studies. Of the three linkage studies, only the Australian study¹ shows evidence of significant linkage between the gene and bone mineral density.

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Authors' reply

EDITOR,—Munro Peacock and colleagues' discussion of the three published sets of data on twins apparently ignores the increasing number of studies that have confirmed the association between vitamin D receptor genotype and bone mineral density.¹⁻³

Although the intraclass correlation in dizygotic twin pairs concordant for vitamin D receptor genotype was consistently higher than that observed in the dizygotic twin pairs that were discordant for the genotype, none of these differences reached significance. Intraclass correlation, however, is a measure of similarity, not of magnitude or direction of effect. Our conclusion of association (not linkage) between vitamin D receptor genotypes and bone mineral density was based not on the analysis of differences between intraclass correlations but on the analysis of covariance of all dizygotic twins irrespective of zygosity. In this model we adjusted bone mineral density for potential confounders (that is, use and duration of use of hormone replacement therapy, age, weight, years since menopause, etc) before the analysis of the genotypic effect by using a multiple linear regression model as described in the paper in considerable detail. In this analysis we found a significant effect of the vitamin D receptor genotype on bone mineral density at all skeletal sites except the distal radius. Another method of analysis of the association between the vitamin D receptor gene locus and bone mineral density is obtained by performing a modification of the Haseman-Elston sib pair analysis.⁴ In this method we regressed the squared difference in bone mineral density of each dizygotic pair against the proportion of vitamin D receptor alleles shared. The results of this analysis confirmed the vitamin D receptor genotypic effect obtained from the analysis of covariance.

In both zygosityes there was no difference between genotypes with respect to the proportion of women who had ever used hormone replacement therapy (that is, TT 42.7%, Tt 42.0%, and

tt 36.2%; $\chi^2=0.89$, $P=0.64$). In dizygotic twins there were no significant differences in the proportion of women currently using hormone replacement therapy ($\chi^2=3.33$, $P=0.19$) or in the duration of use ($P=0.41$). Also, we detected no interaction effect between use of hormone replacement therapy and genotypes, suggesting that the effect of hormone replacement therapy was equal among genotypes and that the analysis of covariance model was justified. Thus it is unlikely that use or duration of use of hormone replacement therapy was a confounder in the study. Indeed, when the analysis was confined to those women who had not taken hormone replacement therapy the effect of the vitamin D receptor genotype ($P<0.05$) was observed at the femoral neck, Ward's triangle, and whole body but not at the lumbar spine or distal radius. This analysis, however, obviously had lower power since the number of subjects was reduced by 44%.

Interestingly, the data in Peacock and colleagues' figure include two twin pairs whose bone mineral density differs by more than 3-5 SD. This difference suggests appreciable unrecognised environmental or other genetic factors that may be affecting bone mineral density in their population and confounding the analysis.

In summary, we disagree with Peacock and colleagues and believe that our data, on the largest group of twins studied, have shown a significant association between vitamin D receptor genotypes and bone mineral density independent of hormone replacement therapy, age, weight, and years since the menopause. Discrepancies between populations may be better addressed by examination of specific gene and environmental interactions that may influence the phenotypic expression of the effect of the vitamin D receptor gene on bone mineral density. In addition, the candidacy of the vitamin D receptor gene must be critically addressed since a role for flanking polymorphic genes which might explain the discrepancies between populations has yet to be evaluated.

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Psychosis is also common in users of "normal" cannabis

EDITOR,—A S Wylie and colleagues report that three of eight patients on a methadone programme experienced psychotic symptoms after using modest amounts of "skunk" cannabis.¹ The tetrahydrocannabinol content of cannabis resin seized in 1984-9 varied widely among batches, years, and

countries of origin,² the average content being between 5.78% (in 1987) and 11.3% (in 1984). The tetrahydrocannabinol content in samples of Moroccan cannabis—the most commonly available variety in south Wales—varied between 6.8-8.9% (in 1988) and 11.7-26% (in 1984). These figures do not support Wylie and colleagues' suggestion that "normal" cannabis contains less than 5% tetrahydrocannabinol.

There are few published data on the prevalence of psychotic symptoms related to use of cannabis. Cannabis users attending alcohol and drug clinics in south Wales smoke large amounts of cannabis (10.5 g a week), 60% being daily users.⁴ In a self report study of 100 people attending a clinic in south Wales 43% reported having suffered acute toxic confusional states after using cannabis and 18% reported psychotic symptoms in clear consciousness.³ Fluctuations in the tetrahydrocannabinol content of all varieties of cannabis may contribute to these high rates in high dose users. In a study of 199 users of cannabis in New Zealand, identified through an electoral register survey, 15% reported psychotic symptoms after smoking cannabis (H Thomas, unpublished findings). These studies suggest that psychotic symptoms related to use of cannabis are common, particularly in clinic populations, and are not confined to users of skunk.

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Allocating census data to general practice populations

Survey data have their problems too

EDITOR,—Glen Scrivener and David C E F Lloyd conclude that the linkage of general practice data and census data is too inaccurate to use.¹ But this conclusion is not warranted by their findings. Whether such linkage is too inaccurate depends on the use in question and is a personal judgment; it cannot be determined by the correlation coefficient. Furthermore, by using correlation the authors fail to display the limits of the agreement and gain maximum benefit from their work.

Correlation measures the degree of linear association and not agreement.² The agreement of the two proportions of people aged over 64 is better shown by the difference between the two proportions plotted against the mean of those proportions. The 95% confidence interval for this can be calculated and gives a useful view of the accuracy of the agreement. In this study it is not surprising that the correlation was not 1.0. One proportion was derived from a source known to be inaccurate: general practice lists that contain ghosts. The other proportion was estimated indirectly. The accuracy of the general practice lists will probably vary from practice to practice. The limits of agreement are not as well shown by the authors in table II, which gives the actual and predicted percentages of patients aged over 64, as by the method proposed by Bland and Altman.³

The authors suggest that the best way to know