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Review Article

Seasonality of births in schizophrenia and bipolar disorder: a review of the literature

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Abstract

More than 250 studies, covering 29 Northern and five Southern Hemisphere countries, have been published on the birth seasonality of individuals who develop schizophrenia and/or bipolar disorder. Despite methodological problems, the studies are remarkably consistent in showing a 5–8% winter–spring excess of births for both schizophrenia and mania/bipolar disorder. This seasonal birth excess is also found in schizoaffective disorder (December–March), major depression (March–May), and autism (March) but not in other psychiatric conditions with the possible exceptions of eating disorders and antisocial personality disorder. The seasonal birth pattern also may shift over time. Attempts to correlate the seasonal birth excess with specific features of schizophrenia suggest that winter–spring births are probably related to urban births and to a negative family history. Possible correlations include lesser severity of illness and neurophysiological measures. There appears to be no correlation with gender, social class, race, measurable pregnancy and birth complications, clinical subtypes, or neurological, neuropsychological, or neuroimaging measures. Virtually no correlation studies have been done for bipolar disorder. Regarding the cause of the birth seasonality, statistical artifact and parental procreational habits are unlikely explanations. Seasonal effects of genes, subtle pregnancy and birth complications, light and internal chemistry, toxins, nutrition, temperature/weather, and infectious agents or a combination of these are all viable possibilities. © 1997 Elsevier Science B.V.

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1. Introduction

Although Hippocrates (460 BC) recognized the importance of season of birth on the development of some diseases, modern medicine has been slow to accept or utilize this information. Bailar and Gurian (1965) noted that season of birth research was "slightly disreputable to many scientists ... The field has attracted an undue proportion of enthusiasts and fadists". In 1969, Sankar said that season of birth research "smacks of pseudo-psychological or even magical flavor." As late as 1974, the American Journal of Psychiatry published a Brief Report by Woodruff et al., 'Psychiatric Illness and Season of Birth', in which the authors divided

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their data by signs of the zodiac rather than calendar months, because they said that "use of the astrological calendar made esoteric and arcane speculation possible".

In fact, serious studies of the effects of season of birth on the development of severe psychiatric illnesses began in 1929 with Tramer's publication of birth data for 3100 Swiss patients diagnosed with various types of psychoses. Tramer undertook the research because he believed that seasonally varying diet, vitamins, and sunlight affects psychical development, and he therefore suspected that an individual's month of birth might permanently influence such development. In the United States, this was followed by Petersen's 1934 study of patients in a state psychiatric hospital in Illinois and Huntington's 1938 publication of birth data from state psychiatric hospitals in eight states. Barry and Barry reviewed these studies and published additional data in the Archives of General Psychiatry in 1961 and 1964. In addition, Knobloch and Pasamanick (1958) published data showing that individuals with mental retardation also had a seasonal birth pattern. Interest in seasonal birth factors was further stimulated by the observation of large numbers of congenital anomalies in children born following the 1963–64 spring rubella pandemic. By the late 1960s, Edward Hare (Hare and Price, 1968) in England and Per Dalén (1968) in Sweden had begun extensive studies of seasonal birth patterns of individuals with serious psychiatric disorders. Because they utilized large numbers of patients, adequate controls, and more sophisticated statistical analyses, Hare and Dalén are regarded as the founders of modern psychiatric studies in this field.

This paper will review all studies located by the authors concerning birth seasonality in schizophrenia and bipolar disorder; such studies now number over 250. The last extensive reviews were done by Bradbury and Miller in 1985 and Boyd et al. in 1986, although brief reviews have appeared in the intervening years (Hare, 1988; Iannuzzo et al., 1990; Fossey and Shapiro, 1992; Cotter et al., 1996). Only season of birth studies will be included; studies of season of onset or hospitalization will not be discussed. In addition to analyzing studies of birth seasonality in schizophrenia and bipolar disorder, the review will also examine correlations between the seasonal births and clinical aspects of these diseases; discuss possible causes of birth seasonality in schizophrenia and bipolar disorder; and indicate promising directions for future research.

2. Methodological problems

Methodologically, there are many problems with studies of birth seasonality in schizophrenia and bipolar disorder. They can be enumerated as follows:

2.1. Accuracy of birth data

Month and year of birth were frequently not accurately recorded in hospital records prior to about 1920, so data in some of the earliest studies are suspect. For example, in Barry and Barry's 1964 study of two private psychiatric hospitals, the authors noted that "in both hospitals, the records indicated that several patients had been admitted on the day they were born". Another type of error in birth date was noted by Torrey et al. (1977) in South Carolina, where it had been common practice to put 30 June as the birth date for any patient with an unknown birth date being admitted to the state hospitals, thus producing a spurious June birth peak.

2.2. Duplication of subject count

In some of the large studies that utilized computerized databases, there was some duplication of subject count if the person was admitted to hospitals more than once during the study period. Thus, in the 19-state study by Torrey et al. (1977), some duplication was thought to exist in many of the states. Individuals who had been admitted in more than one of the states during the study period would also have produced a duplicate count. Studies based on case registers have avoided this problem.

2.3. Diagnosis

Standardization of diagnosis has plagued virtually all studies of schizophrenia and bipolar disorder, including studies of seasonality. Most of the studies have used either the International Classification of Diseases (ICD) or Diagnostic and Statistical Manual (DSM) systems, although a few have used Kraepelian (Shimura et al., 1977), Schneiderian (Danneel, 1973; Koehler and Jacoby, 1976a), or Feighner's (Milstein et al., 1976; Rihmer, 1980) diagnostic criteria. One study used psychotic responses to the Rorschach test to establish the diagnosis (Orme, 1963), and many of the smaller studies did not indicate what diagnostic criteria were used. Diagnostic issues are especially problematic for bipolar disorder, since the older definition of manic-depressive psychosis included individuals with depression without any manic episodes, whereas bipolar disorder requires a manic episode; thus, comparability of the older and newer studies is difficult.

2.4. Controls

A few of the birth seasonality studies apparently used no controls (Barry and Barry, 1964; Rihmer, 1980; Corgiat et al., 1983; Lo, 1985; Ede et al., 1985; Hsieh et al., 1987); this is unsatisfactory, since it is known that there is a seasonality to general births and that this seasonality varies both geographically and over time (Cowgill, 1966; Warren et al., 1986; James, 1990; Russell et al., 1993). A few studies used non-psychotic psychiatric patients as controls (Woodard and Feldman, 1990; García Hildebrandt, 1992; Lynge and Jacobsen, 1995), which is also unsatisfactory since it is known that individuals with diagnoses such as severe depression may also have a seasonal birth pattern (Torrey et al., 1996). One study used controls taken from a registry in which birth months were recorded as the date of birth registration rather than the date of birth, with there frequently being a month or more between the two events (Parker, 1978a).

The majority of studies used as controls all general births for the same years as the study subjects. In a few cases, the same years could not be used because general birth data for those years were not available (Hare and Price, 1968; Krupinski et al., 1976; Parker and Neilson, 1976; Gallagher et al., 1983; d'Amato et al., 1991; Modestin et al., 1995). Norris and Chowning (1962) selected general birth data from four random years to compare to the 45 birth years of their study population and found that they sometimes got different results when they selected four different random years.

2.5. Immigration and emigration

Since most studies of birth seasonality in schizophrenia and bipolar disorder compare the affected individuals in that state or country with all persons born there at the time that the subjects were born, they fail to account for individuals who were born there and later emigrated elsewhere or individuals who were born elsewhere and immigrated to that state or country. In countries and states with high rates of immigration (e.g. Canada, Australia, New York State) or emigration (e.g. Ireland), the number of individuals who move may be high enough to influence the results. A few researchers have taken this into account by deleting all subjects born in other countries (Hare and Price, 1968; Dalén, 1975) or by including controls from the area from which the study population emigrated (Gallagher et al., 1983, 1984).

2.6. Period of analysis

Most studies have analyzed the data by months, which are the most satisfactory. In a few countries (e.g. Ireland, England, and Wales), general birth data were available only by quarter, thereby restricting data analyses to 3-month periods. This is unsatisfactory because a birth excess for an individual month (e.g. March) or for two contiguous months in different quarters (e.g. March and April) may not be statistically significant if analyzed as part of a quarter and the birth excess thereby missed. Some studies have also used seasons, trimesters, or divided the year in half (e.g. December–May, June–November).

2.7. Sample size

An inadequate number of subjects is probably the largest single methodological problem in birth seasonality studies. More than 20 years ago, Hare (1975b) calculated that in order to obtain statistical significance at a level of $p < 0.05$, if it is assumed that there is an 8% deviation in seasonal birth distribution, "at least 1500 subjects will be needed when the distribution is considered by quarters of the year, and 4500 subjects when the distribution is considered by month". If the seasonal birth deviation is less than 8%, then even more subjects will be needed. James (1976) elaborated on Hare's calculations and recommended the use of a standard formula to determine the necessary number of subjects.

2.8. Statistical tests

The vast majority of birth seasonality studies have utilized the chi-square test. As noted by Shensky and Shur (1982), this test can "detect any form of deviation from expected figures, regardless of pattern". However, they added that "where trends are presumed cyclic, this test is insensitive and may not be the most appropriate". Cotter et al. (1996) also noted that for cyclic data, the chi-square test is limited, and "its disadvantages undoubtedly outweigh its advantages." The selection of a correct statistical test for the data being analyzed is essential.

For cyclic data, the most frequently used test is the Edwards test (Edwards, 1961), which has as an hypothesis that the seasonality curve is a sinusoidal curve with one peak and one trough. Cave and Freedman (1975) developed a test that has, as an alternative hypothesis, a sinusoidal curve with two peaks and two troughs. Pocock (1974) developed a test that has, as an alternative, a seasonality curve of arbitrary shape. Marrero (1983), using a computer simulation, examined the type I and type II error rates for eight different seasonality tests for sample sizes up to 1000. The results of the simulations for single sinusoidal or double sinusoidal alternatives are complex, being dependent upon the sample size and the alternative. In the case of a 3-month pulse, none of the tests performed adequately.

In order to determine a sample size of adequate power for a seasonality curve of arbitrary shape, one can run computer simulations for the Pocock test. However, some preliminary estimates of the sample sizes can be obtained by using a goodness-of-fit test (Agresti, 1990). Under the null hypothesis, the counts consist of independent Poisson observations with equal intensity in each month. If the counts are collapsed across the years, then the 12 monthly counts are independent Poisson observations with an equal intensity in each month, and it can be shown that the counts can be considered to derive from a multinomial distribution. It is then possible to test the null hypothesis that the proportions of data in each of the 12 months are all 1/12. This can be performed with the goodness-of-fit test, which has the distribution x^2 ($df = 11$). This test was suggested by Hare (1975b), who showed that a sample of 4500 is needed to detect an 8% deviation in the seasonal birth distribution. For large sample sizes, it will be necessary to adjust the proportion, 1/12, to account for the months of unequal length.

It should be noted that a significant seasonality test does not necessarily imply that seasonality is present (i.e. a fixed yearly cycle persists over the years). One of the factors that can affect the interpretation of the seasonality test results is the population at risk. Since there is frequently a seasonality present in the general birth population, it is important to account for this effect in the seasonality analysis. A significant x^2 could be the result of an effect induced by the general birth seasonality. A seasonality test for the general birth series can also be performed with the goodness-of-fit test. If both goodness-of-fit tests are significant, then one can compare the monthly proportions of the two series and determine months of deficit or excess relative to the general birth monthly proportions. Walter and Elwood (1975) developed an extension of the Edwards test that allows for a variable population at risk and months of unequal length. This test has, as an alternative, a sinusoidal seasonal cycle.

The rejection of the null hypothesis does not necessarily imply that seasonality exists.

Seasonality is present only if a periodicity exists across the years. To determine whether such a periodicity exists, one can use trigonometric regression. For the general birth series, one can perform a trigonometric regression and test for lack-of-fit of the derived model. If the model contains some non-zero coefficients corresponding to a yearly cycle and its harmonics and if the model is not rejected, then seasonality exists. For the birth series being studied, one can modify the series with the square root transform of Bartlett (1947). Then, the same analysis can be performed as for the general birth series.

It is possible that the general birth series has a trend as well as a seasonality effect, so that it will be necessary to account for this trend. Jones et al. (1988) have developed a model based on a time-varying intensity function that accounts for a varying population at risk (trend and seasonal terms) and months of unequal length. This methodology has, as an alternative, a seasonality of arbitrary shape and allows for comparisons among groups and a goodness-of-fit test. Rejection of the goodness-of-fit tests may be a result of serial correlation in the data so that time series methods may be required. The series can be detrended and a seasonal ARIMA model can be fitted, as described in Brockwell and Davis (1987). Time-series regression methods can be used to obtain an estimate of the trend and seasonality, but, as discussed in Grenander and Rosenblatt (1957), asymptotically efficient estimates will generally not be available. Another possibility for obtaining an estimate of the deterministic trend and seasonality is to use the wavelet methods discussed in Johnstone and Silverman (1996). The time series methods require a long series, so that large sample sizes of greater than 10 years are necessary. Time series methods are being increasingly recommended and used for analysis of seasonality data in psychiatry (Welham et al., 1995; Cotter et al., 1996; Torrey et al., 1996).

3. Schizophrenia

Table 1 lists 86 separate studies, 76 from 29 Northern Hemisphere countries and 10 from five Southern Hemisphere countries. Only published studies have been included, thus omitting the large unpublished study of five US states by Kline et al., which was referred to in several earlier studies. The studies are listed in order of sample size by number of individuals with schizophrenia or manic-depressive/bipolar disorder. One of the most striking findings is how few studies have sample sizes sufficient to demonstrate a 5–10% monthly or quarterly birth excess or deficit either for schizophrenia or for manic-depression/bipolar disorder. Studies that were published in multiple journals or that were published in various stages of development have been consolidated into single entries, with the pertinent references noted. Studies for which diagnostic criteria were stated are so noted in the tables.

The 86 studies include a total of 437 710 individuals with schizophrenia, 411 874 in Northern and 25 836 in Southern Hemisphere countries. Sample sizes vary from 71 278 (Torrey et al., 1996) to 22 (Woodruff et al., 1974). The birth seasonality for the 19 largest Northern Hemisphere studies, each of which had samples of 3500 or more and included controls [therefore not including Corgiat et al. (1983) or Barry and Barry (1964)], is shown in Fig. 1. All except one of the 19 studies reported a statistically significant winter-spring birth excess for schizophrenia, and the exception had a trend ($p<0.07$) in the same direction. These 19 studies included 324 630 individuals with schizophrenia or 79% of the total Northern Hemisphere sample. The months that have excess births for schizophrenia are January (15 studies), February (13 studies), March (11 studies), April (eight studies), May and December (five studies each), June (three studies), and November (two studies). It should be noted that June had an excess only in studies in which the second quarter was analyzed as a whole. The schizophrenia birth excess, therefore, may be said to be predominantly from December to May, with its maximum peak in January and February.

In addition to the 19 largest studies, it should be noted in Table 1 that almost all the smaller studies have excess schizophrenia births for winter or spring months; many of these would have achieved statistical significance if the sample sizes

Table 1
Studies of birth seasonality in schizophrenia and bipolar disorder

Authors, year of publication, location	Study group	Control group	Results
NORTHERN HEMISPHERE			
Torrey et al. (1996), US (OH, PA, VA, NC)	Inpatients, born 1925–75: ●71 278 schizophrenia, including 34 024 'process' and 37 254 paranoid ●23 202 schizoaffective ●18 021 bipolar disorder ●14 486 major depression (DSM-III-R)	All births in same states for same years	●Excess births in Dec., Jan., Feb., and Mar. for 'process' schizophrenia. (5.0%), paranoid schizophrenia (3.4%), schizoaffective (3.8%), and bipolar (5.8%) ($p<0.0001$) ●Excess births in Mar., Apr., and May for major depression (5.4%) ($p<0.0001$) ●Time series analysis showed high coherences between bipolar and major depression, bipolar and paranoid schizophrenia, bipolar and schizoaffective, and 'process' schizophrenia and schizoaffective
Torrey et al. (1977), US (19 states)	Mostly inpatients, born 1920–55: ●53 584 schizophrenia (DSM-II)	All births in same states for same years	●Excess schizophrenia births for Jan. ($p<0.01$), Mar. ($p<0.001$), Apr. ($p<0.001$), and May ($p<0.05$) ●Mar. (6.4%) and Apr. (6.0%) had the greatest excesses
Torrey et al. (1991), US (10 states)	Mostly inpatients, born 1950–59: ●43 814 schizophrenia (DSM-II and DSM-III)	All births in same states for same years	●5.9% excess schizophrenia births for Dec., Jan., and Feb. ($p<0.0001$) ●For Jan. alone, the excess was 12.4% ($p<0.0001$)
Torrey et al. (1993), US (NY)	Inpatients, born 1908–59: ●30 467 schizophrenia (DSM-I)	All births in NY for same years	●Excess schizophrenia births for Nov., Dec., Jan., and Feb. ($p=0.0000$, time series analysis)
Corgiat et al. (1983), US (MO)	First admissions 1961–83: ●25 278 schizophrenia	No controls	●Excess births Dec.–Mar.
Hare et al. (1973, 1974, 1979), Hare (1975a,b, 1978, 1983, 1986), England and Wales	National register, first admissions 1970–79, born 1921–60: ●22 453 schizophrenia ●7122 manic-depressive psychosis ●40 769 neurosis ●13 842 personality disorder ●16 161 all other non-psychotic mental disorders (ICD)	All births in England and Wales, 1921–60	●7.6% excess schizophrenia births for first quarter and 3.6% excess for second quarter ($p<0.001$) ●5.5% excess manic-depressive psychosis births for first quarter ($p<0.01$) ●No significant seasonal variation for other diagnoses
Ødegård (1974), Norway	Patients from national case register, born 1870–1939: ●19 740 schizophrenia ●6762 manic-depressive psychosis ●16 097 'reactive psychoses' ●14 917 other psychoses ●4674 not psychotic	All births in Norway for same years	●Excess schizophrenia births Jan., Feb., Mar. and Apr. ($p<0.001$) ●No significant seasonal deviation for manic-depressive psychosis, although May has a definite excess

Table 1 (*continued*)
Studies of birth seasonality in schizophrenia and bipolar disorder

Authors, year of publication, location	Study group	Control group	Results
Dalén (1968, 1969, 1975), Sweden	National case register, inpatients discharged 1962–68, born 1901–40: ●17 592 schizophrenia ●2591 paranoia ●14 566 manic-depressive psychosis and involutional melancholia ●32 541 neurotic depression ●10 482 other neuroses ●3540 pathological personality ('male criminal cases') (ICD)	All births in Sweden, 1901–40	●5.6% excess schizophrenia births, Jan.–Apr. ($p<0.005$) ●8.5% excess pathological personality births, Dec.-Mar. ●No significant seasonal trend for manic-depressive psychosis and involutional melancholia, but when those with mania ($n=1949$) were considered alone, there were excess births in Jan., May and Oct. ●No significant seasonal trends for other diagnoses
Huntington (1938), US (13 states)	Hospitalized patients, born mostly 1885–1914: ●10 420 schizophrenia ●3683 manic-depressive psychosis	All births in MA for same years	●Approximately 8% excess schizophrenia births in Feb. and Mar. ●Approximately 9% excess manic-depressive pscyhosis births in Feb. and Mar.
Templer et al. (1992), Denmark	National case register, onset 1970–87: ●9094 schizophrenia	All births in Denmark, 1901–60	●Excess schizophrenia births Dec.-May ($p<0.07$), N.S., calculated by present authors
Videbech et al. (1974), Denmark	National case register admissions 1969–73: ●7427 schizophrenia ●8212 manic-depressive psychosis (ICD)	All births in Denmark for same years	●Excess schizophrenia births for first quarter ($p<0.001$) ●No significant seasonal deviation for manic-depressive psychosis, but Apr. has a definite excess
Shimura et al. (1977), Japan	Hospital admissions 1879–1973, born 1841–1950: ●7960 schizophrenia (Kraepelian criteria)	●1841–1900: population sample ($n=18\,333$) ●1901–50: all births in Tokyo	●1841–1900: 20% excess in May births ($p<0.01$) ●1901–50: 12% excess in Apr. births ($p<0.03$)
Barry and Barry (1964), US (CT)	Admissions to two private hospitals 1907–62: ●6751 schizophrenia	No controls	●No significant seasonal deviation ●Greatest number born in Mar. and May
Hare and Price (1968), England and Wales	Maudsley Hospital inpatients and outpatients 1951–63, mostly born 1925–35: ●3596 schizophrenia ●5672 manic-depressive psychosis (ICD)	14 076 patients diagnosed with neuroses, for whom data was said to be similar to available data for all births in England and Wales, 1951–60	●5% excess schizophrenia births Jan.–Mar. ($p<0.05$) ●6% excess manic-depressive psychosis births Jan.–Apr. ($p<0.05$)

Table 1 (*continued*)
Studies of birth seasonality in schizophrenia and bipolar disorder

Authors, year of publication, location	Study group	Control group	Results
O'Hare et al. (1980), Ireland	Inpatients, born 1921–55: ●4855 schizophrenia (ICD)	All births for same years, available only by quarters	11% excess schizophrenia births for second quarter ($p<0.001$) ●Raw data suggest that Mar. also has excess but not Dec., Jan. or Feb.
Lang (1931), Germany (Bavaria), as reanalyzed by Barry and Barry (1961) and Diebold (1975)	Inpatients: ●3976 schizophrenia ●1879 manic-depressive psychosis ●876 alcoholism	●17 379 general hospital admissions ●All births in Bavaria, 1905–14	●9–15% excess schizophrenia births for Jan., Feb. and Mar. ($p<0.05$) ●12% excess manic-depressive psychosis births for Jan. and 7% excess for Apr. ($p<0.05$)
Bourgeois et al. (1990), France (Bordeaux)	Identified by mail survey sent to psychiatrists: Inpatients and outpatients born 1921–60: ●3944 schizophrenia	●All births in France ●Births of patients admitted to a general hospital	●9% excess schizophrenia births for first quarter and 7% excess for second quarter ($p<0.001$)
Chen et al. (1996), Taiwan	Inpatients 1987–88, born 1952–66: ●3749 schizophrenia (ICD-9)	All births in Taiwan, 1952–66	●Excess births for Nov. and Jan. ●Logrank test for homogeneity significant for males ($p<0.001$) and females ($p<0.05$)
Norris and Chowning (1962), Canada (all provinces)	Admissions 1959, born 1919–44: ●3617 schizophrenia	All births in Canada for 1923, 1934, 1937, and 1940	●9–11% excess births in Jan., Apr. and May and 12% deficit in Jul. ($p<0.05$) ●Selection of four different years for control births showed excesses and deficits in the same months, but did not achieve significance
Watson et al. (1982, 1984a), US (MN)	Hospital discharges 1963–78, born 1915–59: ●3556 schizophrenia (DSM-I and DSM-II)	All births in MN, 1910–59	●7.2% excess schizophrenia births in Dec., Jan., Feb. and Mar. ($p<0.001$)
Parker and Balza (1977), Philippines	Hospital inpatients and outpatients born over a broad but unspecified range of years: ●3508 schizophrenia	All births in the Philippines, 1956–60	●14.8% excess schizophrenia births for Dec.–Feb. by quarter ($p<0.001$)
Petersen (1934), US (IL)	Inpatients in a state hospital: ●3467 schizophrenia ●691 manic-depressive psychosis	All births in US, 1917–29	●Excess schizophrenia births in Nov., Dec. and Jan. (25% for Jan.) ●Excess manic-depressive psychosis births in Jan., Mar., Apr. and May (37% for May)
Tam and Sewell (1995), Taiwan	Inpatients 1981–91, born 1955–66: ●3346 schizophrenia	All births in Taiwan, 1955–66	●Excess births Nov.–Feb. ($p<0.05$) ●Time series analysis confirmed seasonal pattern
O'Callaghan et al. (1995), Ireland	Case registers: ●3253 schizophrenia (ICD-9)	All births for the same counties, 1921–60	●5% excess sch/ births for first quarter ($p=0.13$, N.S.)

Table 1 (*continued*)
Studies of birth seasonality in schizophrenia and bipolar disorder

Authors, year of publication, location	Study group	Control group	Results
Tramer (1929), Switzerland	Inpatients 1876–1927: ●3100 diagnosed with psychoses, types not specified	All births in Switzerland 1987–1910	●15% excess births in Dec.–Mar. ($p<0.001$, computed by Barry and Barry (1961) ●20% deficit births in May
Rodrigo et al. (1992), US (MS)	Hospital admissions 1986–88, born 1920–70: ●2892 schizophrenia (DSM-III)	All births in MS, 1920–70	●15% excess births in Dec. ($p<0.02$) and 21% in Mar. ($p<0.01$) ●17% deficit births in May ($p<0.02$) and 17% in Jul. ($p<0.01$)
Kendell and Kemp (1987), Scotland	First admissions 1970–81, born 1930–66: ●2653 schizophrenia ●2420 manic-depressive psychosis (ICD)	All births in Scotland for 1940, 1950, and 1960	●8.7% excess schizophrenia births for first quarter ●3.0% excess manic-depressive psychosis births for first quarter
de Sauvage Nolting (1934), The Netherlands	Inpatients: ●2589 schizophrenia ●1556 manic-depressive psychosis	All births in The Netherlands	●Excess schizophrenia births Dec.–Apr. with Mar. peak ●No significant seasonal trens for manic-depressive psychosis
Aschauer et al. (1994), Austria	Inpatients 1971–92, born 1921–75: ●2450 schizophrenia ●682 schizoaffective (ICD-8 and ICD-9)	All individuals living in Vienna and born 1921–75	●10% excess schizophrenia births for first quarter ($p<0.05$) ●15% excess schizophrenia births for first quarter ($p<0.05$)
Deng et al. (1993), Taiwan	Inpatients 1981–89: ●2400 affective disorder, including 1824 bipolar disorder and 312 unipolar disorder	Not stated	●'Excess of winter-born patients'
Ede et al. (1985, 1986), Canada (Alberta)	Hospital admissions 1923–79, born 1898–1960: ●2271 schizophrenia	No controls	●Trend for more schizophrenia births Jan.–Jun. than Jul.–Dec.
Laestadius (1949), Sweden	Inpatients and outpatients: ●2232 schizophrenia ●358 manic-depressive psychosis	All births in Gothenburg, 1901–40	●4% excess schizophrenia births Jan.–May, with peak in Feb. but N.S. ●Excess manic-depressive psychosis births in Jun. but N.S.
de Sauvage Nolting (1951), The Netherlands	Inpatients: ●2090 schizophrenia ●1228 manic-depressive psychosis	All births in The Netherlands	●Approximately 10% excess schizophrenia births for Feb. and Mar. ●Approximately 10% excess manic-depressive psychosis births for Feb., Mar. and Sep.
Hafner et al. (1987), Germany (Mannheim)	Case register: ●2020 schizophrenia ●3409 depression ●5615 neuroses and personality disorders (ICD)	All births in Mannheim	●Excess schizophrenia births for Apr. and May ($p<0.05$) ●Excess births for males but not females for Mar., Apr. and May for other two groups ($p<0.01$)

Table 1 (*continued*)
Studies of birth seasonality in schizophrenia and bipolar disorder

Authors, year of publication, location	Study group	Control group	Results
Kim et al. (1994), Korea	Inpatients and outpatients 1991, born 1941–70: ●1606 schizophrenia (DSM-III)	4582 age- and sex-matched controls, mechanism of selection unclear	●18% excess schizophrenia births in Dec. and 9% in Mar., but N.S.
Koehler and Jacoby (1976b), Germany (Hamburg)	Inpatients 1962–72: ●1576 schizophrenia ●1473 neurosis ●1062 personality disorder (Schneiderian criteria)	All births in Germany, years not specified	●5% excess schizophrenia births for first quarter and 7% deficit for third quarter but N.S.
Frangos et al. (1978), Greece	Inpatients 1975–76: ●1470 schizophrenia	All births in Greece, 1920–60	●Excess schizophrenia births for Mar. (27%), Apr. (12%) and Aug. (16%); excess for Jan.–Apr. significant ($p<0.01$)
Pile (1951), US (VA)	Inpatients 1949, born 1890–1925: ●1469 schizophrenia	All births in VA, 1947 only	●Pile reported no significant seasonal deviation, but Barry and Barry (1961) reanalyzed the data and reported 9% excess schizophrenia births in Dec.–Feb. ($p<0.05$)
Pulver et al. (1983), US (MD)	Case register, admitted 1963–68, born 1942–46: ●1455 schizophrenia (DSM-III)	All births in MD 1942–46	●35% (male) and 38% (female) excess births in Jan.–Mar. ($p<0.01$)
Barry and Barry (1961), US (NJ and MA)	Inpatients 1933–45, born 1880–1930: ●1453 schizophrenia	All births in MA 1883–90, 1903–10, 1923–30	●13–24% excess births in Jan.–Feb. and Apr. and 16–19% deficit births in Jul. and Aug. ($p<0.01$)
Franzek and Beckmann (1992), Beckmann and Franzek (1992), Germany (Berlin)	Inpatients and outpatients, born 1896–1965: ●1299 schizophrenia (DSM-III-R)	All individuals born prior to 1966 and living in West Berlin in 1990	●2.3% excess schizophrenia births 'in the first half of spring' ($p<0.05$)
Newman and Bland (1988), Canada Alberta)	Admissions 1976–83, born 1921–68: ●1101 schizophrenia [includes many of the same patients studied by Ede et al. (1985)]	All births in Alberta, 1921–68	●Excess births in Nov. ($p=0.01$ but N.S. with Bonferroni correction) ●Jun. and Jul. also had excess births but N.S.
Cortes and Periz-Rincon (1990), Mexico	Inpatients: ●1086 schizophrenia ●318 'affective disease'	Matched neurological patients	●Excess births in autumn for paranoid schizophrenia only
Pallast et al. (1994), The Netherlands	Inpatients, born 1962–66: ●1037 schizophrenia (ICD)	All births in The Netherlands 1962–66	●16% excess schizophrenia births Dec.–Mar. ($p=0.04$)

Table 1 (*continued*)
Studies of birth seasonality in schizophrenia and bipolar disorder

Authors, year of publication, location	Study group	Control group	Results
Shur (1982), England	Inpatients 1967–78, mostly born 1936–60: ●975 schizophrenia	'Average live-birth figures' for 1936–60, England and Wales	●No significant excess or deficit for any quarter
Cazzullo et al. (1987), Italy	Inpatients, born 1930–52: ●953 schizophrenia (DSM-III)	Total population born 1930–52	●'An increase was observed' in schizophrenia births 'during the winter months', not further defined
de Sauvage Nolting (1954), The Netherlands	Inpatients: ●941 schizophrenia	All births in The Netherlands	●Excess schizophrenia births December–May
Pulver et al. (1981), US (NY)	Case register, admitted 1969–76: ●918 schizophrenia (DSM-II)	All persons living in Monroe County in 1970; data available only by quarters, so births were assumed to be equally distributed within each quarter	●Test of homogeneity of month effect significant for females ($p<0.001$) but not males ●Maximum excess February and maximum deficit August, September and October
Bojanovský and Gerylovová (1961), Czechoslovakia	Inpatients, born 1920–39: ●896 schizophrenia ●368 manic-depressive psychosis and involutional melancholia ●1167 neuroses	All births in Czechoslovakia for same years	●Excess schizophrenia births in December but N.S. ●Excess manic-depressive psychosis and involutional melancholia births in December, January, March and May, but N.S. ●Excess neuroses births in March and July ($p<0.001$)
Diebold (1975), Germany (Heidelberg)	●730 schizophrenia ●730 affective psychosis ●730 psychopathy	3650 consecutive admissions to general hospital	●Excess schizophrenia births for November, December and January ($p<0.02$) and deficit for February, March, August and September ($p<0.05$) ●Deficit births for affective psychosis for March
Gallagher et al. (1983, 1984), US (PA)	Inpatients, born 1884–1961: ●630 schizophrenia (whites) ●94 schizophrenia (blacks)	All births 1944–61: ●Whites: PA ●Blacks: PA and southern states	●Whites have first-quarter deficit, N.S. ●Blacks have first-quarter excess, N.S.
Danneel (1973), Germany (Bonn)	Treated at university clinic, 1968–71: ●698 schizophrenia (Schneiderian criteria)	All births in Germany, years not specified	●No significant seasonal deviation ($p=0.32$)

Table 1 (*continued*)
Studies of birth seasonality in schizophrenia and bipolar disorder

Authors, year of publication, location	Study group	Control group	Results
Fortuny et al. (1991), Spain	●683 schizophrenia (DSM-III)	Not stated	●'No seasonal predominance of birth'
Khiari et al. (1994), Tunisia	Inpatients 1967–92, born 1930–75: ●631 schizophrenia ●69 schizoaffective disorder ●138 major affective disorder (DSM-III-R)	All individuals in Tunisia born 1975–90	●Excess birth for January, for undifferentiated schizophrenia ($n=402$) ($p<0.05$) ●Excess births for October ($p<0.01$) and deficits for July ($p<0.01$), August ($p<0.05$) and September ($p<0.05$) for schizophrenia and schizoaffective disorder combined ●Deficit for July ($p<0.05$) for major affective disorder
O'Callaghan et al. (1991), Ireland	Inpatients 1983–88: ●616 schizophrenia (ICD-9)	All births in Ireland, 1921–70	●9% excess schizophrenia births for first quarter (N.S.) and 17% deficit for fourth quarter ($p<0.05$)
Kendler (1982), US	Twin registry: ●536 schizophrenia ●1991 neuroses (ICD-8)	12 085 normal twins	●4% excess schizophrenia births January–March, N.S.
Hsieh et al. (1987), US (NE)	Hospital discharges 1979–83: ●472 schizophrenia (ICD-9)	No controls	●Authors report that 'the seasonal variation is non-significant', except for excess births in male paranoid group in first quarter ($p<0.05$)
Malesu et al. (1996), Barbados	Inpatients, born 1915–76: ●466 schizophrenia (DSM-III-R)	All births in Barbados	●No significant monthly or quarterly deviation
Woodard and Feldman (1990), US (NC)	Inpatients 1985–86: ●376 schizophrenia	867 non-schizophrenic psychiatric patients and 2529 general hospital admissions	●No significant seasonal deviation
Watson et al. (1984b), US (MN)	Hospital discharges 1963–78, born 1915–59: ●320 major affective disorder ●989 neuroses ●713 personality disorder ●2870 alcoholism	All births in MN 1915–59	●No significant seasonal deviation for any diagnostic group
Brochard et al. (1994), France (Toulouse)	Inpatients 1981–91: ●294 bipolar disorder ●287 unipolar disorder ●582 neurotic depression ●214 major depression ●244 schizophrenia ●52 schizoaffective ●1433 other diagnoses (modified DSM-III-R)	1943 surgical patients in same hospital and a sample of all births in France 1977–89	●Excess births for unipolar disorder for first and fourth quarters ($p<0.0005$) ●Excess births for major depression for first quarter ($p<0.005$) ●Excess births for bipolar disorder (15%) for first quarter, N.S. ●Excess births for schizoaffective disorder (43%) for second quarter, N.S. ●Excess births for schizophrenia (7%) for first and fourth quarters, N.S.

Table 1 (*continued*)
Studies of birth seasonality in schizophrenia and bipolar disorder

Authors, year of publication, location	Study group	Control group	Results
Dassa et al. (1993), France (Marseille)	Inpatients 1983–92: ●294 bipolar disorder (DSM-III-R)	All births in France	●12% excess births in first quarter, N.S.; however, for bipolar I alone, the excess was 18% ($p<0.05$)
Bersani and Minnielli (1979), Italy	Inpatients 1970–77: ●290 schizophrenia ●153 manic-depressive psychosis	443 non-psychotic patients	●Excess schizophrenia births December–March ($p=0.003$) ●No significant deviation for manic-depressive psychosis
Modestin et al. (1995), Switzerland	Male inpatients 1985–87, born 1909–69: ●282 schizophrenia ●261 affective disorder ●360 alcoholism (RDC and DSM-III-R)	All males born in Berne 1969–92	●Excess schizophrenia births January–March ($p<0.05$) ●Excess alcoholism births March–July ($p<0.005$) ●No seasonal excess for affective disorders, including 82 who met criteria for bipolar disorder
d'Amato et al. (1991), France (Lyon)	Hospital admissions 1950–79, mostly born 1920–60: ●230 schizophrenia (DSM-III-R)	Births of all individuals living in France, born 1949 and later	●Excess births January–March alone ($p<0.04$) and November–April ($p<0.01$)
Lo (1985), Hong Kong	Patients of one psychiatrist: ●188 schizophrenia	Not stated	●October–January appear to have excess births, but no statistical test utilized
King et al. (1985), Northern Ireland	Inpatients: ●184 schizophrenia ●60 affective disorder	103 hospital staff and blood donors	●Excess schizophrenia births in March, April and May ($p<0.05$) ●No excess for affective disorders
Fananas et al. (1989), Spain	Inpatients and outpatients in 1985: ●142 schizophrenia	●All persons living in Barcelona ●198 controls matched for age, sex, and SES	●Excess schizophrenia births for December, January and February significant using first control group ($p=0.007$), but N.S. using second control group ($p=0.10$)
Michitsuji et al. (1987), Japan	Inpatients and outpatients, first onset: ●107 schizophrenia	2052 individuals matched for sex, year of birth, and area of residence	●Excess schizophrenia births in December and January ($p<0.05$)
Orme (1963), England	Inpatients: ●97 psychoses (defined by response to Rorschach test)	No controls	●No significant deviation by season
Rihmer (1980), Hungary	Inpatients 1972–77: 92 bipolar disorder (Feighner criteria)	No controls	●More bipolar I births in spring and autumn and more bipolar II births in summer and winter ($p<0.02$)
Koehler and Jacoby (1976a), Germany	Inpatients 1962–72: ●68 mania ●1147 psychotic depression ●746 neurotic depression (Schneiderian criteria)	All German births, years not specified	●No significant excess or deficit for any diagnostic category by quarter

Table 1 (*continued*)
Studies of birth seasonality in schizophrenia and bipolar disorder

Authors, year of publication, location	Study group	Control group	Results
Mimica et al. (1996), Croatia	Case register: 59 catatonic schizophrenia (ICD)	Not stated	●'No significant excess of winter births'
Milstein et al. (1976), US (IN)	Study patients, born 1896–1952: ●56 manic-depressive psychosis (Feighner criteria)	All births in IN for same months and years as study patients	●No significant seasonal deviation
Lynge and Jacobsen (1995), Greenland	Inpatients, first admissions 1980–83: ●37 schizophrenia (ICD-8)	159 psychiatric admissions with diagnoses other than schizophrenia (28 were diagnosed with other psychoses)	●16/37 (43%) schizophrenia, born December, January and February, vs. 23% of controls ($p=0.002$)
Woodruff et al. (1974), US (MO)	Outpatients: ●22 schizophrenia ●158 primary affective disorder ●100 neuroses ●138 undiagnosed	No controls; seasons were divided by signs of the zodiac rather than by months	●No significant seasonal deviations, except for non-random distribution for the undiagnosed ($p<0.02$)
SOUTHERN HEMISPHERE			
McGrath et al. (1995), Australia (Queensland)	Case register, born 1914–74: Born in Southern Hemisphere: ●8027 schizophrenia Born in Northern Hemisphere: ●1321 schizophrenia (ICD-8 or ICD-9)	All births in Queensland, 1914–74	●7% excess births in July, August and September ($p<0.0001$) for those born in Australia and New Zealand ●Those born in the Northern Hemisphere showed March–April peak and differed from those born in Australia and New Zealand ($p=0.002$)
Krupinski et al. (1976), Australia (Victoria)	Case register, treated 1961–71, born 1910–59: Born in Southern Hemisphere: ●3919 schizophrenia ●2202 depressive psychosis ●3530 alcoholism ●18 815 non-psychotic diagnoses Born in Northern Hemisphere: ●2372 schizophrenia ●699 depressive psychosis ●905 alcoholism ●5270 non-psychotic diagnoses	Controls for Southern Hemisphere sample were all births in Victoria, 1963–71	●No significant seasonal deviation ●For Northern Hemisphere, there were excess schizophrenia and depressive psychosis births in winter ●For Southern Hemisphere, there were excess schizophrenia and depressive psychosis births in spring, but a deficit of schizophrenia births in winter
Dalén and Roche (1975), South Africa	Inpatients in 1971, born 1900–49 in South Africa of European descent: ●2947 schizophrenia	All births in South Africa, 1921–49, of European descent	●Excess births in May, June, July and October, but N.S.

Table 1 (*continued*)
Studies of birth seasonality in schizophrenia and bipolar disorder

Authors, year of publication, location	Study group	Control group	Results
Parker and Neilson (1976), Australia (New South Wales)	Inpatients 1970–74, birth years not specified, born in New South Wales: ●2256 schizophrenia ●220 mania ●1097 psychotic depression ●2813 other psychoses ●4040 neurotic depression ●1116 other neuroses ●1487 personality disorders ●6281 other non-psychotic mental disorders ●(ICD-8)	All births in New South Wales, 1962–71	●No significant seasonal deviation, except a spring excess for other neuroses ($p<0.001$) ●Trend for 5% excess winter births for schizophrenia, which was statistically significant for females only ($p<0.01$)
Parker (1978a), Australia (Tasmania) and New Zealand	Tasmania: first admissions 1970–75: ●236 schizophrenia New Zealand: first admissions 1972–75: ●1811 schizophrenia	Tasmania: birth registrations 1969–73 (which do not necessarily correspond to birth dates) New Zealand: all births in New Zealand 1964–73	●No significant seasonal deviation in either study ●13% excess winter births in Tasmania but N.S.
Jones and Frei (1979), Australia (Victoria)	Inpatients, born in Australia: 915 schizophrenia (ICD)	915 controls born in Australia, matched for year of birth, selected from patients in general medical practices	●No significant seasonal deviation ●Trend for 5% excess winter births (maximum, June and July), which achieved significance for males ($p<0.01$)
d'Amato et al. (1996), Reunion Island	All identified patients born on the island 1910–69: ●668 schizophrenia (DSM-III)	All births on the island 1910–69	●5% excess winter births (July–September), but N.S.
Berk et al. (1996), South Africa	White inpatients, born in South Africa: ●559 schizophrenia (DSM-III-R)	All births in South Africa 1953–77	●Excess schizophrenia births in December, January and February ($p<0.005$)
Syme and Illingworth (1978), Australia (Western Australia)	Admissions to mental health services 1966–75, born 1920–50 in Western Australia: ●455 schizophrenia ●383 anxiety neurosis ●577 depressive neurosis (ICD-8)	All births in Western Australia 1920–50	●Excess schizophrenia births for males in June ($p<0.05$) and females in September ($p<0.02$) ●No significant seasonal deviation for other diagnoses

Table 1 (*continued*)
Studies of birth seasonality in schizophrenia and bipolar disorder

Authors, year of publication, location	Study group	Control group	Results
García Hildebrandt (1992), Peru	Outpatients 1970–90, born 1945–64: ●350 schizophrenia (DSM-III-R)	350 controls matched for sex and age, diagnosed with dysthymia	●Excess schizophrenia births in June, July, August, September, and October, 15–21% each month ●Significant third-quarter excess ($p<0.005$)

had been larger. Only one Northern Hemisphere study (Gallagher et al., 1983, 1984) reported a deficit of schizophrenia births for the first quarter of the year; that study had a small sample ($n=630$) and used controls that were poorly matched to the study group.

The 10 Southern Hemisphere studies consist of much smaller samples because of the lesser population of these countries. The study by McGrath et al. (1995) from Queensland, Australia, is especially interesting because it is the largest, utilized a case register, and divided the individuals with schizophrenia into those born in the Southern Hemisphere ($n=8027$) and those born in the Northern Hemisphere ($n=1321$) who had later immigrated to Australia. Those who had been born in the Southern Hemisphere had a 7% birth excess in the Australian winter (July, August, and September) ($p<0.0001$), whereas those who had been born in the Northern Hemisphere had a marked March–April birth excess similar to that found in many Northern Hemisphere studies.

Regarding the magnitude of the winter/spring schizophrenia birth excess in studies done to date, it consistently ranges between 5 and 8% in the larger studies. There are exceptions, however, such as 11% in Ireland (O'Hare et al., 1980), 12% in Japan (Shimura et al., 1977), and 15% in the Philippines (Parker and Balza, 1977). In studies with small sample sizes, the magnitude of the birth excess is more variable.

Although birth seasonality studies in schizophrenia almost always focus on the periods of excess births, it is important to note that many of these studies also show periods of deficit births. These deficit periods are concentrated in the summer and fall months, and in some studies, the magnitude of the deficit births is greater than that of the excess births (e.g. Hare, 1975b; Torrey et al., 1977; O'Callaghan et al., 1991; Rodrigo et al., 1992).

Only four of the 86 studies included individuals with schizoaffective disorder as a separate group, although diagnostic problems for this group are well known. The largest of these, with a sample of 23 202 (Torrey et al., 1996), reported that this group had a significant excess of births for December, January, February, and March, with a birth pattern very similar to the pattern found in schizophrenia and bipolar disorder ($p=000$). Time series analysis verified a significant coherence between the birth pattern of individuals with schizoaffective disorder with those in the other two groups, thereby supporting the common belief that schizoaffective disorder is not a separate entity but rather is part of schizophrenia and bipolar disorder. Aschauer et al. (1994), studying 682 individuals with schizoaffective disorder, also reported a significant 15% excess in the first quarter for these individuals ($p<0.05$). The other two studies that included schizoaffective disorder had very small samples of 69 (Khiari et al., 1994) and 52 (Brochard et al., 1994).

4. Manic depressive psychosis/bipolar disorder

In 20 of the 86 studies of birth seasonality listed in Table 1, a total of 60 974 individuals with manic-depressive psychosis were included. An additional five studies included a total 20 525 individuals with bipolar disorder. Understanding the difference between these diagnoses is important for understanding the birth seasonality findings: bipolar

■ Statistically significant excess births, analyzed by month
▨ Statistically significant excess births, analyzed by quarter

Authors	Sample Size	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov
Torrey et al. 1996, US	71,278	■	■	■	■								
Torrey et al. 1977, US	53,584		■		■	■	■						
Torrey et al. 1991, US	43,814	■	■	■									
Torrey et al. 1993, US	30,467	■	■	■									■
Hare et al. 1973-86 Eng. & Wales	22,453		▨	▨	▨	▨	▨	▨					
Odegard, 1974, Norway	19,740		■	■	■	■							
Dalen, 1968-75 Sweden	17,592		■	■	■	■							
Huntington, 1938, US	10,420			■	■								
Templer et al. 1992, Denmark	9,094												
Shimura et al, 1977, Japan	7,960					■							
Videbech et al, 1974, Denmark	7,427		▨	▨	▨								
O'Hare et al, 1980, Ireland	4,855					▨	▨	▨					
Lang, 1931, Germany	3,976		■	■	■								
Bourgeois et al, 1990, France	3,944		▨	▨	▨	▨	▨	▨					
Chen et al, 1996, Taiwan	3,749		■										■
Norris & Chowning, 1962, Canada	3,617		■			■	■						
Hare & Price 1968, England & Wales	3,596		▨	▨	▨								
Watson et al, 1982, & 84, US	3,556	■	■	■	■								
Parker & Balza, 1977, Philippines	3,508	▨	▨	▨									

Fig. 1. Studies of birth seasonality for schizophrenia in Northern Hemisphere countries in which the sample size was over 3500 and controls were used. ■, statistically significant excess births, analyzed by month; ▨, statistically significant excess births, analyzed by quarter.

disorder requires that the person has had at least one episode of mania, whereas manic-depressive psychosis does not; consequently, the majority of individuals diagnosed with manic-depressive psychosis have had episodes of severe depression but have not had mania.

The birth seasonality findings for manic-depressive psychosis are less consistent than the findings for schizophrenia. The largest sample was Dalén's (1975) study, which included 14 566 individuals with manic-depressive psychosis or involutional melancholia (ICD 301 and 302); he found no significant seasonal deviation, with the greatest birth excesses being 3% for May and July. However, Hare and Price (1968), studying 5672 individuals with manic-depressive psychosis, reported 6.0% excess births for January through April; Hare (1975a), studying 7122 individuals with this diagnosis, found 5.5% excess births for the first quarter; and Huntington (1938), studying 3683 individuals with this diagnosis, showed, using a graph, a birth excess of approximately 9% for February and March. Other large studies that show excess winter–spring births for individuals with manic-depressive psychosis are those by Videbech et al. (1974, $n=8212$, April excess), Ødegård (1974) ($n=6\,762$, May excess), Kendell and Kemp (1987) ($n=2420$, first-quarter excess), Krupinski et al. (1976) ($n=2202$, spring excess in the Southern Hemisphere), and Lang (1931) ($n=1879$, January excess).

Turning to bipolar disorder, Torrey et al. (1996) included 18 021 individuals with this diagnosis and reported a 5.8% birth excess for December, January, February, and March ($p=0.000$). Especially interesting were the findings of North Carolina, which had birth excesses of 17.5% for February and 21.8% for March for bipolar disorder ($n=3872$) and birth excesses of 28.3% for February and 21.6% for March for schizoaffective disorder ($n=2812$). Four other studies of bipolar disorder had small sample sizes, but all reported excess winter and/or spring births (Rihmer, 1980, $n=92$; Brochard et al., 1994, $n=294$; Dassa et al., 1993, $n=294$; Deng et al., 1993, $n=1824$). It is also of interest that two studies of manic-depressive illness that analyzed separately those individuals who had mania (and thus would probably meet diagnostic criteria for bipolar disorder) reported a 13% first quarter (Hare, 1975a, $n=1180$) and a 14% January (Dalén, 1975, $n=1949$) birth excess.

The study by Torrey et al. (1996) also included 14 486 individuals diagnosed with DSM-III-R major depression; under other diagnostic systems, most of these individuals would be included within the category of manic-depressive psychosis. The individuals with major depression were found also to have a seasonal birth pattern but one that differed from bipolar disorder in that it had its maximum birth excess in March (5.7%), April (2.1%), and May (8.3%). January and February even had slight (2.2 and 1.9%) birth deficits for major depression. These findings suggest that bipolar disorder, which requires an episode of mania, and major depression are two relatively distinct conditions. If this is so, it also might explain the less consistent birth seasonality findings in studies of manic-depressive psychosis, which includes individuals with mania (December–March peak) as well as individuals with major depression (March–May peak).

5. Specificity of the winter–spring birth seasonality

Given the evidence for winter–spring birth excesses for schizophrenia, manic-depressive psychosis/bipolar disorder, and major depression, the question arises as to whether this seasonal birth pattern extends to other psychiatric diagnoses or is specific to these few diagnoses. Multiple researchers have addressed this issue.

Six studies have examined the birth pattern of individuals with childhood schizophrenia. The largest of these (Sankar, 1969) included 2106 children with childhood schizophrenia in a New York psychiatric hospital. Compared to all births in New York City, the individuals with childhood schizophrenia had an excess of both winter (December–March) and summer (June–August) births. The other studies all included very small numbers of children. A French study (Fombonne, 1989) reported that 208 individuals with "childhood psychoses" at a psychoanalytic day treatment center had excess births in the last quarter ($p<0.01$), especially December, compared to 1040 non-psychotic controls from the same clinic. Studies in Sweden (McNeil et al., 1971), England (Garralda and Watt, 1989), and the United States (Atlas, 1989; Livingston et al., 1993) each included less than 100 children and thus were too small to be meaningful.

Nine studies have been carried out on the seasonal birth pattern of childhood autism. Although limited by small sample sizes, these studies are interesting in that five of them, each from a different country, reported a statistically significant increase in March births for these children (Bartlik, 1981, $n=810$; Konstantareas et al., 1986, $n=179$; Gillberg, 1990, $n=100$; Mouridsen et al., 1994, $n=118$; Barak et al., 1995, $n=188$). The first three of these also reported a significant increase in August births but not the intervening months, suggesting the possibility of two separate etiological subgroups. Two additional studies also reported trends toward an increase in spring births (Parker, 1978b, $n=162$; Tanoue et al., 1988, $n=80$), but the other two studies did not (Sankar, 1969, $n=133$; Bolton et al., 1992, $n=196$).

Eleven studies have examined the seasonal birth pattern of individuals diagnosed with neuroses; most of them utilized hospitalized populations, so it can be assumed that these patients were relatively severely affected. Three of the smaller studies reported a significant excess of spring births (Bojanovský and Gerylovová, 1961, $n=1167$; Parker and Nielson, 1976, $n=1116$, anxiety neurosis only; Parker, 1978c, $n=197$). However, eight other studies, including two with large sample sizes, found no significant deviation from the birth pattern of controls (Dalén, 1975, $n=43\,023$; Koehler and Jacoby, 1976b, $n=1473$; Parker and Neilson, 1976, $n=4040$; Syme and Illingworth, 1978, $n=960$; Hare et al., 1979, $n=40\,769$; Greenberg, 1981, $n=946$; Kendler, 1982, $n=1991$; Watson et al., 1984b, $n=989$).

Seasonal birth studies have also included individuals with personality disorders. Hare (1978) found no significant seasonal deviation in the births of 13 842 individuals with personality disorders. Other negative findings were published by Parker and Neilson (1976) ($n=1487$) and Koehler and Jacoby (1976b) ($n=1062$). Hafner et al. (1987), studying a sample of 5615 individuals with either neurosis or personality disorder, reported a trend for increased births in March through May that reached statistical significance only for males ($p<0.01$). The most interesting seasonal birth study of personality disorders was Dalén's (1975) finding that individuals with pathological personality disorder (ICD 320), whom he described as "mostly male criminal cases", had a December-through-March birth excess of 8.5%, virtually identical to his findings for individuals with schizophrenia. Huntington (1938) earlier had noted that "the schizophrenic [birth] curve is almost identical to that of the prisoners" (p. 402).

Individuals with alcoholism have also been included in birth seasonality studies. Negative findings were reported by Krupinski et al. (1976) ($n=4435$), Watson et al. (1984b) ($n=2870$), and Lang (1931) ($n=876$). A significant summer and fall birth excess was reported in a small study ($n=292$) by London (1987). Another small study ($n=457$) reported that severely opiate-addicted individuals had excess births in October through January, but the researchers were unable to replicate their findings among two much larger samples (Kell, 1995).

Two recent studies have examined the seasonal birth pattern of individuals with eating disorders. Nielsen (1992) in Denmark reported a significant ($p<0.01$) April birth peak for females with anorexia nervosa with onset of illness prior to age 15. Rezaul et al. (1996) in England found a significant ($p<0.05$) birth excess in May among 1939 individuals with eating disorders.

Finally, some birth seasonality studies have included categories of non-psychotic psychiatric patients without specifying the diagnoses. Krupinski et al. (1976) ($n=24\,085$) and Parker and Neilson (1976) ($n=6281$) in Australia both reported no significant seasonal birth deviation for such groups, whereas Ødegård (1974) ($n=4674$) in Norway found a significant increase in births in May and September ($p<0.05$).

In summary, it appears that the winter–spring birth excess found for individuals with schizophrenia, manic-depressive psychosis/bipolar disorder, and major depression is relatively specific to those diagnoses and is not found in psychiatric patients in general. The possible exceptions to this are individuals with childhood autism, eating disorders, or pathological personality disorders of the criminal type. Further research is needed to clarify this.

6. Shifts of birth seasonality over time

Huntington (1938) in the United States was apparently the first to note that seasonal birth patterns for individuals with severe mental illnesses do not necessarily remain fixed but, compared to controls, may shift over time. For schizophrenia, his 1114 cases born before 1885 had a definite October–January birth excess, whereas in the decades after 1885, there was a February–March peak. For manic-depressive psychosis, the 1772 cases born before 1885 had a February–March birth excess of approximately 15%, whereas the 1911 individuals born from 1885 onwards had a February–March birth peak only half as great, and there also developed a secondary peak in August and September.

Dalén (1975) in Sweden also observed a changing seasonal birth pattern for individuals with schizophrenia born in the 19th and the 20th centuries. For those born in 1881–90 ($n=1685$), compared to the expected normal birth pattern, there were deficits for each month from December through April, except for February, whereas September (17% excess) and June (11% excess) had the largest excesses. By the 1901–10 period, the winter–spring pattern of excess births for schizophrenia had become established, and it remained relatively fixed for each of the four succeeding decades studied by Dalén.

Shimura and Miura (1980) in Japan collected birth data from 1841 to 1940 on 7472 individuals with schizophrenia and 1036 individuals with manic-depressive psychosis. Compared with general births, both diagnostic groups showed a similar and remarkably consistent 'fall-excess pattern' (September through November) for individuals born before 1890 and a 'spring-excess pattern' (March through May) for those born thereafter. Thus, studies from the United States, Sweden, and Japan all suggest that the seasonal birth pattern for schizophrenia and probably for manic-depressive psychosis shifted between the later years of the 19th century and the early years of the 20th century.

In the 20th century, seasonal shifts in the births of individuals with schizophrenia have been observed in some studies, but not in others. Torrey and Torrey (1979), in a study of 16 910 individuals diagnosed with schizophrenia in Missouri, reported a shift from births in 1921–30 (February peak) to 1931–40 (March and April peak) to 1941–50 (April and May peak). However, no such shift was observed among 10 889 individuals with schizophrenia in five New England states. In England, Hare (1978) also reported a shift in the birth pattern of individuals with schizophrenia and those with affective psychosis between 1921 and 1960, from a fourth-quarter excess to a first-quarter excess and noted the similarity to the shift reported from Japan for earlier years. Recently, Eagles et al. (1995) examined schizophrenia birth data in a Scottish case register for seven decades, from 1900 through 1969. They divided the year into winter–spring (December through May) and summer–autumn (June through November). For 1900–1909 and 1910–29, summer–autumn births were more numerous than winter–spring births for individuals with schizophrenia, but for each decade thereafter, winter–spring births predominated. Eagles et al. also found an unexpected and highly significant increase in the magnitude of the winter–spring seasonal excess that was caused exclusively by an increase in winter–spring births among males ($p=0.00009$).

In summary, it seems clear that the seasonal birth patterns found in individuals with schizophrenia and manic-depressive psychosis/bipolar disorder are not fixed and may shift over time. This makes the selection of appropriate controls for such studies very important.

7. Correlations with clinical features

From the earliest studies of birth seasonality for schizophrenia and bipolar disorder, there have been attempts to correlate winter or winter–spring births with specific clinical features of these diseases. These features include family history, gender, social class or race, urban birth, a history of pregnancy and birth complications, clinical subtypes, and neurological, neuropsychological, neurophysiological, and neuroimaging findings. Since the majority of birth seasonality studies have been carried out on individuals with schizophrenia, that has also been true for the correlation studies. Perhaps the most striking aspect of these correlation studies is the small sample size used in many of them.

7.1. Family history

The definition of positive family history varies considerably from study to study. Most often, ascertaining family history involves asking a family member whether any first degree relative has or has had a serious mental illness. Furthermore, family size varies considerably in different countries, and this also affects the chances of having a positive family history.

Seventeen studies have examined the relationship between birth seasonality in schizophrenia and family history for this disorder. Kim et al. (1994) ($n=1606$) and d'Amato et al. (1996) ($n=668$) both reported that family history had no effect on the seasonality of births. Ten of the remaining studies, including those with the largest samples (Franzek and Beckmann, 1993, $n=1229$; Chen et al., 1996, $n=3749$), reported that individuals with schizophrenia who had a negative family history for the disease were more likely to show a winter birth excess (Kinney and Jacobsen, 1978; Shur, 1982; McNeil, 1987; Zipursky and Schulz, 1987; d'Amato et al., 1991; O'Callaghan et al., 1991; Roy et al., 1994; Dassa et al., 1996). One of the studies, on reanalysis, found that individuals with schizophrenia with a positive family history did have more births in April and May (Shensky and Shur, 1982).

The five remaining studies reported that individuals with schizophrenia who had a positive family history for the disease were more likely to show a winter birth excess (Lo, 1985; Baron and Gruen, 1988; Owen and Lewis, 1988; Pulver et al., 1992a; Kitamura et al., 1995). However, the sample sizes of these studies were all small, ranging from 55 to 381.

7.2. Gender

Nineteen studies have examined the relationship between the sex of individuals with schizophrenia and their birth seasonality, and one of them also included a sample of individuals with manic-depressive disorder. Dalén's (1975) Swedish study ($n=17\,592$), Torrey and Torrey's (1980) American study (Torrey and Torrey, 1980, $n=17\,251$), Ødegård's (1974) Norwegian study (Ødegård, 1974, $n=19\,740$), and Hare et al.'s (1979) English study (Hare et al., 1979, $n=6547$) each looked for male–female differences in the seasonal birth pattern and found little or none. Other smaller studies that reported negative findings on male–female differences for birth seasonality were Parker and Balza (1977), Pulver et al. (1983); Hsieh et al. (1987), Kendell and Kemp (1987), Goldstein et al. (1990), Rodrigo et al. (1991) and Kim et al. (1994),

Four studies reported that the winter–spring birth excess in schizophrenia was more pronounced in, or found exclusively among, female patients. Two of the studies had sample sizes of 2947 (Dalén and Roche, 1975) and 2256 (Parker and Neilson, 1976), but the other two had small sample sizes of 918 (Pulver et al., 1981) and 350 (García Hildebrandt, 1992). Interestingly, three of these four studies were carried out in Southern Hemisphere countries. Three other studies reported the winter–spring birth excess to be more pronounced among men (Jones and Frei, 1979; Michitsuji et al., 1987; Chen et al., 1996), and one small Southern Hemisphere study reported markedly different seasonal excesses for men (in winter) and women (in spring) (Syme and Illingworth, 1978). The only study that looked at seasonal birth patterns among males and females with manic-depressive disorder was that by Kendell and Kemp (1987), and they reported no difference.

7.3. Social class or race

Barry and Barry (1964) were the original proponents of the idea that winter seasonal birth excesses for individuals with schizophrenia were restricted to those from lower socio-economic classes. They contrasted their lack of seasonal findings from two private psychiatric hospitals, in which the patients were from upper socio-economic classes, with their findings from state psychiatric hospitals in which most of the patients were from lower classes. However, because Barry and Barry used no controls in their second study, their findings are of limited value. Since that time, Ødegård (1974) published data on the socio-economic status and seasonal birth pattern of 19 740 individuals with schizophrenia; he not only failed to confirm Barry and Barry's findings but reported a trend in the opposite direction. Hare et al. (1972) and Kendell and Kemp (1987) also failed to confirm Barry and Barry's findings.

Only two analyses of seasonal births by race have been carried out. Gallagher et al. (1983, 1984) compared birth data for 630 whites and 94 blacks with schizophrenia hospitalized at a state hospital in Pennsylvania and reported that black individuals were much more likely to be winter-born. However, the control group used in their study, consisting of general births from 1944 to 1961, poorly matched their study group, who had been born between 1884 and 1961. Rodrigo et al. (1991) analyzed birth data on 1814 individuals with schizophrenia at a state hospital in Mississippi and found no difference in the seasonal birth pattern between whites and blacks.

7.4. Urban birth

Recent studies have established that being born in, or raised in, a city is a risk factor for being diagnosed later with schizophrenia (Lewis et al., 1992; Takei et al., 1995b; Torrey et al., 1997). Six research groups have looked for an association between urban births and winter–spring births in schizophrenia.

Dalén in Sweden was apparently the first to notice that the excess winter births in individuals with schizophrenia "is somewhat higher... in the group of patients born in urban areas" (Dalén, 1975, p. 83), although he did not use any statistical measurement of this difference. Machón et al. (1983) in Denmark utilized a small number of individuals with schizophrenia ($n = 17$) who were known to be at high genetic risk because their mothers had also had schizophrenia. For this high-risk group, Machón et al. reported that "among the urban births, significantly more schizophrenics result from winter [Jan.–Mar.] births (23.3 per cent) as opposed to not-winter births (8.4 per cent)" ($p < 0.028$, Fisher's exact probability test).

Takei et al. (1995a) examined the place and season of birth for 6533 individuals with schizophrenia in England and Wales. Using logistic regression analysis, they determined that "city birth did not increase the risk of schizophrenia among those born in summer, but was associated with a 19% increase among the autumn born and a 21% increase among the winter born". A limitation of Takei et al.'s study is that they used patients with affective psychosis, personality disorders, and neurotic disorders as controls; since there is evidence that individuals with affective psychosis may also have excess winter–spring births, their inclusion as controls may have weakened the findings.

O'Callaghan et al. (1995) in Ireland utilized two psychiatric case registers to compare the place and season of birth for 3253 individuals with schizophrenia with the place and season of birth of the general population. They reported "a significant ($p = 0.04$) difference in quarterly distribution of births between urban-born patients ($n = 1362$) and urban-born controls; patients who were urban-born were more likely (+13%) than controls to be born in the winter". This effect was much more pronounced for females than for males. The authors also noted "a trend for an excess (+8%, $p = 0.14$) of spring births among rural-born patients ($n = 1799$) relative to rural-born controls". A limitation of this study is that control data were available by quarters only, thereby obscuring the monthly patterns.

Additional studies of the interactive effects of place and season of birth have recently been reported from The Netherlands and France. Van Os et al. (1996) utilized a Dutch national sample of 22 361 individuals with schizophrenia and 27 718 individuals with affective psychosis. They compared their birth seasonality by quarters with an index of population density for their municipality of birth. The analysis found a significant association between urban and winter birth for broadly defined schizophrenia ($p = 0.05$) and for narrowly defined schizophrenia ($p = 0.007$) for females but not for males. No association between place and season of birth was found for affective psychosis. A limitation of the study is that the measure of population density was based on 1993 data, whereas the patients had been born from 1894 to 1971.

Verdoux et al. (1997) in France studied 4139 individuals with schizophrenia and compared their season of birth by quarters with the population density of their 'département' of birth. The individuals born in the most highly populated areas had a 20% increase in winter (January–March) births compared to those born in other areas ($p=0.02$). This urban-winter birth effect was found equally for males and females. A limitation of this study is the lack of standardized diagnostic criteria for schizophrenia in France.

7.5. Pregnancy and birth complications

Pregnancy and birth complications (PBCs) have been shown, in many but not all studies, to be increased in individuals who later develop schizophrenia. Four studies have asked whether PBCs occur more commonly in individuals with schizophrenia who were born in the winter and spring. The results have been contradictory.

Machón et al. (1987) in Denmark reported on 16 individuals with schizophrenia; PBCs were reported to have occurred among six of the seven individuals born in the winter and among five of the nine individuals born in non-winter months. Jones et al. (1991) in England compared PBCs in a sample of 111 individuals with schizophrenia. Among those born in the summer or autumn, 12 of 51 had a history of PBCs, whereas among those born in the winter or spring, only four out of 60 had a history of PBCs ($p<0.05$). Kinney et al. (1994), in an American study of 29 individuals with schizophrenia and using 39 unaffected siblings as controls, also reported that PBCs were significantly more common in patients born May–November than December–April ($p=0.01$). However, Cantor-Graae et al. (1994) found exactly the opposite; in their Swedish study of 70 individuals with schizophrenia using a matched-pair, case-control method, they reported that "obstetric complications increased risk for schizophrenic outcome by 80% in cases born during the winter months" ($p=0.02$) and concluded that this study was "the first to show an overrepresentation of obstetric complications in winter-born schizophrenics in general".

7.6. Subtypes, symptoms, and signs

Many attempts have been made to correlate winter birth seasonality for individuals with schizophrenia with specific subtypes, symptoms, or signs of illness as measured neurologically, neuropsychologically, neurophysiologically, or using imaging techniques.

The most common subtyping of schizophrenia is into paranoid and non-paranoid types. Large studies by Torrey et al. (1977) ($n=18\,123$), Kendell and Kemp (1987) ($n=2653$), and Hafner et al. (1987) ($n=2020$) all reported no difference in birth seasonality between paranoid and non-paranoid schizophrenia.

However, Dalén (1975), in a study of 2586 individuals with paranoia (ICD 303), not paranoid schizophrenia, found markedly increased births from December through April, but especially in February ($p<0.001$). Templer and Veleber (1982) ($n=10\,495$), Rodrigo et al. (1991) ($n=1814$), and Kitamura et al. (1995) ($n=55$) reported that individuals with paranoid schizophrenia had more winter births than those with non-paranoid schizophrenia. Hsieh et al. (1987) ($n=472$) and Michitsuji et al. (1987) ($n=107$) reported that males, but not females, with paranoid schizophrenia had more winter births than individuals with other types of the illness. Finally, Nasrallah and McCalley-Whitters (1984) ($n=577$) found no seasonal birth difference for all individuals with paranoid and non-paranoid schizophrenia; when analyzed by sex, the paranoid males (trend) and non-paranoid females ($p<0.05$) were more likely to have been born in the winter months.

Two studies have examined seasonality of birth for the disorganized subtype of schizophrenia. d'Amato et al. (1991) ($n=2215$) reported that this subtype had a marked preponderance of winter (November–January) births ($p<0.001$). Khiari et al. (1994, $n=700$) found that individuals with disorganized schizophrenia had been born disproportionately in October ($p<0.01$). Wolyniec et al. (1993) ($n=362$) found that individuals with schizophrenia who had had 'manic-like syndromes' had been born disproportionately in the winter and spring.

Another common division of schizophrenia is into individuals with predominantly positive and those with predominantly negative symptoms. Roy et al. (1995) ($n=269$) found no difference in birth seasonality when their sample was divided by positive and negative symptoms. Kronengold et al. (1995) ($n=132$) reported that winter births "showed significantly decreased levels of positive symptoms". Two studies, both with very small numbers of subjects, reported a significant association between winter births and increased negative symptoms (Opler et al., 1984, $n=18$; Öhlund et al., 1990, $n=32$). Similarly, Watson et al. (1987), in a larger study ($n=511$), reported that individuals with schizophrenia who were born following winters with high rates of infectious diseases had higher scores on the anhedonia scale ($p<0.05$).

Individuals with schizophrenia can also be divided by age of onset or age of initial hospitalization, although these two measures do not always correlate with each other. Corgiat et al. (1983), in a large study of this question ($n=25\,278$), reported that individuals with schizophrenia who were older at the time of their first hospitalization were significantly more likely to have been born in the winter ($p<0.05$). Chen et al. (1996) ($n=3749$) found that individuals with schizophrenia who had had an early age of onset were more likely to have been born in the winter only if they were male and had no family history of the disease. No associations between winter births and age of onset or age of initial hospitalization (Roy et al., 1995, $n=269$), age of onset (Baron and Gruen, 1988, $n=88$), or age of initial hospitalization (Modestin et al., 1996, $n=282$) have been reported by other researchers.

Still another way to divide individuals with schizophrenia is by acuteness or chronicity of symptoms or by duration of hospitalization. Dalén (1975) in a large study of 21 442 individuals, found a non-significant trend between winter–spring (February–April) births and hospitalization for less than 3 years. Pulver et al. (1983) ($n=1455$) and Rodrigo et al. (1991) ($n=1, 814$) similarly found a significant association between winter birth in schizophrenia and shorter duration of hospitalization. Two small studies found no such association (Jones and Frei, 1979, $n=915$; Modestin et al., 1996, $n=282$), and a larger study that divided patients into acute and chronic on duration of illness also found no association with winter births (Hafner et al., 1987, $n=2020$).

Researchers have also examined winter-born and non-winter-born individuals with schizophrenia for possible differences on neurological, neuropsychological, and neurophysiological measures. Roy et al. (1995, $n=210$) looked for differences on a variety of neurological soft signs and developmental reflexes and found none. di Michele et al. (1992) ($n=73$) also looked for season of birth differences on neurological soft signs and found none. Similarly, on neuropsychological tests Roy et al. (1995) ($n=134$) utilized the Wechsler Adult Intelligence Scale (WAIS) and the Continuous Performance Test (CPT), wheras Faustman et al. (1992) ($n=112$) utilized a wide battery of neuropsychological measures to try to distinguish individuals with schizophrenia born in the winter months, but in both cases, the results were completely negative.

Neurophysiological studies of birth seasonality in individuals with schizophrenia have yielded more interesting results. In two studies Öhlund et al. (1990, 1991) studied 26 individuals with schizophrenia in each study and reported that those born January–April had lower electrodermal activity (as measured by the skin conductance response) ($p<0.05$ in first study, $p=0.04$ in second study). Katsanis et al. (1992) replicated these findings among 49 individuals with schizophrenia and further showed that the winter birth-related lower skin conductance was specific to schizophrenia since it was not found in individuals with schizophreniform disorder ($n=28$), bipolar disorder ($n=32$), major depression ($n=32$), or normal controls ($n=130$). However, Schnur et al. (1995) were unable to replicate the above studies among 83 individuals with schizophrenia, 59 with depression, and 81 normal controls divided into winter-born (January–April) and non-winter-born (May–December). Their findings led them to conclude that "birth season was unrelated to the proportion of nonresponders" when either the skin conductance response or the finger pulse amplitude response was examined.

Finally, ten research groups have attempted to correlate winter birth seasonality in individuals with schizophrenia or bipolar disorder with neuroanatomical findings as measured by computerized tomography (CT) or magnetic resonance imaging (MRI). The results have been decidedly contradictory. Sacchetti et al. (1987) used CT to measure the lateral-ventricle to brain ratio (VBR) in 155 individuals with schizophrenia and found a significant correlation between increased VBR and December–April births ($p=0.008$). Zipursky and Schulz (1987) found a similar correlation between increased VBR and December–March births in 32 individuals with schizophrenia ($p<0.05$). Degreef et al. (1988) ($n=30$), defining winter births as January–March, reported a trend in the same direction for VBR ($p=0.15$) and also found more sulcal atrophy in the winter-born individuals ($p=0.05$).

Sacchetti et al. (1992), in another CT study of 206 individuals with schizophrenia and 107 with major affective disorder (53 bipolar disorder, 54 major depression), found that those born December–April compared with May–November had increased VBR ($p=0.04$), especially marked for those with no family history of the disease ($p=0.03$). Among the individuals with schizophrenia, however, there was no seasonal birth difference for atrophy. The individuals with major affective disorder showed no seasonal birth differences for either VBR or atrophy. Moore et al. (1996), in an interesting MRI study of 29 patients with bipolar disorder, reported that nine had subcortical white matter lesions and that all nine had been born in February or March. The final study with positive findings was done by d'Amato et al. (1994) using CT on 42 individuals with schizophrenia and 24 controls. Individuals with schizophrenia born January–March compared with July–September had larger VBRs ($p<0.03$) and larger third ventricles ($p<0.001$).

Four other studies have found no correlation between birth seasonality and neuroanatomical measures. Jones et al. (1991), studying 88 affected individuals who had a negative family history for schizophrenia, reported that on a CT scan, those born in the summer and autumn had significantly larger VBRs compared to those born in winter and spring ($p=0.03$), exactly the opposite of the other studies. Wilms et al. (1992), studying 42 individuals with schizophrenia by CT, found no seasonal birth trends in the VBR. Roy et al. (1995) studied 109 individuals with schizophrenia using MRI and compared the winter-born (November–April) with the non-winter-born (May–October). No differences were found on measurements of VBR, lateral ventricular asymmetry, third ventricle, temporal horn, lenticular nucleus, or cerebellum. Finally, DeQuardo et al. (1996), studying 54 individuals with schizophrenia by CT, found no difference in VBR or third ventricle size, no matter how winter was defined (December–March, December–April, January–March, or January–April).

In summary, attempts by researchers to correlate winter–spring births in individuals with schizophrenia and, rarely, bipolar disorder with a variety of clinical features of these diseases have yielded a few promising leads. All six studies of urban and winter–spring births suggest that these two known risk factors may interact in a way that is at least additive, if not synergistic, for schizophrenia; the single study of individuals with affective psychosis was negative. A majority of studies also suggest that individuals with schizophrenia who do not have a family history of the disease are disproportionately represented among the winter–spring birth cohort, with opposing studies having relatively small numbers of subjects. If both of these correlations hold up with additional studies, they suggest that the seasonal birth factor in schizophrenia is more likely to affect individuals not genetically predisposed to the disease and those born in, or raised in, urban areas.

Two other areas that deserve further study in schizophrenia are possible correlations between winter–spring births and neurophysiological measures, such as skin conductance response, and with individuals with an older age of initial hospitalization and/or briefer hospital stays. The latter suggests that individuals with schizophrenia who are born in the winter and spring months may possibly have a better prognosis, although this remains to be confirmed.

Correlations between winter–spring births and other clinical features appear much less promising. Studies done to date on gender, social class or race, pregnancy and birth complications, most clinical subtypes, and neurological, neuropsychological, and neuroimaging measures have not yielded results that suggest that these measures correlate with winter–spring births. Given the presumed heterogeneity of schizophrenia and bipolar disorder, however, it is possible that sample sizes to date have been too small and lack the statistical power to yield positive correlations.

8. Discussion of possible causes

An excess number of winter–spring births for individuals with schizophrenia appears to be one of the most firmly established and consistently replicated aspects of this disease. An excess number of winter–spring births is also found in individuals with bipolar disorder, although for manic-depressive psychosis, it is clearly established only for those who have had manic episodes and not for those with depression alone. Except for known infectious diseases, no other diseases have seasonal birth excesses as clearly established as those for schizophrenia and bipolar disorder.

In thinking about causes of this seasonal birth excess, two things should be kept in mind. First, a 5–8% seasonal birth excess does not necessarily indicate the true magnitude of this effect. If the seasonal factor exerts its effect only in the winter and spring months, then it may account for only 5–8% of all individuals with these diseases. If, however, the seasonal factor exerts its effect all year long but merely peaks in the winter and spring months, then it may account for any proportion of the total cases.

Second, although we measure the effect of the seasonal factor by measuring the excess of winter and spring births, that does not necessarily mean that the seasonal factor exerts its effect at that time. It could theoretically also exert its effect on the second trimester of these pregnancies (a fall factor), on the first trimester of these pregnancies (a summer factor), or in the first few postpartum months (a spring or summer factor). In short, the actual timing of the seasonal factor is completely unknown, and it may well exert its effect at more than one part of pregnancy and the postpartum period.

Ten major theories have been proposed to account for the seasonal excess births of individuals who later develop schizophrenia and bipolar disorder. The first two have been disproved, but the others must be considered until more definitive etiological information becomes available.

8.1. Statistical artifact

Lewis and Griffin (1981) and Lewis (1989) claimed that the winter–spring seasonal birth excess for schizophrenia and bipolar disorder is a statistical artifact caused by age incidence and age prevalence effects. Lewis described the age incidence effect as follows:

> People born in January, February, and March of a given year are older than people born in later months, and therefore they should produce more new cases. An investigator seeing this excess incidence might mistakenly attribute it to winter. (1989, p. 61)

Lewis labeled age prevalence “an especially strong form of age incidence” (1989, p. 61) and explained it as follows:

> For example, people who are 30 years old have a higher incidence of schizophrenia than people who are 29 years old. Therefore, people born in 1937 may have a higher incidence in 1967 than in 1966. When first admissions from 1967 are pooled with first admissions from 1966, people born in 1937 and admitted in 1967 will have more influence on the final result than people born in 1937 and admitted in 1966. The difference in influence between any 2 years is not great, but over the course of an entire data set it becomes noticeable and should be corrected. (Lewis and Griffin, 1981, p. 590)

Both Dalén (1975) and Hare (1975b) had earlier raised the age incidence effect as a source of error, and Hare had proposed a formula for correcting it. Similarly, Lewis and Griffin (1981) proposed a formula to correct for the age prevalence effect.

Although the age incidence and age prevalence effects have elicited extensive and spirited discussion among statisticians and psychiatric researchers (Watson et al., 1982; Shur and Hare, 1983; Bradbury and Miller, 1985; Boyd et al., 1986; Dalén, 1990; Torrey and Bowler, 1990), these effects have been shown to be negligible. At least 13 studies of birth seasonality in schizophrenia or manic-depressive psychosis have corrected for the age incidence or age prevalence effects, but the winter–spring birth excess was still statistically significant (Hare, 1975b, 1978; Pulver et al., 1981, 1983; Watson et al., 1982, 1984a; Shur and Hare, 1983; O'Callaghan et al., 1991; Rodrigo et al., 1992; Aschauer et al., 1994; Kim et al., 1994; Pallast et al., 1994; Tam and Sewell, 1995).

The age incidence effect predicts that the greatest birth excesses should be in January and February and the greatest deficits in November and December, yet December and occasionally November have had excess births in some studies. The age incidence effect also predicts that the seasonal birth excess should be maximal in young age cohorts and become less pronounced in older age cohorts, yet analysis of the seasonal effect by age cohorts shows no differences (Torrey and Bowler, 1990). The age incidence and age prevalence effects also predict that studies in Southern Hemisphere countries should show a January and February birth excess, but the findings are in the opposite direction. Finally, age incidence and age prevalence effects should produce a winter excess in birth seasonality studies of other psychiatric or non-psychiatric disorders, but these are not found in most studies.

8.2. Exaggeration of normal seasonal birth curves

For reasons that are not fully understood, there are seasonal patterns to normal births (Cowgill, 1966; Warren et al., 1986; James, 1990; Russell et al., 1993). In Europe, the peak months for normal births occur in the spring. Since births of individuals with schizophrenia also peak in the early months of the year, this suggested to Ødegård (1977) that "the pronounced maximum in schizophrenia results from the same causes as the somewhat lower maximum in the general population". In North America, however, the peak months for normal births are in the fall; since the peak birth months for schizophrenia and bipolar disorder are in the winter and spring, this effectively refutes this hypothesis.

8.3. Procreational habits

Huntington (1938) appears to have been the first to explain the seasonal birth pattern in individuals with schizophrenia by postulating that their parents have an idiosyncratic seasonal conception pattern. As described by James (1978), "in the summer, people wear fewer clothes in bed, and... a schizoid spouse is more likely then to notice his (or her) co-spouse there and accordingly to initiate sexual behaviour". Hafner et al. (1987) has been a contemporary proponent of this theory, and Bleuler (1991) included affective disorders as well by noting that conceptions among depressed individuals are more likely to take place in the spring, when depression is less severe.

The procreational habits hypothesis predicts that individuals with schizophrenia who have a family history of the disease should show a greater winter–spring birth excess since their parents would presumably have been more affected by the seasonal conception proclivities. As noted above, studies on family history and seasonality go predominantly in the opposite direction.

The procreational habits hypothesis also predicts that unaffected full siblings of individuals with schizophrenia and bipolar disorder should also have a winter–spring birth excess. Six studies have examined this question. McNeil et al. (1976), with a sample of 288 siblings, compared January–April births against May–December births and reported that "the full siblings showed a birth pattern much closer (non-significant) to that of the schizophrenics than to that of the general population". Hare (1976) examined birth data on 219 well siblings of individuals with schizophrenia and 451 well siblings of individuals with manic-depressive psychosis. He reported that the siblings of "the psychotic group show an excess [of births] over expectation in the first quarter". However, as Watson et al. (1984a) later pointed out, the excess in first-quarter sibling births noted by Hare was almost entirely due to the siblings of the individuals with manic-depressive psychosis.

Four other studies, with sample sizes of 558, 1039, 1321, and 2639, have reported no seasonal birth deviation in the births of siblings of individuals with schizophrenia (Larson and Nyman, 1976;

Buck and Simpson, 1978; Torrey, 1989; Pulver et al., 1992b). One of the studies (Torrey, 1989) further divided the siblings into first-born siblings and siblings born immediately following the one with schizophrenia to ascertain whether the planned spacing of births might have affected the seasonal pattern; there was no evidence that it did so. It appears, therefore, that there is no evidence to support a procreational habits explanation for the seasonal birth pattern of individuals with schizophrenia. Given the findings from Hare's (1976) study, however, this remains a possible explanation for the seasonal birth pattern of individuals with manic-depressive psychosis/ bipolar disorder and needs additional study.

8.4. Genetic

A variety of genetic hypotheses have been offered to explain the seasonal birth patterns of individuals with schizophrenia and bipolar disorder. Hare and Price (1968) proposed that "an increased robustness associated with the schizophrenic genotype may lead to an increased survival of winter-born babies prone to schizophrenia". Conversely, Pulver et al. (1981), noting that insufficient attention has been directed to the months of deficit births rather than excess births, proposed that in the summer and fall there might be "a seasonally varying factor that increases the risk to fetal loss of individuals with genes predisposing to schizophrenia". Both hypotheses would predict that the seasonal birth deviations should be more pronounced among individuals with a family history of the disease, which does not appear to be the case. Dalén (1988) discussed evidence linking increasing maternal age to birth seasonality in schizophrenia and concluded that the evidence was mixed. Crow (1987) proposed that the seasonal birth pattern in schizophrenia might be explained by a high rate of mutation that was modified by an environmental factor such as heat.

8.5. Pregnancy and birth complications

Some studies have reported that individuals who later develop schizophrenia experience an increased number of pregnancy and birth complications. Since many such complications are seasonal in nature, that has lead to speculation that "the excess proportion of births during the early months of the year might have been due to prematurity" (Hare, 1975a). Müller and Kleider (1990) have developed this hypothesis in relation to schizophrenia and theorized that "seasonal variation of conception... leads to seasonal variation of the risk of preterm birth... [and] preterm babies were found to have an increased risk for schizophrenia". Unfortunately, such theories provide no methods for separating pregnancy and birth complications as causal factors for severe psychiatric illnesses from the possibility that pregnancy and birth complications and severe psychiatric illnesses are both sequelae of yet a third factor.

8.6. Seasonal variation in light and internal chemistry

Several researchers have postulated that the winter–spring birth excess observed in schizophrenia and bipolar disorder might be caused by variations in internal chemistry or neural development brought about by seasonal variations in light. For example, Turnquist (1993) proposed that "seasonal changes in maternal hormonal levels" could affect neuronal pruning or other developmental events and thereby "provide an explanation for the greater winter birthrate among schizophrenic patients". Similarly, Quested (1991) speculated that "variations in photoperiod could mediate the establishment of inappropriate development patterns", thereby accounting for the schizophrenia birth pattern. Morgan (1978) focused on circadian abnormalities in schizophrenia and proposed that "abnormal setting of body clock speed in infancy may be the factor linking spring birth with schizophrenia". Another hypothesis has been promoted by Jongbloet (1975) and Pallast et al. (1994), in which they theorize that seasonal light changes lead to seasonal variations in the release of overripe ova by the ovary, with these ova being more susceptible to 'teratogenic consequences' and schizophrenia.

All such hypotheses predict that seasonal birth deviations for schizophrenia and bipolar disorder should be most prominent at latitudes that have the most marked changes in light and least prominent at the equator. Some studies of schizophrenia birth seasonality have suggested the existence of such a latitude gradient (Dalén, 1975; Torrey et al., 1977), whereas other studies have not (Torrey et al., 1991). The 15% winter birth excess reported by Parker and Balza (1977) for the Philippines, just north of the equator, is also contrary to these hypotheses.

8.7. Seasonal variation in external toxins

Since it is known that the developing nervous system is sensitive to minor changes in its chemical environment, external toxins that have seasonal fluctuations should be considered as possible causes of the seasonal birth pattern in schizophrenia and bipolar disorder. Deficiencies of heavy metals such as magnesium (Yassa et al., 1979), zinc (Andrews, 1990), and selenium (Foster, 1988; Berry, 1994; Brown, 1994) have been reported to cause schizophrenia-like syndromes. Similarly, exposure to industrial chemicals, such as toluene, is also known occasionally to cause schizophrenia-like syndromes (Goldbloom and Chouinard, 1985). Although such toxins are unlikely to cause large numbers of cases of severe psychiatric illness, if a small number of cases were caused by such toxins in the winter and spring months, it might account for the seasonal birth pattern.

8.8. Nutritional deficiencies

This is the oldest theory of causation for the observed winter–spring birth excess in severe psychiatric illnesses, put forward by Tramer in his original 1929 study. de Sauvage Nolting (1954), in his studies of schizophrenia birth seasonality in The Netherlands, postulated that it was due to a seasonal deficiency of vitamin C and even carried out animal studies to try to prove it. Dalén (1975) was interested in vitamin K deficiency at the time of birth as an explanation for schizophrenia's winter–spring excess births. In addition, Pasamanick (1961) speculated that protein deficiency during the summer months, at the time of conception, might be the cause of excess winter–spring births for schizophrenia, mental retardation, and a variety of other neurodevelopmental conditions. Nutritional deficiency hypotheses, however, predict that the seasonal birth excess should be more pronounced in developing nations in which nutritional deficiencies are widespread as well as more pronounced in the early years of this century, when nutrition was less adequate in Western nations; the data that exist would not appear to support either of these observations.

8.9. Temperature and weather effects

This hypothesis to explain the seasonality of births in schizophrenia was originally put forward by Petersen in 1934. Its strongest proponents have been Pasamanick (1986), who believed that hot summers were the cause of protein deficiency at the time of conception, and Templer et al. (1978), who reported "a rather consistent trend of schizophrenics being born in cold months and conceived in warm months". McNeil et al. (1975), studying a sample of 13 440 individuals with schizophrenia in Sweden, was unable to corroborate an association between summer temperatures at the time of conception and winter births of individuals with schizophrenia. Hare and Moran (1981) and Watson et al. (1984a) also reported no association between summer temperatures and winter births.

Attempts to correlate the temperature at birth with winter–spring birth patterns for schizophrenia have met with mixed success. Hare and Moran (1981) found "the schizophrenia birth rate to be consistently higher in the coldest years". More recently, Kinney et al. (1993) reported "a highly significant excess of schizophrenic births in months associated with physiologically stressful weather". Bark and Krivelevich (1996), studying 'rigidly defined heatwaves' in New York, found "significant increases in schizophrenia when heatwaves occurred in pregnancy in all but the first and seventh months". However, Watson et al. (1984a), studying 3246 individuals with schizophrenia, Ede et al. (1985), whose sample included 2275 such individuals, and Torrey and Torrey (1979), studying 16 910 inpatients in Missouri, all found no association between winter temperatures and excess schizophrenia births.

8.10. Infectious agents

Since most infectious agents have seasonal variations in their incidence, they have received considerable attention as possible explanations for the winter–spring birth excess in schizophrenia and bipolar disorder. Viruses have been especially well studied in this regard (Yolken and Torrey, 1995). Influenza, which has a marked seasonal occurrence, has been linked to an excess number of schizophrenia births following mid-trimester, in-utero exposure in 14 studies, whereas five other studies found no such link [reviewed by Wyatt et al. (1996)]. Significantly, however, two studies that examined the records of women who were not merely exposed to, but actually had, influenza during pregnancy did not find an excess of schizophrenia in the offspring (Crow and Done, 1992; Cannon et al., 1996).

Other attempts to link infectious agents to the seasonal schizophrenia birth pattern include Watson et al.'s study (Watson et al., 1984a) of eight seasonal diseases in Minnesota, Torrey et al.'s study (Torrey et al., 1988) of six reportable viral diseases in Connecticut and Massachusetts, and O'Callaghan et al.'s study (O'Callaghan et al., 1994) of 16 infectious diseases in England and Wales. Watson et al. reported that excess births of individuals with schizophrenia were significantly greater "in the years directly following those marked by high levels of infectious disorders" ($p<0.05$), most marked for diphtheria, pneumonia, and influenza. Torrey et al., using a time series analysis, found statistically significant correlates between schizophrenia births and the occurrence of measles, polio, and varicella-zoster. O'Callaghan et al. reported that increased deaths from bronchopneumonia "preceded, by three and five months respectively, increased numbers of schizophrenic births". Still other researchers have speculated that specific viruses, such as the agent that caused Von Economo's disease (Jones and Frei, 1979), Japanese encephalitis virus (Shimura et al., 1987), or summer enteroviruses (Khiari et al., 1994), were responsible for the schizophrenia seasonal birth pattern they observed.

If infectious agents are responsible for the seasonal birth pattern in schizophrenia and bipolar disorder, there are several plausible mechanisms for transmission. Any infectious agent that varies seasonally could infect the developing fetus via transplacental transmission from the mother. There is also known to be a seasonal (spring) increase in coitus in pregnant women, with a consequent increase in infectious agents reaching the developing fetus via the vaginal tract (Naeye, 1980). Infections can also be transmitted from mother to baby during delivery, as commonly occurs with human immunodeficiency virus (HIV) infections (Landesman et al., 1996). Both pregnant women and new-born children are exposed on a seasonal basis to some infectious diseases from other children in the family, and this may explain the findings of Sham et al. (1993) that "having siblings three to four years older was associated with a significantly increased risk of schizophrenia" in children born at that time. Finally, environmental factors may promote the transmission of infectious agents on a seasonal basis; for example, pet cats are kept inside more often in the colder months, at which time they might infect pregnant women (as, for example, occurs with toxoplasmosis) or new-born children through close contact with them (Torrey and Yolken, 1995).

Finally, in thinking about possible causes of the winter–spring birth excess in schizophrenia and bipolar disorder, it should be kept in mind that both conditions are probably heterogeneous and also that the possible causes may interact. Genetic predisposition, variations in light and internal chemistry, temperature, nutritional status, and immune status may all affect infectious agents, and infectious agents may affect many of them. This potential interaction has furthered speculation about a 'two-hit hypothesis,' in which schizophrenia or bipolar disorder might be predisposed by a seasonal factor occurring during the perinatal period and then precipitated by another factor, not necessarily seasonal, many years later.

9. Directions for future research

The winter–spring birth excess, firmly established for schizophrenia and strongly suggested in studies done to date for bipolar disorder, offers promising leads for etiological research. If we can ascertain the cause(s) of these seasonal birth patterns, we may then understand the etiology of at least some cases of these diseases. Directions for future research include:

(1) Bipolar disorder: More season of birth studies are needed for this disorder. For example, do individuals whose illness includes episodes of mania really have a different seasonal birth pattern than individuals with severe depression alone?

(2) Deficits: Almost all research done to date for schizophrenia and bipolar disorder has focused on the birth excesses in the winter and spring months. Equally interesting, and sometimes statistically more significant, are the birth deficits in the summer and fall months. Öhlund et al. (1991) speculated that some protective factor might be operant for births at this time. Eagles et al. (1995) also noted the possibility "that the accent of theory on the season-of-birth effect in schizophrenia is misplaced and that instead of searching for explanations for the excess of winter/spring births, we should be focusing on possible reasons for low birth rates of future schizophrenics in the autumn".

(3) Statistical methods: More sophisticated methods, including time series analysis, should be used. Each of the above studies has a different population at risk and possibly different tests for seasonality with different alternative hypotheses. Attempting to combine these studies in a meta-analysis in order to increase the power for detecting seasonality is unlikely to be useful at this stage.

(4) Correlations: The most promising areas for research on correlations between winter–spring birth excesses and specific clinical features of schizophrenia appear to be family history and urban birth/raising. Virtually no correlation research has been carried out for bipolar disorder.

(5) Comparisons with other disorders: The specificity of the schizophrenia and bipolar disorder winter–spring birth excess needs to be further studied in comparison to other psychiatric disorders. Preliminary data on childhood autism, eating disorders, and antisocial personality disorder (Dalén's 'male criminal cases') suggest similarities.

(6) Causes: Although parental procreational habits have been effectively refuted as a possible cause of winter–spring birth excesses for schizophrenia, further investigation is needed regarding their relationship to bipolar disorder. Research on infectious agents would also seem to be especially promising. However, given our limited knowledge, almost all the areas of causal research discussed above are legitimate areas for further study.

Finally, it is important to point out that season of birth studies for individuals with schizophrenia and bipolar disorder are merely statistical assertions; the vast majority of individuals with these diseases are not born during the months of excess births, and most individuals born during these months do not develop schizophrenia or bipolar disorder. As noted by Barry and Barry (1961): "It should be emphasized for the sake of the layman who may read this paper that the differences in seasonal incidence of birth are small and have no predictive value for any individual."

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