tailored to the hypothesis under consideration at a local level, rather than, as seems to have been done, merely abstracting information from the national case control study of CJD. To expect a local consultant in communicable disease control to have the time or resources to undertake such a study may well be unrealistic. However, it would be an appropriate task for a national centre, such as the CJD Surveillance Unit, since any positive findings would have national implications and a negative investigation would offer some direct reassurance and complement the approach that Cousens and colleagues take.

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Authors' reply

Sir—Since our report was submitted for publication a further 12 cases of vCJD have been diagnosed in the UK (excluding Northern Ireland), for 11 of whom lifetime residential histories are available. Only one of these 11 cases had ever lived in Kent. This individual moved to Kent 8 months before disease onset and lived at a distance of about 10 km from plant B. With the long disease incubation periods seen in human growth hormone-related CJD cases[1] and kuru,[2] it seems unlikely that this individual became infected with the vCJD agent after moving to Kent.

Four of 37 identified vCJD cases were resident in Kent at disease onset and the same number were living within 50 km of plant B on Jan 1, 1988. With 37 cases, the number expected to have been living within 50 km of plant B on this date under the null hypothesis of no clustering around plant B is now about 1·06. Assuming the observed number of cases follows a Poisson distribution, the four recorded cases represent a statistically significant excess (p=0·02). This p-value may be taken at face value by someone who postulated that plant B might be a transmission source for the vCJD agent without knowing that any cases had been identified in individuals who had lived near the plant, but not by anyone who raised the hypothesis in the knowledge that one or more cases of vCJD had already been recorded in such individuals. Repeating the stimulations given in our paper for 37 cases indicates that the occurrence of four or more cases in a population of about 1·5 million (the population of Kent and that living within 50 km of plant B) is not unexpected (p=0·53) in the absence of any underlying clustering mechanism.

A C F Colchester indicates that he first raised concerns after two cases of vCJD had been identified in the vicinity of plant B, but states that his concerns were unrelated to these cases. We do not know whether David Williams and Michael Steed postulated that plant B might be transmitting the vCJD agent to the surrounding population before there had been any cases there. We do know that Steed's interpretation of hypothesis tests and p-values is incorrect. A p-value of 0·18 indicates that under the null hypothesis one would expect to obtain results as or more extreme than those noted 18 times out of 100. It cannot be interpreted as indicating "four-to-one odds such a cluster did not arise by chance". Colchester argues that including cases who had lived close to plant B at times other than 1998 would increase the statistical evidence for a cluster; this may be true, but it is a difficult computation to do because we do not know what proportion of the population have ever lived near plant B. Cases had lived on average at about six addresses during their lifetimes and in 2·2 different counties.

Steed and Salmon and Hillier raise the possibility that there might be a raised frequency of vCJD in Kent for reasons unrelated to the presence of plant B. The Kent cases show no evidence of any direct links or contacts between them, they share no common occupational exposure, nor is history of a surgical procedure common to all. All consumed beef products during the 1980s, as did most of the UK population.

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Past lives of twins

Sir—The report by Paul Gringras (Feb 13, p 562)[1] of physical differences between a pair of monozygotic twins was informative, but could have been more so if he had described differences, if there were any, in the twins' behaviours.

We have examined a pair of twins in Sri Lanka with very different stature and facial appearance. An analysis of their blood groups and subgroups showed that they were monozygotic. The twins also showed widely different behaviours from an early age. The older twin was calm and gentle; his brother was "tough" and inclined to violence. The older twin was more intelligent and had a better memory than his brother. The older twin enjoyed schoolwork and was good at it; his brother did not like school and did poorly there. The older twin held himself somewhat aloof from other members of the family, whereas the younger twin was open and affectionate toward them. Finally, the older twin had a phobia of vehicles and was unusually fond of chillies; his brother had neither of these traits.

The twins' parents had no reason to believe that their behaviour toward the twins could have inculcated or even encouraged these behavioural differences. They did, however, have another explanation for the differences. When the twins were aged about 3 years they spoke about previous lives they claimed to remember. The younger twin said he had been shot by the police. Because his family laughed at his statements, he stopped speaking about a past life. The older twin spoke copiously about a life he said he remembered as a schoolboy in a distant town. His many statements were sufficiently precise to allow his family to trace the family, previously unknown to them, of a deceased young boy whose life corresponded to these statements and whose behaviour corresponded closely to the older twin's behaviour.[2]

My colleagues and I have investigated 42 twin pairs, one or both of whom have claimed to remember a previous life. The cases are mostly in Asia, and tests of zygosity have so far been feasible with only six pairs. One other pair—this one in the UK—is monozygotic; and these twins showed physical differences (including two birthmarks on only one of the twins) and also behavioural ones that corresponded to the previous lives they seemed to remember.

Between 5%[3] and 18%[4] of monozygotic twins are not identical, if

judged by questionnaires alone. Genetics and postnatal influences may not be able to explain all such differences. Gestational factors may account for some differences.

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The Cardiac Insufficiency Bisoprolol Study II

Sir—The Cardiac Insufficiency Bisoprolol Study II (CIBIS-II) investigators (Jan 2, p 9)[1] are unable to account for their finding that the benefit of β-blockers for heart failure occurred in those patients with coronary heart disease, whereas in the first CIBIS[2] the treatment effect, if any, seemed to be greatest in patients with non-ischaemic heart failure or without a history of myocardial infarction. There is a simple explanation that may have substantial clinical significance.

In CIBIS, idiopathic dilated cardiomyopathy was diagnosed when no known cause of cardiomyopathy could be found. Patients were classified as having ischaemia when there was a typical history of coronary artery disease, a history of myocardial infarction, or the presence of a coronary stenosis greater than 70% shown by coronary angiography. The proportion of patients in the trial with idiopathic dilated cardiomyopathy was 36%.

In CIBIS-II, idiopathic dilated cardiomyopathy was considered as the diagnosis only when patients were shown to have normal coronary arteries on angiography; this diagnosis was made in 317 (12%) of 2647 patients. This result is in stark contrast to CIBIS, and almost certainly reflects the substantial uncertainty in making the diagnosis of idiopathic dilated cardiomyopathy without coronary angiography. What constituted a normal coronary angiogram is not stated. The proportion of patients with coronary heart disease in CIBIS-II was somewhere between 50% and 88%.

β-blockers are of value in the treatment of hypertension, after myocardial infarction, and in angina. The use of β-blockers for angina alleviates symptoms, but β-blockers have not been shown to affect mortality in patients with chronic angina, probably because of the obvious difficulties in undertaking such a study. β-blockers have a powerful anti-ischaemic effect and would be expected to be a benefit in patients with a coronary occlusion and full thickness myocardial infarction but almost normal remaining coronary arteries.

Thus, the mortality benefit shown in CIBIS among patients without established myocardial infarction probably reflects a population in whom there is substantial coronary heart disease and active ischaemia. The patients were misclassified because a coronary angiography was not used to make the diagnosis. This same group benefited in CIBIS-II. This argument is supported by the observation that after myocardial infarction the benefit of β-blockers is apparent, irrespective of the presence or absence of heart failure.[3]

What CIBIS-II shows is that β-blockers are effective anti-ischaemic therapy in patients with coronary heart disease. The benefit has been shown in patients with mild or moderate heart failure, because this subset of patients has a high event rate so that a mortality effect can be shown in a study of limited size. If true, this interpretation has substantial clinical implications. β-blockers would be expected to exert their greatest benefit in patients with mild-to-moderate heart failure with an aetiology of coronary heart disease and that would be the group on which clinicians should focus. The use of β-blockers in patients who are elderly, have a normal ejection fraction, are female, or have severe heart failure is either not established or less certain and should await the outcome of future studies.

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Authors' reply

Sir—Philip A Poole-Wilson draws attention to the apparent disparity between CIBIS and CIBIS-II, in that patients with ischaemic heart disease benefited most in CIBIS-II, whereas those with no history of previous myocardial infarction seemed to benefit most in CIBIS. He suggests that the benefit of bisoprolol in CIBIS-II was entirely due to the well described anti-ischaemic effects of β blockade and that the apparent benefit in patients classified as having non-ischaemic heart failure in CIBIS was because most of them actually had ischaemic heart disease.

Poole-Wilson postulates the lack of effect in patients with previous myocardial infarction in CIBIS was because they had single vessel disease associated with a full thickness scar and no residual or remote areas of jeopardised myocardium for β blockade to protect. Since coronary angiography was not a mandatory inclusion criteria but was carried out only to diagnose ischaemic heart disease in some cases, we have insufficient information to confirm or refute this complex hypothesis. However, this hypothesis is not plausible since the prevalence of single vessel disease in a group of patients whose average age is 60 years and who have chronic heart failure is unlikely to be high. Nevertheless, although rates of myocardial infarction or admission for angina were not reduced by bisoprolol in CIBIS-II, we completely agree that a major part of the effect of β blockers in a population of patients with heart failure in whom coronary artery disease is usually the major cause is likely to be anti-ischaemic. Subendocardial ischaemia could, of course, result from the low trans-myocardial pressure gradient resulting from raised end diastolic pressure, especially in association with a low systemic blood pressure. Reduction in demand for myocardial oxygen due to β blockade would be expected to be beneficial in this situation, even if coronary heart disease were not the cause of heart failure.

The impressive reduction in sudden death and of serious ventricular arrhythmias, however, suggests that an antiarrhythmic effect is an important component, explicable not only on an anti-ischaemic basis but also by blockade of sympathetic activity. There is no reason to suppose that Poole-Wilson's putative group of patients with full thickness infarct would not also stand to benefit from this favourable property of β blockers.