value practices stress that the actual problem is inappropriate low value use, and better targeting and implementation of treatment thresholds is needed. Our objective was to use Cochrane Reviews to identify low value practices to support local disinvestment decisions.

Methods: New or updated reviews were included if the authors concluded that the uncertain effectiveness of an intervention meant it should only be used in research, or that it was ineffective or harmful and should not be used. The reviews go through a production and quality assurance process, and are published as 'Cochrane Quality and Productivity topics' through the NHS Evidence website (http://www.library.nhs.uk/qipp/).

Results: Over a six-month period, 65 Cochrane reviews were processed by the National Institute for Health and Clinical Excellence (NICE). Of these, 28 identified potentially low value practices in the UK context. This was primarily due to a lack of randomized evidence of effectiveness, rather than robust evidence of a lack of effectiveness, or evidence of harm.

Conclusions: Identifying low-value health care practices for local disinvestment (total or partial) is both practically and politically challenging, yet it is necessary to manage health budgets. This project identified that Cochrane Reviews can potentially identify low value health care practices. However, each review has to be reinterpreted for the UK context and additional analysis has to be undertaken to facilitate local implementation. Recommendations to improve the usability of systematic reviews are made.

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Minocycline for acne vulgaris: efficacy and safety.

Reducing unnecessary practice: What are Cochrane 'Quality and Productivity' topics?

NICE has developed the Cochrane Quality and Productivity (QP) topics to help the NHS identify practices which could be significantly reduced or stopped completely, releasing cash and/or resources without negatively affecting the quality of NHS care.

Each Cochrane QP topic has been derived from a systematic review undertaken by reviewers from the Cochrane Collaboration. Each month the UK Cochrane Centre notifies NICE about new or updated Cochrane reviews that conclude that:

- the evidence shows that the practice is harmful or ineffective and should not be used
- there is insufficient evidence to support widespread use of the practice, suggesting that it should be used only in a research or audit project.

NICE has assessed this Cochrane QP topic against the QIPP criteria and has summarised the topic, supporting evidence, likely ease of implementation, impact on productivity savings (cash and resources) and on the quality of NHS care. The topic has also been mapped onto any existing NICE guidance and other guidance accredited by NHS Evidence.

This NICE assessment has not been informed by evidence of practical implementation. If a Cochrane QP topic has been implemented users are encouraged to submit their experience as a QIPP example using the QIPP user guide in order to inform other NHS users.

Summary

The 'Implications for practice' section of Cochrane review stated:
'The 27 studies included in this review do not provide any clear and unbiased evidence to support the first-line use of minocycline in the treatment of acne. Although it has been shown to be an effective treatment for moderate acne vulgaris at a dose of 100 mg per day, no study has conclusively shown any important clinical difference between the tetracycline antibiotics or other commonly used therapies. Given that it is 2.9 to 4.8 times more expensive than (oxy)tetracycline in the UK (Drug Tariff Jan 2000) depending on the formulation, the additional cost of minocycline is not justified on the basis of clinical efficacy alone.

Similarly, there is no evidence that it is more effective in acne resistant to other therapies or that it has a faster onset of action or a more prolonged effect. Insufficient information was located to make any recommendations concerning the appropriate dose that should be used. The relative safeties of the tetracyclines have still not been adequately determined and little further information could be derived from the studies due to their inherent inability to detect rare events. Recent reviews of case reports and case series suggest that minocycline therapy for acne may be associated with a broader spectrum and a higher incidence of severe adverse drug reactions that other tetracyclines.

The lack of a denominator in nearly all of the studies means that the risks for minocycline compared to other tetracyclines cannot be compared. Only in the case of lupus-like

Potential productivity savings

Estimate of current NHS usage	An estimated 1.2 million people in England currently seek medical advice for acne. Prescribing data from 2008 show just over 260,000 prescriptions issued for minocycline.
Level of productivity savings anticipated	Using the October 2010 BNF prices (which exclude VAT), the estimated savings of substituting minocycline for an alternative tetracycline is approximately £2.2 million
Type of saving	The savings are likely to be cash-releasing efficiency savings
Any costs required to achieve the savings	There is not likely to be a cost barrier to change
Other information	The savings are likely to impact on community prescribing

Results

- The process was resource-intensive
  - rejection rate of 57%
  - 40 man-hours per topic
    - Project management
    - Costing
    - Clinical adviser
    - Sign-off
    - Publishing
  - Approximately £1500

Why the difficulties?

- Recommendations to stop have to be robust

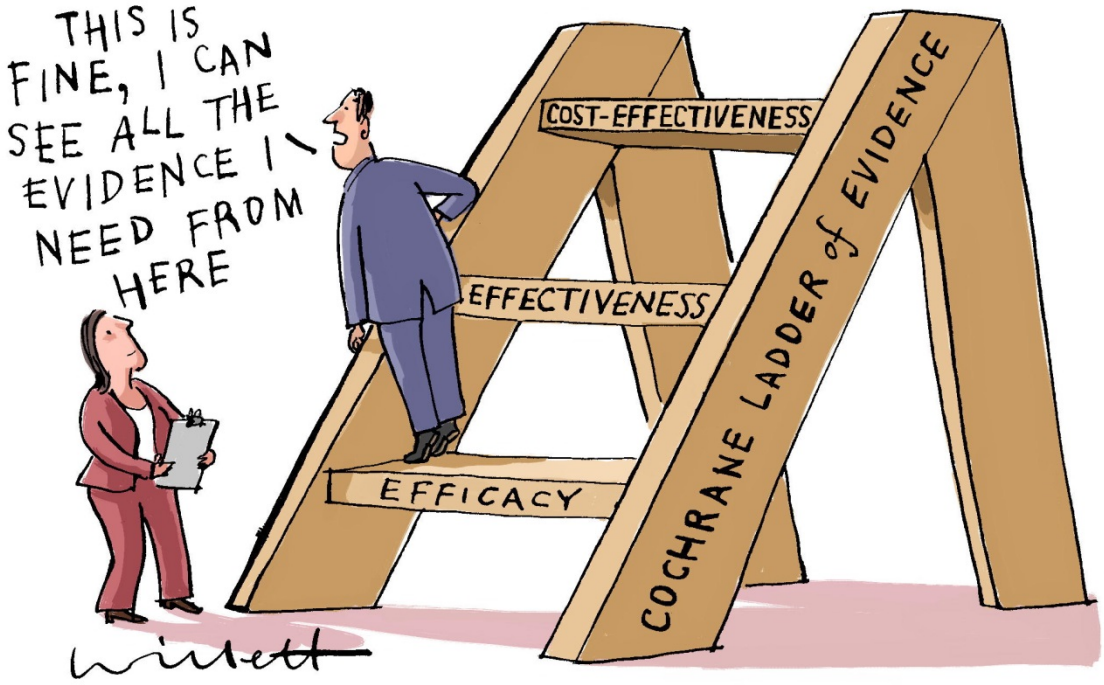
- The context of the reviews differed from our objectives
  - Did not reflect current UK practice
    - Experimental drugs
    - Practice already stopped
  - PICO differed

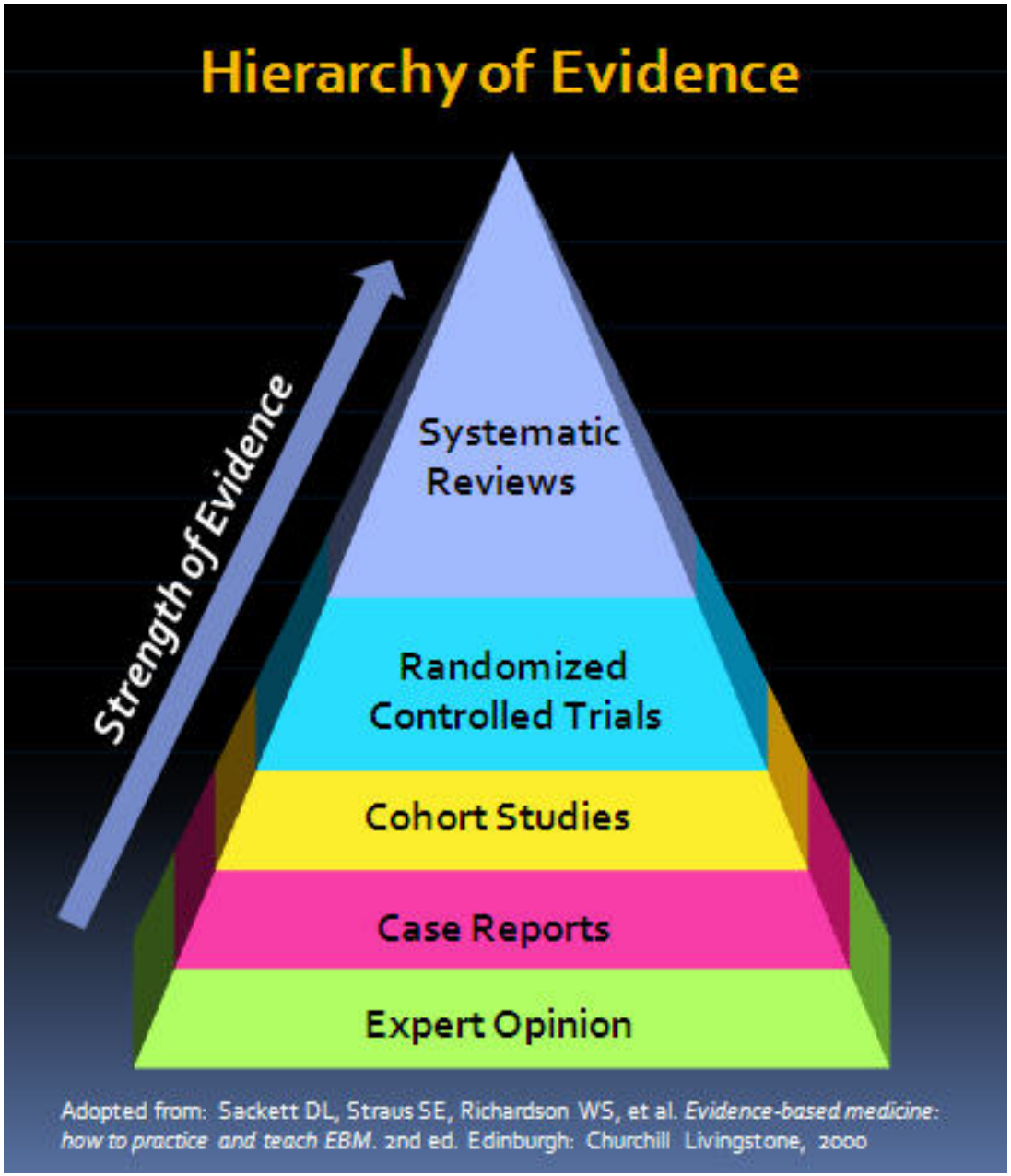
More editing required…

- PICO in trials not made explicit in conclusions
- Risks and benefits not clearly described
- Abstract and review not aligned
- Lack of summary data
- Conclusions that go beyond evidence and are not precise
- Reviews did not differentiate well between
  - Evidence of lack of (cost) effectiveness or harm
  - Uncertainty- lack of evidence of (cost) effectiveness
  - Low quality or no evidence, lack of clinical or statistical significance

The evidence base…

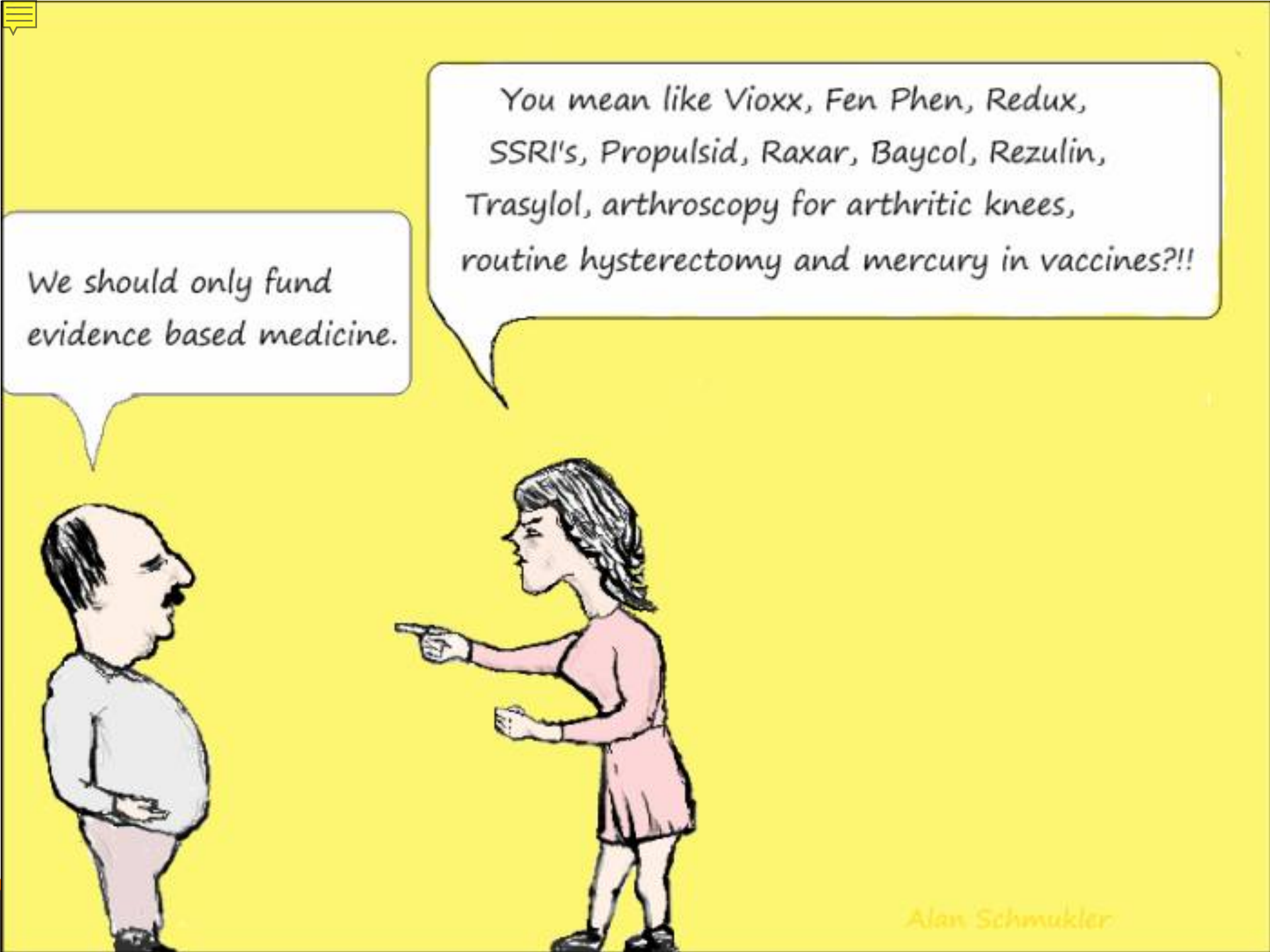
- Systematic review did not provide the full clinical picture. Guidelines needed.
- Systematic reviews rarely look at comparator
- Conflicting evidence
- RCTs are not the only source of evidence




Hierarchy of Evidence
Strength of Evidence
Systematic Reviews
Randomized Controlled Trials
Cohort Studies
Case Reports
Expert Opinion
Adopted from: Sackett DL, Straus SE, Richardson WS, et al. Evidence-based medicine: how to practice and teach EBM. 2nd ed. Edinburgh: Churchill Livingstone, 2000

Efficacy v effectiveness

- Efficacy
  - patient benefit and harm in experimental and closely monitored research studies, normally RCTs.
  - major advantages in minimising bias
  - generalisability questionable
    - restricted entry criteria
    - unrepresentative settings
- Effectiveness
  - patient benefit and harm when the technology is actually applied in everyday practice.
    - pragmatic clinical trials
    - adverse event reporting
    - clinical audit
    - Registries?


We should only fund evidence based medicine.
You mean like Vioxx, Fen Phen, Redux, SSRI's, Propulsid, Raxar, Baycol, Rezulin, Trasylol, arthroscopy for arthritic knees, routine hysterectomy and mercury in vaccines?!!
Alan Schmukler

Hierarchies of evidence should be replaced by accepting—indeed embracing—a diversity of approaches.

This is not a plea to abandon RCTs and replace them with observational studies. Nor is it a claim that the bayesian approaches to the design and analysis of experimental and non-experimental data should supplant all other statistical methods.

Rather, it is a plea to investigators to continue to develop and improve their methods; to decision makers to avoid adopting entrenched positions about the nature of evidence; and for both to accept that the interpretation of evidence requires judgment.

THE HARVEIAN ORATION OF 2008

DE TESTIMONIO

On the evidence for decisions about the use of therapeutic interventions

Professor Sir Michael David Rawlins
MD FRCP FFPM FMedSci

Royal College of Physicians
Setting higher medical standards

The world is changing…

- Personalized medicine
- Comparative effectiveness agenda in the US
  - PCORI
  - Registry of patient registries
- Data linkage initiatives eg UK CPRD
- Electronic Healthcare records and PROMS
- CONSORT statements
- ISPOR and GRACE critical appraisal for non-RCTs
- Cochrane non-RCT methods working group
- Innovative Medicines Initiative: GetReal Consortium
- Adaptive Licensing: EMA to pilot

Helping the policy maker…

- Do sensitivity analysis
- Be precise with conclusions
- Be explicit about strengths and weaknesses
- If time…explore other data sources
- Get involved with methods development

"The research proves tall rats are more confident than short rats. At least I think it does. I've never been good at this."