Brit. J. Psychiat. (1983), **143**, 389–396

Risk Factors in Schizophrenia: Season of Birth in Maryland, USA

ANN E. PULVER, WALTER STEWART, WILLIAM T. CARPENTER, Jr. and BARTON CHILDS

Summary: The association between the risk for schizophrenia and season of birth was studied using a standard actuarial life table method. This method of analysis eliminates the possibility of the previously described statistical artifacts from the data. An increased risk for schizophrenia for winter born individuals was demonstrated. The analyses also supported the hypothesis that season of birth is associated with an increased risk for a subtype of schizophrenia.

A statistically significant increased risk of schizophrenia for individuals born in the winter has been reported (Videbech *et al*, 1974; Hare *et al*, 1974; Dalen, 1974; Torrey, 1980; Pulver *et al*, 1981). This has led to suggestions that either some seasonally varying factor, occurring during intrauterine life or during the first postnatal months, alters the central nervous system and increases the risk for schizophrenia, or that mothers of schizophrenics are more likely to conceive in the spring or early summer. The increased risk, reported for winter born individuals, is reported to be between 5 per cent and 15 per cent, which indicates that the season of birth is only a minor risk factor for schizophrenia. However, since schizophrenia is aetiologically heterogeneous, it may be that the seasonally varying factor is important only for a subgroup of patients. If analysis were limited to that subgroup, the winter excess would be of far greater magnitude than any previously reported and the need to enquire into the cause of this finding would be increased.

The validity of this association has been repeatedly questioned (Barry and Barry, 1964; Norris and Chowning, 1962; Dalen, 1974; Lewis and Griffin, 1981). These criticisms have been reviewed and answered in many publications, (Dalen, 1974; Hare, 1978; Pulver *et al*, 1981). The most recent of these criticisms is that of Lewis and Griffin (1981) who suggested that the association between month of birth and risk for schizophrenia is due to a statistical artifact. This artifact, called the age prevalence effect, is distinct from the age incidence effect (Dalen, 1974; Hare, 1978; Pulver *et al*, 1981) but also results in an artificially increased risk for individuals born in the early months of the year. The artifact diminishes as the length of the age period of risk increases. The analysis by Lewis and Griffin suggests that the age prevalence effect accounts for the winter excess; however, they noted that this effect could not explain the winter excess reported in the southern hemisphere.

The objective of our investigation was twofold: to determine if the season of birth association is present when the possibility of the described statistical artifacts are completely removed from the data and to determine if the season of birth phenomena is more likely to be associated with a subgroup of schizophrenic patients.

Method

I. Study population

The sample consisted of all individuals who were reported to the Maryland Psychiatric Case Register and who met the following criteria:

- diagnosed as schizophrenic for the first time during the period 1/1/63–31/12/65
- admitted to a psychiatric facility at least once during the period 1/1/63–31/12/68
- diagnosed as schizophrenic for the first time between 17 and 23 years of age
- white

The Maryland Psychiatric Case Register includes the names of Maryland residents who were on the rolls of psychiatric inpatient or outpatient facilities in Maryland or the District of Columbia. During the period 1/7/61–1/7/68 all residents seen in these facilities have been reported to the Register. Record linkage allowed the accumulation of diagnostic and treatment data for a population of approximately four million individuals. Standard American Psychiatric Associ ation nomenclature (DSM III) was used to record diagnoses. Special tabulation of the data was made so that no individual could be identified.

The population at risk

The population at risk included all white male and female individuals reported to have been born in Maryland between 1/1/42–31/12/46 and who survived the first month of life. These data were obtained from vital statistics tables published by the U.S. Department of Commerce (1944–1948). The calendar time covered does not include cohorts born before 1942 because data on births and neonatal deaths by sex, race and month have only been available in Maryland since 1942. The live birth frequencies were adjusted for deaths occurring during the first month of life because there is a differential rate of mortality by month of birth. Data concerning neonatal deaths were also obtained from tables published by the U.S. Department of Commerce (1944–1948).

II. **Data analysis**

The patients and population at risk data were divided into 24 cohorts defined by sex and month of birth. The number of patients born in each month (numerators) is listed in Table I. Standard actuarial life table methods were used to estimate the cumulative probability of being diagnosed as schizophrenic for each of these 24 cohorts for the 204–276 month age period (17–23 years of age) Peto *et al*, 1977. The period 204–276 months of age was chosen because it is the longest age period for which race, sex and month of birth specific denominators were available and also because it is the longest age period for which each of the 24 cohorts have a population at risk for all 73 age of month intervals. It should be noted that by restricting the life table analyses for each cohort to exactly the same age range some data are lost but the possibility of a statistical artifact (i.e. age incidence or age prevalence effect) is completely eliminated. Coincidentally, the age period of risk used for the life table calculations coincides with the highest risk period for schizophrenia.

The effort to determine whether the seasonal effect was associated with an identifiable subtype of schizophrenia was somewhat limited by the data in the register but age, sex, and length of hospital stay were available. The length of the first psychiatric hospitalization is useful since duration of hospitalization is associated with prognosis in schizophrenia (Strauss and Carpenter, 1977). Patients were arbitrarily divided into two subgroups: those hospitalized more than six months (chronic) and those hospitalized less than six months (not chronic). Each of these two subgroups was further divided into 24 cohorts defined by sex and month of birth. So, for the subgroup analyses, there was a total of 48 unique cohorts defined by length of stay in the hospital, sex and month of birth. The number of patients in each cohort is listed in Tables II and III.

Results

The cumulative probabilities of being diagnosed as schizophrenic between the age 17 and 23 years (204–276 months of age) for white males and females born during 1942–1946, in Maryland by month of birth are listed in Table I and displayed in Fig 1. The chi-square test was used to test for homogeneity of the cumulative probability of being diagnosed as schizophrenic; the test was significant for both females ($\chi^2 = 26.08$, $P < .01$) and males ($\chi^2 = 25.62$, $P < .01$). In Maryland there is an increased risk for both males and females born during the winter months to receive this diagnosis.

The cumulative probabilities of being diagnosed as schizophrenic and hospitalized for more than 180 days between the ages of 17 and 23 years (204–276 months of age) for white males and females born during 1942–1946 in Maryland by month of birth are listed in Table II and displayed in Fig 2. The chi-square statistic for the test for homogeneity of the probabilities is not significant for the females ($\chi^2 = 9.29$, $P > 0.05$) or for the males ($\chi^2 = 3.44$, $P > 0.05$). The risk for individuals to be diagnosed as schizophrenic and hospitalized more than 180 days is not associated with the month of birth.

The cumulative probabilities of being diagnosed as schizophrenic and being hospitalized less than 181 days between the ages of 17–23 years for white males and females by month of birth are listed in Table III and displayed in Fig 3. The test for the females is significant ($\chi^2 = 25.85$, $P < .01$) and also for the males ($\chi^2 = 33.41$, $P < .005$). In Maryland there is an increased risk for both males and females born during the winter months and who were hospitalized less than 181 days.

Discussion

I. **The association between the risk for schizophrenia and season of birth**

These analyses confirm the association between the risk for schizophrenia and season of birth in population data from the state of Maryland. The risk for winter born males (i.e. males born in January-March) is approximately 35 per cent greater than for nonwinter born males (i.e. males born April-December); the risk for winter born females is approximately 38 per cent greater than for nonwinter born females. Previously, studies have revealed that the excess risk was on the average 15 per cent. What accounts for this difference? Three possibilities are:

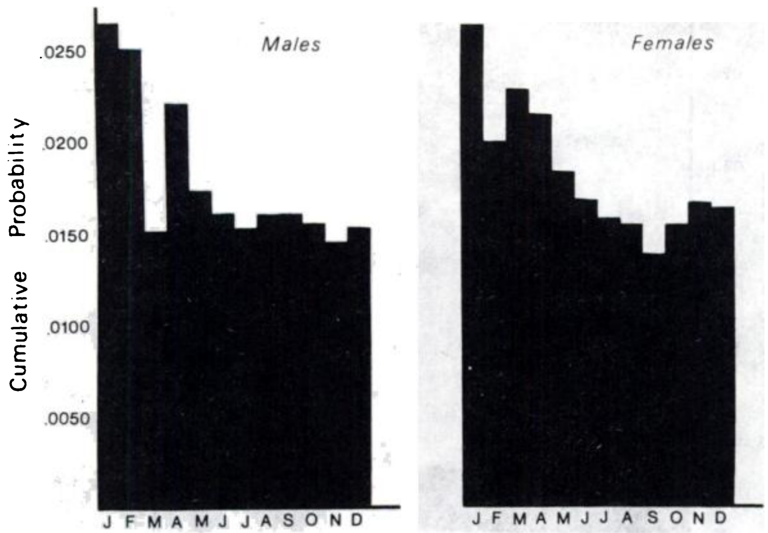

FIG 1.—The cumulative probability of being diagnosed as schizophrenic between the ages of 17 and 23 years of age (204–276) months of age) for white Maryland residents born during 1942–46 by month of birth and sex.

TABLE I

The cumulative probability of being diagnosed as schizophrenic between the ages of 17 and 23 years of age (204–276 months of age) for white Maryland residents born during 1942–46 by month of birth and sex

	Male			Female		
Month	Number of cases	Cumulative probability	Standard error	Number of cases	Cumulative probability	Standard error
January	78	.0262	.0033	87	.0261	.0036
February	67	.0248	.0037	61	.0199	.0035
March	51	.0150	.0028	73	.0225	.0028
April	60	.0217	.0037	63	.0213	.0028
May	48	.0172	.0025	60	.0182	.0024
June	50	.0160	.0023	59	.0167	.0025
July	54	.0152	.0024	59	.0155	.0020
August	58	.0160	.0021	60	.0153	.0020
September	54	.0160	.0021	54	.0137	.0018
October	62	.0155	.0024	62	.0154	.0022
November	54	.0144	.0019	61	.0165	.0020
December	60	.0152	.0019	60	.0163	.0020

(a) Risk period: All of the previously reported season of birth studies examined the association between season of birth and the risk for schizophrenia over a lifetime. The investigation reported here examined the association for a defined risk period i.e. between the ages 17 and 23. Hare (1978), and Pulver *et al* (1981), have suggested previously that age of onset may influence the relationship between schizophrenia and season of birth i.e. the season of birth association may be limited to a subgroup of schizophrenic patients and this subgroup may be differentiated by the age at which schizophrenia is diagnosed. The excess risk

https://doi.org/10.1192/bjp.143.4.389 Published online by Cambridge University Press

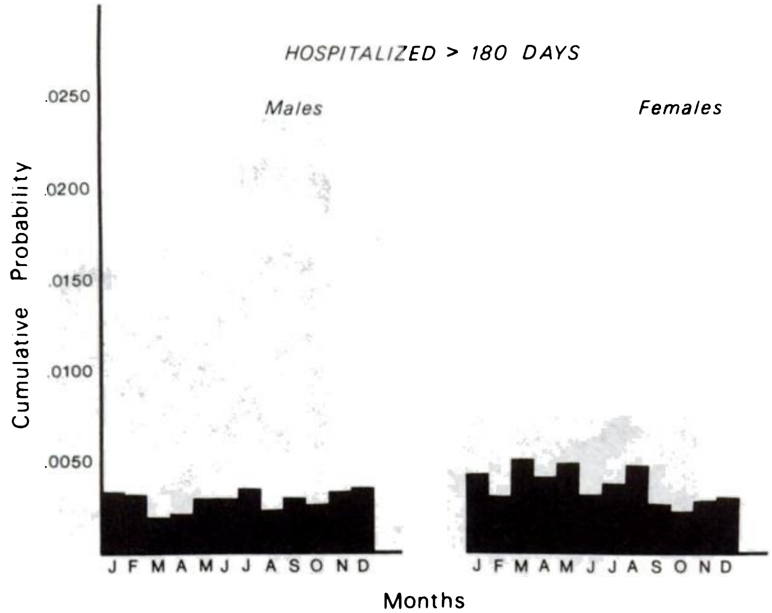

FIG 2.—The cumulative probability of being diagnosed as schizophrenic and hospitalized more than 180 days between the ages of 17 and 23 years of age (204–276 months of age) for white Maryland residents born during 1942–46 by month of birth and sex.

TABLE II

The cumulative probability of being diagnosed as schizophrenic and hospitalized more than 180 days between the ages of 17 and 23 years of age (204–276 months of age) for white Maryland residents born during 1942–46 by month of birth and sex

	Male			Female		
Month	Number of cases	Cumulative probability	Standard error	Number of cases	Cumulative probability	Standard error
January	9	.0033	.0012	14	.0043	.0012
February	8	.0032	.0013	11	.0030	.0019
March	7	.0019	.0018	17	.0051	.0012
April	6	.0021	.0008	13	.0041	.0012
May	10	.0030	.0009	17	.0051	.0011
June	9	.0030	.0010	10	.0032	.0010
July	13	.0035	.0016	13	.0037	.0010
August	9	.0024	.0008	17	.0048	.0011
September	9	.0030	.0008	11	.0027	.0008
October	10	.0026	.0008	9	.0024	.0007
November	12	.0034	.0009	11	.0028	.0008
December	14	.0035	.0009	12	.0031	.0009

found in these data is consistent with the results of the analysis of data from Monroe County, New York (Pulver *et al*, 1981) which revealed the greatest seasonal effect for the early onset female cases.

(b) The diagnostic criteria used in Maryland during the 1960's may somehow include more patients who are the 'seasonal type.'

(c) The putative environmental factor which influences the development of the central nervous system, and increases an individual's risk for schizophrenia

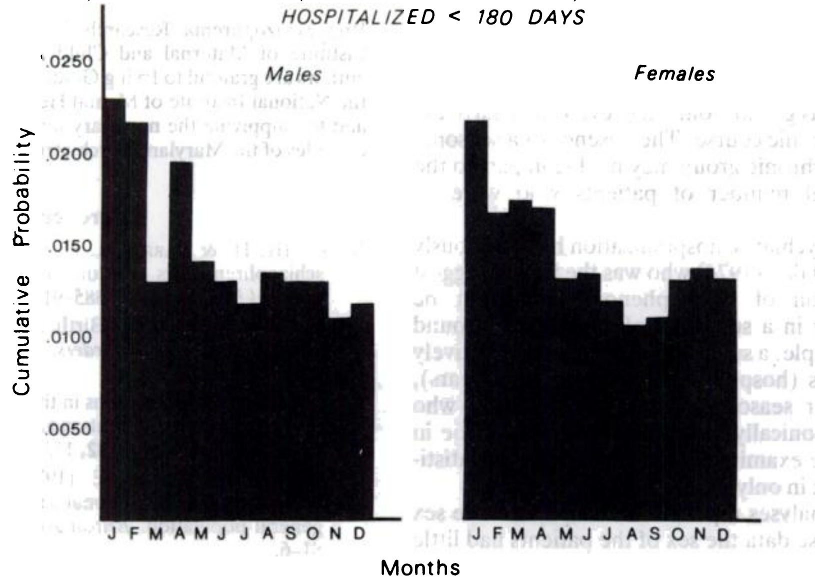

FIG 3.—The cumulative probability of being diagnosed as schizophrenic and hospitalized less than 181 days between the ages of 17 and 23 (204–276 months of age) for white Maryland residents born during 1942–46.

TABLE III

The cumulative probability of being diagnosed as schizophrenic and hospitalized less than 181 days between the ages of 17 and 23 (204–276 months of age) for white Maryland residents born during 1942–46

	Male			Female		
Month	Number of cases	Cumulative probability	Standard error	Number of cases	Cumulative probability	Standard error
January	69	.0229	.0031	73	.0218	.0034
February	59	.0217	.0034	50	.0168	.0029
March	44	.0131	.0021	56	.0174	.0025
April	54	.0196	.0036	50	.0171	.0025
May	38	.0142	.0023	43	.0132	.0021
June	41	.0131	.0021	49	.0135	.0023
July	41	.0118	.0018	46	.0120	.0017
August	49	.0136	.0019	43	.0106	.0017
September	45	.0130	.0019	43	.0111	.0017
October	52	.0130	.0022	53	.0131	.0021
November	42	.0110	.0017	50	.0137	.0018
December	46	.0117	.0017	48	.0132	.0018

may have been (or may be) more prevalent in Maryland.

II. **Subgroup analyses**

These analyses suggest that season of birth is associated with an increased risk for a subtype of schizophrenia which does not have a chronic course. Month of birth was not associated with the risk for schizophrenia for patients hospitalized more than six months. Duration of first psychiatric hospitalization is the only datum available from the Register which provides a means for identifying a group of patients who may have a chronic disease. The division of the sample at 180 days is arbitrary and many factors affect the timing of hospital discharge so that there will be patients who have been misclassified. We are confi dent that patients who required more than 180 days in the hospital represent a group of chronic patients, while those who stayed less than 181 days are probably a heterogeneous group; some may eventually have experienced a chronic course. The absence of a seasonal pattern in the chronic group may be due in part to the relatively small number of patients who were so classified.

Length of psychiatric hospitalization had previously been used by Dalen (1974) who was the first to suggest that the season of birth phenomenon might be important only in a subgroup of patients. He found that in one sample, a subgroup selected for a relatively good prognosis (hospitalized less than three years), showed greater seasonal deviation than those who were more chronically hospitalized. This was true in two samples he examined; the difference was statistically significant in only one.

All of the analyses reported in this paper were sex specific. In these data the sex of the patients had little effect on the results. Previously, six investigators subdivided their samples of patients by sex (Parker and Nielson, 1976; Roche and Dalen, 1974; Parker and Balza, 1977; Pulver *et al*, 1981; Torrey and Torrey, 1980; Syme and Illingworth, 1978). Five investigators reported a sex difference in the season of birth effects and four of them found the season effects to be more marked among the females.

Other evidence supporting the idea that the season of birth association may only be important to a subgroup of patients comes from three recent studies. Kinney and Jacobson (1978) divided their sample of 34 schizophrenic patients into (a) patients with a family history of schizophrenia or a history of postnatal brain damage and (b) patients with neither of these factors. The patients with neither risk factors were more likely to be born during the winter months. Shur (1982) divided his sample of 975 schizophrenic patients according to a family history of psychiatric disease. The patients with a family history of either severe psychiatric illness or schizophrenia were born less often in the first quarter of the year. Pulver *et al* (1981) reported that the effect of month of birth on the risk for schizophrenia was related to the sex and the age of subsets of the whole population.

In conclusion, our findings are consistent with Dalen (1974), Kinney and Jacobson (1978), Pulver *et al* (1981), Shur (1982), Shensky and Shur (1982) in suggesting that the season of birth phenomenon is important to the aetiology of a subgroup of schizophrenia.

Acknowledgements

This work was supported in part by grants from the Scottish Rite Schizophrenia Research Program and the National Institute of Maternal and Child Health, HD 00486. The authors are grateful to Irving Goldberg and William Eaton of the National Institute of Mental Health for their suggestions and for supplying the necessary tabulation of data from the case files of the Maryland Psychiatric Case Register.

References

BARRY, III, H. & BARRY, JR. H. (1964) Season of birth in schizophrenia: Its relation to social class. *Archives of General Psychiatry*, **11**, 385–91.

DALEN, P. (1974) Season of Birth. *A Study of Schizophrenia and Other Mental Disorders*. Amsterdam: North Holland/American Elsevier.

HARE, E. H. (1978) Variations in the seasonal distribution of births of psychotic patients in England and Wales. *British Journal of Psychiatry*, **132**, 155–8.

—— PRICE, J. & SLATER, E. (1974) Mental disorder and season of birth: A national sample compared with the general population. *British Journal of Psychiatry*, **124**, 81–6.

KINNEY, D. K. & JACOBSON, B. (1978) Environmental factors in schizophrenia: new adoption study evidence. In *The Nature of Schizophrenia: New Approaches to Research and Treatment* (eds. L. C. Wynne, R. L. Cromwell and S. Matthysse), pp 38–51. New York: Wiley.

LEE, E. T. (1980) *Statistical Methods for Survival Data Analysis*, Belman 4, California: Lifetime Learning Publication.

LEWIS, M. S. & GRIFFIN, P. A. (1981) An explanation for the season of birth effect in schizophrenia and certain other diseases. *Psychological Bulletin*, **89**, 589–96.

NORRIS, A. S. & CHOWNING, J. R. (1962) Season of birth and mental illness: a critical examination. *Archives of General Psychiatry*, **7**, 207–12.

PARKER, G. & BALSA, B. (1977) Season of birth and schizophrenia—an equatorial study. *Acta Psychiatrica Scandinavica*, **56**, 143–6.

—— & NEILSON, M. (1976) Mental disorder and season of birth—a southern hemisphere study. *British Journal of Psychiatry*, **129**, 355–61.

PETO, R. & PIKE, M. C. *et al* (1977) Design and analysis of randomized clinical trials requiring prolonged observation of each patient. II. Analysis and examples. *British Journal of Cancer*, **35**, 1, 1–39.

PULVER, A. E., SAWYER, J. W. & CHILDS, B. (1981) The association between season of birth and the risk for schizophrenia. *American Journal of Epidemiology*, **114**, 735–49.

ROCHE, S. D. & DALEN, P. (1974) In *Season of Birth: A Study of Schizophrenia and other Mental Disorders*. Amsterdam: North Holland.

SHENSKY, T. & SHUR, E. (1982) Season of birth of schizophrenics: cyclic trends and their analysis. *British Journal of Psychiatry*, **141**, 316–17.

SHUR, E. (1982) Season of birth in high and low risk schizophrenics. *British Journal of Psychiatry*, **140**, 410–15.

STRAUSS, J. S. & CARPENTER, JR., W. T. (1977) Prediction of outcome in schizophrenia. *Archives of General Psychiatry*, **34**, 159–62.

SYME, G. J. & ILLINGWORTH, D. J. (1978) Sex differences in birth patterns of schizophrenics. *Journal of Clinical Psychology*, **34**, 633–5.

TORREY, E. F. (1980) *Schizophrenia and Civilization*. New York: Aronson.

—— & TORREY, B. B. (1980) Sex differences in the seasonality of schizophrenic births. *British Journal of Psychiatry*, **137**, 101–4.

U.S. DEPARTMENT OF COMMERCE, VITAL STATISTICS OF THE U.S. (1944) Part 2. Natality and Mortality Data for the U.S. Tabulated by Place of Residence. Washington, D.C.: Government Printing Office, 1944.

—— (1945) Part 2. Natality and Mortality Data for the U.S. Tabulated by Place of Residence. Washington, D.C.: U.S. Government Printing Office.

—— (1946) Part 2. Natality and Mortality Data for the U.S. Tabulated by Place of Residence. Washington, D.C.: U.S. Government Printing Office.

—— (1947) Part 2. Natality and Mortality Data for the U.S. Tabulated by Place of Residence. Washington, D.C.: U.S. Government Printing Office.

—— (1948) Part 2. Natality and Mortality Data for the U.S. Tabulated by Place of Residence. Washington, D.C.: U.S. Government Printing Office.

VIDEBECH, T., WEEKE, A. & DUPONT, A. (1974) Endogenous psychoses and season of birth. *Acta Psychiatrica Scandinavica*, **50**, 202–28.

Appendix

The cumulative risk of schizophrenia (Q) between months of age 204–276 was calculated as one minus the probability of surviving this age period without a diagnosis of schizophrenia (P).

$$Q = 1 - P = 1 - (p_{204}\, p_{205} \cdots p_{276})$$

$$= 1 - \prod_{i=204}^{276} p_i$$

$$= 1 - \prod_{i=204}^{276} (1 - q_i)$$

$$= 1 - \prod_{i=204}^{276} \left(1 - \frac{Di}{O_i - W_{i/2}}\right)$$

where:

i = i^{th} month of age

p_i = probability of surviving through the i^{th} month of age without schizophrenia, for those at risk at the beginning of the interval

q_i = probability of being diagnosed schizophrenic during the i^{th} month of age for those at risk at the beginning of the interval

D_i = number of individuals diagnosed schizophrenic during the i^{th} month

O_i = number of individuals at risk at the beginning of the i^{th} month

W_i = number of individuals withdrawn from the population at risk during the i^{th} month

O'_i = $O_i - W_{i/2}$

The standard error of Q (SE(Q)) was derived as shown below (Lee, 1980).

$$SE(Q) = P\sqrt{V}$$

where:

$$\log(P) = \sum_{i=204}^{276} \log(p_i)$$

$$V = \mathrm{Var}[\log(P)] = \sum_{i=204}^{276} \mathrm{Var}[\log(p_i)]$$

$$= \sum_{i=204}^{276} \frac{q_i/p_i}{O'_i}$$

The log rank test (Peto and Pike, 1977) was used to test for differences in life table risk between each of the month of birth cohorts among males and between each of the month of birth cohorts among females.

The test is of the chi-square type, i.e., $(O-E)^2$, where expected (E) case events are calculated by allocating the total number of events (all months of the birth cohorts) for an interval (age in month) in proportion to the fraction of subjects at risk for a specific month of birth cohort to the total subjects at risk for the interval. The expected numbers for each interval are then summed to give the expected number of events for a given population which is used in the χ^2 calculation.

$$\chi^2_{k-1} = \sum_{j=1}^{k} (O_j - E_j)^2 / E_j$$

where:

O_j = total observed number of schizophrenics in cohort j for the age period 204–276 months

E_j = expected number of schizophrenics for cohort j,

In general, the logrank procedure requires that the data be tabulated by, more or less, exact times to the event. However, an interval of time is an approximation for a logrank test as

https://doi.org/10.1192/bjp.143.4.389 Published online by Cambridge University Press

long as none of the intervals are so wide as to make an assumption of constant risk throughout the interval doubtful. This condition holds when using monthly intervals for the schizophrenia data.

*Ann E. Pulver, SC.D., *Assistant Professor of Psychiatry, University of Maryland School of Medicine, Maryland Psychiatric Research Centre P.O. Box 3235, Baltimore, Maryland 21228, USA and Assistant, Department of Pediatrics, Johns Hopkins University School of Medicine*

Walter Stewart, M.P.H., *Research Associate, University of Maryland School of Medicine, Maryland Psychiatric Research Center and Doctoral Candidate, Department of Epidemiology, Johns Hopkins University, School of Hygiene and Public Health*

William T. Carpenter, Jr., M.D., *Professor of Psychiatry, University of Maryland School of Medicine and Director, Maryland Psychiatric Research Center*

Barton Childs, M.D., *Professor Emeritus, Department of Pediatrics, Johns Hopkins University School of Medicine*

*Correspondence.

(Received 18 November 1982; revised 17 March 1983)