It is therefore disquieting that manifestly inappropriate confidence intervals, presented by Paul J Turnbull and colleagues in their paper on the prevalence of HIV infection among ex-prisoners, passed the editorial process.[1] The usual asymptotic formula of p±1·96 SE, which produces a symmetric interval, yields inappropriate limits for proportions such as prevalences when the number of positive results is low: a negative lower limit can occur, uninterpretable as a "margin of error." When the observed proportion is 0 the symmetric method produces the interval 0 to 0, irrespective of the preset confidence interval; Turnbull and colleagues have shied away from quoting this degenerate interval for the prevalence in homosexual/bisexual men (0 out of 20 sampled), for which an upper limit of zero is singularly inappropriate.

An "exact" but more complex method is recommended for small samples and proportions away from 0·5.[2] For sample sizes up to 100 this method is used by the program CIA,[3] and tabulations are available.[4] For sample sizes above 100 when the number of positive results is low an approximate method uses tables for the Poisson distribution.[4] Thus for the "Others" group in the authors' table, with an observed prevalence of HIV positive samples of 3/188, the 95% confidence interval is (0·6187 to 8·7673)/188—that is, 0·3 to 4·7%. Accordingly, the published table should be replaced by the one given here. For the first few rows of the table the symmetric method gives a reasonable approximation to the exact interval, but for the last three it does not. In every instance the symmetric method gives an interval that is shifted to the left compared with the interval produced by the exact or Poisson method; hence it gives a falsely reassuring upper limit for the prevalence.

Ex-prisoners in England: results of testing saliva samples for HIV antibodies

Group	No tested	HIV antibody positive: No (%)	HIV antibody positive: 95% Confidence interval (%)
Total sample	385	19 (4·9)	3·0 to 7·7
Injectors:	148	15 (10·1)	5·7 to 16·7
Men	103	8 (7·8)	3·3 to 15·3
Women	45	7 (15·6)	6·5 to 29·5
Non-injecting women	29	1 (3·4)	0·1 to 17·8
Homosexual/bisexual men	20	0	0·0 to 16·8
Others	188	3 (1·6)	0·3 to 4·7

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Carpal tunnel syndrome and hormone replacement therapy

SIR,—Ronit Confino-Cohen and colleagues report on two women in whom the carpal tunnel syndrome resolved with hormone replacement therapy.[1] We have found that the syndrome is one of many musculoskeletal conditions seen at the menopause that may respond to hormone replacement therapy.

We examined 42 perimenopausal women (≤3 years since their last menstrual period) attending a menopause clinic to identify rheumatological disorders and to assess the response to hormone replacement therapy. For each patient 10 somatic and psychosomatic menopausal symptoms were graded 0-3 (0=none, 3=severe). The pain scores (graded 0-3 for each joint) that had been symptomatic for three months within the past three years were totalled. Patients completed visual analogue scales for pain (0-10 cm) and were examined by the same observer for evidence of rheumatic disorders. Joints were scored for tenderness (0-3). The carpal tunnel syndrome was diagnosed according to the criteria of the American State Health Department,[2] and one point was scored for the presence of each of Tinel's and Phalen's signs and median nerve sensory loss in each arm (maximum 6). Modified criteria of Yunus *et al* were used to diagnose fibromyalgia[3] and a count of tender points used (0-14). Patients were then assessed by a gynaecologist, and oestrogens (subcutaneous implant, transdermal patch or cream, or oral treatment) were started. Progestogens were prescribed when appropriate. Patients were reassessed after six months with the same clinical evaluation, and a visual improvement scale was used to score musculoskeletal symptoms and general wellbeing.

The table shows the diagnoses and response to hormone replacement therapy. Twenty eight patients complained of rheumatic symptoms and 34 diagnoses were made (six women had more than one diagnosis). Five patients reported a non-specific arthralgia affecting the hands with digital swelling, but examination and investigations yielded normal results. Other diagnoses included spondylosis (three patients) and tendonitis (two). A further two women had symptoms of the carpal tunnel syndrome but not signs. Overall, psychosomatic scores correlated with pain ($r=0·33$, $p=0·03$). Thirty seven women were reassessed after six months. Somatic scores ($p<0·001$), psychosomatic scores ($p<0·001$), and pain scores on the visual analogue scale ($p=0·02$) had improved significantly. Improvement scores for general wellbeing and musculoskeletal symptoms correlated strongly ($r=0·66$, $p<0·001$).

Previous authors have noted musculoskeletal symptoms at the menopause but have not detailed specific rheumatological disorders.[4,5] Surprisingly, 17% of our 42 women had the carpal tunnel syndrome and a further 5% had symptoms without signs. A recent study found evidence of the carpal tunnel syndrome in 32% of women after oophorectomy.[6] Changes in forearm fat content that occur at the menopause, which are prevented by hormone replacement therapy,[7] may explain these findings and the impressive response to hormone replacement therapy seen in our group and the women reported on by Confino-Cohen and colleagues.

We found that 14% of our patients had fibromyalgia, and low oestrogen concentrations were seen in those with persistent symptoms. Oestrogen withdrawal lessens rapid eye movement sleep and heightens depression,[8] both of which are associated with fibromyalgia, and hormone replacement therapy seems a logical option in this group. Although there is undoubtedly a strong placebo effect with hormone replacement therapy[9] and our study was uncontrolled with few patients, hormone replacement therapy seemed to be highly efficacious in many patients, suggesting the need for further randomised studies. Many common rheumatological disorders, including the carpal tunnel syndrome, seen in middle aged women may be part of the climacteric syndrome, for which hormone replacement therapy should be encouraged.

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Commoner rheumatological diagnoses and response to hormone replacement therapy (HRT) over six months in 42 perimenopausal women

	Osteoarthritis	Carpal tunnel syndrome	Fibromyalgia
No of patients	8	7	6
Mean age (years)	48·5	49·5	46·3
No treated with HRT	7	6	4
Mean menopausal symptoms score (0-10):			
Somatic:			
At entry	4·9	4·7	6·8
At 6 months	1·7	1·3	0·8
Psychosomatic:			
At entry	8·0	6·8	7·5
At 6 months	3·0	1·0	3·3
Mean pain score:			
At entry	6·4	NA	24·5
At 6 months	5·4		6·25
Mean visual analogue pain scale (0-10 cm):			
At entry	3·6	NA	5·4
At 6 months	3·3		4·6
Mean visual analogue improvement scale (−5 to +5 cm):			
General wellbeing	3·7	3·3	3·2
Musculoskeletal pain	1·7	NA	2·4
Mean examination score:			
At entry	4·0	3·0	12·9
At 6 months	2·3	0·5	4·5

NA=Not applicable.

Passive smoking and otitis media with effusion

SIR,—Several points arise from Anthony Hinton's letter[1] commenting on my and A P Coatesworth's paper.[2] The difference in findings between our survey[2] and his[3] may result from differences in

design features. Case matching is a more reliable means of eliminating errors than comparing the study group with a control group of a different size as in Hinton's survey.

The question of the season in which our data were collected is largely irrelevant but raises other issues. Patients attending the clinics in Cheltenham and Gloucester with suspected otitis media with effusion had waited four or five months for their first outpatient appointment and before their referral had had symptoms for several months. This time added to three months' follow up in an outpatient clinic and time on the waiting list for surgery brings the period of symptoms to roughly 12 months.

Some children have a seasonal deafness, which is usually worse in the winter or early spring. As these children's middle ear effusions resolve spontaneously the indication for surgery—or even for diagnosing otitis media with effusion—is less substantial.

Therein lies our criticism of the Edinburgh study of 892 schoolchildren aged 7, which found an association between salivary cotinine concentrations from passive smoking and tympanometric abnormalities.[4] Tympanometry alone is insufficient for diagnosing otitis media with effusion; otoscopy and audiometry are required to increase the sensitivity and specificity for diagnosing the cause of childhood deafness. Furthermore, the Edinburgh children were examined only once. As over 80% of children have a middle ear effusion at some stage it is difficult to know whether these children were normal or had a pathological process.

There is no firm evidence to suggest that tobacco smoke, whether inhaled directly or by passive smoking, causes otitis media with effusion. If smoking does cause the condition an increase in otitis media with effusion in teenage girls might be expected as this group has recently increased its tobacco consumption. As most patients in our survey were from lower socioeconomic groups smoking would be more prevalent among their parents. To date the only firm evidence linking otitis media with effusion with passive smoking has been associative.

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Drug treatment for acute upper gastrointestinal bleeding

SIR,—In their editorial on drug treatment for acute upper gastrointestinal bleeding Colin Brown and W D W Rees make light of the evidence for benefit from tranexamic acid[1] on the grounds that in the largest controlled trial, in which 256 patients were randomised to receive tranexamic acid and 260 to receive placebo, the treatment groups were poorly matched in terms of important prognostic factors.[2] In fact, adjustment for these baseline differences made negligible difference to the overall outcome as mortality was consistently lower among patients receiving tranexamic acid within all the high risk subgroups.[2] In any case, dismissing the results of such a study on the basis of mismatching is usually based on a logical fallacy.

In a properly blinded randomised controlled trial baseline differences between treatment groups occur only by chance. Thus the p value obtained for the difference in outcome (<0·01 for the fatality rates in this particular trial) must reflect the probability that the result was simply due to mismatching.

The most surprising feature of the trial of tranexamic acid, done in Nottingham, was the failure to detect any differences in rates of rebleeding and operation to account for the reduction in deaths.[2] This contrasts with the large trial of omeprazole reported by T K Daneshmend and colleagues, in which endoscopic signs of bleeding were reduced in patients receiving active treatment yet there was no reduction in death rates.[3] In both trials roughly three quarters of deaths were associated with continued or recurrent bleeding.

Postoperative mortality in the trial of tranexamic acid was strikingly different between the two groups (four deaths out of 44 operations compared with 10 out of 35 in the placebo group), yet there was no difference in the timing of surgery. This suggests that fibrinolytic inhibition may have conferred benefit independent of any haemostatic effect. Recent analysis of the data from the large trials of fibrinolytic treatment for myocardial infarction (R Collins, Cardiovascular Symposium presentation) showed an early excess of deaths in patients receiving active treatment, mainly due to cardiac rupture. Thus it seems possible that fibrinolysis impairs (and thus tranexamic acid might improve) tissue healing.

This hypothesis is clearly speculative but deserves investigation. In particular, further large trials of tranexamic acid or similar drugs, possibly combined in a factorial design with other new treatments for acute upper gastrointestinal bleeding, are urgently needed. The only published statistical overview of such trials indicates a consistent reduction in mortality with tranexamic acid of around 40% (95% confidence interval 11 to 60%), an apparent benefit that is hard to ignore.[4] Brown and Rees suggest that this meta-analysis was biased by the results of the Nottingham trial. Such statistical reviews are much more likely to suffer from the omission of unpublished studies (probably with negative results) than from the inclusion of large published trials. It seems that the narrative approach to reviews of published work is more prone to bias than the statistical.

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Omeprazole for acute upper gastrointestinal bleeding

SIR,—T K Daneshmend and colleagues are to be congratulated on their remarkable feat of performing over three years the largest controlled trial ever of treatment for gastrointestinal haemorrhage and concluding that their "data do not justify the routine use of acid inhibiting drugs in the management of haematemesis and melaena."[1] Unfortunately, even this trial does not answer the question at issue—Would abolition of gastric acid improve mortality from gastrointestinal haemorrhage?—because neither the effects nor the side effects of a therapeutic intervention can be attributed to a drug alone: they depend on the dose, defined as the amount needed to produce the required effect.

The gastric acid outputs or acidities of the authors' patients with bleeding were not measured, and it was assumed that these patients would behave in response to omeprazole as did their patients with inactive duodenal ulcers tested with their intravenous injection regimen,[2] which they claim produced "rapid and profound inhibition of acid secretion"—transmogrified in Colin Brown and W D W Rees's editorial to "virtually to abolish acid secretion."[3] In their acidity studies, however,[2] although the pH rose above 4 in 90% of samples with this intravenous injection regimen of 80 mg, then three doses of 40 mg at eight hourly intervals, it was below 7 in almost every sample.

In our studies in healthy doctors the same eight hourly intravenous injection regimen gave a mean 24 hour pH of 7·05 but half the samples had a pH below 7.[4] Even with our novel continuous 24 hour intravenous infusions of omeprazole, which resulted in a mean 24 hour pH significantly higher at 7·33, a quarter of the samples had a pH less than 7.

I still look forward to a trial of the abolition of gastric acid (pH above 7) in gastrointestinal bleeding, but that must wait until we have available a regimen (drug, route, frequency, and dose) that has been shown to produce sustained anacidity in such patients.

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Audit of gastrointestinal bleeding in a district general hospital

SIR,—T K Daneshmend and colleagues report their study of omeprazole in patients presenting with acute upper gastrointestinal bleeding.[1] In 1990 we established a protocol for managing patients admitted with gastrointestinal bleeding. We have now completed a retrospective audit of such patients over the six months from 1 January to 31 June 1991. We have evaluated how closely the protocol was adhered to, identified shortcomings in the management and protocol, and revised the protocol in the light of these observations.

There were 104 admissions for acute gastrointestinal bleeding, but only 58 case notes were available for assessment. The average age of the patients studied was 66 years, and 15 were over 80. Thirty nine patients underwent diagnostic endoscopy, the results of which were similar to those of a study by Madden and Griffiths.[2] Four patients underwent surgery, none of whom died. Altogether seven patients died: three had carcinomatosis, two had massive bleeding from a duodenal ulcer (one) and oesophageal varices (one), and two (aged 88 and 94) had been managed conservatively.

Evaluation of the protocol as applied to these patients led to several conclusions.

Firstly, the frequency of observations to be made was often not recorded in the notes or satisfactorily communicated to the nursing staff,