

ON KNOWLEDGE AND PIGS

Bandolier concentrates in finding evidence in systematic reviews and meta-analysis, on large randomised trials, and on informative observational studies. Each has its place in helping us shape our views on what to do, when, and for whom. Each adds to our knowledge, and sometimes also to our understanding.

Meta-analysis has been under the spotlight of late, with papers and editorials in the *NEJM* and *BMJ*. What can we learn from all this? Firstly, anyone wanting a readable exposition of what this all means could do no better than to read David Naylor's balanced and sensible editorial in the *BMJ* [1]. Then for those who are troubled that meta-analysis of small trials may not be the best thing, there is reassurance from a number of reports [2,3] that most of the time (four times out of five) questions answered both by meta-analysis and by large randomised trials give much the same answer.

Randomness and confidence

Most of the arguments about small trials and meta-analysis occur where only a small proportion of the people involved in the study have a particular outcome - small effects in large populations. In trials of magnesium in acute heart attack, for instance, if only about 7% of people die without treatment, then demonstrating a relative risk reduction of 50% means only three fewer deaths per 100 patients. You therefore need large numbers of patients to make sense of small changes.

But meta-analysis is also done where there are large effects in small populations. Here the issue may be one of effectiveness, in which case a large number of events may be found with smaller numbers of patients. But it can also be one of avoiding bad things which might be consequences of treatment (oral contraceptives being a good example), and again because these happen rarely many patients need to be studied to get accurate and precise information.

When *Bandolier* reads these papers, what it finds striking are the wide confidence intervals reported in statistical outputs like odds ratios, both for trials and for meta-analysis. That reflection of uncertainty tells us something about how little high quality information we have in the face of the random effects seen in clinical trials. Clearly, for more accurate estimates with better precision, more data is needed.

Give me a break

We live in a real world where decisions need to be taken now. So while it is often convenient to say that more research is needed, *Bandolier* sympathises with those who have to make decisions. The good news is that meta-analysis is continually

improving our knowledge about clinical research, how to do it, and how to use the knowledge we gain from it. Anyone forced to sit and read in detail even ten trials on the same topic would soon come up with reasons why some should be kicked to touch.

In praise of observation

Lest you worry that all this is too *recherché*, think about circumstances in which you would be really confident that observations can provide you with high quality evidence.

Imagine that we tell you that *Bandolier* has trained a pig to talk. What foolishness you say. But we bring this talking pig before you and the pig says "Good evening", and proceeds to summarise the day's news for you. Hopefully you would be amazed by this phenomenon, and would not immediately demand a randomised selection of 100 pigs to check it out. The fact that *any* pig can talk is what is important.

Pidgin & creole

Teasing out how language develops involves observational studies and phenomena like the talking pig - or wolf child. Pidgin languages arise "when speakers of different languages have to communicate to carry out practical tasks but do not have the opportunity to learn one another's languages"[4]. Bickerton observed that children exposed to the pidgin at the age when they acquire their mother tongue inject grammatical complexity, and the pidgin becomes a Creole - rules of grammar seem to be innate.

The problem for us in medicine is that we are often looking for cause and effect. Does a class of oral contraceptives cause thrombosis? The observations may generate a hypothesis, but proof may require more stringent study architecture.

In this issue

Knowledge & Pigs	p. 1
BRCA genes - potential & problems	p. 2
Long-term outcome after head injury	p. 4
<i>Bandolier</i> conferences	p. 5
Reducing unnecessary consultations	p. 6
HIV infection - ACTG320 NNTs	p. 7
Health Technology Assessment	p. 8
NNT or IYDT correspondence	p. 8

The views expressed in Bandolier are those of the authors, and are not necessarily those of the NHSE Anglia & Oxford

GENEWATCH: BRCA GENES - POTENTIAL AND PROBLEMS

The same problem of observations and causation is described beautifully by Oliver Sacks [5]. He talks of his visit to Guam and describes the endemic "lytico-bodig" disease. This can present as a progressive paralysis (lytico) or as parkinsonism (bodig) or as dementia. Cycad seed made with fadang flour was a putative cause, but a continued puzzle of this geographical isolate was the fact that the younger people were not affected and the condition may be disappearing (sounds a bit like Kuru!).

It's all done by mirrors

A final observation is about alleviating phantom pain. If the phantom pain is of tightly clenched fingers digging into the absent hand, then putting the "good" hand in front of a mirror (so that it looks like the phantom hand) and unclenching the fist can diminish the phantom pain [6]. The brain is tricked by the mirror into thinking of the good hand as the absent one. Sounds crazy, but this one had been seen to work for a grateful patient.

Talking pig evidence rules sometimes for efficacy, and often for rare and serious adverse events.

References:

- 1 D Naylor. Meta-analysis and the meta-epidemiology of clinical research. *British Medical Journal* 1997 315: 617-9.
- 2 JC Cappelleri, JP Ioannidis, CH Schmid et al. Large trials vs meta-analysis of smaller trials. *Journal of the American Medical Association* 1996 276: 1332-8.
- 3 J LeLorier, G Grégoire, A Benhaddad et al. Discrepancies between meta-analyses and subsequent large randomized controlled trials. *New England Journal of Medicine* 1997 337: 536-42.
- 4 Steven Pinker. *The Language Instinct*; Penguin.
- 5 Oliver Sacks. *The Island of the Colour-blind and Cycad Island*; Picador.
- 6 Ramachandran VS, Rogers-Ramachandran D. Synaesthesia in phantom limbs induced with mirrors. *Proc R Soc Lond B Biol Sci* 1996; 263:377-86.

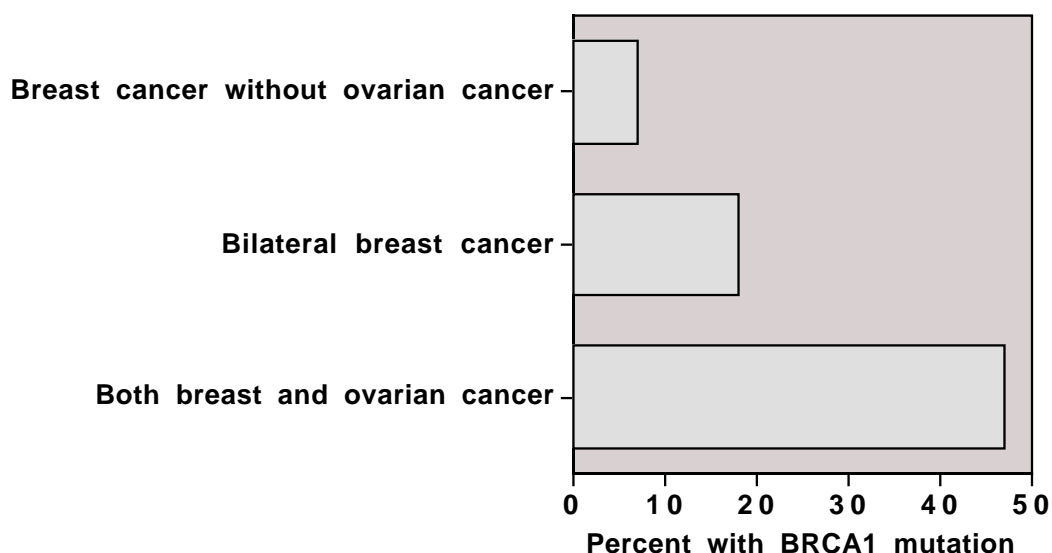
The New England Journal of Medicine had a headline back in May of which *Bandolier* would be proud - "BRCA genes - Bookmaking, Fortunetelling, and Medical care" [1]. It pulled together information in four papers in that issue which examined new research on these genes involved with breast and ovarian cancer. The correspondence published in September is also interesting for those contemplating how to make the best use of new genetic information.

Statistical prophecies

The discovery of the so-called breast cancer genes, BRCA 1 in 1994 and BRCA 2 in the following year, were clearly landmarks in the study of breast cancer. It was naturally hoped, indeed almost assumed, that such important discoveries would quickly be followed by rationally designed improvements in prevention and treatment of this dread disease. The message that a woman with a strong family history of breast and/or ovarian cancer who carries a germ line mutation in one of these genes carries a lifetime risk of breast cancer of about 85%, and about 60% for ovarian cancer, is a very frightening one. Not surprisingly the pressure created for the practical application of these discoveries was almost immediate and very great.

The situation was further complicated by the potential economic returns of genetic testing and the speed with which commercial companies were able to offer their services. Although the ethical and socio-economic problems raised by this were quickly appreciated, ongoing discussions between well informed representatives of the public, patient groups and the relevant professions will be required before any consensus can be reached. It is at least some comfort to note that government regards the situation as sufficiently important to have set up (even if only after severe pressure from the professions!) both a Human Genetic Commission and a Genetics Testing Advisory Group.

Strong family history of breast and ovarian cancer and association with BRCA1 gene mutation



Although the emerging information is of great scientific value and interest, it does have a great potential for misunderstanding and misapplication. The editorial [1] refers to the making of gene-based statistical prophecies - but not necessarily with all the evidence yet in.

Inappropriate optimism

One of the papers in the NEJM issue was a study of the prevalence of BRCA1 mutations in a population of women with breast cancer. Clinical information, family histories and blood was given by 263 women, and DNA sequencing was used to identify BRCA1 mutations. Women were consecutive referrals who were referred either because there was a strong familial risk factor for breast cancer (169 women) or breast cancer was diagnosed before 40 years of age (94 women). There was an average of 4 breast cancers per family and 1.5 cases of ovarian cancer in the women with a family history.

BRCA 1 mutations were identified in 9/124 (7%) women where there was a family history of breast cancer without ovarian cancer, 10/57 (18%) where family members had bilateral breast cancer, 28/60 (47%) with family members with both breast and ovarian cancer or a single member with both cancers.

Implication for screening

This suggests that even when subjects are selected from families with a strong history of breast cancer only about 7 in 100 will be found to have BRCA 1 mutations. So more than 9 out of 10 tests would be negative, with 10% or fewer positive, if screening for BRCA1 mutations were instituted. The implication is that BRCA1 mutations may account for fewer than half of hereditary cases of breast cancer, not much higher figures suggested previously (see *Bandolier* 18). Routine screening, even where there is a family history, will be wasteful in that it will require enormous back up, both scientific and medical, including counselling, to undertake responsibly. Furthermore, women who do not have a mutation have to be cautioned to prevent a false sense of security, because, in the striking words of the article, "negative tests are not truly negative". That is, women with negative results for BRCA1 mutation are still at risk of cancer.

BRCA1 gene

Scientists have already identified more than 200 different mutations in the two BRCA genes. But we do not know how these different mutations differ in their relative contributions to breast, ovarian and other cancers. Clearly some mutations are responsible for the very high risks identified in some families, but others are likely to be within the normal variations found in many genes (polymorphisms) and not be relevant to cancer. It is also likely that different mutations will determine different types of cancers with different pathologies and different outcomes. There are some very preliminary indications that mutations towards one end of the BRCA1 gene are more likely to lead to breast cancer while those towards the other end of the gene are more likely to give ovarian cancer. It is also suggested that mutations in the BRCA2 gene are less likely to be found in early onset breast cancer than are BRCA1 mutations.

Moreover the same mutations may behave differently in different populations of women. This emphasises the importance of modifying factors in determining the final outcome (eg, reproductive history, hormone therapy, diet, smoking and other genes which, for example, control the metabolism of hormones). We must not forget that all cancers are ultimately determined by a combination of genetic and environmental factors and the interplay of these is one of our most urgent subjects for research.

Statistical prediction

The problem of statistical prediction becomes especially worrying when irreversible decisions are based on it. The question of whether to have prophylactic mastectomies or oophorectomies for carriers of BRCA mutations is a particularly difficult one. A theoretical model [3], based on a number of statistical assumptions, estimated that prophylactic mastectomies would add 2.9 to 5.3 years of life expectancy for a 30 year old carrier of a mutation and an oophorectomy would add 0.3 to 1.7 years. Estimated gains in life expectancy decline with age, however. Gains would be minimal for a 60 year old, less than one year on average, very little more than the estimated gain in life expectancy of 8 months for a woman without a mutation.

But as correspondence suggests [4], even this reported gain in life expectancy may overstate the benefit of prophylactic surgery to the patients for several reasons:

- ◆ The effects of surgery on quality of life are ignored.
- ◆ Risks associated with surgery are immediate. Benefits (prevention of cancer) accrue over time.
- ◆ The reported gain in life expectancy applies only to women who already know they have the gene mutations. Screening to find the mutation would carry its own demerits - not least those of false positive or false negative results in circumstances where prevalence may not be high.

So this information should encourage a conservative approach to prophylactic surgery. But patients are individuals rather than units of a statistical study and each needs to be given individual consideration. Where this involves changes in genes which predispose to breast cancer this means access to experts who themselves are in possession of the latest information and are able to communicate this in a digestible form to worried people who do not understand the science or statistics.

References:

- 1 B Healy. BRCA genes - Bookmaking, Fortunetelling, and Medical Care. *New England Journal of Medicine* 1997 336: 1449-9.
- 2 FJ Couch, ML DeShano, A Blackwood et al. BRCA1 mutations in women attending clinics that evaluate the risk of breast cancer. *New England Journal of Medicine* 1997 336: 1409-15.
- 3 D Schrag, KM Kuntz, JE Garber, JC Weeks. Decision analysis - effects of prophylactic mastectomy and oophorectomy on life expectancy among women with BRCA1 or BRCA2 mutations. *New England Journal of Medicine* 1997 336: 1465-71.
- 4 JD Birkmeyer, HG Welch. Risk of breast cancer in carriers of BRCA gene mutations. *New England Journal of Medicine* 1997 337: 787.

LONG-TERM OUTCOME AFTER HEAD INJURY

Bandolier often wonders about the natural history of disease or disorder. Observational studies which give us answers are hard to find, but the long-term outcomes after head injury have been described in a good study from France [1].

Trauma and its sequelae are major health problems, and it is one of the major if not the major cause of death in children and young adults. Head injury has a reported incidence of 150 to 300 per 100,000 and is one of the most frequent injuries in trauma.

Study

The study was conducted in Aquitaine (population 2.7 million), using data from a 1986 population-based study looking at all injuries serious enough to result in death or hospital admission. Out of the 7,281 patients identified, a cohort of 1,005 which included 407 head injury patients was selected for follow up (selection criteria were not given other than that three centres were involved).

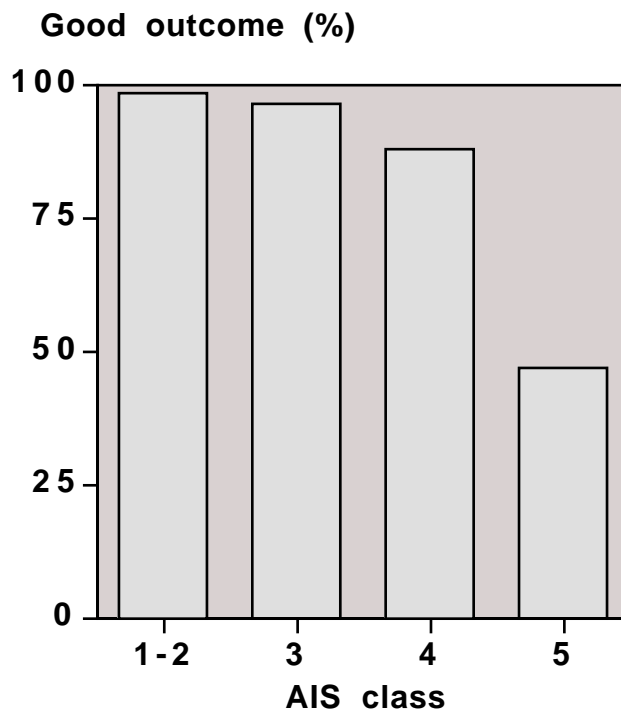
Head injury was defined as loss of consciousness, abnormal neurological examination, abnormalities on computerised tomography, or skull fractures. Trauma severity was rated using the Abbreviated Injury Scale (AIS):

AIS 1-2	short period of unconsciousness or linear skull fracture
AIS 3	complex skull fracture or cerebral contusion
AIS 4	prolonged unconsciousness or intracranial haematoma
AIS 5	unconsciousness >24 hours, diffuse brain lesions, or severe mass effect.

Survivors were sent a letter five years after the initial trauma and were interviewed with a 200 item questionnaire at the institution or at home, or by phone, or by filling in the questionnaire at home and sending it back by post. Wherever possible a close family member was interviewed separately to supply information on the patient's behaviour. Out of the 407 head injury patients, 64 had died, 36 were lost to follow up, and three refused to participate, so data were available on 304 patients.

Results

Patients in the cohort were predominantly under the age of 60 years (90%), and 50-60% were under 30 years at the time of their injury. About two thirds were male, and almost all had received their head injury in a traffic accident or fall. Almost all the patients lived at home. About 4% needed family support because of behavioural or cognitive problems, and this was



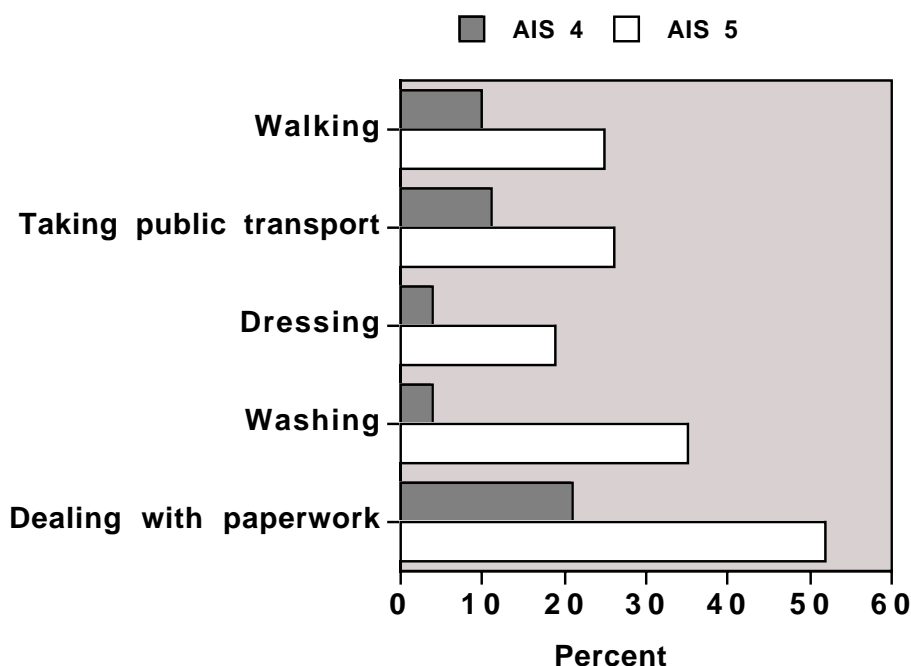
permanent in about 20% of the most severe cases. Epilepsy and hemiparesis were present in 0.7% of the whole head injury cohort.

But overall outcome was good. Using the Glasgow Outcome Score, recovery in survivors was good in 98, 97, 88 and 47% of patients in AIS 1-2, 3, 4 and 5 respectively.

Impairment

An impairment was defined as any loss or abnormality in body structure or function. Headaches, dizziness, memory disturbance, depressive mood, irritability and anxiety were common. They occurred in 25% or more of patients of all AIS classes, and there was a tendency for some of these to be more severe in those in AIS 5.

Disability rates in patients with head injury scores:



Disabilities

A disability was defined as a change in ability to perform an activity within the range considered normal. Few patients in AIS 2-3 were affected, but disability was higher in AIS classes 4 and 5, with difficulty in walking, taking public transport, dressing, washing and dealing with paperwork.

Handicap

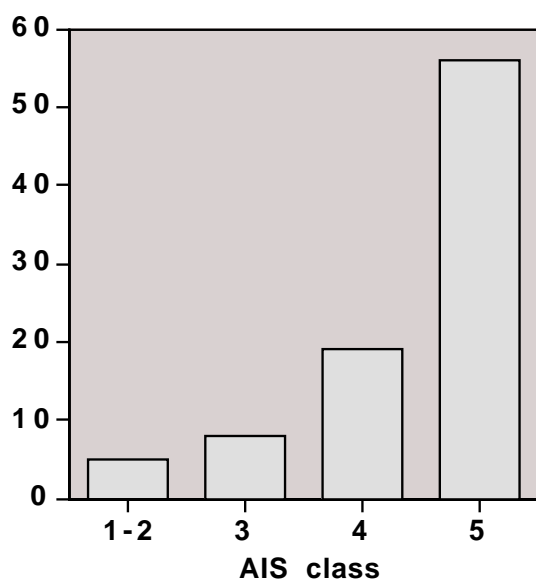
A handicap was defined as a disadvantage which limited the fulfilment of a role that was normal for that individual. At the time of their injury 37% of patients were working. After five years 15% could not work any more because of their injury.

Ninety-six patients were children at school in 1986. It was estimated that 7% of these students had problems in studying again, mostly because of behavioural changes.

Death

Death rates were class dependent. They were 5, 8, 19 and 56% in AIS 1-2, 3, 4 and 5 respectively.

5 year death rate (%)



Comment

Bandolier liked this paper because it gave information of the likely five year outcome following a head injury. The study may be criticised because it looked at a cohort, rather than the whole head injury population of the region. The datum point was people who had a head injury as long ago as 1986, and it is possible that management has improved since then.

But it probably gives a fair impression of what can be expected in terms of recovery and problems for someone having a head injury. Useful for doctors, patients and families.

Reference:

- 1 F Masson, J Vecsey, LR Salmi et al. Disability and handicap 5 years after a head injury: a population-based study. *Journal of Clinical Epidemiology* 1997 50: 595-601.

BANDOLIER CONFERENCES

The fifth *Bandolier* conference on New Horizons on HIV and AIDS takes place at the Wellcome Trust in London on Wednesday December 17th. The programme is being finalised right now, but will include:

- History and size of the problem in the UK.
- An idiots guide to HIV immunology.
- Advances in treatments, including multiple drug therapies with protease inhibitors.
- Treatment strategies - which patients should get what treatment - an important issue this because the evidence is coming in that triple therapy is beneficial in patients with low CD4 counts. But what about HIV-infected patients with high plasma viral loads who have not developed AIDS, or those with low plasma viral loads?
- Post exposure prophylaxis?
- Are there any health economic arguments that are important?
- What does the future hold for HIV treatments, and for their funding in the UK?

The conference will start in mid morning and finish at about 5 pm, with lots of time for discussion and some horizon scanning in this fast-moving area. The conference aims to be particularly helpful for those outside the main centres treating HIV to bring their knowledge up to date, and to provide information to inform future commissioning policy. The cost will be £135 (NHS) or £270 (Commercial).

There will be a small number of bursaries (half-price places) for students and those in training posts. To apply you need to write and explain why the full costs cannot be met by your host institution.

For details and preliminary booking please fax Eileen Neill on 01865 226879. Those travelling to London who are likely to need overnight accommodation should also write to Eileen, as we are trying to negotiate special rates at nearby hotels.

Bandolier back numbers

Bandolier 2nd Annual is available inside the NHS for £14 from Eileen Neill, and overseas or credit card orders (£18) from Hayward Medical (Angie Stagg on +44 1638 751517 (fax) or hayward.newmarket@dial.pipex.com (email).

Bandolier costs

Non-NHS subscribers should note that the cover price goes up to £36/year (£72 overseas) from January 1 to cover increased costs. We very much regret this, but it reflects the costs of handling single orders.

Costs inside the NHS do not change, of course. Because NHS E R&D Directorates purchase *Bandolier* for whole regions, the cost per copy within the NHS is less than the cost of photocopying it. So anyone doing lots of copying is wasting money - just ask for more copies!

REDUCING UNNECESSARY CONSULTATION – A CASE OF NNNT?

Tom Marshall
Specialist Registrar in Public Health Medicine
Northamptonshire Health Authority

Introduction

Readers of *Bandolier* will be familiar with the concept of NNT as a convenient summary of the beneficial impact of a treatment. But what if the treatment has an effect – such as encouraging unnecessary consultation – which we want to avoid? We could think of this in terms of NNNT (numbers needed to not treat).

Consultation for throat infection

Throat infection is a common reason for a GP consultation. There is not much support for using antibiotics. The Cochrane Collaboration's most recent review confirmed the extremely modest effects of antibiotics in reducing the duration of throat infection [1]. Because simple analgesics are all that is needed, dealing with it can also be a frustrating exercise. Yet patients still consult. Could GPs have an influence on this pattern of behaviour? A recent randomised controlled trial explored this question in a novel way [2].

Patients were randomly allocated to immediate antibiotics, an offer of delayed antibiotics (three days later, if symptoms persisted) and no antibiotics. However, patients were not blind to their treatment. The clinical outcomes and patient satisfaction were the same for each strategy. However, compared to either offering a delayed prescription or not prescribing, issuing a prescription for an antibiotic tended to persuade patients that they were effective. It also affected their intention to consult in the future.

Numbers-needed-to-not-treat (NNNT)

From this we can work out a NNNT (numbers needed to not treat - Table 1). For every 3 patients we “not treat” (avoid or delay prescribing antibiotics) we persuade an additional one that they are not effective. Similarly for every 4 patients whom we “not treat” we persuade one that they need not consult with the problem in the future.

Rather than simply relying on patients' stated intentions, a follow up to the initial study looked at the factors which led patients who had suffered one throat infection to consult again in the next year [3]. Again the message was fairly clear. An immediate prescription for antibiotics increases the number of patients who consult again (Table 2). It was also clear that those patients who did consult again were much more likely to have been prescribed antibiotics for throat infection at some time in the past.

Conclusion

We can sum this up by illustrating what would happen if a GP prescribed antibiotics to 100 fewer patients with throat infection in a year. Thirty three fewer would believe antibiotics were effective, 25 fewer would intend to consult with the problem in the future and 10 fewer would come back within the next year. Game, set and match to masterly inactivity.

References:

- 1 CB Del Mar, P Glasziou. Antibiotics for the symptoms and complications of sore throat. In: *The Cochrane Database of Systematic Reviews*. Available in The Cochrane Library [database on disk and CDROM]. The Cochrane Collaboration; Issue 1. Oxford: Update Software; 1997. Updated quarterly.
- 2 P Little et al. Open randomised controlled trial of prescribing strategies in managing sore throat. *British Medical Journal* 1997 314: 722-7.
- 3 P Little et al. Reattendance and complications in a randomised trial of prescribing strategies for sore throat: the medicalising effect of antibiotics. *British Medical Journal* 1997 315: 350-2.

Table 1: Effect of prescribing an antibiotic for throat infection on patients' beliefs and intentions

Effect on patient	Penicillin V prescribed	No Penicillin V or offer delayed for 3 days	NNNT
Believe “antibiotics are effective”	87%	57%	3
Say that they “will consult next time”	79%	55%	4
“satisfied” with consultation	96% (ns)	92% (ns)	

Table 2: How prescribing antibiotics affects patients' re-attendance with throat infection

Effect on patient	Penicillin V prescribed	No Penicillin V or offer delayed for 3 days	NNNT
Consult again with throat infection	38%	27%	10
	Penicillin V prescribed in the past	No Penicillin V prescribed in the past	NNNT
Consult again with throat infection	50%	27%	4

HIV PROTEASE INHIBITORS

Bandolier 41 discussed the importance of the concentration of HIV virus in plasma or serum (viral load) as a surrogate marker for beating the disease. We gave some exciting results of the ACTG 320 trial taken from an Internet source. The full paper has now been published [1], and the pukka results are in the Table.

ACTG 320 trial

Briefly, this was a randomised, double-blind, placebo-controlled trial in which people with HIV-1 infection and CD4 cell counts of no more than 200/ μ L received either a two nucleoside regimen plus protease inhibitor (indinavir), or the same regimen plus placebo. Stratification was by CD4 count more or less than 50 cells/ μ L. Follow up was at 4, 8, and 16 weeks, and every 8 weeks thereafter up to 40 weeks.

Results

1156 people were randomised, and the median duration was 38 weeks. Patients lost to follow-up were few, at 5%. There were 227 (20%) premature discontinuations, of which a major portion was patients seeking open-label treatment with protease inhibitor.

AIDS or death

Addition of protease inhibitor halved the rate of progression to AIDS or death. Overall the NNT was 19, but in those patients with the lowest CD4 cell counts of ≤ 50 / μ L (that is, the most advanced disease), the same halving of the rate produced an NNT of 11 because of the higher progression rate.

Plasma viral load

Protease inhibitor was very effective in reducing the plasma viral load to levels below the sensitivity limit of the assay

(500 molecules/mL). Sixty percent of patients treated with protease inhibitor had such low values, compared with 9% in the placebo group. The NNT was 2. A similar NNT of 2 for reducing plasma viral load to such low levels was seen in an accompanying article [2].

CD4 cell count

CD4 cell counts rose substantially in patients given protease inhibitor, by nearly 150/ μ L over 40 weeks. Placebo-treated patients had rises which were below 50/ μ L.

Adverse effects

Neutropenia was much less common in patients on protease inhibitor, but both hyperbilirubinaemia and renal colic were more common with protease inhibitor.

Comment

Bandolier has already said that this is exciting stuff. The one fly in this particular ointment may be the need to generate more certainty about the use of plasma viral load as a prognostic factor. It's fine to chase it as an end point of treatment, but the ACTG 320 trial, for instance, fails to couple data from viral load to outcome. Trialists and their commercial sponsors, who have the original data, could do us all a favour by doing a bit more on this.

References:

- 1 SM Hammer, KE Squires, MD Hughes et al. A controlled trial of two nucleoside analogues plus indinavir in persons with human immunodeficiency virus infection and CD4 cell counts of 200 per cubic millimeter or less. *New England Journal of Medicine* 1997 337: 725-33.
- 2 RM Gulick, JW Mellors, D Havlir et al. Treatment with indinavir, zidovudine, and lamivudine in adults with human immunodeficiency virus infection and prior antiretroviral infection. *New England Journal of Medicine* 1997 337: 734-9.

Protease inhibitor and HIV: results from ACTG320 trial [1]

Outcome	Nucleosides plus indinavir	Nucleosides plus placebo	Relative risk	Absolute risk reduction	NNT
All patients					
Aids or death	33/577	63/579	0.53 (0.35 - 0.79)	0.05	19 (12 - 50)
Death	8/577	18/579	0.45 (0.20 - 1.03)*	0.02	58 (29 - >1000)
Plasma viral load <500 molecules/mL	52/577	347/579	6.7 (5.1 - 8.7)	0.51	2.0 (1.8 - 2.2)
Neutropenia	29/577	87/579	0.33 (0.22 - 0.49)	0.10	10 (7.5 - 15)
Hyperbilirubinaemia	35/577	6/579	5.9 (2.5 - 14)	0.05	20 (14 - 34)
Renal colic	21/577	5/579	4.2 (1.6 - 11)	0.03	36 (22 - 93)
Aids or death CD4 ≤ 50 /cu mm	23/219	44/220	0.53 (0.33 - 0.85)	0.09	11 (6.2 - 35)
Aids or death 51-200 CD4/cu mm	10/358	19/359	0.53 (0.25 - 1.12)	0.02	40 (18 - ∞)
Plasma viral load <500 molecules/mL From [2]	24/28	5/28	2.0 (1.3 - 3.2)	0.43	2.3 (1.5 - 4.9)

* Statistically significant by hazard ratio calculation in original article

What would you like to see assessed?

The NHS HTA Programme aims to ensure that high quality research information on costs, effectiveness and broader impact of health technologies is produced in the most economical way for those who use, manage and work in the Health Service. *Health technologies* are defined very broadly as:

- ◆ all methods used by health professionals to promote health, diagnose, prevent and treat disease, and improve rehabilitation and long term care.

Health technology assessment is defined more tightly to include the following features:

- ◆ the health technology under assessment should be clearly defined, sufficiently stable, and able to be compared with competing health technologies and/or no intervention;
- ◆ evaluating new applications of existing health technologies is part of HTA, but work aiming to develop new applications of health technologies would not normally be included;
- ◆ the end-point of the assessment should be the identification of patient outcomes and/or the relative cost-effectiveness of alternative means;
- ◆ work aimed solely at auditing established good practice or current practice would not normally fall under the definition of HTA.

The HTA programme is now starting its identification of priorities for 1998. We are asking for suggestions of health technologies you would like to see assessed. These suggestions will be considered by the programme's six expert panels who advise on acute care, population screening, primary and community care, diagnostics and imaging, pharmaceuticals and the methodology of health technology assessment. The Standing Group for Health Technology will take the final decision on the most important 40 or 50 priorities in which research will be commissioned. Suggestions previously prioritised by the programme include:

- √ Management of venous leg ulcers in the community
- √ Management of irritable bowel syndrome in primary care
- √ Long term follow up following psychotherapy and cognitive behaviour therapy
- √ Acupuncture for the management of pain in primary care
- √ Day care services for the severely mentally ill
- √ Outreach ophthalmology clinics in general practice
- √ The use of acute diagnostic ultrasound in general practice
- √ Community support teams for people with learning disabilities and challenging behaviour
- √ SSRI anti-depressants in comparison to tricyclics
- √ Treatments for eczema
- √ Different treatments for severe psoriasis

If you would like to make a suggestion, please visit our web site on <http://www.soton.ac.uk/~wi/hta>or alternatively write to NCCHTA, Highcroft, Romsey Road, Winchester, SO22 5DH requesting an 'identification pack'.

Bandolier has received considerable correspondence on the use of NNTs in economic analysis. We are not sure that's the best way to use them, so a challenge to all those health economists out there - does Stephen Gray strike a chord? Is there one example where NNTs or IYDTs can be used? Any 500 word (one table) piece selected for publication gets a free *Bandolier* annual.

IYDT vs NNT

Dear *Bandolier*,

I was interested to read your correspondence from Jon Brassey (*Bandolier* 42) concerning the psychology of expressing things as a cost rather than a benefit. One simple way of calculating the priority for doing a particular intervention can be expressed as the cost of delaying the intervention divided by the amount of scarce resource required to do the intervention. This theory has been developed for use in forestry. However it could be used to compare medical interventions as well, by simply substituting '1/IYDT' (the higher the IYDT, the less useful the treatment) for the 'cost of delay'.

Thus priority could be given to interventions with a low value of IYDT x cost. These figures could be calculated as If You Do not Treat for 1 year (e.g. stick someone on a waiting list!) and the cost of treatment for one year.

It would certainly be interesting to see if some treatments, for which NNTs are known, could be compared in this way.

Yours sincerely,

Stephen Gray e-mail Graypharm@compuserve.com
 Grays Pharmacy
 20 Main Street
 Tweedmouth
 TD15 2AA

Bandolier does publish correspondence, but space is limited. So we have an Internet correspondence section which is updated from time to time. Many thanks for your letters of support, and answers for Question Time - a report on the outcome of that exercise next month.

EDITORS

Dr Andrew Moore
 Dr Henry McQuay

Dr J A Muir Gray

Pain Relief Unit
 The Churchill, Oxford OX3 7LJ

Editorial office: 01865 226132

Editorial fax: 01865 226978

Email: andrew.moore@pru.ox.ac.uk

Internet: <http://www.jr2.ox.ac.uk/Bandolier>

ISSN 1353-9906