

## Tools not rules

*Bandolier's* move to the new Pain Research building in Oxford is now about complete. We'll try and get a picture for January's addition. The most difficult part is getting new furniture, because desks, chairs, cupboards have been around for so long that, tatty or no, they are comfortable, just like *Bandolier's* old cardie.

New things chafe. Using best evidence chafes with some people too, especially when it is introduced through a challenge - a new piece of evidence that experience does not necessarily support. If that is a meta-analysis or systematic review, then the immediate reaction is that these are useless. But if our car fails to start in the morning, that doesn't mean we never use a vehicle with an internal combustion engine ever again! These methods are tools not rules, but the right tool has to be used for the right job. Anyone know the best DIY manual on this topic?

## Bandolier conference on stroke

A *Bandolier* conference on optimising secondary prevention and follow-up care is being planned. The suggested date is 24 March 1999, with a venue in London, probably at the Royal College of Pathologists, which is conveniently situated a short walk from the Mall or Trafalgar Square.

More details will appear in future issues, but if you want to be sure you are sent a booking form and programme, please fax your details to Eileen Neill on (+44) 1865 226978.

## Bandolier correspondence

*Bandolier* occasionally receives correspondence about articles. Because we have limited space, these are displayed on our Internet pages (<http://www.jr2.ox.ac.uk/Bandolier/letters/letters.html>). Two people have written to disagree about our article on tonsillectomy in *Bandolier* 55, and to take exception to our approach to NNTs for antiepileptic drugs. Please read them and (where appropriate) our responses.

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

## NNTs FOR MS

*Bandolier* has been asked on more than one occasion to visit the difficult area of beta-interferon treatment for multiple sclerosis (MS). It is a hard subject - because the disease is itself awful, treatments have limited efficacy, and cost-benefit calculations are riven with hard decisions. But more evidence is emerging, and so, with much trepidation, it seemed that perhaps the time had come to see if NNTs could be calculated for clinical outcomes understandable to most of us.

One of the difficult issues is that of clinical outcomes versus surrogate markers from brain imaging. Frequent MRI scanning of the brains of patients with MS provides a dynamic picture of the disease process. Areas with increased water content seen on the T2-weighted images, known to some as "unidentified bright objects", appear in the cortical matter with surprising frequency. They enlarge, shrink, and often disappear at intervals of two to eight weeks. Most, possibly over 80% of them, are silent, in that they have no link to episodes of appreciable neurological deficit.

When biopsied, these lesions show inflammatory responses with invading T-cells and activated macrophages. Demyelination of nerves may be subtle, or frank, and repair processes are often seen. Plaques in brain tissue of people with evolved MS seen at post mortem show almost complete demyelination and an absence of inflammatory processes [1].

Many MS lesions are reversible and asymptomatic, but as one attack follows another repair mechanisms may fail and areas of permanent damage (plaques) enlarge or coalesce. Irreversible difficulties with gait, coordination, vision, and bladder and bowel control accumulate. Areas of demyelination, and of axonal loss, interrupt impulse conduction along nerve tracts. If the optic nerve is involved, vision will be compromised. If pyramidal tracts are involved, spasticity and weakness will follow, possibly leading to an inability to walk. If cerebellar pathways are involved, there may be loss of coordination. If sensory pathways are involved, there may be dysaesthesia or frank loss of sensation. If the pathways controlling bladder and bowel function are involved, there may be urinary and faecal incontinence.

## Interferon-β

Interferon-β interferes with the local inflammatory processes. It may impede those processes involved with initiating or propagating the immune response, or enhance those which end an episode. This is an area of immense complexity, and the important point is that interferon-β1b can be shown to have pharmacological properties which should be beneficial in MS. The question is whether these benefits transfer from the laboratory to the clinic.

## Expanded Standard Disability Status Scale (EDSS)

The EDSS scale extends from 0 (normal neurological examination) to 10 (death from MS complications) in 0.5 unit increments. EDSS 1.0 to 4.5 refers to patients who are fully ambulatory. The precise steps are denoted by functional scores which are graded from normal (0) to maximal impairment (5 or 6) for pyramidal, cerebellar, brain stem, sensory, bowel and bladder, visual, cerebral or mental, and other functions. EDSS 5.0 to 9.5 are defined by impairment to ambulation. The definitions for points 3 to 7 are given below:

- 3.0 Moderate disability in one functional score or mild disability in three or four functional scores, though fully ambulatory.
- 4.0 Fully ambulatory without aid; self-sufficient; up and about some 12 hours a day despite relatively severe disability consisting of one functional score grade 4 (others 0 or 1) or combinations of lesser grades exceeding limits of previous steps; able to walk 500 metres without aid or rest.
- 5.0 Ambulatory without aid or rest for about 200 metres; disability severe enough to impair full daily activities (unable to work a full day without special provision); usual functional scores are grade 5 alone (others 0 or 1) or a combination of lesser grades, usually exceeding those for step 4.0.
- 6.0 Intermittent or unilateral constant assistance (walking stick, crutch, brace) required to walk about 100 metres with or without resting; usual functional score equivalents are combinations of more than two functional scores grade 3+.
- 7.0 Unable to walk beyond about 5 metres even with aid; essentially restricted to a wheelchair; wheels self in standard wheelchair and transfers alone; up and about in wheelchair some 12 hours a day; usual functional score equivalents are combinations with more than one functional score grade 4+; very rarely, pyramidal grade 5 alone.

## Secondary progressive MS

This study [2] involved 718 patients who had clinically or laboratory-supported definite MS in the secondary progressive phase, with two relapses or a 1-point deterioration in the Extended Disability Severity Scale (EDSS, see box) in the previous two years. The EDSS score had to be between 3.0 and 6.5 at entry, with no relapse or deterioration in the month before starting treatment. Patients were randomised between interferon- $\beta$ 1b 8MIU subcutaneously every other day for 36 months, with lower doses in the first 15 days, and intermittent dose interruption, if indicated.

Outcomes were assessed at a planned interim time when all patients had 24 months of treatment. It was stopped at this point because of clear evidence of efficacy. The primary outcome was confirmed neurological deterioration by a 1-point

deterioration in the EDSS scale, from baseline, on two consecutive visits at least three months apart. For patients with greater disability and an initial EDSS score of  $\geq 6.0$  a 0.5 increase was regarded as confirmed neurological deterioration. These outcomes were assessed by a neurologist not involved with the ongoing management of MS patients and who had no knowledge of the treatment assignment. A number of prespecified secondary endpoints were also used, which included time to becoming wheelchair bound (EDSS of 7.0), annual relapse rate, use of steroids, hospital inpatient episodes, and MRI T2 lesion volume.

## Results

Over 80% of patients had baseline EDSS scores of  $\geq 4.0$ . The main results are shown in Table 1, with number needed to treat based on an intention-to-treat analysis of all patients randomised.

Analysis when all patients had been treated for at least 24 months showed that, counting any patients lost to follow up as deteriorated, 178/358 (50%) of patients given placebo deteriorated, compared with 140/360 (39%) with interferon- $\beta$ 1b. The NNT to prevent progression over two years was 9.2 (95% confidence interval 5.5 to 28). The treatment effect (relative benefit) was consistent across all baseline EDSS scores. This was equivalent to a delay of about 12 months in progression over two to three years.

Interferon- $\beta$ 1b reduced the incidence of patients becoming wheelchair-bound (EDSS score of 7). With interferon- $\beta$ 1b 60/360 (17%) of patients became wheelchair-bound, compared with 88/358 (26%) with placebo. The NNT was 13 (95% CI 7.2 to 49).

Interferon- $\beta$ 1b reduced the incidence of patients having moderate or severe relapses. With interferon- $\beta$ 1b 203/360 (56%) of patients had either no relapse or only a mild relapse, compared with 168/358 with placebo. The NNT was 11 (95% CI 6.0 to 46).

Interferon- $\beta$ 1b reduced the incidence of patients needing high-dose steroids. With interferon- $\beta$ 1b 167/360 (46%) of patients did not require steroids, compared with 115/358 (32%) with placebo. The NNT was 7.0 (95% CI 4.7 to 14).

Interferon- $\beta$ 1b reduced the incidence of patients needing any hospital admission. With interferon- $\beta$ 1b 193/360 (54%) of patients needed no hospital admission, compared with 169/358 (48%) with placebo. The NNT was 16 (95% CI 7.3 to no benefit, though in the paper this was a statistically significant difference using different statistical tests).

Interferon- $\beta$ 1b reduced the cumulative mean number of new lesions detected by MRI. The mean lesion volume increased by 8% with placebo, but declined by 5% with interferon- $\beta$ 1b. These results were statistically significant at more than the 1 in 10,000 level.

## Adverse effects

Interferon- $\beta$ 1b was associated with increased rates of adverse effects. There were mostly those of the 'flu syndrome associated with interferons, injection site inflammation and reac-

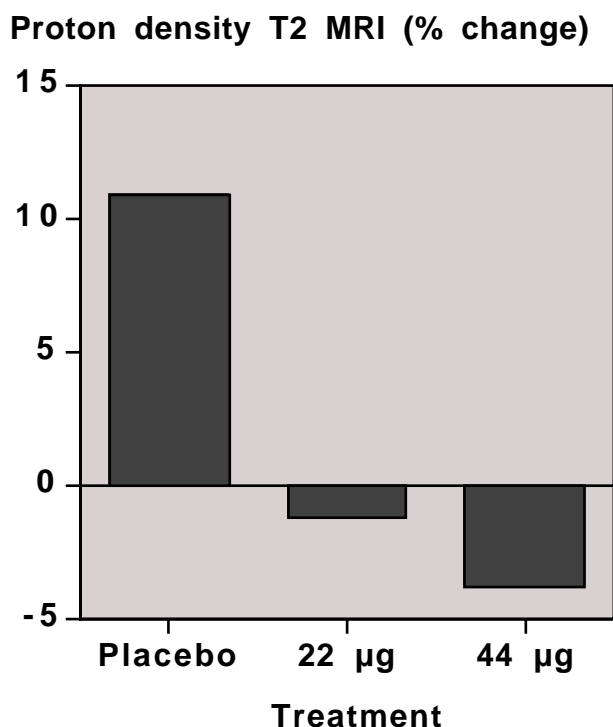
**Table 1: Effects of treatment for two years with Interferon  $\beta$ -1b on various clinical outcomes in a randomised trial in 718 patients with secondary progressive multiple sclerosis (Intention to treat analysis) [2]**

Event	NNT (95%CI)
Prevent confirmed progression	9.2 (5.5 to 28)
Prevent becoming wheelchair bound	13 (7.2 to 49)
Prevent moderate or severe relapse	11 (6.0 to 46)
Prevent MS-related steroid use	7.0 (4.7 to 14)
Prevent any hospital admission	16 (7.3 to no benefit)

**Table 2: Effects of treatment for two years with Interferon  $\beta$ -1a on various clinical outcomes in a randomised trial in 560 patients with relapsing/remitting multiple sclerosis [3]**

Event	22 $\mu$ g dose	44 $\mu$ g dose
	NNT (95%CI)	NNT (95%CI)
Prevent any relapse	9.1 (5.2 to 37)	6.2 (4.1 to 13)
Prevent moderate or severe relapse	5.4 (3.5 to 12)	5.1 (3.4 to 10)
Prevent MS-related steroid use	7.0 (4.1 to 23)	5.9 (3.7 to 14)

**Effect of interferon- $\beta$ 1a over two years on brain scans in MS**



tion, and increased muscle tone. While about 60% of patients receiving interferon- $\beta$ 1b had 'flu-like symptoms in the first three months of treatment, this reduced to 10-20% after six months.

## Relapsing/remitting MS

Another study [3] examined the effects of interferon- $\beta$ 1a in relapsing/remitting disease. This was well conducted and randomised 560 patients with EDSS scores of 0 to 5 to placebo, 22  $\mu$ g or 44  $\mu$ g of interferon- $\beta$ 1a subcutaneously three times a week over two years. Neurological examinations were done every three months and MRI twice a year.

Outcomes included the number of relapses, progression of disease by at least 1 EDSS point confirmed after three months, use of steroids and hospital admissions, as well as MRI outcomes.

## Results

The main results are shown in Table 2. The relapse rate over two years was lower for both doses of interferon- $\beta$ 1a than for placebo with an NNT to prevent any relapse of 6.2 (4.1 to 13) for the higher dose. Time to first relapse was delayed by three and five months with the 22  $\mu$ g and 44  $\mu$ g doses respectively.

Both doses appeared to be equally effective in preventing a moderate or severe relapse over two years, with NNTs of 5.4 (3.5 to 12) and 5.1 (3.4 to 10) for 22  $\mu$ g and 44  $\mu$ g doses respectively.

Both doses were effective in preventing the need for steroids, with NNTs of 7.0 (4.1 to 23) for 22  $\mu$ g and 5.9 (3.7 to 14) for 44  $\mu$ g. There was an overall reduction in the number of hospital admissions for the 44  $\mu$ g dose.

Interferon- $\beta$ 1a reduced the cumulative mean number of new lesions detected by MRI. The mean lesion volume increased by 10.9% with placebo, but declined by 1.2% with 22  $\mu$ g and by 3.8% with 44  $\mu$ g (Figure).

Injection site reactions were higher with the interferon- $\beta$ 1a than with placebo, but other adverse effects, like headache and influenza-like symptoms, were not different between the groups.

## Comment

How are these results to be judged? It is about more than just NNTs and outcomes. The results are good without being startling, but the costs are high. Patients with MS and their carers, and decision-makers in the NHS may well view the results differently, in part because of the high treatment costs. It is possible for these treatment to appear to be good value for individuals and/or society as a whole while appearing to be poor value in the NHS.

The remarkable results of interferons in reducing the number of brain lesions and of the number of new lesions, a feature of both these studies, needs to be put in perspective. MRI scans appear, without too much thought, to be just another surrogate end point. But in other circumstances we have seen surrogate end points to be the bees' knees, as with viral load in HIV infection (*Bandolier* 41 and 49). There seems to be a missing link here, that between the MRI results and long term effects, or perhaps we have to wait for results from audits of patients treated with interferon, or open label extensions of these and other studies.

### References:

- 1 BG Arnason, A Dayal, ZX Qu et al. Mechanism of action of interferon- $\beta$  in multiple sclerosis. *Springer Seminars in Immunopathology* 1996 18: 125-148.
- 2 L Kappos and European Study Group. Placebo-controlled multicentre randomised trial of interferon  $\beta$ 1b in treatment of secondary progressive multiple sclerosis. *Lancet* 1998 352: 1491-7.
- 3 GC Ebers & PRISMS Study Group. Randomised double-blind placebo-controlled study of interferon- $\beta$ 1a in relapsing/remitting multiple sclerosis. *Lancet* 1998 352: 1498-504.

## THEATRE NURSING TRUST FUND FOR SYSTEMATIC REVIEWS

The Theatre Nursing Trust has made funds available for UK based theatre nurses to undertake and maintain systematic reviews as part of the Cochrane Collaboration. Successful applicants will be supported in the development and publication (in the Cochrane Library) of a protocol and then the review. Support, including training and education, will be provided by the UK Cochrane Centre, the Cochrane Wounds Group.

For further particulars, please contact Roz Thompson, Department of Health Studies, University of York, telephone 01904 434109 / fax 01904 434102 / email [mrt4@york.ac.uk](mailto:mrt4@york.ac.uk)

## URINARY CATHETERS

Apparently about one hospital patient in four has an indwelling urinary catheter. Urinary catheters are associated with urinary tract infection in about 5% of those with an indwelling catheter, and with bacteraemia also in some of these patients. *Bandolier* calculates from these figures that out of every 1000 patients in hospital, about 12 will have urinary tract infection because of their indwelling urinary catheter.

What can be done to reduce this? Work has been done to give the catheters themselves antimicrobial properties. This has included incorporating antibiotic drugs onto the surface of the catheters using chemical methods, and using silver-coated catheters, because of the antimicrobial actions of silver. The idea is that surfaces with antimicrobial properties (which may be on the inside of the catheter, or on the outside, or both) will inhibit the growth of nasty bugs and so prevent health problems occurring.

Do they work? A meta-analysis [1] of silver catheters says yes and no, depending on the type of silver coating employed.

## Process issues

The searching was with MEDLINE, not limited to English, and other ways of obtaining trial data were pursued, including grilling the manufacturers (not literally, just asking questions about what trials they had or had not done). To be included trials had to have compared a silver-coated catheter with an uncoated catheter. The outcome chosen was bacteriuria as judged by urine culture. No studies were analysed in the meta-analysis in which patients were bacteriuric at baseline, or where there was an open urinary drainage system.

Eight trials were identified, four using silver alloy coating both inside and outside the catheter, and four using silver oxide coating, two of which had the coating on both internal and external surfaces, while two had external coating only. The patient groups were mixed, with urology, surgical and medical patients being included in the various trials. Definitions of bacteriuria used in the trials varied. All were above 200 colony forming units per mL (two studies); two were at 1000 and four were at 100,000 colony forming units per mL.

## Results

Six of the studies were randomised by individual patients. Two allocated patients by week or month. Neither investigators nor patients were blinded to type of catheter used in any study.

For silver alloy catheters, 11% of patients had bacteriuria, compared with 32% with uncoated catheters (Figure). The number needed to treat with a silver-alloy coated catheter to prevent one case of bacteriuria was 4.6 (Table).

For silver oxide catheters, 12% of patients had bacteriuria, compared with 14% with uncoated catheters (Figure). The number needed to treat with a silver-oxide coated catheter to prevent one case of bacteriuria was 51 (Table).

## Comment

This is a fascinating report. There are many reasons to consider the validity of the results, which include:

- ◆ Bacteriuria is a surrogate end-point, rather than overt urinary tract infection or catheter-associated bacteraemia, or death.
- ◆ Methodological issues over randomisation, blinding, the use of prophylactic antibiotics, and gender (men and women may differ in their susceptibility to infections with urinary catheters).
- ◆ The very variable rates of bacteriuria with control, from 10% to 55% in individual studies, and the effect of trial size, with larger studies having lower rates of control infection.
- ◆ The overall rate of 14% with silver oxide controls and 32% for silver alloy controls.
- ◆ The fact that all four silver alloy studies were done at the same institution by the same investigators.

Given some of these concerns, can we be sure of the results? *Bandolier* thinks caution is needed, as, to be fair, do the authors. But the clear and well-written nature of the report makes it ideal for anyone wanting to use it for critical appraisal work, and going on from there to design a trial which might prove the point without dispute.

There is also an interesting health economics perspective here. According to the authors, a silver alloy coated catheter costs twice that of an uncoated catheter in the USA (about US\$7 difference). What are the health economic implications? It should be possible to examine how much better silver alloy catheters would have to be for them to be cost-effective, given some reason-

able assumptions about rates of infection with uncoated catheters. And if the "back-of-stamp" health economics suggests that catheters with antimicrobial properties save money, then what trials do we need to prove it, and to get better practice implemented?

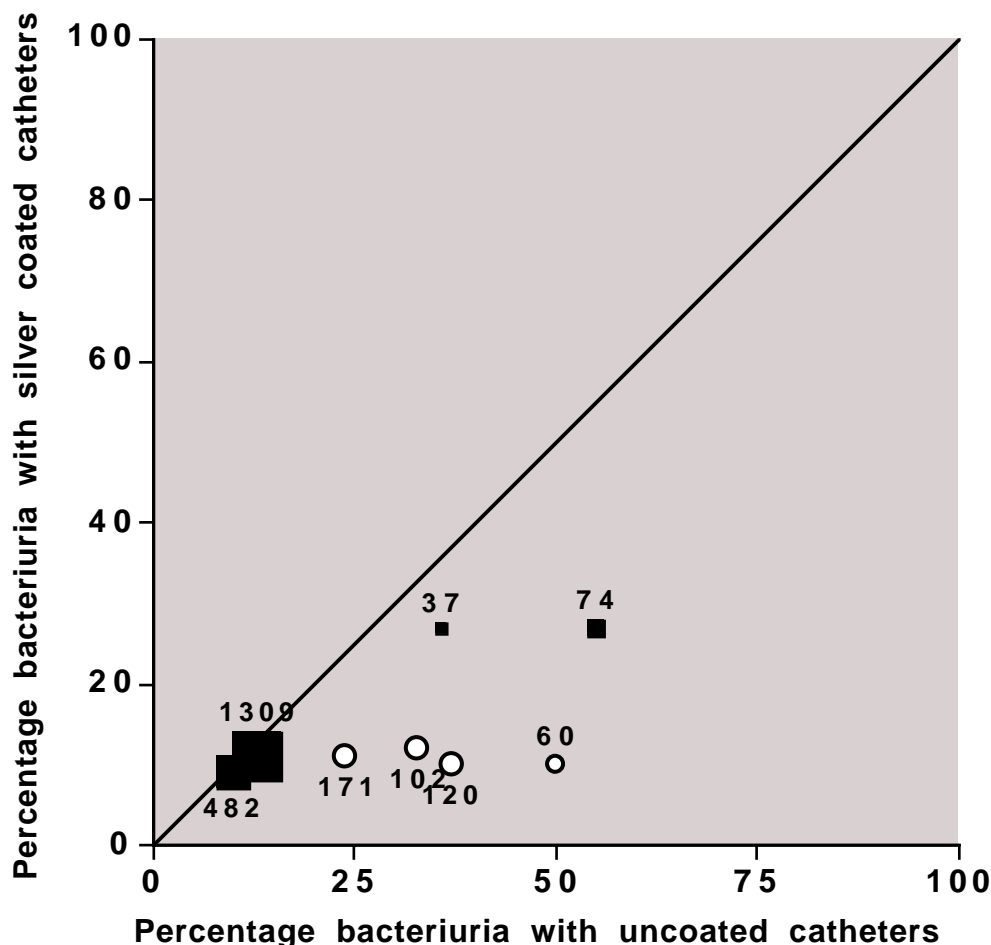
This paper makes you think, especially about issues like technology creep, where innovations may be small in their costs and consequences, but

where the pennies add into many pounds. It also makes you think we should be doing more, and better, and faster, than we seem to be doing now.

### Reference

- 1 S Saint, JG Elmore, SD Sullivan et al. The efficacy of silver alloy-coated urinary catheters in preventing urinary tract infection: a meta-analysis. *American Journal of Medicine* 1998 105: 236-41.

## Rates of bacteriuria with silver-alloy catheters (circles) and silver-oxide catheters (squares) compared with uncoated catheters



### Efficacy of silver-coated urinary catheters

Number (%) of patients with bacteriuria

	Silver-coated	Uncoated	Relative risk (95% CI)	NNT (95% CI)
<b>Alloy</b>	23/216 (11)	77/237 (32)	0.32 (0.21 to 0.49)	4.6 (3.4 to 6.9)
<b>Oxide</b>	122/1019 (12)	123/883 (14)	0.82 (0.65 to 1.03)	51 (20 to no benefit)

# CAFFEINE AND HEALTH

Drinking coffee, or taking in caffeine from tea or cola, or wherever, always seems to be popping up in the newspapers with one message or another, sometimes with conflicting results. So it is comforting that epidemiologists and others are beginning to pull together information so that we can make sense of it. Three recent studies, two of which are meta-analyses, helps us understand the proper place of caffeine, and when to avoid it. It may help formulate better advice for people as part of evidence-based guidance for healthy living.

In interpreting what follows, where data are often analysed in terms of caffeine consumption in milligrams per day, one cup of coffee is equivalent to about 75 mg caffeine, one cup of tea to about 30 mg and one can of cola about 50 mg. But beware espresso or café solo - there the caffeine content can be double at 150 mg a cup!

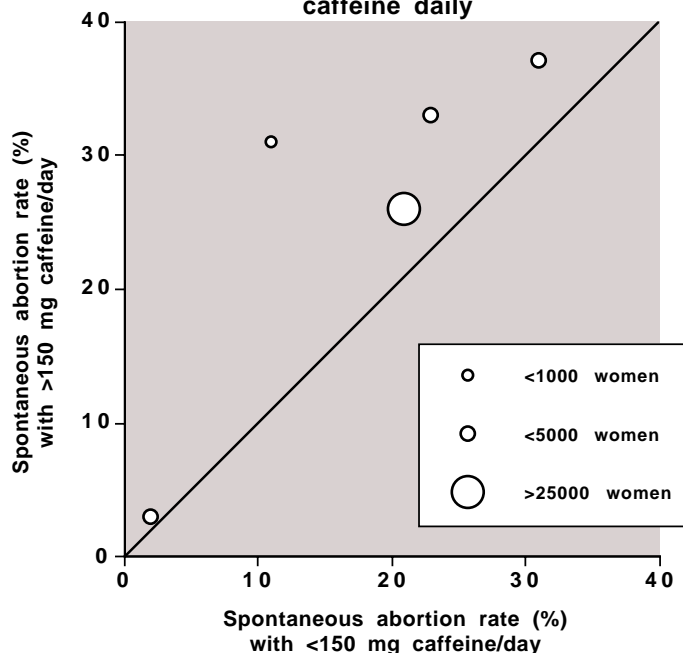
## Caffeine in pregnancy

A meta-analysis examined the effects of caffeine consumption on spontaneous abortion and low birthweight pregnancies [1]. Spontaneous abortion was defined as expulsion from the uterus of products of conception before about 20 weeks (including foetal loss, foetal death and miscarriage). Low birthweight was defined as less than 2,500 g. The control subjects were women who consumed less than 150 mg caffeine a day (two cups of coffee or less), and exposed women those who consumed more than this. Searching was thorough.

## Results

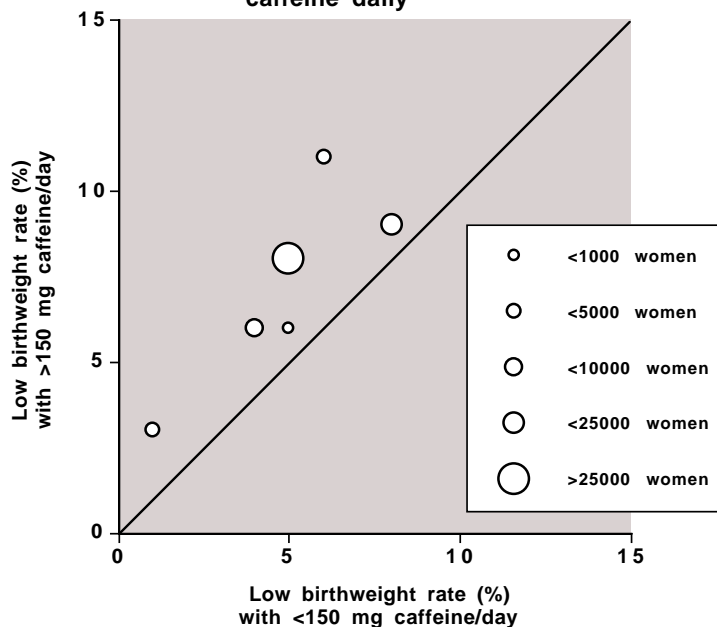
In 42,889 women the rate of spontaneous abortion was 24.4% in exposed women, and 20.0% in controls, with consistency between studies (Figure 1). The number needed to harm we calculated as 23 (Table 1). This means that for every 23 pregnant women who consume more than two cups of coffee or six cups of tea a day, one will have a spontaneous abortion who would not have had they not consumed this much caffeine.

**Figure 1: Spontaneous abortions in women consuming more or less than 150 mg caffeine daily**



In 64,691 women the rate of low birthweight infants was 7.7% in exposed women, and 5.5% in controls, with consistency between studies (Figure 2). The number needed to harm we calculated as 46 (Table 1). This means that for every 46 pregnant women who consume more than two cups of coffee or six cups of tea a day, one will have a baby weighing less than 2500 grams who would not have had they not consumed this much caffeine.

**Figure 2: Low birthweight infants (<2500 g) in women consuming more or less than 150 mg caffeine daily**



## Comment

This is a useful and thoughtful review, which explains, for instance, how each study deals with confounding issues like maternal age and smoking. That does not exclude unknown confounding factors, but an association between maternal caffeine intake and spontaneous abortion or low birthweight is more likely to be true than not. The review tells us that caffeine is cleared from the body much less rapidly in the second and third trimesters of pregnancy, and advises pregnant women to limit their caffeine intake to less than 150 mg a day. This seems sensible.

## Coffee and colorectal cancer

Another meta-analysis comes to a somewhat tentative conclusion that high coffee consumption (perhaps four cups a day or more) reduces the risk of colorectal cancer [2]. Methodologically it is sound, and it does a nice job of discussing the subject, but it gives us relative risks for high versus low coffee consumption in people with colorectal cancer.

So the overall figure for all 17 studies with 6,192 cases was that colorectal cancer was 24% less likely in people who drink four or more cups of coffee a day - relative risk 0.76 (95% confidence interval 0.66 to 0.89).

The finding was consistent across geographically distinct areas, and in most studies except five small cohort studies with fewer than 15% of the patients studied. In three studies with 883 cases with adenomas, the relative risk was 0.57 (95% confidence interval 0.44 to 0.72).

## Caffeine intake, spontaneous abortion, and low birthweight infants

	Number (%) of women affected		Relative risk (95%CI)	NNH (95% CI)
	Caffeine >150 mg/day	Caffeine <150 mg/day		
<b>Spontaneous abortion</b>	1994/8181 (24.4)	6941/34708 (20.0)	1.27 (1.22 to 1.33)	23 (19 to 30)
<b>Low birthweight infant</b>	713/9308 (7.7)	3033/55383 (5.5)	1.50 (1.39 to 1.62)	46 (36 to 62)

### Coffee and stroke in hypertensive non-smokers

Coffee consumption in hypertensive men in older middle-age and the risk of stroke has been examined in a long-term study in Hawaii. Coffee intake (inter alia) was measured in a large cohort of men in the late 1960s, and the incidence of stroke observed over the next 25 years in almost all the men in the study. These were men aged 55 to 68 years who were nonsmokers with hypertension (defined as systolic or diastolic blood pressure above 140 or 90 mmHg respectively).

There were 499 men, and 76 developed a stroke, 55 of which were thromboembolic. After adjusting for age, the risk of thromboembolic stroke, but not haemorrhagic stroke, was significantly related to the amount of coffee consumed (Figure 3). For non-drinkers the five-year incidence was 2%, compared with 4% in those drinking more than three cups a day.

The risk of thromboembolic stroke was more than doubled (relative risk 2.1, 95% confidence interval 1.2 to 3.7) in those who consumed three cups of coffee a day as compared with non-drinkers.

#### Comment

This is probably the first study to show any relationship between coffee consumption and stroke. It is well done, and long-term, and discusses elegantly the methodological issues, especially the difficulty of disentangling coffee and cigarette smoking, as both are highly positively related one to the other.

#### Overall comment

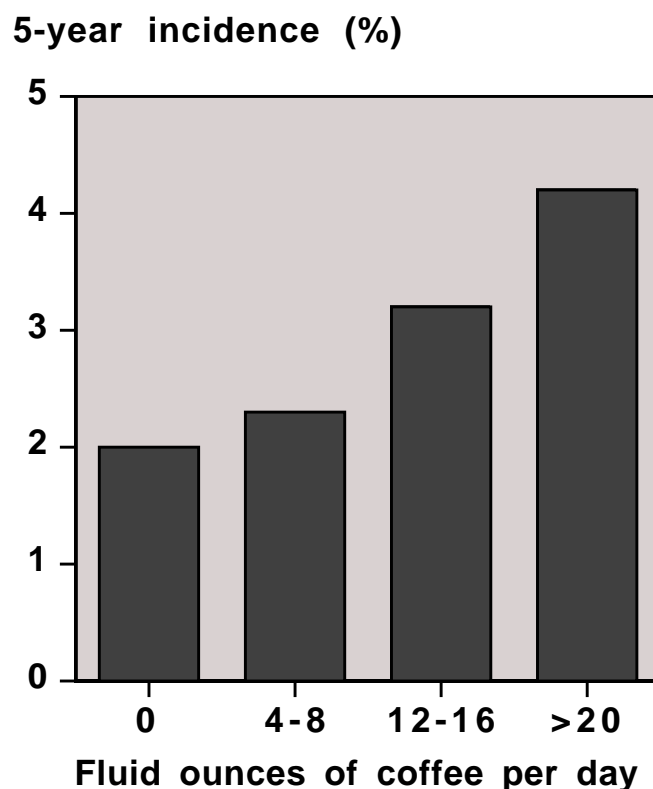
These three studies show us how careful we need to be in giving advice about lifestyle. It's a bit like Heisenberg's uncertainty principle - if you see it, it's not there any more. With lifestyle advice, any change for the good in one direction may be a change for the bad in another.

For coffee and men with hypertension, stopping drinking it may reduce the chance of a stroke, but increase the risk of colorectal cancer. Difficult, isn't it? But for pregnant women the evidence seems strong - limiting caffeine consumption will reduce the chance of a spontaneous abortion and a low birthweight infant.

#### References:

- 1 O Fernandes, M Sabharwal, T Smiley et al. Moderate to heavy caffeine consumption during pregnancy and relationship to spontaneous abortion and abnormal fetal growth: a meta-analysis. *Reproductive Toxicology* 1998 12: 435-44.
- 2 E Giovannucci. Meta-analysis of coffee consumption and risk of colorectal cancer. *American Journal of Epidemiology* 1998 147: 1043-52.
- 3 AA Hakim, GW Ross, JD Curb et al. Coffee consumption in hypertensive men in older middle-age and the risk of stroke: the Honolulu heart program. *Journal of Clinical Epidemiology* 1998 51: 487-94.

**Figure 3: Effect of increasing coffee consumption on incidence of thromboembolic stroke in hypertensive non-smokers**



# LAPAROSCOPIC APPENDECTOMY

Newer surgical techniques are sometimes unfairly criticised for not having been subjected to what has been called the "purifying heat" of a randomised controlled trial. This criticism cannot be levelled at laparoscopic appendectomy, and a new meta-analysis has pulled together all the studies to give us a pretty good picture of the results of this new technique [1].

## Searching

The review had a heroic search strategy, which included contacting many people for unpublished results (including abstracts submitted to meetings) and sending them data and information forms to complete and return. The authors used randomised trials with pre-specified outcome measures of operation time, complications (wound infections, intra-abdominal abscesses), postoperative pain, length of hospital stay and return to full activity.

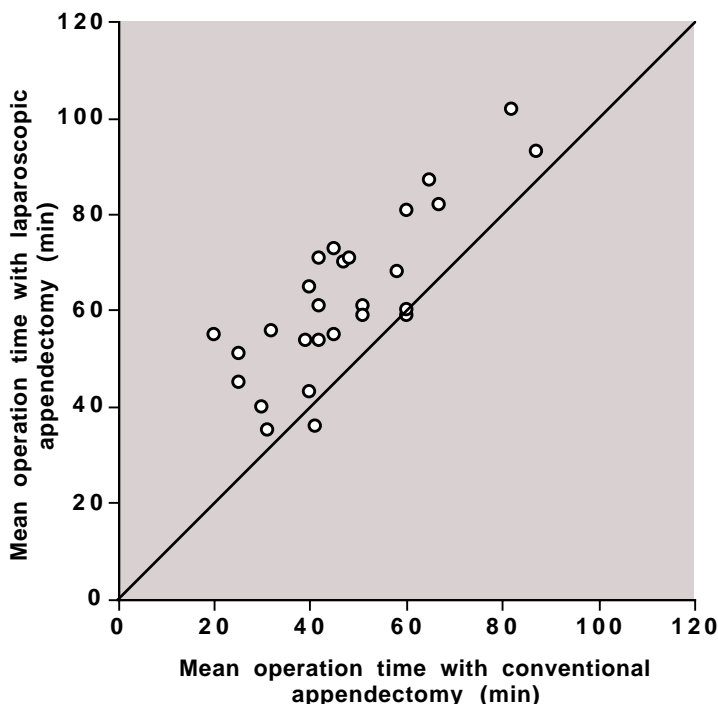
## Results

The analysis was on 28 randomised trials with 2877 patients. Only two trials were blinded (not unexpected). There was a wide range of inclusion and exclusion criteria in the studies, like sex, age and whether the appendix had burst or not.

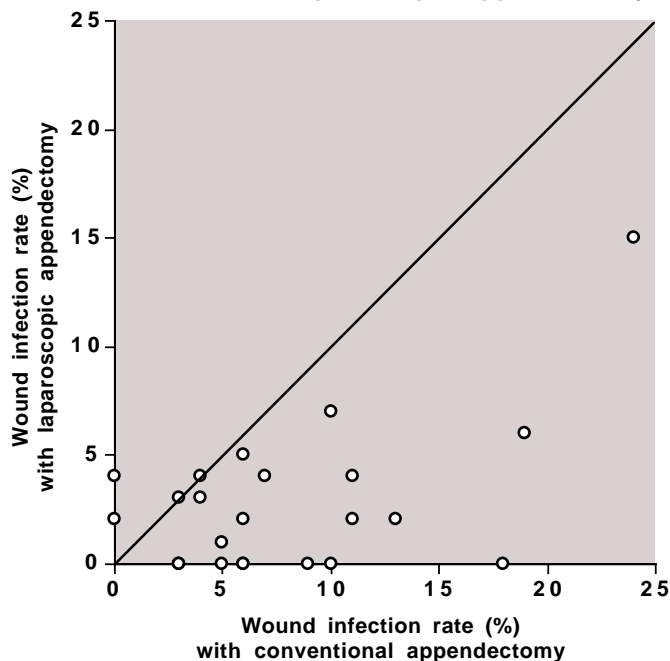
On average 8% of operations which started as laparoscopy were converted to open appendectomy (range 0% to 27%). Operating time was 16 minutes longer for laparoscopy (Figure 1). The length of hospital stay was an average of 15 hours less, and return to full activity 6.5 days earlier than with conventional appendectomy.

Wound infections were significantly less frequent with laparoscopic techniques; 36/1309 (2.8%) of laparoscopies had a wound infection compared with 93/1187 (7.8%) in conven-

**Figure 1: Comparison of mean operation time of conventional and laparoscopic appendectomy in randomised trials**



**Figure 2: Wound infection rates with conventional and laparoscopic appendectomy**



tional surgery. This is a NNT of 20 (95% confidence interval 15 to 31). The risk of developing an intra-abdominal abscess was 22/745 (3.0%) with laparoscopic and 10/653 (1.5%) with conventional surgery, with a relative risk of 1.8 (0.9 to 3.5).

## Comment

This is a thoughtful review which gives not only outcome data but an interesting discussion of issues of technical importance to surgeons and others. It could form an interesting base for discussing whether the benefits of a 5% reduction in wound infection was balanced by a 2% increase in intra-abdominal abscesses. Such a discussion could include issues about severity (how much worse is an average intra-abdominal abscess than an average wound infection), and how much weight should be put on the non-significant (just, statistically) incidence of abscesses. Important when as many as 1 in 12 of us will have our appendix out in our lifetime. The discussion ends with a quote "Laparoscopic appendectomy is an excellent operation, but we don't need it." Enjoy!

Reference:

- 1 S Sauerland, R Lefering, U Holthausen, EA Neugebauer. Laparoscopic vs conventional appendectomy - a meta-analysis of randomised controlled trials. *Langenbeck's Archives of Surgery* 1998 383: 289-295.

## 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](mailto:andrew.moore@pru.ox.ac.uk)  
Internet: <http://www.jr2.ox.ac.uk/Bandolier>

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