detection rate for a given false positive rate than screening using maternal age alone.¹

We examined the effect of the variation in the age distribution in different health districts in England and Wales in 1991.² To determine the effect at the extremes of the distribution we selected, firstly, the three districts with the highest proportion of births among women aged 35 or older (Richmond, Twickenham, and Roehampton; Hampstead; and Riverside), which in 1991 together had 19% of the births occurring among such women; and, secondly, the three districts with the lowest proportion of births among women aged 35 or older (Hartlepool; Barnsley; and Pontefract), which together had 5% of the births among such women.

The detection rate in the three districts with the highest proportion of births among older women would be, on average, 60% for a 5% false positive rate compared with 55% in the three districts with the lowest proportion for the same false positive rate. In England and Wales as a whole (with 9% of births among women aged 35 or more) the detection rate would be 58% for a false positive rate of 5%.

An important point that we did not make in our letter is that if the same risk cut off level was used there would be a notable difference in screening results between the two groups of districts. For example, with a risk cut off level of 1 in 250, the three districts with the highest proportion of pregnancies among older women would expect a 70% detection rate for a 9.0% false positive rate. In the three districts with the lowest proportion of pregnancies among older women the detection rate would be 52% for a 4.4% false positive rate. This represents the range of expected screening results. Roughly 90% of districts will have detection rates between 55% and 65%, with false positive rates between 5% and 8%. We would be pleased to supply the precise estimates for any particular district on request.

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Simulation model for planning renal services

EDITOR,—P G Bolger and R Davies use the Southmead renal programme to demonstrate a computer simulation model for renal services.¹ Unfortunately, we did not see their paper before publication. Had we done so we would have corrected some of the misleading information in it.

The paper uses information obtained in 1988-9 but presents it as current practice. The information in itself is inaccurate. The stated stock and acceptance rates on our renal programme for 1989, the starting point for simulation, are incorrect as they include children from a huge area not serviced by the adult unit. The distribution of new patients between haemodialysis and continuous ambulatory peritoneal dialysis is also incorrect: over the past three years the true ratio has been roughly the reverse of that quoted. The implication that haemodialysis is the preferred treatment, with continuous ambulatory peritoneal dialysis as the second choice if this is not possible, also misrepresents our practice. The stated upper limit for hospital haemodialysis is false, as at present there are some 70% more patients receiving this form of treatment than the quoted ceiling. The simulation also ignores the development of a full haemo-

dialysis and continuous ambulatory peritoneal dialysis service at the Gloucester Royal Hospital, which has greatly changed the population we serve.

The costs quoted were not validated by discussion with those of us working in the renal unit. They are inaccurate, especially as they contain no element for inpatient stays—relevant particularly to continuous ambulatory peritoneal dialysis and to some extent for the support of home haemodialysis. The costs for unit haemodialysis are overestimated. Thus it is not surprising that, based on the simulations for 1990-2000, the predicted pattern of our practice for 1992 is considerably different from what is actually happening, especially with regard to the costs.

The stated level of acceptance of new patients (40 per million population per year) is below our current practice and well below the accepted national need of 70-80 million population per year; this is recognised both by our purchasers and by us as providers. The purchasers have publicly announced their intention to increase investment in renal services and are working with us to increase treatment rates.

The computer model described may be excellent but is, of course, only as good as the data fed into it. The impression given in the paper of the practice, costs, and policies of Southmead Renal Unit is misleading. We are working with our purchasers to improve the quality, quantity, and efficiency of the service we provide. We do use a computer simulation program to help us with this; we have been careful to feed into it accurate information, but it is not the program that Bolger and Davies described.

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1 Bolger PG, Davies R. Simulation model for planning renal services in a district health authority. *BMJ* 1992;305:605-8. (12 September.)

AUTHOR'S REPLY,—We reported simulation runs using costs estimated in 1991, data collected in 1990, and assumptions about resource availability discussed with Southmead Renal Unit in 1989-90. The costs were obtained through the district finance department and were the best available at the time.

The purpose of our paper was to show what could be done with a simulation model, not to say anything specifically about Southmead. It was not our intention to present the work as reflecting the current practice of Southmead Renal Unit. We apologise to our colleagues at Southmead for any embarrassment caused by such an impression being given since their cooperation in the project was invaluable.

The data used came from Southmead's own computer system. We were aware that they included data on children. The simulation model can be used to produce projections for various age groups, but in this case we thought that the numbers were too small to produce reliable results. For simplicity we included the whole of the programme in the projections. Thus children were included in the numbers of patients and in survival curves used to produce projections.

It is important to appreciate that simulation models cannot predict the future. Good models predict what will happen given certain circumstances and can be adapted easily to accommodate changes in policy and practice. In view of the inevitable delay to publication of the paper we could have described the quite recent changes in service provision and costs. Despite this our projections showed that, even without an increased uptake rate, the demand for hospital dialysis facilities would almost immediately be at the former upper limit.

We believe that use of this model by purchasers has improved understanding of the service and its increasing resource demands.

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EDITOR,—P G Bolger and R Davies state that the number of new patients taken on for treatment in Southmead in 1989 was 40 per million population per year. This is exceptionally low: it is lower than the national average, much lower than the modest targets set by the Renal Association of Great Britain, and less than half the rates in other parts of the country, including Cornwall and Wales.

Why is there such a large difference? It cannot be explained demographically. In Wales a deliberate policy decision was made to devolve dialysis facilities to the districts, and the subsequent diaspora of nephrologists away from the teaching centres, together with provision for more hospital based haemodialysis, has led to the rate of new patients being taken on for dialysis being over 100 per million population per year in many areas. A similar pattern has developed in Cornwall, as well as in other parts of Europe where facilities for hospital based haemodialysis are not restricted.

One way to keep the cost of dialysis down is to limit access to it. This is best done by concentrating services in one centre, preferably on the periphery of the catchment area it is supposed to serve. The indifference of many British nephrologists to this situation has become known internationally.² Nephrologists in Britain are apparently content that at least half the people who would benefit from their skills are either not referred or told that they "have the type of kidney disease that does not respond to dialysis treatment."

We believe that the answer is to develop renal services in each district general hospital, but this would undoubtedly increase the total expenditure on renal services, and no district health authority will seek this option unless forced to do so. The treatment is costly but no more so than keeping an elderly demented patient in residential nursing care, and our society prides itself on being able to look after these unfortunate people.

We question who is going to ensure that equitable provision of dialysis is maintained in each district health authority and what powers there will be to correct the situation when it is clearly shown to be deficient.

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1 Bolger PG, Davies R. Simulation model for planning renal services in a district health authority. *BMJ* 1992;305:605-8. (12 September.)

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Heterosexual AIDS epidemic

EDITOR,—Chris Ford objects that information about AIDS "is still male dominated" and gives examples of recent medical literature that she or he considers ignores women.¹ It is indeed important

that heterosexual transmission of HIV is understood and that manifestations of AIDS and HIV infection that are particular to women are recognised—notably, disease of the female genital tract. But the overwhelming evidence shows that most manifestations of HIV infection are gender non-specific in type and incidence.

Ford is unfair and, indeed, incorrect in citing the recent clinical teaching text by my colleagues Parkin and Peters.² Their case oriented book, based on actual patients, uses a problem solving approach to help clinicians learn about AIDS. Most cases of AIDS in the developed world have been in men, and so real patients are described as man/he/him; it would be offensive to those men gratuitously to change their gender. Sadly, as heterosexual spread of HIV and ignorance and denial of it continue more cases will be seen among women, but the delay between infection and disease means that this spread will not be apparent as clinical disease for some years.

Current cumulative figures on AIDS in the United Kingdom show 5215 cases in men and 341 in women. In the vast majority of case histories, radiographs, and histological material, and most clinical slides, however, gender would be indistinguishable. Furthermore, Ford says that only two of 153 presentations in this book are of women, but, in fact, of 138 cases, 10 are in women and for 27 the gender is not specified; of 63 clinical photographs, six are of women and one shows a family.

Parkin was a coauthor of a report on one of the first women in the United Kingdom (a monogamous English housewife) to acquire AIDS through heterosexual transmission.¹ Parkin and other members of my team have repeatedly emphasised the importance of heterosexual spread over many years and have learnt much from patients; we have endeavoured to pass this on to our colleagues and the public in many forums. Ford's attack on young and enthusiastic colleagues is unwarranted.

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- 1 Ford C. Heterosexual AIDS epidemic. *BMJ* 1992;305:772. (26 September.)
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3 Jenkins P, Malthouse SR, Baughan CA, Parkin JM, Pinching AJ. AIDS: the African connection. *BMJ* 1985;290:1284-5.

EDITOR,—We agree with Chris Ford that services for diagnosing, treating, and preventing HIV infection in women have lagged behind those targeted at people whose major risk behaviour is male homosexual contact.¹ The pattern of risk behaviour has changed in recent years; of the 263 HIV seropositive heterosexuals who attended St Stephen's Clinic to the end of 1991, 110 were female and 49 of these presented after January 1990. In response to this change a clinic for women only was initiated in April 1991 to attract women with a range of risk behaviours who were not using existing facilities. This clinic is staffed exclusively by women for women and has proved to be popular.² Similarly, a clinic providing genitourinary medicine services for lesbians has been instituted in the district as the sexual health of this group is underresearched and lesbians have had difficulty in gaining access to appropriate medical services.

Ford also cites a short article by one of us as an example in which "information about the disease is still male dominated."³ This article was intentionally written without specific references to either the sex or orientation of the infected subjects and to apply equally to all with HIV infection or AIDS. We hope that HIV infection will be regarded as a multi-system disorder that may affect people from any walk of life but is amenable to risk reduction—

the adoption of measures such as safer sex and not sharing drug using equipment.

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Tachycardia during cisapride treatment

EDITOR,—Sten Olsson and I Ralph Edwards report seven cases of tachycardia or palpitations associated with treatment with cisapride.¹ These presumably represent all or most of these events reported spontaneously to four national centres over three years.

We have studied cisapride in 13 233 patients and have compared the rates of palpitations, tachycardia, and extrasystoles with data collected under substantially identical conditions from 240 381 patients in 23 recent prescription event monitoring studies. This database, which comprises about 40% of our records, includes 1960 records of tachycardia, palpitations, or extrasystoles, 595 of which were noted to have occurred during the first month of observation (table).

Number of cases of palpitations, tachycardia, and extrasystoles recorded during first month in 23 prescription event monitoring studies: rates per thousand in descending order*

Drug	No	Rate/1000
Nicardipine	160	14.6
Lisinopril	99	8.0
Xamoterol	35	6.5
Enalapril	72	4.7
Fluvoxamine	44	4.0
Buspirone	43	3.9
Diltiazem	25	2.5
Fluoxetine	29	2.3
Betaxolol	2	1.3
Ornepazole	20	1.2
Terodiline	14	1.1
Cisapride	11	0.8
Nedocromil	10	0.6
Flunitrazepam	6	0.8
Misoprostol	9	0.7
Tenoxicam	4	0.4
Etozolac	3	0.3
Famotidine	3	0.3
Nizatidine	2	0.3
Nabumetone	2	0.2
Acrivastine	1	0.1
Cetirizine	1	0.1
Loratadine	0	0
All studies	595	2.5

*Includes patients who had stopped treatment with relevant drug.

The rate of these events during the first month was 0.8/1000 for cisapride compared with a mean rate of 2.5/1000 in all the studies. Even allowing for the fact that several studies were of drugs used to treat cardiovascular conditions in which tachycardia would be expected to be common, our results provided no epidemiological support for Olsson and Edwards's hypothesis. We therefore examined all relevant records in our study of cisapride individually. There were 104 such records—67 of palpitations, 23 of tachycardia, five of extrasystoles, and nine of heart block. Fifty five of the events occurred during the follow up period, up to a year after the patient had stopped using cisapride. Only eight patients using cisapride experienced one of these events during the first

month of treatment. We consider that all these events were coincidental and almost certainly unrelated to cisapride. For all 104 patients, no doctor stopped treatment with cisapride because of these events or attributed them to the drug.

The few reports to the World Health Organisation's programme suggest an extremely low risk, even if there has been considerable underreporting. We believe that these reports represent only a small fraction of the events of this type that would be expected with or without treatment with cisapride. Palpitations and tachycardia are common and have occurred coincidentally in all of the groups we have studied. Spontaneous reporting systems were designed to detect previously unsuspected reactions that were too infrequent to be identified during premarketing clinical trials. When events are reported that commonly occur in the absence of any recognisable association with treatment it is inappropriate to draw conclusions from them, especially if alternative causes have not been eliminated.

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- 1 Olsson S, Edwards IR. Tachycardia during cisapride treatment. *BMJ* 1992;305:748-9. (26 September.)

EDITOR,—Sten Olsson and I Ralph Edwards report that treatment with cisapride may induce tachycardia.¹ They conclude that the mechanism of this action is not obvious but may be a procainamide-like effect. A tachycardic response to cisapride has, however, been reported previously,² and we suggest that activation of serotonin-4 receptors is a more likely explanation for this effect.

The existence of serotonin-4 receptors has only recently been established.¹ These receptors are positively coupled to adenylyl cyclase¹ and are present on pig heart,⁵ where they mediate a chronotropic response. Experiments have also shown the presence of serotonin-4 receptors on human right atrium, where they mediate an inotropic response.⁶ In this atrial tissue the response to serotonin was associated with raised levels of cyclic AMP⁷; thus, although the rate response was not measured, it is likely that, as in pig heart, stimulation of serotonin-4 receptors mediates a chronotropic as well as an inotropic response. Furthermore, it is well documented that cisapride is an agonist at serotonin-4 receptors,¹ and, in particular, exhibits partial agonist activity at the serotonin-4 receptor found in human right atrium.⁸

We conclude that the tachycardic response to cisapride in humans may be due to activation of atrial serotonin-4 receptors. Possibly this occurs infrequently in clinical practice because cisapride is a particularly weak partial agonist at serotonin-4 receptors in the human heart.⁹

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