Psychosis and Place

One important line of epidemiologic inquiry implicating social context in the etiology of psychosis is the examination of spatial variation in the distribution of psychotic illness. The authors conducted a systematic review of evidence from urbanicity and neighborhood studies regarding spatial variation in the incidence of psychosis in developed countries since 1950. A total of 44 studies (20 of urbanicity and 24 of neighborhood) were culled from three databases with similar time frames: Medline (1950–2007), PsychInfo (1950–2007), and Sociological Abstracts (1952–2007). With a special emphasis on social factors potentially relevant to etiology, the authors elucidated contributions, limitations, and issues related to study design, measurement, and theory. Evidence from both arenas supports a possible etiologic role for social context. Studies of urbanicity indicate that early-life exposure may be important; dose-response relations, spatial patterning of schizophrenia, and interactions with other factors may exist. Neighborhood studies indicate heterogeneity in rates, hint at spatial patterning of schizophrenia, and offer intriguing evidence implying more proximal social (as opposed to physical) exposures. The authors encourage the exploration of social pathways engaging theory, methodological advances, and the life-course perspective. They also propose a conceptual shift from studies of spatial variation in outcomes to research addressing the etiologic effect of exposures shaped by place as a reservoir of risk or resilience.

geography; incidence; psychotic disorders; residence characteristics; schizophrenia; social environment

INTRODUCTION

Accumulating evidence implicates social context in the etiology of psychosis. One important line of epidemiologic research pointing to a potentially causal role of social context is the examination of spatial variation in the distribution of psychotic illness. Such investigations have a rich history, in which social theory featured prominently in the first half of the 20th century. Eclipseed for a period of time, interest in the etiologic role of social context has been revived (1), and a new era of research has begun, stimulated in part by methodological advances and studies of migration and race/ethnicity (2). However, more recent studies have been somewhat disconnected from potentially enriching social theoretical perspectives that shaped earlier investigations. As recent work has indicated (3), integrating methodological advances and social theory with the life-course approach (4, 5) can help in unraveling the meaning of important findings, such as the spatial distribution of psychosis. Toward that end, we conducted a systematic review of evidence regarding spatial variation in psychosis. Here we present our findings and critically discuss their implications.

We first sketch the history and current relevance of classic research investigating the spatial distribution of psychosis, and follow it with a synthesis and interpretation of incidence studies carried out in developed countries since 1950. With an emphasis on social factors potentially relevant to etiology, we elucidate contributions, limitations, and issues related to study design, measurement, and theory. Finally, in

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History

Attempts to characterize the spatial distribution of psychosis have produced a rich history of empirical research. In the United States, these efforts can be traced back to the sixth decennial Census, conducted in 1840 (6). Though plagued with methodological problems, notorious errors, and misinterpretations later exposed by Edward Jarvis (7), it constituted the first attempt to enumerate the “insane” in the general population. Subsequently, Jarvis himself conducted a survey (8) marking the beginnings of descriptive psychiatric epidemiology in the United States (9). Later in the 19th century, other researchers put forward environmental conditions such as climate, meteorologic phenomena, and topographic features to explain the purported spatial distribution of insanity (10). Around the turn of the century, however, the emphasis on the physical environment began to shift to the social environment, and classifications of psychotic disorders began to emerge (9, 11).

The first half of the 20th century witnessed several seminal contributions to our understanding of the social and geographic distribution of psychosis. In 1932, Ødegård (12) demonstrated a doubling of rates of first hospital admission for psychosis among Norwegian migrants to Minnesota, as compared with native Minnesotans and with Norwegians living in Norway. This work provided a foundation for investigations of migration and psychosis by generating several testable hypotheses to explain this pattern of findings, including selective migration, dismissed only recently as a generally applicable explanation (13).

Several years later, Faris and Dunham (14) published their classic ecologic study of psychosis in Chicago, Illinois, Mental Disorders in Urban Areas. This work explored the relation between the spatial distribution of psychosis and social organization, a construct formed from sociologic theories relating the social architecture of urban settings to various social problems, of which mental disorders constituted one set. Faris and Dunham posited social isolation and poor communication among people in various communities as sociologic explanations for mental disorders, which they empirically tested by applying the concentric zone model of urban organization, developed by Park and Burgess (15) a decade earlier (figure 1). In this model, social organization increased with distance from the epicenter. Inner urban zones consisted of the most disorganized and unstable communities, characterized by isolation and poor communication among residents; outer zones were the most organized and stable communities, with the least isolation and better communication. Faris and Dunham hypothesized and found an inverse relation between social organization and rates of schizophrenia: The least socially organized inner urban zones had the highest rates. Similar ecologic patterns were found in other cities in the United States (14, 16).

While best known for these ecologic findings, Faris and Dunham’s Chicago study also examined ethnic density (i.e., proportion of a given ethnic group in a defined area), concentration of immigrants, and social class. Thus, in addition to the findings regarding social organization, Mental Disorders in Urban Areas provided a stimulus for two important lines of investigation. First, it gave rise to research centered on neighborhood composition (e.g., proportions of ethnic minorities and immigrants) and other aspects of the social environment in relation to severe mental illness (17). Second, it invigorated the debate regarding social class and mental illness, taken up in depth by Hollingshead and Redlich (18) a century after it was first noted by Jarvis in 1855 (8).

As research regarding the spatial distribution of psychosis continued to take shape, a prominent area of inquiry was defined by the question of whether lower social class was a cause or consequence of mental illness (19, 20). Two processes by which social class could result from mental illness are selection (the intergenerational process by which individuals are selected into various social positions before and during the prodromal phase of disorder) and drift (the intragenerational process by which mentally ill persons, after onset, ultimately occupy various social positions). While distinct, both have been folded into a general category of selection. Although the social causation-selection debate is still not entirely resolved, for schizophrenia, results overall tend to favor selection as the dominant explanation—that is, people with schizophrenia either drift into or are selected into lower social classes because of disability or
discrimination. Such findings created a context wherein the findings of Faris and Dunham, which largely supported social causation, were increasingly viewed as having reached the wrong conclusions about the causal direction between social conditions and psychoses (20, 21). The skepticism extended to their findings regarding urban ecology: Were higher rates of schizophrenia in inner urban areas due to the social disorganization of such areas or to people with schizophrenia drifting or being selected into them? However, the fact that Faris and Dunham catalyzed thinking about the spatial and social patterning of severe mental illness beyond the scope of social selection, drift, and causation remains often overlooked.

Currency

Between the 1960s and the 1990s, with notable exceptions (22), a once-prominent social emphasis in etiologic research receded alongside a sharpening focus on biologic underpinnings. Studies of migration and psychosis in the United States (8, 14, 17) literally migrated to Western Europe (23) and, over time, revived interest in the role of social context in the etiology of psychosis. Interest in the spatial distribution of psychosis itself also expanded, exemplified by interest in urban areas and psychosis (24) and increasingly rigorous comparative studies of urban and rural areas (25, 26) and landmark studies of countries and cultures (27, 28). In a recent review, McGrath et al. (29) concluded that there is heterogeneity in rates. Given the rich history of and current interest in social etiology, a synthesis and critical examination of epidemiologic studies of the spatial distribution of psychosis is perhaps a timely contribution.

RESULTS

Of the approximately 28,000 references returned in our search and articles cited in those publications, a total of 44 studies (26, 30–72) met the inclusion criteria. Thirty-nine of the 44 studies were identified with an initial title sift, followed by an abstract sift, and finally, a paper sift. Five additional studies (50–52, 56, 57) were identified in the paper sift by examination of references not returned in our search. Results were separated into two primary domains that constitute the vast majority of research in the developed world regarding the spatial distribution of psychosis: variation by level of urbanicity and variation by neighborhood. While urbanicity is a characteristic of neighborhoods, we considered the two as distinct entities in this review. In table 1, the characteristics and relevant principal findings of studies published in the last decade are categorized by urbanicity and neighborhood and presented according to location.

Results from studies included in this review suggest heterogeneity in the distribution of psychoses by urbanicity and neighborhood. Regarding this heterogeneity, there are two main questions that can be asked. The first deals with the direction of causation: Does exposure to or residing in certain areas increase the risk of psychosis or confer protection from psychosis? The second asks, If so, what factors are culpable? This review responds to these two questions by providing a systematic examination of the nature and quality of data that can address them. Rather than conduct a meta-analysis, which would focus on effect sizes of reported results, we opted to critically evaluate the validity and meaning of the literature.

Variation by urbanicity

In 20 studies, rates of psychosis were examined according to urbanicity (26, 30–48). All studies except the earliest, conducted in the United States by Eaton (30), were carried out in Western Europe: nine in Denmark (34–36, 38, 39, 43–45, 48)—the bulk by members of a research group using the Danish psychiatric registry; three in Sweden (26, 41, 42); three in the United Kingdom (37, 46, 73); two in the Netherlands (32, 33); and one each in Finland (47) and Italy (31). The evidence indicates an association between urban life and rates of psychosis; in most studies, urbanicity is associated with an approximately twofold increase in risk of psychosis, though associations indicating a risk increase as high as fourfold have been reported in early-onset cases (35). In only two (26, 31) of the 20 studies were no significant differences in rates of psychosis found according to urbanicity.

Studies of urbanicity have defined exposure to urban environments in two primary ways: by dichotomies, consisting of
urban-rural comparisons, and by degrees, defined as three or more categories of urbanicity according to population density. Two studies included in this review examined urbanicity in terms of the urban-rural dichotomy (31, 37); in parallel, one study classified areas of interest as cities and noncities (73). In another investigation, researchers examined two urban areas, one of which was more urbanized, and a mixed urban-suburban-rural area (46). The majority of investigators defined urbanicity by degrees of population density, defined either as population per square kilometer (32, 33, 42) or, most commonly, number of inhabitants within a defined location (e.g., capital, city, or town) (26, 30, 34–36, 38, 39, 41, 43, 44, 48). Among studies in which urbanicity was defined categorically as opposed to dichotomously, investigators in more than one third reported a dose-response relation between exposure to urban environments and risk of psychosis (30, 32, 35, 36, 39, 42).

The timing of exposure has been examined in the urbanicity literature in some detail—a valuable methodological contribution to the characterization of etiologically relevant social factors. Analyses have been facilitated by the employment of psychiatric case registers linked to population registers and other registers. Although associations between population density and psychosis at illness onset have been reported (31, 36, 37, 42, 46), we focus on exposure prior to illness onset because such findings are less likely to be due to drift across places.

From studies assessing the impact of urbanicity as defined by population density prior to illness onset, there is good evidence that elevated rates in urban areas are not simply the products of drift. In a number of studies examining exposure at birth (32–35, 38, 39, 41, 43–45, 47, 48, 73), investigators reported an approximate doubling in risk of psychosis in adulthood. Among these studies, several attempts to further refine understanding of the timing of exposure to urbanicity have been made. A classic study of Swedish conscripts by Lewis et al. (26) examined place of upbringing; men brought up in urban areas were more likely to develop schizophrenia than those brought up in rural areas. In another analysis employing the psychiatric case register in the Netherlands, Marcelis et al. (33) sought expressly to determine whether urbanicity operates before or around the time of illness onset. The highest rates of schizophrenia were seen among persons born in urban areas, regardless of urban residence at illness onset; in accord with other studies assessing risk of urban birth, there was an approximately twofold elevation in incidence. In contrast, persons not exposed to urban areas at birth but exposed around the time of illness onset showed no increase in risk (33). In one study using the psychiatric case register and the civil registration system in Denmark, Pedersen and Mortensen (39) probed the possibility of particular periods of vulnerability prior to illness onset and the role of cumulative exposure by examining urban residence at birth and over 5-year intervals during upbringing. In this study—the lone investigation examining duration of exposure to urbanicity in this review—risk increased with cumulative exposure to the most urbanized areas; persons who resided in the most urbanized areas during the first 15 years of life had the highest (nearly threefold) increase in risk (39). Finally, some of the most recent evidence from the Danish case register indicates that the risk(s) conferred by urban life prior to conception and/or birth may affect offspring born in areas less urbanized than those in which the family previously resided (44), providing evidence counter to drift and selection explanations. Together, these studies indicate that urbanicity confers a risk of psychosis early in the life course; moreover, they flag accumulation and persistence of exposure both across the life course and across generations as areas for further exploration.

The urbanicity effect does not seem entirely attributable to drift or selection. Whether the reported associations are artifacts of health-care service utilization should also be considered. In a number of early studies comparing urban and rural areas, service utilization cannot be dismissed as an explanation for the findings. More recent studies, which have assessed the timing of exposure, permit an evaluation. For instance, Pedersen and Mortensen (39) reported a linear relation between degree of urbanization at birth and risk of schizophrenia, given fixed urbanization at age 15 years, in a large population-based Danish cohort. Since the relation between exposure to increasing urbanicity at birth and psychosis cannot be explained alternatively by service use around the time of illness onset, such findings offer support that the observed associations are not completely explained by the availability of psychiatric services that may differ according to degree of urbanization.

Consistent with the findings of Faris and Dunham (14), two analyses indicated spatial patterning of schizophrenia, though not of affective psychoses. Eaton et al. (35) reported a dose-response relation between degree of urbanization and risk of schizophrenia but not risk of affective psychoses in Denmark. Kirkbride et al. (46) found three times more non-affective psychoses and the highest rates of schizophrenia in the most urbanized (South East London) of three centers studied in the United Kingdom; this was not the case, however, for affective psychoses. Though these findings are not supported unanimously (32), accumulating evidence from several large, prospective, population-based observational studies (74–77) suggests an absence of spatiality in affective psychoses.

Despite reports of a dose-response relation, findings regarding timing of exposure, and some indication of diagnostic specificity with schizophrenia, little regarding what is etiologically operative about urban life is known. High rates of schizophrenia in two studies of highly urbanized areas in London were partly explained by elevated rates in ethnic minorities (37, 46), consistent with the growing body of literature indicating elevated incidence among ethnic minority and immigrant groups in developed countries (23, 78, 79). However, this does not account for the bulk of the findings in the urbanicity literature.

Several interactions reported in the urbanicity literature may offer clues to etiology. Persons with familial liability seem to be particularly at risk (80). van Os et al. provided evidence of an additive interaction between urbanicity and family history of schizophrenia and severe mental illness in the Netherlands (81) and in Denmark (43). Winter birth has also been reported to be a modifier of the urbanicity effect (73), which might indicate gestation as a period of vulnerability to factors associated with urban life, such as
<table>
<thead>
<tr>
<th>Country, author(s), and year (ref. no.)</th>
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<th>Principal findings</th>
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<tr>
<td>Denmark Mortensen et al., 1999 (34)</td>
<td>Five categories of urbanicity: capital, capital suburb, provincial city with &gt;100,000 residents, provincial town with &gt;10,000 residents, rural area</td>
<td>Schizophrenia (ICD-8)</td>
<td>Population-based cohort study of administrative incidence among 1.75 million residents alive in 1968 or born in 1968–1993 whose mothers had been born in 1935–1978</td>
<td>Increased risk of schizophrenia in urban (capital) areas vs. rural areas (RR* = 2.40, 95% CI*: 2.13, 2.70); highest risk found in persons with an affected mother (RR = 9.31, 95% CI: 7.24, 11.96)</td>
<td>Controls drawn from 10% sample of medical birth register</td>
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<td>Denmark Eaton et al., 2000 (35)</td>
<td>Five categories of urbanicity: capital, capital suburb, large city, small city, rural area</td>
<td>Schizophrenia and affective psychosis (ICD-8)</td>
<td>Population-based case-control study of administrative incidence among persons born in 1973–1993</td>
<td>Dose-response relation found between degree of urbanization and risk of schizophrenia (for capital city vs. rural area, OR* = 4.20, 95% CI: 2.4, 7.4) but not affective psychosis; association not mediated by obstetric complications</td>
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<td>Denmark Schelin et al., 2000 (36)</td>
<td>Three regions, classified by degree of urbanicity: capital; capital suburb and provincial cities with &gt;100,000 residents; rural counties, including towns with &lt;100,000 residents</td>
<td>Schizophrenia (ICD-8)</td>
<td>Population-based administrative incidence study of first hospital admissions occurring in 1978–1982 with diagnosis at least once in 10 years following first admission</td>
<td>Dose-response relation between degree of urbanization and risk</td>
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<tr>
<td>Denmark Pedersen and Mortensen, 2001 (39)</td>
<td>Five categories of urbanicity: capital, capital suburb, provincial city with &gt;100,000 residents, provincial town with &gt;10,000 residents, rural area</td>
<td>Schizophrenia (ICD-8 or ICD-10)</td>
<td>Population-based cohort study; persons born in Denmark between 1956 and 1983 with a known maternal identity who were alive at age 15 years</td>
<td>Significant dose-response relation between number of changes in municipality during the age bands between 5 and 15 years (ages 5–10, 10–13, and 13–15 years) and risk of schizophrenia; living in a more urbanized area than in the prior 5 years conferred increased risk (RR = 1.40, 95% CI: 1.28, 1.51)</td>
<td>Change of address within the same municipality had no effect, indicating the importance of contextual change</td>
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<tr>
<td>Denmark Pedersen and Mortensen, 2001 (38)</td>
<td>Five categories of urbanicity: capital, capital suburb, provincial city with &gt;100,000 residents, provincial town with &gt;10,000 residents, rural area</td>
<td>Schizophrenia (ICD-8 or ICD-10)</td>
<td>Population-based cohort study; persons born in Denmark between 1950 and 1993 with a known maternal identity</td>
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<tr>
<td>Denmark Torrey et al., 2001 (48)</td>
<td>Five categories of urbanicity in 217 geographic divisions: capital, capital suburb, provincial city with &gt;100,000 residents, provincial town with &gt;10,000 residents, rural area</td>
<td>Schizophrenia (ICD-8)</td>
<td>Population-based administrative incidence study of 2,199 people admitted to a hospital and diagnosed, 1970–1993</td>
<td>Significant heterogeneity across divisions ($r^2 = 0.203$, 95% CI: 0.147, 0.276), associated with urban birth, age-sex interaction, and calendar period</td>
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</table>
van Os et al., 2004 (43)  
Five categories of urbanicity: capital, capital suburb, provincial city with >100,000 residents, provincial town with >10,000 residents, rural area; family history defined as ICD schizophrenia or severe mental illness and inpatient care before cohort member’s 25th birthday.

Administrative incidence of schizophrenia or schizophrenia spectrum disorder (ICD-8 or ICD-10) before age 25 years.

Population-based birth cohort study; administrative incidence study of persons born in 1950–1976 and residing in Denmark at age 25 years; mothers of cohort members born in 1935 or later.

Family history of schizophrenia increased risk from 0.33% to 2.0%; in controlled analyses, there was a significant positive interaction between urbanicity and family history of schizophrenia ($\chi^2 = 8.09$, 1 df; $p < 0.005$) or severe mental illness ($\chi^2 = 42.22$, 1 df; $p < 0.0001$).

Pedersen, 2006 (82)  
Municipalities categorized by degree of urbanization: capital area, provincial area, rural area.

Schizophrenia (ICD-8 or ICD-10).

Population-based cohort study; administrative incidence study of persons born in Denmark in 1910–1986, followed from their 15th birthday or April 1, 1970 (later date) until date of first diagnosis from April 1, 1970, onwards or date of death, emigration, or December 31, 2001 (first date).

Urban-rural differences were consistent for persons born between 1945 and 1986; risk was greater for males than for females and higher for persons aged <20 years than for persons aged ≥20 years.

Pedersen and Mortensen, 2006 (44)  
Municipalities categorized by degree of urbanization: capital area, provincial area, rural area.

Schizophrenia (ICD-8 or ICD-10).

Population-based cohort study; administrative incidence study of persons born in Denmark in 1956–1986, alive on their 15th birthday, whose parents were born in Denmark (mother after April 1, 1935)

Urban risk potentially carried by family: risk of schizophrenia was greater for persons who lived in a rural area until age 15 years if their nearest older sibling had been born in an urban area (RR = 1.59, 95% CI: 1.10, 2.30).

Pedersen and Mortensen, 2006 (45)  
Municipalities categorized by degree of urbanization: capital area, provincial area, rural area.

Schizophrenia (ICD-8 or ICD-10).

Population-based cohort study; administrative incidence study of persons born in Denmark in 1956–1983 who were alive on their 15th birthday.

Living 500–1,000 m from the nearest major road was significantly associated with the risk of schizophrenia (RR = 1.30, 95% CI: 1.17, 1.44).

The Netherlands

Marcelis et al., 1998 (32)  
Residence in 646 municipalities categorized in two ways: 1) <500 addresses per km$^2$ and >1,500 addresses per km$^2$; 2) birth in area with highest population density.

All psychoses (ICD-9).


Significant dose-response relation between urbanicity and risk of all psychoses—broadly defined schizophrenia, narrowly defined schizophrenia, affective psychoses, and other psychoses; associations were stronger in more recent birth cohorts and in cases with earlier age of onset.

Results were analyzed to minimize diagnostic misclassification.

Marcelis et al., 1999 (33)  
Exposure status in the three most densely populated areas of the Netherlands, defined by four combinations of place of birth and place of residence at illness onset: nonexposed born–nonexposed resident (NbNr); nonexposed born–exposed resident (NbEr); exposed born–nonexposed resident (EbNr); exposed born–exposed resident (EbEr)

All psychoses (ICD-9).


Risk of broad and narrow schizophrenia was significantly increased among persons exposed to an urban area at birth, regardless of residence area at illness onset; highest in the EbEr group for broad schizophrenia (RR = 2.29, 95% CI: 1.64, 3.22).

Effect of urbanicity seemed to operate before the time of illness onset.
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<tr>
<th>Country, author(s), and year (ref. no.)</th>
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<tr>
<td>Sweden</td>
<td>Nine categories of urbanicity: main city; suburb of main city; large city (population 50,000–200,000); medium city (population 20,000–50,000); industrial municipality with &gt;40% employed in industrial sector (irrespective of size); other large municipality (population 15,000–50,000); rural municipality; sparsely populated area; other municipality (population &lt;15,000)</td>
<td>Nonaffective psychosis and schizophrenia (ICD-9 or ICD-10)</td>
<td>Population-based cohort study; study of administrative incidence among 696,025 persons born in 1973–1980 who were followed during 1989–1997</td>
<td>Adjusted for age and sex; incidence of nonaffective psychosis was highest in sparsely populated areas (hazard ratio = 2.32, 95% CI: 1.15, 4.66) and significantly elevated in main cities, suburbs, large cities, industrial municipalities, and other large municipalities; incidence of schizophrenia was highest in main cities (hazard ratio = 1.63, 95% CI: 0.90, 2.95), though not significantly elevated in any area; associations were not mediated by obstetric complications or maternal education</td>
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### Finland

**Haukka et al., 2001 (47)**

559 municipalities, classified into 57 functional small areas

**Schizophrenia (ICD-8 or ICD-9)**

Birth cohort study of administrative incidence; persons born in 1950–1969 who were followed during 1969–1991

Significant variation in incidence by place of birth; significant clustering in eastern Finland; higher incidence in males than in females (RR = 1.28, 95% CI: 1.24, 1.33); incidence was increased in every age band except 36–41 years and was highest in the age category 12–22 years (RR = 2.35, 95% CI: 2.19, 2.51); incidence declined between the 1950s cohort and the 1960s cohort; significant interactions were found between sex and age, urban-rural birth and birth cohort (risk was higher in rural areas for 1950–1954 cohort, higher in urban areas for 1964–1969 cohort), and age and cohort

### United Kingdom

**Boardman et al., 1997 (60)**

71 electoral wards in North Staffordshire

**Psychotic disorders (ICD-9)**

Ecologic study of administrative incidence, 1987–1993

Heterogeneity in rates of psychosis; incidence of psychotic disorders was significantly related to areas of deprivation (adjusted $R^2 = 0.68$, 95% CI: 0.45, 0.83) in a random sample of 36 wards

1999 census was used; other mental disorders were examined; rates of nonpsychotic disorders were slightly more associated with deprivation than psychosis

**Croudace et al., 2000 (61)**

104 electoral wards in Nottingham

**Psychosis (ICD-10)**

Administrative incidence study, 1992–1993

Nonlinear relation between ward-level social deprivation and administrative incidence of psychosis (Spearman's $\rho = 0.44$)

Primarily a test of the Mental Illness Needs Index, used to predict population prevalence of mental health-related hospital admissions; 1991 census was used for neighborhood boundaries and characteristics

**Boydell et al., 2001 (63)**

15 electoral wards in London borough of Camberwell

All psychotic illness (ICD-9 or ICD-10); Research Diagnostic Criteria were employed

Multilevel ecologic study of administrative incidence, 1988–1997

Inverse dose-response relation observed between proportion of non-White ethnic minority groups in wards and administrative incidence of schizophrenia in such groups, compared with majority White population, after adjustment for age, sex, and ward deprivation (in highest tertile, IRR = 2.38, 95% CI: 1.49, 3.79; in middle tertile, IRR = 3.63, 95% CI: 2.38, 5.54; in lowest tertile, IRR = 4.4, 95% CI: 2.49, 7.75)

Proportion of non-White ethnic minorities in wards was divided into tertiles (lowest tertile proportion, 8–22.8%; middle tertile proportion, 23–28.1%; highest tertile proportion, 28.2–57%); addresses at first contact were used to place individuals in wards

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<tr>
<td>Allardyce et al., 2005 (64)</td>
<td>Postcodes in Scotland</td>
<td>Schizophrenia; schizoaffective disorder; delusional disorder; mania; acute, transient, or unspecified psychotic disorder; or drug-induced disorder (ICD-9)</td>
<td>Population-based study of administrative incidence, 1989–1993</td>
<td>Areas with high social fragmentation had higher incidence of psychosis than areas with low social fragmentation, independently of deprivation and urbanicity (OR = 12.8, 95% CI: 5.7, 28.9); dose-response relation was observed between social fragmentation and rates of psychosis; no statistically significant interaction between social fragmentation, deprivation, and urbanicity</td>
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<td>Kirkbride et al., 2007 (66)</td>
<td>33 CAS wards in South East London</td>
<td>All psychoses (ICD-10)</td>
<td>Population-based case-control study of administrative incidence, 1997–1999; CAS wards from the 2001 census were used to estimate population at risk</td>
<td>Indirectly standardized for age, sex, and ethnicity; significant heterogeneity in risks of broad and nonaffective psychoses but not for affective psychoses; results were not explained by individual-level factors</td>
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<tr>
<td>Kirkbride et al., 2007 (68)</td>
<td>33 CAS wards in South East London</td>
<td>All psychoses (ICD-10)</td>
<td>Population-based case-control study of administrative incidence, 1997–1999; CAS wards from the 2001 census were used to estimate population at risk</td>
<td>Significant neighborhood variation was found for schizophrenia, which remained after adjustment for individual-level age, sex, and ethnicity; this accounted for 23% of variation in incidence rates; social capital was significantly inversely related to incidence of schizophrenia and other nonaffective psychoses; ethnic fragmentation was significantly directly related to incidence of schizophrenia but not other nonaffective psychoses, while population density and ethnic density were not; no evidence of interaction between neighborhood-level ethnic density and individual ethnicity</td>
<td>Ethic fragmentation (i.e., ethnic segregation) was estimated using the Index of Dissimilarity; neighborhood deprivation was estimated using the Index of Multiple Deprivation from geographic levels above and below the ward level; social capital was estimated by voter turnout in wards</td>
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<td>The Netherlands van Os et al., 2000 (62)</td>
<td>35 neighborhoods in Maastricht</td>
<td>Schizophrenia and related disorders (ICD-9)</td>
<td>Multilevel study of administrative incidence, 1986–1997</td>
<td>After adjustment for individual-level characteristics, risk of schizophrenia was significantly related to proportion single (RR = 1.02, 95% CI: 1.00, 1.03; p = 0.013) and proportion divorced (RR = 1.12, 95% CI: 1.04, 1.21; p = 0.003) in the neighborhood; after adjustment for individual-level characteristics, neighborhood-level welfare dependency, foreign birth, and unemployment were also significantly related to risk</td>
<td>Six small and industrial neighborhoods were excluded; neighborhood characteristics were obtained from the municipal authority; neighborhood-level effects were treated as both random and fixed, while individual-level effects were fixed</td>
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<td>Study</td>
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<tr>
<td>Drukker et al., 2006 (65)</td>
<td>36 residential neighborhoods in Maastricht</td>
<td>Schizophrenia (DSM-IV)</td>
<td>Multilevel case-control study of cumulative administrative incidence, 1998–2002</td>
<td>Neither neighborhood-level deprivation nor social capital was associated with administrative incidence; there was an inverse relation between individual-level socioeconomic status and administrative incidence. Address at first contact was used to define neighborhood residence; individual-level socioeconomic status was extracted from the psychiatric case register.</td>
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<tr>
<td>Veling et al., 2008 (72)</td>
<td>44 neighborhoods in The Hague</td>
<td>Schizophrenia (DSM-IV)</td>
<td>Multilevel study of administrative incidence, 1997–1999, 2000–2005</td>
<td>After adjustment for neighborhood socioeconomic deprivation, IRRs were significantly lower for immigrants living in high-ethnic-density neighborhoods (IRR = 1.25, 95% CI: 0.66, 2.37) than for those living in low-ethnic-density neighborhoods (IRR = 2.36, 95% CI: 1.89, 2.95).</td>
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<tr>
<td>Germany</td>
<td>23 districts in Mannheim and 14 districts in Heidelberg</td>
<td>Schizophrenia (ICD-9)</td>
<td>Population-based ecologic study of administrative incidence, 1987–1989</td>
<td>Results were compared with those from previous studies in Mannheim; incidence of schizophrenia remained stable over 25 years; highest concentration of schizophrenia was seen in the inner city in poor and unfavorable living conditions; individual biographies indicated that social drift begins to take place long before first admission.</td>
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<tr>
<td>Sweden</td>
<td>8,482 SAMS areas</td>
<td>Psychosis (ICD-9 or ICD-10)</td>
<td>Population-based study of administrative incidence in entire population aged 25–64 years ((n = 4,516,787)), followed from 1997 to occurrence of an event (hospital admission, death, or emigration) or study’s end in 1999</td>
<td>Dose-response relation between neighborhood-level deprivation and rates of psychosis; inverse linear relation between linking social capital and rates of psychosis (highest in low-social-capital areas: for males, OR = 2.89, 95% CI: 2.72, 3.07; for females, OR = 2.62, 95% CI: 2.47, 2.78); low-linking social capital at the neighborhood level remained significantly associated with risk of psychosis after adjustment for individual-level variables and neighborhood-level deprivation.</td>
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*ICD:* International Classification of Diseases; RR, relative risk; CI, confidence interval; OR, odds ratio; SAMS, small-area market statistics; DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition; CAS, Census Area Statistics; IRR, incidence rate ratio.
infection, toxins, or nutrition. Furthermore, more robust effects have been reported in early-onset cases (32, 35, 82) and in males (42, 82), though contrary reports (34) exist with respect to sex.

Other factors have been examined as potential mediators of the urbanicity effect. Neither obstetric complications (35, 41) nor childhood socioeconomic circumstances (41) appear to mediate the risk of psychosis conferred by urbanicity. Likewise, according to one report (45), traffic-related pollution in urban areas does not seem to mediate the association. However, these few reports cannot be considered to rule out such explanations entirely; more work addressing potential mediators is much needed in the urbanicity literature.

In sum, the urbanicity literature reviewed here creates a pattern of findings that does not seem attributable to either reverse causation or service utilization. The timing, consistency, and dose-response relation reported in some studies provide evidence for an etiologic effect of urbanicity. Overall, the studies of urbanicity concerned with causation support a hypothesis that exposure at some point early in the life course could play a role in the etiology of psychosis, yet the explanation for the apparently psychotogenic effect of urban life remains unknown. This literature demonstrates the need for theory to inform investigations of mediators of the urbanicity effect, ideally employing competing hypotheses. As is discussed below, further research might more directly measure and examine both physical (e.g., toxins, infections, and nutrition) and social exposures, as well as characteristics of and changes in urban social context itself over time, and their respective impact on the development of psychosis in a diverse range of settings.

**Variation by neighborhood**

In 24 studies, investigators directly compared the incidence of psychosis among neighborhoods and/or examined specific neighborhood-level characteristics in relation to the incidence of psychosis (49–72). Nineteen studies (49, 53–55, 58–72) were returned in our database search, and five additional studies were included because they were referenced (50–52, 56, 57) in one of the articles returned. Most studies were conducted in Western Europe: 11 presented results from studies conducted in England (50, 51, 54, 58–61, 63, 66, 68, 69), four from Germany (55–57, 71), three from the Netherlands (62, 65, 72), and one each from Scotland (64) and Sweden (67). Four studies were carried out in the United States (49, 52, 53, 70).

Like studies of urbanicity, neighborhood studies have relied on administrative geographic units. Neighborhood boundaries in this literature have been formed most commonly by community analogs such as districts, electoral wards, municipalities, and tracts. In very few studies (69, 72) were neighborhoods constructed on the basis of similarity of social characteristics, although these, too, relied on administrative units as bases. One of the limitations of exposure definition is thus the fact that administrative units serve as crude proxies for neighborhoods as they are defined and experienced in the lives of their constituents.

Compared with studies of urbanicity, far fewer neighborhood studies have systematically examined the timing of exposure. Thus, as a group, neighborhood studies are more vulnerable to interpretations of drift across places. Only two studies (52, 58) measured neighborhood both at birth and at illness onset. The most complete assessment of timing was made by Dauncey et al. (58), who also examined neighborhood during childhood and adolescence to address questions regarding lifelong residential mobility. A third study conducted by Veling et al. (72) measured neighborhood at illness onset, and also accounted for drift by determining whether cases were residing in their parental home at first treatment contact. All other studies assessed neighborhood at first treatment contact and could not entirely dismiss drift as an explanation for variation in rates of psychosis. To date, no neighborhood studies have directly examined the duration of exposure in relation to psychosis. In order to determine whether exposure to or living in certain neighborhoods is important in the etiology of psychosis, the timing and duration of exposure must be systematically examined; absence of this systematic evaluation constitutes a primary limitation of the neighborhood literature.

Investigators in a number of studies reported spatial variation in psychoses at the neighborhood level. Aside from drift and selection, which cannot be eliminated conclusively as an explanation in many analyses, what can explain the reported variation in rates? The neighborhood literature, which has relied more on social theory to inform analyses, offers some of the most intriguing evidence that the variation may be due to group-level social processes. One signal, ripe for further investigation in a range of settings, comes from research regarding neighborhood composition; such investigations lie at the crossroads of spatial variation, immigration, and ethnicity. In three studies included in this review, researchers reported a significant protective effect of ethnic density (i.e., percent composition of persons of a given ethnicity in a geographic area) (53, 63, 72), consistent with the initial findings of Faris and Dunham (14). An early study of Italian Americans conducted by Schwartz and Mintz (53) in Boston, Massachusetts, neighborhoods found that rates of schizophrenia among Italian Americans were lower in communities with higher proportions of Italian-American residents. Two more recent studies provided even stronger evidence that the protective effect conferred by ethnic density is both social and group-level. In the African-Caribbean population in South East London, Boydell et al. (63) found an inverse linear relation between ethnic density and rates of schizophrenia that remained even after adjustment for neighborhood-level deprivation. A multilevel analysis conducted by Veling et al. (72) in The Hague, Netherlands, also found that ethnic density conferred a significant protective effect, even in the most deprived areas. Recently, investigators in several studies have examined other neighborhood-level social structural correlates of ethnicity, such as ethnic fragmentation (i.e., segregation), and have found direct relations with psychosis (64, 68).

Other findings also suggest that the nature of neighborhood social ties may be related to the distribution of psychosis. The earliest relevant report included in this review is that of Jaco (49), who found direct relations between several indicators of social isolation in communities in Texas and high rates of schizophrenia, which accords with other
evidence (83). More recently, social capital—community-level characteristics that foster participation for mutual benefit—has been tested by several investigators (65, 67, 68). In two (67, 68) of the three studies, researchers found significant inverse relations between social capital and incidence of psychosis; in one report (68), this included both schizophrenia and other nonaffective psychoses. These results remained significant after adjustment for individual-level variables and neighborhood-level deprivation.

It is unclear whether, at the neighborhood level, population density is related to risk of psychosis. A classic study conducted by Hare (51) found a significant relation between population density and psychosis in neighborhoods in Bristol, United Kingdom, while a more recent study by Kirkbride et al. (66) in South East London did not. Temporality could not be established, and thus ambiguity at the level of neighborhood remains.

A number of other neighborhood characteristics have been examined in relation to psychosis. The most commonly examined in these studies was socioeconomic deprivation, the factor most subject to drift across places. In nine studies (52, 58–61, 64, 65, 67, 71), researchers directly examined the association with deprivation; overall, the studies suggested a relation between neighborhood-level deprivation and incidence of psychosis. One early study in the United States found the overwhelming majority of schizophrenia incidence in neighborhoods that were in the lowest half of their socioeconomic categories (52). Another investigation in Nottingham, United Kingdom, found the rate of schizophrenia in the most deprived neighborhoods to be nearly three times that in the least deprived areas (58). Two other recent studies conducted in Sweden (67) and Scotland (64) found a linear relation between neighborhood-level deprivation and rates of psychosis. In another study conducted in Nottingham, Croudace et al. (61) demonstrated an excess incidence (i.e., a higher proportion than expected) of psychosis in neighborhoods with above-average social deprivation, which suggests a possible threshold effect. Only one analysis of data collected in the Netherlands failed to find an association between neighborhood-level deprivation, defined at first contact, and incidence of schizophrenia (65). Together, these findings suggest that neighborhood deprivation is related to heterogeneity in rates of psychosis. However, these results are still subject to a drift interpretation, because people might have moved into deprived neighborhoods before first contact for treatment.

As suggested by studies addressing socioeconomic deprivation, some findings (e.g., ethnic density, social isolation) in the neighborhood literature may be more prominent for schizophrenia; for other psychoses, the association is less clear. Some neighborhood studies also hint at spatial patterning of schizophrenia. Kirkbride et al. (61) recently demonstrated significant neighborhood variation in incidence rates of schizophrenia, but not affective psychoses, in the concentrated urban area of South East London, and they reported that the observed variation was not due to individual-level factors, which accords with some urbanicity studies (35, 46). Consistent with the findings of Faris and Dunham (14), investigators in several earlier studies reported the highest concentration of schizophrenia to be in the inner city (54, 56, 57); stability in spatial patterning has been reported in Mannheim, Germany (56), though this remains relatively unexplored in other locations. As with other findings in the literature reviewed here, drift across places is a plausible explanation for the findings suggesting spatial patterning at the neighborhood level.

To summarize, the great majority of these studies report heterogeneity in incidence rates of psychosis at the neighborhood level in developed countries. Among the most intriguing findings in the neighborhood literature are those reported from studies of ethnic density. These findings indicate an interaction between the individual context and the social context, and they offer the possibility of a group-level social explanation for spatial variation, as opposed to an effect mediated by purely material factors, such as toxins. Moreover, these findings are also the least vulnerable to drift and selection interpretations, which pose barriers to causal inference in the neighborhood literature reviewed here. If drift or selection were an explanation, one might expect an increase in psychosis rates in high-ethnic-density, socioeconomically deprived areas; however, studies of ethnic density show a fairly consistent protective effect, which is more consistent with social causation. The measurement of exposure—both timing and duration—constitutes one of the primary limitations of neighborhood-level studies of psychosis incidence. While the use of administrative boundaries to define neighborhoods enables this sort of research, such boundaries do not necessarily capture neighborhoods as they are experienced and shaped by their inhabitants. One of the strengths of the neighborhood studies reviewed here is the employment of social theory to define constructs that form the basis for the definition of covariates. Social context itself has been measured in greater detail; a corollary strength is that social groups have been examined within neighborhoods, which helps shape our etiologic knowledge about social processes themselves.

DISCUSSION

In developed countries, spatial variation in rates of psychosis appears to be common in studies of both urban areas and neighborhoods. However, several differences exist between these two domains. The most basic distinction is that urbanicity is usually a broad and undifferentiated construct, which permits only general conclusions about the etiologic role of urban living; the neighborhood literature, in contrast, consists of studies of specific contextual factors—narrower constructs, such as ethnic density and social capital. Another notable difference is the statistical approach employed to model variation. In studies of urbanicity, variation is often modeled as a few parameters in the mean specification, which permits estimation of the direction of the variation. The mean is not specified in neighborhood studies in which all variation is modeled—except those that specify a variable (e.g., percent minority composition)—thus, estimation of its direction is prohibited (see Torrey et al. (48) for a comparison). Finally, the findings from each arena are distinct. Urbanicity studies point to early life as a period of elevated risk. Evidence largely from neighborhood investigations

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indicates that both risk and protective social factors at the group and individual levels may be etiologically relevant. Though they both suggest that social context might play a role in etiology, each domain is subject to methodological limitations, particularly inconsistent use of designs that permit the determination of causal direction and eliminate selection and drift as potential explanations for observed spatial variation.

An interesting finding noted here and observed consistently for nearly 70 years is the spatiality of nonaffective psychoses and the apparent absence of spatiality of affective psychoses. In this review, we have observed that this finding holds both between settings (46) and within settings (14, 66). While both disorders have been associated with ethnic minority status (78), putative explanations for factors associated with nonaffective psychosis, specifically schizophrenia—such as ethnic density (63, 72) and societal-level discrimination (84)—are inherently spatial. Still, whether these two broad sets of disorders are etiologically distinct per their respective spatial distributions remains to be conclusively established. It is possible that unspecified factors at other levels (e.g., the family) may explain the distinction between affective and nonaffective psychoses. Given the phenomenological overlap with affective psychoses, studies of common mental disorders may offer clues: After accounting for individual- and family-level variation, researchers have consistently failed to observe significant neighborhood-level variation (85, 86). Understanding the full specification of effects across multiple levels of organization in psychosis research may offer parallel insights with respect to spatial variation.

### Social pathways: from space to place

The findings highlighted in this review beg further characterization of social and contextual factors, as we simply do not know what processes produce the observed associations, or at what level. In studies of the spatial variation of psychosis, two distinct questions are often conflated, which complicates the determination of causality. The first question, whether there is spatial heterogeneity of the outcome, is a descriptive question that is particularly important for establishing the demand for psychiatric services. Processes of group-level selection and individual-level drift probably contribute to spatial heterogeneity of psychosis, though each has been assessed largely in cross-sectional studies. The second, whether exposure either to or in certain conditions (e.g., urban environs) produces variation in the outcome, is the central etiologic question. Answering this question is challenging and requires understanding of the conditions produced by broader social processes; characterization of specific social and contextual factors and knowledge of the interrelations between factors that form social processes is essential. The multilevel processes responsible for spatial variation in psychosis operate alongside those that produce conditions resulting in relevant exposures, and may overlap. As a result, disentangling extant evidence to answer the etiologic question is difficult.

However, this inherently challenging problem and the limitations of the studies reviewed here can be minimized if not overcome. One possibility for future research is to focus on key social pathways—the social processes by which exposures of interest are created and maintained—that may affect the development of psychosis. Social pathways comprise cascades of social processes across multiple levels that produce a variety of conditions in a given place, which shape exposures more proximal to the individual (87).

Place, then, is broadly defined as a reservoir of risk or resilience. As a reservoir, place consists of the natural and built environment, physical structures, and material resources that shape experience within a designated geographic location. The physical and social architecture of place both shapes and reflects relationships among individual inhabitants, social groups, and social structures and institutions. Place thus harbors the dynamics of power, varies by culture, and changes over time. Given these characteristics, the study of social pathways requires consideration of place, since both risk and protective factors accumulate therein.

Social pathways might operate etiologically in two ways, which are not mutually exclusive. First, social processes might create conditions that ultimately result in physical exposures. For instance, as a number of authors have hypothesized, the association between urban birth and psychosis could be attributable in part to exposure to infection during gestation. Large-scale social processes of migration into and urbanization in a range of social, political, and economic contexts could produce a variety of conditions, including crowding, which could increase person-to-person contact and thereby alter the dynamics of infectious disease transmission. Therefore, a pregnant woman living in crowded conditions is more likely to be exposed to infections, such as influenza, that have been associated with adult-onset psychosis in offspring (88–91). Similarly, living in a deprived neighborhood could increase risk of psychosis through exposure to pollutants or toxins (45). Structural discrimination and its associated social processes relegate members of minority groups and/or lower social classes to living in neighborhoods with unhealthy conditions—for example, proximity to highways, landfills, and other potential sources of pollutants and toxins (92–94).

Second, social processes might operate directly, in the absence of physical exposures. Studies of ethnic density suggest social processes resulting in exposures more proximal to the individual that are social, as opposed to physical, in nature. Ethnic density could confer a protective effect with respect to psychosis through group-level social cohesion that provides a buffer against interpersonal discrimination and social exclusion, which may be etiologically important (84). Ethnic density might also partially provide a buffer against structural discrimination, since its protective effect seems to hold even in the most deprived neighborhoods (63, 72). Ultimately, whether social pathways result in individual-level exposure that is physical or social in nature, social processes at some level are etiologically important.

### Research strategies

Understanding social pathways, and therefore relevant exposures, requires systematic investigation of social processes and the conditions they create in a given place at a particular
period in time. Integration of the life course perspective (95) to better understand both critical and sensitive periods of exposure (96) is also necessary (97). For example, a number of urbanicity studies indicate that early life may be the critical time of exposure with respect to psychosis, meaning that urbanicity—or whatever exposure is truly operative—cannot have an etiologic effect later in life. However, urbanicity or the factor(s) responsible for the observed associations may also operate as a precipitating factor closer to illness onset (98), and thus early life may be a sensitive period—a period during which risk is simply greater. In contrast, little is known about the relevant timing of exposure in the neighborhood investigations of psychosis reviewed here. For instance, studies of ethnic density have examined exposure around the time of illness onset (63, 72), although the observed protective effect might be exerted much earlier in life, either during gestation or during childhood and adolescence.

Although determining the relevant timing of exposure poses an enormous challenge, it is possible with longitudinal birth cohort data that can be linked to area characteristics, such as population density or neighborhood ethnic density, over the life course. Using this type of data would permit assessments of whether changes in context itself matter, especially for persons living for extended periods in one place that changes over time. It would also facilitate assessments of whether residential mobility matters. However, two circumstances must be considered: Contexts change at various rates, and people move, both within and between contexts, at different rates. Examining prospective population data in urban areas before and after the influence of key social processes, such as urban development or renewal and changing racial or ethnic composition, could enrich our understanding of the relative impact of these processes.

Both risk and protective social factors in psychosis research could be examined more rigorously over the life course with the assistance of theory, much as the study of complicated factors in developmental psychopathology has been (99). Classical studies of psychosis tested theories to better understand etiology. For example, Faris and Dunham (14) examined social organization, while Jaco (49) and others (83) explored social isolation as potential explanations for psychosis. In recent studies, such as those that have examined the relation between social capital and psychosis (65, 67, 68, 100), investigators have begun to employ social theory to understand risk and protective factors. This could be explored further to distinguish among the group-level construct (101), the individual-level conceptualization (102), and other seemingly distinct constructs (e.g., social fragmentation and social isolation).

If grounded in theory and integrated with the life-course perspective, the study of social pathways could capitalize on conceptual and methodological advances to help investigators determine whether and how certain places act as reservoirs of risk for—or protection from—psychosis. We could determine the conditions under which the exposures ultimately produced by social pathways might give rise to different predictions; both between- and within-location and social group strategies might be employed gainfully (103), and differential spatial distributions of affective and non-affective psychoses could be probed further. Moving beyond the question of whether spatial heterogeneity exists in the outcome to the more difficult question of whether place-based social processes are etiologically relevant would effectively constitute a conceptual shift from space to place. Such a shift could offer a dual advantage: By understanding how social processes at various levels of organization create the conditions in a given place that shape individual-level exposures, whether physical or social, we could better characterize etiologically relevant exposures and uncover potential points of public health intervention.

Once we have a better handle on what social processes result in etiologically relevant exposures, we can systematically integrate this with investigations of the distribution of psychoses across places to better understand spatial variation in the outcome. In this way, we will be better able to understand how processes of social causation operate with processes of social selection and drift to produce observed distributions of various psychoses across social strata, geographic locations, and time periods.

The study of social pathways should not be viewed as an alternative to studying biologic pathways. Rather, the two are complimentary. One particularly accessible example is the well-documented association between paternal age at conception and schizophrenia in offspring (104–111). Societal norms shape paternal age at conception; links between paternal age and de novo mutations have been put forward to explain the reported relation to schizophrenia (105, 109, 112).

Studying how various social processes create certain conditions in a given place—essentially, how exposures become emplaced—could be a fruitful strategy for understanding social causes, whether they result in more proximal physical or social exposures. Furthermore, investigation of the nature and timing of exposure to putative social causes could point to potential biologic mechanisms, including gene-environment interactions (80), de novo mutations (112), and epigenetics (113), among others. Understanding how what is emplaced ultimately becomes embodied could facilitate the integration of social and biologic knowledge, and thus elucidation of the full range and sequence of causes of psychosis and potential points of intervention.

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REFERENCES

March et al.

31. Eldar J, Pedersen CB, Mortensen PB. Are the cause(s) responsible for urban-rural differences in schizophrenia risk rooted in families or in individuals? Am J Epidemiol 2006;163:971–8.
34. Torrey EF, Mortensen PB, Pedersen CB, et al. The influence of sex, urbanicity, migrant status and method.


