late 30s would have traversed almost none of the risk period. Although there are a number of deficiencies outlined by the authors with their high-risk strategy, there are some limitations which they do not outline. The actual risk to illness differs substantially across individual subjects.

To my surprise, the authors never precisely define what they mean by 'well'. In the middle of the 'Results' section, they do make the statement that "no one in either group reached the criteria of a current psychiatric disorder in the PSE or SADS–L". Is that their definition? If someone had a prior episode of psychosis or depression or alcohol dependency from which they recovered and are no longer symptomatic, does that render them well? What about an individual who has four of the nine criteria for schizotypal personality disorder. Would this person be considered 'well'?

The statement on page 547 of the risk for schizophrenia in children of one parent with schizophrenia could hardly be cited in such a definitive way. There is a range of risks and the most recent empirical risk figures from the New York and Copenhagen high-risk studies are different from the summary results presented here. Curiously, they discuss preliminary data supported by Kendler *et al* on the Structured Interview for Schizotypy, but do not cite or comment on complete analysis of the schizotypal symptoms and signs in the Rosscommon Family Study (Kendler *et al*, 1995).

Kendler, K. S., McGuire, M., Gruenberg, A. M., *et al* (1995) Schizotypal symptoms and signs on the Roscommon Family Study: their factor structure and familial relationship with psychotic and affective disorders. *Archives of General Psychiatry*, **52**, 296–303.

Stromgren, E. (1935) Zum Ersatz des Weinbergschen "Abgekurzten Verfahrens". Zugleich ein Beitrag zur Frage von des Erblichkeit des Erkrankungsalters bei der Schizophrenie. *Zeitschrift Gesamte für Neurologie und Psychiatrie*, **153**, 784–797.

Professor Kenneth S. Kendler Department of Psychiatry, Virginia Institute for Psychiatric and Behavioral Genetics, Medical College of Virginia Commonwealth University, 800 East Leigh Street, PO Box 980126 Richmond, Virginia 23298-0126, USA

NEED FOR MORE RIGOROUS PRELIMINARY REPORTING

The study describes the design, methods and selected 'baseline' characteristics in a set of 'high-risk' subjects representing 50% of the projected sample size of 100, and in 30 control individuals. The study is prospective by design. The authors also intend to include 30 patients with 'sporadic' schizophrenia. Apart from demographic data, the manuscript includes items from previous history (psychiatric and forensic) and a selection of scores from the Structured Interview for Schizotypy (SIS).

This is a potentially important study which takes a novel approach to the study of risk factors for schizophrenia. However, there is little in this manuscript to justify its publication, since none of the preliminary findings about this half of the sample contributes any new substantive knowledge about the precursors or risk factors in schizophrenia. Hopefully, such knowledge will be forthcoming. The authors should have considered a shorter, tightly written preliminary report outlining more clearly the design of the study and the main background variables describing the study population. Some specific questions that should have been addressed are: (a) Were the SIS interviews conducted blind to the high-risk/control status? (b) How many individuals met the DSM–IV or ICD–10 criteria for schizotypal disorder? A table giving a breakdown of the sample by number of affected family members and degree of relatedness (i.e. affected sibling pairs, parent–sibling, etc.) could have been included as well as a table listing the neuropsychological assessments and the magnetic resonance imaging measures being collected.

Professor Assen Jablensky Department of Psychiatry and Behavioural Science, University of Western Australia, Medical Research Foundation Building, Level 3, Rear 50 Murray Street, Box X2213 GPO, Perth, WA 6001, Australia

FAMILIES WITH A GENETIC 'TAINT' OR THE TIP OF UBIQUITOUS VARIATION FOR THE HUMAN CAPACITY FOR LANGUAGE?

At first evaluation it seems as though the findings of this study are predictable. Psychiatric illness, forensic contacts and delinquency are higher in the at-risk group than the control group. This could be genetic predisposition or it could presumably be reactive to illness in the family. The increase in premorbid personality anomalies (social isolation, restricted affect etc.) is perhaps more likely to reflect the genetic predisposition. It is consistent with the findings from cohort studies.

The conclusions the authors draw are that the differences may represent increased risk but "their true significance will not be revealed until the cohort has been followed through the at-risk years". An unsympathetic reader might conclude 'let's wait for the full analysis and see – there's no justification for publication at this stage'. Even so, one can ask whether, if the conclusions are relatively predictable at this stage, much more will be achieved with a larger sample and a longer follow-up. Is it not likely that the group who develop a psychotic illness will be more abnormal on these same indices than those who do not? That is, there will be quantitative deviations along the axes of abnormal behaviour and 'schizotypy'.

This question is worth asking because a salient feature of the paper (and maybe the study) is the absence of hypotheses about the nature of the genetic predisposition and the nature of the illness. That there is a category of illness that can be readily isolated and labelled schizophrenia is taken as read (the criteria adopted are not mentioned in the summary), but this is doubtful (see Endicott *et al*, 1982). There are different criteria and there is almost certainly a spectrum or continuum of illness (see Crow, 1994, 1995).

These considerations are no doubt well known to the investigators, but they may be relevant to the way the analysis of the study proceeds in the future. Thus, this background has had no impact on the rather naïve genetic models presented. A further important point (relevant to the issue of the survival of genetic predisposition, considered in the 'Discussion') is uniformity of incidence across populations. As has been argued in the papers cited above, this finding, which has now to be considered relatively securely established, has had no impact on the psychiatric genetic literature or on genetic models. It must mean that predisposition to schizophrenia is a part of variation that crosses the population as a whole. It is the nature of this variation – what are the critical dimensions of variation of which psychosis is the extreme – that is the key question. It seems as though the data in this study, particularly when considered in conjunction with the structural and psychometric studies which, although not mentioned here, are presumably a major part of the

https://doi.org/10.1192/S0007125000262648 Published online by Cambridge University Press

justification for the study, could cast new light on these questions if the authors are able to adopt a hypothesis-testing approach to the data they are accumulating. Relevant to these issues is the nature of the speech and communication difficulties that are described in the Structural Interview for Schizotypy assessments.

The 'Discussion' considers methodological problems that are specific to this study, but also touches on the theoretical issues. Neither has a significant impact on the guarded conclusion in the summary.

There may be a case for interim publication on the progress of this study, but if so it seems that much of the introduction and some of the discussions which relate to theoretical issues that are not addressed at all in the conclusions of the study could be omitted. More importantly, it seems that this interim report provides an opportunity for the authors to review their study in the light of the questions concerning the nature of psychosis that have now come into focus and towards which they are moving. What is the nature of the genetic predisposition? To what function do these genes relate (Crow, 1997)? What is the relationship between brain change and genetic predisposition? Can the early or precursor symptoms be interpreted as language-related and how do these change with onset of frank psychosis?

Crow, T. J. (1994) The demise of the Kraepelinian binary system as a prelude to genetic advance. In *Genetic Approaches to Mental Disorders* (eds E. S. Gershon & C. R. Cloninger), pp. 163–192. Washington, DC: APA.

— (1995) A continuum of psychosis, one human gene and not much else – the case for homogeneity. *Schizophrenia Research*, **17**, 135–145.

— (1997) Is schizophrenia the price *Homo sapiens* pays for language? *Schizophrenia Research*, **28**, 127–141.

Endicott, J., Nee, J., Fleiss, J., *et al* (1982) Diagnostic criteria for schizophrenia: reliabilities and agreement between systems. *Archives of General Psychiatry*, **39**, 884–889.

Dr T. J. Crow University Department of Psychiatry, Warneford Hospital, Warneford Lane, Headington, Oxford OX3 7JX

AUTHOR'S RESPONSE

We are sorry that Professors Farmer and Jablensky do not think that this paper warrants publication at the present time. It is perfectly true that there is no clear message from the paper; it describes case identification and very preliminary findings in a study which one of the other commentators is kind enough to describe as unique. The sample is certainly unusual and the fact that these subjects, although not complaining or seeing themselves as unwell, have been able to be recruited in such numbers to a complex and ongoing study, could be considered as worthy of report. The purposes of the presentation and the study as a whole are both briefly described. The purposes of the study as a whole will be discussed in full detail when it is complete.

Power calculations have been conducted and a detailed account of these was given in the proposal for funding. We did not think it appropriate to present them here, as they relate to the numbers of subjects who may be expected to develop psychosis over the period of the study, and this issue cannot yet be addressed.

We entirely agree that a 10-year follow-up would be more useful, and we very much hope that those who fund us will share this view. Funding agencies like to see evidence of the diligence of those they support, and for this reason, as well as because of other pressures such as the Research Assessment Exercise, young investigators are encouraged by older ones to get their findings in print if they can.

Professor Kendler is correct in drawing attention to the difficulty of selecting appropriate controls. 'Screened controls' would probably be a good term, as he suggests, although 'supernormal' seems a little excessive.

Potential controls were only excluded if they had first-degree relatives with functional psychotic illness. Alcohol misuse, minor depression, neurotic illness, or dementia in old age did not lead to exclusion. In fact, disorders such as alcohol misuse and neurotic illness were widely described in the families of both the high-risk subjects and the controls. We would have liked to meet the criterion that the control group should be identical to the index group in all characteristics except the presence of the initial diagnosis, but we did not achieve this. Controls were excluded if they said that they had relatives with bipolar affective disorder, and high-risk cases were included if they had relatives with bipolar affective disorder (in addition to sufficient relatives with schizophrenia). This situation arises because we were not in a position to obtain the case notes of the relatives of the control subjects and we wanted to be as sure as we could be that the controls did not have relatives with schizophrenia.

We are very well aware of the fact that age of onset of schizophrenia varies from family to family. The power calculations of the proposal for the study depend upon the actual ages of onset in the initial families identified. We are aware that some of the subjects are at much greater risk than others. We are developing a complex statistical model based upon detailed knowledge of the health of individual members of all the extended families involved in the study. This will allow us to take this variable risk into account, but for the central purpose of the main study it is probably not important. What we are trying to do is to look at possible precursors of schizophrenia and to see how they evolve towards the onset of psychotic illness. In order to do this, we have to be able to examine in detail adequate numbers of people who are destined to develop schizophrenia, before they have complaints suggestive of the condition or features that would indicate to others that such a diagnosis would be appropriate. For that purpose, all we require is a sufficiently large sample of individuals who, on average, have a risk that is increased enough beyond that of the general population for interpretable numbers to reach set criteria for the diagnosis of schizophrenia during the period of the study, in order that they may be contrasted with those who do not meet such criteria.

We have defined what we mean by 'well' in our protocol and should have noted it in the paper. The criteria are that the subjects do not complain of features suggestive of current psychiatric disorder and that they have no history that would suggest that they have had a psychotic illness, no history that any doctor has ever considered that they may have had features of such an illness, and no history of ever having been prescribed antipsychotic medication.

Professor Jablensky sets out specific questions and makes specific suggestions:

(a) Sometimes the SIS interviews were conducted blind to high-risk/control status and sometimes they were not. Recruitment throughout the country meant that our raters were sometimes involved in case ascertainment/identification, although it had not originally been intended that this would happen.

(b) No individuals met the DSM–IV or ICD criteria for schizotypal disorder at the time of first assessment.

https://doi.org/10.1192/S0007125000262648 Published online by Cambridge University Press