



BOND UNIVERSITY
MEDICAL PROGRAM

Putting Evidence into Practice

Mieke van Driel

Professor of General Practice

Ghent University, Belgium

Bond University, Queensland, Australia



FACULTEIT GENEESKUNDE EN
GEZONDHEIDSWETENSCHAPPEN

-
- The roots of EBM
 - EBM today
 - Why is EBM important?
 - How to use EBM in patient care?
-



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The roots of EBM



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James Lind
(1716-1794)



Pierre-Charles-Alexandre Louis

(1787-1872)



Pierre Louis

Paris, 1836

FIGURE 2. Duration of disease and number of bleedings in patients who survived, by day of the first bleeding [17]. The original legend is reproduced.

	1	2	3	4	5	6	7	8	9									
10	3	7 3	19 3	19 3	28 2	13 1	24 2	19 2	35 1									
12	2	10 2	29 3	12 2	17 3	16 2	12 4	12 1	11 2									
14	2	12 2	20 2	15 2	40 2	23 3	19 2	18 1	17 2									
			20	22 4	13 2	35 5	18 2	20 3	30 3									
			16 3	12 4	21 2	17 2	15 2	13 2										
			17 4	21 2	13 2		27 2	21 2										
				25 3														
				28 4														
				40 2														
				16 2														
				12 4														
<hr/>																		
	12	2½	10	2½	20	3	20	8	22	2	21	2½	19	2½	17	2	23	2

The figures upon the horizontal line above the columns indicate the day when the first bleeding was performed; the figures on the left in each column mark the duration of the disease; those on the right, the number of bleedings; and those on the horizontal line below, show the mean duration of the disease and the average number of bleedings.

	1	2	3	4	5	6	7	8	9
6	5 18	53 5 65	4 1 57	29 2 19	16 4 58	62 4 20	20 2 68	25 1 40	22 1 50
		12 3 69	16 2 54	29 4 46	8 2 63	10 2 40			
		8 2 65	6 3 30	12 1 85	9 4 24	29 3 24			
		12 1 55	6 4 47	15 3 37					
		17 7 75	47 2 75	17 1 67					
			11 4 45	20 3 22					
<hr/>									
6	5 18	20 3 3.5 66	15 3 51	20 2½ 49	11 3 48	33 3 28	20 2 68	25 1 40	22 1 50

FIGURE 3. Duration of disease, number of bleedings and age in patients who died, by day of the first bleeding [17]. See Figure 1 for explanations.



Look for causalities,

but...

are the inferences correct?
what is the role of chance?



Randomized Controlled Trial - RCT

Comparable groups

Intervention



Outcome

Allocated by chance

Control



Outcome



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EBM today

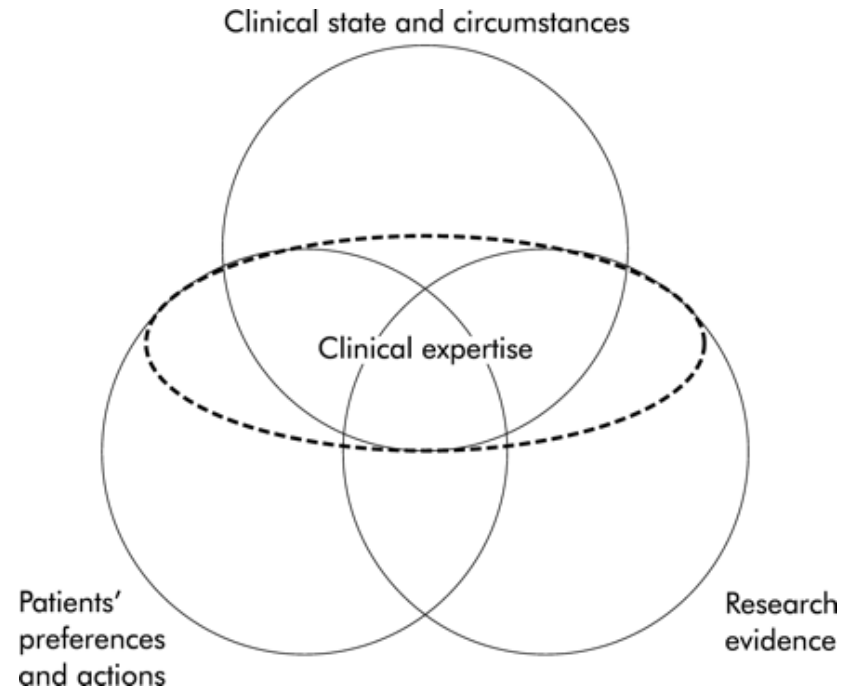


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Evidence-Based Medicine

“Evidence-based medicine is the integration of **best research evidence** with **clinical expertise** and **patient values**”

Sackett & Straus, 2001





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Why is EBM important?



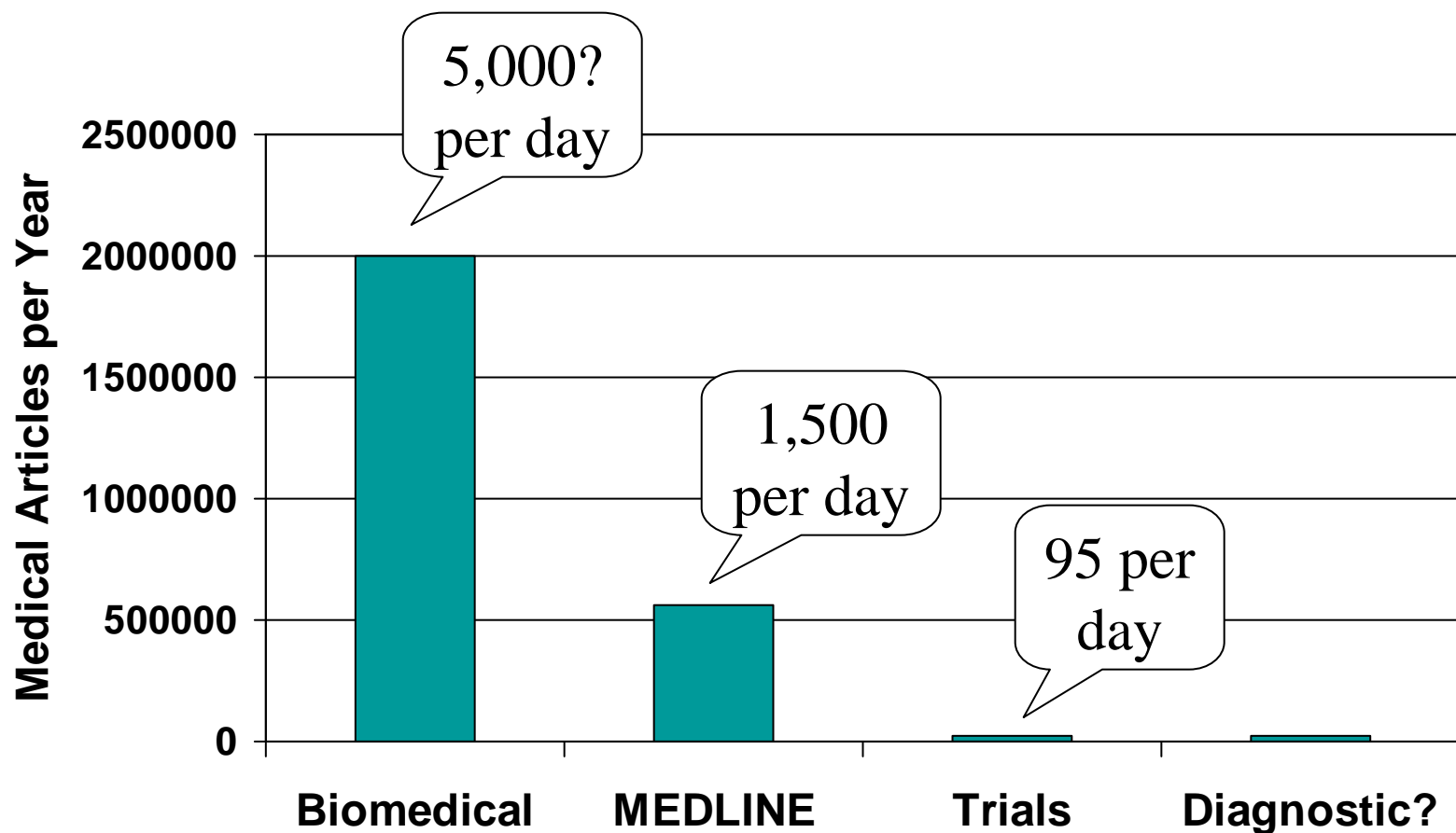
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Why is EBM important?

- Need for valid information daily on Diagnosis, Treatment, Prognosis and Prevention
 - Inadequate traditional sources:
 - ☞ Outdated (Textbooks)
 - ☞ Frequently wrong (Expert opinions)
 - ☞ Ineffective (Didactics/CME)
 - ☞ Too overwhelming in volume and variable in validity (Medical Journals)
-

Rule 31 – Review the World Literature Fortnightly*

*"Kill as Few Patients as Possible" - Oscar London



Why is EBM important?

- Time constraints in clinical practice
 - Primary care doctors would need over 17 hours/day just to review reasonable pertinent material
 - Specialists in one narrow field would need 6+ hrs/week
 - Practicing doctors average around 1-1.5 hrs/wk
 - Relevant information is widely scattered
-

An impossible task to keep up to date?

We are on a slippery slope...

Knowledge
of best
hypertension
care

Shin et al,
CMAJ, 1993

$r = -.54$

$p < 0.001$

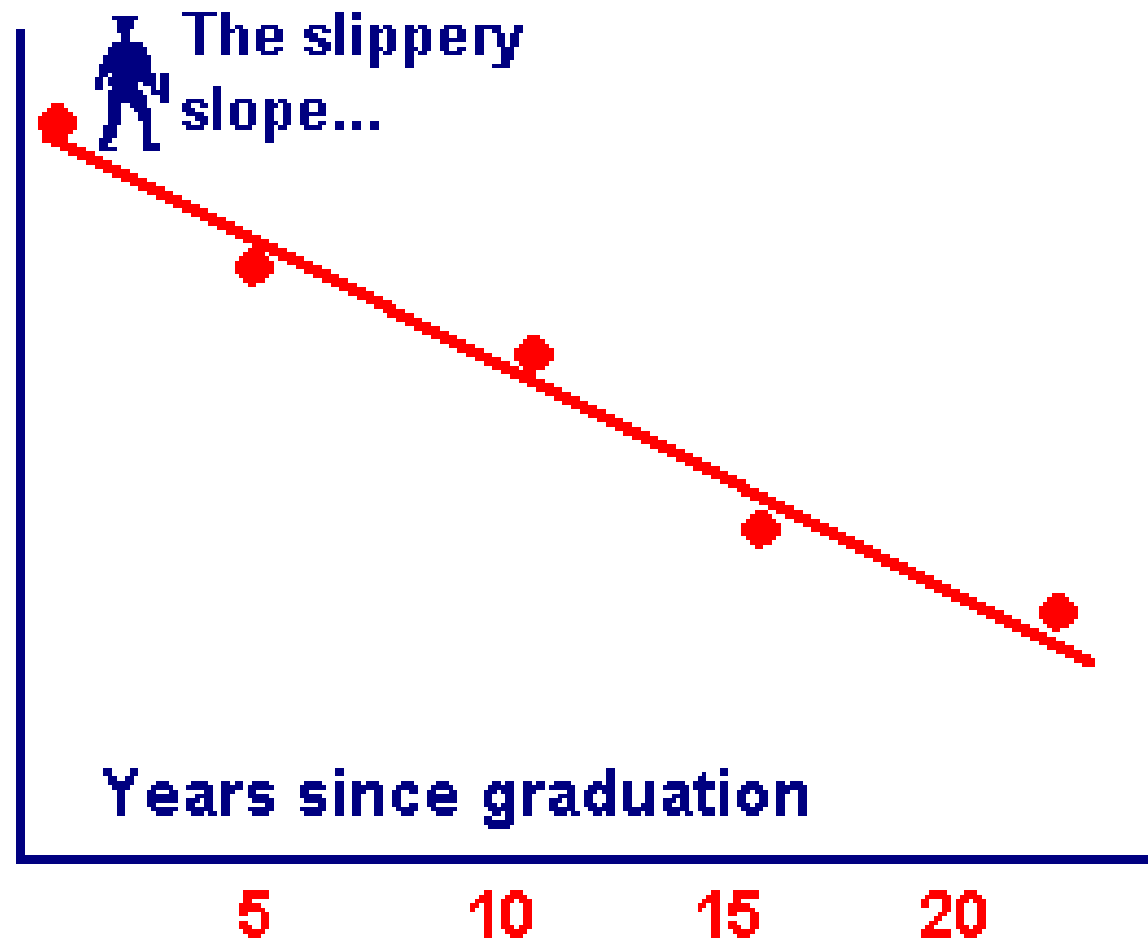
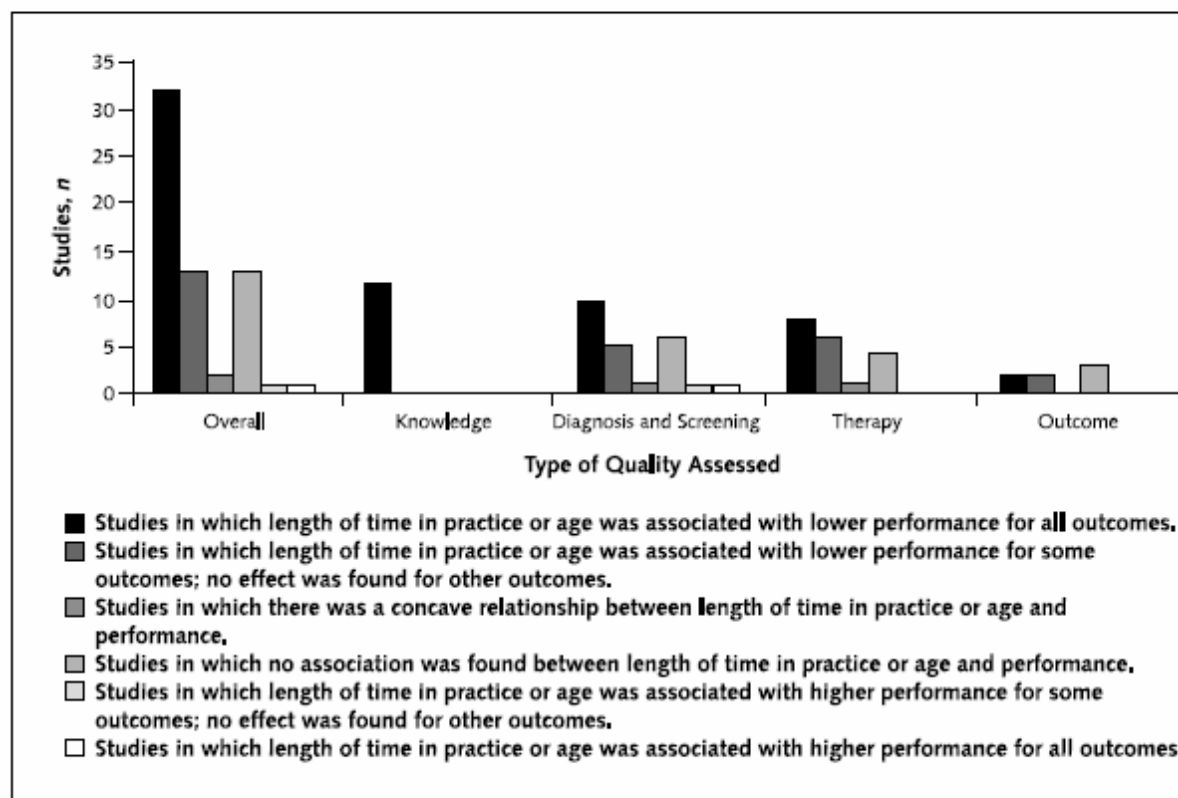


Figure 2. Distribution of study results relating physician age to clinical performance in various domains.



Is EBM the answer?

How does evidence inform us?

Would you use drug X?

- Drug **X** has been studied in preterm delivery
 - Of 7 randomised trials:
 - 5 trials showed no significant difference;
 - 2 showed significant benefit
-

Would you use drug X?

- Drug **X** has been studied in preterm delivery
 - Of 7 randomised trials:
 - 5 trials showed no significant difference;
 - 2 showed significant benefit
 - Drug **X** is corticosteroids
-

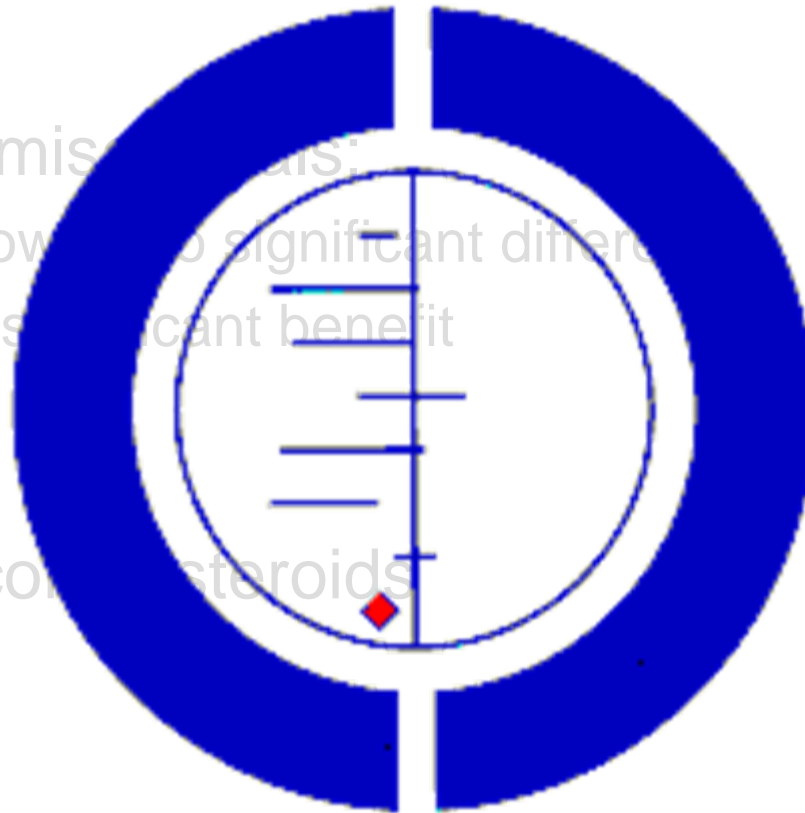
Would you use drug X?

- Drug X has been studied in preterm delivery

- Of 7 randomised trials:

- 5 trials showed no significant difference
- 2 showed significant benefit

- Drug X is compared to steroids



Would you recommend Drug Y?

- Drug **Y** has been studied in trials of myocardial infarction
 - Of 24 randomised trials:
 - 4 showed a significant benefit;
 - 20 showed no significant benefit
-

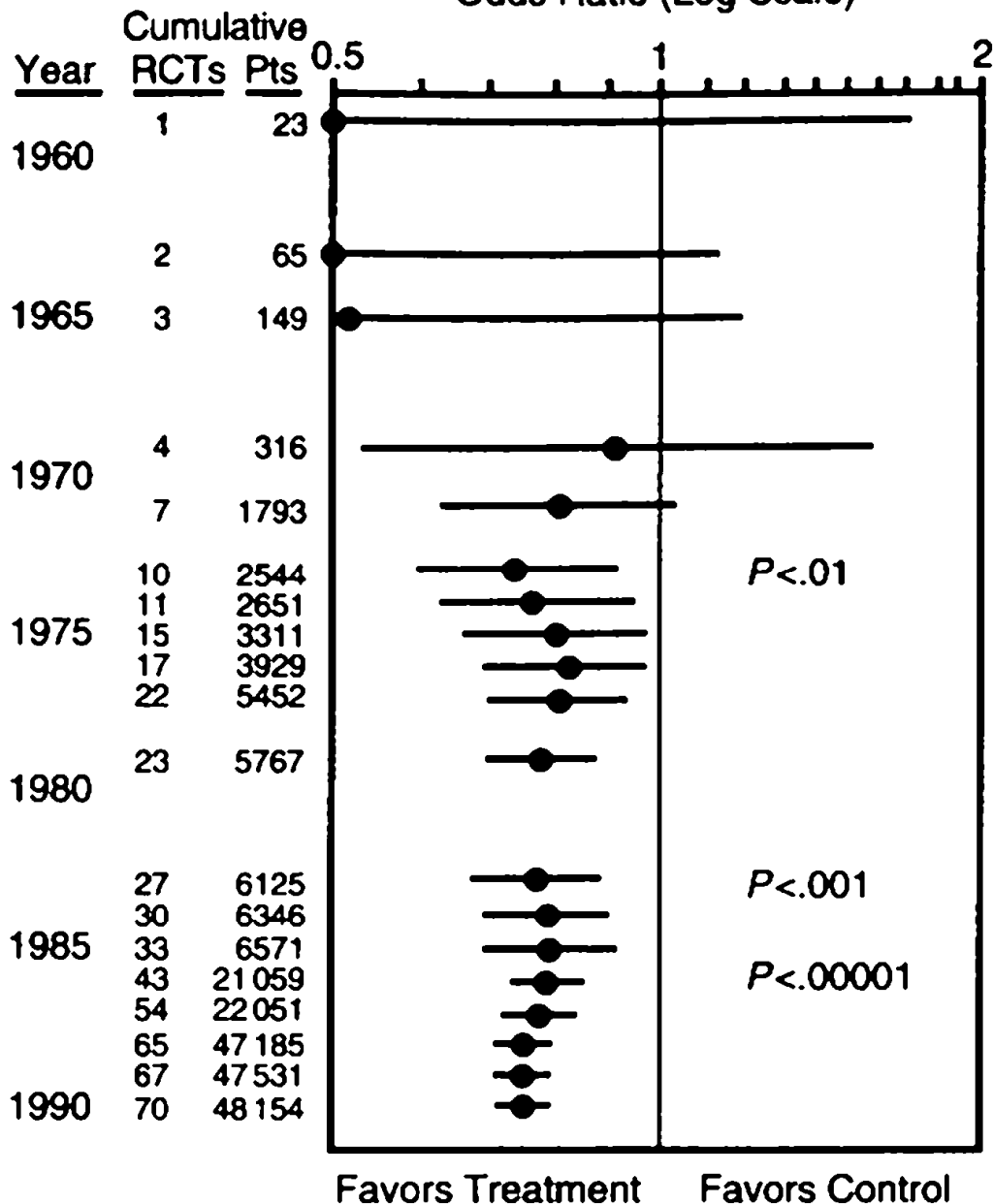
Would you recommend Drug Y?

- Drug **Y** has been studied in trials of myocardial infarction
 - Of 24 randomised trials:
 - 4 showed a significant benefit;
 - 20 showed no significant benefit
 - Drug **Y** is streptokinase (circa 1982)
-

A. Thrombolytic Therapy

Odds Ratio (Log Scale)

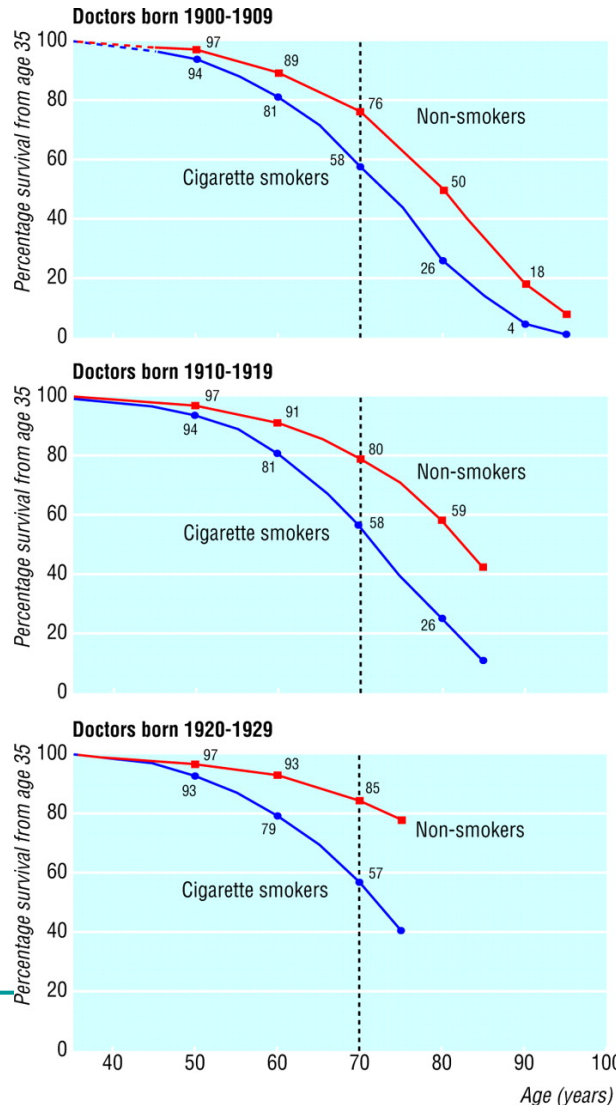
Textbook/Review Recommendations



	Routine	Specific	Rare/Never	Experimental	Not Mentioned
					21
					5
				1	10
				1	2
				2	8
					7
					8
		1			12
M		1		8	4
M		1		7	3
M		1		7	3
M	5	2		2	1
M	15	8			1
M	6	1			

Smoking and lung cancer / CV Risk

Men born in 1900-1930 who smoked only cigarettes and continued smoking died on average about 10 years younger than lifelong non-smokers.

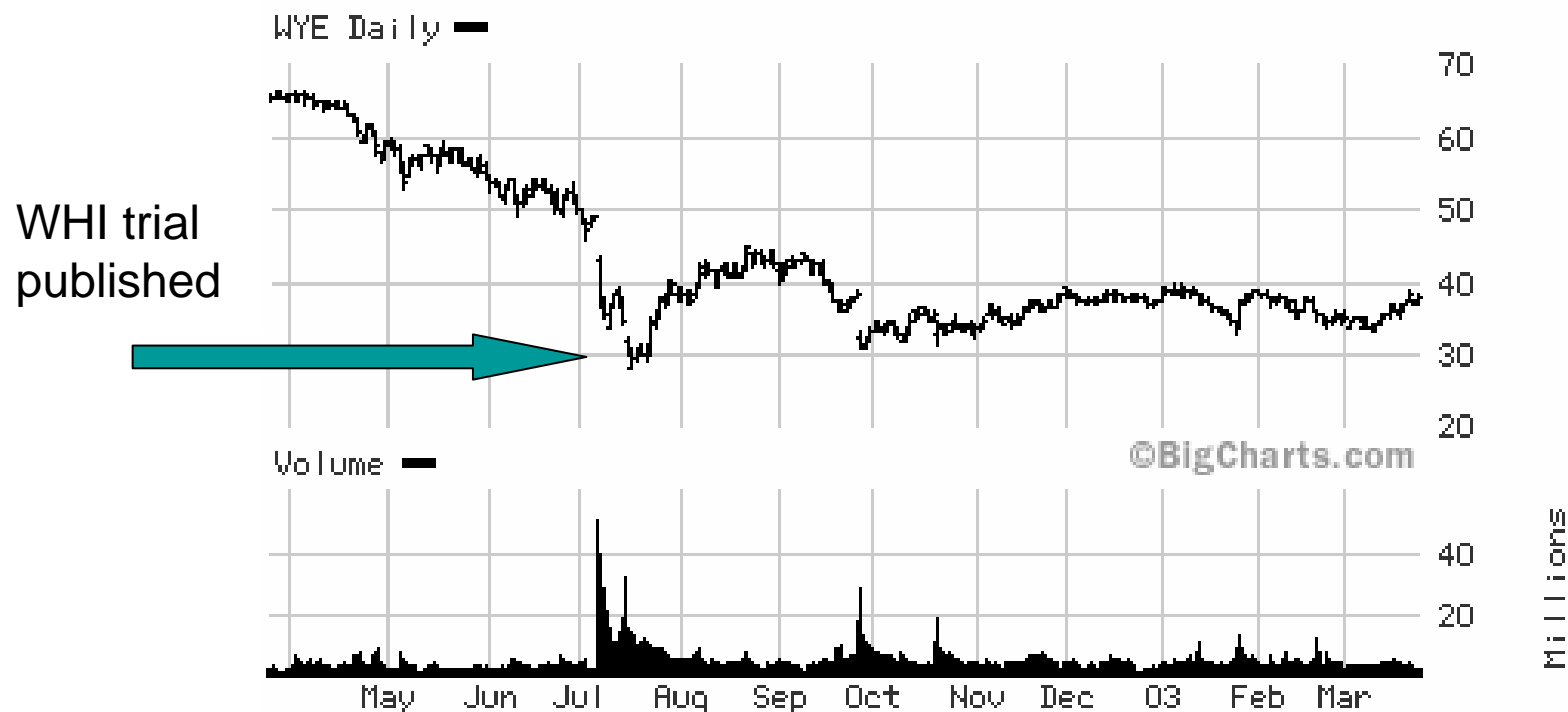


Hormone Replacement Therapy

- **1991**: *Cohort study* showed relationship between use of HRT and CV disease and mortality
 - *World wide use of HRT promoted*
 - **1995**: *PEPI trial* shows effect on CV risk factors (surrogate end points)
 - **2002**: *WHI trial* shows increased risk of cancer and no proven CV benefit
-

Wyeth stock chart

25 March 2003



EDITORIAL

Postmenopausal Hormone Replacement Therapy: How Could We Have Been So Wrong?

While the public is hungry for medical discoveries that will immediately change clinical practice, evidence typically accumulates piecemeal and practice changes

abling vasomotor disturbances without it. An ongoing arm of the WHI may find that the balance of benefits and harms is different in women taking unopposed estrogen

Christine Laine, MD, MPH
Senior Deputy Editor

SSRI dangers for children 'suppressed'

Press Association

[Society Guardian](#), Friday April 23 2004 [Article history](#)

Drug companies have deliberately suppressed evidence that many antidepressants are unsuitable or even dangerous for children, according to psychiatrists and child health experts.

Rofecoxib withdrawal sparks criticism of FDA and overaggressive marketing of coxibs

Zosia Chustecka

Oct 4, 2004

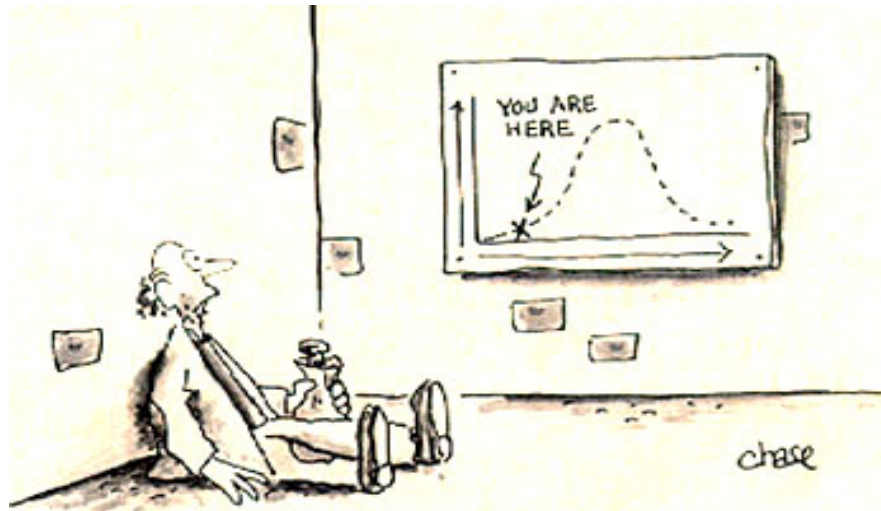
The withdrawal of **rofecoxib** (Vioxx, Merck & Co) has sparked questions about the way that the FDA handled the issue as well as the way this group of drugs was marketed.

Information from Industry

Explore an agent offering persistent pain relief with extended benefits. Learn about around-the-clock treatment with potential to reduce the number of breakthrough pain episodes and a demonstrated improvement in pain related sleep parameters. [Read more](#)

The Epidemiology of Ignorance in Health Care - *P. Glasziou*

What do we know about what we know?

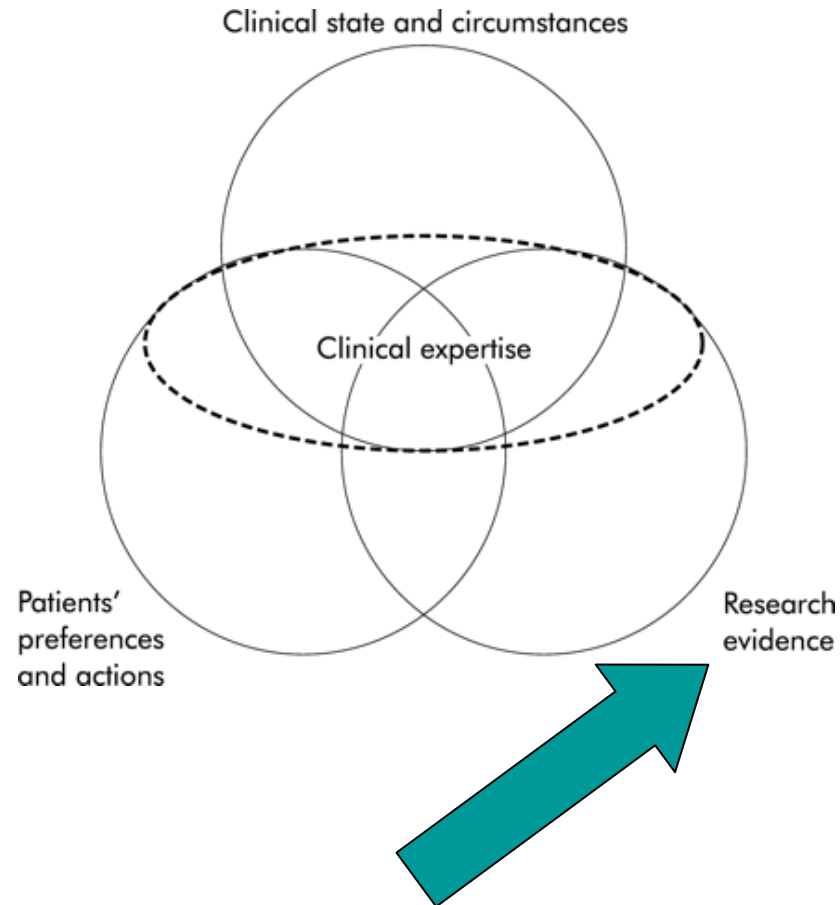




How to use EBM in patient care

“Evidence-Based Practice”

Evidence-Based Medicine



Steps of EBP: the four 'A's

1. **A**sk ...an answerable **Q**uestion
2. **A**ccess ...literature for the **A**nswer
3. **A**ppraise ...the quality of the **A**nswer
4. **A**pply ...the **A**nswer to your specific environment/patient

Questions and Answers...

Step 1 of the four 'A's

- **Ask** ...an answerable **Question**
- Access ...literature for the Answer
- Appraise ...the quality of the Answer
- Apply ...the Answer to your
specific environment/patient

Set out the **Question** in a way that is answerable

Another case of
"economy" class
syndrome.
Shouldn't everyone
take an aspirin and
wear stockings?

© 1992, 1994 H. L. SCHWADRON



What do you think about "flight socks" ?

What do you think about “flight socks” ?

What do you think about “flight socks” ?

PICO:

Population/patient

Intervention

Control

Outcome



What do you think about “flight socks” ?

PICO:

Population/patient

Intervention

Control

Outcome

P people on long haul flights

I compression stockings

C no stockings

O incidence of DVT

What do you think about “flight socks” ?

PICO:

Population/patient

Intervention

Control

Outcome

P people on long haul flights

I compression stockings

C no stockings

O incidence of DVT

“Do flight socks compared with no stockings reduce the incidence of DVT after long haul flights?”

Step 2 of the four 'A's

- Ask ...an answerable Question
 - **Access** ...literature for the **Answer**
 - Appraise ...the quality of the Answer
 - Apply ...the Answer to your
specific environment/patient
-

Examples



Systems

Computerized decision support system (CDSS)

Ideal, still theoretical, links to best research evidence, always updated, drills down

Synopses

Evidence-based journal abstracts

Provide enough information to support a clinical action

Syntheses

Cochrane reviews

More details, summaries based on exhaustive search for evidence, explicit scientific reviews, and systematic assembly of evidence

Studies

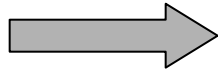
Original published articles in journals

When all above fails, more recent or not reviewed topics

Examples



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When all above fails, more recent or not reviewed topics

Updated
and expanded
every six months

8 ISSUE

DECEMBER 2002

clinical evidence

The international source of the
best available evidence for
effective health care

www.clinicalevidence.com

BMJ
Publishing
Group

<http://clinicalevidence.bmj.com/>

BMJ Clinical Evidence

[Sections](#)

[Full review list](#)

Summary

Post-thrombotic syndrome

Compared with no treatment, Compression stockings reduce post-thrombotic syndrome at 2 years compared with no treatment ([high-quality evidence](#)).

ACP Journal Club

March/April 1997
Volume 126 • Number 2

Linking Research to Practice in Internal Medicine

Published
Bimonthly
by the
American College
of Physicians

■ THERAPEUTICS

Lowering LDL cholesterol levels reduced fatal coronary events in patients with acute MI and average cholesterol levels	29
Amlodipine did not increase morbidity or mortality rates in severe heart failure	30
Meta-analysis: Mortality is reduced when fibrinolytic therapy is started soon after the onset of MI symptoms	31
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■ PROGNOSIS

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LDL particle size was smaller in CAD, but other lipid parameters were stronger predictors of CAD	48
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Low cholesterol levels were associated with suicide in men	50

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Low-molecular-weight heparin was cost-effective for perioperative prevention of DVT	51
Cost-effectiveness of pravastatin in the secondary prevention of CAD in men varied with the risk profile of the patient	52
Intensive therapy extended life and was cost-effective for IDDM	53

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Vol. 2 No. 5 pp. 129-160

SEPTEMBER/OCTOBER 1997

Evidence-Based Medicine



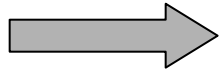
American College
of Physicians

BMJ
Publishing
Group

Examples



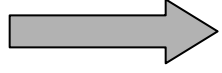
Computerized decision support system (CDSS)



Ideal, still theoretical, links to best research evidence, always updated, drills down

Synopses

Evidence-based journal abstracts



Provide enough information to support a clinical action

Syntheses

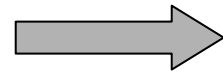
Cochrane reviews



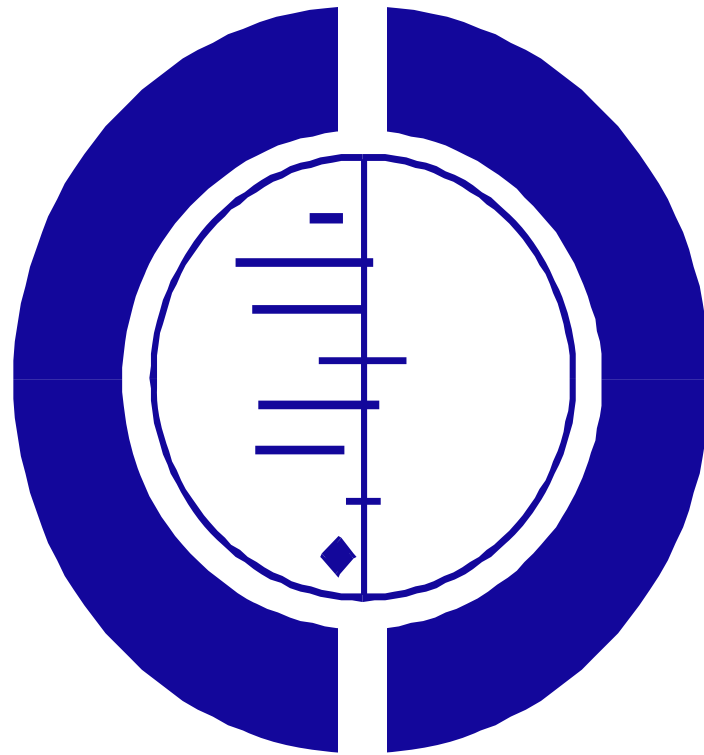
More details, summaries based on exhaustive search for evidence, explicit scientific reviews, and systematic assembly of evidence

Studies

Original published articles in journals



When all above fails, more recent or not reviewed topics



www.theCochraneLibrary.com

Cochrane Systematic Reviews (5412)

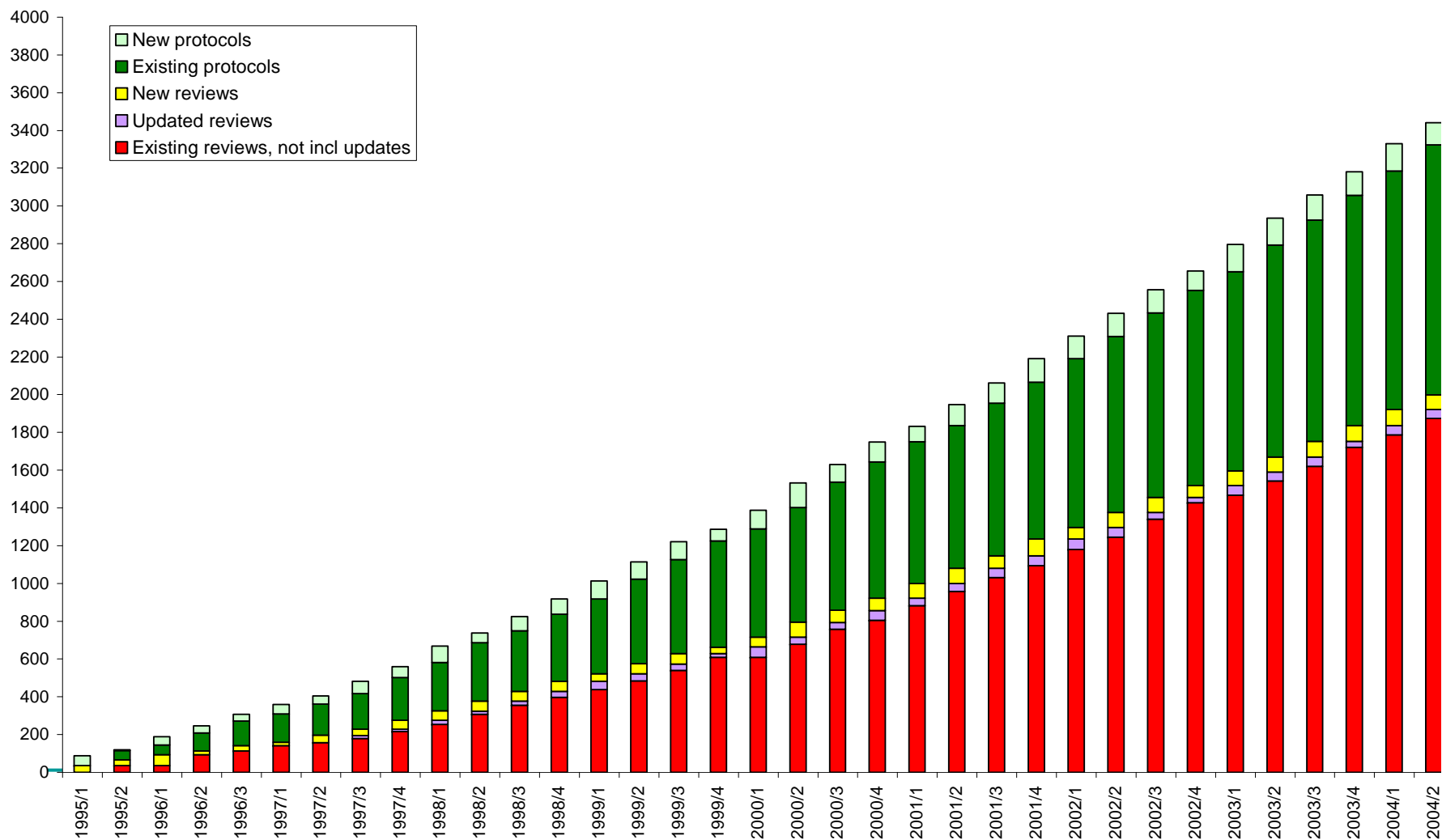
Database of Abstracts of Reviews of Effectiveness (8349)

Registry of Randomised Controlled Trials (540,156)

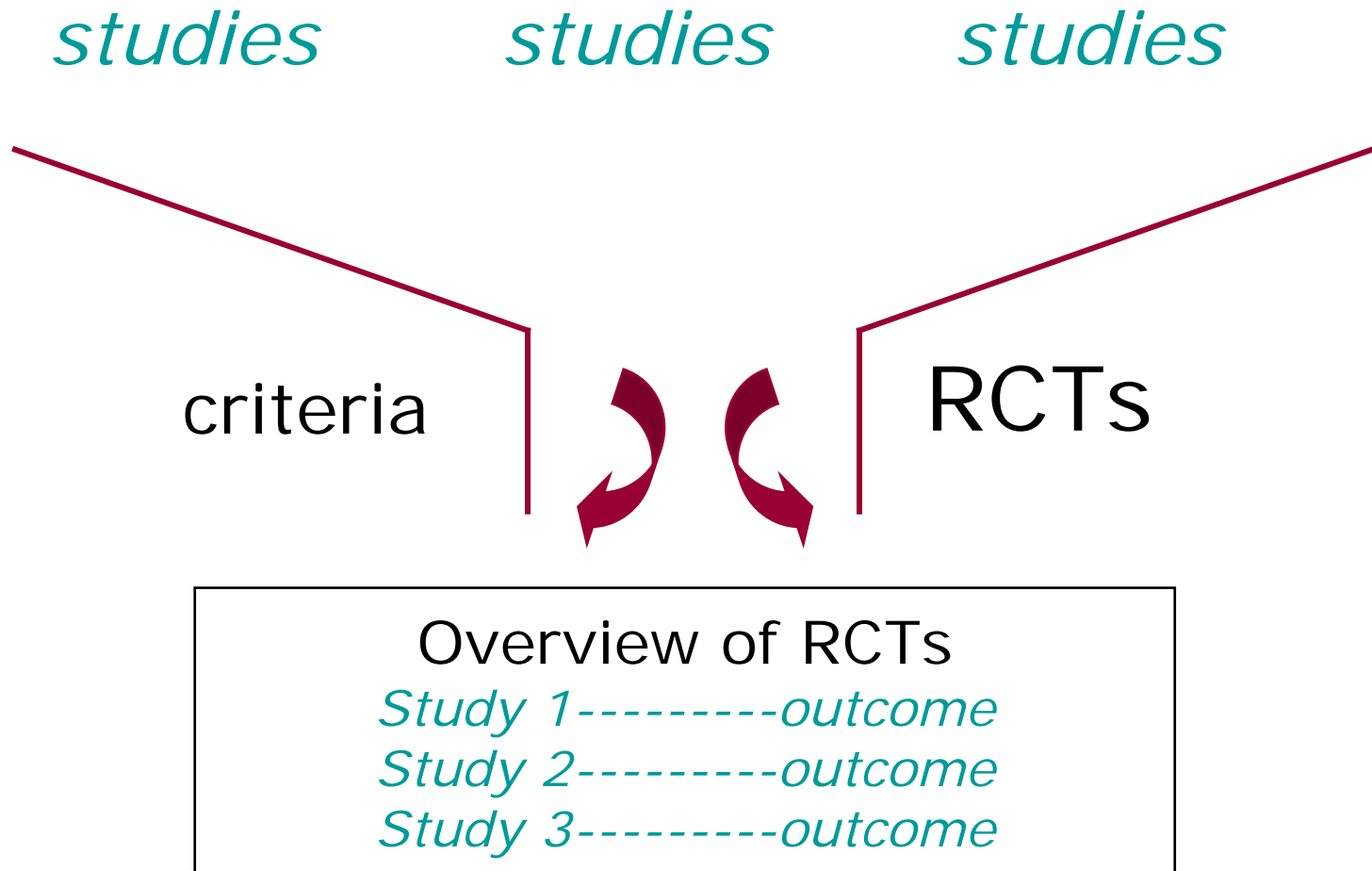
Systematic Reviews - mostly for therapy

Reviews and protocols for reviews on
The Cochrane Database of Systematic Reviews
Issue 1/2005

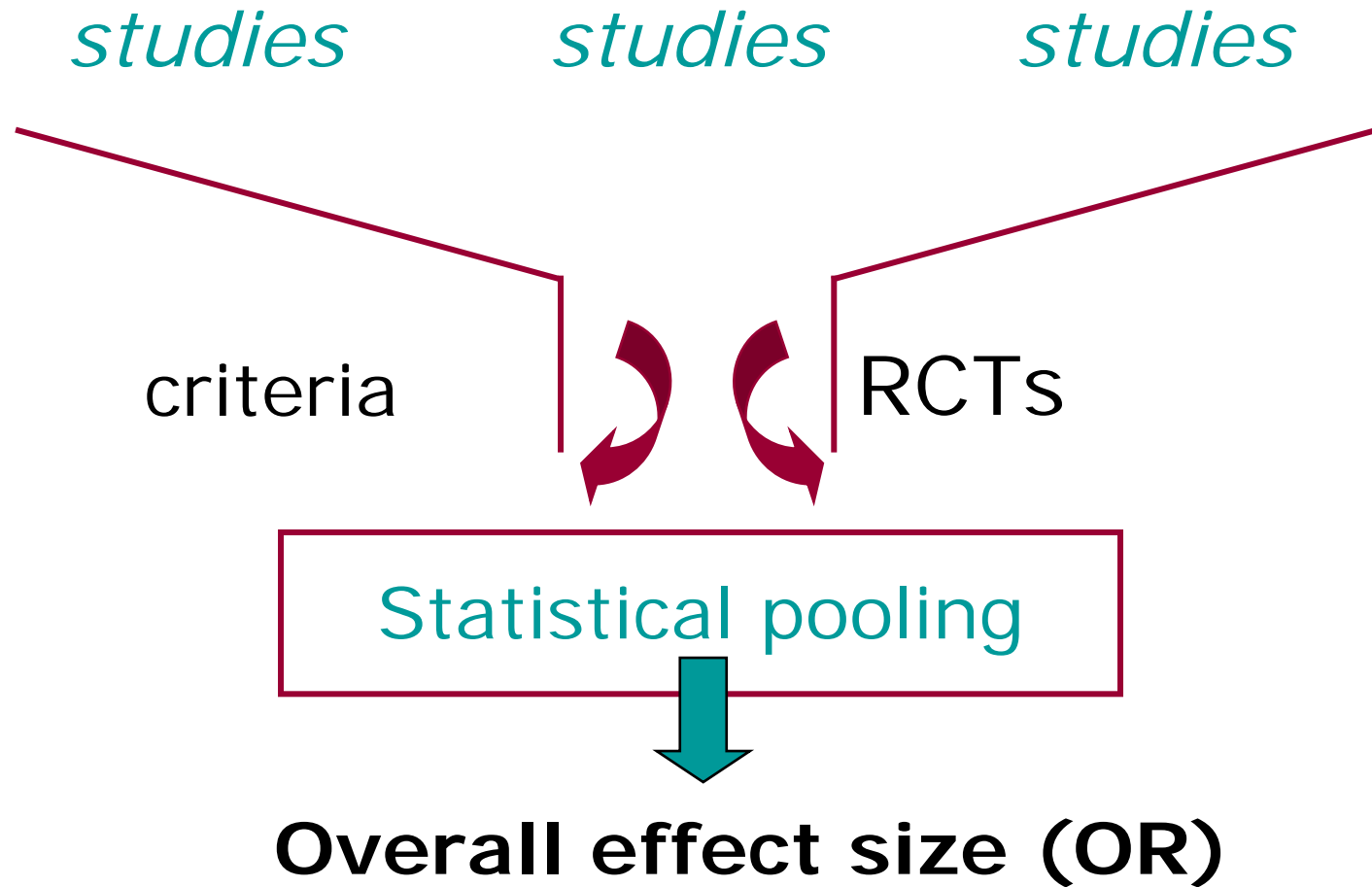
Alderson, 2005



Systematic Review



Meta-analysis



Compression stockings for preventing deep vein thrombosis in airline passengers

M Clarke, S Hopewell, E Juszczak, A Eisinga, M Kjeldstrøm

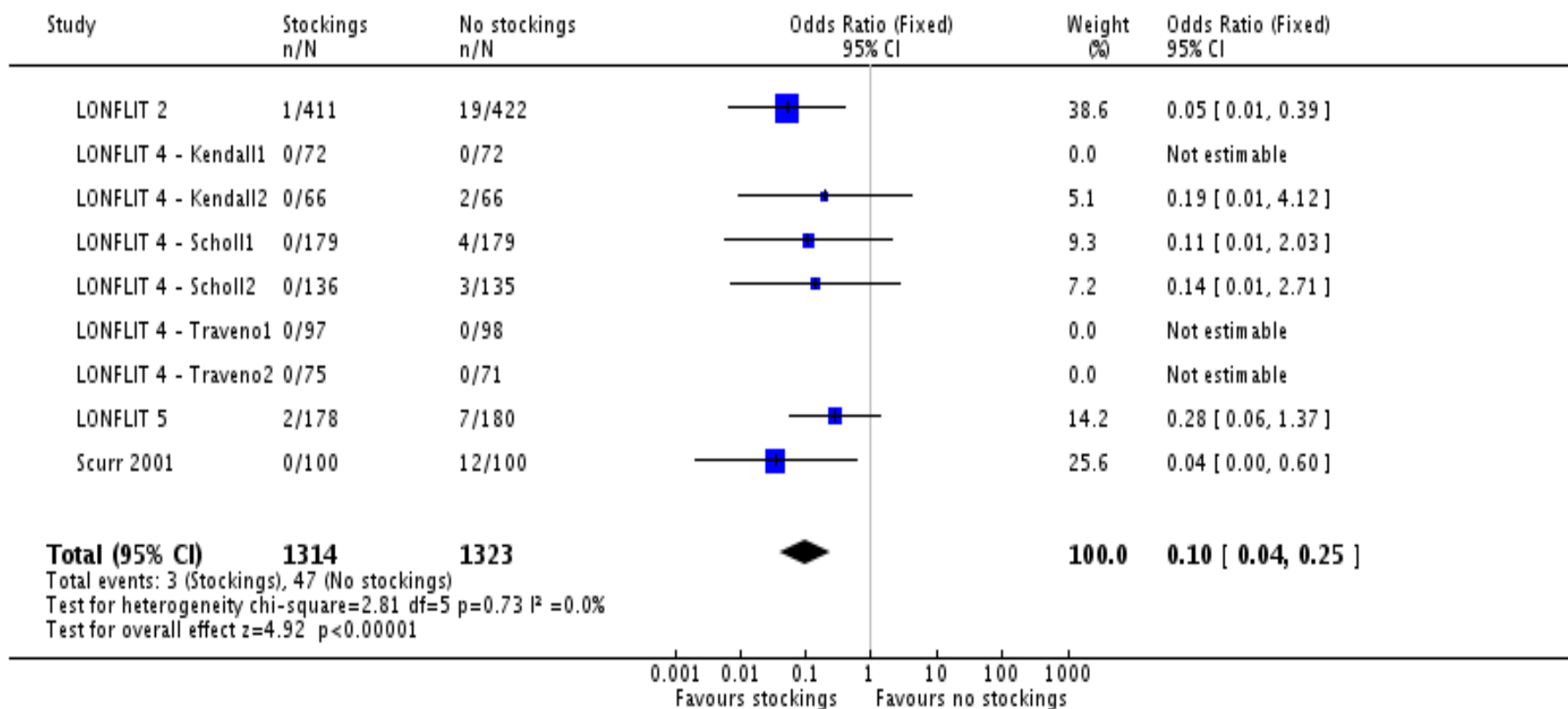
Cochrane Database of Systematic Reviews 2008 Issue 3 (Status: *Unchanged*)

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Review: Compression stockings for preventing deep vein thrombosis in airline passengers

Comparison: 01 Wearing stockings versus not wearing stockings

Outcome: 01 Symptomless deep vein thrombosis





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Critical appraisal



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Step 3 of the four 'A's

- Ask ...an answerable Question
 - Access ...literature for the Answer
 - **Appraise** ...the quality of the Answer
 - Apply ...the Answer to your
specific environment/patient
-

Critical appraisal – assessing the risk of **BIAS**

1. What?
 2. Who?
 3. How? - study design
 4. Result?
 5. Risk/Cost-Benefit for **my patient?**
-

1. What is studied?

- Is the research question relevant for me/my patient?

2. Who is studied?

- Population – “mice or men”
 - Setting
 - In- and exclusion criteria
 - Age and sex
 - Comorbidity
 - Groups comparable
-

3. How is the study conducted?

- Study design – observational vs experimental
 - Method
 - if RCT
 - Randomisation – *allocation concealment*
 - Blinding: *single-double-triple blind*
 - Placebo
 - Outcome measurement
 - Intention to treat
-

Study Pyramid for Clinical Research



4. Results

- How are the results reported?
 - “Hard” (*e.g. morbidity, mortality*) vs “surrogate” (*e.g. Blood pressure, serum cholesterol*) outcomes
 - Relative vs absolute risks – NNT
 - $RR = R_i/R_c$
 - $ARD = R_i - R_c$
 - $RRR = (R_i - R_c)/R_c$
 - $NNT = 1/ARD$
 - Estimate of accuracy – 95% CI; p-value
-

5. What is the cost-benefit for my patient?

- If the results are valid, is it good for my patient?
 - Access
 - Availability
 - Acceptability
 - Benefit-harm balance
 - Informed choice for each individual patient
-

-
- Exercise with critical appraisal

Critical appraisal checklist

1. **What?** – research question relevant?
 2. **Who?**
 1. patients in PHC
 2. in/exclusion
 3. comparable groups
 3. **How?** – research method
 1. Randomisation
 2. Blinding
 3. Placebo
 4. Outcome measurement
 5. Intention to treat
 4. **Results**
 1. hard/surrogate outcome – risk measurement
 2. accuracy (95%CI; p-value)
 5. **Cost benefit** for my patient
-

Step 4 of the four 'A's

- Ask ...an answerable Question
 - Access ...literature for the Answer
 - Appraise ...the quality of the Answer
 - **Apply** ...the Answer to your
specific environment/patient
-

Would you use the vaccine to prevent
OMA in children?

So... Why EBM?

- Answer questions about patients when we need it
 - Keep up to date
 - Better informed doctors and patients
 - Better patient care...
-

EBM

“more certain uncertainty”

“more uncertain certainty”

(Richards, BMJ 1997)
