Evidence-Based Medicine: What is it and why does it matter?

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Kingston University London

I like David’s hair!

team GB

KING’S
I am here because?
One day Introduction to Evidence-Based Medicine

08:45      Arrival & Registration
09:00      Plenary: What is Evidence-based practice
09:45      Group Tutorial: Asking well-formulated questions

10:30     Morning Coffee

10:45      Plenary: Finding the best evidence (searching basics)
            (Outreach Librarian at Bodleian Health Care Libraries)
11:15      Lab Tutorial: Cochrane and PubMed Searching (hands-on)
            (Outreach Librarian at Bodleian Health Care Libraries)

12:15     Lunch

1:30       Plenary & Small Group Tutorial: Rapid Critical Appraisal of Randomised Controlled Trials

3:15       Plenary & Small Group Tutorial: Critical Appraisal of Systematic Reviews
           – Tea served in the room

4:45       Where to from here? / Evaluation / Close
Aims of this session

1. To understand Evidence-Based Practice in clinical care and it’s importance

2. To introduce the steps of EBM

3. Develop skills for asking focussed & answerable clinical questions

4. To inspire you to want to learn more
EBM in a nutshell

Patient values & preferences

Improved patient outcomes

Best available evidence

Clinical expertise & judgment


http://www.bmj.com/content/312/7023/71
Pre-EBM thinking....
Pre-EBM thinking....

- Unsystematic observations from clinical experience guided decisions

- Sufficient to apply basic mechanisms of disease and pathophysiologic principles to clinical practice

- Traditional medical training and common sense sufficient to allow one to evaluate new tests and treatments

- Content expertise and clinical experience sufficient base from which to generate valid guidelines for clinical practice

BASING CLINICAL DECISIONS ON OPINION
Baby and Child Care” has actually sold more than 50 million copies, only outmatched in sales by the Bible.
‘...disadvantages to a baby’s sleeping on his back. If he vomits he’s more likely to choke on the vomitus.

..I think it is preferable to accustom a baby to sleeping on his stomach from the start.’

Dr Benjamin Spock
Over four fold increase risk of sudden infant death syndrome

“By 1970, there was a statistically significantly increased risk of SIDS for front sleeping compared with back (pooled odds ratio (OR) 2.93; 95% confidence interval (CI) 1.15, 7.47)”
Sudden infant death syndrome (SIDS) – also known as cot death – is the sudden, unexpected and unexplained death of an apparently well baby.

In the UK, at least 300 babies die suddenly and unexpectedly every year. This statistic may sound alarming, but SIDS is rare and the risk of your baby dying from it is low.

Most deaths happen during the first six months of a baby’s life. Infants born prematurely or with a low birthweight are at greater risk, and SIDS is also more common in baby boys.

SIDS usually occurs when a baby is asleep, but it can occasionally happen while they are awake.

Parents can reduce the risk of SIDS by not smoking while pregnant or after the baby is born, and always placing the baby on their back when they sleep (see below).
MECHANISTIC REASONING
Antiarrythmics

- USA 1980s
- Oral drug to used to prevent irregular heart rhythms

Patients have a heart attack (post MI) → At risk of irregular heart rhythm → Death

Flecainide

“Mechanistic approach”
ORAL FLECAINIDE ACETATE FOR THE TREATMENT OF VENTRICULAR ARRHYTHMIAS

JEFFREY L. ANDERSON, M.D., JAMES R. STEWART, M.D., BENJAMIN A. PERRY, M.D., DANIEL D. VAN HAMERSVELD, M.D., THERESA A. JOHNSON, R.N., GORDON J. CONARD, PH.D., SHAW F. CHANG, M.S., DONALD C. KVAM, PH.D., AND BERTRAM PITT, M.D.

Abstract The antiarrhythmic efficacy and safety of oral flecainide acetate were assessed during a controlled, short-term dosage-maintenance study. Thirteen patients with chronic ventricular ectopy entered a placebo control period, and 11 with persistent, frequent (>600 per 12 hours) premature ventricular complexes (PVCs) advanced to drug therapy. Of 10 patients completing a trial of different doses, nine responded completely, with a mean PVC suppression of 98.3 per cent. Repetitive PVCs were eliminated. The mean effective dose was 189 mg per 12 hours, and the effective plasma concentration before administration of a dose averaged 635 ng per milliliter. One patient responded partially (68 per cent of PVCs suppressed). Flecainide continued to be effective and well tolerated at the end of a two-week outpatient trial in the nine complete responders, maintaining an average PVC suppression of 94.6 per cent. The PR and QRS intervals were mildly prolonged. The echocardiographic ejection fraction was unchanged during treatment. The elimination half-life was long — 18.8±3.8 hours. Flecainide thus appears to be a highly effective and well-tolerated antiarrhythmic agent with favorable pharmacokinetics. (N Engl J Med. 1981; 305:473-7.)

MANAGEMENT of ventricular arrhythmias remains problematic. A drug’s failure to control arrhythmia may be attributed to inadequate antiarrhythmic activity, intolerable side effects, or compliance problems stemming from unfavorable pharmacokinetics. These considerations suggest the need for additional, more promising antiarrhythmic agents.

Flecainide acetate is a new antiarrhythmic compound (Fig. 1) that has had favorable pharmacologic effects in animals, suggesting therapeutic potential in human beings. Results of electrophysiologic testing Initial studies with intravenous flecainide in human beings have suggested its potential for sustained antiarrhythmic activity. Single-dose studies in normal subjects have indicated a long (14-hour) plasma elimination half-life. Hoback et al. reported a 93 per cent average decrease in premature ventricular complexes (PVCs) in 12 patients given 1 to 2 mg per kilogram of body weight, and Somani reported complete suppression of PVCs in nine of 10 patients. When larger doses (1.5 to 2.0 mg per kilogram) were administered, Seipel et al. noted substantial prolongations of
10 patients who had had an MI

Given alternating placebo/ Flecainide

Number of irregular contractions counted over 14 days

Flecainide – Mechanistic approach
Flecainide – Mechanistic approach

1989 – 200,000 patients were being treated with flecainide post MI
EBM advocates critical thinking

• Are 10 people enough to make this conclusion?
  – Sample size?

• What is the evidence for the safety of antiarrhythmic drugs in the longer term?
  – Appropriate follow up period?

• Is this the best study design to answer the question?
  – RCT = higher quality environment to prove theory?
MORTALITY AND MORBIDITY IN PATIENTS RECEIVING ENCAINIDE, FLECAINIDE, OR PLACEBO

The Cardiac Arrhythmia Suppression Trial


Abstract  Background and Methods. In the Cardiac Arrhythmia Suppression Trial, designed to test the hypothesis that suppression of ventricular ectopy after a myocardial infarction reduces the incidence of sudden death, patients in whom ventricular ectopy could be suppressed with encainide, flecainide, or moricizine were randomly assigned to receive either active drug or placebo. The use of encainide and flecainide was discontinued because of excess mortality. We examined the mortality and morbidity after randomization to encainide or flecainide or their respective placebo.

Results. Of 1498 patients, 857 were assigned to receive encainide or its placebo (432 to active drug and 425 to placebo) and 641 were assigned to receive flecainide or its placebo (332 to active drug and 318 to placebo). After a mean follow-up of 10 months, 89 patients had died: 59 of arrhythmia (43 receiving drug vs. 16 receiving placebo; P = 0.0004), 22 of nonarrhythmic cardiac causes (17 receiving drug vs. 5 receiving placebo; P = 0.01), and 8 of noncardiac causes (3 receiving drug vs. 5 receiving placebo). Almost all cardiac deaths not due to arrhythmia were attributed to acute myocardial infarction with shock (11 patients receiving drug and 3 receiving placebo) or to chronic congestive heart failure (4 receiving drug and 2 receiving placebo). There were no differences between the patients receiving active drug and those receiving placebo in the incidence of nonlethal disqualifying ventricular tachycardia, proarrhythmia, syncope, need for a permanent pacemaker, congestive heart failure, recurrent myocardial infarction, angina, or need for coronary-artery bypass grafting or angioplasty.

Conclusions. There was an excess of deaths due to arrhythmia and deaths due to shock after acute recurrent myocardial infarction in patients treated with encainide or flecainide. Nonlethal events, however, were equally distributed between the active-drug and placebo groups. The mechanisms underlying the excess mortality during treatment with encainide or flecainide remain unknown. (N Engl J Med 1991; 324:781-8.)
After having a heart attack.....

For every 100 people treated with the placebo:
- 2 people died

For every 100 people treated with flecainide:
- 6 people died
Clinical Implications

The CAST study has demonstrated that the use of encainide or flecainide to treat asymptomatic or mildly symptomatic ventricular arrhythmias in patients with left ventricular dysfunction after myocardial infarction carries a risk of excess mortality. This study emphasizes the need for placebo-controlled clinical trials of antiarrhythmic drugs with end points of related mortality. It also demonstrates the necessity for a data- and safety-monitoring board to establish guidelines for monitoring and discontinuing a study to protect patients.

The lack of benefit of the two Class IC agents used in this study suggests that, despite their increased risk, asymptomatic or mildly symptomatic patients with ventricular premature depolarizations or nonsustained ventricular tachycardia after a myocardial infarction may not benefit from therapy beyond the general use of beta-adrenergic–blocking agents. 32 Al-
Why do we need RANDOMIZED CONTROLLED TRIALS?

By 1990, more than a decade after these drugs were introduced, it has been estimated that they were killing more Americans every year than died in action in the Vietnam war.
AN OVER RELIANCE ON TEXTBOOKS/REVIEWS
(WHICH ARE OFTEN OUT OF DATE)
Accumulating data from randomized control trials of treatments for acute MI

Versus

Recommendations of clinical experts writing review articles and textbook chapters.

“there are often discrepancies between the most current evidence of effective practice as derived from randomized trials and the recommendations of reviewers.”

What's so special about EBM?

• “de-emphasizes intuition, unsystematic clinical experience, and pathophysiologic rationale as sufficient grounds for clinical decision making and stresses the examination of evidence from clinical research”

• “EBM requires new skills of the physician, including efficient literature searching and the application of formal rules of evidence evaluating the clinical literature”

“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
Practising EBM – the 5 A’s

Step 1: Ask a clinical question
Step 2: Acquire the best evidence
Step 3: Appraise the evidence
Step 4: Apply the evidence
Step 5: Assess the impact and performance
Practising EBM – the 5 A’s

Step 1: Ask a clinical question
Step 2: Acquire the best evidence
Step 3: Appraise the evidence
Step 4: Apply the evidence
Step 5: Assess the impact and performance
Size of Medical Knowledge

• NLM MetaThesaurus
  – ~1.0 million concepts
  – 2.14 million concept names

• Diagnosis Pro
  – 13,000 diseases
  – 30,000 abnormalities (symptoms, signs, lab, X-ray,)
  – But there’ll be new one’s (4-5 per week)!

To cover the vast field of medicine in four years is an impossible task.
- William Olser
How many randomized trials are published each year you would have to read 500 RCTS per week in 2008 to cover the published RCTs in PubMed.
Angela is a patient on the general medical ward who recently moved to the area to be closer to her son and his family.

She is 72 years old and has a history of congestive heart failure. She was admitted 2 days ago having presenting with non specific chest pain, shortness of breath, an enlarged liver, swollen ankles and has been diagnosed with a Non –ST elevation MI.

She has been hospitalized twice within the last 6 months for worsening of heart failure.

At the present time she says she is pain free and is extremely diligent about taking her medications (lisinopril and aspirin), and wants desperately to stay out of the hospital. She reports being mobile and lives alone with several cats.

She also tells you she is a bit hard of hearing, has a slight cough, is a smoker of 20 cigs a day for 40 years. When you examine her: BP is 170/90, her ankles are slightly swollen, her pulse is 80 and irregular.

She is about to be discharged home on her previous medications plus 25mg spironolactone od. She is happy to be going home and asks you if this new medication will help her stay out of hospital?

What are your questions?
Experience and skill base

Types of questions

About the disorder, test, treatment, etc.
2 components:
a. Root* + Verb: “What causes ...”
b. Condition: “... SARS?”
- Textbooks/online

About patient care decisions and actions
4 (or less) components:
a. Patient, problem, or population
b. Intervention, exposure, or maneuver
c. Comparison (if relevant)
d. clinical Outcomes
   (including Time horizon)
<table>
<thead>
<tr>
<th><strong>Patient or Problem</strong></th>
<th><strong>Intervention</strong></th>
<th><strong>Comparison intervention</strong></th>
<th><strong>Outcomes</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Describe a group of patients similar to your own</td>
<td>What intervention are you considering</td>
<td>What is the main alternative to the intervention</td>
<td>What do you hope to accomplish with the intervention</td>
</tr>
<tr>
<td>“In elderly patients with congestive heart failure ...”</td>
<td>...does treatment with spirinolactone ...</td>
<td>...when compared with standard therapy alone...</td>
<td>...lead to a decrease in hospitalization “</td>
</tr>
</tbody>
</table>
Types of questions

About the disorder, test, treatment, etc.

2 components:

a. Root* + Verb: “What causes ...”

b. Condition: “… SARS?”

- Textbooks/online

Experience and skill base
Bell’s palsy is a facial paralysis, usually unilateral, and of sudden onset. It is a lower motor neurone palsy usually diagnosed by exclusion. Typically, presentation is with facial distortion, loss of taste, hyperacusis and a watery eye.

- Bell’s palsy was previously considered as an idiothetic lower motor neurone nerve palsy but there has been increasing evidence to suggest that the main cause of Bell’s palsy is latent herpes viruses (herpes simplex virus type 1 and herpes zoster virus), which are reactivated from cranial nerve ganglia.
  - polymerase chain reaction techniques have isolated herpes virus DNA from the facial nerve during acute palsy.
  - inflammation of the nerve initially results in a reversible neurapraxia - however ultimately Wallerian degeneration ensues.
  - herpes zoster virus appears to exhibit more aggressive biological behaviour than herpes simplex virus type 1 - this is because it spreads transversely through the nerve by way of satellite cells.

Note that a fifth of cases of acute facial palsy have an alternative cause that should be managed appropriately.

Reference:
- (1) N Julian Holland, Graeme M Weiner, Recent developments in Bell’s palsy, BMJ, 2004, September 04;329:553-557
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
1 Signs and symptoms
2 Cause
3 Pathology
4 Diagnosis
5 Treatment
5.1 Steroids
5.2 Antibiotics
5.3 Surgery
5.4 Complementary therapy
5.5 Physiotherapy

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

ICD-10  Q51.0
ICD-9  351.0
DiseasesDB  1303
MedlinePlus  000770
Types of questions

About patient care decisions and actions
4 (or less) components:

a. Patient, problem, or population
b. Intervention, exposure, or maneuver
c. Comparison (if relevant)
d. clinical Outcomes (including Time horizon)
‘Foreground’ Questions – PICO(T)

About patient care decisions and actions

• 4 (or 2-3) components:
  
  • a. In Patients with Bell’s Palsy
  • b. Do (I) corticosteroids
  • c. Compared to placebo
  • d. Improve facial function (O) (at 3 months (T))
Clinical scenario

- Mr Whish, is a 69 yr retiree. He comes to see you today as she is frustrated by the symptoms of his irritable bowel syndrome. He feels that they have got worse and despite trying numerous things that you have suggested nothing has helped. He read an article in The Daily Mail suggesting that probiotic drinks help and wonders what you think?
<table>
<thead>
<tr>
<th></th>
<th>Broad</th>
<th>Specific</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient/Population</strong></td>
<td>Adults with IBS</td>
<td>Gender? Age? How long have they had IBS?</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>Probiotics</td>
<td>Type? Tablet? Drink?</td>
</tr>
<tr>
<td><strong>Comparison</strong></td>
<td>No probiotics</td>
<td>Placebo? Standard therapy?</td>
</tr>
<tr>
<td><strong>Outcome</strong></td>
<td>Improve symptoms</td>
<td>Which ones? All?</td>
</tr>
</tbody>
</table>
Short exercise...

• Think of a clinical question/scenario
• Frame it using PICO tool
Practising EBM – the 5 A’s

- Step 1: Ask a clinical question
- Step 2: Acquire the best evidence
- Step 3: Appraise the evidence
- Step 4: Apply the evidence
- Step 5: Assess the impact and performance
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
Levels of evidence tables

<table>
<thead>
<tr>
<th>Question</th>
<th>Step 1 (Level 1*)</th>
<th>Step 2 (Level 2*)</th>
<th>Step 3 (Level 3*)</th>
<th>Step 4 (Level 4*)</th>
<th>Step 5 (Level 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>How common is the problem?</td>
<td>Local and current random sample surveys (or censuses)</td>
<td>Systematic review of surveys that allow matching to local circumstances**</td>
<td>Local non-random sample**</td>
<td>Case-series**</td>
<td>n/a</td>
</tr>
<tr>
<td>Is this diagnostic or monitoring test accurate? (Diagnosis)</td>
<td>Systematic review of cross sectional studies with consistently applied reference standard and blinding</td>
<td>Individual cross sectional studies with consistently applied reference standard and blinding</td>
<td>Non-consecutive studies, or studies without consistently applied reference standard**</td>
<td>Case-control studies, or <em>poor or non-independent reference standard</em>*</td>
<td>Mechanism-based reasoning</td>
</tr>
<tr>
<td>What will happen if we do not add a therapy? (Prognosis)</td>
<td>Systematic review of inception cohort studies</td>
<td>Inception cohort studies</td>
<td>Cohort study or control arm of randomized trial*</td>
<td>Case-series or case-control studies, or poor quality prognostic cohort study**</td>
<td>n/a</td>
</tr>
<tr>
<td>Does this intervention help? (Treatment Benefits)</td>
<td>Systematic review of randomized trials or n-of-1 trials</td>
<td>Randomized trial or observational study with dramatic effect</td>
<td>Non-randomized controlled cohort/follow-up study**</td>
<td>Case-series, case-control studies, or historically controlled studies**</td>
<td>Mechanism-based reasoning</td>
</tr>
<tr>
<td>What are the COMMON harms? (Treatment Harms)</td>
<td>Systematic review of randomized trials, systematic review of nested case-control studies, n-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect</td>
<td>Individual randomized trial or (exceptionally) observational study with dramatic effect</td>
<td>Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)**</td>
<td>Case-series, case-control, or historically controlled studies**</td>
<td>Mechanism-based reasoning</td>
</tr>
<tr>
<td>What are the RARE harms? (Treatment Harms)</td>
<td>Systematic review of randomized trials or n-of-1 trial</td>
<td>Randomized trial or (exceptionally) observational study with dramatic effect</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is this (early detection) test worthwhile? (Screening)</td>
<td>Systematic review of randomized trials</td>
<td>Randomized trial</td>
<td>Non-randomized controlled cohort/follow-up study**</td>
<td>Case-series, case-control, or historically controlled studies**</td>
<td>Mechanism-based reasoning</td>
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http://www.cebm.net/ocebmln-evidence-levels-of-evidence/
Practising EBM – the 5 A’s

Step 1: Ask a clinical question

Step 2: Acquire the best evidence

Step 3: Appraise the evidence

Step 4: Apply the evidence

Step 5: Assess the impact and performance
Levels of evidence tables: Bias bingo

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<th>Step 4 (Level 4*)</th>
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<td>How common is the problem?</td>
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<td></td>
<td></td>
<td>n/a</td>
</tr>
</tbody>
</table>


Bias
Bias in RCTs

Table 8.4.a: A common classification scheme for bias

<table>
<thead>
<tr>
<th>Type of bias</th>
<th>Description</th>
<th>Relevant domains in the Collaboration’s ‘Risk of bias’ tool</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selection bias.</td>
<td>Systematic differences between baseline characteristics of the groups that are compared.</td>
<td>• Sequence generation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Allocation concealment.</td>
</tr>
<tr>
<td>Performance bias.</td>
<td>Systematic differences between groups in the care that is provided, or in exposure to factors other than the interventions of interest.</td>
<td>• Blinding of participants and personnel.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Other potential threats to validity.</td>
</tr>
<tr>
<td>Detection bias.</td>
<td>Systematic differences between groups in how outcomes are determined.</td>
<td>• Blinding of outcome assessment.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Other potential threats to validity.</td>
</tr>
<tr>
<td>Attrition bias.</td>
<td>Systematic differences between groups in withdrawals from a study.</td>
<td>• Incomplete outcome data</td>
</tr>
<tr>
<td>Reporting bias.</td>
<td>Systematic differences between reported and unreported findings.</td>
<td>• Selective outcome reporting (see also Chapter 10).</td>
</tr>
</tbody>
</table>

estimates showed the presence of this bias could exaggerate treatment effect from 5 percent to 51 percent

http://handbook.cochrane.org/chapter_8/8_assessing_risk_of_bias_in_included_studies.htm
Bias in observational studies
Confounding factors

Other patient features/causal factors, apart from the one being measured, that can affect the outcome of the study e.g..
Validity of the study

Outside the study: external validity
Can the findings be applied to different settings (e.g., given patient population)?

Critical appraisal

Inside the study: internal validity
Can we believe the results?
Practising EBM – the 5 A’s

Step 1: Ask a clinical question

Step 2: Acquire the best evidence

Step 3: Appraise the evidence

Step 4: Apply the evidence

Step 5: Assess the impact and performance
‘Forefront’ Questions – PICO(T)

About patient care **decisions** and **actions**

- 4 (or 2-3) components:
  - a. In **P**atients with Bell’s Palsy
  - b. Do (I) corticosteroids
  - c. **C**ompared to placebo
  - d. Improve facial function (O) (at 3 months (T))
Early Treatment with Prednisolone or Acyclovir in Bell's Palsy


BACKGROUND
Corticosteroids and antiviral agents are widely used to treat the early stages of idiopathic facial paralysis (i.e., Bell’s palsy), but their effectiveness is uncertain.

Full Text of Background...

METHODS
We conducted a double-blind, placebo-controlled, randomized, factorial trial involving patients with Bell’s palsy who were recruited within 72 hours after the onset of symptoms. Patients were randomly assigned to receive 10 days of treatment with prednisolone, acyclovir, both agents, or placebo. The primary outcome was recovery of facial 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 76.7% among patients who did not receive acyclovir.
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.
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
In the control group 64 people out of 100 will have recovered facial function, compared to 83 out of 100 for the active treatment group.
Shared decision making is the process of clinician and patient jointly participating in a health decision after discussing the options, the benefits and harms, and considering the patient's values, preferences, and circumstances.
### Table 4. Adverse Events.

<table>
<thead>
<tr>
<th>Event</th>
<th>Prednisolone–Placebo</th>
<th>Acyclovir–Prednisolone</th>
<th>Placebo–Prednisolone</th>
<th>Acyclovir–Placebo</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dizziness</td>
<td>5</td>
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<tr>
<td>Death</td>
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<td>2</td>
<td>1</td>
<td>3</td>
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<tr>
<td>Total</td>
<td>24</td>
<td>25</td>
<td>20</td>
<td>19</td>
<td>88</td>
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</table>

* Patients with two or more symptoms (e.g., dizziness and vomiting) are listed in this category only and are not duplicated in categories corresponding to a separate symptom (i.e., dizziness or vomiting).
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

Relative risk = 83/64 = 1.29 or 29%
Risk difference = 83-64 = 19%
Number Needed to Treat (for benefit) = 100/19 = 6

Give/not give corticosteroid AND send to ENT
Does SDM work?

“moderate quality evidence that interventions that aim to facilitate shared decision making reduce antibiotic use for ARIs in primary care (immediately after or within six weeks of the consultation), compared with usual care, from 47% to 29%: risk ratio (RR) 0.61, 95% confidence interval (CI) 0.55 to 0.68”
Practising EBM – the 5 A’s

- **Step 1**: Ask a clinical question
- **Step 2**: Acquire the best evidence
- **Step 3**: Appraise the evidence
- **Step 4**: Apply the evidence
- **Step 5**: Assess the impact and performance
HOW DID I DO?
Assess the impact and performance

- How is your patient?
  - Short and long term, safety netting, follow up, handover

- Did the decision improve the outcome of interest?
  - Log of activities, recall of patient encounters

- What did I learn from that?
  - Reflection, significant event analysis

- How might I use this experience again?
  - Building clinical expertise, personal development, write about it

- How might I share this experience with others?
  - Dissemination of good (and bad) practice
**Abstract**

**Background**—Although several prospective studies have shown that low folate intake and low circulating folate are associated with increased risk of coronary heart disease (CHD), the findings are inconsistent.

**Methods and Results**—We studied the associations of dietary intake of folate, vitamin B₆, and vitamin B₁₂ with the risk of acute coronary events in a prospective cohort study of 1980 Finnish men 42 to 60 years old examined in 1984 to 1989 in the Kuopio Ischemic Heart Disease Risk Factor Study. Nutrient intakes were assessed by 4-day food record. During an average follow-up time of 10 years, 199 acute coronary events occurred. In a Cox proportional hazards model adjusted for 21 conventional and nutritional CHD risk factors, men in the highest fifth of folate intake had a relative risk of acute coronary events of 0.45 (95% CI 0.25 to 0.81, \( P = 0.008 \)) compared with men in the lowest fifth. This association was stronger in nonsmokers and light alcohol users than in smokers and alcohol users. A high dietary intake of vitamin B₆ had no significant association and that of vitamin B₁₂ a weak association with a reduced risk of acute coronary events.

**Conclusions**—The present work in CHD-free middle-aged men is the first prospective cohort study to observe a significant inverse association between quantitatively assessed moderate-to-high folate intakes and incidence of acute coronary events in men. Our findings provide further support in favor of a role of folate in the promotion of good cardiovascular health.

**Key Words:** cardiovascular diseases · diet · epidemiology · follow-up studies · nutrition
**Abstract 2**

<table>
<thead>
<tr>
<th><strong>P</strong></th>
<th><strong>I</strong></th>
<th><strong>C</strong></th>
<th><strong>O</strong></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Folate, Vit B6, and Vit B12 supplements</td>
<td>No supplements</td>
<td>Death from CV causes, MI and stroke</td>
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</table>

**METHODS**

We randomly assigned 5522 patients 55 years of age or older who had vascular disease or diabetes to daily treatment either with the combination of 2.5 mg of folic acid, 50 mg of vitamin B6, and 1 mg of vitamin B12 or with placebo for an average of five years. The primary outcome was a composite of death from cardiovascular causes, myocardial infarction, and stroke.

**RESULTS**

Mean plasma homocysteine levels decreased by 2.4 μmol per liter (0.3 mg per liter) in the active-treatment group and increased by 0.8 μmol per liter (0.1 mg per liter) in the placebo group. Primary outcome events occurred in 619 patients (18.8 percent) assigned to active therapy and 647 (19.8 percent) assigned to placebo (relative risk, 0.95; 95 percent confidence interval, 0.84 to 1.07; P=0.41). As compared with placebo, active treatment did not significantly decrease the risk of death from cardiovascular causes (relative risk, 0.96; 95 percent confidence interval, 0.81 to 1.13), myocardial infarction (relative risk, 0.98; 95 percent confidence interval, 0.85 to 1.14), or any of the secondary outcomes. Fewer patients assigned to active treatment than to placebo had a stroke (relative risk, 0.75; 95 percent confidence interval, 0.59 to 0.97). More patients in the active-treatment group were hospitalized for unstable angina (relative risk, 1.24; 95 percent confidence interval, 1.04 to 1.49).

**CONCLUSIONS**

Supplements combining folic acid and vitamins B6 and B12 did not reduce the risk of major cardiovascular events in patients with vascular disease. (ClinicalTrials.gov number, NCT00106885; Current Controlled Trials number, ISRCTN14017017.)
Abstract 3

**P** Children diagnosed with headaches

**I**

**C** Frequency and type of headaches in adulthood

**O**

Background: Headaches affect most children and rank third among illness-related causes of school absenteeism. Although the short-term outcome for most children appears favorable, few studies have reported long-term outcome.

Objective: To evaluate the long-term prognosis of childhood headaches 20 years after initial diagnosis in a cohort of Atlantic Canadian children who had headaches diagnosed in 1983.

Methods: Ninety-five patients with headaches who consulted 1 of the authors in 1983 were previously studied in 1993. The 77 patients contacted in 1993 were followed up in 2003. A standardized interview protocol was used.

Results: Sixty (78%) of 77 patients responded (60 of the 95 of the original cohort). At 20-year follow-up, 16 (27%) were headache free, 20 (33%) had tension-type headaches, 10 (17%) had migraine, and 14 (23%) had migraine and tension-type headaches. Having more than 1 headache type was more prevalent than at diagnosis or initial follow-up (P<.001), and headache type varied across time. Of those with headaches at follow-up, 80% (35/44) described their headaches as moderate or severe, although an improvement in headaches was reported by 29 (66%). Tension-type headaches were more likely than migraine to remit (P<.04). Headache severity at diagnosis was predictive of headache outcome at 20 years. During the month before follow-up, nonprescription medications were used by 31 (70%) of those with ongoing headaches, and prescription medications were used by 6 (14%). However, 20 (45%) believed that nonpharmacological methods were most effective. Medication use increased during the 10 years since last follow-up. No patient used selective serotonin receptor agonists (triptans).

Conclusions: Twenty years after diagnosis of pediatric headache, most patients continue to have headache, although the headache classification often changes across time. Most patients report moderate or severe headache and increasingly choose to care for their headaches pharmacologically.
Useful resources

Principles of EBM:

Critical appraisal:

Geeky fun: