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Evidence-Based Practice
Nov 2015

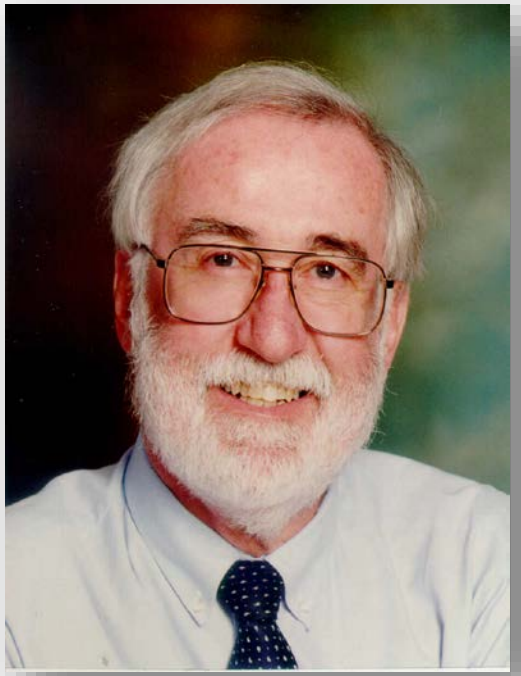
Roya Safari
Assistant Professor in Epidemiology

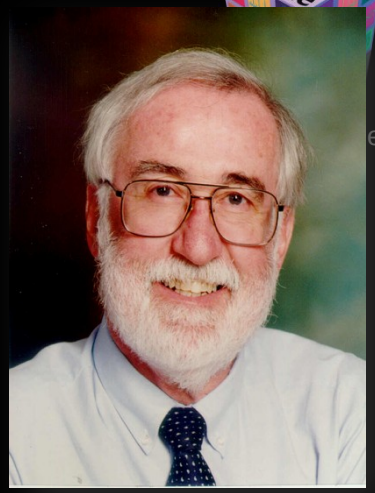
Professor Carl Heneghan
University of Oxford
Director CEBM


I am here because?
•I wanted 3 days of work
•Formulate an answerable question

What is Evidence-Based Medicine?

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





et

http://www.bmj.com/content/312/7023/71

Patient values & preferences

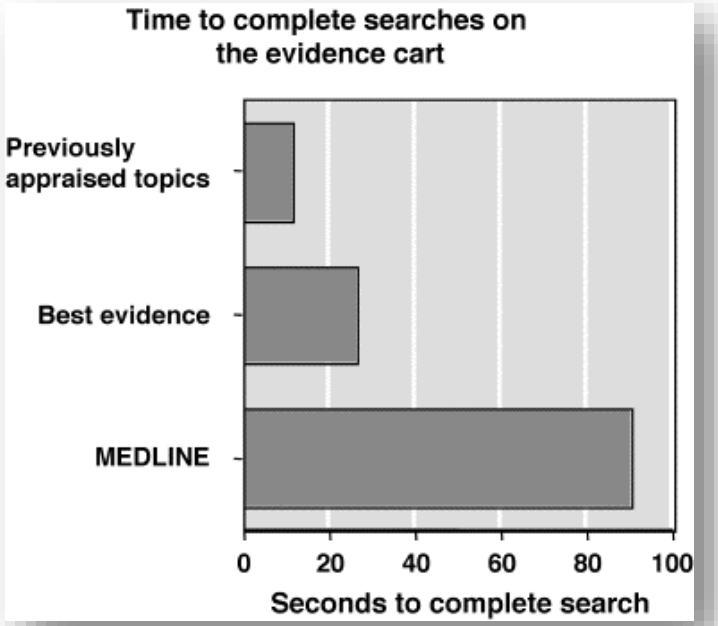
Improved patient outcomes

Best available evidence

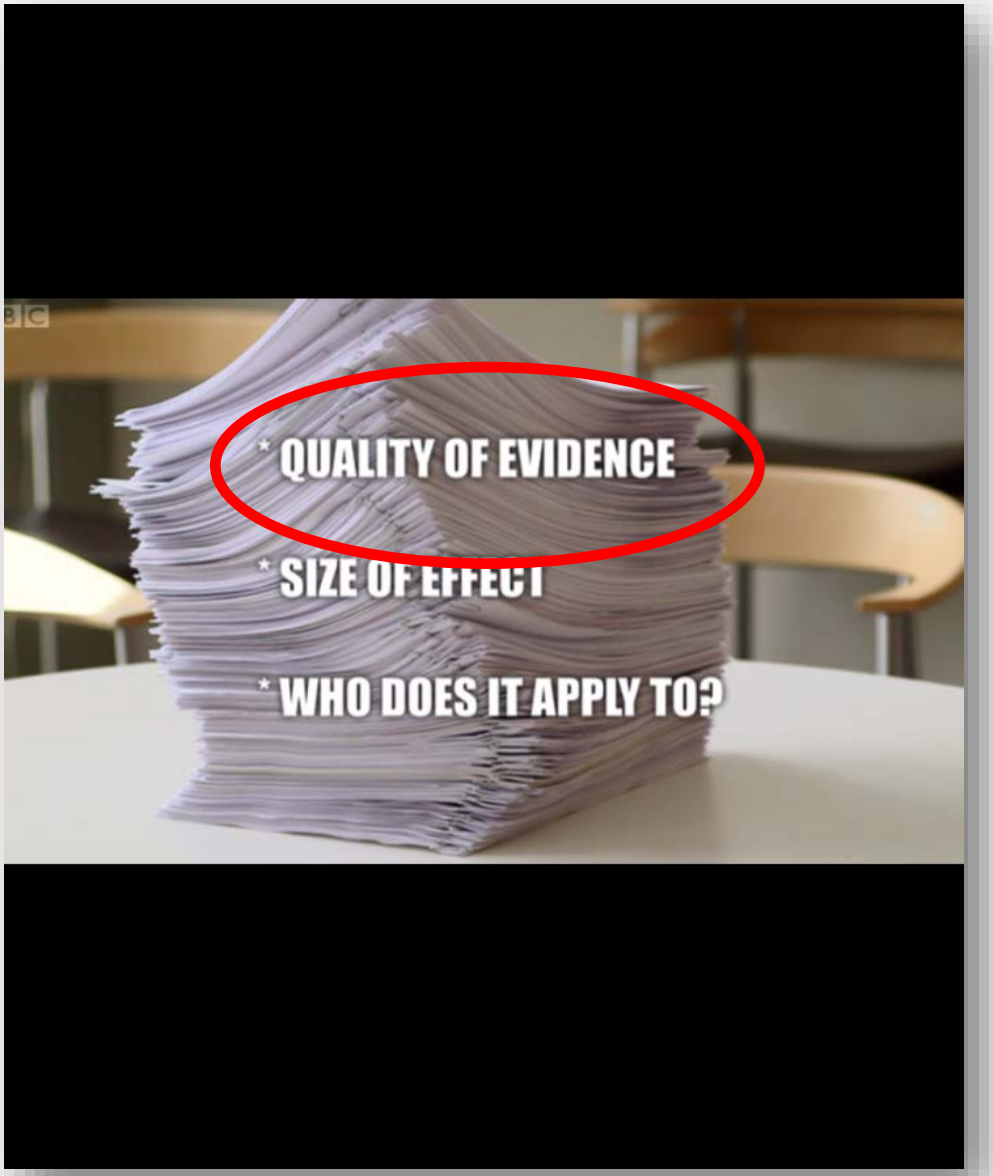
Clinical expertise & judgment

“Just in Time” learning
The EBM Alternative Approach

- Shift focus to current patient problems (“just in time” education)
  - Relevant to YOUR practice
  - Memorable
  - Up to date
- Learn to obtain best current answers



Develop strategies to assess the quality of evidence for health claims, effectiveness and applicability.



• Pharma Blog » 2010 » September » 16

Do You Know Who Frances Kelsey Is?

By Ed Silverman // September 16th, 2010 // 12:35 pm 6 Comments

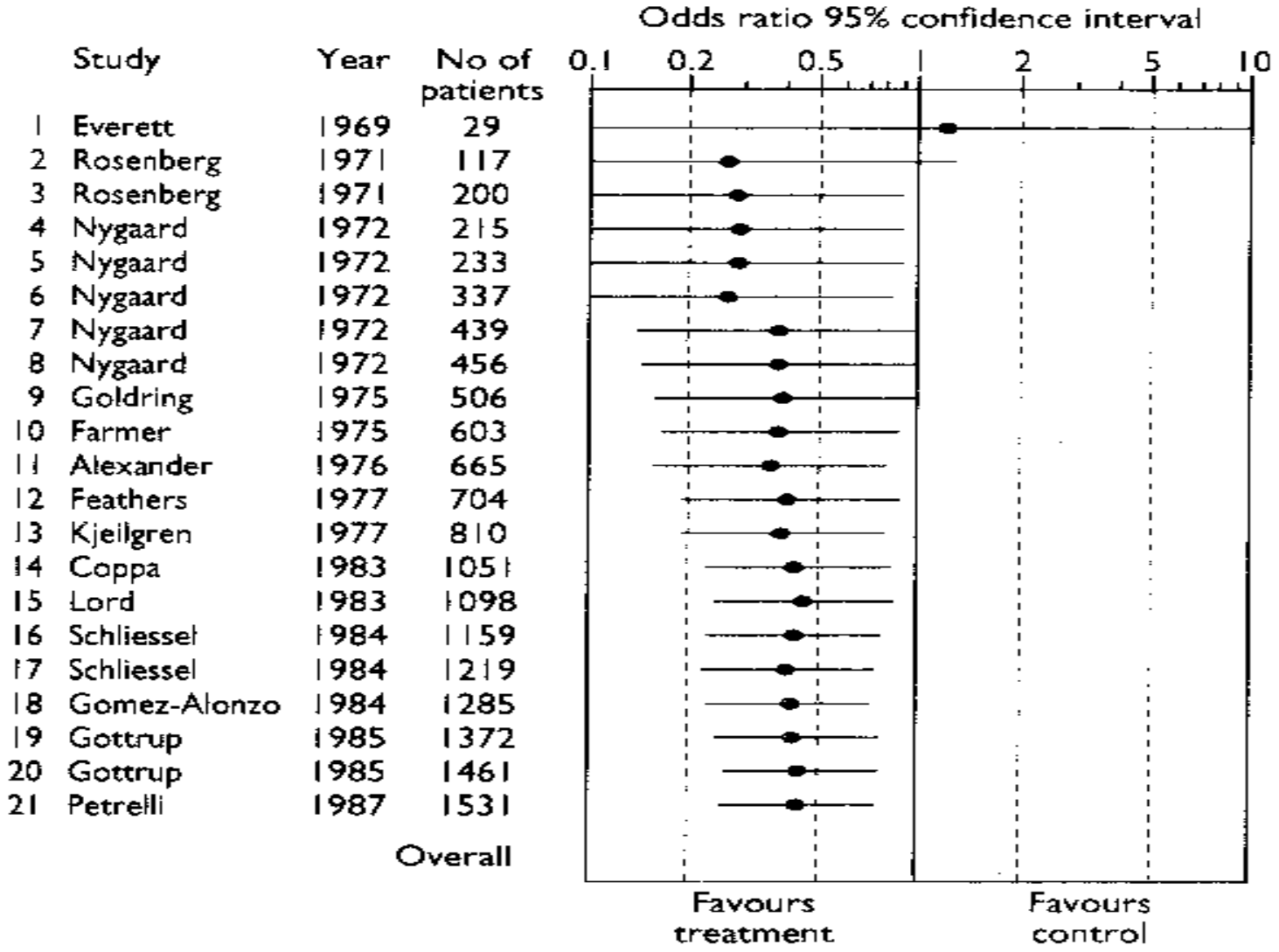
The odds are that you don't, but her actions a half-century ago helped transform the way prescription drugs are tested and approved. Kelsey, you see, was a new FDA employee in 1960, when she was assigned to review Kevadon, which was the brand name for thalidomide. The drug caused severe birth defects in thousands of babies born overseas after being prescribed to help women sleep or manage morning sickness. But babies often had limbless arms, malformed legs or extra appendages.

A physician and pharmacologist, Kelsey questioned its safety. "It just came with so many extravagant claims that I didn't believe," Kelsey, now 96, tells The Washington Post. Her decision set in motion a lot of intrigue as the manufacturer, Merrell, pushed back by complaining about her to the FDA. But kelsey held her ground and after the scandal became known, President John Kennedy gave her the Federal Civilian Service award.

Congress, meanwhile, amended the Food, Drug & Cosmetic Act to require safety and effectiveness testing and informed consent in clinical trials. What did informed consent have to do with it? As the paper notes, Merrell gave the drug to more than 1,000 US docs to distribute to 20,000 patients as part of a so-called investigational trial, but some patients were not informed they were participating in a trial. The upshot - about 40 babies in US were born with deformities.

Would any of you have agreed to participate in a placebo controlled trial of prophylactic antibiotics for colorectal surgery after 1975?

Reduction of perioperative deaths by antibiotic prophylaxis for colorectal surgery

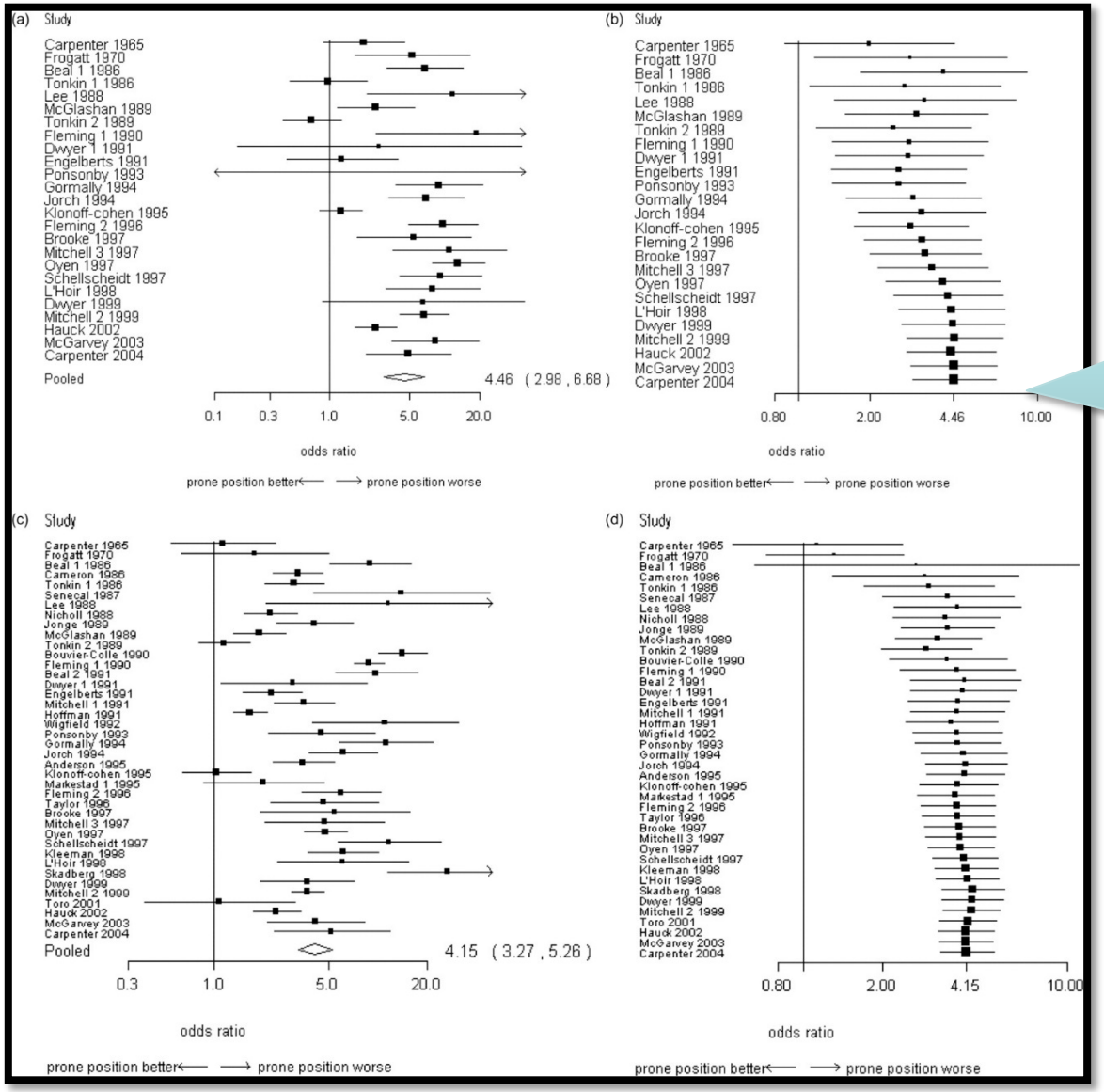


	Study	Year	No of patients
1	Everett	1969	29
2	Rosenberg	1971	117
3	Rosenberg	1971	200
4	Nygaard	1972	215
5	Nygaard	1972	233
6	Nygaard	1972	337
7	Nygaard	1972	439
8	Nygaard	1972	456
9	Goldring	1975	506
10	Farmer	1975	603
11	Alexander	1976	665
12	Feathers	1977	704
13	Kjellgren	1977	810
14	Coppa	1983	1051
15	Lord	1983	1098
16	Schliessel	1984	1159
17	Schliessel	1984	1219
18	Gomez-Alonzo	1984	1285
19	Gottrup	1985	1372
20	Gottrup	1985	1461
21	Petrelli	1987	1531
	Overall		

Would you ever have put babies to sleep on their tummies?

Expert opinion

Baby and Child Care" has actually sold more that 50 million copies, only outmatched in sales by the Bible

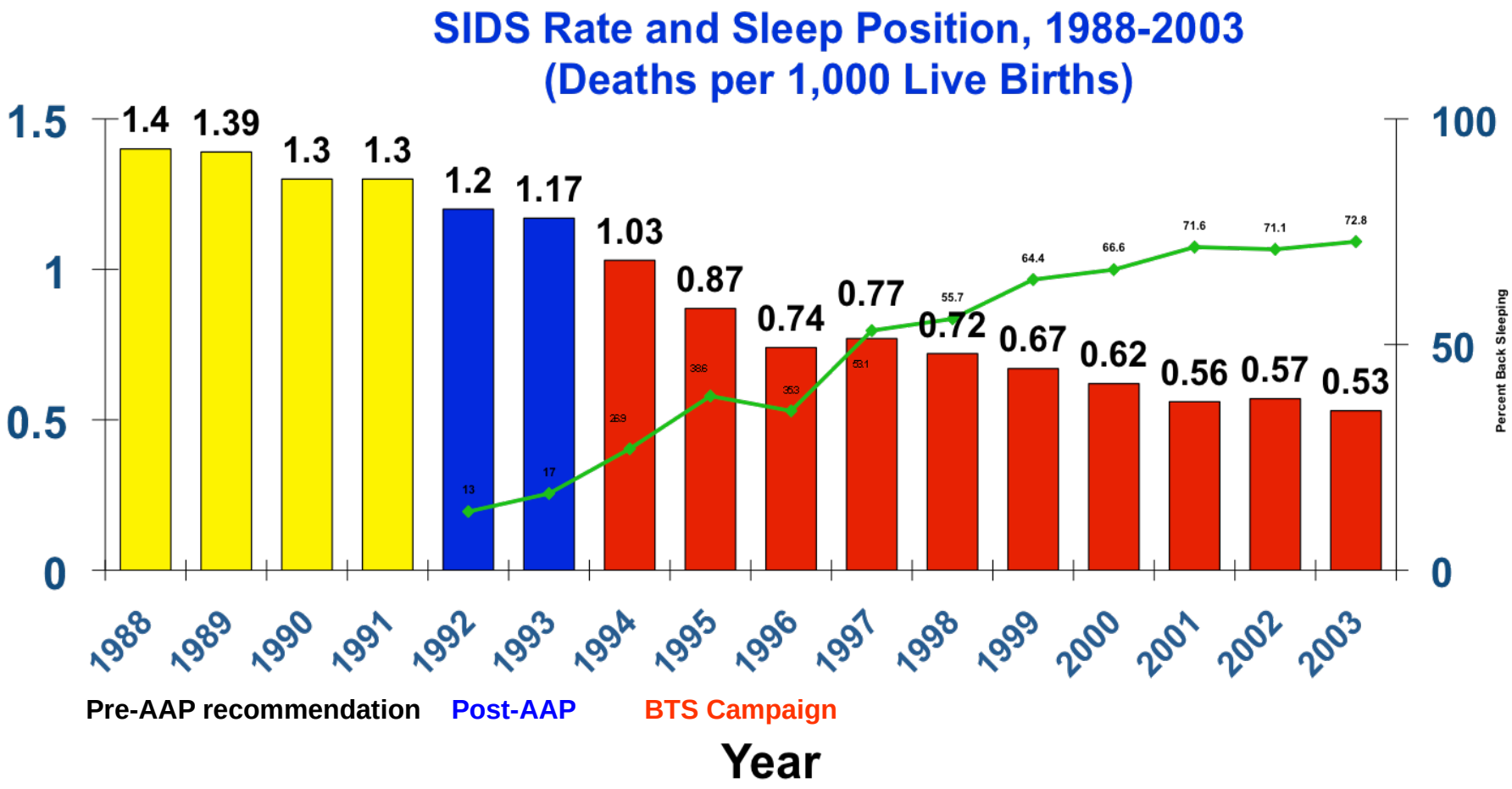


Front vs. back

Over four fold increase risk of sudden infant death syndrome

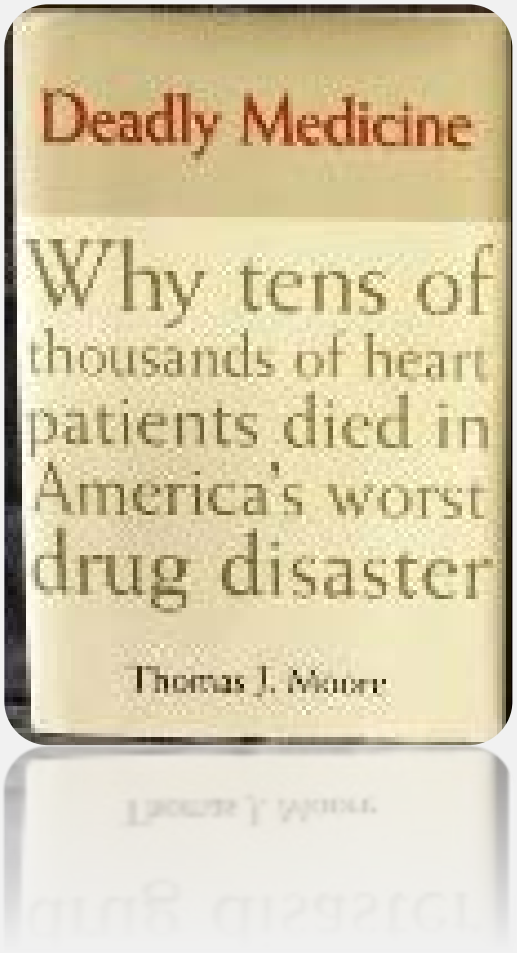
front vs. non-front

Ruth Gilbert et al. Int. J. Epidemiol. 2005;34:874-887



Sleep Position Source: NICHD Household Survey
SIDS Rate Source: National Center for Health Statistics, CDC

Why do we need RANDOMIZED CONTROLLED TRIALS ?



In the early 1980s newly introduced antiarrhythmics were found to be highly successful at suppressing arrhythmias.

Not until a RCT was performed was it realized that, although these drugs suppressed arrhythmias, they actually increased mortality.

The CAST trial revealed Excess mortality of 56/1000.

By the time the results of this trial were published, at least 100,000 such patients had been taking these drugs.

Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial

*The DREAM (Diabetes REduction Assessment with ramipril and rosiglitazone Medication) Trial Investigators**

Published Online
September 15, 2006
DOI:10.1016/S0140-6736(06)69420-8

*Group members are listed at the end of the report

Correspondence to:
DREAM Project Office, Population Health Research Institute, 237 Barton Street East, 2nd Floor, Hamilton, Ontario L8L 2X2, Canada
dream@cardio.on.ca

Summary

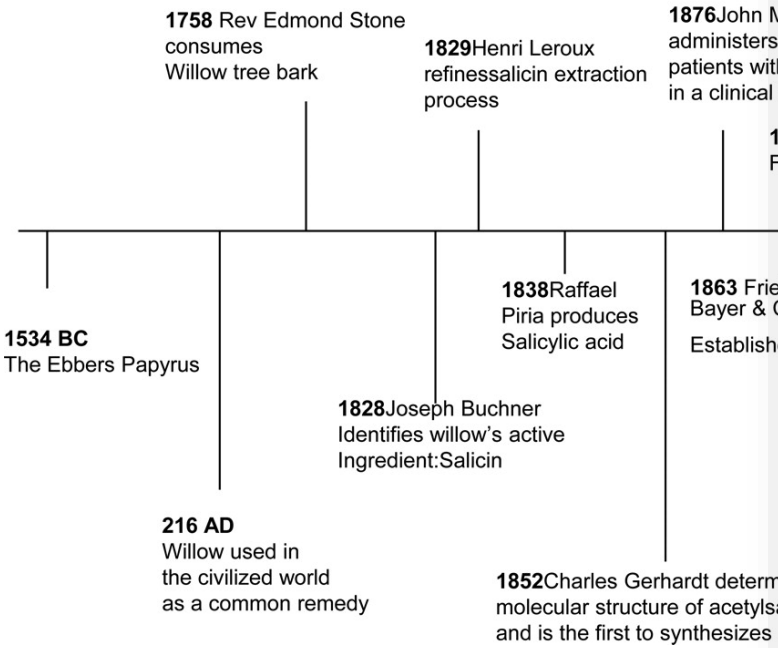
Background Rosiglitazone is a thiazolidinedione that reduces insulin resistance and might preserve insulin secretion. The aim of this study was to assess prospectively the drug's ability to prevent type 2 diabetes in individuals at high risk of developing the condition.

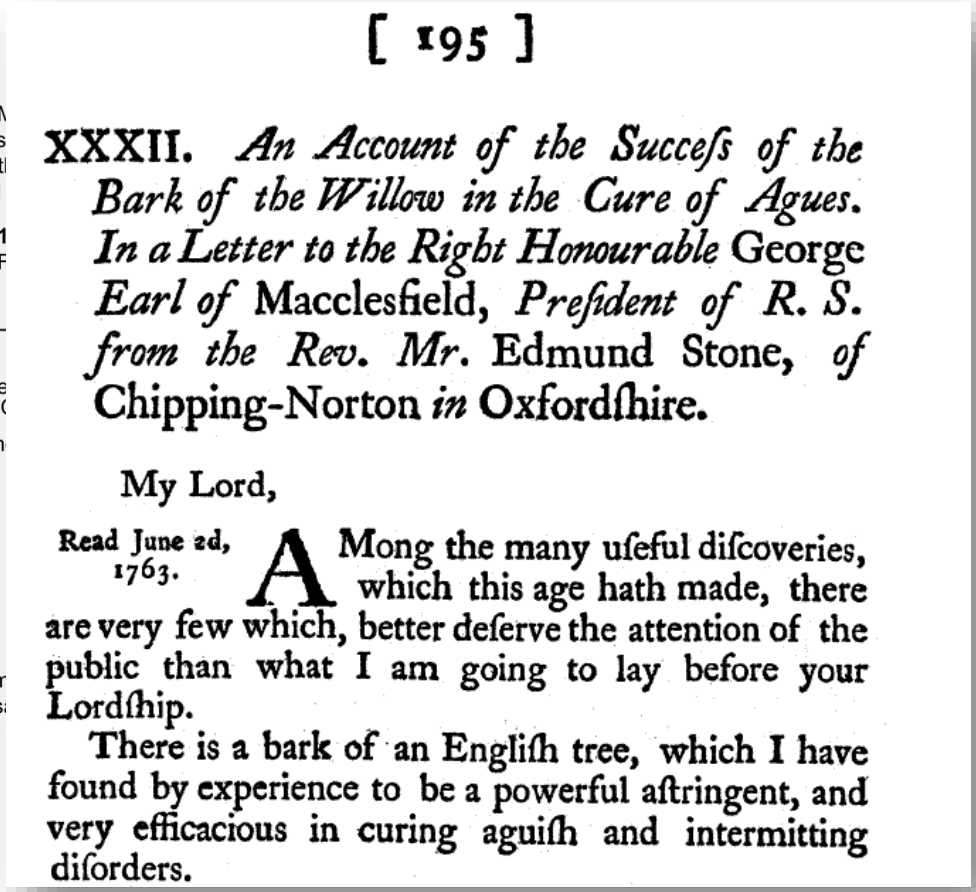
Methods 5269 adults aged 30 years or more with impaired fasting glucose or impaired glucose tolerance, or both, and no previous cardiovascular disease were recruited from 191 sites in 21 countries and randomly assigned to receive rosiglitazone (8 mg daily; n=2365) or placebo (2634) and followed for a median of 3 years. The primary outcome was a composite of incident diabetes or death. Analyses were done by intention to treat. This trial is registered at ClinicalTrials.gov, number NCT00095654.

Findings At the end of study, 59 individuals had dropped out from the rosiglitazone group and 46 from the placebo group. 306 (11·6%) individuals given rosiglitazone and 686 (26·0%) given placebo developed the composite primary outcome (hazard ratio 0·40, 95% CI 0·35–0·46; p<0·0001); 1330 (50·5%) individuals in the rosiglitazone group and 798 (30·3%) in the placebo group became normoglycaemic (1·71, 1·57–1·87; p<0·0001). Cardiovascular event rates were much the same in both groups, although 14 (0·5%) participants in the rosiglitazone group and two (0·1%) in the placebo group developed heart failure (p=0·01).

Interpretation Rosiglitazone at 8 mg daily for 3 years substantially reduces incident type 2 diabetes and increases the likelihood of regression to normoglycaemia in adults with impaired fasting glucose or impaired glucose tolerance, or both.

Timeline of historical events in the development of aspirin.





[195]

XXXII. *An Account of the Succeſs of the Bark of the Willow in the Cure of Agues. In a Letter to the Right Honourable* George *Earl of* Macclesfield, *Preſident of R. S. from the Rev. Mr.* Edmund Stone, *of* Chipping-Norton *in* Oxfordſhire.

My Lord,

Read June 2d, 1763.

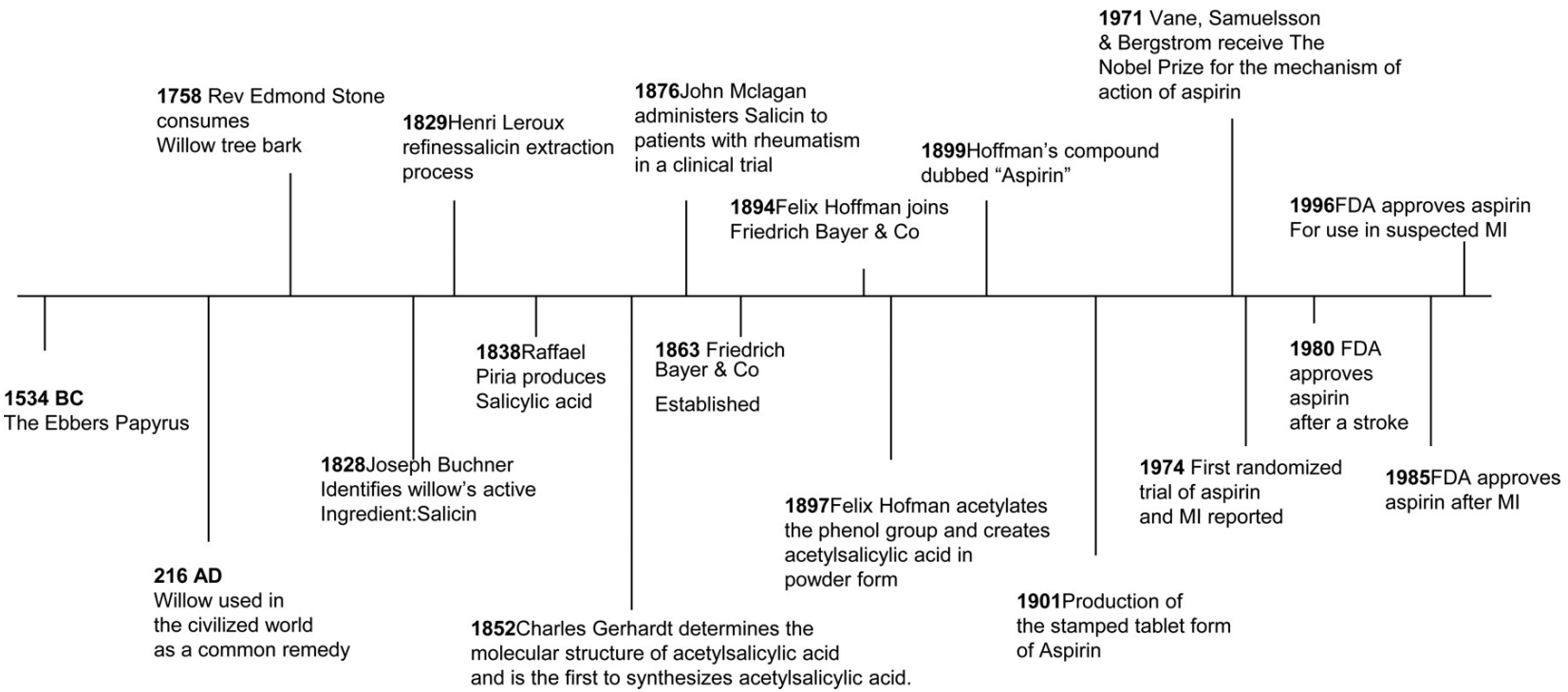
AMong the many uſeful diſcoveries, which this age hath made, there are very few which, better deſerve the attention of the public than what I am going to lay before your Lordſhip.

There is a bark of an Engliſh tree, which I have found by experience to be a powerful aſtringent, and very efficacious in curing aguiſh and intermitting diſorders.

Fuster V , and Sweeny J M Circulation 2011;123:768-778

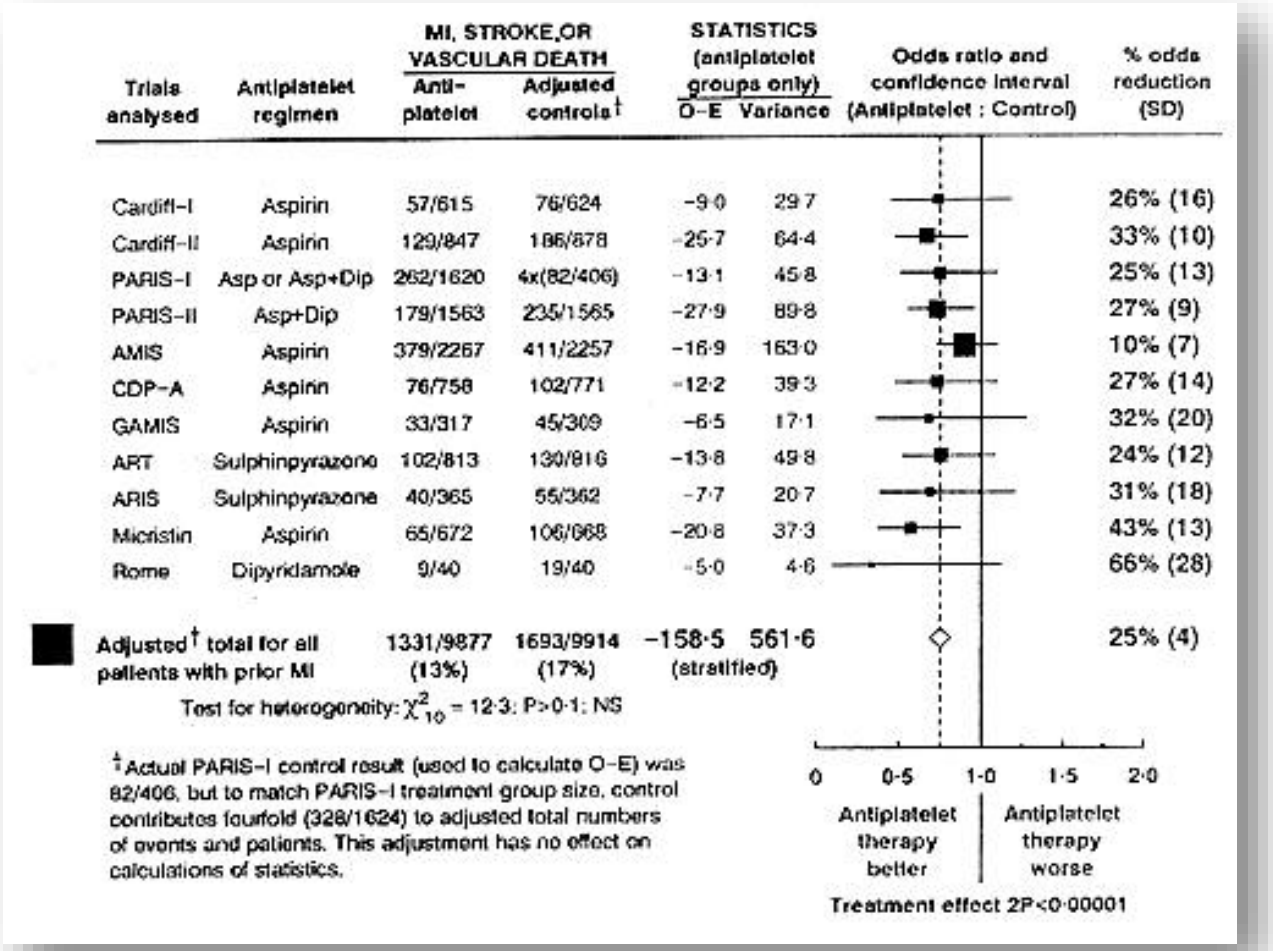
American Heart Association
Learn and Live

Timeline of historical events in the development of aspirin.



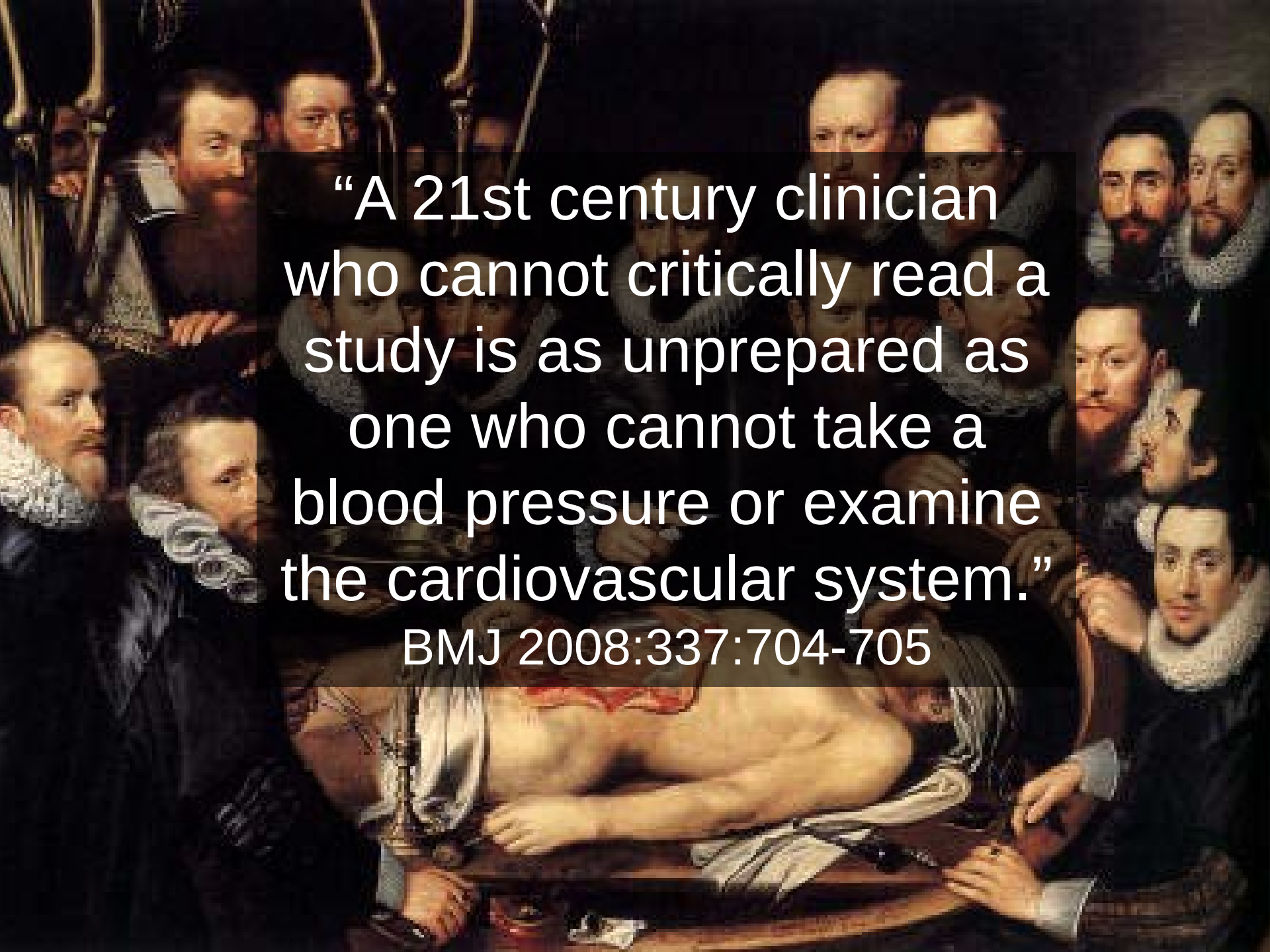
Fuster V , and Sweeny J M Circulation 2011;123:768-778

Proportional effects on vascular events (myocardial infarction, stroke, or vascular death) in 11 randomised trials of prolonged antiplatelet therapy (for one month or more) versus control in patients with prior myocardial infarction.



Antiplatelet Trialists' Collaboration BMJ 1994;308:81-106

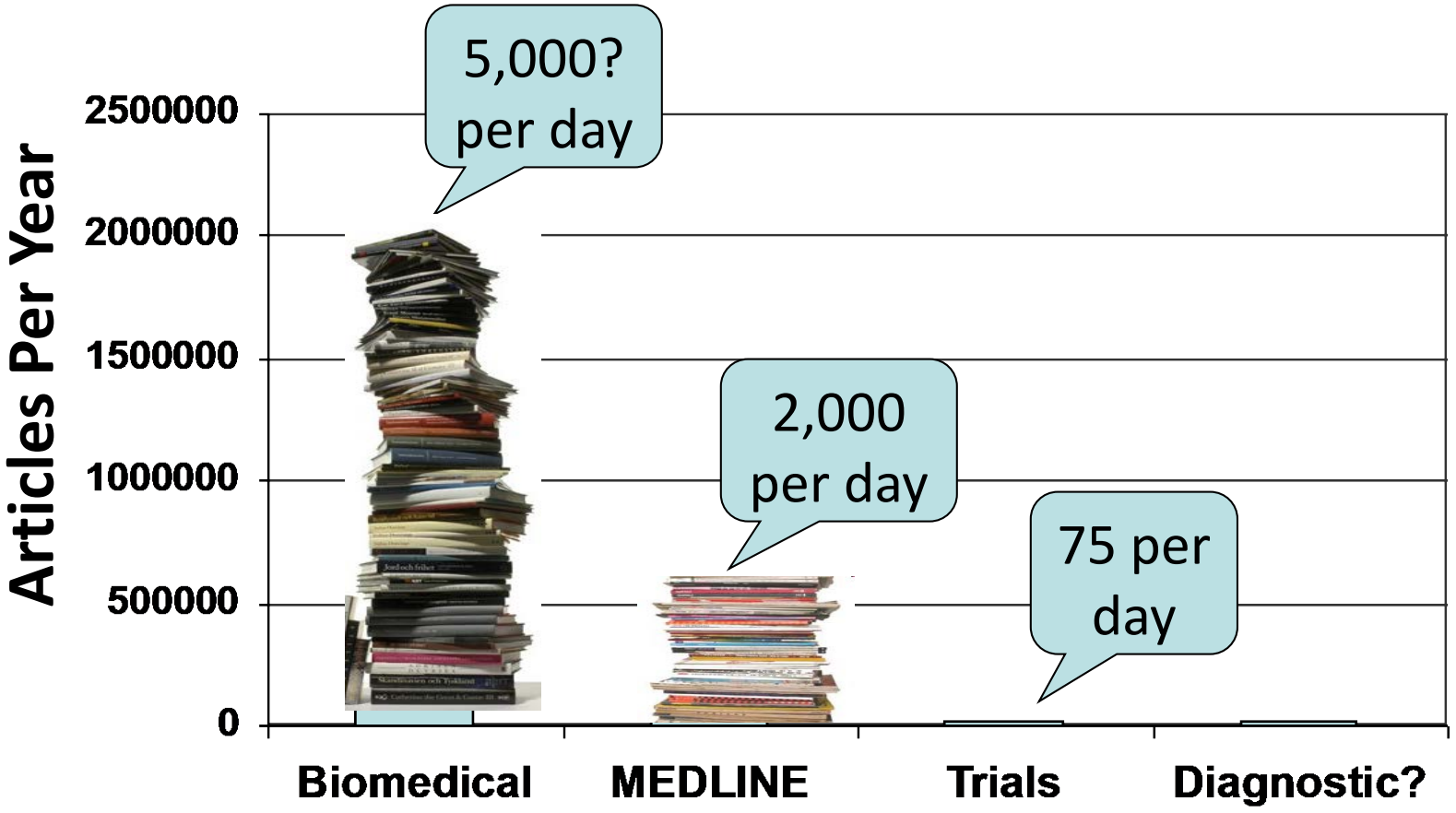
Types of evidence affect the quality


“A 21st century clinician who cannot critically read a study is as unprepared as one who cannot take a blood pressure or examine the cardiovascular system.”
BMJ 2008:337:704-705

The 5 steps of EBM

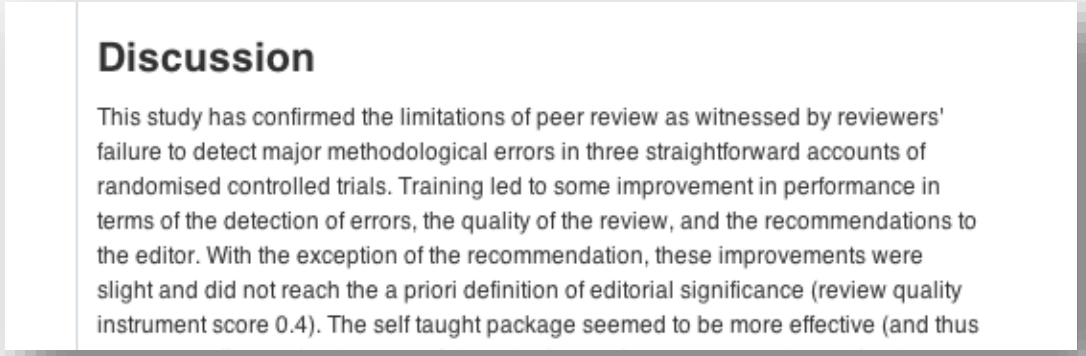
1. Formulate an answerable question
2. Track down the best evidence
3. Critically appraise the evidence for validity, clinical relevance and applicability
4. Individualize, based clinical expertise and patient concerns
5. Evaluate your own performance

Why do we need to use evidence efficiently?



But we are (currently) poorly equipped to tell good from bad research

- BMJ study of 607 reviewers
  - 14 deliberate errors inserted
- Detection rates
  - On average <3 of 9 major errors detected
  - Poor Randomisation (by name or day) - 47%
  - Not intention-to-treat analysis - 22%
  - Poor response rate - 41%



Discussion

This study has confirmed the limitations of peer review as witnessed by reviewers' failure to detect major methodological errors in three straightforward accounts of randomised controlled trials. Training led to some improvement in performance in terms of the detection of errors, the quality of the review, and the recommendations to the editor. With the exception of the recommendation, these improvements were slight and did not reach the a priori definition of editorial significance (review quality instrument score 0.4). The self taught package seemed to be more effective (and thus

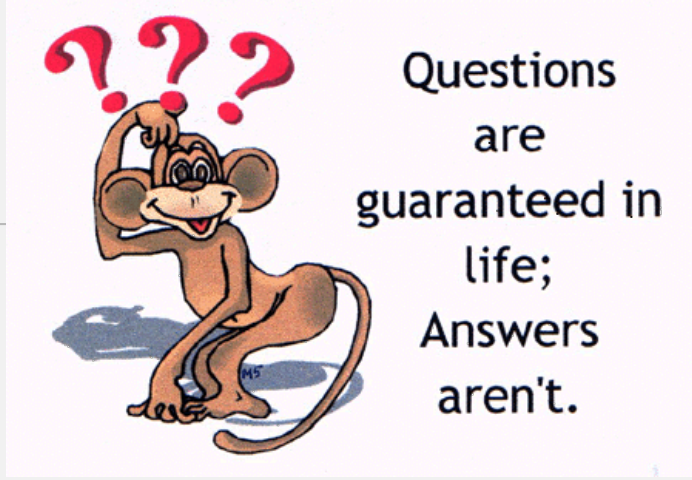
Schroter S et al

Managing Information
"Push" and "Pull" methods

- "Push" - alerts us to new information
  - "Just in Case" learning
    - Use ONLY for important, new, valid research
- "Pull" – access information when needed
  - "Just in Time" learning
    - Use whenever questions arise
    - EBM Steps: Question; search; appraise; apply

Your Clinical Questions

- Write down one recent patient problem
- What was the critical question?



: Asking well-formulated questions

In your books

Angela is a new patient who recently moved to the area to be closer to her son and his family

She is 69 years old and has a history of congestive heart failure brought on by a recent myocardial infarctions.

She has been hospitalized twice within the last 6 months for worsening of heart failure and has a venous leg ulcer.

At the present time she reports she is extremely diligent about taking her medications (lisinopril and aspirin) and wants desperately to stay out of the hospital. She is mobile and lives alone with several cats but reports sometimes she forgets certain things.

She also tells you she is a bit hard of hearing, has a slight cough, is an ex-smoker of 20 cigs a day for 40 years. Her BP today is 170/90, her ankles are slightly swollen and her ulcer is painful and her pulse is 80 and slightly irregular.

What are your questions?

‘Background’ Questions

- **About the disorder, test, treatment, etc.**

2 components:

a. Root* + Verb: “What causes …”

b. Condition: “… Ebola?”

- *** Who, What, Where, When, Why, How**

‘Foreground’ Questions

- **About patient care decisions and actions**

4 (or 3) components:

a. Patient, problem, or population

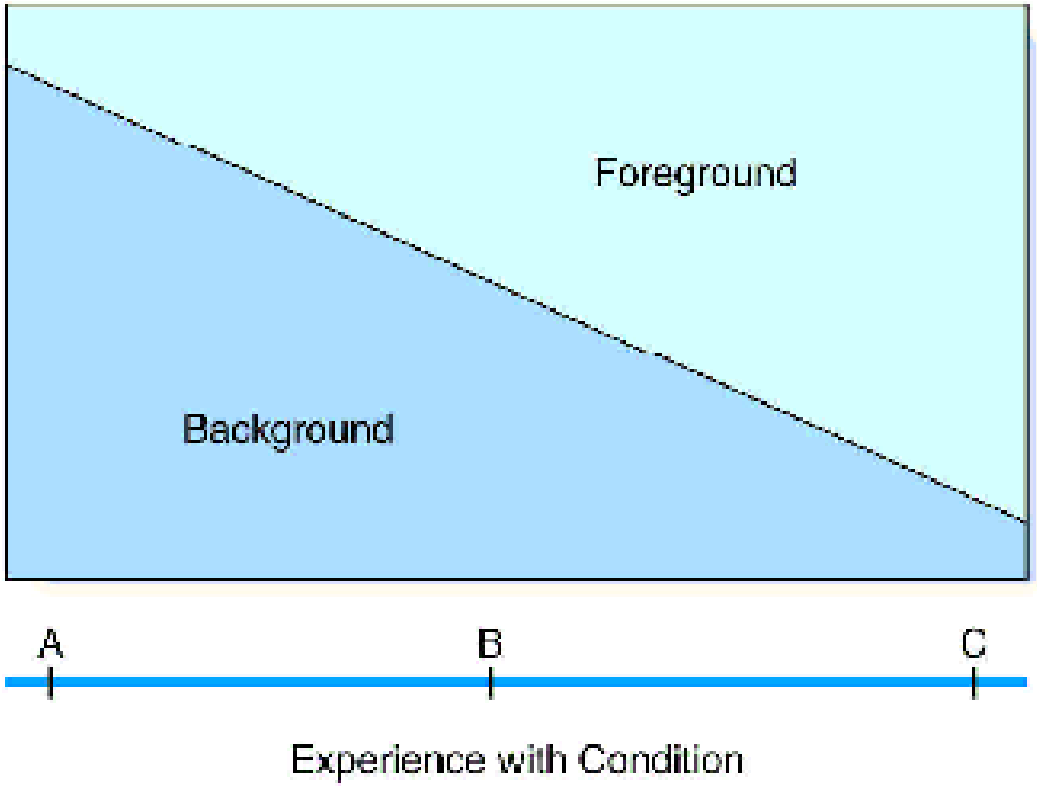
b. Intervention, exposure, or maneuver

c. Comparison (if relevant)

d. Clinical Outcomes (including time horizon)

Background & Foreground

Figure 1.1 Background and foreground questions.



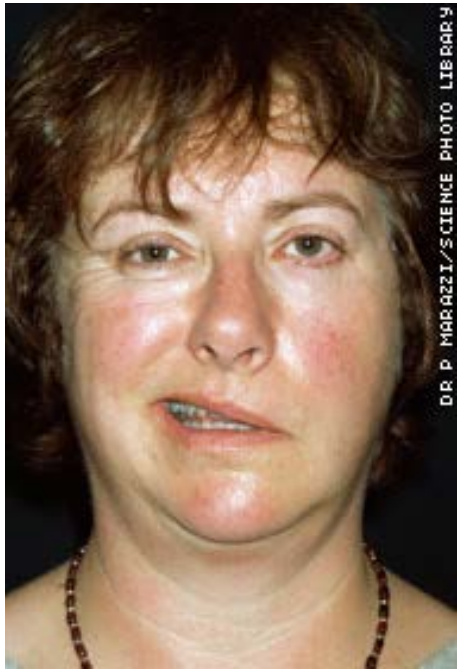
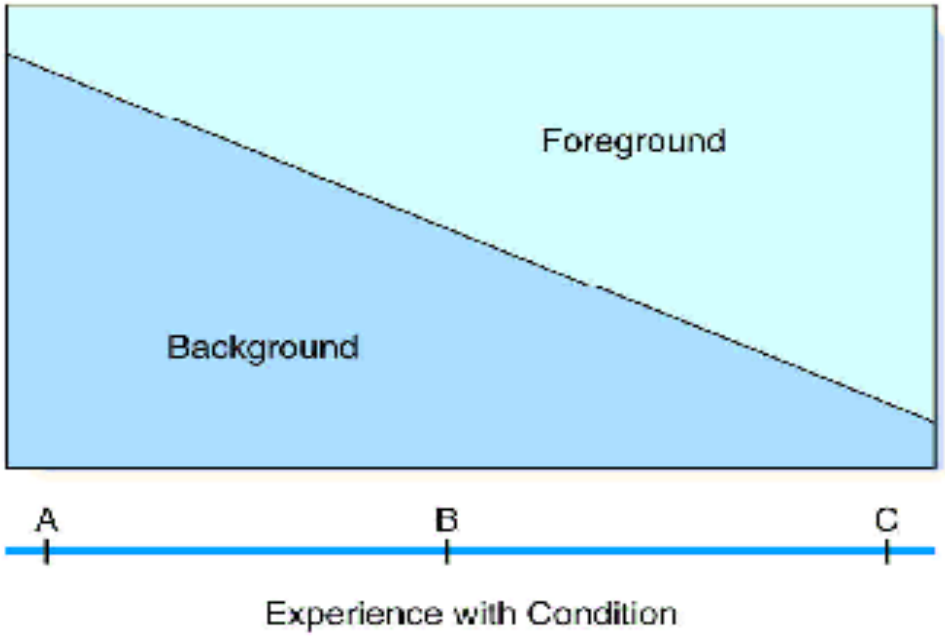


Figure 1.1 Background and foreground questions.



Bell's palsy

From Wikipedia, the free encyclopedia

Bell's palsy is a form of facial paralysis resulting from a dysfunction of the cranial nerve VII (the facial nerve) that results in the inability to control facial muscles on the affected side. Several conditions can cause facial paralysis, e.g., brain tumor, stroke, and Lyme disease. However, if no specific cause can be identified, the condition is known as Bell's palsy. Named after Scottish anatomist Charles Bell, who first described it, Bell's palsy is the most common acute mononeuropathy (disease involving only one nerve) and is the most common cause of acute facial nerve paralysis.

Bell's palsy is defined as an idiopathic unilateral facial nerve paralysis, usually self-limiting. The hallmark of this condition is a rapid onset of partial or complete palsy that often occurs overnight. In rare cases (1%), it can occur bilaterally resulting in total facial paralysis.[1]

It is thought that an inflammatory condition leads to swelling of the facial nerve. The nerve travels through the skull in a narrow bone canal beneath the ear. Nerve swelling and compression in the narrow bone canal are thought to lead to nerve inhibition, damage or death. No readily identifiable cause for Bell's palsy has been found.

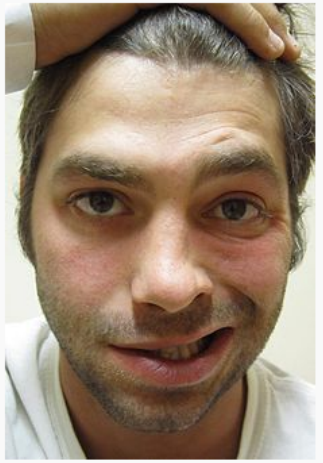
Corticosteroids have been found to improve outcomes while anti-viral drugs have not.[2] Early treatment is necessary for steroids to be effective. Most people recover spontaneously and achieve near-normal to normal functions. Many show signs of improvement as early as 10 days after the onset, even without treatment.

Often the eye in the affected side cannot be closed. The eye must be protected from drying up, or the cornea may be permanently damaged resulting in impaired vision. In some cases denture wearers experience some discomfort.

Contents [hide]

Bell's palsy

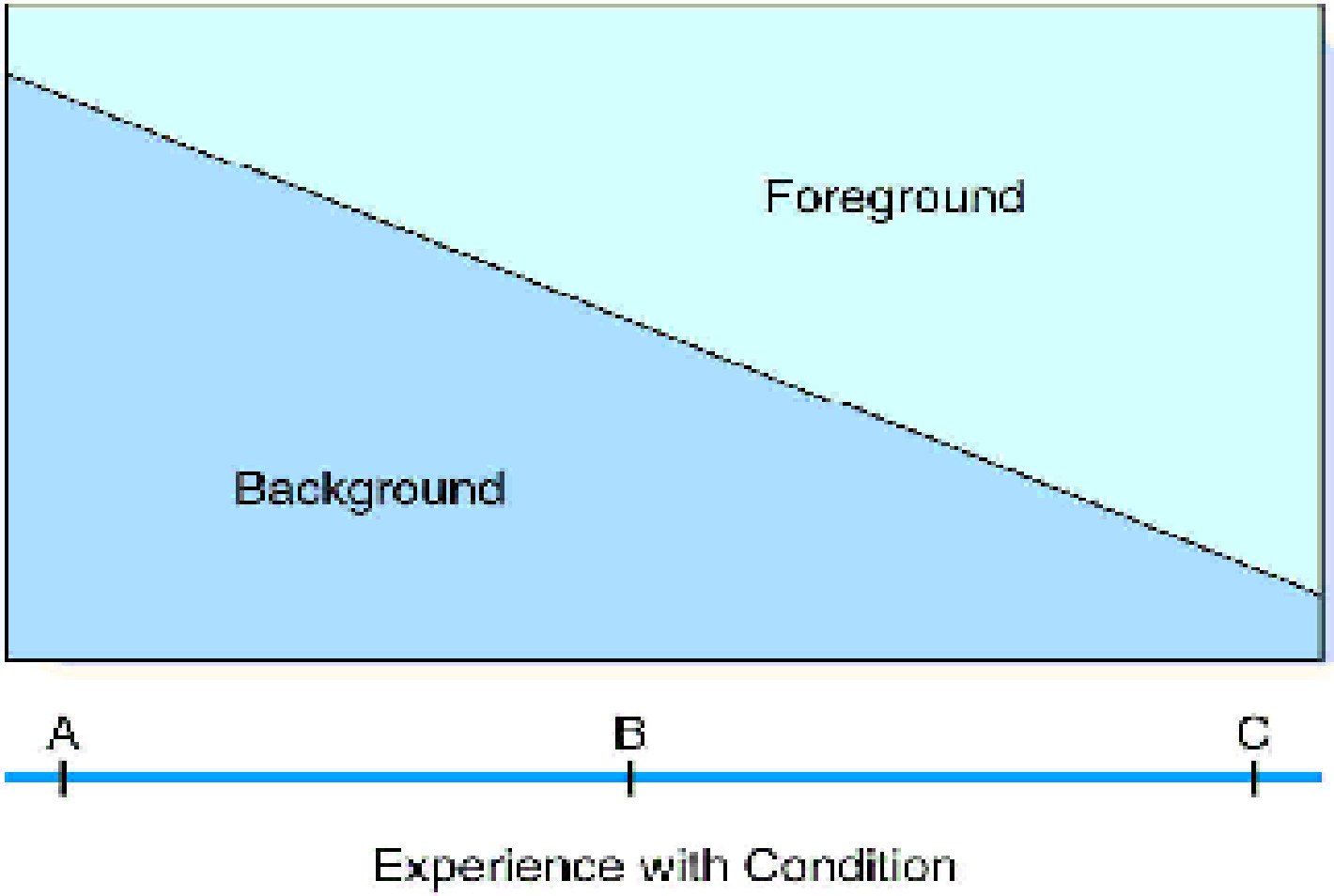
Classification and external resources



A person attempting to show his teeth and raise his eyebrows with Bell's palsy on his right side.

ICD-10	G51.0
ICD-9	351.0
DiseasesDB	1303
MedlinePlus	000773

Figure 1.1 Background and foreground questions.



‘Foreground’ Questions

About patient care decisions and actions

- **4 (or 3) components:**

- **a. In Patients with Bell’s Palsy**
- **b. Do (I) corticosteroids**
- **c. Compared to placebo**
- **d. Improve facial function (O) at 3 months**

ORIGINAL ARTICLE

Early Treatment with Prednisolone or Acyclovir in Bell's Palsy

Frank M. Sullivan, Ph.D., Iain R.C. Swan, M.D., Peter T. Donnan, Ph.D., Jillian McKinstry, M.D., Richard J. Davenport, D.M., Luke D. Vale, Ph.D., Janet E. C Hayavi, Ph.D., Anne McAteer, M.Sc., Ken Stewart, M.D., and Fergus Daly, M

N Engl J Med 2007; 357:1598-1607 | October 18, 2007

Abstract | Article | References | Citing Articles (43)

BACKGROUND

Corticosteroids and antiviral agents are widely used to treat stages of idiopathic facial paralysis (i.e., Bell's palsy), but th effectiveness is uncertain.

Full Text of Background...

METHODS

We conducted a double-blind, placebo-controlled, randomize factorial trial involving patients with Bell's palsy who were rec within 72 hours after the onset of symptoms. Patients were assigned to receive 10 days of treatment with prednisolone, both agents, or placebo. The primary outcome was recovery function, as rated on the House–Brackmann scale. Secondary outcomes included quality of life, appearance, and pain.

Full Text of Methods...

RESULTS

Final outcomes were assessed for 496 of 551 patients who underwent randomization. At 3 months, the proportions of patients who had recovered facial function were 83.0% in the prednisolone group as compared with 63.6% among patients who did not receive prednisolone (P<0.001) and 71.2% in the acyclovir group as compared with 75.7% among patients who did not receive acyclovir (adjusted P=0.50). After 9 months, these proportions were 94.4% for prednisolone and 81.6% for no prednisolone (P<0.001) and 85.4% for acyclovir and 90.8% for no acyclovir (adjusted P=0.10). For patients treated with both drugs, the proportions were 79.7% at 3 months

Slide

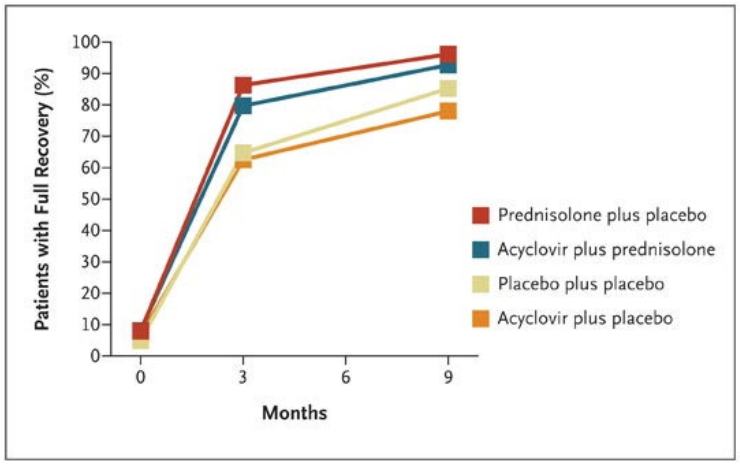


Figure 2 Patients Who Had a Full Recovery at 3 Months and 9 Months, According to Study Group.

Full recovery was defined as grade 1 on the House–Brackmann facial-nerve grading scale, which ranges from 1 to 6, with higher grades indicating worse facial paralysis.

Patients Who Had a Full Recovery at 3 Months and 9 Months, According to Study Group.

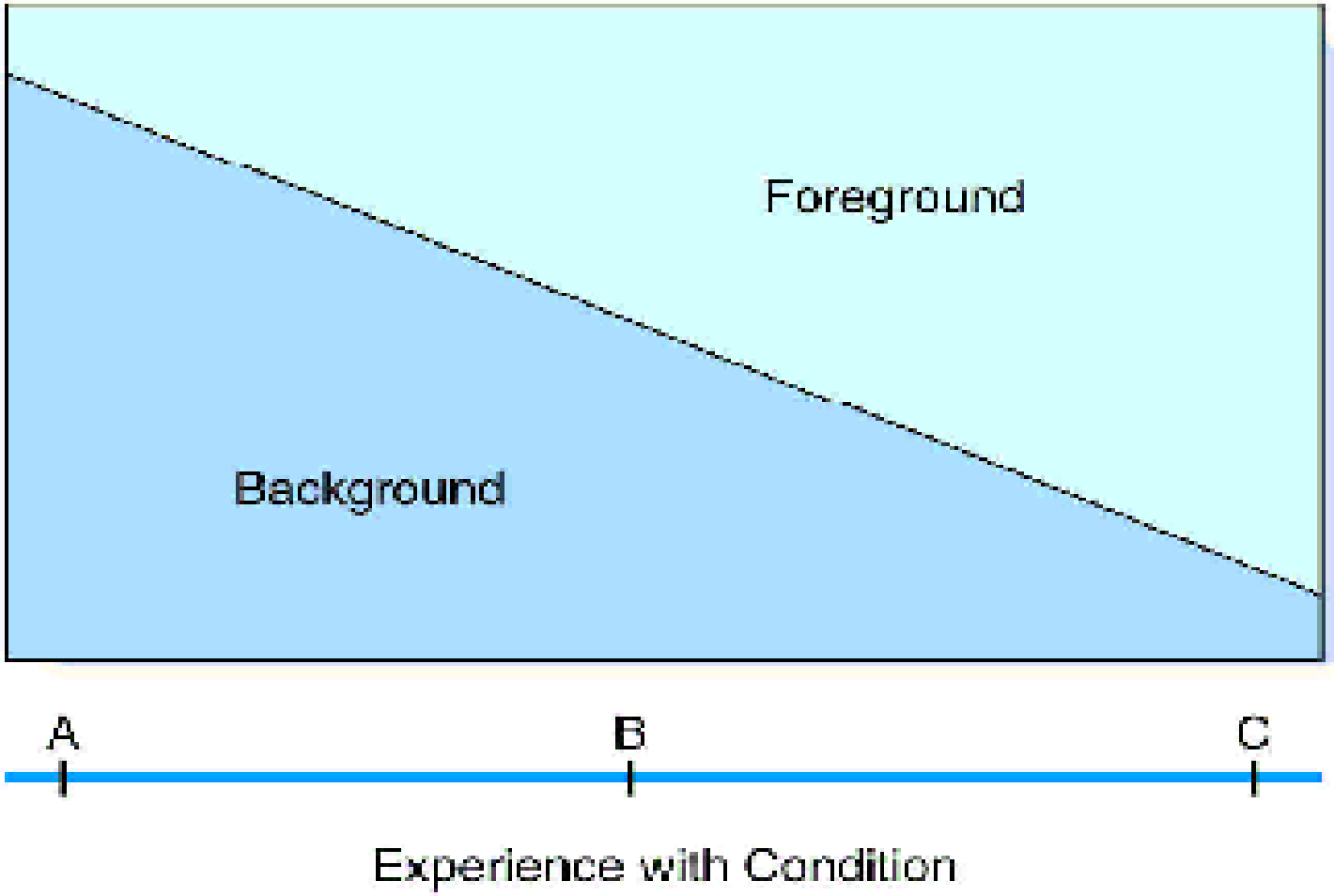
Does this intervention help?

For every 100 people with Bell's palsy at 3 months

- 83 in the corticosteroid group will have recovered facial function &
- 64 in the placebo group will have recovered facial function

- Risk difference = 19%
- Relative Risk Reduction = 23%
- Number Needed to Treat = 6
- Natural Frequency 19 per 100

Figure 1.1 Background and foreground questions.



Background:

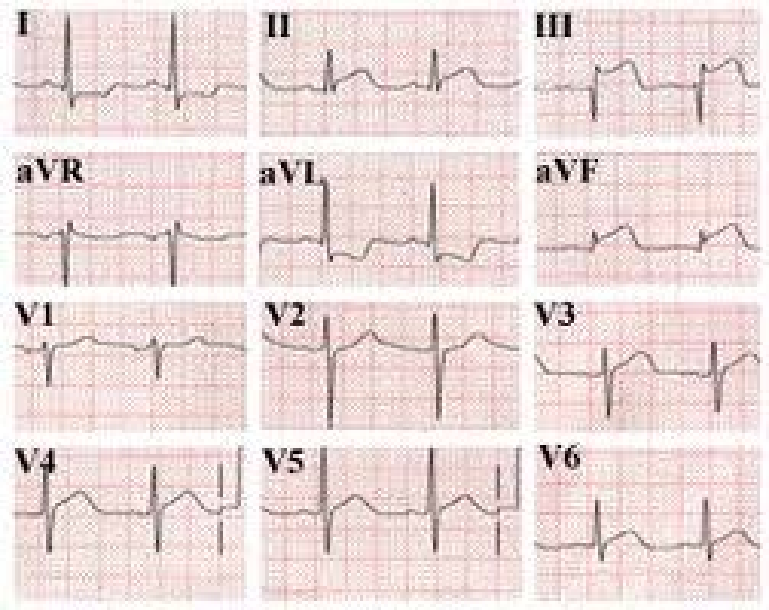
Patient presenting with MI

1. What are the symptoms and signs of someone presenting with MI?

1. What are the diagnostic tests for MI?

1. What are the causes of MI?

1. What are the treatments of MI?



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Česky
Cymraeg

Myocardial infarction

From Wikipedia, the free encyclopedia

"Heart attack" redirects here. For other uses, see Heart attack (disambiguation).

Not to be confused with Cardiac arrest.

Myocardial infarction (**MI**) or **acute myocardial infarction** (**AMI**), is the medical term for an event commonly known as a **heart attack**. It happens when blood stops flowing properly to part of the heart and the heart muscle is injured due to not getting enough oxygen. Usually this is because one of the coronary arteries that

Myocardial infarction
Classification and external resources

Signs and symptoms [edit source | edit beta]

The onset of symptoms in myocardial infarction (MI) is usually gradual, over several minutes, and rarely instantaneous.[17] Chest pain is the most common symptom of acute myocardial infarction and is often described as a sensation of tightness, pressure, or squeezing. Chest pain due to ischemia (a lack of blood and hence oxygen supply) of the heart muscle is termed angina pectoris. Pain radiates most often to the left arm, but may also radiate to the lower jaw, neck, right arm, back, and epigastrium,[7][18] where it may mimic heartburn. Levine's sign, in which the patient localizes the chest pain by clenching their fist over the sternum, has classically been thought to be predictive of cardiac chest pain, although a prospective observational study showed that it had a poor positive predictive value.[19]

Shortness of breath (dyspnea) occurs when the damage to the heart limits the output of the left ventricle, causing left ventricular failure and consequent pulmonary edema. Other symptoms include diaphoresis (an excessive form of sweating),[1] weakness, light-headedness, nausea, vomiting, and palpitations. These symptoms are likely induced by a massive surge of catecholamines from the sympathetic nervous system[20] which occurs in response to pain and the hemodynamic abnormalities that result from cardiac dysfunction. Loss of consciousness (due to inadequate cerebral perfusion and cardiogenic shock) and sudden death (frequently due to the development of ventricular fibrillation) can occur in myocardial infarctions.[7]

Female, elderly, and diabetic patients report atypical symptoms more frequently than their male and younger counterparts.[21][22] Women also report more numerous symptoms compared with men (2.6 on average vs 1.8 symptoms in men).[21] The most common symptoms of MI in women include dyspnea (shortness of breath), weakness, and fatigue. Fatigue, sleep disturbances, and dyspnea have been reported as frequently occurring symptoms that may manifest as long as one month before the actual clinically manifested ischemic event. In women, chest pain may be less predictive of coronary ischemia than in men.[23]

At least one-fourth of all myocardial infarctions are silent, without chest pain or other symptoms.[3][24] These cases can be discovered later on electrocardiograms, using blood enzyme tests or at autopsy without a prior history of related complaints. Estimates of the prevalence of silent myocardial infarctions vary between 22 and 64%.[3] A silent course is more common in the elderly,[3] in patients with diabetes mellitus[25] and after heart transplantation, probably because the donor heart is not fully innervated by the nervous system of the recipient.[26] In people with diabetes, differences in pain threshold, autonomic neuropathy, and psychological factors have been cited as possible explanations for the lack of symptoms.[25]

Any group of symptoms compatible with a sudden interruption of the blood flow to the heart are called an acute coronary syndrome.[27]

The differential diagnosis includes other catastrophic causes of chest pain, such as pulmonary embolism, aortic dissection, pericardial effusion causing cardiac tamponade, tension pneumothorax, and esophageal rupture. Other non-catastrophic differentials include gastroesophageal reflux and Tietze's syndrome.[28]

Causes [edit source | edit beta]

Know your background

Patient presenting with MI

Foreground’ Questions

About actual patient care decisions and actions

For treatment
4 (or 3) components:

In Patients with a MI
Does (I) cholesterol lowering therapy
Compared to placebo
reduce mortality (O)

Patient presenting with MI (7 types of questions)

1. How common is the problem	Prevalence
2. Is early detection worthwhile	Screening
3. Is the diagnostic test accurate	Diagnosis
4. What will happen if we do nothing	Prognosis
5. Does this intervention help	**Treatment**
6. What are the common harms of an intervention	
7. What are the rare harms of an intervention	

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FORMULATING THE CLINICAL QUESTION

PICO

- Patient/ Population
- Intervention
- Comparison group
- Outcome

Patient or **P**roblem	**I**ntervention	**C**omparison intervention	**O**utcomes
Describe a group of patients similar to your own	What intervention are you considering	What is the main alternative to the intervention	What do you hope to accomplish with the intervention
“In elderly patients with congestive heart failure …	…does treatment with spirinolactone …	…when compared with standard therapy alone…	…lead to a decrease in hospitalization ”

Example 1

Jean is a 55 year old woman who quite often crosses the Atlantic to visit her elderly mother. She tends to get swollen legs on these flights and is worried about her risk of developing deep vein thrombosis (DVT), because she has read quite a bit about this in the newspapers lately. She asks you if she would wear elastic stockings on her next trip to reduce her risk of this.

Example 2

CHILDHOOD SEIZURES

Childhood seizures are common and frightening for the parents, and the decision to initiate treatment is a difficult one. What is the risk of further recurrences following a single seizure of unknown cause? Are there any identifiable factors that modify this risk?

Example 3

VACCINATION AND NEEDLE LENGTH

You are the practice nurse and one of your colleagues tells you it is better to use a short needle than a long needle when immunising babies for their first ever vaccinations, as it reduces the swelling and decreases the parents anxiety about further vaccinations. You wonder if your colleague is correct?

Example 4

CHILDREN AND ANTIVIRALS

You are the GP and the next patient brings their 3 year old child who is unwell with a fever, the mother wants to know whether she should give the child tamiflu?

Further Example

Susan is expecting her first baby in two months. She has been reading about the potential benefits and harms of giving newborn babies vitamin K injections. She is alarmed by reports that vitamin K injections in newborn babies may cause childhood leukaemia. She asks you if this is true and, if so, what the risk for her baby will be.

Your Clinical Questions

- Write down one recent patient problem

- What is the PICO of the problem?