

NNTs FOR PREVENTATIVE INTERVENTIONS

Bandolier presents three examples of numbers-needed-to-treat for preventative interventions, antibiotics in acute otitis media (NNT 7), antibiotics after dog bites (NNT 16) and compression stockings for postoperative DVT (NNT 9).

Interpreting NNTs for prophylactic interventions requires thought. How serious is the event you are trying to prevent. Could it be treated effectively as and when it arises? Does the prophylaxis have any adverse effects? And then there is cost.

Two examples may help, from opposite ends of the spectrum. From the ISIS2 trial, using streptokinase and aspirin after myocardial infarction had an NNT of 20 to prevent 1 death at 5 weeks compared with doing nothing. Here is prophylaxis against a serious event, by definition not treatable if it occurs. The NNT for the adverse effect of haemorrhagic stroke with streptokinase was 1000.

From the less dramatic end of the spectrum is prophylaxis after dog bite. If no prophylactic antibiotics are given any

subsequent infection (10%) should be treatable. The NNT for antibiotic prophylaxis was 16, so that only one patient out of 16 receiving prophylaxis actually avoids infection as a result. The other 15 have antibiotics that they did not need, and which may have adverse effects. And then there is cost.

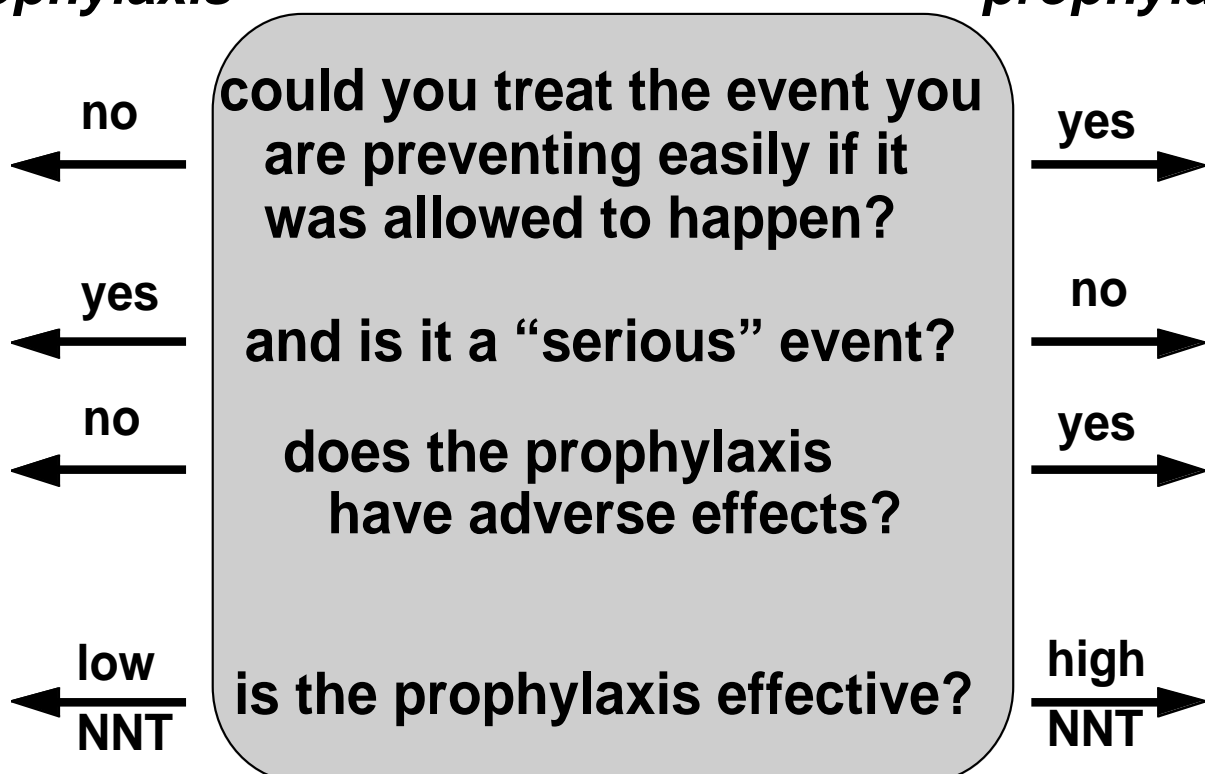
The NNTs for prophylactic interventions not only require thought but reinforce the message that NNTs are by definition relative. There is no rule that says that an NNT of 2 is always good and one of 100 is always bad: it depends on the context. A NNT of 20 in a fatal condition could be terrific - one person in 20 could be saved. The same NNT would not be terrific for prevention of postoperative vomiting if accompanied by significant adverse effects.

DOG BITES MAN

A classic headline, and an event that is common enough. But what happens next? Obviously treatment for the immediate effects of the bite are needed, but what of the possibility of infection? Is there a role for prophylactic antibiotics, and are they effective if used?

bias towards prophylaxis

bias against prophylaxis



Meta-analysis

A meta-analysis of randomised controlled trials of the use of prophylactic antibiotics found eight RCTs [1], six in the USA and two in the UK. All the studies used oral antibiotics, three using penicillin and three penicillinase-resistant penicillins. The overall occurrence of infection rates ranged from 3.2% to 45.8% (the latter in Middlesbrough, which had much the highest rate of infection; in this study 93% of patients had dog bites, the remainder being bitten by other humans, cats, a ferret and a rabbit). The cumulative incidence of infection was 16%.

Limited effect of prophylactic antibiotics

There were 323 patients who received placebo, of whom 52 became infected. There were 306 patients who received prophylactic antibiotics, of whom 30 became infected.

The relative risk of infection with antibiotics was 0.56 (95% confidence intervals 0.4 - 0.8), so antibiotics significantly reduced the risk of infection. It was interesting that while the meta-analysis demonstrated this clearly, only one of the eight trials individually showed results for antibiotics to be statistically superior to placebo.

Number-needed-to-treat

The NNT for antibiotic prophylaxis to prevent infection after dog bites was 16 (95% CI 9 - 92). If 100 patients with dog bite wounds seen in casualty are given oral antibiotics, on average 84 patients would escape infection regardless of therapy, nine will become infected despite medication, and seven will avoid infection because of the medication.

Is it worth treating 100 patients with antibiotics to prevent infection in seven? Cost benefit analysis is missing, so the answer is left to the reader. In the meantime, try to avoid being bitten in Middlesbrough!

Reference:

P Cummings. Antibiotics to prevent infection in patients with dog bite wounds: a meta-analysis of randomized trials. *Annals of Emergency Medicine* 1994 23: 535-40.

ANTIBIOTICS FOR ACUTE OTITIS MEDIA

Ear infections in children are common. In the USA there are 12.8 million episodes a year (about 45,000 per million population), usually in children aged 5 years or younger and most involve seeing a doctor. Despite there being over 170 published clinical trials there is no consensus on the best drug for the initial therapy for acute otitis media (AOM).

Meta-analysis

A meta-analysis of 35 randomised studies involving antimicrobial drugs in 5400 children may help. This very detailed study [1] is an exemplar of how systematic reviews can be done; the authors started with a written protocol defining the methods and objectives of the meta-analysis.

Study inclusion

Studies to be included had to be randomised controlled trials of antimicrobial drugs for the initial empirical treatment of simple AOM. The authors give exact definitions of what they mean for each of these important words to avoid any doubt about the definitions they used:

- Simple AOM - new or recurrent episodes of AOM in patients without underlying disorders.
- AOM - bulging or opacification of the tympanic membrane with or without reddening, with symptoms of acute infection.
- Initial empirical therapy - treatment of new-onset AOM without knowledge of the specific causative agent.
- Therapeutic antimicrobial agents - drugs administered to treat established AOM - with individual drugs defined.
- Randomised controlled studies - allocation of subjects by chance to one or more concurrent treatment groups, at least one of which involving a study drug as defined.

Their initial searching strategy identified 286 studies. The progress from that to the final tally of 30 included papers is set out with the reasons for each exclusion given.

Outcome measures

The primary end point was the clinical response to antimicrobial therapy. This was defined as the absence of all presenting signs and symptoms of AOM at the evaluation point closest to 7 - 14 days after therapy started. The appearance of the tympanic membrane, if reported, should be improved.

Neither middle ear effusion nor the lack of a bacteriologic cure was grounds for considering a specific treatment a failure. All outcomes less than success as defined, including unilateral resolution of bilateral AOM, were considered primary end point failures.

Patients, rather than ears, were the unit of analysis.

Results

Sixty-nine study arms were identified in the 30 trials and gave the following results:-

Intervention	N	Resolution (Mean ± SD)
Controls	4	70 ± 17
Standard spectrum antibiotics	26	77 ± 17
Extended-spectrum antibiotics	39	86 ± 13

Pre treatment tympanocentesis increased the primary control rates by 6.5% (95% CI 3 - 10%).

This paper has many different comparisons between different drugs, and a number of sensitivity analyses. The main findings of effect were the comparisons of penicillin, aminopenicillin or any antimicrobial against placebo or no drug controls. The odds ratios and rate difference (RD: same as absolute rate reduction x 100) for these were:-

Intervention	Odds Ratio (95% confidence interval)	Rate Difference
Penicillin	2.1 (1.2 - 4.0)	16 (5 - 27)
Aminopenicillin	3.0 (1.7 - 5.8)	13 (7 - 19)
Any antimicrobial	2.9 (1.8 - 4.9)	14 (8 - 19)

Number-needed-to-treat

The number needed to treat is calculated in the paper as 7. Six of every seven children with AOM either do not need antibiotics for primary control or will not respond to antibiotic therapy. All seven children have to be treated because we cannot predict which one of the seven is both at risk for failure and responsive to antibiotics.

Provided that the antibiotic given is safe, well-tolerated and affordable this need to treat many to control a few would be offset by a 14% higher primary control rate and a potentially lower incidence of suppurative complications.

Conclusion

The authors give a qualified yes to the question whether antibiotics should be part of the initial empirical therapy for AOM in children. As always there are qualifications, and these are elegantly dissected. As is so often the case, no single paper, or meta-analysis in this case, gives the entire result. But meta-analyses like this provide policy makers with the raw material from which to forge guidelines based on solid evidence.

Reference:

RM Rosenfeld, JE Vertrees, J Carr et al. Clinical efficacy of antimicrobial drugs for acute otitis media: metaanalysis of 5400 children from thirty-three randomized trials. *Journal of Pediatrics* 1994 124: 355-67.

GRADUATED COMPRESSION STOCKINGS TO PREVENT POSTOPERATIVE VENOUS THROMBOEMBOLISM

Postoperative venous thromboembolism can be prevented by methods that reduce the coagulability of blood or by methods that reduce blood stasis in the deep veins of leg. Graduated compression stockings reduce stasis, are a simple prophylactic approach, are inexpensive, easy to use and free of side effects.

Graduated compression stockings may be used alone or in combination with other methods of prophylaxis. They may be used in circumstances where the risk of venous thromboembolism is relatively low (as with abdominal surgery) or where it is high (after hip replacement).

The question is whether they are effective. A recent meta-analysis has gone a long way towards proving the point.

Meta-analysis

A group from Hamilton, Ontario, has performed a first class meta-analysis on published papers. They had a prior set of criteria for inclusion or exclusion based on methodology and diagnosis of thromboembolism. The inclusion criteria included:-

- Only randomised trials with proper randomisation
- Reliable objective tests of proven accuracy for the diagnosis of postoperative deep vein thrombosis
- Independent and blind interpretation of venography (when this was the outcome measure) by observers without knowledge of the patients' assignment or symptoms, and predefined criteria for an abnormal result.

Results

The searching strategy yielded 122 articles, of which only 35 were randomised trials. After further exclusions because of methodological inadequacy, the result was 12 trials for analysis, one in orthopaedic surgery and the others in moderate risk non-orthopaedic (mainly abdominal) surgery.

In the 11 moderate risk studies there were 1752 patients - some of whom were their own controls in studies where legs rather than patients were randomised.

In the control group without compression stockings 930 legs suffered 164 episodes of venous thromboembolism. In the group treated with graduated compression stockings, 932 legs had 58 episodes of venous thromboembolism. The pooled odds ratio was 0.28 (95% CI 0.23 - 0.42, $p < 0.001$), with a risk reduction of 68% (95% CI 53 - 73).

Number-needed-to-treat

The NNT was 9 (95% CI 7 - 13). If 100 postoperative patients are treated prophylactically with graduated compression stockings, 82% will not have a venous thrombosis anyway, 6 will have a thrombosis despite the treatment, but 12

will have had an episode of venous thrombosis prevented.

Conclusion

Surveys have shown that the use of graduated compression stockings varies greatly from less than 3% to over 70%. There is confusion over whether they are effective. Clearly, in moderate risk patients graduated compression stockings are highly effective, and given that they are cheap, easy to use, and have negligible adverse effects their use should be promoted widely in these patients.

In patients at high risk of venous thromboembolism, those undergoing hip replacement, for instance, there is insufficient evidence of their effectiveness either alone or in combination with anticoagulant prophylaxis. The single RCT identified in this paper where graduated compression stockings were used alone in orthopaedic patients did not show a significant reduction in episodes of venous thromboembolism.

Reference:

PS Wells, AWA Lensing, J Hirsh. Graduated compression stockings in the prevention of postoperative venous thromboembolism. Archives of Internal Medicine 1994 154: 67-72.

EVIDENCE-BASED JOURNALISM

The power of the press and other media to influence opinion is well understood. It can be used for purposes of which many of us would approve, but when, inevitably, it gets something wrong it can drive us to distraction. For instance, an episode of "The Chief" recently perpetrated the myth that radioactivity at nuclear power plants causes childhood leukaemia - disappointing when many years of painstaking research has investigated this and shown it be a population mixing phenomenon found in many non-nuclear projects.

It is more of a concern when a medical journalist writes to propose actions which are not based on evidence and which are, at best, controversial. The Times of May 16 carried an article by Dr Thomas Stuttaford on the health checks that every man and woman needs each year. Dr Stuttaford is an influential medical journalist, but we would take issue with the 18 checks he advocates shown in the box.

The following letter was *not* printed in The Times.

Sir,

The dose of Dr Thomas Stuttaford's customary common sense is lower than usual in his article on screening, which is written with evangelical zeal.

Screening is, of course, a deliciously attractive idea. A stitch in time is said to save nine and forms the basis of the enthusiasm for screening. However, for 18 of the tests recommended by Dr Stuttaford there is insufficient evidence to support their recommendation. There is, for example, no good evidence that women

under 50 benefit from mammography.

Because a disease is found early it does not mean that survival is improved. In some cases the only result is that the individual knows they have a disease for a longer period of time.

Ineffective screening is not only inefficient, it is also harmful, causing anxiety and exposing people who have false positive tests to further tests and treatment, each of which carries its own risks. Screening has an important part to play in health care, but it is not so extensive as indicated by Dr Stuttaford.

In health care decisions are increasingly evidence-based - namely backed by good scientific evidence. Perhaps The Times should follow this example and give references to support the assertions made by correspondents where evidence is available. Evidence-based journalism has a vitally important part to play in public education, but unsubstantiated assertions, with recommendations to attend clinics offering ineffective tests at high cost are more likely to do harm than good.

Yours faithfully,

J A Muir Gray

Is there evidence for effectiveness for these screening tests recommended by The Times of May 19?

The *Bandolier* screening blacklist:

- Chest X-ray in older patients, smokers and travellers.
- Haemoglobin for anaemia.
- ESR for inflammatory infective or malignant disease.
- Liver function tests in blood.
- Renal function tests.
- Calcium in blood.
- Uric acid in blood.
- Glucose in blood.
- Cholesterol.
- HDL / LDL ratio.
- Mammography in women over 40 years.
- Ultrasound examination of the ovaries.
- Bone density in women.
- Resting ECG.
- Exercise ECG on a treadmill.
- Ultrasound examination of the aorta in men over 55 years.
- PSA in men over 50 years.
- Helicobacter pylori.

Some of these, like cholesterol screening, have been examined and found wanting. Others, like PSA testing in men, are the subject of active research. *Bandolier* would like to know from any reader who is aware of evidence of effectiveness for the use of these tests as screening tests.

We would also like other examples of tests of unproven efficacy or of proven ineffectiveness to extend the *Bandolier* Screening Blacklist. We were tempted to offer prizes - first prize one private health check, second prize two etc. - but decided to depend on the public spiritedness of our readers.

SCREENWATCH

Readers of *Bandolier* frequently request that we carry the best available knowledge about screening programmes. Screenwatch will try regularly to do this.

Current thoughts on ovarian cancer for screening, treatment and follow-up have been summarised in the Journal of the American Medical Association reporting the conclusions of an NIH Consensus Conference (JAMA 1995, 273: 491-7). This is a thorough and useful description of where we are now, and a signpost to future developments. Reading it in detail is a must for those interested in ovarian cancer screening.

Dr Mike Bedford of the North Derbyshire Health Authority has sent us a paper entitled "Ovarian cancer screening - The Evidence". It contains much useful information, especially about the performance of currently available tests, and can be obtained from him at the address below. Mike Bedford has also written the following article on screening for ovarian cancer in asymptomatic women

Ovarian cancer screening in asymptomatic women

Ovarian cancer is a major public health problem. It is the most common, insidious, and lethal gynaecological malignancy. Despite this there is no mass screening programme to detect it. This has arisen because of the nature of the disease itself (the deep abdominal site of the ovaries, and a lack of a clear understanding of the disease), and the absence of a simple, cheap, and suitable, screening test.

Mortality from the disease depends on what stage it is detected. Changes in treatment over the last 30 years have not significantly improved survival. Hence, research work has centred around screening methods which could diagnose the condition earlier, and thus improve prognosis.

The size of the problem

It is the fifth most common malignancy in females. In England and Wales there are approximately 3900 deaths a year from the condition. The incidence is approximately 17 per 100,000 women per year. Although there is a low incidence, ovarian cancer often accounts for more deaths than cancer of the cervix and uterus combined. This is due to poor survival rates from the disease. Overall 5 year survival is around 35%.

Compared with this, the rates for early stage disease (stage 1) are excellent at around 80%. 5 year survival from late stage disease (stage 4) is around 5%. The death rate increases with age, the main number of deaths falling in the 65-75 year age group.

Risk factors

Migration studies have suggested Western lifestyle may be a contributory factor. Lifetime number of ovulations are closely associated with ovarian cancer risk so that

nulliparity, few pregnancies, early menarche, and late menopause, are all risk factors. Talc dusting of the perineum has been suggested, although the evidence for this is debatable.

Oral contraceptive use may decrease lifetime risk by as much as 40%. Other protective effects have been noted with high gravidity, hysterectomy, and sterilisation.

The most significant risk is a positive family history. Heredity is thought to account for between 5 to 10% of ovarian malignancies. There are three types of ovarian cancer namely epithelial (which accounts for the vast majority), sex-cord mesenchyme, and germ cell. Work on genetic inheritance has looked at epithelial cancer.

Three clinical types have been identified [1,2]:

Familial ovarian cancer

- Breast/ovary syndrome - families with an increased risk of both.
- Lynch type II syndrome - where clusters of ovarian, endometrial, and colorectal cancer are seen (sometimes called family cancer syndrome).
- Site specific - families with increased risk for ovarian cancer only.

All probably have autosomal dominant pattern with variable penetrance. Hence, healthy males can transmit the disease to their daughters. There have been suggestions that a woman who has one first degree affected relative (mother/sister/daughter), has an increased lifetime risk from 1.4% to approximately 3%.

Bruce Ponder [3], reviewing population based data [4], suggests that if there is only one close affected relative then this corresponds to a 1 in 40 (2.5%) risk of death from ovarian cancer by the age of 70. For a women with two or more affected close relatives the risks may be in the order of 30 to 40%. There is often an earlier onset with familial risk.

To further study family sets, a register of families with ovarian cancer in two or more close relatives has been set up by the United Kingdom Co-ordinating Committee for Cancer Research (UKCCCR) and Cancer Family Study Group called the UKCCCR Familial Ovarian Register [5]. This provides a resource in this area. Women can be referred to the study for investigation of the family tree, and the study will confirm the histological diagnosis in relatives. The study itself does not undertake actual screening but will make appropriate recommendations for screening to the original source of referral.

Screening tests available

There is a general consensus that pelvic examination, tumour markers, and ultrasound examination form the three most likely candidates for a screening programme. Pelvic examination is particularly poor in screening for ovarian cancer and there is little to recommend it.

The most intensively investigated serum tumour marker is CA 125. Problems encountered include the fact that it is not specific for ovarian cancer, and there is a lack of specificity and sensitivity particularly in early disease.

Both trans-abdominal and trans-vaginal ultrasound have been used in screening trials. Because of the low incidence of the disease it is difficult to attain a high positive predictive value from the screening tool. This is particularly important in ovarian screening where a positive test may result in laparotomy. Increasing the incidence in the screened group by focusing on high risk groups (such as those with familial risk) allows the test to more easily attain reasonable predictive values.

What should purchasers provide?

A major drawback is the lack of a randomised controlled trial to show a reduction in mortality from screening. The European Randomised Trial of Ovarian Cancer (ERTO) is about to start, and should provide evidence in this area. Ovarian cancer is a high profile media issue. This often results in women requesting advice. Thus a decision must be made on what can be identified as best practice based on the available evidence.

There is no evidence to support screening asymptomatic women in the general population for ovarian cancer.

Screening asymptomatic women with one affected relative should be confined to recognised research studies [3].

Women with two or more first (mother/daughter/sister) or second (grandmother/aunt) degree affected relatives with the disease are at a markedly increased risk. There is no evidence as yet to support actively seeking these women out in the community, as due to the lack of RCT evidence on reduction in mortality, benefit cannot be guaranteed. If a woman with this history presents requesting screening, she should be referred for further advice. This might be to a Gynaecologist or to the UKCCCR Familial Ovarian Cancer Study. Any decision to undergo screening must be based on a fully informed choice.

The current criterion for the UKCCCR study is two first or second degree relatives living or dead with (epithelial) ovarian cancer. The protocol suggests yearly screening from the age of 25 or 30 with a method such as trans-vaginal or trans-abdominal ultrasound.

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References

- 1 HT Lynch, P Watson, C Bewtra, et al. Hereditary ovarian cancer - Heterogeneity in age at diagnosis. *Cancer* 1991; 67: 1460-6.
- 2 HT Lynch, W Kimberly, WA Albano, et al, Hereditary nonpolyposis colon cancer (Lynch syndrome I and II). *Cancer* 1988; 56: 934-8.

- 3 Non-surgical aspects of ovarian cancer. Report of a meeting of Physicians and Scientists, Institute of Cancer Research and the Royal Marsden Hospital, London. *Lancet* 1994. 343: 335-40.
- 4 BAJ Ponder, DF Easton, J Peto. Risk of ovarian cancer associated with a family history. In: Sharp F, Mason W D, Leake R, eds. *Ovarian cancer*. London: Chapman and Hall, 1990. 3-6.
- 5 UK Familial Ovarian Cancer Study, Box 238, Addenbrookes' Hospital, Hills Road, Cambridge, CB2 2QQ.

LATEX ALLERGY

Bandolier #7 carried a review of latex allergy. A recent publication [1] reviews the clinical symptoms of latex rubber allergy and provides guidelines for its management.

A big problem

In the four years between 1988 and 1992, about 13 billion latex gloves were used in the USA - about 11 gloves per year per person. In the same period the FDA received reports of more than 1,000 systemic allergic reactions to latex, 15 of which were fatal. The prevalence of latex allergy in health care workers is between 7% and 10%, but is up to 24% in those with atopic allergy.

Guidelines

Some of the key points reported:-

- All persons at risk from latex allergy should have a careful history taken and should complete a standardised latex questionnaire (given in the paper).
- High risk patients should be offered clinical testing for latex allergy. This includes children with spina bifida and atopic health care workers.
- A latex-free environment is defined as one in which there is no latex glove use by any personnel, nor direct contact with other latex devices.
- Procedures on children with spina bifida should be done in a latex-free environment.
- Procedures on all patients with positive skin tests results should be done in a latex-free environment.

Reference:

- 1: GL Sussman, DH Beezhold. Allergy to latex rubber. *Annals of Internal Medicine* 1995 122: 43-6.

THE UK COCHRANE CENTRE AND THE NHS CENTRE FOR REVIEWS AND DISSEMINATION: THEIR RESPECTIVE ROLES

Dr Chris Hyde, The UK Cochrane Centre

The following summarises an article published in 1994 [1].

Background:

- The UK Cochrane Centre and the NHS Centre for Reviews and Dissemination are both part of the Information Systems Strategy of the NHS Research and Development Programme.
- The third element of this strategy is an NHS Projects Registers System.

The UK Cochrane Centre and its role:

- Established at the end of 1992 in Oxford.
- In addition to its place in the NHS, is part of an international collaboration - The Cochrane Collaboration.
- Is one of nine centres established world-wide, within the Cochrane Collaboration.
- Specific role: "To collaborate with others to build, maintain and disseminate a database of systematic, up-to-date reviews of randomized controlled trials of health care."
- This role holds within both the NHS Information Systems Strategy and the Cochrane Collaboration.
- The database produced is called *The Cochrane Database of Systematic Reviews*.

The NHS Centre for Reviews and Dissemination and its role:

- Established at the end of 1993 in the University of York.
- Has two roles within the NHS, the first relating to reviews and the second to dissemination.
- The Centre "proactively commissions or itself carries out reviews on behalf of the NHS". The reviews "focus on specific questions of importance to the NHS, principally in areas of effectiveness, and cost-effectiveness of health care interventions, management and organisation of health services".
- The Centre "disseminate(s) the results of research to the NHS in order to enhance effective decision making". In this respect the Centre will "develop and maintain databases of published reviews and studies reporting economic evaluation of health care and will develop an enquiry service for handling appropriately filtered requests for information on the availability of reviews."

on the availability of reviews." The Centre will in addition "assist the Cochrane Collaboration to disseminate the contents of *The Cochrane Database of Systematic Reviews* to the NHS".

Summary:

- There are substantial areas of common interest between the UK Cochrane Centre and the NHS Centre for Reviews and Dissemination. Commensurate with this both organisations are committed to collaborate closely and avoid unintended duplication.
- In this context, the difference in emphasis of the roles of the two centres in the NHS may be summarised as:

REVIEWS:

The UK Cochrane Centre facilitates individuals to undertake and maintain systematic reviews of randomised controlled trials in response to the interest expressed by those individuals, whereas the NHS Centre for Reviews and Dissemination commissions individuals to undertake systematic reviews of research evidence in response to questions of current importance to the NHS. Thus the main differences lie in the starting point for, and the long-term commitment to maintain the review, not the rigour of the review's method.

DISSEMINATION:

Only the NHS Centre for Reviews and Dissemination will have the capacity to respond to requests from individuals in the NHS about the availability of reviews of research. Despite this, both centres are committed to the effective dissemination of the information they produce, within the constraints of the resources with which they are provided. The UK Cochrane Centre is committed to work with others to disseminate *The Cochrane Database of Systematic Reviews* and to make this database as accessible as possible. The NHS Centre for Reviews and Dissemination will take a more direct and active role in the dissemination to the NHS of key messages arising from particular systematic reviews.

Reference:

- 1 Sheldon T, Chalmers I. The UK Cochrane Centre and the NHS Centre for Reviews and Dissemination: respective roles within the Information Systems Strategy of the NHS R&D Programme, coordination and principles underlying collaboration. *Health Economics* 1994;**3**:201-203.

CORRESPONDENCE

Focus on drips: helpful heparin - not for free thyroxine!

Heparin may help catheter sampling and life [1] but it is most unhelpful for free thyroxine measurements. Parenteral heparin, even at low doses, produces an artefact with free thyroxine assay methods [2]. Whether thyroid function should be assessed in sick patients (who are likely to have a peripheral catheter) is debatable [3]. However, if this request is indicated a prudent step would be to check with the laboratory before the sample is collected.

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References:

- 1 D Carroll. Focus on Drips. **Bandolier** 1995 14: 1-3.
- 2 R Mardell, TR Gamlen. Artefactual reduction in circulating free thyroxine concentration by radio-immunoassay. *lancet* 1982 i: 973-4.
- 3 RJ Mardell, TR Gamlen. Thyroid function tests. 1: Effects of illness. *Hospital Update* 1995 21: 231-6.