British Journal of Psychiatry (1992), **160**, 65–71

Risk Factors in Schizophrenia
Season of Birth, Gender, and Familial Risk

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The risk for schizophrenia among first-degree relatives of schizophrenic probands obtained from an epidemiological sample using family history methods was examined to determine whether month of birth of the proband was associated with familial risk. The results of this study of the first-degree relatives of 106 female schizophrenics and 275 male schizophrenics suggested that the relatives of probands born in the months February to May had the highest risk, although the association between month of birth and familial risk among the male probands was present only for those relatives who had onset of schizophrenia before the age of 30.

The distribution of birth dates of schizophrenic patients differs from that of the general population. Schizophrenics are more likely to be born in the winter and early spring, and less likely to be born in the late spring and summer (Bradbury & Miller, 1985; Boyd *et al*, 1986). Several explanations have been offered. One is that a seasonally varying factor, occurring during either the intra-uterine life or the first post-natal months, alters the central nervous system and increases the risk for schizophrenia for some especially vulnerable group. The seasonally varying risk factor has been hypothesised to be a virus, a low-protein diet, or pregnancy and birth complications (Bradbury & Miller, 1985; Boyd *et al*, 1986). A second explanation is that individuals genetically at risk for schizophrenia have a biological advantage which protects them against allergies or infections which may cause mortality and may be more prevalent in the winter. Thus, there may be a preferential survival of infants who are genetically predisposed to schizophrenia who are born in the winter (Bradbury & Miller, 1985; Boyd *et al*, 1986). A third explanation is that the parents of schizophrenics (those with the 'schizophrenia genotype') have an unusual seasonal pattern of conception. Investigators have tested this idea by studying the distribution of dates of birth of the sibs of schizophrenic probands, but the results have been conflicting (McNeil *et al*, 1976; Hare, 1976; Buck & Simpson, 1978; Machon *et al*, 1983; Watson *et al*, 1984).

Since it has been established that genetic factors increase an individual's risk for schizophrenia, it is not surprising that investigators have tried to understand the seasonal phenomenon in relation to genetic risk. Two strategies have been employed: the study of the association between month of birth and the probability of development of schizophrenia among the offspring of schizophrenic women, and the study of the months of birth among cases classified as either familial or non-familial. Machon *et al* (1983) studied the offspring of schizophrenic women to determine whether or not their place of birth (i.e. urban v. rural) as well as their season of birth was associated with their risk of schizophrenia. They hypothesised that neonates born in urban environments are more likely to be exposed to viral infections because individuals living in the city are living at closer proximity to each other. They found a significant interaction effect between season of birth and place of birth in predicting risk of schizophrenia for the offspring: the offspring of schizophrenic women born in the city during the winter and spring months were most likely to develop schizophrenia.

There have been six studies reported which compared the birth months of familial and non-familial schizophrenic patients. The results of these studies have been contradictory. Some found that the familial patients were less likely to be born during winter months (Kinney & Jacobsen, 1978; Shur, 1982; Shensky & Shur, 1982) while others reported that the familial patients were more likely to be born during the winter and spring months (Lo, 1985; Baron & Gruen, 1988; Owens & Lewis, 1988). The studies are summarised below. Three of these studies were reported in papers (Kinney & Jacobsen, 1978; Shur, 1982; Baron & Gruen, 1988) and the other three were described in letters to the editor (Shensky & Shur, 1982; Lo, 1985; Owens & Lewis, 1988).

Kinney & Jacobsen (1978) tested the hypothesis that schizophrenics born in the winter and early spring (January to April) are less likely to have a relative affected with schizophrenia or to have any sign of post-natally incurred brain damage than schizophrenics born during the rest of the year. Among a small sample of schizophrenic patients

($n = 34$) they showed that those with either an affected relative or evidence of post-natal brain damage were significantly less likely to be born in the period January to April.

Similar results were reported by Shur (1982), who used a χ^2 test to compare the distribution of birth dates (by quarter of the year) of 377 familial patients with that of 598 non-familial patients. He found that the familial patients were less likely to have been born during the first quarter. Shensky & Shur (1982) later re-analysed these data using a method described by Edwards (1961) and later amended by Roger (1977) which tests for cyclic trends and the identification of the time of year when the birth rate is maximal. The non-familial patients were more likely to be born in October; patients with affected schizophrenic relatives were more likely to be born in April and May.

Baron & Gruen (1988) studied 88 schizophrenic patients and their 375 first-degree relatives. Using a χ^2 analysis (with four seasons) they found that there were no statistically significant differences in the season-of-birth distribution between the familial and non-familial patients. However, when the relatives' morbidity risks for schizophrenia and schizophrenia spectrum disorders were calculated as a function of season of birth of the proband, they found that the relatives of winter- and spring-born schizophrenics had similar morbidity risks and that these risks were greater than those of the relatives of schizophrenics born in the summer or autumn. The results of the morbidity risk analyses are consistent in part with the results of the cyclic analysis reported by Shensky & Shur (1982), which identified April and May as the period when the familial patients were most likely to be born. However, the results of the morbidity risk analyses are not consistent with other studies which compared the schizophrenic probands who had a family history with those who did not.

The morbidity risk analysis is superior to the conventional χ^2 analysis comparing the familial and the non-familial because of the increased power of the analysis. The familial/non-familial paradigm has reduced power because of misclassification, since the probability of having affected relatives is dependent on family size and the ages of the relatives.

The results from the studies reported by Owens & Lewis (1988) and Lo (1985) were in agreement with the results from the morbidity risk analysis. Owens & Lewis (1988) reported that a positive family history was found in 37% of the patients born during the winter or spring (December to May) in contrast to 20% born during the summer or autumn (June to November). Lo (1985), studying a sample of schizophrenics in Hong Kong, reported that more schizophrenic patients with a positive family history were born during the cool months (October to March) than during the remainder of the year.

In this paper, we compare the morbid risk for schizophrenia among the first-degree relatives of schizophrenic patients as a function of the month of birth of the proband. This study has several advantages over many of the previous studies. They include the following. (a) A large, systematic sample of schizophrenic probands identified in 15 hospitals was studied. (b) The research diagnosis of the probands was made from multiple sources of information, with demonstrated high reliability. (c) Diagnosis for the relatives was based on information obtained from two informants. (d) The analyses were not limited to a comparison of the months of birth of schizophrenic patients classified as familial and non-familial. Cox proportional-hazards models were used which allowed us to adjust for the number of first-degree relatives and for their ages, genders and characteristics. (e) Gender-specific analyses were conducted. (f) The analyses examined the effect of age at onset of psychoses on the relationship between season of birth and familial risk. (g) The analyses avoided making any assumptions about the periods of excess or decreased risk.

Method

The 381 schizophrenic patients are participating in an epidemiological and genetic investigation. Details of the sample selection are described elsewhere (Pulver *et al*, 1989*a*; Pulver & Bale, 1989*b*). Briefly, the probands for this study were selected from a larger sample of patients who were ascertained over six years by a systematic approach to all patients admitted to any one of 15 psychiatric facilities who met the following criteria.

Patients had to be white, to be at least 16 years of age, and to have one of the following hospital diagnoses: schizophrenia, schizophreniform or schizoaffective disorder, bipolar disorder, major depression with psychotic features, drug-induced psychosis, atypical or brief reactive psychosis, paranoid disorder, or schizotypal, schizoid or borderline personality disorder. At 11 of the 15 hospitals, patients with a hospital diagnosis of schizophrenia, schizophreniform disorder, schizoaffective disorder, atypical psychosis or brief reactive psychosis were eligible if they had had less than four psychiatric admissions; at the remaining four hospitals the admission number criterion for these patients was dropped in order to increase the number of schizophrenic patients screened into the sample. At all of the hospitals, patients with the remaining diagnoses were eligible only if they were currently in hospital for the first time. These criteria increased the heterogeneity of the sample (i.e. the proportion of older, chronic schizophrenic patients was

restricted). Recording patient names assured that each patient appeared in the data set only once.

Patients, who gave their informed consent, were interviewed before discharge from hospital. The major component of the interview was a modified version of the Diagnostic Interview Schedule (DIS; Robins *et al*, 1981). The modifications which have been described in previous publications (Pulver *et al*, 1989*a*) were made to address a concern for the lack of sensitivity and specificity of the DIS/lay interviewer approach in identifying psychotic symptoms.

A best-estimate research diagnosis, formulated by a psychiatrist six months after the patient's index admission, was based on the following information: (a) six-month outcome functioning (i.e. information regarding social and occupational functioning, presence or absence of psychiatric symptoms, and time spent in the hospital); (b) a review of the patient's hospital records, including admission and discharge summaries; and (c) a review of the information reported by the patient during the hospital interview. The diagnosis was made by a psychiatrist who, during a telephone interview with the patient or an informant, clarified the patient's clinical picture and determined the six-month outcome status. The diagnosis, based on DSM–III criteria (American Psychiatric Association, 1980), was made provided that one of the two sources of information (i.e. contact with the patient or an informant, or medical records) in addition to the hospital interview was available. Reliability exercises were conducted throughout the data collection.

For diagnoses in the relatives, the family history method was used instead of direct-assessment methods because of the reduced cost. A family history was obtained from two informants judged by the proband to be knowledgeable about his/her family. Details of this procedure have been described previously (Pulver *et al*, 1989*a*; Pulver & Bale, 1989*b*). Briefly, Family History Research Diagnostic Criteria were used to classify the psychiatric illnesses in the relatives (Endicott *et al*, 1975). The family interviewers were blind to the proband's research diagnosis and to the research hypotheses. In this report, the disorder of concern is schizophrenia. Two inter-rater reliability exercises consisting of interviewers rating case vignettes were completed. The intraclass correlation coefficient for the diagnosis of schizophrenia averaged 0.77 across the exercises, demonstrating good inter-rater reliability. Although the family-informant data may have lower sensitivity than data obtained by direct assessment, we do not think that the probability of misclassification is associated with the proband's month of birth. Therefore, any misclassification in these analyses will tend to reduce the statistical power.

The patients involved in this report are limited to those who (a) were admitted to the study between 15 June 1983 and 30 April 1989, (b) received a best-estimate lifetime research diagnosis of schizophrenia, and (c) gave their informed consent to allow us to contact two relatives to participate in a telephone interview about the psychiatric history of the family. This results in a total of 381 patients (275 males and 106 females) and their families. The small proportion of females may be attributed in part to sampling from hospital populations.

Statistical methods

Cox proportional-hazards models (Cox, 1972) were used to assess the familial risk for schizophrenia among first-degree relatives of male and female schizophrenic probands. Gender-specific analyses were carried out because it has been shown that gender is associated with familial risk in this sample (Wolyniec *et al*, 1992) and in others (Goldstein *et al*, 1990).

In the Cox proportional-hazards model, a hazard function for relatives of probands is calculated using the relative's reported age at onset of schizophrenia. The hazard rate (i.e. the chance that a currently unaffected person will develop the disorder within a small amount of time) is dependent on the season of birth of the proband. The model assumes that the hazard rate varies by a constant proportionality factor across the relatives' ages at onset.

This proportional-hazards assumption was tested for each model by plotting the hazards curves. Whenever the proportional-hazards assumption was violated, time-dependent covariates were included in the model. The addition of these time-dependent covariates allowed us to assess the relationship between proband season of birth and familial risk for schizophrenia for specific age-at-onset intervals of the relatives.

The Cox regression model has two analytical benefits. First of all, it allows us to evaluate the simultaneous contribution of proband characteristics and relative characteristics to the relative's chance of having a disorder. Secondly, this model allows us to adjust for different ages of the relatives; this is an important factor since a relative's chance of having a disorder at the time of the interview is dependent on how far along he is in his risk period. The relative's age at first onset is used if the family-informant information has identified a relative as affected; otherwise, the current age of the relative is entered and the case is treated as censored, that is, the psychopathology may or may not appear at a later time. Thus, Cox proportional-hazards modelling and censoring allows us to make use of all existing information about each subject while making mild assumptions about the form of the hazard rate across time.

The relationship between proband birth month and familial risk was hypothesised to involve a step function of birth month. To fit such a model, dummy variables representing clusters of consecutive months were entered as predictor variables in the model. Because the literature on relationships between season of birth and familial risk for schizophrenia suggested somewhat different findings for months of highest risk, we chose to evaluate seven different models involving proband's birth month, categorised into three or four consecutive months. For the first four models we divided the months into sets of four consecutive months. The first model, for example, included January to April, May to August, and September to December, and the other three models started with February, March and April respectively. The remaining three models included

https://doi.org/10.1192/bjp.160.1.65 Published online by Cambridge University Press

all sets of three consecutive months. Based on the results of Cox regression analyses, we then chose those combinations of birth months which showed the highest risk.

Results

In this sample there was a clear difference in risk for schizophrenia in the relatives of male and female probands (Wolyniec *et al*, 1992). The risk of schizophrenia (hazard rate) in relatives of female probands was over twice the risk in relatives of male probands (95% confidence interval 1.3–4.3). There was also a suggestion of an interaction between gender of proband and proband's birth month (significant about the 0.10 level), so separate analyses were done by proband's gender.

After fitting the seven different models for females (number of relatives = 578), we selected one single model which was the most statistically significant ($P = 0.02$). The risk of schizophrenia among first-degree relatives of females born during February to May was approximately seven times that for relatives of female probands born between October and January (95% confidence interval 1.98–25.64) and over twice that for relatives of female probands born between June and September (95% confidence interval 0.95–6.95) (Table 1). The final model adjusts for gender of the relative and season of birth of the relative. The plot of the hazards curve revealed that the proportionality assumption was not violated.

The results of the analyses for male probands (number of relatives = 1353) were somewhat different from those for the females. The plot of the hazards curves revealed that the proportionality assumption was violated: up to the age of 30 the February to May group had the highest risk; after 30 it did not. A time-dependent covariate was therefore introduced into the model which allowed us to determine the risks for schizophrenia in the relatives before and after 30. The results of this analysis indicated that the relatives under the age of 30 of probands born during February to May were over six times as likely to be schizophrenic as those of probands born during October to January (95% confidence interval 0.77–53.00) and over 100 times as likely to be schizophrenic as those of probands born during June to September (95% confidence interval 5.30–4054.72) (Table 1). This association between season of birth of the male proband and familial risk for schizophrenia was not found when we looked at the relatives aged 30 and over (Table 1).

As an alternative, simpler, method for examining the familial aggregation of schizophrenia by proband birth month, we report unadjusted (for age) proportions of affected first-degree relatives by proband's season of birth (see Table 2). For both female probands and male probands whose relatives were aged under 30 years at onset of illness, those born during February to May had relatives who were at highest risk for schizophrenia.

We also explored the possibility that some differences in the sociodemographic make-up or clinical characteristics of the proband groups could explain this season-of-birth difference (Table 3). Among the proband characteristics of marital status, being a parent, levels of education of the proband and the head of household, age at first hospital admission, hospital type, duration of illness and chronicity, we found no significant differences by birth-month grouping. However, considering female probands who became psychotic before 17, we found a much higher proportion in the February to May group than in the other groups (see Table 3). Inclusion of this early-psychosis variable in the model did not, however, affect the season-of-birth results, nor did we find early psychosis

Table 1
Season-of-birth models for schizophrenia among relatives by gender of the proband

Probands	Relative hazards	95% CI
Female probands[1]: for all relatives		
born Feb.–May	7.13	1.98, 25.64
born June–Sept.	2.78	0.69, 11.13
born Oct.–Jan.[3]	1	-
Male probands[2]: for relatives under 30 years		
born Feb.–May	6.37	0.77, 53.00
born June–Sept.	0.04	0.0005, 4.16
born Oct.–Jan.[3]	1	-
Male probands[2]: for relatives 30 years and over		
born Feb.–May	0.61	0.16, 2.38
born June–Sept.	1.21	0.37, 4.00
born Oct.–Jan.[3]	1	-

1. Model adjusted for gender of the relative and season of birth of the relative.
2. Model adjusted for gender of the relative, season of birth of the relative, and time-dependent covariates.
3. Reference group.

Table 2
Proportion of relatives affected with schizophrenia by gender and season of birth of the proband

	Proportion of first-degree relatives affected
Female probands: for all relatives	
born Feb.–May	12/123 = 0.098
born June–Sept.	7/206 = 0.034
born Oct.–Jan.	4/231 = 0.017
Male probands: for relatives under 30 years	
born Feb.–May	11/159 = 0.069
born June–Sept.	3/118 = 0.025
born Oct.–Jan.	4/127 = 0.031
Male probands: for relatives 30 years and over	
born Feb.–May	0
born June–Sept.	4/292 = 0.014
born Oct.–Jan.	3/298 = 0.010

https://doi.org/10.1192/bjp.160.1.65 Published online by Cambridge University Press

Table 3
Characteristics of schizophrenia probands by gender and season of birth

	Female probands			Male probands		
	February–May ($n=26$)	June–September ($n=36$)	October–January ($n=44$)	February–May ($n=95$)	June–September ($n=89$)	October–January ($n=91$)
% married	52.0	51.4	39.0	13.3	21.8	15.3
% with children	48.0	51.4	38.1	10.1	20.7	14.3
Proband education:						
⩽11 years	25.0	28.6	33.3	25.6	19.3	27.1
12 years or general education diploma	45.8	37.1	42.9	43.3	45.5	42.4
⩾13 years	29.2	34.3	23.8	31.1	35.2	30.6
Head-of-household education:						
⩽11 years	30.0	33.3	44.1	29.9	26.3	13.3
12 years or general education diploma	30.0	33.3	26.5	31.2	32.9	37.3
⩾13 years	40.0	33.3	29.4	39.0	40.8	49.3
% first admission	15.4	19.4	15.9	20.0	23.6	20.9
Hospital type:						
state	57.7	80.6	54.5	63.2	61.8	54.9
university	11.5	8.3	18.2	12.6	10.1	11.0
private	11.5	5.6	13.6	12.6	16.9	16.5
community	19.2	5.6	13.6	11.6	11.2	17.6
Age first admitted to hospital: years						
mean	22.5	26.12	24.29	23.72	23.59	22.78
s.d.	6.37	8.88	7.92	7.19	8.07	5.75
range	10–38	14–54	14–45	15–63	12–64	14–38
% ⩽16	20.8	8.8	21.4	4.3	6.9	12.5
Age at first psychotic episode: years						
mean	19.53	23.54	20.95	21.43	20.52	20.43
s.d.	6.86	6.57	6.03	5.68	5.59	5.70
range	7–35	14–41	10–42	7–40	7–37	7–38
%⩽16	41.7*	11.4	24.4	13.0	13.8	18.4
Duration of illness: years						
mean	11.17	12.34	12.54	8.79	10.26	8.93
s.d.	9.93	11.09	9.82	7.72	9.34	7.86
range	0–36	0–36	0–37	0–37	0–40	0–26
Chronicity:						
% with duration >2 years	83.3	77.1	87.8	78.3	75.9	72.4
% with duration >5 years	62.5	65.7	70.7	57.6	64.4	56.3

*$P=0.03$.

to be a predictor of higher risk for schizophrenia among the relatives of female probands.

Discussion

We previously reported that the first-degree relatives of female schizophrenic patients have a higher risk for schizophrenia than do first-degree relatives of male schizophrenics. The results of the analyses reported in this paper suggest that this increase in risk may be attributed to the high risk among relatives of female probands where the proband was born in the months February to May. The risk of schizophrenia for these relatives was approximately seven times that for relatives of probands born in other months. The lowest risk of schizophrenia in relatives of female probands occurred when probands were born during October to January. Neither the relative's gender nor month of birth was associated with familial risk.

The results of the analyses of families with male probands suggest that the association we observed among the female probands was also present among the male probands; however, it was specific to the risk of schizophrenia before age 30 in the relatives. The proband's month of birth was not important to the risk of schizophrenia with onset at or above age 30 in the relatives.

Owing to the differences in research design, it is difficult to make a direct comparison between the

https://doi.org/10.1192/bjp.160.1.65 Published online by Cambridge University Press

results of our investigation and the earlier studies which classified the probands into familial and sporadic cases based on the presence of schizophrenia among close biological relatives (Kinney & Jacobsen, 1978; Shur, 1982; Lo, 1985; Owens & Lewis, 1988). The study reported by Baron & Gruen (1988) is most similar to ours in that consideration was given to the age and number of relatives at risk (i.e. morbidity risks were calculated for the relatives). The sample was smaller than ours (88 cases: 58 males and 30 females), and was selected from two hospitals which may somehow limit representativeness and diminish the generalisability of the findings. However, the study had the advantage of having direct-interview data on the relatives (85% of the first-degree relatives were interviewed direct; thus it was possible to identify those relatives with a 'spectrum personality disorder'). Seasons of birth were defined as winter (December to February), spring (March to May), summer (June to August) and autumn (September to November). The data were analysed in two ways. First, the seasons of birth of the schizophrenic patients with and without a family history were compared and no differences were found. Then morbidity risks for schizophrenia, schizotypal personality disorder and paranoid personality were calculated for proband groups based on the above-defined seasons, using the Strömgren method. The relatives of winter–spring schizophrenic patients were found to have a greater risk for schizophrenia and related personality disorders than the relatives of schizophrenics born in the summer or autumn. Season of birth was not associated with proband characteristics such as gender, birth order, age at onset and clinical subtypes.

Our findings are consistent with Baron & Gruen's finding of an excess risk for schizophrenia among the relatives of schizophrenic probands born during February to May. However, our analyses did not suggest that there was an excess risk for schizophrenia among the relatives of probands born in December to January. We do not have a good explanation for this inconsistency.

Given our use of family informants to obtain information about the relatives, we were not able to identify relatives with personality disorders with sufficient reliability, so we are not able to make the necessary comparison.

Effect of proband's gender and age at onset

In our initial analyses, we found that gender of the proband was important to the relationship between familial risk for schizophrenia and month of birth of the proband. In our analysis of both male and female probands combined, we had a marginally significant interaction between gender and season which suggested to us that the relationship between season of birth and familial risk may be different for the genders. We conducted gender-specific analyses and found a greater seasonal effect on risk for the relatives of the female schizophrenics than for the relatives of male schizophrenics. However, when we plotted hazard curves to test the proportionality assumption for the Cox models, we found that although the assumption was met for the analyses of the female probands, it was not for the male probands. There appeared to be cross-over in the hazard curves for the relatives of the male probands which suggested that it was important to introduce a time-dependent covariate in the analyses to allow for the possibility that the relationship between the risk for schizophrenia and season of birth among the male probands was not consistent across all relatives' ages. This model with the additional variable allowed us to see that among male probands the association between season of birth and familial risk was present only if the onset of the schizophrenia in the relative occurred before the age of 30, the time when all but a few cases were observed. As with the female probands, the risk to relatives was greatest for the probands born February to May. Unfortunately, we know of no other study with which we can compare this result. The Strömgren method, used by Baron & Gruen (1988), did not permit tests for interactions, and the authors did not report gender-specific analyses. This may be due to the relatively small number of probands (58 males and 30 females).

Although we did not find an interaction between proband's age at onset and season of birth in predicting familial risk, we did find that female probands born during February to May were younger than female patients born during the other months.

It has previously been suggested that either age at onset or year of birth may be important to the identification of 'the seasonal subgroup' (those patients for whom risk is increased by season of birth) (Shimura & Miura, 1977; Hare, 1978; Pulver *et al*, 1981). Results from previous investigations which controlled for potential statistical artefacts in the relationship between month of birth and risk for schizophrenia suggested that there may be greater seasonal effects among the early-onset cases (Pulver *et al*, 1981, 1983). Baron & Gruen (1988) did not find differences in age at onset for the patients born in the different seasons.

Conclusion

The association between the risk for schizophrenia and time of birth is helping us to identify a group

https://doi.org/10.1192/bjp.160.1.65 Published online by Cambridge University Press

of patients for whom aetiology is associated in some way with a seasonally varying factor. We suggest that some subgroup of individuals at an increased risk of developing schizophrenia because of their genetic background may also be more vulnerable to some seasonally varying factor which further increases their risk. The way the seasonally varying factor interacts with the genetic-risk factors awaits elucidation. We suggest the following two possibilities for further exploration: (a) that there may be some seasonally varying factor that causes an unusual pattern of conception among those with 'the schizophrenic genotype'; and (b) that some seasonally varying complication of pregnancy or birth may be associated with the risk for schizophrenia.

Acknowledgements

We acknowledge with thanks the helpful comments from Charles Rohde, and from an anonymous reviewer of a previous draft of this manuscript. We also acknowledge the assistance of the staff of the participating hospitals, the staff of the Epidemiology/ Genetics Program, and the patients and their relatives who have participated in this research, and the support of the Maryland Psychiatric Research Center. This work was supported by NIMH grants RO1-MH35712 and RO1-MH45588.

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Season of Birth of Siblings of Schizophrenic Patients

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The hypothesis that mothers of winter–spring-born schizophrenics have an unusual pattern of conception which results in an excess of winter–spring births was tested by studying the distribution of birth-dates of 401 siblings of 120 winter–spring-born schizophrenics and 157 siblings of 59 winter–spring-born controls. All analyses were gender-specific. The results suggest there is no association between the probability of a winter–spring date of birth and being a sibling of a winter–spring-born schizophrenic or control.

It has been reported repeatedly that the distribution of birth-dates of schizophrenic patients differs from that of the general population. Schizophrenics are more likely than the general population to be born in the winter and early spring and less likely to be born in the late spring and summer (Bradbury & Miller, 1985; Boyd *et al*, 1986). The increased risk for schizophrenia in winter-born individuals is reported to be 5–15% in most studies, suggesting that time of birth is a minor risk factor for schizophrenia, or that it may be important for only a subgroup of schizophrenic patients – the remaining schizophrenics being born in the winter group by chance. Among schizophrenic patients, the relationship of season of birth to gender, time spent in hospital, age at onset and familial risk has been studied in order to search for this possible subgroup of schizophrenic patients (Boyd *et al*, 1986; see also preceding paper, this issue). The results of these studies are not consistent.

Three hypotheses have been put forward to explain the excess of winter birth-dates among schizophrenic patients (see preceding paper). The hypotheses are that certain babies born at that time of year are affected by an unknown factor which makes them more likely to develop schizophrenia; that babies genetically at risk for schizophrenia are more likely than others to survive winter infections; and that mothers of schizophrenics have an unusual pattern of conception.