FREQUENTLY ASKED QUESTIONS

In the last few months many of our readers have written, faxed, E-mailed and telephoned to obtain back numbers, to ask questions about Bandolier and how they might obtain it, and to pass on messages of support. To all of you, thanks.

We are struggling to keep up with you. In the best British traditions Bandolier is run on a shoestring, written in a leaky Portacabin, and has no secretarial support. Our telephone line is overloaded, so please write or fax unless it’s urgent.

Origins and policy

Bandolier was financed as an experiment by the former Oxford RHAR&D Directorate (in Feb ’94) to bring evidence to the coal-face, and to highlight problems in assessing evidence. Circulation has risen steadily towards 20,000 as R&D Directors of other regions purchase Bandolier at cost for purchasers and GPs. The raw cost of writing, printing and distributing Bandolier is about 60p per copy.

Bandolier is also made available to non-NHS subscribers. They pay the full economic cost of production and distribution, which is why we have a £2.50 price on the masthead. Bandolier receives no funds or other support from non-NHS sources other than from these subscriptions.

Bandolier responds to questions from our readers (mainly GPs), and from stimulating evidence-based articles, mainly in major medical journals.

Bandolier is available on the Internet at the address shown below. This is important because back numbers are now all but exhausted. If you want copies of stories from back numbers, your library information service should be able to download and print the relevant bits. In addition, we are exploring the possibility of a bumper annual reprint - of which more as plans firm up.

The future of Bandolier

We think Bandolier is appreciated from the comments in your letters, calls, and even Christmas cards. Now we need you to tell us in droves that Bandolier is appreciated and needed. The reason is that we are reaching a watershed as the Regional Health Authorities cease to exist in April 1996 - so Bandolier’s funding will necessarily have to change.

If you want Bandolier to continue (and we believe that the experiment should continue for another 3 years with Bandolier free within the NHS), then please write or fax (01865 226978) and tell us so. Please don’t ‘phone, as we can’t write and answer the ‘phone at the same time.

PILLS, PURCHASING & PRESENTATION

Readers will be well aware that Bandolier has a bee in its bonnet about the way that information is presented. The number-needed-to-treat (NNT) has been used frequently to convey the numerical power of clinically relevant end-point.

If the manner of presentation affects the way in which the information is used, then presentation becomes as important or even more important than the information itself.

Perhaps this is self-evident. It explains the clever advertisements which appear in our papers, on our TV screens, and in many of the medical and scientific journals we read.

Pills

The “Dear Doctor” letter from the Committee on the Safety of Medicines of October 18 stated that “combined oral contraceptives containing desogestrel and gestodene are associated with around a two-fold increase in the risk of thromboembolism”. It is not easy to advise an anxious patient on the basis of this statement.

The Sunday Times of October 22 gave some numerical estimates of the increased risk. With the suspect pill the risk “appeared to be double that of other, older brands - at a rate of 30 incidents per 100,000 women”. It also helpfully stated that “the risk for a healthy woman not on the pill is 5 per 100,000, while the risk of thrombosis during pregnancy is 60 per 100,000”.

Bandolier has no knowledge that these numbers form the evidence upon which the CSM based its decision. They can, however, form the basis on which to calculate NNTs for this intervention (though perhaps here we should be using the NNH - numbers-needed-to-harm!). In any event, using these numbers Bandolier calculates that:

- Compared with other pill brands there is an increased risk of a thrombosis (odds ratio 1.95, 95%CI 1.1 - 3.5). One woman in 6667 on the suspect brands would have a thrombosis who would not have had a thrombosis if she had been taking other brands (NNT 6667, 95%CI 3553 - 53950).
- Compared with not being on the pill there is an increased risk of a thrombosis with the suspect brands (odds ratio 4.2, 95%CI 2.2 - 8.1). One woman in 4000 on the suspect brands would have a thrombosis who would not have had a thrombosis if she had not been on the pill (NNT 4000, 95%CI 2733 to 7459).
Compared with being pregnant there is a significantly lower risk of thrombosis with the suspect brands (odds ratio 0.5, 95% CI 0.34 - 0.78).

*Bandolier* believes that these clinically interpretable numbers, one in 6,667 versus other pill brands and one in 4,000 versus no pill, would have made the 'Dear Doctor' letter more useful (above and beyond all the arguments about the process of letting everyone know).

Many other questions are, of course, left unanswered until the data from the trials on which the CSM based its conclusions are published. Was there, for instance, any evidence of some benefit from the use of the suspect pills which could be set against the increased risk of thromboembolism?

**Purchasers and presentation**

The importance of the way in which information is presented is emphasised by Fahey et al [1], who gave 182 health authority members results from a randomised trial on breast cancer screening and results from a systematic review on cardiac rehabilitation. The results were presented to them (shown in the table below) in four different ways:

- relative risk reduction
- absolute risk reduction
- proportion of event-free patients
- numbers of patients treated to prevent one death

From the 140 questionnaires returned the willingness to fund either programme was influenced significantly by the way in which results were presented.

Relative risk reduction produced significantly higher inclination to purchase, followed by NNT. Intriguingly only three respondents, “all non-executive members claiming no training in epidemiology” said that they realised that all four sets of data summarised the same results.

**Doctors and presentation**

It is not only members of health authorities who are susceptible to altered perceptions of effectiveness according to the way in which the results of studies are presented to them. Two studies have looked at the effects of presentation on decisions by doctors in teaching hospitals in Canada [2] and on GPs in Italy [3]. Both used data from the Helsinki heart study.

<table>
<thead>
<tr>
<th>Data on &quot;any myocardial infarction&quot; scored by teaching hospital doctors according to method of presentation</th>
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<tbody>
<tr>
<td><strong>Relative RR</strong></td>
</tr>
<tr>
<td><strong>Absolute RR</strong></td>
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<tr>
<td><strong>NNT</strong></td>
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<tr>
<td>Score</td>
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<td>0</td>
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In the first of these studies, David Naylor and colleagues [2] compared clinicians’ ratings of therapeutic effectiveness by looking at different end-points presented as percent reductions in relative risk, absolute risk, and numbers-needed-to-treat. The study was conducted using random allocation of questionnaires which used relative data or absolute data, each with NNT data, among doctors of various grades at Toronto teaching hospitals. They used an 11-point scale anchored at “no effect” and running from -5 “harmful” to +5 “very effective”.

Relative presentation consistently showed a tendency to higher scores - that is the intervention was interpreted as being more effective. Where data from a single end point, that for any myocardial infarction, was examined, both relative and absolute comparison was scored consistently higher than NNT presentation of the same data.

<table>
<thead>
<tr>
<th>Information presentation</th>
<th>Mammography</th>
<th>Cardiac rehabilitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative risk reduction</td>
<td>34%</td>
<td>20%</td>
</tr>
<tr>
<td>Absolute risk reduction</td>
<td>0.06%</td>
<td>3%</td>
</tr>
<tr>
<td>Percent of event-free patients</td>
<td>99.82 vs 99.8%</td>
<td>84 vs 87%</td>
</tr>
<tr>
<td>Number-needed-to-treat</td>
<td>1592</td>
<td>31</td>
</tr>
</tbody>
</table>
The results are shown in the figure above. NNT reporting of the same information produced a reduction of about 2 points in the effectiveness scale, reducing the judgement from quite effective to one of only slight effect.

**General practitioners**

This second study [3] presented information to 148 GPs using information from the trial as if it referred to five different drugs. The presentations were:

- relative risk reduction
- absolute risk reduction
- difference in event-free patients
- NNT to prevent one event
- events reduction and mortality

For each statement about effects, the GPs were asked to mark a 10 cm line labelled “I would definitely not prescribe this drug” on the left and “I would definitely prescribe this drug” on the right. The statements were presented in random sequences.

The results are shown in the figure. Presentation as relative risk reduction produced a very large tendency towards prescribing with a mean score of 7.7 out of 10. All other presentations produced scores of between about 2.5 and 3.5.

**Comment**

This is all very interesting, but what does it mean? One simple message comes from all three studies. For those who want to influence others, use the relative risk reduction as your means of presenting data. For those who are likely to be influenced by data presentation, never, ever, accept information on the basis of relative risk reduction alone.

There is a more complicated message, for which, to some extent, we need to answer the question about what should be the “true” or “appropriate” response to these various forms of data presentation? This is not answerable, however, at least not in any simple way.

A secondary response is then to ask whether you actually understand the result - is the difference in event free patients or absolute risk reduction immediately useful to you? Would you rather have a few words which conveyed the message - something like “X patients have to be treated for one to benefit”? Perhaps that is why NNT is becoming the presentation method of choice.

In any event, armed with this information it will be an interesting experience to examine articles, talks and advertisements to see how the information is being presented.

**References:**

Bell’s palsy

Bell’s palsy is more and more frequently being asked by GPs about particular problems. Not all can be answered, but we thought we could try for the question “Should steroids be used to treat Bell’s palsy?”, and whether it is important that treatment should be started within the first 24 hours for it to be effective. Little did we realise!

The textbook answer is straightforward. Cecil (17th edition, 1985) states: “Most authorities recommend treatment with prednisone” and “it is claimed that prednisone treatment should be instituted as soon as possible”. The Oxford Textbook of Medicine (1996, 3rd edition) says “There is some evidence that corticosteroids may be advantageous by reducing oedema in the nerve”, and “it is justifiable to treat all cases with corticosteroids if seen within a few days of onset, providing no contraindications to such treatment exists.”

Not much equivocation here. But neither source uses references in support of their statements - and, indeed, why should they? Textbooks are not original articles, but condensates of knowledge, or general maps of a subject. If we want to know more, then we should consult maps with more miles to the inch - and do some searching of our own, even though here is a problem which is not rare (one case per GP per year) and for which there are clear textbook statements.

The searching strategy to find relevant studies used the freetext terms “Bell’s” and “palsy” between the years 1966 and 1995. We found three reports since 1990, only one of which was relevant. This is reported in detail below and is followed by a commentary about the quality of the study and the level of evidence that it represents.

Prednisolone in Bell’s palsy

The study [1] was relatively recent, being published in November 1994 from the University of Alexandria in Egypt. It was not randomised because it was considered unethical to withhold steroids from patients with no contraindications. It was an open study, and blinding of treatments was not used.

Patients

One hundred and sixty patients with acute non recur rent unilateral Bell’s palsy of no more than six days duration were studied. All had complete or nearly complete facial paralysis. None had severe hypertension, glaucoma, peptic ulcer, cardiac disease, diabetes or were pregnant.

The study group of 97 patients received prednisolone tablets at a dose of 1 mg/kg body weight (maximum 70 mg) in divided doses with meals for six days, and the dose was then reduced gradually over the next four days.

The control group of 67 patients were not given prednisolone or any other treatment other than oral paracetamol for pain. This group comprised patients who had refused prednisolone because of fears of complications or who had a relative contraindication like heartburn or moderate hypertension.

All patients received superficial muscle heating, massage and electrical muscle stimulation for all the paralysed facial muscles, three sessions a week until complete recovery or up to six months.

Initial clinical gradings and later evaluations were made by a doctor who was blind to the patients’ grouping. Electrophysiological measurements were also made of nerve function. Four categories of clinical recovery were defined:

- **Excellent recovery** - patients with no evidence of facial muscle denervation and no residual facial asymmetry within six months without complication.
- **Good recovery** - patients with minimal or no facial muscle denervation, but had negligible residual facial asymmetry only on close inspection during maximum effort on smiling and within six months of onset.
- **Fair recovery** - patients with partial facial muscle denervation and mild residual facial muscle

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Satisfactory recovery/total patients</th>
<th>Odds Ratio (95% CI)</th>
<th>NNT (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control patients</td>
<td>46/67 (69%)</td>
<td>2.6 (1.2 - 5.5)</td>
<td>6.1 (3.4 - 33.2)</td>
</tr>
<tr>
<td>All treated patients</td>
<td>79/93 (85%)</td>
<td>5.7 (1.9 - 17.2)</td>
<td>3.2 (2.4 - 4.9)</td>
</tr>
<tr>
<td>Treated within 24 hours</td>
<td>23/23 (100%)</td>
<td>2.3 (0.7 - 6.8)</td>
<td>6.1 (2.8 - ∞)</td>
</tr>
<tr>
<td>Treated between 24 and 48 hours</td>
<td>17/20 (85%)</td>
<td>1.5 (0.5 - 4.6)</td>
<td>12.8 (3.2 - ∞)</td>
</tr>
<tr>
<td>Treated between 2 and 3 days</td>
<td>13/17 (76%)</td>
<td>1.6 (0.7 - 4.1)</td>
<td>9.9 (3.6 - ∞)</td>
</tr>
<tr>
<td>Treated between 3 and 5 days</td>
<td>26/33 (78%)</td>
<td></td>
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</table>

Data are taken from [1], with effective treatment defined as a clinically excellent or good result.
weakness on maximal effort within one year of disease onset.

- **Poor recovery** - patients with facial nerve denervation and incomplete clinical recovery (obvious facial weakness) in spite of physical therapy for one year after disease onset.

A satisfactory recovery was defined as excellent or good, and an unsatisfactory recovery was defined as fair or poor.

**Results**

The results are shown in the table and figure. Without steroid treatment there was a high rate of satisfactory recovery (by 46 of 67 patients, 69%).

The rate of satisfactory recovery in all steroid treated patients was higher (79 of 93 patients, 85%). This produced an NNT of 6; that is, for every six patients treated with prednisolone within 24 hours of onset of the paralysis, one extra patient had a satisfactory recovery compared with no treatment.

Treatment after 24 hours failed to show a statistically significant difference from the recovery rate in the control group. There was a higher recovery rate in all treatment subgroups than in the control group, the lowest rate of satisfactory recovery being 76%.

**Comment**

There are very serious problems with this paper. Foremost is the fact that the study was not random (perhaps for good reasons), and, while the evaluations were said to be blind, it is very difficult to limit leakage of blinding in a study which must have taken at least two years. Absence of randomisation and blinding will lead to overestimation of treatment effects. Neither is the design of the study a classical case-control design.

The numbers in the subgroups were not large. With larger numbers of patients (or more patients included in a meta-analysis), beneficial effects which may be present with corticosteroid administration later than 24 hours after the onset of the facial paralysis. A case perhaps of absence of evidence not being the same as evidence of absence [2].

However it is also the case that there are at least two randomised controlled trials [3,4], published over 20 years ago, one of which [3] examined large numbers of patients treated with steroid and placebo. They both came to a negative conclusion, that treatment with corticosteroid did not increase overall cure rates. Neither, however, looked specifically at the effects of early treatment, and the preponderance of patients in these studies began steroid treatment more than 24 hours after the onset of facial paralysis.

A number of non-randomised studies, also in the 1970s, showed significant benefit with steroid. In Bandolier 17, the way in which inadequate randomisation and blinding led to over-estimation of treatment effects was examined, and steroid treatment of Bell's palsy seems to be an example of that.

Only one report in our search mentioned the effects of early treatment. This study in an Indian journal is still awaited, but there was no indication that it was randomised.

**What should GPs do?**

Make up their own minds based on local guidelines and their experience, just as now.
randomised trials. We know that these are likely to exaggerate the effects of treatment; two randomised trials were negative.

This is a classic problem, where textbooks appear to be regurgitating the advice from non-randomised studies and ignoring the randomised. What is needed for Bell’s palsy is a thorough systematic review of the literature, and we hope that friends of Bandolier will undertake it.

Even then, this may not be enough. To answer the original questions, especially that of the benefits of early administration of steroids, a new randomised controlled trial may yet be needed.

References:


GENE WATCH

Two reports about genetics have recently been published by the NHS Central R&D Committee [1,2]. They are complementary and are worth having on the shelf as useful aides memoir.

Genetics Research Advisory Group

This report [1] concentrates on the impact of advances in genetic testing and understanding of disorders at a biochemical level, and looks forward to preventative medicine through screening for genes which predispose to certain diseases. Cystic fibrosis, muscular dystrophy, haemophilia, immune deficiencies and coronary artery disease are discussed. There are useful chapters (short, readable and pertinent) about genetic techniques, laboratory services and the delivery of genetic services in the NHS.

The recommendations of the group are mainly about the need for directed research in particular areas - concentrating, for instance, on screening for Down’s syndrome and cystic fibrosis, but with the important proviso that genetic screening with its ethical overtones will need, like cancer screening, careful thought, evaluation and counselling.

Genetics of common diseases

The second report [2] examines the genetics of common diseases. It has much to commend it. Because much of the groundwork was covered in the first report, this second report is more expansive. It has a useful glossary for those of us unused to this area, some intriguing maps of chromosomes with the gene loci so we can actually see where the problem lies, and it has a valuable set of appendices bringing together genetic information on particular topics - diabetes, breast cancer, colon cancer, cardiovascular disease, coronary artery disease, rheumatoid arthritis, Alzheimer’s disease and venous thrombosis. The way each of these is handled in text and appendices really brings the reader up to the present state of the art with remarkably little brain ache.

Each topic has its own interesting questions. Venous thrombosis, for example, may be associated with a defect in blood coagulation factor V. This genetic defect (Factor V Leiden) may be present in up to 5% of the population. Since these individuals are at higher risk of venous thrombosis (in one study of men over 60 years with venous thrombosis, 26% had the mutation), a key question is whether screening for this genetic defect is practical for patients undergoing major surgery where thrombosis is common, and if practical whether it is effective or cost effective. The jury is hardly selected yet, but some centres are considering research projects.

Summarising the reports:

1. Progress in genetics is very rapid, partly as a by-product of the human genome mapping programme.
2. Almost all major disease susceptibility genes (and some genes conferring protection) will be identified in the next 5-10 years and techniques will be available to detect mutations and polymorphisms in them.
This will lead to:

- a better understanding of the pathophysiology of common diseases
- a new taxonomy of disease
- opportunities to prevent some diseases and for earlier and more effective treatment of others
- more accurately targeted therapies
- fewer side effects from therapy
- more effective use of limited health care resources

If the potential benefits of this progress are to be achieved a carefully planned programme of research and development will need to be implemented in:-

- education, both public and professional
- screening for high risk groups and perhaps whole populations
- counselling
- service organisation and development involving ongoing formal evaluations and integration of primary care into genetic services

Educational programmes are needed to increase public and professional understanding of the new genetics.

Consequences of progress in molecular genetics will not be limited to the areas currently considered under the umbrella of genetics but will impinge widely on many aspects of clinical and laboratory medicine, and indeed to horizons beyond medicine.

Other sources

There are other places to go to look for useful and accessible information on the new genetics. The House of Commons Science and Technology Committee report [3] is longer and a bit more technical. The Welsh Health Planning Forum document [4] examines some of the implications of the new genetics for the NHS.

Internet sources

There are increasing sources on genetic information available on-line and downloadable from the Internet. Dr Eric Sidebottom has produced a list of some useful addresses, shown in the box. Some are UK addresses, and therefore will be quite readily accessible most of the time without some of the delays occasionally found when accessing US sources.

References:
**OTTAWA ANKLE RULES OK**

*Bandolier* 13 was taken with a Canadian newsletter which was the source of interesting evidence-based information. It described the Multicentre Ankle Rules Study which developed and tested a decision aid algorithm in Ontario.

The full results are now published in the BMJ [1], and interesting reading it is. The article describes a simple set of clinical decision rules used as an aid in deciding whether ankle or foot X-rays are needed. The rules are described in full in the BMJ article and are not rehearsed here, therefore.

The important issue was the way in which the rules (guidelines) were implemented to the benefit of patients and the healthcare system.

**The study**

All adult patients seen in eight hospitals in Ontario were studied during a control period of one year before and one year after the introduction of the rules. The control group had nearly 6,300 such patients and the intervention group nearly 6,500. The total population covered was not mentioned, but the individual hospitals included small community to large teaching establishments.

The Ottawa ankle rules were introduced by means of a lecture, handouts, pocket cards and posters in the emergency departments. The main outcome measures were the proportion of patients receiving X-rays and whether that was appropriate, the number of “missed” fractures, patient waiting times, and data on cost effectiveness.

**Results**

The main result was a reduction in the proportion of patients given X-rays from 83% during the control year to 61% during the intervention year. These results were consistent across hospitals and doctors and most doctors used the rules correctly most of the time (over 95%).

So 1081 of 6288 patients with foot or ankle injuries did not have X-rays in the control period, compared with 2534 of 6489 patients in the intervention period. This is statistically significant with an odds ratio of 2.94 (95%CI 2.7 - 3.2).

The number-needed-to-treat (NNT) for the implementation of this intervention was 4.6 (95%CI 4.3 - 4.9). This means that the implementation of the Ottawa ankle rules saved one patient with ankle or foot injury from having an unnecessary X-ray for every five examined compared with not using the rules.

**Benefits and cost-effectiveness**

The patients without fracture spent on average 30 minutes less in the emergency department if they had no X-ray. The average cost differential between those who had and those who did not have an X-ray was $90 - about £50.

**Comment**

What makes the Ottawa ankle rules successful? Probably four things:-

1. The rules were devised and tested with some rigour before they were more generally used.
2. They had a sensitivity of 100%, or close to it. In layman’s terms, they worked. This is an important issue, since many diagnostic and treatment decisions are made on the results of clinical, laboratory or other tests which have sensitivities and specificities far below 100%.
3. They were simple and easy to remember, and so simple and easy to use.
4. Their use produced a simple yes/no decision as to whether to X-ray the foot or ankle.

What are the implications of implementing the Ottawa ankle rules? Probably three things, but putting numerical estimates to them is difficult because the denominator of population was absent from the paper. However, in eight hospitals in one year it:

1. Saved 1713 patients from having an X-ray.
2. Saved 36 patient-days waiting in a hospital emergency room.
3. Saved $154,000.

Divided between eight hospitals this may not seem much compared with the totality of their activity but implementing many things that are simple, cheap and effective can make a big difference over time, especially when the driving force is benefit to patients. This is a splendid example of implementation in action.

**Reference**


**Missed fractures?**

Nearly 2,200 patients without fracture in the intervention period were followed up at about 10 days by telephone call with a response of 94%. Three of 732 (0.4%) who had had an X-ray subsequently had a fracture diagnosed compared with seven of 1,301 (0.5%) who had not had an X-ray.