Letters

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Rectal bleeding and colorectal cancer

Inclusion criteria of study need clarification

EDITOR—Wauters et al report on the diagnostic value of rectal bleeding in terms of subsequent development of colorectal cancer.[1] We feel that this study requires clarification for several reasons.

Firstly, the authors do not report the pre-test probability of colorectal cancer in age specific categories in their population. The diagnostic value of a symptom such as rectal bleeding and the impact on post-test probability and subsequent referral threshold are maximised when the pre-test probability of the disease is known.[2]

Secondly, they fail to mention that less than half of patients with rectal bleeding have no other symptoms.[3] More often it is associated with other bowel symptoms that have higher diagnostic value than rectal bleeding alone.[4]

Thirdly, the reported positive likelihood ratio of 68.3 "rules in" a diagnosis of colorectal cancer, irrespective of the pre-test probability of the disease.[2] The reported specificity of 99.5% has the same effect of ruling in the target disorder of colorectal cancer. These findings imply that any patients attending their general practitioner with rectal bleeding need referral and further evaluation. Our own clinical experience and other community based studies of rectal bleeding indicate that such a high specificity and likelihood ratio is unlikely and may well be misleading.[4 5]

Finally, the most likely explanation for the results relates to general practitioners underreporting rectal bleeding in the prospective arm of the study. Wauters et al chose "rectal bleeding as the reason for visiting a general practitioner" as the inclusion criterion for their study. They should clarify whether this means that patients in whom rectal bleeding was not the primary reason for consulting their general practitioner were excluded. A prospective study in the Netherlands showed that among patients presenting with rectal bleeding, 51% stated this as the primary reason for consulting their general practitioner; 49% consulted for a different reason, but rectal blood loss was subsequently mentioned during the consultation.[4] Another prospective study found that 3% (95% confidence interval 1.4% to 5.8%) of patients with rectal bleeding subsequently developed colorectal cancer, and even in this study patients with "clinically relevant rectal bleeding" were overrepresented.[5] In Wauters et al's study, 27 patients with rectal bleeding (7%, 4.6% to 10%) developed colorectal cancer.

In summary, there may have been a systematic bias in excluding less severe forms of rectal bleeding which may have not been the primary reason for consulting a general practitioner. This has resulted in inflated values for specificity and positive likelihood ratio. Before their results are incorporated into clinical practice Wauters et al should clarify their inclusion criteria and provide age specific two by two tables so that readers can judge for themselves the diagnostic value of isolated rectal bleeding in general practice.

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Results of study were incorrectly interpreted

EDITOR—The diagnosis of colorectal cancer is an important subject, but the paper by Wauters et al is flawed on several counts.[1]

To determine the value of rectal bleeding in the diagnosis of colorectal cancer the authors correctly analysed retrospectively all patients with a diagnosis of colorectal cancer in 1993-4 to calculate the sensitivity and analysed prospectively all patients presenting with rectal bleeding in 1993-4 to calculate the positive predictive value. They then claim to have estimated the specificity and negative predictive values from these results. However, the retrospective and prospective parts of the study were carried out on different populations of patients, and the data collected did not give a measure of the relative size of the population who neither had colorectal cancer nor presented with rectal bleeding. Hence it was not possible to make valid estimates of the specificity and negative predictive values. For the same reasons, valid estimates of the likelihood ratios cannot be made.

The authors stated that the probability of colorectal cancer increases greatly in association with fatigue and weight loss. However, the figure of 7.1% for the positive predictive value associated with fatigue must be wrong as the mean is outside the 95% confidence interval (8.3% to 15.8%). The positive predictive value associated with weight loss of 16.0% (4.5% to 36.1%) is not statistically different from the overall positive predictive value of 7.0%.

The authors argued that "people should be better informed and encouraged to seek medical advice if bleeding occurs."[1] Although this advice might be appropriate, the conclusion was not justified by their results, which did not show that any of the patients failed to seek appropriate medical advice.

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Authors' reply

EDITOR—We present some additional information that could not be included in the short report.

The pre-test probability of colorectal cancer in our population was 63 per 100 000 patient years; for the age groups <50, 50-59, 60-69, 70-79, and >80 it was 3, 72, 162, 296, and 401 respectively. These figures are largely similar to the incidences found by the regional cancer registry.[1]

We registered additional signs and symptoms that contribute to the diagnosis of colorectal cancer. The positive predictive values of the association of rectal bleeding and each factor are presented in the table. The positive predictive value for anal blood loss without any additional symptom was 4.4%.

The likelihood of cancer in a patient with anal blood loss is represented by the (age specific) positive predictive value and not by the likelihood ratio. The latter gives an indication of the increase of the odds of cancer by the emergence of the symptom. The positive predictive value is low (0.7%) below age 50, but increases in older patients, leading to both the conclusion that rectal bleeding should prompt referral in these age groups and a high overall positive likelihood ratio. Similar reasoning applies to the specificity.

Fijten et al found that rectal bleeding is underreported by both patients and physicians.[2] This may also have occurred in our study. However, we only studied rectal bleeding presented to the general practitioner. General practitioners were instructed to register all cases of rectal bleeding, whether or not this was the main reason for the consultation. Prospectively, rectal bleeding was the main reason for consultation in 56/386 (15%) cases, even less than was found by Fijten.[2] This does not support the fears of Fahey et al.

Leung correctly states that sensitivity and positive predictive value were directly identified from our data but specificity and negative predictive value only indirectly from the two by two table based on the data resulting from both arms of the study. As it was impossible to perform invasive tests in all patients visiting their general practitioner, we opted for a follow up period as a reference standard. The use of two arms within one study is then the only option. The combination of the resulting time shift and possible recall bias results in a small difference in the left upper cell of the two by two table (27 in the prospective arm and 31 in the retrospective arm). However, this difference does not affect the results of our calculations.

Finally, we concluded from our data that most cases of rectal bleeding do not require referral in connection with possible colorectal cancer. This does not apply, however, to patients aged over 60 or to those with additional signs or symptoms. These conclusions still hold.

Positive predictive values of rectal bleeding and associated symptoms for diagnosis of colorectal cancer

	Rectal bleeding		
Associated symptom	All patients	Patients with colorectal cancer	Positive predictive value (95% CI)
Pain	34	0	0 (0 to 10.2)
Spasms	111	6	5.4 (2.0 to 11.3)
Fatigue	70	5	7.1 (2.3 to 15.8)
Weight loss	25	4	16.0 (4.5 to 36.0)
Palpable tumour	19	6	31.5 (12.5 to 56.5)

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All epidemiological evidence is important in colorectal cancer

EDITOR—Boyle and Langman summarised descriptive features and risk factors of colorectal cancer in their article.[1] They seem, however, rather selective (or not well informed) of recent literature regarding dietary and nutritional factors in the aetiology of colorectal cancer. Boyle and Langman state that the intake of dietary fat and meat is positively related to risk of colorectal cancer. A high intake of meat is probably associated with increased risk of colorectal cancer, but the epidemiological evidence for fat and colorectal cancer is not as strong as they say. They referred in detail to the results in the nurses' health study published by Willett et al in 1990,[2] a single prospective study that showed an increased risk of colon cancer associated with high intake of total or animal fat after adjustment for total calorie intake.

Epidemiological evidence should not be relied on from the result of a single study, but the total evidence must be considered. At least seven large prospective studies were reported in Europe and the United States up till 1999. None of these studies found a clear, positive association between fat and colon or colorectal cancer; reported relative risks for the highest versus lowest intake ranged from 0.5 to 1.2 with adjustment for total calorie intake. Six of these studies also addressed the relation between saturated fat and colorectal cancer and found no material association, with relative risks of 0.7-1.4 for the highest versus lowest intake. Giovannucci et al noted that the increased risk associated with animal fat intake in the American nurses disappeared when red meat intake was taken into account.[3] Furthermore, in the combined analysis of 13 case-control studies, Howe et al showed no measurable positive association between either total fat intake or intake of saturated fat and colon cancer with adjustment for total calorie intake.[4] While animal studies have suggested an aetiological role for high fat intake in colorectal carcinogenesis, such evidence is very hard to extrapolate to humans living freely.

Boyle and Langman also say that both vegetables and fruits may be protective against colorectal cancer. There is, however, little evidence regarding the protective effect of fruit against colorectal cancer; readers will relish a more accurate and succinct review article regarding dietary factors and colorectal cancer,[5] which Boyle and Langman missed in the list of further readings.

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Competing interests: None declared.

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Impact of NHS Direct on demand for immediate care

NHS Direct must be better marketed and deal with problems more effectively

EDITOR—In their responses to the paper by Munro et al,[1] who found that NHS Direct had no appreciable impact on the use of ambulance services and accident and emergency departments, McInerney et al[2] and Lawson et al[3] addressed two important points: do the patients know about NHS Direct; and does NHS Direct make any difference to the use of emergency services anyway? At the moment, the answer to both questions seems to be "no."

We are studying consultations with our out of hours general practitioners' cooperative (Bridgwater Out-of-hours and Night Emergency Service, BONES), comparing the outcomes for two groups of patients who have called our service: those who have previously contacted NHS Direct about their problem and those who have not.

Preliminary results show that, of the 1153 consultations with BONES over four weeks in October, in 1005 cases (87%) the patients said they had not tried NHS Direct. We had a similar number of contacts over the same period in 1997, before NHS Direct became operational. Even if NHS Direct is preventing a small upward trend in calls out

of hours,[1] the fact therefore remains that most patients do not use NHS Direct.

But would it make any difference to the outcome if they did? The purpose of NHS Direct is to deal effectively with problems that can be dealt with on the telephone, and pass on to the emergency services those problems that are likely to need some kind of intervention. Therefore, those who call NHS Direct and then consult the emergency services should end up needing more face to face consultations, on the spot treatment, visits, and hospital admissions, and fewer consultations by telephone alone. On the contrary, we found that 53% of the problems that had already been presented to NHS Direct could still be dealt with over the telephone by BONES, compared with 47% of those that had not involved NHS Direct.

Furthermore, the NHS Direct callers ended up needing fewer treatments or admissions to hospital. NHS Direct has the potential to alleviate some of the increasing demands on primary care, both in and out of hours, but if the government wants it to be useful it must be better marketed and must deal more effectively with the problems presented to it.

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1 Munro J, Nicholl J, O'Cathain A, Knowles E. Impact of NHS Direct on demand for immediate care: observational study. *BMJ* 2000;321:150-3. (15 July.)
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Meaningful review is still outstanding

EDITOR—The comments by Munro et al and the responses by McInerney et al and Lawson et al relate to a time when the volume of calls to NHS Direct and their impact were very small.[1 2–3] Today three different structures to NHS Direct remain, pending the adoption of the NHS clinical assessment system this year. A meaningful review of a whole service, therefore, is still a way off.

Clinicians participating in NHS Direct see the profound changes that can come from the application of decision support logic to historical models of care. To others it remains outside their experience, and its first application (NHS Direct) seems a costly irrelevance. The vision of our professional leaders has remained focused on the politics of NHS Direct rather than its clinical potential.

The north east site has piloted integrated care out of hours since July 1999. Recent comparative data for two large areas of the integrated cooperative (Northern Doctors Urgent Care) and adjacent accident and emergency departments are shown in the table. The brief is to improve patient access and appropriate direction, but it is reassuring that NHS Direct apparently does not accelerate acute demand as the volume of calls grows.

Domestic visiting rates for the cooperative (12.1%) are half the rates before integration. For every two patients referred to a higher level of care, three are directed to a lower level of intervention.[4] Patient satisfaction is over 90%, yet 72% are diverted from their original intention and many no longer see doctors. All this, while the service is still in its infancy.

The NHS clinical assessment system piloted by NHS Direct will produce important changes in the behaviour of patients and clinicians over time and outcome studies of a high quality will be needed. The partnership experiment is working, and integrated acute care departments behind the triage platform will be piloted next year. Many teething troubles and a long way in a short time for the NHS certainly, but "a beleaguered service"? I don't think so.

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NHS Direct can help accident and emergency departments

EDITOR—McInerney et al found low awareness of NHS Direct in patients attending their accident and emergency department, and wondered whether a proper national publicity campaign would help.[1] Such a national campaign started on 20 November to mark the service becoming available throughout England. It would be worth repeating their study after the campaign. Replicating the study in other sites seems a useful way to assess awareness among the population. We intend to perform a similar study in accident and emergency departments in Hampshire, where NHS Direct has been established for 19 months.

Lawson et al have been unable to divert telephone calls for clinical advice from their accident and emergency department to NHS Direct.[2] Such a scheme has been in place in Portsmouth for over a year now and was recently extended to Southampton. As Lawson et al noted, call diversion to NHS Direct offers significant advantages in quality of service, including staff trained specifically in telephone advice, computerised protocols, and improved documentation. It can also increase time for direct patient contact. In Portsmouth we estimate that the removal of the need to respond to telephone calls has freed up the equivalent of two whole time equivalent senior nurses, enabling them to improve the quality of service to patients requiring face to face advice.

Along with other published evaluations,[3] Lawson et al comment on the lack of impact of NHS Direct on numbers attending established healthcare services. Such evaluations oversimplify the objectives of the service. NHS Direct was set up to improve access to healthcare services, which it has achieved, with over 3 million callers to the service already. Many callers indicate a prior intention to call their general practitioner or attend accident and emergency wards, and yet they are advised about self care, potentially saving a visit. It is, however, evident that other callers would not otherwise have accessed healthcare services. Some of these patients, who would normally fall "below the water level" of the "iceberg of illness,"[4] are advised to seek further clinical advice and will thus move into the system. The net numerical effect of these flows on existing services may be neutral. But those accessing services should be doing so more appropriately. Evaluations of NHS Direct must tackle this challenge of measuring appropriateness. This is the third side of the triangle of evaluation—increased access to healthcare information and advice, and demand on existing services being the others.

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Comparative data for two of the largest areas of general practice cooperative and adjacent accident and emergency departments in September 1999 and 2000

	September 1999	September 2000	Percentage change
Out of hours contacts with two largest divisions of cooperative:			
Telephone advice	1 048	712	–32.1
Visits to centre	899	842	–6.3
Home visits	749	656	–12.4
Contacts with local accident and emergency departments (24 h)	6 397	6 153	–3.8
Calls to NHS Direct North East	10 122	17 559	73.5

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Should NICE's advice be handled centrally or locally?

EDITOR—Smith's editorial on the failings of the National Institute for Clinical Excellence (NICE) addresses the right issue but attacks the wrong target.[1] It is not the recommendations emanating from the institute's deliberations that have an impact on the NHS but the subsequent executive letter that issues from the Department of Health.

The institute has many strengths, but its remit is weak in at least four areas[2]:

- It often has to rely on evidence from studies whose criteria on patient selection exclude people at the extremes of age, non-compliant people, and those with comorbidity
- Economic appraisal is a factor in its assessments. In complex interventions, sweeping generalisations have to be made about typical costs in typical hospitals and typical clinical outcomes in a range of treatment centres and populations. At local level the costs (especially marginal costs and opportunity costs) and outcomes can be very different from the norm. Briggs, in the editorial preceding Smith's, warns of trials that are underpowered with respect to economic variables[3]
- The institute usually looks at a single link in a patient pathway, and the Department of Health translates its recommendations into requirements. But in a local health economy the more pressing bottlenecks in the patient's journey might be at the diagnostic stage or in palliative care
- The institute does not have to consider trade offs within whole programmes of care, such as women's health. The forthcoming review of infertility treatments will be a fascinating worked example. In east Norfolk last year we lengthened screening intervals for cervical cancer from 36 months to 54 months, at a small but tangible health loss. But we are now able to sustain our substantial in vitro fertilisation programme as well as allow sterilisations on the NHS, giving a favourable net health gain; this has been supported at public consultation. A neighbouring health authority claims that in vitro fertilisation and sterilisations are unaffordable and continues its 36 month cervical screening cycle.

The job of the National Institute for Clinical Excellence is not to ration but to advise. The institute works best at arm's length. Smith's Committee for Honest and Open Rationing is the Department of Health. The real debate is whether openness, honesty, and responsibility should be handled centrally (on the assumption that the centre always knows best and one size fits all) or delegated to local level, where we would celebrate the differences that emerged as an indicator of a lively and responsive NHS. I prefer the latter.

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Competing interests: The author has participated in several public and professional educational events on health economics, including support for the case for health authority funding of infertility within the NHS, sponsored by a variety of pharmaceutical companies, notably Serono, Bristol Myers-Squibb, Zeneca, Novartis, and Janssen-Cilag.

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Catheter ablation for cardiac arrhythmias

Ablation should not be denied to elderly patients on basis of age

EDITOR—Peters in his editorial fails to justify his conclusion that older patients with longstanding atrial fibrillation can be managed by controlling their ventricular rate and by giving them anticoagulation treatment without need for input from a specialist.[1] Elderly people are underrepresented in clinical trials of cardiovascular disease and are less likely to have appropriate cardiological investigations.[2 3]

The reason for valuing the life of younger patients over that of older ones is not made explicit. Harris argues that what is valued by each of us is the rest of our lives, the duration of which is unknown.[4] An antiageist argument is of particular relevance to catheter ablation, a procedure that is applicable to patients of all ages and considered by some to be first line treatment in selected elderly patients.[5] If catheter ablation is denied to elderly patients on the basis of age then they are subject to the same injustice as if the procedure had been denied to the young on some equally spurious premise.

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Author's reply

EDITOR—Bourne seems to make an assumption that is common in clinical practice, of considering older patients with atrial fibrillation to encompass all elderly patients with an arrhythmia. Not all complaints of palpitations and irregularities of the pulse in elderly people can be assumed to be atrial fibrillation.

Atrial fibrillation is recognised to be common and a major clinical challenge among elderly people (affecting 9% of those older than 70 years), but other arrhythmias must be considered, particularly atrial flutter or the possibility of ventricular tachycardia, if there is evidence of previous myocardial infarction. Although they are considerably less likely than atrial fibrillation, other arrhythmias such as these for which radiofrequency ablation may be appropriate are not uncommon in this age group. For older patients with longstanding atrial fibrillation, Bourne's assertion that the paper by Van Gelder et al concludes that radiofrequency ablation should be first line treatment is incorrect. In chronic atrial fibrillation, radiofrequency ablation cannot be considered first line treatment to abolish the arrhythmia in any age group. If, however, control of the ventricular rate cannot be achieved by other means, radiofrequency ablation of the atrioventricular node accompanied by implantation of a ventricular pacemaker may provide appropriate symptomatic relief.

I thank Bourne for the opportunity to raise these important issues in response to his drawing ageist conclusions from the editorial. In so doing, however, he seems to have missed the point.

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Surveillance of *Haemophilus influenzae* infection

Surveillance data for assessing impact of vaccination are valid

EDITOR—Olowokure et al suggest that routine surveillance of *Haemophilus influenzae* is incomplete, that completeness declined after the vaccine was introduced, and that the effectiveness of vaccination programmes is overestimated.[1] We question this.

The authors suggest that the same weakness may affect the surveillance of the group C meningococcal vaccination programme. We accept that routine reporting is often incomplete, but, because of this, all vaccine preventable infections are under enhanced surveillance. The 15-fold reduction in the incidence of *H influenzae* type b disease after the introduction of the *H influenzae* type b vaccine was observed in an enhanced active surveillance scheme operating in five NHS regions,[2] not by the use of routine laboratory reports to the Public Health Laboratory Service (PHLS) Communicable Disease Surveillance Centre.

This surveillance scheme was established before the vaccine was introduced and was continued until 1995, when an enhanced national scheme was implemented.[3] Completeness of data can be maximised by reconciling reports to the Communicable Disease Surveillance Centre, isolates referred to the PHLS Haemophilus Reference Unit, and notifications of *H influenzae* type b meningitis, and by active reporting of cases to the British Paediatric Surveillance Unit.

A similar scheme—reconciling reference laboratory reports, notified infections, cases known to consultants in communicable disease control, and laboratory reports to the Communicable Disease Surveillance Centre—was used to determine the burden of infection before the introduction of meningococcal group C vaccine[4]; this scheme has now been extended nationally.

Olowokure et al do not mention the most important weakness of surveillance systems for vaccine preventable disease. When the incidence of a disease is being ascertained after the introduction of a vaccine, the specificity of clinical case definitions and laboratory tests is critical. If specificity is low, when the true incidence of an infection declines the predictive value of the case definition falls and the proportion of false positive diagnoses increases.

Since 1990 in five regions, and since 1995 in the whole of England, all reports of confirmed invasive haemophilus infections have been followed up by referral of the isolate to the PHLS Haemophilus Reference Unit, where additional confirmation is carried out with molecular typing techniques. Between 1995 and 1999, of 136 putative type b isolates referred, only 108 were confirmed as type b.

The evaluation of surveillance data for *H influenzae* type b vaccine should be based only on confirmed type b infections. The collaboration between the Communicable Disease Surveillance Centre and the national reference laboratories for meningococcal and haemophilus infections ensures that national surveillance data for England and Wales for assessing the impact of vaccination are valid.

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Authors' reply

EDITOR—Ramsay et al misrepresent the conclusions of our study. We suggested that routine surveillance was incomplete, that the underascertainment worsened after the vaccine was introduced, and that if routine surveillance data are used the effectiveness of the vaccine is overestimated. Thus we make the argument for the introduction of enhanced surveillance before the introduction of the intervention (to set baselines) and its continuation, with the same methods, after the introduction (to detect change).

At the time that we performed our analysis the relevance to the introduction of meningococcal type C vaccine was that no funding had been agreed for ongoing enhanced meningococcal surveillance, even though the immunisation programme had started. Enhanced national surveillance has now been set up, although there are methodological differences to the subnational system that was in place before the vaccine was introduced.

Because our paper was published as a short report (maximum 600 words) we did not have space to mention several weaknesses in surveillance systems. The use solely of laboratory confirmed cases obtained by testing routinely generated clinical specimens presupposes that no changes occur in the clinical practice that generates these isolates. Experience with meningococcal infection suggests that preadmission antibiotics and an increased reluctance to perform lumbar puncture in recent years have reduced the likelihood of obtaining an isolate of the infecting organism[1] and that other methods of case ascertainment are required.[2]

Ramsay et al, and others, expend enormous effort in improving surveillance data. They should interpret our report as supportive of the need for their efforts.

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Outcome of pregnancy in diabetic women

Authors did not define criterion for case selection

EDITOR—Hawthorne et al claim to show that women with diabetes have a much more unfavourable outcome of pregnancy in England than Norway.[1] But what does their study really show?

Their criterion for case selection ("diabetes") was not defined. But the prevalence differs hugely between the countries: 1 in 335 pregnant women in northeast England and 1 in 90 in Norway were reported to have diabetes. This suggests that selection in the two countries was based on different clinical criteria. In northeast England most women included in the northern diabetic pregnancy survey were taking insulin before pregnancy, and all cases were confirmed by the clinicians and from the patient record.[2] The data from Norway are from the centralised medical birth registry, and the possible pitfalls of this are illustrated by experience in Scotland.

I checked national registry listings of diabetes as part of the protocol for the SIGN (Scottish Intercollegiate Guidelines Network) guideline on management of pregnancy.[3] Some women recorded as having diabetes did indeed have this, but some had only impaired glucose tolerance; some had had a glucose tolerance test but the result was normal; some had only a relative with diabetes; and some did not have diabetes, had not had a glucose tolerance test, and did not have a relative with the condition. Even if the diagnosis in the Norwegian registry was always reliable and was recorded before pregnancy, as stated, here is one further specific source of possible systematic error.

Women who did not have type 1 or type 2 diabetes but who had had an abnormal result of a glucose tolerance test during a previous pregnancy may have been included as cases. The higher the proportion of women without diabetes in the case group the better the outcome will be.

The outcome of pregnancy may be better in Norway, but this comparison looks flawed. The authors need to define the condition to be studied to ensure that data assembly includes only those cases, and thus like is compared with like.

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More investigation is needed into whether control of diabetes is really poorer in England than Norway

EDITOR—Hawthorne et al compared the outcome of pregnancy in women with pregestational diabetes between northeast England and Norway.[1] They note a wide discrepancy in both perinatal mortality and congenital defects, with Norway having much lower rates of adverse outcome than northeast England. They state that the registration system in Norway results in identical data being collected in the two countries.

Apparent from the table—but not commented on by the authors—is the striking contrast in prevalence of maternal diabetes between the two countries: 0.3% (304/101 516) in northeast England and 1.1% (2019/179 754) in Norway. This raises the question as to whether this difference is a true reflection of the prevalence in the two countries. There are at least four possible alternative explanations: the Norwegian data include data for cases of gestational diabetes and the English data are for only

cases of more severe uncontrolled diabetes; the Norwegian data have a higher rate of keying or editing errors (which will serve to increase the apparent numbers with a rare disorder and dilute any effect); the Norwegians do have a higher rate of diabetes in young women; or the criteria for diagnosis differ between the two countries.

We hope that these four possibilities will be investigated before any conclusion is reached on poorer control of diabetes causing an excess of problems in the United Kingdom. We have strong reasons to think that the English data on prevalence are accurate since data from the prospective Avon longitudinal study of parents and children show a similar rate (0.4%) of pregnancies in women with non-gestational diabetes to that in Hawthorne et al's study.[2]

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Authors' reply

Editor—Johnstone suggests that the case selection for diabetes was not defined and that this invalidates the finding that the outcome of pregnancy is better in Norway than northeast England. He acknowledges that diabetes was confirmed in most cases from northeast England before entry into the study, but he questions the data from Norway. Golding et al draw attention to the contrast in prevalence of maternal diabetes between the two countries and suggest possible explanations for this.

We accept that there are pitfalls in using centralised data. However, data collection by the medical birth registry in Norway has documented a decline in perinatal mortality for diabetic pregnancy, from 155.1/1000 for 1967-72 to 18.1/1000 for 1986-92.[1] During this time the number of births delivered in hospitals with more than 3000 births a year has increased from less than 10% to 34%.

During the 1990s gestational glucose intolerance was a particular focus in clinical work as well as in the registration. This has ensured the option of removing cases of gestational glucose intolerance from the analysis. The fact that there has been no secular decrease in the occurrence of macrosomia in the infants adds to the validity of the diagnoses registered by the medical birth registry.[2]

There are clear clinical guidelines recommending centralisation of clinical care of diabetic pregnancy. These guidelines distinguish the management of diabetes and glucosuria during pregnancy.[3] The improved mortality figures are thought to relate to an updated intensified follow up module for pregnant diabetic patients, improved diabetes care in general, home glucose monitoring, and measurement of haemoglobin A_{1c} concentrations.

Norway has a documented high and increasing incidence of diabetes in children[4] and young people.[5] In 1991 Joner and Sovik showed that there was a twofold increase in the incidence of diabetes mellitus in the 15-29 year age group.[5] The finding that there is an increased prevalence of diabetic pregnancies in Norway compared with northeast England is consistent with these data.

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Ultrasonography in diagnosis of acute appendicitis

Diagnostic laparoscopy is often more useful than ultrasonography

Editor—Douglas et al's trial of ultrasonography in the diagnosis of acute appendicitis, and the accompanying editorial, highlight the importance of an accurate diagnosis of acute abdominal pain in the right iliac fossa and the need to avoid unnecessary appendicectomy.[1 2] The results indicate that ultrasonography has little practical value in the diagnosis of acute appendicitis because of false positive and false negative results and the inability to identify alternative diagnoses.

Neither article mentioned the increasing use of diagnostic laparoscopy in these cases. This technique makes an accurate diagnosis clearly; this is especially useful in female patients of any age and in elderly men, in whom diagnostic doubt is common. As well as preventing inappropriate appendicectomy, diagnostic laparoscopy defines the correct operative intervention if an alternative diagnosis necessitates surgery. If surgery is not required a definitive management plan is usually clear. A further advantage of laparoscopy is that if surgeons have appropriate training and experience the appendix can be removed laparoscopically, with advantages in patient recovery.[3]

If the abdominal signs are sufficiently clear to indicate peritonism in the right iliac fossa in elderly patients or female patients of reproductive age there is little to be gained from ultrasonography. Laparoscopy should be undertaken and surgical intervention proceeded to as appropriate.

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Active observation is often sufficient to make diagnosis

Editor—Douglas et al have added to the debate on the role of imaging in the diagnosis of acute appendicitis.[1] Reasons for using ultrasound, and perhaps computed tomography, need to be viewed against the background of the epidemiology of acute appendicitis.

When all children admitted with acute abdominal pain were studied in the 1960s it was found, surprisingly, that in 30-40% (mostly referred as having "?acute appendicitis") the condition settled without treatment. This syndrome, which for 12-24 hours closely resembles acute appendicitis, was named acute non-specific abdominal pain[2] and was soon found to occur equally commonly in adults.[3]

The knowledge that as many as one third of patients with acute abdominal pain will prove to have a self limiting condition must have an effect on management. At the time of admission about one third of patients clearly need emergency surgery. Then the task among the remainder is to distinguish, with the minimum of delay, those with suspicious signs who are developing surgical or medical disease requiring treatment from those with non-specific abdominal pain.

When the frequency of non-specific abdominal pain is not allowed for there is a tendency to regard every doubtful case as a possible perforated appendix, and this still leads to as many as 15-30% of appendicectomies being unproductive. If a policy of active observation is adopted, experience over 25 years in many centres has shown that repeated bedside examination is a safe method of separating the two groups; an unproductive appendicectomy rate of 14% in the 1960s had fallen to 3-5% in the 1990s.[4] Concern is expressed that delay during observation allows perforation to occur, but most patients with a perforated appendix show appreciable signs on admission; recovery has been good in the few cases that have been recognised during active observation.[4]

The existence of imaging (especially computed tomography, with its high dose of radiation) is not a reason for using it if a simpler method is effective and safe, and experience with active observation suggests that it is rarely required. Douglas et al and

Weyant et al[5] have found that reliance on ultrasound and computed tomography produces problems from false negative and positive results that have to be resolved at the bedside; both groups emphasise the central role of "more precise patient selection by clinical criteria."[5]

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Interrupting antiretroviral treatment needs particular care

Editor—Noble and Kehlet raise an important issue in their editorial about the interruption of drug treatment during the postoperative period.[1] We would emphasise the particular problems of drug interruptions in HIV infected patients receiving combination antiretroviral treatment; in these patients the general rule that some drugs are better than none does not apply.

Efavirenz and nevirapine are both non-nucleoside reverse transcriptase inhibitors with long plasma half lives (44-55 hours and 25-30 hours respectively) relative to the other main classes of antiretroviral drugs (nucleoside reverse transcriptase inhibitors (1-6 hours) and protease inhibitors (1-7 hours)).[2] Thus if a patient is taking efavirenz or nevirapine as part of his or her HIV treatment in combination with two nucleoside reverse transcriptase inhibitors, and all the drugs are stopped at the same time, the long half lives of the inhibitors will result in a period of monotherapy with these agents perioperatively.

A similar situation may arise when antiretroviral drugs with dietary restrictions (for example, indinavir, nelfinavir, didanosine) are stopped earlier or restarted later in the perioperative period than other drugs in the regimen without such restrictions (for example, stavudine, lamivudine, zidovudine, nevirapine, efavirenz). HIV-1 has a rapid mutation rate, and so even brief periods of monotherapy may result in the rapid accumulation of drug resistant strains and loss of virological control (L Guay et al, seventh conference on retroviruses and opportunistic infections, San Francisco, 2000; abstract S12). This is a particular problem for antiretroviral drugs with a low genetic barrier (such as efavirenz, nevirapine, lamivudine), where a single mutation may result in phenotypic resistance.[3]

If possible, antiretroviral treatment should not be interrupted in patients undergoing general anaesthesia or other procedures for which they must be nil by mouth for a period. When an interruption is unavoidable all antiretroviral drugs should be stopped and restarted together, except for those with a long half life, which should be stopped two to four days before the others. We recommend that specialist HIV advice should be sought about antiretroviral management in individual patients.

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Smoking and use of mobile phones

Data have been wrongly interpreted

Editor—Charlton and Bates's use of data was breathtaking in its inaccuracy.[1] For a start, the chart has no data points before 1996, so we have no way of judging how large the downturn in teenage smoking has been. But more importantly, the chart shows clearly that teenage smoking was falling before the sharp rise in mobile phone ownership. And, even worse, at the point where phone ownership sharply increases, the decline in smoking actually levels off.

This is a clear case of not letting the facts get in the way of an interesting hypothesis. It is even more regrettable given that the letter caught the national headlines. This sad misuse of numbers is a great deal worse—because it is so obvious—than the more technical statistical liberties I often find in *BMJ* articles.

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Italian data don't show the same pattern

Editor—The hypothesis of a beneficial effect of mobile phones on adolescents' attitudes to smoking is appealing, and the explanations suggested by Charlton and Bates are attractive.[1] Italians lead the European Union in ownership of mobile phones, so the influences of this particular social habit on teenage behaviour could be studied appropriately in our country.

Percentage of smokers among Italians aged 15-24 years in 1995 and 1998*

	1995	1998
Male	27.7	26.2
Female	12.7	15.4

However, data from the Italian Institute for Statistics do not suggest a decrease in the prevalence of smoking among people aged 15-24 in Italy (table). On the contrary, although rates of smoking among boys seem to be stable, rates in girls have been rising during 1995 to 1998.[2 3] Only a survey intended specifically to study the possible correlations between smoking and use of mobile phones will be able to verify this interesting hypothesis.

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No correlation in Switzerland either

Editor—The link between smoking and use of mobile phones by young people suggested by Charlton and Bates is not supported by Swiss data.[1] The prevalence of smokers aged between 15 and 24 in Switzerland increased disproportionately between 1992 and 1997 (table). The number of mobile phone subscribers increased from 215 000 in 1992 to 1 044 000 in 1997. Even though I do not have the specific numbers for the age group 15 to 24 year olds, it is likely that there was at least a proportional, if not even more rapid, growth in this age group.

Proportion of population that smokes and ownership of mobile phones in Switzerland 1992 and 1997

	1992	1997
Smokers of all ages[2]	30.1%	32.7%
Smokers aged 15-24	31%	43%
No of mobile phone owners[3]	215 000	1 004 000

This question should be resolved through a prospective study in which other known promoters and demoters of smoking in various countries are considered together with use of mobile phones.

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Hospital mergers may be painful but have positive aspects too

EDITOR—Most of us would agree with Harvey's comments in her personal view about the problems of hospital mergers.[1] A merger is more like a divorce than a marriage. It introduces vulnerabilities, sensitivities, suspicion, and redirections that often seem inappropriate.

The developing paranoia that Harvey expresses—concerning the perceived low morale and poor standards of the interloping hospital—is only too common. It is overcome by communication and joint decision taking, which, in itself, is extremely difficult, not only because of the separation of the units but also because of the lack of time in one's clinical practice.

There is, though, a positive side to a merger. The larger population that we serve allows a more efficient use of resources, particularly in smaller specialties. Merged departments allow a more efficient use of junior hospital doctors, especially specialist registrars; this is a bonus in view of both the European directive to reduce their hours and the reduction in Calman numbers. The Royal College of Obstetricians and Gynaecologists has considered the increasing risk in obstetric practice, litigation, governance, and training of junior hospital doctors.[2] In addition it is implementing standards that include 40 hours a week of consultant presence on labour wards and a delivery rate per consultant that falls from the national yearly average of 543 to 300.[2]

The surgical process of the merger might be painful but the improved health care of patients and quality of practice should make it worth while.

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The fragile male

Male zygotes are often formed at suboptimal times in fertile cycle

EDITOR—Kraemer adduced large quantities of data to substantiate the proposition that, from conception, males are more vulnerable than females.[1] Postnatal vulnerability has some social causes, which are known, but the causes of the prenatal vulnerability of males are not established, so I wish to suggest one.

During the menstrual cycle women have a fertile window lasting several days.[2] There is strong direct[3] and indirect[4] evidence that the regression of the sex ratio of the offspring (proportion male) on the time of fertilisation is U shaped across this fertile window. In other words, females are formed disproportionately often in the middle of this window and males at either end of it. There is also strong evidence that zygotes formed at either end of the window are more likely to be spontaneously aborted.[5]

Thus it would seem that, compared with female zygotes, male zygotes are formed disproportionately often at suboptimal times in the cycle. This suggestion would explain three factors: the additional prenatal vulnerability of males, the suspected higher sex ratio in spontaneously aborted fetuses than in live births, and the male excesses in those adult diseases suspected of being related to suboptimal intrauterine environments.

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Men should follow example of women's health movement

EDITOR—As Kraemer points out, being a man can seriously damage your health.[1] The Men's Health Forum (www.menshealthforum.org.uk), with a membership of over 180 organisations ranging from the BMA and the Department of Health to the Royal College of Nursing, and from the Post Office to Marks and Spencer, has campaigned on this issue for six years. Politicians now seem to realise that men's health is often a contradiction in terms and urgently needs more attention and resources.

Extensive research shows that the health of both sexes is often inextricably entwined; this is clearly shown by chlamydial infection. A joint approach to the health of women and men is required, rather than a "them and us" confrontation.

It is no coincidence that men's health is increasingly highlighted in areas where women are taking their place as policymakers. Half of the elected representatives of the Men's Health Forum are female, with a woman as deputy chair. It was two women—Tessa Jowell and Yvette Cooper (minister for public health and minister for health, respectively)—not Frank Dobson or Alan Milburn (previous and current health secretaries) who brought men's health as an issue to the attention of parliament.

Perhaps men should take a leaf from the women's health movement's book rather than begrudge women their success. With spending on women's health in the United Kingdom the lowest in Europe, it would serve both sexes well to improve spending generally in the NHS.

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Title of Dr should be sufficient for all doctors

EDITOR—I applaud Loudon's questioning of the title of Mr for surgeons,[1] but he is much too gentle with our sensitive colleagues. My history genes could grudgingly accept Mr for male consultant surgeons, but the absurdity is complex.

Married multiparous surgeons are usually referred to as Miss, a title more appropriate to an actress than a doctor. Gynaecologists and ophthalmologists are Dr in Scotland but Mr or Miss in England and Wales. Patients, who erroneously consider that all consultants are Mr or Miss, become confused when a young surgical senior house officer or registrar converts overnight from being addressed as Dr to being addressed as Mr or Miss on passing the fellowship of the Royal College of Surgeons.

I have no doubt that some patients fret with anxiety over getting the great man's (or woman's) title right. I am a physician, and I well recall one of my elderly patients whispering to her husband as she left my consulting room, "He was Dr Crisp, not Mr Crisp. He must be one of them junior doctors."

British medicine makes itself ridiculous with its multiplicity and inconsistency of titles for practising doctors. The title Dr should be sufficient for all doctors regardless of age, sex, specialty, and distinction. I applaud the North American practice of preferring to use the title Dr rather than Professor when treating patients.

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