Unbiased Prescribing Information

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* The project benefits from a grant from Iceland, Liechtenstein and Norway through the EEA Grants.

What this presentation covers

- Background to advertising analysis
- What type of evidence is needed to guide prescribing decisions?
- A few useful measures: NNT, ARR, etc.
- Critical appraisal – judging research quality

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To decide whether to prescribe, what do you need to know?

- About the condition?
- About the treatment?
- About the patient

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All medicine use is a balance

Benefit

- Drug effect
- Health problem
- Personal characteristics

Harm

- Drug effect
- Other exposures
- Personal characteristics

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"Evidence based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients."

- Sackett D. BMJ 1996; 312:71-72

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What defines best evidence'?

- Completeness: full body of scientific research
- Strength of evidence: design and quality of studies, results replicated
- Magnitude of effect: is there enough of a difference to make a difference?
- Health impact: effects important to patient health
- Balance: benefits clearly outweigh harm

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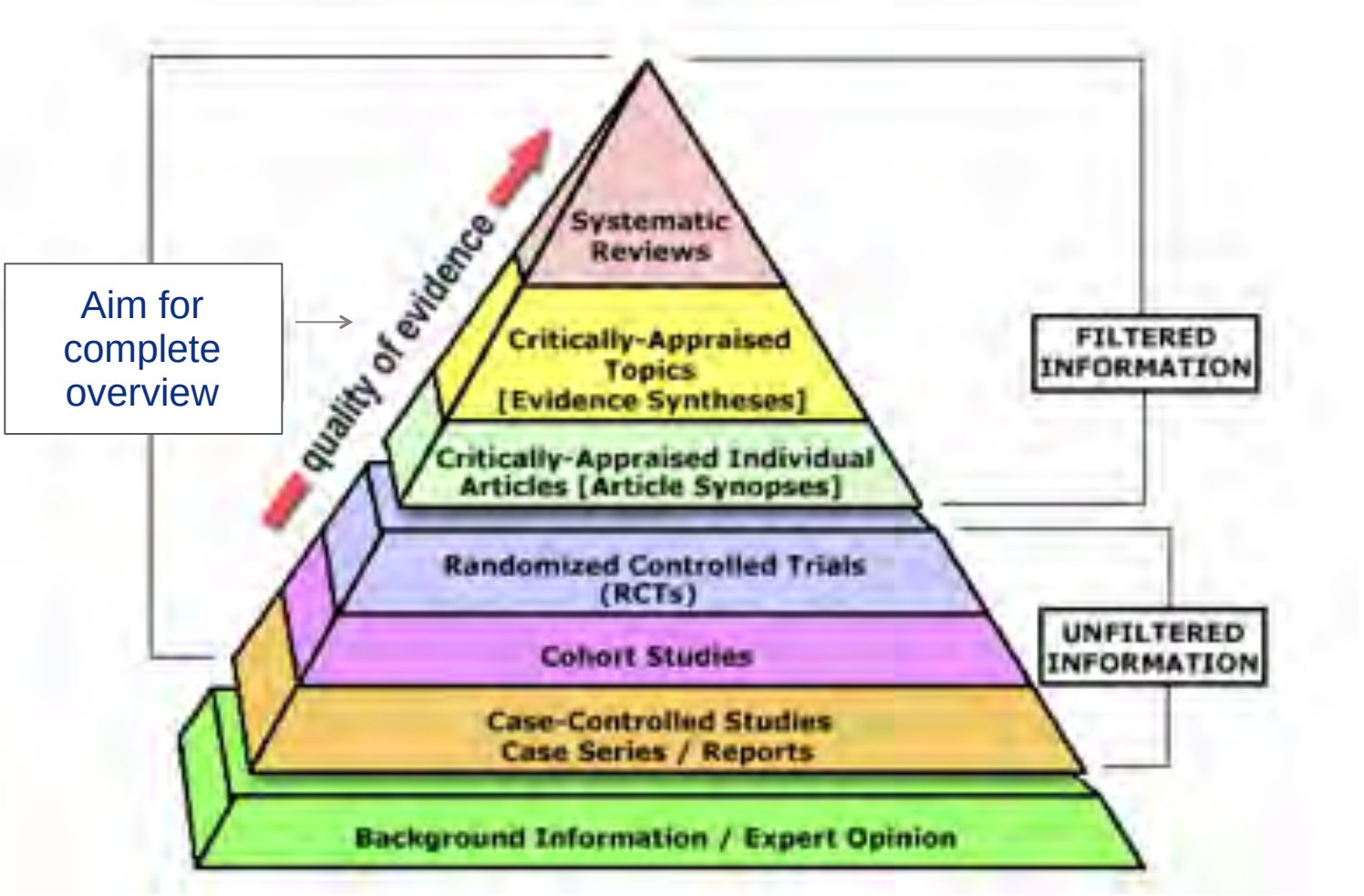
Hierarchy of evidence



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What is a systematic review?

"A concise summary of the best available evidence that addresses a sharply defined clinical question and attempts to answer it using explicit and rigorous methods to identify, critically appraise and synthesize all relevant studies."

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An example – systematic review results versus advertising messages

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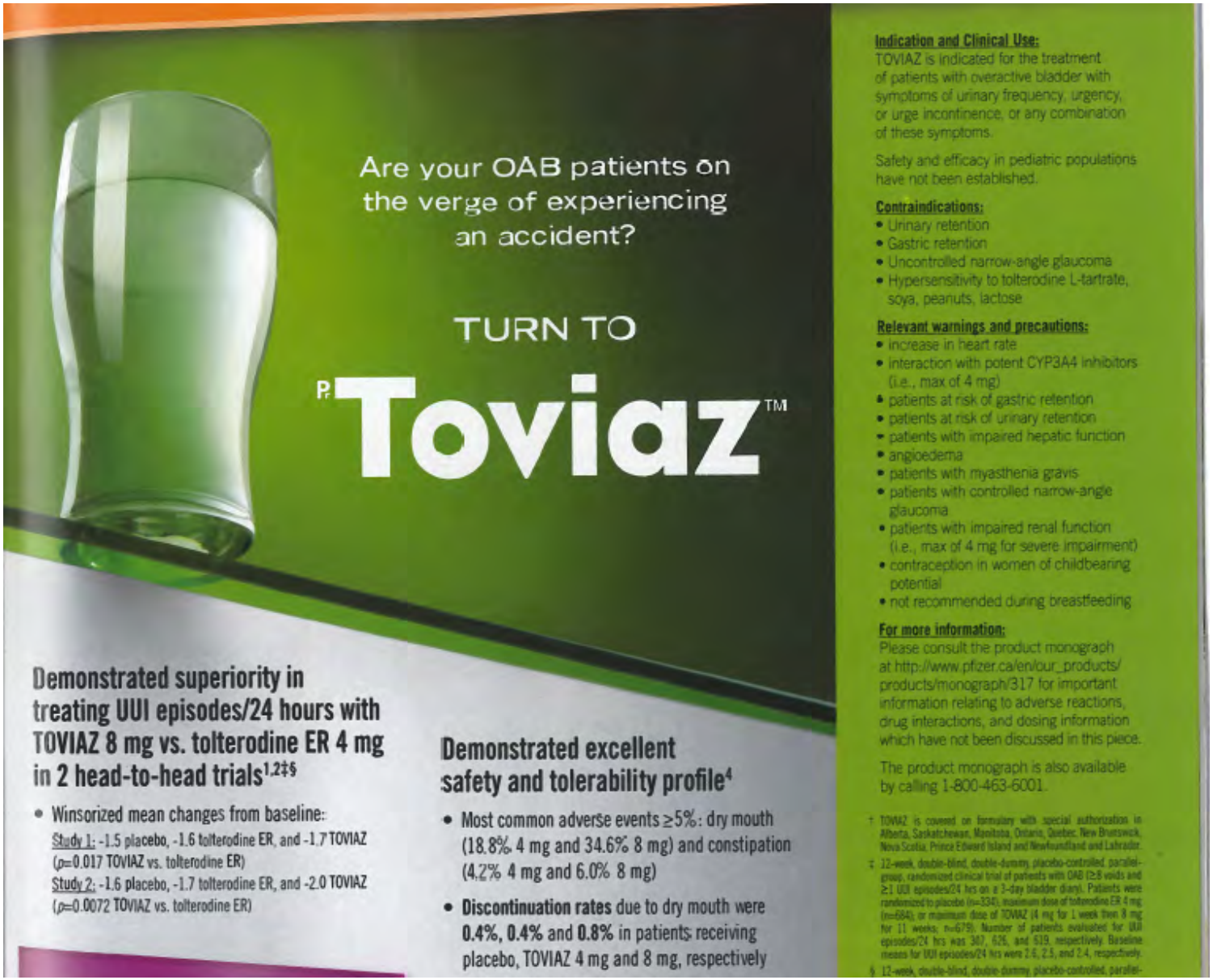

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Do benefits outweigh harm?

Medicines for Treating Urgency Incontinence	
Fesoterodine (Toviaz®)	**Benefits** About 1 out of 10 women became continent using this medicine.  About 1 out of 10 women improved their symptoms using this medicine.  **Side Effects** About 2 out of 10 women had dry mouth using this medicine.  Less than 1 out of 10 women had constipation using this medicine.  Less than 1 out of 10 women had dry eyes using this medicine. 

Agency for Healthcare Research and Quality (AHRQ). Non-surgical treatments for urinary incontinence. Consumer Summary 2012. www.ahrq.gov

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How does it compare to non-drug options?

Options for Treating Urgency Incontinence	
Non-drug Treatments: Lifestyle Changes	
Bladder training	**Benefits** The number of women who became continent was not reported. 4 out of 10 women improved their symptoms using bladder-control exercises.  Combining PFMT with bladder training improved continence in women with urgency incontinence. **Side Effects** Not known, but most researchers think there are few if any.

Agency for Healthcare Research and Quality (AHRQ). Non-surgical treatments for urinary incontinence. Consumer Summary 2012. www.ahrq.gov

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Can drug treatment lead to serious harm?

Warning: Doctors and patients have also reported some serious side effects that can occur with these medicines. Although they do not happen very often, they are more dangerous than the common side effects listed above. These side effects include rapid irregular heart rate, hallucinations, problems with thinking, and rarely death. The chance of having a serious side effect is greater for elderly patients, for patients who take many different medicines at the same time, and for patients who take some antihistamines (allergy medicines) and antibiotics along with these UI medicines. Ask your doctor about these more serious side effects.

Agency for Healthcare Research and Quality (AHRQ). Non-surgical treatments for urinary incontinence. Consumer Summary 2012. www.ahrq.gov

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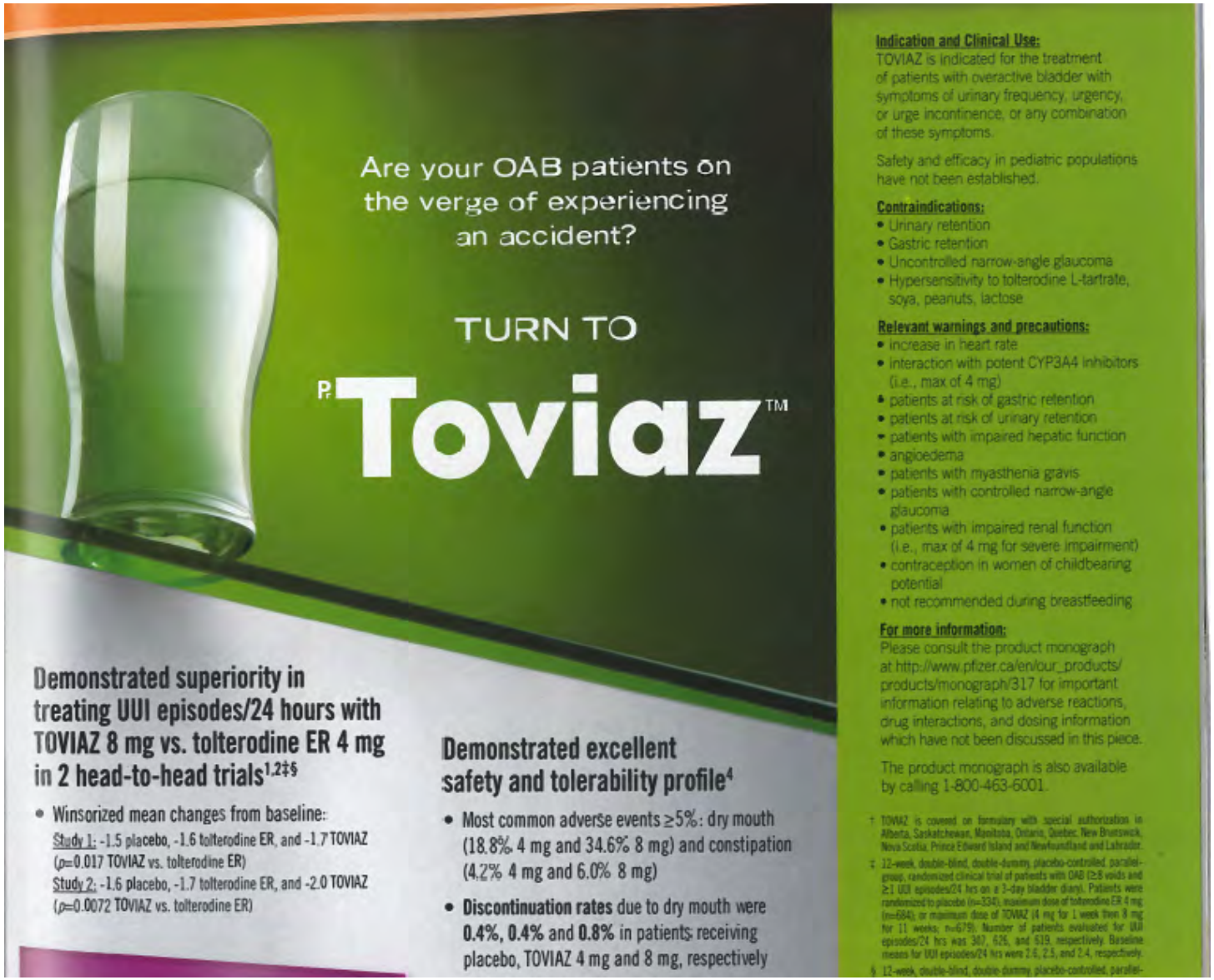

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Communicating treatment outcomes

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Have I got a deal for you!

- Special offer: 50% off
- Any takers?

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Relative or absolute risk difference

- 1 in 100 patients improve on placebo
- 2 in 100 patients improve on drug

- Relative risk reduction = (1/100) ÷ (2/100)
- Absolute risk reduction (ARR) = 0.02 – 0.01

- Number needed to treat for 1 to benefit = NNT 1 ÷ absolute risk reduction

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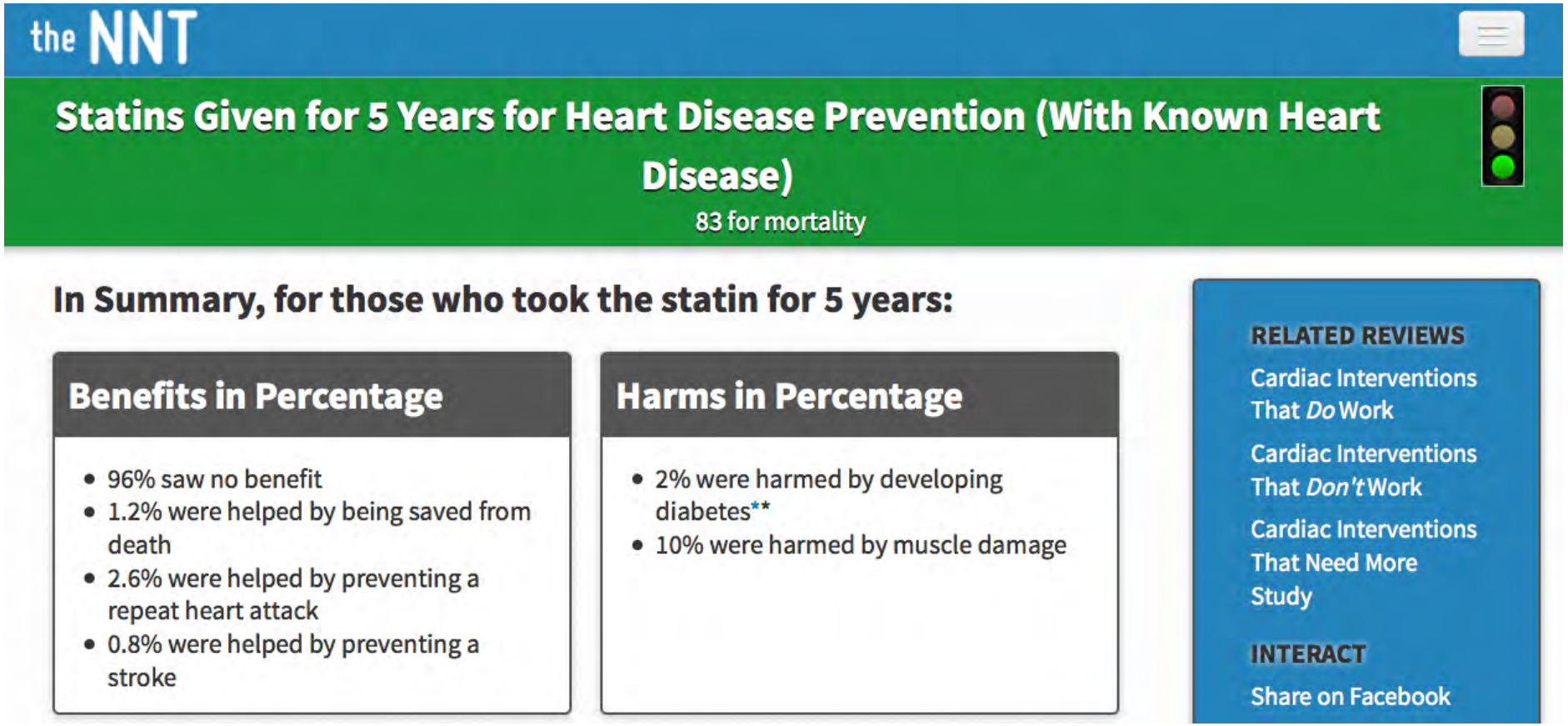

www.thennt.com/nnt/statins-for-heart-disease-prevention-with-known-heart-disease/

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Veselības projekti | hai | Sabiedrības integrācijas fonds | eea grants | Ojārs Vēlde Scholarship Fund

the NNT

Statin Drugs Given for 5 Years for Heart Disease Prevention (Without Known Heart Disease)

60 for non-fatal heart attack

In Summary, for those who took the statin for 5 years:

Benefits in Percentage

- 98% saw no benefit
- 0% were helped by being saved from death
- 1.6% were helped by preventing a heart attack
- 0.4% were helped by preventing a stroke

Harms in Percentage

- 2% were harmed by developing diabetes**
- 10% were harmed by muscle damage

RELATED REVIEWS

Cardiac Interventions That *Do* Work

Cardiac Interventions That *Don't* Work

Cardiac Interventions That Need More Study

INTERACT

Customize This NNT

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THERAPEUTICS INITIATIVE Evidence Based Drug Therapy

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An imperfect evidence base

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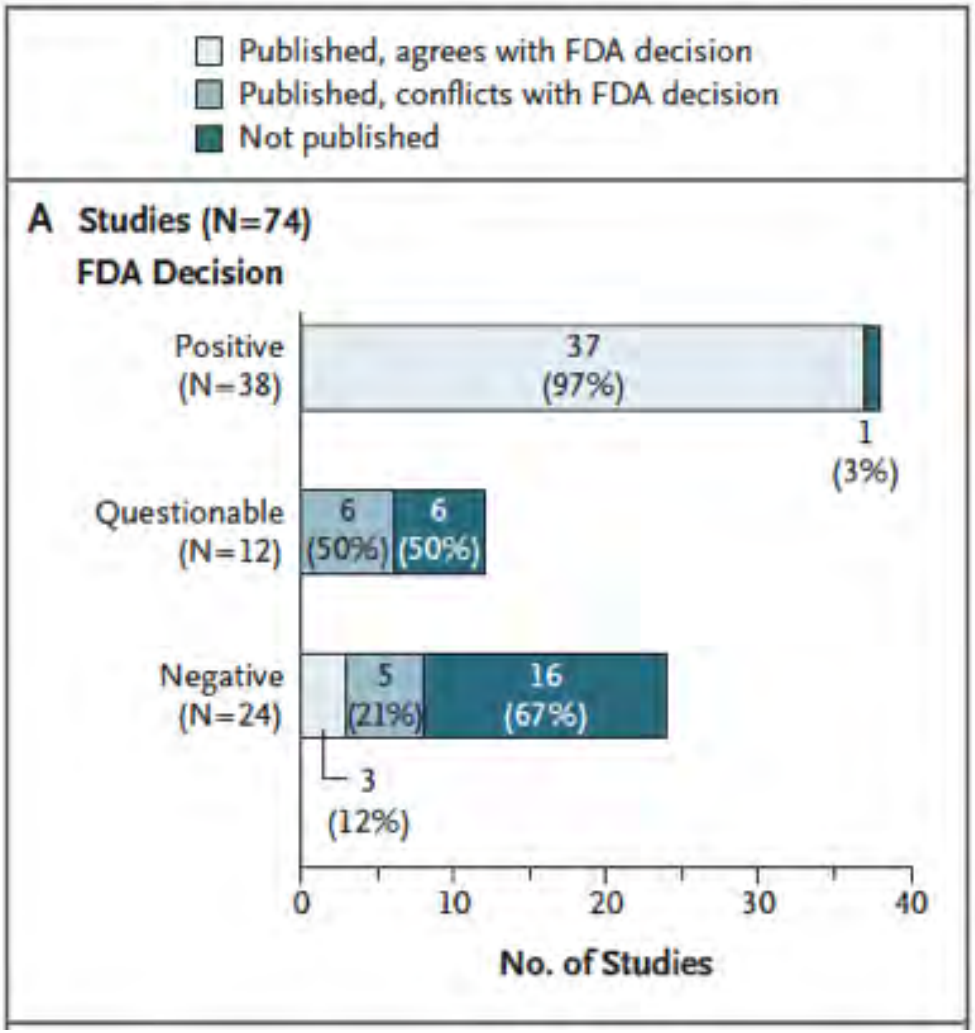
Antidepressant effectiveness



- *Turner et al. N Engl J Med 2008;358:252-60*

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A Cochrane group's attempt to reproduce an analysis underpinning the use of oseltamivir in pandemic influenza hit a brick wall. **Deborah Cohen** retraces its steps

COMPLICATIONS

Tracking down the data on oseltamivir

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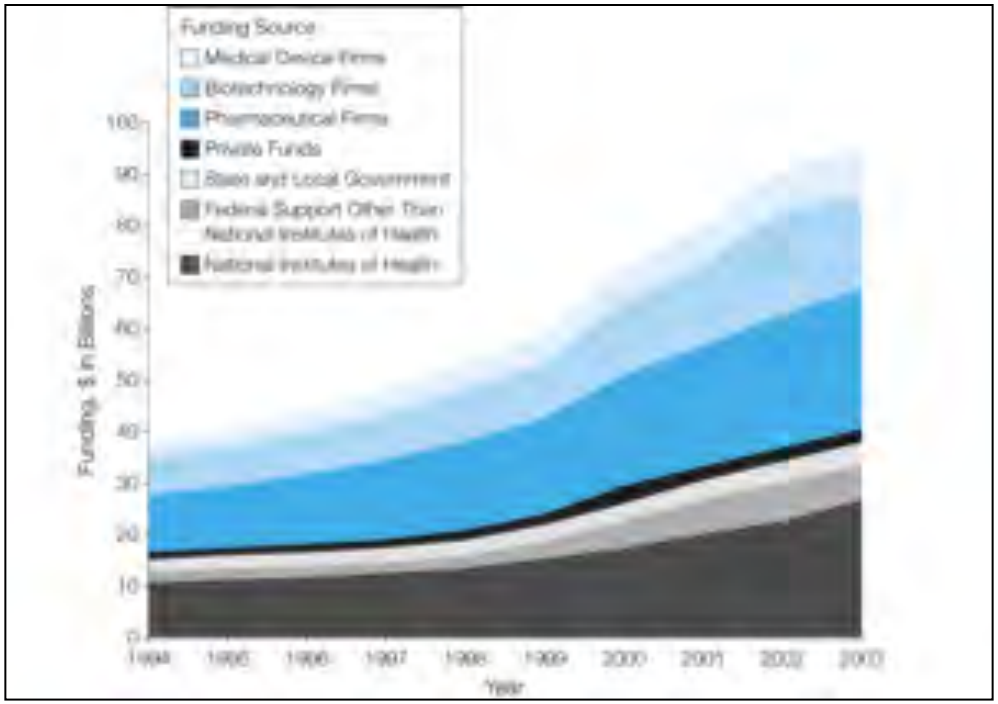
Industry research sponsorship

- twice the odds of favourable results
  - Odds ratio = 2.15 (95% CI 1.7-2.7)

Lundh et al. Cochrane library 2012



Moses et al. JAMA. 2005;294(11):1333-42

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Trials comparing 2 or more cholesterol-lowering drugs

- Bero et al. PLoS Med 2007; 4(6):e184

- Systematic review; n=192 studies
- 95 (50%) industry-sponsored
- Sponsor strong predictor of which drug did best
  - OR=20 (95% CI 4 - 93) – results favour sponsor's drug
  - OR=35 (95% CI 7 – 168) – conclusions favour

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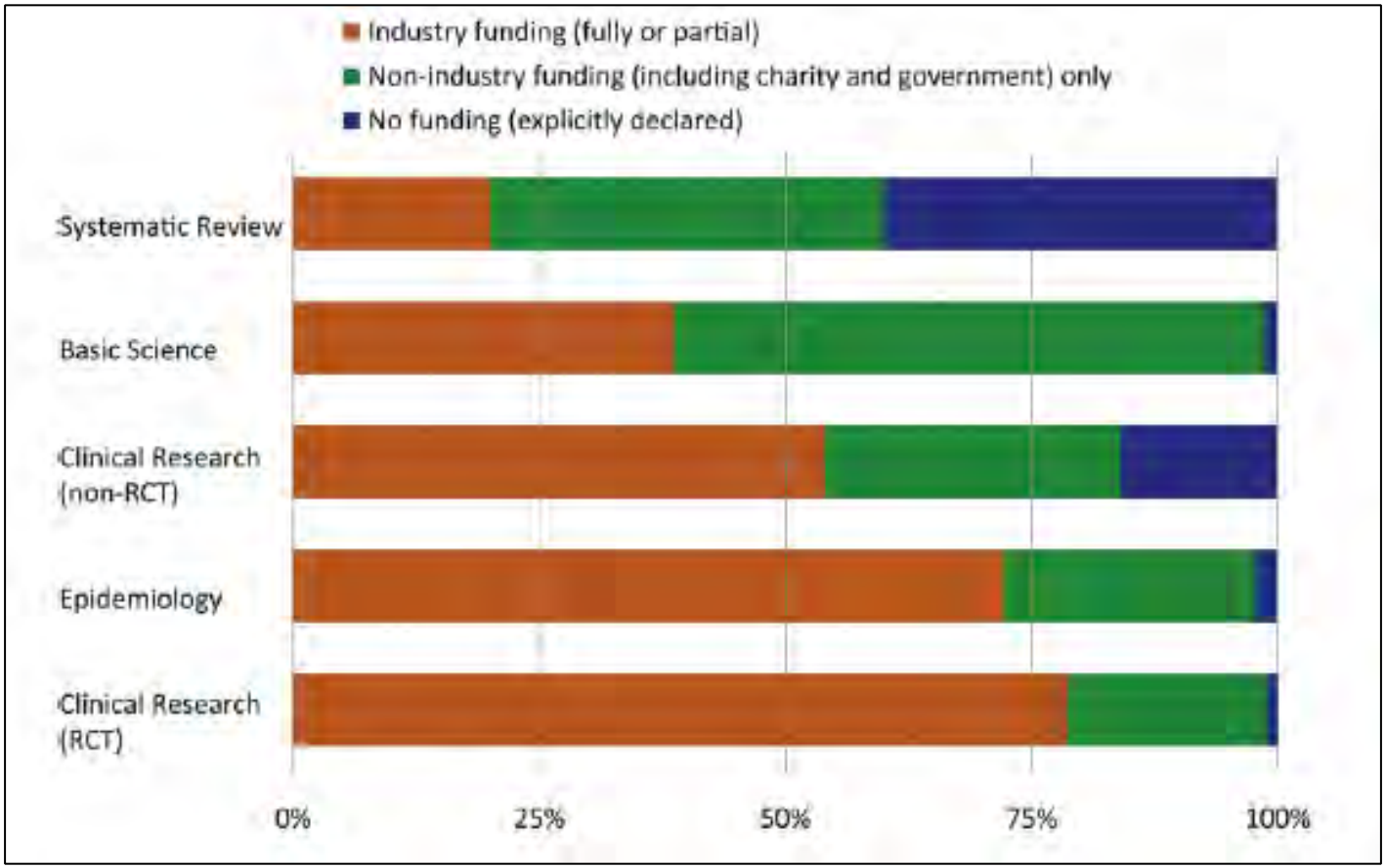
Body of research literature on overactive bladder



Tikkinen et al. Europ Urol 2012; 61: 746-8

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Reshaping disease diagnoses

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Critical appraisal – evaluating study quality and risk of bias

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Critical appraisal “in a nutshell”

- How strong is the study design?
- How well was it carried out?
- Can you trust the results?
- Can you apply them to ‘real life’ patients?

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Cochrane Risk of Bias Tool

(biases known to exaggerate estimated effects)

Type of bias	
Selection bias	***Randomization, allocation***
Performance bias	Blinding of participants and caregivers
Detection bias	***Blinding of outcome assessment***
Attrition bias	Incomplete outcome assessment
Reporting bias	***Selective outcome reporting***

http://handbook.cochrane.org/

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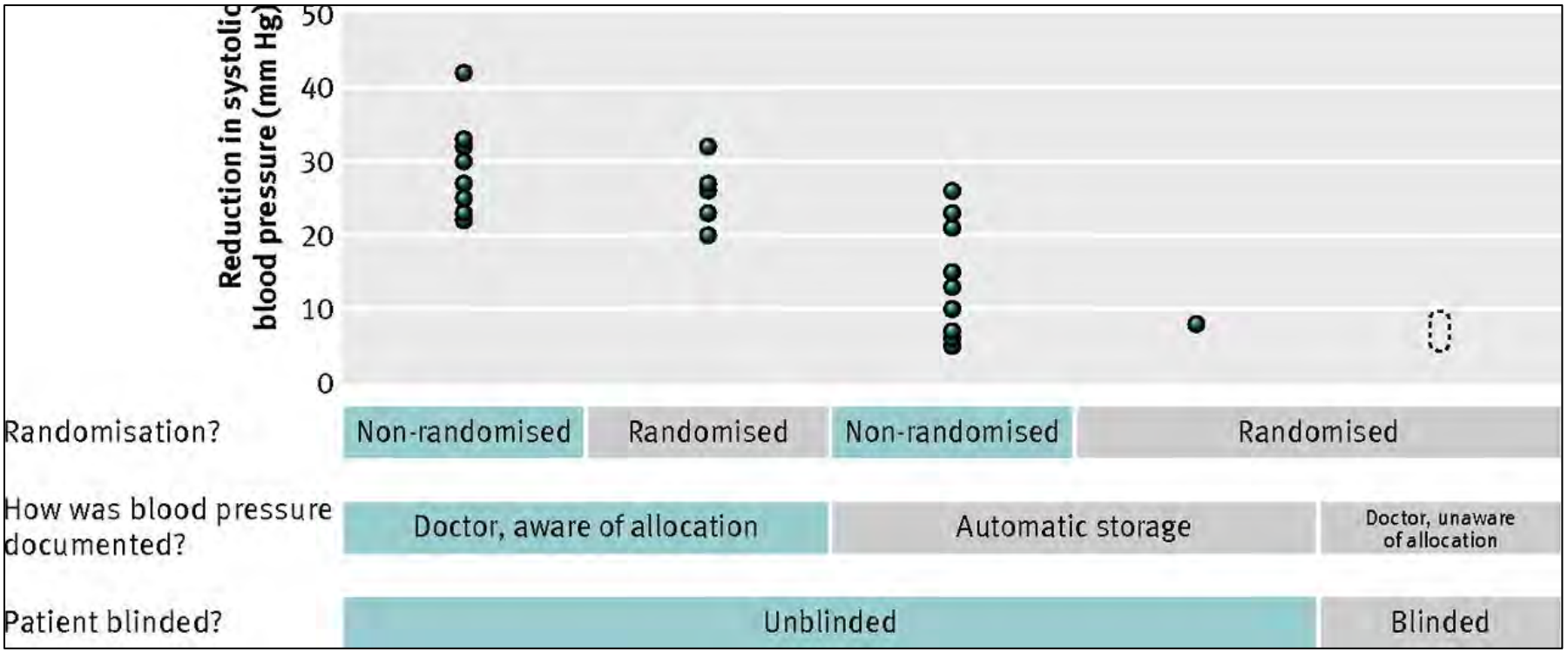

"Measurement of a noisy variable by unblinded optimistic staff is a known recipe for calamitous exaggeration."

Shun-Shin et al. Removing the hype from hypertension. BMJ 2014;348:bmj.g1937

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Counting and accounting for all study participants

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Post hoc subgroup analyses

…there are many ways to cut a pie

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How to get the results you want

- Compare to an inferior treatment
- Compare to too low or too high a dose
- Use too small a sample
- Report only the most favourable results (endpoints; trial centres; subgroups)
- Present results for strongest impact

- Smith R. PLoS Med 2005; 2(5) e138

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Critical appraisal of advertisements

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Hitchhiker's guide to drug ads

1. Beauty is only skin deep- seductive images
2. What's the point? – main message
3. Examine the claims – check the evidence
4. The great picture show (graphs & data)
5. "Lies, damned lies, and statistics"
6. Non sequiturs – irrelevant information
7. References – listed and obtainable?

www.healthyskepticism.org

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A few sources of independent drug information

- Cochrane Database of Systematic Reviews
  - www.cochrane.org
- Therapeutics Letter
  - www.ti.ubc.ca
- Drug & Therapeutics Bulletin of Navarre
  - www.navarra.es
- US “Worst Pills, Best Pills” - $20/ year subscription
  - www.worstpills.org
- Prescrire International
  - http://english.prescrire.org/en/
- UK Drugs & Therapeutics Bulletin – subscription
  - http://www.dtb.org.uk/
- NPS Radar – Australia
  - www.nps.org.au
- US Agency for Health Research and Quality (AHRQ)
  - www.ahrq.gov
- UK National Institute of Clinical Excellence (NICE)
  - www.nice.org.uk
- The number needed to treat
  - www.nnt.com

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Comments?

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