do not does not in itself prove that the drug is useful in some patients and not in others.

The question then arises whether an individual doctor would not be wiser to base his decision on what to prescribe on the averages reported from conventional clinical trials rather than on the individual results from an n of 1 trial. The ideal solution is probably a compromise between the two extremes. Standard statistical analyses of conventional trials do not reflect the tendency of different patients to react differently to treatment and, as Dr Johannessen notes, averages can be misleading. On the other hand, to base a decision to prescribe or not on the result of an n of 1 trial alone is to treat each man as an island and cast away relevant information.

If we wish to use the large amount of less relevant information that becomes available from studying many patients together with the small amount of more relevant information provided by studying a given patient for whom we wish to make a recommendation we shall need to study many patients many times. Whether we describe such a programme as a cross over trial or a series of n of 1 trials is a matter of taste. Where, however, we use the information so obtained to make a specific recommendation in the interest of a given patient the most usual objection to bayesian methods, that the results are not communicable, is not relevant and there seems to be no reason not to use them. Whatever approach is adopted, basing a decision to prescribe on a p value from an n of 1 trial is hardly likely to be sensible.

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AUTHOR'S REPLY,—I agree with Dr Senn that the outcome of n of 1 trials should be interpreted carefully. It is, however, important to discriminate between the two different applications of the n of 1 approach: the practical aim of determining the effect of a new treatment in one patient versus the scientific aim of making more general conclusions from series of similarly conducted n of 1 trials.

I do not claim that decisions on treatment in single subjects should be based on a controlled trial alone and that we should throw away all other relevant information. Probably the n of 1 trial should be reserved for chronic clinical conditions in which there is uncertainty about the effect of treatment.[1] Compared with the trial and error approach otherwise used, which is strongly biased towards a false positive effect of treatment, the n of 1 trial may afford the clinician more certainty on whether to prescribe the drug or not.

In research projects we report an individual outcome by means of a p value and a confidence interval, and I agree that this is not sensible in clinical work. It is cumbersome to do the calculations and you need a computer. In daily work simple score models may suffice, but statistical tests are necessary to validate such models.

Combining series of n of 1 trials to extend the conclusions beyond the individual is obviously more controversial, as shown by Dr Senn's comments. This research method will, however, never replace the conventional group trial. In my opinion the approach could be helpful in heterogeneous conditions and in the development of new drugs by generating hypotheses that could subsequently be tested in conventional trials.[2]

Thus, unlike in the parallel group trial, the main objective of the combined n of 1 study is to identify a group of responders and to see if it has common features that may serve as inclusion criteria in a subsequent conventional trial. If such a study shows an overall effect of the drug, the group of responders is significantly larger than could be expected by pure chance, and the responders have specific characteristics[3] then true responders are likely to exist. The concept of aggregating the results from many similarly conducted n of 1 trials is similar to a meta-analysis of conventional randomised controlled trials.[4] The objectives are also the same: to strengthen the evidence of an effect of treatment and to suggest directions for future research.

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Waiting for coronary angioplasty

SIR,—Minerva does interventional cardiologists and their patients a disservice by suggesting that patients with coronary occlusions "would be well advised to stay on the waiting list a bit longer."[1] The longer the occlusion has been present the harder it is to re-establish worthwhile flow by percutaneous angioplasty without causing damage.[2] The main reason for the multitude of devices is that none is yet established in clinical practice to tackle the common problem of occlusion.[3]

A recent audit of 102 consecutive patients awaiting elective conventional balloon angioplasty at our centre found wide variation in the timing of the procedure. Poor procedural outcome was associated with a longer wait (median 42 days *v* 15). In six patients conventional angioplasty failed because of interim progression to occlusion in the target vessel. To reduce the impact of this potentially avoidable problem we now have a routine policy of scheduling elective angioplasty early after diagnostic angiography. When occlusion is suspected to be recent the need to get on with the task is all the more pressing.

Patients with occlusions may have difficult symptoms inadequately controlled by medical treatment yet are not ideal for coronary surgery or conventional balloon angioplasty. In the United Kingdom many will have waited a long time for their diagnostic coronary angiography, and who knows what proportion may have developed total occlusions while waiting? Minerva adds insult to injury by dispensing ill conceived advice that further jeopardises the chances of successful revascularisation in such patients.

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Cervical samplers

SIR,—I was closely involved in drawing up the British Society for Cervical Cytology's guidelines for judging the adequacy of a cervical smear[1] and take issue with Dr N S Dallimore's criticism of this document.[2] He questions whether there is good scientific evidence for these guidelines and states that "the introduction of these criteria would produce a rate of inadequate smears of 40%."

It is precisely because, as Dr Dallimore points out, the single criterion of the presence or absence of endocervical cells is not a satisfactory method of judging the adequacy of a cervical smear that an attempt has been made to give guidelines on assessing the smear as a whole using several variables. Because most carcinomas of the cervix originate in the transformation zone it would seem logical to use the presence of cells from this region for making this assessment. This has been confirmed in our trials in 1984 of the Aylesbury spatula compared with the Ayre spatula.[3] It was shown that the increase in dyskaryotic smears taken by the Aylesbury spatula was accompanied by a decrease in the number of smears that did not contain at least three of the four elements found in the transformation zone and by an increase in the number of smears containing all four elements. In 1986 we studied the outcome of 419 women reported as having a negative but inadequate smear according to these guidelines and in whom a further smear was obtained within four months. One of these women had cervical intraepithelial neoplasia grade III and three had grade II confirmed within one year. This is comparable to a pick up rate of 1·02% of cases of cervical intraepithelial neoplasia grades II and III and invasive carcinoma of the cervix in the 30 858 women having a cervical smear taken in the whole of that year.

Our own inadequate smear rate using the Aylesbury spatula is approximately 6% and I find Dr Dallimore's claim that he would be rejecting 40% of smears as inadequate extraordinary. This has certainly not been the experience of laboratories in the Oxford region that have adopted these guidelines.

For any screening programme to be successful it is essential that the test is conducted correctly; it may be that Dr Dallimore would find the British Society for Cervical Cytology's video and booklet on taking cervical smears[4] useful in improving the skill of those who take smears in his district.

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Cervical screening and the new contract

SIR,—Dr G S Reid and colleagues claim that "the introduction of the new contract for general practitioners has brought about a further sustained increase in population coverage for cervical screening."[1] It is not at all clear from the evidence presented in their paper, however, whether and to what extent the improvements described could be attributed to the new contract itself. Indeed, before the new contract coverage rates in the area had already risen by 7% (from 71% to 78%) after a more efficient call-recall scheme was introduced. Rates continued to rise a further 7% to 85% after April 1990, with a higher proportion of smears originating from general practice. Their figures for trends in the source of smears show a decrease in smears from sources other than general practice which predated the new contract.

Though it may be superficially attractive to ascribe improvements in cervical cytology coverage

to the new contract, I believe that it is important to acknowledge the impact of other improvements in the provision of primary care services. The improvement in the call system in Perth could be said to be the most significant change in service provision, which perhaps "kick started" the recent rise in coverage rates.

Locally in South Glamorgan, where coverage is now 82%,[2] the increase in provision of cervical cytology in general practice started well before the new contract, aided by an improved call-recall scheme and the provision of improved training for practice nurses.

In our practice we attributed coverage of over 80% in 1987 not only to the efficiency of the call system but also to the provision of a sensitive, flexible, and timely service.[3] Such qualities can more readily be provided in general practice than in a traditional cytology service based in a clinic.

I do, however, concur with Dr Reid and colleagues' comments about the need to modify the payment system. In particular I would strongly support the introduction of a "more extensive and graduated system of remuneration." This should provide improved rewards to those practices with high proportions of working class, immigrant, or mobile populations, where the task of improving coverage is most challenging and demands careful, sensitive, and time consuming work by the practice team. The present payment system often fails to reward such work, which requires diligent adherence to long established principles of primary care practice.

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SIR,—Dr G S Reid and colleagues raise a number of interesting issues, one of which is choice.[1] Fife Health Board, a neighbour of Tayside also using the OCCURS computer program, has a network of 18 well woman and family planning clinics serving a population of about 100 000 women aged 20-60. A survey indicated that women in Fife, if given a choice, would opt for cervical screening by their general practitioner or at a local health board clinic in roughly equal numbers.[2] Despite this clear message from Fife women, there has been a significant move towards taking smears in general practice over the past six years (table). Although the general practitioner contract has undoubtedly helped to boost the uptake of cervical screening, this has been achieved at the cost of loss of choice.

In Fife the crude hysterectomy rate as notified by general practitioners is 5·12%. Interestingly, the range across all 64 practices in Fife is much wider than 1·9%. The age standardised hysterectomy ratio, based on a figure of 100 for the whole of Fife, varies from zero to 222, with practices in the same areas of Fife having widely differing ratios. This simple audit information is being fed back to individual general practitioners.

The upper limit of the banding for payment should be higher than 80%. Many practices in Fife have now achieved this level of uptake for smears taken within the past five years and there is very little incentive for them to screen the remaining eligible women. This is important because women who are reluctant to attend for screening may represent a subgroup that is at relatively high risk of cervical cancer.

One issue that the article does not deal with is the routine screening interval. For several years this has been three years in Fife, but the present payment system militates against achieving a high uptake of three yearly screening. As of December 1990 the uptake of cervical screening in Fife, corrected for hysterectomies, was 80% in the past five years and 72% within the past three years, but it is unlikely that the latter figure will be maintained after the rush to recruit women into the screening programme has subsided. Until general practitioners have a system of payments based on three yearly rather than five yearly screening the cervical screening programmes will not operate as effectively as they could.[4]

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Number of cervical smears taken in Fife, 1985-91

	1985	1989	1990	First 6 months of 1991
General practice	8562	18588	28675	12748
Health board's well woman or family planning clinics	8565	7987	7262	3083
Hospital clinics	5895	5112	4746	1771
Total	23022	31687	40683	17602

Vitamin D deficiency in elderly people

SIR,—In replying to a question Professor J S Garrow states that the vitamin D requirements in adults can normally be met by synthesis under the influence of sunshine.[1] This is also true for normal ambulant elderly people.[2] We agree with Mr J Chalmers, however, that this is not so in elderly people who are housebound, residents of nursing homes, and geriatric inpatients.[3]

In collaboration with Professor R Bouillon we found, as others have done, that residents of nursing homes were severely deficient in vitamin D when compared with healthy young controls. They had significantly lower concentrations of 25-hydroxycholecalciferol and of total and free 1,25-dihydroxycholecalciferol and thus also lower serum calcium and serum phosphate concentrations for equivalent creatinine values.[4] In another study of elderly people (also done in collaboration with Professor Bouillon) those who had low 25-hydroxycholecalciferol concentrations had significantly low serum calcium concentrations, low concentrations of albumin and of total 1,25-dihydroxycholecalciferol, and high alkaline phosphatase activity for the same serum creatinine and urea concentrations when compared with elderly people without vitamin D deficiency. Histomorphometric analysis showed that these elderly people did not have osteomalacia but had the features of hypovitaminosis osteopathy with an increase in eroded surfaces.[4]

We agree entirely that, this being a high risk population, vitamin D should be provided. A dose of 1000 IU (25 μg) daily is effective in preventing osteomalacia or hypovitaminosis osteopathy, or both, and is harmless.[5,6] Even 800 IU (20 μg) daily significantly increases serum calcium and phosphate concentrations to normal while decreasing alkaline phosphatase activity.[7] This was confirmed by Chapuy *et al* with the same dose but with the simultaneous administration of calcium supplements (1 g elemental calcium daily).[8] This regimen significantly decreases the concentration of immunoreactive parathyroid hormone. Seemingly, even 400 IU (10 μg) daily may be sufficient to increase 1,25-dihydroxycholecalciferol concentration slightly but significantly. Serum intact immunoreactive parathyroid concentration fell about 15% and serum osteocalcin concentration tended to fall. Another, perhaps more practical method, to ensure an adequate vitamin D concentration is to provide 100 000 IU (2·5 mg) twice yearly.[9]

We do not agree with Mr Chalmers when he states that the risks of overdosage in elderly people have been much overstated.[3] Doses of 10 000-50 000 IU/day are known to thin the cortical bone of the metacarpals as assessed by radiography and to affect the vertebrae adversely as measured by the spine score.[10] Such doses should never be prescribed.

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Condylomata acuminata and risk of cancer

SIR,—Dr Bárður Sigurgeirsson and colleagues found no significant increased risk of genital cancer in women with genital warts[1] despite the similar incidence of carcinoma in situ (2·4%) to that in the earlier Mayo Clinic study (2·6%), which came to quite the opposite conclusion.[2] To attribute this, as they do, to the use of a better method of assessing the baseline risk is to obscure the fact that both studies compared the incidence of carcinoma in situ in patients with warts with an expected incidence derived from the general population.

The Swedish study does not give details of any other diseases in their 711 women with warts, but the 500 women in Rochester had had 91 trichomonas infections, 41 cases of gonorrhoea, 38 cases of non-gonococcal pelvic inflammatory disease, 28 cases of genital herpes, 22 cases of pediculosis or scabies, and five cases of syphilis—possibly not typical of a general population? A voluminous recent review arguing the benefits of cervical screening despite an apparently low return