Letters

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Impact of NHS Direct on demand for immediate care

Target communities show poor awareness of NHS Direct

Editor—Munro et al found that NHS Direct had no discernible effect on the use of emergency ambulances or accident and emergency departments in the first year of operation, leading to a suggestion that this service may not prove cost effective.[1] The study is limited by an assumption that the population studied had complete awareness of the service. Six months after the introduction of East Midlands NHS Direct we had anecdotal evidence to suggest that many patients attending our accident and emergency department were unaware of the telephone advisory service.

Consequently we undertook a survey of 300 consecutive ambulatory patients (or their parents) who referred themselves to the accident and emergency department and had not contacted NHS Direct. We wanted to find out whether they were aware of the service. Altogether 266 (89%) questionnaires were completed, with 166 (62%) patients claiming to have had no previous awareness of NHS Direct. Furthermore, of the 100 patients who were aware of the service, only 36 were aware of the telephone charge while 51 thought that calls were taken by doctors. Only eight "aware" patients, however, said that they would distrust advice given by a nurse, a finding that supports a study by O'Cathain et al.[2]

The survey also determined which sections of the community were unaware of NHS Direct. Patients aged over 65 (all 9), patients from ethnic minorities (41/59; 69%), patients from predominantly less affluent postcodes (101/129; 78%), and young men (20/28; 71%) were overrepresented. The survey also found that 240 (90%) patients claimed to have access to a telephone and that 56 (21%) might have been redirected away from our department by NHS Direct.

In the light of these findings we would say that NHS Direct has failed to market its existence to those members of the community who frequently access urgent health care. The results of NHS Direct impact studies have consequently been confounded by this oversight. Whether a proper national publicity campaign can improve the impact of this beleaguered service remains to be seen.

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2 O'Cathain A, Munro JF, Nicholl JP, Knowles E. How helpful is NHS Direct? Postal survey of callers. *BMJ* 2000;320:1035. (15 April.)

Service has not decreased attendance at one paediatric A and E department

Editor—Our experience in a paediatric accident and emergency department supports the data showing that NHS Direct has had little or no impact on attendance rates in primary care.[1] We audited the attendance at Sunderland Royal Hospital's paediatric accident and emergency department before and after NHS Direct started operating. Admissions increased from 844 to 860.

The paper from Sheffield did not look at the impact on the number of telephone calls to the accident and emergency department for medical advice.[1] This is a large and often forgotten workload. We received 453 calls before NHS Direct began and 576 after, a 27% increase. Fourteen calls to the department were redirected there from NHS Direct.

We controlled for the time of year and the population. The annual attendance at the accident and emergency department did not increase over the two years of the audit. It would have been better if we could have done a crossover trial in the same population with and without NHS Direct. This criticism could also be made of the Sheffield work. Such a trial, however, would mean the temporary withdrawal of a popular public service.[2]

Our service does not provide documentation, computerised protocols, or staff training for the telephone advice given. It had been planned that all calls would be redirected to NHS Direct. This would have provided equity and safety for patients and staff. It has not been possible, however, to divert calls to NHS Direct because of the unexpectedly high volume of calls that it has received.

NHS Direct has not decreased the attendance at our paediatric accident and emergency department and has coincided with an increase in the number of telephone calls to our informal service. This decreases the time for patient contact. The situation needs further research and consideration if NHS Direct is to be a success.

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We thank the paediatric accident and emergency nursing and medical staff and audit department for their help.

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2 O'Cathain A, Munro JF, Nicholl JP, Knowles E. How helpful is NHS Direct? Postal survey of callers. *BMJ* 2000;320:1035. (15 April.)

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Evidence on endometriosis

Elitism about randomised controlled trials is inappropriate

Editor—The article by Farquhar focuses on evidence from randomised controlled trials for the effective treatment of endometriosis.[1] A casual reader could conclude that these trials are the only evidence for effective treatment.

The definitive treatment of endometriosis is simple: surgical eradication. The success of surgical treatment is best assessed by determining how much disease, if any, remains after operative intervention. This must include appropriate mapping of endometriotic deposits. Excision biopsy is the most effective way of treating both superficial and deeply invasive disease and allowing histological confirmation. It has been shown to have a cure rate of 57-66% at re-evaluation.[2 3]

There are no such follow up data for patients treated by laser vaporisation or electrocoagulation. The randomised controlled trials cited in Farquhar's article have focused on pain or infertility. They do not answer the question of efficacy in destroying the disease.

If symptoms of pain and infertility are a result of endometriosis it follows that destroying the disease will cure the pain and infertility. Pelvic pain and infertility are not solely caused by endometriosis, and therefore studies that focus on symptom response are limited in their ability to determine how successful a type of treatment is.

Randomised controlled trials are often viewed as better evidence than observational cohort follow up or case-control studies because of the elimination of bias, but the information they produce is usually no different from that produced by such studies.[4] The many limitations of such trials make them unsuitable to be viewed as the single, preferred way to study clinical questions.[5]

Although the concept of evidence based medicine has focused attention on what is or is not a good type of study, elitism about randomised controlled trials taken to its illogical furthest extent, as in this case, will be harmful to everyone involved in the successful treatment of endometriosis.

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Author's reply

Editor—Redwine et al raise two separate issues: the appropriate outcomes with which to monitor response to treatment of endometriosis and whether randomised controlled trials are the appropriate method to test effectiveness of treatments for endometriosis.

They suggest that the definitive treatment for endometriosis should be surgical eradication and state that the success of surgical treatment is best assessed by whether there is residual disease after operative intervention. Increasingly, the focus has been on using research outcomes that matter to patients.[1] In the report, patient oriented outcomes of relief of pain and pregnancy rate were chosen as the major outcomes as these are the outcomes considered to make a difference to the daily lives of women with endometriosis. Evidence also suggests a poor correlation between disease and symptoms in women with endometriosis. Therefore seeking to eliminate all endometriosis in well patients may not always be of benefit to them.[2]

Redwine et al cite a paper by Benson and Hartz comparing observational data and data from randomised controlled trials. In that article there was no universal agreement between the outcomes from the observational studies and the trial data. The editorial that accompanied the article was critical of the report in several respects and suggested that the studies used were a highly selected sample.[3] It concluded that observational databases can be useful adjuncts to randomised controlled trials, to see whether efficacy under controlled conditions in specialist centres translates into effective treatment in routine practice. There is even an example of observational data misleading treatment decisions in endometriosis: medical treatment for endometriosis and subfertility used to be common practice until the results of randomised controlled trials were available.[4 5]

As mentioned in published reports, in the case of surgical destruction two randomised controlled trials have shown benefit both in relief of pain and in improved fertility, so there is little doubt about the benefit of surgery. I agree with Redwine et al that laparoscopic surgery is very important in the management of endometriosis.

Redwine et al end by suggesting that reliance on randomised controlled trials will be harmful to everyone concerned with the successful treatment of endometriosis. I am not sure whether they mean patients. Assuming they do, then I have to differ. The trial data presented in this report should reduce the risk to patients. For example, women with endometriosis and subfertility should no longer be routinely offered ovulation suppression as a form of treatment as their ability to conceive will be delayed by many months.

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Seeing what you want to see in randomised controlled trials

Authors' choice of study was ill informed

Editor—McCormack and Greenhalgh's suggestion that those involved in running and reporting clinical trials might be able to engineer a worldwide "groupthink" spin on the results is an intriguing notion.[1] But their choice of the United Kingdom prospective diabetes study (UKPDS) as an example to support their hypothesis is ill informed given the manner in which this study was reported.

We note with interest Greenhalgh's earlier commentary on an article by Horton concerning the "spin that authors place on their own work."[2] In this, she highlighted the "unjustified assumption that this spin is necessarily evil, insidious, and the last remaining bastion of caprice in the otherwise objective terrain of scientific publication," and she challenged Horton to "produce a single, clinically important instance of scientific heads being turned by rhetoric and rhetoric alone."

There was a complete embargo on all outcome data from the United Kingdom prospective diabetes study before their presentation at a meeting of the European Association for the Study of Diabetes on 12 September 1998. To avoid the usual scenario whereby conference reports are given wide publicity before peer reviewed manuscripts are available, the UKPDS Group worked closely with the editors of the *Lancet* and the *BMJ* to ensure that as many of the primary results as possible were published in five peer reviewed papers on the same day as our conference presentation. In addition, 100 slides illustrating the published data were made available on our website at midnight that day (www.dtu.ox.ac.uk/ukpds/).

We believe that the manuscripts and the slides present the results without spin and in a scientifically rigorous fashion. The findings in the summary of the main glucose study paper give almost equal prominence to the positive results and those adverse issues of concern.[3] The interpretation states categorically that "intensive blood-glucose control by either sulphonylurea or insulin substantially decreases the risk of microvascular complications, but not macrovascular disease."

McCormack and Greenhalgh's reworking of selected data from the United Kingdom prospective diabetes study adds nothing, since our papers listed the correct absolute and relative event rates for all outcomes. We would agree that it is

important to examine in detail the relation between prevailing haemoglobin A_{1c} concentrations and subsequent clinical outcomes. These analyses, which were shown at the original presentation, have been published in the *BMJ*[4] together with a second paper addressing the relation to prevailing blood pressure.[5] The degree to which the authors of any paper can influence editorials and debate is open to conjecture, but we can confirm that those cited were published without reference to us.

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1 McCormack J, Greenhalgh T. Seeing what you want to see in randomised controlled trials: versions and perversions of UKPDS data. *BMJ* 2000;320:1720-3. (24 June.)
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Meta-analyses may suffer from interpretation bias too

Editor—McCormack and Greenhalgh's article states that interpretation of clinical trials is neither objective nor value free.[1] A colleague and I reached the same conclusion in a letter to the *BMJ* after evaluating two meta-analyses of the effect of antibiotic treatment on acute bronchitis or cough.[2–4] Eight of the nine studies extracted were the same in the two meta-analyses, and 90% of the 750 patients were evaluated in both. The two meta-analyses came to opposite conclusions: one that antibiotic treatment had a modest beneficial effect, the other that it made no significant difference.

We concluded that the different conclusions might lie in different research objectives and different choice of outcome measures. In our opinion two important questions in meta-analyses should be: Which outcome measures are the most clinically relevant? and Are the differences found to be significant also clinically important? The choice of outcome measures may be crucial for the main conclusion, so it should be explicit and well substantiated. We found that in meta-analyses too there is an element of subjectivity in the research question posed, the choice of outcome measures, and the evaluation of whether significant differences are also clinically important.

Our conclusion is in line with McCormack and Greenhalgh's: that the discourse about the meaning and clinical importance of results of research should be strengthened. That is the only way we can apply new results into practice.

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Authors' reply

Editor—We agree with Holman that results from the United Kingdom prospective diabetes study (UKPDS 33 and 34) were presented reasonably fairly in the *Lancet*.[1 2] Our primary concern was not with the study group's publication itself but with the editorialisation of the results by other authors. We did not suggest that a "groupthink" response was "engineered" by the UKPDS Group. One of the most important concepts of groupthink is that it is not something that is engineered—it is simply a process of group dynamics.

Perhaps part of the issue is with the use of the word "spin"; by spin we meant both intentional and unintentional bias in the delivery of information that draws the authors and readers to a set of conclusions. There is virtually no way of presenting or interpreting results without bias. Our paper presented the UKPDS Group's results in the way that we think they should have been presented and reflects whatever internal biases both of us have.

Holman correctly points out that one of us (TG) argued in a commentary on Horton's article in 1995 that the results of scientific studies are generally presented without much spin.[3] As the responses to our paper show, however, the subsequent publication sagas of several high profile clinical trials have made her argument in that article quite untenable and highlight the importance of Horton's message.[3]

Despite Holman's best intention, and his belief "that the manuscripts and the slides present the results without spin," we believe that there are several cases of unintentional bias in the way the information is provided by these investigators. The box contains a few examples of the bias in the UKPDS Group's slide presentation (a synopsis of the results of their study).[4]

We encourage authors and readers to put aside their preconceived notions of the benefit of drug treatment and the value of surrogate markers before reading or writing medical articles and review the objective results as critically as they can.

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4 Diabetes Trials Unit, University of Oxford. UKPDS overview. www.dtu.ox.ac.uk/ukpds/

Some examples of bias in UKPDS Group's synopsis of results[4]

- In the summary and conclusion slides all benefits were presented as relative risk reductions, not as absolute risk reductions
- The relative benefits of treatment were reported over 10 years, but the absolute incidence of hypoglycaemic events was given per year
- Adverse reactions (such as hypoglycaemia and weight gain) were not mentioned in the conclusions
- UKPDS 34 showed that in patients with type 2 diabetes who were obese the use of sulphonylureas and insulin over 10 years did not reduce the chance of microvascular or macrovascular disease. This clinically important finding is not mentioned in any of the slides
- UKPDS 33 showed that 10 years of treatment with sulphonylureas and insulin did not produce a significant reduction in any type of macrovascular complication, yet this was not mentioned in the conclusion slides
- The investigators state in the conclusion slides, "There are no major differences between the therapies tested." Yet UKPDS 34 showed that metformin was the only agent that reduced the chance of macrovascular events, not only compared with placebo but also when compared with the sulphonylurea and insulin group (and perhaps even independently of the reduction in haemoglobin A_1 concentration—another point not mentioned anywhere in the slides)
- On the basis of their results, the investigators recommended the use of combinations of agents with different actions to treat type 2 diabetes; yet the only results presented (albeit a subset analysis) on combination treatment showed that in patients in whom sulphonylureas were started and who then had metformin added, diabetes related death and all cause mortality were significantly increased

Thyroid function tests

Tests must still be done in possible thyroid dysfunction

EDITOR—The article by O'Reilly on reassessment of thyroid function tests raises some important questions but is misleading in several respects.[1] Clinical features must of course be given full consideration in the assessment of possible thyroid dysfunction, but appropriate tests must still be done.

The symptoms of both hyperthyroidism and hypothyroidism are non-specific and can be mimicked by other conditions. Thus the practice of prescribing thyroid treatment on a clinical basis alone without biochemical confirmation carries potential risks. The statement that "the clinical features of hypothyroidism . . . have been relegated to the status of historical curiosities" is absurd. What the doctor aims to do is not simply to categorise a patient into hypothyroidism, hyperthyroidism, or the subclinical variants but rather to make a full diagnostic assessment, of which thyroid function tests are one important facet. Surprisingly, O'Reilly makes no mention of autoantibody tests, which are also helpful in assessing thyroid disease.

With regard to hyperthyroidism, a reduced thyroid stimulating hormone concentration is not in fact diagnostic. Clinical assessment is imperative, and before thyrotoxicosis is diagnosed the thyroxine (and in some cases triiodothyronine) concentration should be checked. The practice of using results of thyroid stimulating hormone tests alone to indicate hyperthyroidism is to be deplored and has led to a mistaken diagnosis in several cases subsequently shown to be cases of hypopituitarism.

O'Reilly mentions the use of thyroid stimulating hormone for screening purposes; the figures quoted for misleading results in the general population are interesting but date from 10 or more years ago. Thyroid stimulating hormone assays have considerably improved since then, and thus these numbers may not now be relevant.

O'Reilly is probably correct in claiming that too many indiscriminate requests for thyroid stimulating hormone tests are made. In some situations, however, notably in pregnancy, thyroid tests are not performed frequently enough. Recent studies have shown that raised maternal thyroid stimulating hormone concentrations or low thyroxine concentrations, or both, in early pregnancy are associated with impaired neuropsychological development of the child.[2 3] There should be greater awareness of this and of the possibility of hypothyroidism in early pregnancy. All women known to be hypothyroid should be advised to increase their dose of thyroxine as soon as pregnancy is diagnosed, and the adequacy of the dose should be monitored by measurement of thyroid stimulating hormone concentration.

In conclusion, thyroid stimulating hormone assays are not infallible and must always be interpreted in the light of clinical features, effects of drug treatment, thyroxine concentrations, and antibody status.

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Thyroid stimulating hormone outside the normal range has important implications

EDITOR—Although O'Reilly suggests that the reference interval for thyroid stimulating hormone could be extended to 21.5 mU/l,[1] this assertion is unjustified by its numerous published reference intervals. As an example we quote our recent experience measuring thyroid stimulating hormone with the Roche Elecsys 2010 analyser in excess serum received in the laboratory for other investigations on 324 patients undergoing either elective surgery or cholesterol screening. Patients taking thyroxine were excluded. We found results ranged from <0.005 to >100 mU/l, but the central 95% portion was 0.5 to 5.8 mU/l. False positive and negative results are possible with any test but can be minimised if the confidence intervals for the limits of the reference interval are calculated, which for our population are 0.22-0.61 and 5.2-6.3 for the lower and upper limit respectively.

The concept of subclinical hypothyroidism is based on the log-linear feedback loop between thyroxine and thyroid stimulating hormone: for one unit change in thyroxine there is a 10 unit change in thyroid stimulating hormone. The prediction of disease by the measurement of an intermediate marker is now well established in the absence of clinical symptoms—for example, calcium concentration, cholesterol concentration, and blood pressure. Since the review by one of us (APW) that seems to have provoked some of the statements made by O'Reilly it has been shown that changes in endothelial function and cholesterol concentration are apparent in subclinical hypothyroidism and even in people whose thyroid stimulating hormone is greater than 2 mU/l.[3 4] This provides a physiological basis for the Rotterdam study, which clearly shows that subclinical hypothyroidism is associated with an increased risk of ischaemic heart disease.[5]

O'Reilly is also concerned that non-specialists cannot understand from the review[2] the implications of a high normal thyroid stimulating hormone (>2 mU/l) compared with one which is outside the reference interval. We trust the *BMJ* readership more. The fact remains that a value outside the reference interval is not simply a minor variation but is important both in terms of predicting future hypothyroidism and in causing biological effects.[3 4]

Finally, the danger we perceive in O'Reilly's article is that it may encourage the mistaken belief that hypothyroidism can be diagnosed clinically. At least let us be clear that symptoms and signs are inadequate for diagnostic purposes and thyroxine is not indicated unless hypothyroidism (clinical or subclinical) is confirmed biochemically.

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Accurate diagnosis depends on both clinical judgment and results of tests

EDITOR—O'Reilly is correct in highlighting the difficulties in interpreting the results of thyroid function tests but overstates his view that the clinical aspects of thyroid disease have been downgraded.[1] Furthermore, he misrepresents the data presented in two of our papers. We did not consider abnormal thyroid stimulating hormone concentrations in isolation when arriving at a diagnosis of subclinical hyperthyroidism. The patients with suppressed serum thyroid stimulating hormone and normal thyroid hormone concentrations on whom we reported also had clinical evidence of thyroid disease.[2] The finding of an abnormal serum thyroid stimulating hormone in some patients taking thyroxine is an indication for adjustment of the dose; we did not imply that these patients were treated with an optimal dose of thyroxine.[3]

The sensitivity of pituitary thyrotrophs to minor changes in thyroid hormone concentrations is such that biochemical evidence of thyroid disease will be apparent before clinical features develop. Thus a patient with an incidental finding of a serum thyroid stimulating hormone concentration of 7.0 mU/l (normal <5.0 mU/l) is unlikely to be clinically hypothyroid but may well have a goitre of Hashimoto's thyroiditis on examination and antibodies in the serum directed against thyroid peroxidase. Treatment with thyroxine would be an acknowledgment not of hypothyroidism but of the well recognised progression of thyroid failure in future years, as shown by the second Whickham survey—in other words, prevention is better than cure.

The finding of a suppressed serum thyroid stimulating hormone concentration, with or without a raised free thyroxine concentration, would perhaps indicate examination for the presence of a nodular goitre. There is then the potential for isotope scanning and measurement of thyroid stimulating hormone receptor antibodies to determine whether thyroid disease is present.

Some doctors argue that clinical judgment is more sensitive than biochemical tests of thyroid function and justify the use of thyroxine to treat non-specific symptoms in patients with normal biochemistry. The only controlled trial of thyroxine in such patients, however, showed no benefit,[4] which is good evidence for the robustness of the currently available tests.

Nothing is to be gained by those who advocate the primacy of thyroid function tests or of clinical examination in the diagnosis of thyroid disease. The correct diagnosis will usually be made on the basis of both.

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Doing more tests is not always better

Editor—O'Reilly's review of thyroid function tests is apposite at a time when most laboratories are experiencing an exponential increase in requests for these tests.[1] It is worrying that clinical diagnosis has been relegated to history and that assessment is based almost entirely on biochemical tests. The only comfort that laboratories can derive from the huge increases in workload and the cost of doing these tests is that doctors apparently have more confidence in laboratory results than in their own clinical assessment.

Thyroid function tests are notorious for producing misleading results in non-thyroidal illness, and yet there are few patients in medical and care of the elderly wards who do not have these tests. Routine preoperative laboratory testing is unnecessary except in specific clinical conditions.[2] Yet most patients who have an asymptomatic euthyroid goitre or are taking adequate thyroxine replacement have their thyroid function tested before elective non-thyroid surgery (even if results of tests were normal a few weeks or months before). Evidence based medicine has been slow to reach thyroid function testing.

While there are no data on the relative importance of biochemical thyroid function tests and clinical symptoms and signs in assessing thyroid dysfunction, laboratories would be well advised to consider ways of reducing unnecessary and excessive testing. We refuse samples on groups of patients who have (*a*) had these tests done within the previous month irrespective of the reason, (*b*) started thyroxine or had the dose changed within the previous six to eight weeks, or (*c*) had normal results on routine screening for primary thyroid disease within the previous year. This has led to a saving of over 100 requests a month—our current daily workload—which, if translated into money, is not an insignificant amount. This is of course only possible because we have a laboratory computer system that can easily identify these patients.

Unless we have data about thyroid function testing related to clinical outcomes it is difficult to justify the increasing trend in the use of these tests. Doing more biochemical tests only leads to more confusion, especially if results do not agree with clinical presentation. This is certainly an area where more is not necessarily better.

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Thyroid function testing means different things to different people

Editor—O'Reilly suggests that the role of thyroid function tests should be reassessed.[1] In any reassessment it needs to be recognised that different specialties may have different requirements for thyroid function testing. Minor degrees of thyroid dysfunction that seem inconsequential in endocrinological settings may be important in groups who are differentially sensitive to changes in thyroid function, such as patients susceptible to mood disorders.

Thyroid dysfunction, including dysfunction classed as subclinical according to existing biochemical norms, is an important factor in the onset of depressive states[2 3] and resistance to antidepressant treatment[4] and can aggravate mood instability in bipolar mood disorders.[2] Treatment with thyroid hormones or antithyroid treatment can be beneficial in these and related cases even when circulating thyroid hormone concentrations fall within the normal range.[2 4 5]

If thyroid stimulating hormone assays are not routinely performed in these groups, subclinical thyroid dysfunction is more likely to be unrecognised and untreated. In these groups at least, the difficulties identified by O'Reilly need to be addressed primarily by further biochemical research. Increased attention to clinical signs of thyroid dysfunction will be of limited help.

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Author's reply

Editor—I agree with Kendall-Taylor that thyroid stimulating hormone assays are not infallible and must be interpreted in the light of clinical features. I also agree with Toft and Beckett that there is nothing to be gained by those who advocate the primacy of thyroid function tests or clinical examination and that the correct diagnosis will be made on the basis of both clinical examination and the results of tests.

I drew attention to the observation that the clinical features of thyroid dysfunction are now rarely discussed in the medical literature and that, as a consequence, the impression is given that they are of little importance. The clinical features are given in publications such as *Thyroid Disease—the Facts*,[1] which I recommend to students and trainees. Sadly, some have the impression that because such publications were written primarily for patients the data they contain that are not available in the conventional medical literature are of little importance.

This view is re-enforced when they note that the clinical features of thyroid disorders have been downgraded in current textbooks. Anyone who consults the definitive *Werner and Ingbar's—the Thyroid*[2] will note that the clinical features of hypothyroidism were given in the 5th edition and effectively abandoned in the 6th, 7th, and 8th editions. The Newcastle thyrotoxicosis index was given, shortly after it was published, in the 2nd edition of the textbook *Fundamentals of Clinical Endocrinology*[3] and dropped from subsequent editions.

I do not advocate extending the reference range for thyroid stimulating hormone to 21.5 mU/l, as suggested by Price and Weetman. I was pointing out that from our first experiences with the measurement of thyroid stimulating hormone it was clear that there was a considerable difference between the reference range (often referred to as the normal range) and what could be considered diagnostic values.

I have no difficulty with cholesterol and triglyceride measurements being used for the diagnosis and monitoring of hyperlipidaemias. However, the statistically derived reference range for plasma cholesterol bears no relation to the cholesterol concentrations used, along with other variables, when establishing risk factor status for coronary heart disease or the therapeutic goals for treatment. Coronary heart disease is one of the major causes of death and morbidity. Yet the number of cholesterol measurements made in hospital laboratories in Scotland in 1999 was 72% of the number of thyrotrophin measurements; figures for England and

Wales are unavailable. As Bulusu highlights, there seems to be some inappropriate requesting of thyroid function tests.

Toft and Beckett state that finding an abnormal serum thyroid stimulating hormone concentration in patients taking thyroxine is an indication for adjustment of the dose. Franklyn et al found that in 55 of 153 patients taking thyroxine the serum thyroid stimulating hormone concentration was below the functional sensitivity of the assay (that is, <0.03 mU/l), which is an order of magnitude below the lower end of the reference range.[4] They stated that "An important finding from the present study was the observation that the serum thyrotropin values were undetectable, even in the most sensitive assays employed, in subjects receiving long term thyroxine therapy."[4] In practice, to maintain the serum thyroid stimulating hormone concentration within the reference range for the population not taking thyroxine is an unachievable goal in some patients if one takes account of their clinical status.

I fully endorse the view that serum thyroid hormone measurements are essential in diagnosing hypothyroidism and hyperthyroidism. The reference range is so narrow that to diagnose hypothyroidism in patients who have a serum thyroid stimulating hormone concentration within the range, in the absence of hypothalamic-pituitary disease, is virtually untenable. This is in keeping with the findings of Pollock et al.[5]

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Incidence and remission of lower urinary tract symptoms

Authors should have used standardised questionnaire

Editor—Møller et al did not describe in detail the questionnaire that they used in their longitudinal study of lower urinary tract symptoms in women,[1] but it seems to have been based on two different instruments.[2 3] The Bristol female lower urinary tract symptoms questionnaire uses a five point scale for reporting symptoms.[3] Respondents can reply "never," "occasionally," "sometimes," "most of the time," or "all of the time" when asked whether they have a particular symptom; when asked about frequency they can reply "never," "once or less a week," "2-3 times a week," "once a day," or "several times a day."

This raises the issue of reproducibility when the questionnaire is completed on more than one occasion. Reproducibility of our instrument was good when a test-retest analysis was performed with a two week interval, there being no apparent change in the underlying condition during that time; 78% of symptom questions were answered identically on both occasions, with no responses changing by more than two categories. The instrument used by Møller et al is reported to have fair to excellent reproducibility, but details are not supplied.

The definition used for incidence in the authors' paper was "the proportion of women in whom symptoms arise or increase from sometimes to weekly or more." Remission was defined as "the proportion of women with symptoms occurring weekly or more in whom symptoms decreased to less than weekly." Thus, seemingly, a change in questionnaire response by one category could be recorded as incidence or remission. If reproducibility is similar to that of the Bristol female lower urinary tract symptoms questionnaire over 20% of women in whom there has been no apparent change in their underlying condition will change their response by one category or more over two weeks.

Standardised questionnaires that have been tested for validity and reliability should be used whenever possible so that these types of measurement errors can be calculated. Møller et al may simply be confirming test-retest error, and the conclusion that there is an incidence and remission rate of 10.0% and 27.8% for female lower urinary tract symptoms over one year should be interpreted with caution.

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Results have practical implications

Editor—Møller et al found that the remission rate of lower urinary tract symptoms was as high as 27.8% in their study; no single treatment modality, including antibiotic treatment, was found to be beneficial on these symptoms overall.[1] This has important practical implications, especially for doctors who see patients with this disorder in primary care. In our hospital we have conducted a study examining the extent of non-compliance among patients prescribed antibiotics in the accident and emergency department; we found that 31% of patients admitted to taking none of the antibiotics, or substantially less than the full course.[2]

A quarter of women with lower urinary tract symptoms have a remission in one year with or without treatment, and on average one out of three patients will not be compliant with the antibiotic treatment. Given this, it seems rational to limit the use of empirical antibiotics, especially in those with equivocal evidence of infection. Perhaps more emphasis should be placed on communication with the patient, together with advice and reassurance—for example, information leaflets.

When treatment is indicated we would advocate a short course (three days) of antibiotics, which has been shown to be as effective as a seven day[3] or 10 day[4] course. This is in line with the recommendation in the Standing Medical Advisory Committee's report striving to reduce the selection pressure for antibiotic resistance.[5]

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Authors' reply

Editor—Jackson et al ask about the reliability of our study. Our questionnaire was based on the Bristol female lower urinary tract symptoms questionnaire, but the number of response categories was reduced to "never," "sometimes," "once or more a week (often)," or "once or more a day (very often)." To test reproducibility a subgroup of 100 women from the study was asked to fill in identical questionnaires two weeks apart. The subgroup comprised 50 women reporting one or more lower urinary tract symptoms and 50 reporting none. Otherwise selection was randomised. The response rate was 77%.

To calculate reproducibility, data were split into those for women with symptoms once or more a week (often and very often) and those for women with symptoms less often or with no symptoms. Classification

into these groups was thought to be clinically relevant as it separated women with bothersome symptoms from those without.[1] Regarding symptoms of urinary incontinence, test-retest analysis showed an agreement of 86.4% in women with bothersome symptoms and of 94.5% in women without (overall 92.2%). For lower urinary tract symptoms, agreements were 93.1% and 97.9% respectively (overall 96.1%).

In comparison, Jackson et al found that overall 78% of symptom questions were answered identically on both occasions.[2] As reproducibility is associated with the prevalence of a specific disease we believe that an overall estimate of reproducibility is a less useful variable. Moreover, by using an overall estimate Jackson et al assume that increasing frequency, as reported in different categories, reflects a continuous scale. We believe that this is not the case: we observed a sharp increase in bothersomeness when shifting category from women with symptoms sometimes to women with symptoms weekly (often).[1] We therefore still believe that our design was adequate for the purpose.

We agree with Lam et al that our study supports a conservative approach to treating lower urinary tract symptoms. Increased knowledge about the natural course of lower urinary tract symptoms is surely a way to allocate the relevant medical resources needed.

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DoH explains thinking behind national service framework for coronary heart disease

Editor—In the cluster of letters on the national service framework for coronary heart disease,[1] two letters (by Lloyd-Mostyn and Cracknell) raise concerns about the recommendation to reduce cholesterol concentration by 30%.[2] I wish to clarify the Department of Health's position. The wording of the advice on cholesterol lowering in the national service framework was intended to read: "Statin therapy should aim to lower cholesterol below 5.0 mmol/l or to reduce total serum cholesterol by 20-25%, whichever would result in the lowest level. Equivalent figures for LDL [low density lipoprotein] cholesterol would be 3.0 mmol/l or by 30% reduction, whichever results in the lowest level." This is consistent with the joint British recommendations.[3]

On the matter of when to start statin treatment after acute myocardial infarction, the joint British recommendations state: "Patients admitted with unstable angina or acute MI [myocardial infarction] … should … be prescribed lipid lowering therapy before discharge."[3] It was our intention to incorporate this professional consensus on treatment into the framework.

Jolly et al suggest that many operators and facilities will not meet the standards set out in the national service framework for number of procedures performed.[1] As with statins, the advice in the framework is consistent with that published by the professions.[4] The key point is that the framework sets out a 10 year programme for improving cardiac services, which will mean that more procedures will be undertaken than ever before, backed up by a substantial investment package.

An important consequence of the national service framework is the opportunity it now provides to bolster the NHS capacity to treat heart disease, alongside our wider effort to reduce mortality through the new national standards for prevention, treatment, and rehabilitation of coronary disease.

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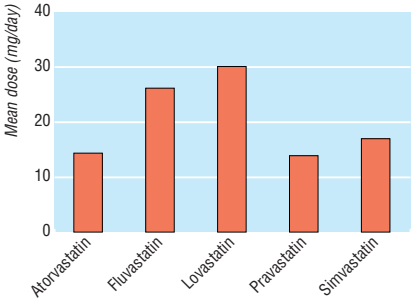
Long standing heart disease should be better screened

Editor—The audit by Irving et al in Scotland in 1997 showed that management of cholesterol concentration was performed less optimally than the treatment of other risk factors in secondary prevention of coronary heart disease.[1] Those who had had coronary bypass operations before 1994—before the Scandinavian simvastatin survival study[2]—were much less likely to receive treatment.

Our experience in the Helsinki area in 1998 was similar.[3] Patients whose coronary heart disease had been diagnosed before 1995 received significantly less lipid lowering treatment than patients whose heart disease had been diagnosed after 1995. Patients with long standing coronary heart disease constitute an important treatment gap in lipid lowering treatment and should be better screened in primary care.

But even if treatment with lipid lowering drugs is started this may not be optimal. In 1999 we performed a survey among the customers of a big pharmacy in Helsinki.[4] One hundred people who consecutively attended to renew their prescriptions of lipid lowering drugs were given a short questionnaire about their drug treatment, possible cardiovascular disease, and latest cholesterol concentrations. Ninety four patients responded.



Mean daily dose of statins among 94 consecutive patients renewing prescription for lipid lowering drug at pharmacy in Helsinki

Of these 93 used statins, 17 taking atorvastatin, 16 fluvastatin, 17 lovastatin, 5 pravastatin, and 38 simvastatin. Thirty nine respondents reported having cardiovascular disease, and 68 knew their cholesterol concentrations while receiving treatment. Of the respondents with or without cardiovascular disease, only 33% (10/30) and 11% (4/38) respectively reported having a serum cholesterol concentration below 5.0 mmol/l, which is the current target of the European guidelines.[5]

The reason for the suboptimal situation is shown in the figure: irrespective of the type of statin the mean dose given was near the lowest strength of tablet available. It is of note that, for example, in the Scandinavian simvastatin survival study the mean simvastatin dose was 27 mg/day.[2]

We think that doctors should pay more attention to patients with long standing diagnoses of coronary heart disease, whose drug treatment in addition to lipid lowering drugs may often need checking. Dose should be adjusted according to the lipid concentrations achieved in all patients who take lipid lowering drugs.

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Competing interests: Dr Strandberg and Professor Vanhanen have cooperated with different companies marketing statins.

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Discontinuation rates for use of statins are high

EDITOR—Packham et al describe an almost fourfold increase in the use of statins between 1996 and 1998.[1] The rationale for this treatment is well established,[2] yet drug discontinuation rates are generally far lower in controlled trials than in routine care.[3] We have conducted an Australia-wide assessment of discontinuation rates in patients newly prescribed lipid lowering drugs.

Using national prescription records, we identified 420 543 patients prescribed a lipid lowering drug in Australia in April 1999; this represented 68% of all lipid lowering drugs dispensed nationally in this month. We extracted records on 32 384 patients who had not received such a drug in the preceding three months. Continuation of treatment was assessed from pharmacist payment claims for the period November 1999 to January 2000 inclusive, representing 6-7 months of treatment with some time allowed for late dispensing of prescriptions.

Altogether 9% of patients (2740) were aged below 50, 47% (15 141) were 50-69, and 44% (14 222) were ⩾70; 52% (17 069) were women; 66% (21 006) were resident in an Australian capital city. The table shows dispensing data at least six months after initial supply.

Around 92% of drugs used were statins. Discontinuation rates averaged 30% and were broadly similar with all statin drugs. Discontinuation rates were higher in those younger than the median age of 68 (32% (2457/7706) *v* 26% (1845/7189) in men, 33% (2947/8879) *v* 29% (2357/8190) in women). In multiple logistic regression the significant predictors of discontinuation were age (relative risk 0.97 for each year of increasing age; 95% confidence interval 0.97 to 0.98) and not living in a capital city (0.87; 0.82 to 0.92.

Statins are a class of drugs with a low rate of adverse events and good cholesterol lowering efficacy. Hence there are likely to be other explanations for a 30% discontinuation rate. These high discontinuation rates represent a considerable wastage of resources and a lost opportunity for proved prevention of heart disease.

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General medical journals should have covered war in Kosovo more

EDITOR—Stott and Holdstock state that the link between war and poverty is critical in the campaign towards improving health.[1] Their letter shows how medical journals are an excellent forum for raising awareness.

Many general medical journals are making an effort to publish literature that addresses the social determinants of health. *JAMA* claims to work towards the "betterment of the public health,"[2] the *BMJ* towards influencing "the international debate on health," and *CMAJ* (the *Canadian Medical Association Journal*) towards fostering "curiosity and debate about all aspects of medicine." As Lock, the previous editor of the *BMJ*, stated, " a general journal without a social conscience is incomplete."[3] Social issues and medicine cannot be divorced—the two are interlaced.

Our database of articles from six leading general medical journals (*Annals of Internal Medicine, BMJ, CMAJ, JAMA, Lancet, and New England Journal of Medicine*) shows how medical journals cover health catastrophes such as war. We examined the coverage of the Kosovo crisis. The database includes articles published since the day that NATO (the North Atlantic Treaty Organisation) began bombing in Kosovo (24 March 1999) until the end of July 1999. Any mention of Kosovo was recorded.

Only 23 of the 85 issues published during this period mentioned the Kosovo crisis, and only 19 of these issues dedicated entire articles to the matter. Interestingly, 17 of the 19 articles that solely discussed Kosovo were news articles. *Annals of Internal Medicine* and the *New England Journal of Medicine* did not mention Kosovo in any issue. In contrast, the *BMJ* addressed the crisis in 10 of its 18 issues. Nine of these 10 issues dedicated an entire article to the crisis. The *CMAJ*, a biweekly journal, published articles on the crisis in two of its nine issues during the four months. The *Lancet* referred to the crisis in 10 of 19 issues and dedicated an article to it in seven of the 10 issues. *JAMA* published only one article on the crisis.

At what point does the Kosovo crisis deserve the attention of internationally distributed medical journals? Is war not one of the world's most ominous threats to health?[4] The Kosovo crisis serves as an example of an issue that is marginalised by general medical journals. One need only refer to the World Health Organization's list of the social determinants of health[5] to recognise that more than half of them are not adequately addressed in the leading general medical journals. These journals need to broaden their focus to include more substantial publications on the social determinants of health.

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Dispensing data six to seven months after initial supply. Figures are numbers (percentages)

Drug dispensed	Patients who started drug	Patients who continued with drug	Patients who switched drugs	Patients who stopped taking drug for lipid lowering
Simvastatin	12 554	8 246 (66)	818 (6)	3490 (28)
Atorvastatin	11 034	6 864 (62)	810 (8)	3360 (30)
Pravastatin	4 776	2 917 (61)	528 (11)	1331 (28)
Fluvastatin	759	411 (54)	119 (16)	229 (30)
Cerivastatin	626	323 (52)	103 (16)	200 (32)
Gemfibrozil	1 808	941 (52)	294 (16)	573 (32)
Resin	424	139 (33)	62 (12)	223 (53)
Nicotinic acid	383	102 (27)	30 (7)	251 (66)
Probucol	20	8 (40)	7 (35)	5 (25)
All lipid lowering drugs	32 384	19 951 (62)	2 771 (9)	9 662 (30)