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Reply

Lawson's letter makes a number of points concerning the importance of spatial autocorrelation in the analysis of geographical disease data with which I cannot agree. This is an area where generalisation may be dangerous, so I would certainly not wish to dispute the possibility that such autocorrelation may be important in some instances. But by the same token, I believe that there are others where it is not of major concern. I restrict my remarks to diseases for which cases may be taken to occur independently of one another conditionally on any underlying variation in risk; the appropriate underlying error model must then be the Poisson process, although we will not necessarily know the true risk at a given point.

In the first place, unrecognised spatial autocorrelation presumably has the effect – at least within the framework of frequentist inference and modelling – of leading to heterogeneity that might be recognised, for example, by a high deviance residual to a fitted model. However, in this respect this heterogeneity is like that resulting from any other factor that has not been properly taken into account in a given model. The crucial question is surely whether this over dispersion leads to misleading conclusions about the factors that have been fitted. Whether it does so will, broadly speaking, depend on whether these factors are themselves associated with whatever spatially varying factors are responsible for the over dispersion. If they are, then of course such factors may be regarded as confounding the effects we are interested in. However, we can never eliminate the possibility of confounding factors anyway; it seems to me to be of limited inferential value to know that such confounding – if it occurs – is mediated through an unidentified spatially varying variable. It is, of course, scientifically much more valuable to try and identify all the factors that matter.

Lawson claims that the heterogeneity induced by spatial autocorrelation is "particularly important in putative source applications". I believe this to be most unlikely. For here the contributions of cases to neighbouring intervals on the distance axis will come in large measure from small areas which are relatively far apart, so that the serial correlation on this axis should be expected to be substantially less than the spatial autocorrelation per unit distance prevailing in two dimensions.

Likewise, the claim that "Leukaemias are known to cluster . . . around putative sources (nuclear power stations)" is highly suspect. There is very little published evidence relating to adult leukaemias, while, for childhood leukaemia in England and Wales, the evidence was recently reviewed in the *British Medical Journal*[1] and found to be largely negative, with the exception of the data relating to Sellafield. The latter excess is extremely hard to interpret because of the post hoc nature of the observation; numerous papers have addressed the possible aetiology, but it seems clear that a purely geographical explanation is far from convincing.

In fact, contrary to numerous claims in the literature, childhood leukaemia does not exhibit strong spatial auto-correlation. The residual deviance exhibited in my own contribution to the session addressed in Lawson's letter suggests that there is very little residual heterogeneity to explain,[2] while methodologically sound and intelligible attempts to demonstrate a spatial explanation for any such heterogeneity have generally produced only equivocal results.[3] For adults, there tends to be substantially more heterogeneity, but the small scale spatial component of this again appears to be very weak.[4]

To assume that spatial auto-correlation is important and to build this assumption into a statistical analysis may at first sight appear to be a sensible defensive strategy. But there is a high price to pay for an unnecessarily elaborate model. Its interpretation becomes more difficult and it is likely that estimates of the parameters of primary interest become less precise and stable as we attempt to gain more information from modest data sets. Important questions of procedure optimality[5] are also much harder to address. These are familiar ideas in applied statistics; the fact that they are hard to make precise in any given case does not make them less important. The onus is on the builder of a more complex model to demonstrate that a simpler one will not suffice.

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Reply

Lawson raises a number of interesting issues, but in our opinion misrepresents what we say in our paper in several respects.

1 We agree that the assumption of an underlying Poisson point process may be violated in practice, which is why we refer to this model as an idealised point process model. We discuss this issue explicitly in the last two paragraphs of our paper.

2 We agree that residential location is an imperfect surrogate for the epidemiologically relevant location or locations of an individual, but again we say this explicitly in the paper. Also, dealing with counts in regions hides, rather than resolves, the difficulty while introducing other potential problems, most obviously the well documented one of ecological bias. Nowhere in our paper do we suggest that our approach (or any other single approach) is a "general panacea"; we seek only to clarify some of the relevant practical issues by deliberately working within an idealised theoretical framework.

3 The problem of "mixed aggregate levels" is much more subtle than simply being able to deal with point cases and aggregated population data (controls). In our opinion, much work remains to be done in developing practical solutions to this problem.

4 Models more complex than our simple equation (8) would undoubtedly be justified if sufficient, and sufficiently precise, data were available for their validation. It does not follow that such models would give better inferences for the necessarily limited and imprecise data available in many applications. We have proposed a general model for decline in risk with distance around the source that approximates to the "threshold" or "peaked exposure" (eg around a stack) scenarios discussed by Lawson (Diggle *et al*, unpublished data).

While recent methodological developments in complex statistical modelling open up exciting possibilities, it should not be forgotten that all models are wrong, and that parsimony is a sound guiding principle.

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The decline in sex ratios at birth, England and Wales, 1973–90

SIR – Dickinson and Parker entitled the letter which was published in this journal,[1] "Why is the sex ratio falling in England and Wales?". The short answer to this question is that the sex ratio does not seem to be falling still. It fell more or less continuously from 1973–90, but in the four succeeding years it rose; and in 1993 it reached the highest level since 1983. It is interesting, however, to consider the causes of the fall during the 1970s and 1980s. Dickinson and Parker[1] mention three possibilities – coital rate, pollution, and hormones – and I should like to comment on these.

Coital rate

The sex ratios of white births in the USA between 1915 and 1988 seemed to show unexplained oscillations across intervals of very roughly 20–30 years.[2] In particular, they rose during the years 1965–75 and fell during the years 1975–88. In that paper,[2] I cited evidence that age standardised reported marital coital rates increased by 22% between 1965 and 1975 and fell by 27% between 1975 and 1988. Moreover, I also reviewed there the hypothesis that parental coital rate (weakly) controls the offspring sex ratio.[2] The evidence seems strong so it appears that in the USA from 1965–88 variations in the sex ratio might be explained by secular variations in the coital rate.

The recent decline in the sex ratio in England and Wales parallels a decline in the USA across the same years. It is possible that the

cause is the same. The growing perception of the danger of AIDS has caused a reduction in the rate of change of sexual partners and hence a reduction in the coital rate. There is also the possibility that coital rates are subject to medium term oscillations synchronised with movements of the economy. Fashionably decreed hemline levels and accompanying measures of sexual permissiveness do not move at random but seem to be subject to forms of homeostatic control which, plausibly, also influence coital rates.

Pollution

Dickinson and Parker[1] also raise the possibility that pollution may be a cause of the decline in sex ratios. However, pollution might have opposing reproductive effects on men and women. There is good evidence that exposure to industrial hazards like heat[3] and to some chemicals like lead,[4] borates,[5] and pesticides[6] causes men to sire a disproportionate number of daughters. And there is evidence that some forms of disease (for example, non-Hodgkin's lymphoma[7] and multiple sclerosis[8] in men are associated with low offspring sex ratios. It seems plausible to suggest that all this variation is hormonally mediated. Low values of testosterone and/or high values of gonadotrophins are associated with many diseases in men[9] and with the above mentioned deleterious industrial exposures.

Only limited data exist on the effects of hazardous occupational exposures and diseases to women on offspring sex ratios. The most suggestive line of evidence comes from the sex ratio of offspring of women with MS. This is high.[8] Moreover the adrenal glands of MS patients are large.[10] Stress produces adrenocorticotrophic hormone which lowers testosterone in men and apparently raises it in women.[11] It is therefore reasonable to propose that in this disease (and perhaps others) raised adrenal androgens occasion a rise in the sex ratio of offspring born to affected women.

The present line of reasoning suggests that the reproductive effects of disease and of hazardous industrial exposure are similar. If this is accepted, one might expect these exposures and diseases to have opposite effects on the offspring sex ratios of men and women. The upshot is that air pollution (if it affects the sexes equally) cannot be expected to reveal itself in a changed offspring sex ratio. Dickinson and Parker[1] cite Williams *et al* (who reported a lowered sex ratio in association with pollution).[12] But one might mention that Lloyd *et al*[13] found raised sex ratios in association with pollution. Thus, though pollution might have caused the decline in sex ratios, the hypothesis that it actually did so would only gain plausibility if it were backed by evidence of a particular pollutant which increased between 1973 and 1990, and decreased thereafter.

Hormones

The question nevertheless arises whether the decline in sex ratios in England and Wales from 1973–90 reflected some sort of increasing hazardous environmental exposure to men. In particular, is it to be associated with the recent suggestion relating diminished sperm counts to environmental oestrogen exposure?[14] If the USA is anything to go by, this seems not to be the case. There (where the data on secular movements in sperm counts are more abundant than in the UK) sperm counts were apparently declining during the 1970s and possibly stable during the 1980s,[15 16] in contrast to the movements of the sex ratio and coital rates described above.

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NOTICES

The 1997 World Congress of the World Federation for Mental Health, 6–11 July 1997, Lahti and Helsinki, Finland. For further information contact: The Secretariat, KaKo Congress Services, PO Box 762, FIN-00101 Helsinki, Finland. Fax: +358 9 492 810. Email: kako-ar@cc.helsinki.fi.

European Conference on Costs and Benefits of Occupational Safety and Health 1997, 28, 29, 30 May 1997, The Hague, The Netherlands. For further information, contact: Conference Secretariat: European Conference on Costs and Benefits of Occupational Safety and Health 1997, c/o Holland Organizing Centre, Parkstraat 29, NL-2514 JD The Hague, The Netherlands. Tel: +31 70 365 7850. Fax: +31 70 364 5748. Email: Conference97@hoc.nl.

Conference on Cities and Addiction: (balancing) public health and public order, 21–23 April 1997, Conference centre De Doelen, Rotterdam, The Netherlands. Scientific Secretariat: GGD, Professor HFL Garretsen, PO Box 70032, Schiedamsedijk 95, 3000 LP Rotterdam, The Netherlands; tel: +31 (0) 10 433 96 20; fax: +31 (0) 10 433 94 93. Conference Secretariat: Van Namen & Westerlaken, Congress Organization Services, PO Box 1558, 6501 BN Nijmegen, The Netherlands; Tel: +31 (0) 24 323 44 71; fax: +31 (0) 24 360 11 59.

Sixth Annual British Epidermo-Epidemiology Society Workshop, 17 January 1997, at the University of Nottingham, England. For further information, contact: Ms Melanie Bowesman, Secretary to Dr Hywel Williams, Department of Dermatology, C Floor, South Block, Queen's Medical Centre, Nottingham NG7 2UH, UK; Tel: 0115 924 9924 ext 44539; fax: 0115 970 9003.

Sixth International Symposium of the International Section of the ISSA for the Prevention of Occupational Risks in the Iron and Metal Industry, 20–22 October 1997, Barcelona. For further information, contact: Secretariat of the ISSA Section "Metal", c/o Kongressbüro, Allgemeine Unfallversicherungsanstalt, Adalbert-Stifter-Strasse 65, A-1200 Vienna, Austria; Tel: +43 1 33111 537; fax: +43 1 33111 469.

Corrigenda

Society for Social Medicine annual meeting 1996 (vol **50**:580–600) – a paper by A Grey, N Fulop, and I Allen entitled, 'Alternatives to acute admission: the national picture', was withdrawn from the meeting at the last minute. As the journal had already gone to press, the abstract still appears on page 586 of the October issue.

Estimating the prevalence of drug misuse in Dundee, Scotland: an application of capture-recapture methods by G Hay and N McKeganey (vol **50**:469–73) – there is an error in table 4 on page 471, row 2 column 2 should read ISD and DPC and row 3 column 2 should read ISD and POL.

BOOK REVIEWS

Evaluation of cancer screening. J Chamberlain and S Moss (eds). (Pp 192; dm54.00) Berlin: Springer Verlag, 1996. ISBN 3-540-19957-8.

Evaluation of cancer screening opens with a discussion of the broad principles of screening. It then looks in turn (possibly intentionally in descending order of effectiveness?) at screening for cancers of the cervix, breast, colon and rectum, melanoma, ovary, prostate, and "other" – lung, stomach, oral, and neuroblastoma. For each site, there are sections on the epidemiology, aetiology, screening test(s), effectiveness (with reviews of published trials where appropriate), acceptability, and conclusions. Finally, there are chapters on both the economic, and the relatively neglected, psychological aspects.