possibility of bias but also the plausible direction in which it might operate.

We were at great pains, even in the title of our paper, to show that our findings supported a familial aetiology and that this might be genetic. On the other hand, the segregation analysis makes the genetic aetiology more plausible; we made it quite clear that this was not proof. We also pointed out that voluntary childlessness might not have been exactly the same in both groups, and therefore we performed a sensitivity analysis to see what effects this bias might have had on our conclusions —a point that Gregson and colleagues overlook.

The high incidence of subfertility would not seem to explain the striking similarity in the sperm counts across the three families in which extended sampling was permitted.

Our paper shows that we were aware of all the biases identified by Gregson and colleagues, and more besides. We believe that our findings should be corroborated and that they are an intriguing clue. If Gregson and colleagues can suggest a method to overcome bias arising from what must inevitably be verbal evidence then we would love to discuss it with them. We would, for example, like to know whether they really think that observers could be blinded in a study of genetic histories and whether this has been accomplished successfully for other topics for which genetic histories are required from cases and controls.

With regard to the letter from F J Stewart and A J Hill, absence of the vas deferens causes azoospermia, whereas we were concerned with oligozoospermia. There is no particular reason for thinking that oligozoospermia might be associated with mutations in the cystic fibrosis gene.

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Natural history of childhood asthma

Other studies have been ignored

EDITOR,—In his editorial Malcolm R Sears concludes that two thirds of children with asthma will outgrow it (especially those with mild asthma).[1] This statement is primarily based on the work of Mark A Jenkins and colleagues,[2] but it does not reflect several other solid research findings that show that asthma persists into adulthood in half of the children who have it.[3-5]

The study of Jenkins and colleagues is presented as a prospective study based on the 1968 Tasmanian asthma survey. In this survey Tasmanian parents were retrospectively asked whether their children, then at school, had ever suffered from asthma or wheezy bronchitis. Jenkins and colleagues did a follow up study 23 years later (again partly retrospectively) in which a random sample of the original population was asked whether they suffered or had previously suffered from asthma. The questionnaire seemingly did not define the term asthma.

Jenkins and colleagues concluded (*a*) that "in most cases, childhood asthma did not seem to persist . . . and most asthma in these adults . . . seems to have developed after the age of 7" and (*b*) that, "onset of parent reported asthma or wheezing before the age of 2 did not predict asthma as an adult." To base findings on parents' recollection, however, has limited scientific merit because the recall bias must be great and the diagnostic reliability small.

Jenkins and colleagues begin their introduction: "Few population based and truly prospective cohort studies have been published of the natural course of asthma from childhood to adult life," but several relevant studies spring to mind. One is Blair's prospective study over 20 years of children from a London group practice.[3] In Blair's study asthma was clearly defined as a minimum of three attacks of paroxysmal dyspnoea with wheezing. Blair concluded that asthma persisted in half of all the cases, irrespective of time of onset, and that it disappeared or was only mild in the other half; that the age of onset of asthma was under 2 years in 57% of the 267 asthmatic children; and that there was no correlation between early age of onset and severity of asthma 20 years later.

Another important study is that of Martin *et al*, which was based on a cohort of 7 year olds in Melbourne.[4] They found that half of the children who started wheezing before the age of 7 years still had asthmatic symptoms at the age of 21. These results were confirmed by Oswald and colleagues when the cohort was 35.[5] Martin *et al* commented that they had not used a control group "because children who had wheezed in infancy probably were not identified because of failure in parents' memory."[4]

Given the introduction to Jenkins and colleagues' paper, I wonder why Sears does not mention or discuss the above studies in relation to the natural history of asthma. Blair's study is a truly prospective follow up study, while Jenkins and colleagues' study is partly retrospective but presented as a prospective study. Conclusions drawn from a study based on the methods used by Jenkins and colleagues seem dubious.

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Author's reply

EDITOR,—Distinctions must be drawn between the natural history of a disease in clinical practice and that determined in an epidemiological study. Blair reported a 20 year follow up of 267 children treated for asthma before the age of 12.[1] In these children, who were not a random sample drawn from the community, asthma persisted into adult life in 21% and went into remission and then caused a relapse in 28%. Very mild asthma was detectable in a further 24% of cases, leading Blair to conclude that most children with asthma did not grow out of their disease. Martin *et al* followed up the same Melbourne cohort as Oswald and colleagues.[2,3] Although initially the Melbourne study used a randomly selected sample, this was "enriched" with subjects with more severe asthma to provide adequate numbers for long term follow up. The outcome was that most (but not all) asthma persisted.

In contrast, Jenkins and colleagues[4] studied a community sample in which the severity of asthma ranged from trivial to severe and a large proportion of subjects had no symptoms. In this population sample mild asthma tended to remit while more severe asthma persisted. This finding is not contradictory to the studies mentioned by Marianne Stubbe Østergaard, but it shows the importance of clearly identifying the population under study when outcome is determined.

The Melbourne sample[2,3] and the children studied by Blair[1] are not epidemiologically representative of their communities but are subjects selected for having asthma. They are therefore likely to have somewhat more severe and persistent disease. Even so, some grow out of asthma, but remission is more evident among subjects with milder disease.

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Epidemic of asthma possibly associated with electrical storms

EDITOR,—Intense nationwide interest has arisen in an epidemic of asthma that occurred overnight on 24 and 25 June in the south of England and coincided with electrical storms. Between 11 pm on 24 June and 7 am on 25 June our accident and emergency and acute admissions departments saw 39 asthmatic patients. Over a similar period last year the two units saw only one patient with asthma. The patients tended to be young adults, with a median age of 28. Thirteen patients had not previously been diagnosed as asthmatic, and 22 were regularly affected by hay fever.

Atmospheric pollution, which has previously been implicated in epidemics of asthma[1] and is the subject of much interest in the media, was high. Zero level ozone measured in centres adjacent to Cambridge and Peterborough was at a two week high (45 ppb, compared with a daily average of 28·7 ppb over the preceding and following weeks). Pollen counts were considerably increased in the 48 hours before the rainfall. It has been shown that an allergy to pollen causes an increase in non-specific bronchial reactivity.[2] The high proportion of patients with regular seasonal hay fever who were affected by the epidemic might support this.

There has been interest in the fungal spore *Didymella exitialis* and the yeast *Sporobolomyces* as aetiological factors in asthma.[3,4] *Didymella* however, showed only a moderate rise in concentration, and *Sporobolomyces* rose only after most of the patients with asthma had attended, but a massive rise occurred in the concentration of ascospores of *Phaeospheria nigrans* and Diatrypaceae, which have not been previously associated with asthma and may merit further investigation.

It has been suggested that electrical storm activity, through the medium of positive ions, may cause bronchospasm,[4,5] but measurement of lightning strikes from cloud to cloud and from cloud to ground by the Meteorological Office showed 37 strikes in the Cambridge catchment area and two in the Peterborough catchment area. The widely varying levels of electrical activity but equivalent attendances for asthma in our two areas do not support this suggestion.

The aetiology of this epidemic was probably multifactorial, and a study relating attendances because of asthma at hospitals and general practices to factors known to precipitate asthma is required to establish the most important causative factors, as Virginia Murray and colleagues have proposed.[6] This would also allow for a more

efficient early warning system for asthmatic patients and those treating them.

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Asthma in runners

EDITOR,—Larrson *et al* reported that out of 42 Swedish élite cross country skiers, 23 had asthma and 31 asthma-like symptoms.[1] In 1984, 11·2% of the athletes in the United States' Olympic team had asthma induced by exercise.[2] Thus, in élite athletes and especially in skiers symptoms of exercise induced asthma are common.[1] Running is the most effective way to provoke such asthma,[3] and bronchoconstriction in connection with exercise is exacerbated by inhalation of cold dry air or allergens.[4,5] However, exercise induced asthma has not yet been thoroughly studied in runners. During winter in countries with four distinct seasons runners train outdoors in cold temperatures or indoors, where air quality may be poor. During spring and summer they are exposed to many pollen allergens.

We studied the occurrence of asthma, asthma-like symptoms, and allergy in élite athletes. Volunteer subjects were 103 runners from the Finnish adult and junior national teams. Their main event ranged from the 400 m to the marathon, and they had run a mean distance in training in the previous year of 4140 km (range 1500-8500 km). Their mean age was 22·9 (SD5·5) years, and they had been active competitors for a mean of 9·3 (4·5) years. They completed questionnaires about allergies, asthma, and asthma-like symptoms connected with exercise (cough, breathlessness, or wheeze) and their relation to training and environmental conditions.

Sixteen of the runners had asthma documented by a physician. Twenty four of the 87 remaining runners (28%) had allergies. All 16 runners with asthma and 14 of the 24 runners with allergies (58%) reported having symptoms like exercise induced asthma. However, 23 of the 63 runners without asthma or allergies (37%) reported having such symptoms occasionally. Thus asthma-like symptoms were strongly associated with allergies as 75% (30/40) of the runners with allergies had symptoms compared with 37% (23/63) of the runners without allergies (χ^2 test, $P<0·01$). Indoor training caused symptoms like exercise induced asthma in 41 of the 103 runners (40%), and outdoor training in cold air caused such symptoms in 31 (30%).

Asthma and symptoms like exercise induced asthma adversely affect not only cross country skiers[1] but also middle and long distance runners, with over half of the runners in our study (52% (53/103)) being affected. In countries with four distinct seasons the circumstances of training may stress the airway mucous membranes to induce exercise induced asthma and symptoms like it in élite athletes, who use large ventilation volumes and train intensively all year round. In runners cold weather may be a minor problem, but allergy and exposure to aeroallergens during the pollen season in spring and indoor training in winter may be important factors in provoking asthma-like symptoms.

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Serum C4 concentration and risk of atherosclerosis

EDITOR,—Judit Kramer and colleagues report a high prevalence of the C4B*Q0 allotype in patients with myocardial infarction.[1] Muscari *et al* showed a significant assocation between serum C4 concentrations and the presence of severe atherosclerosis.[2] We have studied, in our paediatric lipid research clinic, 243 children aged 2·0 to 15·9 years. We determined serum C4 concentrations in 107 children from 79 families who were referred to our clinic from 1990 to 1992 because serum total cholesterol concentrations exceeded the 75th centile for local data (5·17 mmol/l)[3] in at least one child. At the time of diagnosis we analysed the serum lipoprotein profile and C4 fraction with commercially available kits.

The children were divided into three age groups: 2·0-6·9, 7·0-10·9, and 11·0-15·9 years. They were also divided according to atherosclerotic risk, which depended on their concentration of low density lipoprotein cholesterol in comparison with values obtained in the healthy Spanish population[3]: normal risk (values between the 5th and 75th centiles (1·29 and 3·23 mmol/l)); moderate risk (values between the 75th and 95th centiles (3·23 and 3·88 mmol/l)); and high risk (values above the 95th centile (3·88 mmol/l)). Two way analysis of variance with sex and age groups as dependent variables showed a significant effect only for sex. Comparisons between low density lipoprotein cholesterol groups were made by one way analysis of variance (Fisher's test); post hoc testing was done with Scheffe's S test.

We observed significant differences between boys in the high risk group and those in the two other groups (table). The relation between serum C4 concentrations and the risk of atherosclerosis agrees with that previously reported in adults.[2] Despite the high degree of variability in the expression of C4 genes in normal subjects,[4] the association between serum concentrations of C4 or its isotypes and atherosclerosis could be related to the C4B*Q0 allotype. From our data we conclude that monitoring of the C4 fraction and other atherosclerotic risk factors[5] could be useful in diagnosing and evaluating the atherosclerotic process. Now we must investigate the precise relation between all these findings and the pathogenic sequence of the formation of atherosclerotic plaques, which begins in childhood.

Serum C4 concentration (g/l) in children according to risk of atherosclerosis

	Normal risk	Moderate risk	High risk
Boys:			
No	24	14	19
Mean (SD)	0·19 (0·05)	0·18 (0·04)	0·23* (0·08)
Girls:			
No	17	14	19
Mean (SD)	0·18 (0·04)	0·18 (0·06)	0·17 (0·04)

*Boys at high risk *v* boys at normal risk, $P<0·05$; boys at high risk *v* boys at moderate risk, $P<0·05$.

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Emergency transport for neonates after home deliveries

Expectations of flying squads are too high

EDITOR,—Northern region has had a centralised neonatal flying squad for many years, but we agree with Carol Sullivan and colleagues that the title is misleading.[1] It causes confusion and results in an instant response being expected. Such a response has become impossible with the reduction in junior doctors' hours and has always been problematic if the squad is already attending a call.

Community midwives may well have the expectations outlined by the authors,[1] and these should be dispelled. A neonatal flying squad could never, however, react sufficiently quickly to fulfil a primary role in neonatal resuscitation. Northumbria ambulance authority has one of the best response times but would not be able to move a squad from hospital to a patient at home in less than 15 minutes from receipt of a call. In the few cases in which neonatal resuscitation is required[2] it is needed in the first minutes after delivery. Therefore establishing a separately funded flying squad is an inadequate solution. An alternative is to improve the training of the people who deliver babies in the community. If we are able to train