Urban-rural differences in major mental health conditions

Francesca Solmi,[1] Jennifer Dykxhoorn,[1] James B. Kirkbride[1]*

[1]PsyLife Research Group, Division of Psychiatry, UCL, London, W1T 7NF, UK

*Correspondence to: Dr James B Kirkbride, j.kirkbride@ucl.ac.uk

Word count: 8,395

Keywords: Schizophrenia, psychotic disorders, common mental disorders, depression, anxiety, suicide, rural-urban, epidemiology

Author biographies

Dr Francesca Solmi is a Research Associate in psychiatric epidemiology in the PsyLife group, Division of Psychiatry, UCL. She is interested in researching life course risk factors of various mental health problems in childhood, adolescence and young adulthood as well as ways to improve access to mental health services.

Jennifer Dykxhoorn is a PhD student in the PsyLife Lab, Division of Psychiatry, UCL. Her research focuses on social and spatial determinants of psychotic disorders. She has a background in public mental health policy, having previously worked for the Public Health Agency of Canada and Mental Health Commission of Canada.

Dr James Kirkbride is a Reader in Epidemiology in the Division of Psychiatry, UCL. He specialises in investigating the determinants of excess risk of schizophrenia and other psychotic disorders experienced by urban populations and ethnic minority groups. He runs the PsyLife group (www.PsyLife.eu) in the Division of Psychiatry, UCL.

Abstract

In this chapter we review the evidence for rural-urban and spatial variation of three major sets of mental health disorders: schizophrenia and related psychotic disorders; common mental disorders including depression and anxiety, and; suicide. For each, we review the recent literature which has addressed these issues and report the main strengths and limitations of the available evidence. The most consistent evidence for rural-urban gradients in mental health risk are found to exist for schizophrenia and suicide, with more mixed evidence in relation to common mental disorders. For schizophrenia and suicide we go onto review the major hypotheses that have been put forward to account for rural-urban variation in risk.

1 Introduction

How the social and physical environment may affect our mental health – both positively and negatively – is a topic of increasing global importance. By 2014, more than half of the world's population lived in urban areas, and this is set to rise to a staggering 66% by 2050. In this chapter, we examine the potential mental health implications that this global shift towards living in urbanised environments may have at the population level. We have restricted our analysis to three major psychiatric conditions, where most research has been conducted: psychotic disorders, including schizophrenia; common mental disorders i.e. depression and anxiety; and suicide. We have organised the chapter into four main sections. First, we review the current evidence linking psychotic disorders to our urban environments. We identify the main hypotheses which have been proposed to explain such associations and review their plausibility, given the available evidence. We repeat this analysis for common mental disorders in Section 3, and for suicidal outcomes in Section 4. In the final section, our focus turns to consider the extent to which the evidence presented in this chapter informs possible preventive medicine strategies with respect to our urban environments.

For each mental health outcome, we have distinguished between studies which examine urban-rural differences in risk, and those which have provided more detailed examination of small area variation in the rate at which psychiatric conditions occur. These second set of studies have often sought to move beyond rural-urban dichotomies to investigate how differences in the environmental milieu of small areas – or "neighbourhoods" – within a single setting may affect the risk of mental health disorders. Such effects are typically studied using a variety of "multilevel" statistical approaches which are designed to examine whether risk factors which occur at several levels of causation, including both the individual- and neighbourhood-level – are associated with a given outcome of interest. Typically, such small areas have been defined by administrative units to investigate "neighbourhood-level" effects. While the extent to which these represent meaningful neighbourhoods as perceived by their occupants has been debated,[1] small area units typically provide a more homogeneous and precise basis for analytical investigation than simpler rural-urban distinctions. Although primarily used for administrative purposes, such as Census enumeration or elections, area-level units such as postcode tracts, census wards or postal areas are often demarcated by physical barriers such as major roads, rivers or other topographical features, providing some ecological validity to their "neighbourhood" status.

The best data we have on the role cities play in shaping mental health presently come from High Income Country (HIC) settings. The paucity of data on mental health and urbanisation from Low and

Middle Income Country (LAMIC) settings, where economic development, basic services and physical health care may present more fundamental topics for service providers and urban planners, reflects an important gap in the literature. It also presents an opportunity to carefully tailor the best available evidence on mental health and city life from other settings into policy and planning recommendations for the design of mentally healthy cities. Since it has been suggested that population dynamics and urban development trajectories will differ in LAMIC settings,[2] this calls on researchers and funding bodies to invest time, energy and capital into research programs which identify the burden and correlates of psychiatric morbidity in rapidly developing populations. For this reason, in this chapter we endeavour to make special reference to any studies conducted in LAMIC settings, where pertinent and robust evidence is available.

2 Schizophrenia and other non-affective psychoses

Schizophrenia affects between 4.6 (range: 1.9 – 10.0), 3.3 (range: 1.3–8.2) and 4.0 (range: 1.6 – 12.1) people per 1000, depending on whether measured at a single point in time (point prevalence), over the course of a year (annual or period prevalence) or over the entire lifetime (lifetime prevalence) is considered.[3] Incidence, which describes the number of *new* cases within a defined population in one year, is estimated to be appromxitely 15.2 new cases per 100,000 people per year (range: 7.7 – 43.0).[4] However, incidence is heterogeneously distributed throughout the population according to several socio-demographic indicators,[5] including age, sex, ethnicity and place. Schizophrenia and related disorders are more common among men, young adults (before 35 years old) and people from disadvantaged socio-economic backgrounds.[6] Consistent evidence suggests that higher rates are experienced by people from minority ethnic backgrounds, most notably those of black African and black Caribbean origin living in the UK, Netherlands and elsewhere.[7–10] A long history of research, beginning with the pioneering work of two Chicago sociologists Robert E.L. Faris and Warren H. Dunham in the 1930s, have shown that the distribution of the incidence of schizophrenia and other non-affective psychoses is not random, but occurs with greater-than-expected frequency in more densely populated urban settings.[11] Such geographical patterning exists between countries[12], within countries along a urban-rural gradient,[13,14] and between neighbourhoods within urban areas.[13] Over the last 70 years, spatial variation in the incidence of non-affective psychotic disorders such as schizophrenia has been replicated in a number of early[15–17] and more recent studies (Tables 1 & 2 summarise those studies published since 1990).

2.1 Urban vs. rural settings

Perhaps owing to the presence of comprehensive population and hospital registers, Western Europe has provided the setting for the vast majority of the forty studies which have investigated urban-rural differences in the distribution of psychosis since 1990 (Table 1),[5,18–46] with thirteen studies in Denmark,[23–25,27,30,31,37–40,42,44,46] four in The Netherlands,[21,22,32,34] three in Sweden,[18,33,35] three in the UK,[5,20,36] two in Finland, [26,29] two in Ireland,[28,41] one in Italy,[19] one in Spain,[45] and one in France[43]; one study was conducted in Israel.[47] In comparison, research from developing countries has been more sparse.[48–54]

Urbanicity has commonly been defined by grouping geographical areas from the most rural to the most urban on the basis of population density,[21,22,35,47] degree of urbanization,[5,18,23–25,27,30,31,33,36–40,42–44,46,50,52] density of postal addresses[29,32,34] or a dichotomised urban-rural classification.[19,20,26,28,41,45,48,49,51,53,54] With the exception of an Israeli study, which measured diagnosis at military conscription,[47] urbanicity has been measured at the time of diagnosis,[5,19,24,28,32,34–36,41,43,45,48–51,53,54] birth,[20,23,25–27,29,30,33,37,39,40,42,44,46] birth and upbringing,[22,31,52] birth and diagnosis,[21] or upbringing only.[18,38] While methods used to diagnose participants have varied (see Table 1), many studies used standardised clinical interviews to derive a diagnosis of schizophrenia[5,32,34,41,48,50–54] rather than reliance solely on case records. Many studies simultaneously investigated urbanisation in relation to depression (see also Section 3),[35,50–52] affective psychotic disorders (see Section 2.4),[20,22,25,28,40,43,50,53] and other non-affective psychoses.[21,22,26,33,43,50] Finally, an increasing number of studies have employed longitudinal cohorts[5,18,19,21–24,26,28–31,33,35–37,39,40,42,44,46] (which usually provide stronger, prospective evidence of an association) over other types of study design, including cross- sectional[32,45,48,50–54] (more frequent in LAMIC) or case-control[20,25,27] designs. Despite heterogeneity in design, populations, and definitions of urbanicity and diagnosis, all but eight studies[19,26,29,36,49,51–54] found higher schizophrenia risk in urban compared with rural areas.[5,18,20–25,27,28,30–35,37–48,50,55,56] Of those which did not, three reported no urban-rural differences,[36,51,53] while five observed higher rates in rural areas.[19,26,29,49,52,54] Summarising much of the literature from high income countries, a recent meta-analysis estimated that people living in urban areas at birth and upbringing had over twice the odds of developing schizophrenia compared with people living in rural areas (Odds Ratio [OR]: 2.37; 95% confidence interval [95%CI]: 2.01–2.81).[57]

Findings from nine studies conducted in LAMIC countries were less consistent than those reported from High Income countries (see Table 1). Lifetime and 12-month prevalence of schizophrenia seems to be higher in urban areas in Chile (men)[50] and China,[48,55,56] whilst the reverse has been observed in

Table 1: Summary of literature on rural/urban differences in the distribution of schizophrenia (from 1990 onwards, chronologically ordered)

Study ID	Diagnostic criteria & outcome	Case ascertain-ment	Sample size	Definition of urban	Timing of urban	Findings	Confounders	Comments
Lewis et al[18] (1992) Sweden	ICD-8 (schizophrenia)	Register	Sample = 49,191 (male conscripts) Cases = 268	Degree of urbanization	Upbringing	Higher odds of schizophrenia in men who grew up in the city	Family finances, cannabis use, psychiatric diagnosis at conscription, parental divorce, number of friends, 'nervous' feelings, family history of schizophrenia.	Fully-adjusted model showed weaker statistical signficiance between urban & rural risk
Thornicroft et al[19] (1993) Italy	ICD-9 (schizophrenia & other psychoses, including affective)	Registers	Not reported	Urban vs. rural	At diagnosis	Higher prevalence & incidence rates in the rural compared with urban areas	Household composition, employment, population density, number of dependents, number of family members economically inactive, age, number of rooms per person	Living alone, being unemployed, % total population who unmarried, separated or divorced were associated with schizophrenia in urban, but nor rural area
Takei et al[20] (1995) UK	ICD-9 (schizophrenia)	Registers	Sample= 24,858 Cases=6,553	Urban vs. rural	Birth	Risk of schizophrenia higher for people born in urban areas & autumn/winter months	Age, sex, place of birth	Poor control group (psychiatric controls), cross-sectional data
Marcelis et al[22] (1998) The Netherlands	ICD-9 (narrow schizophrenia, broad schizophrenia)	Registers	N=47,721 Narrow schizophrenia (NS) (N=5606) Broad schizophrenia (BS) (N=16716)	Urban vs. rural (based on population density)	Birth & upbringing	People with urban birth & urban exposure had higher risk of narrow & broad schizophrenia	Birth cohort, season of birth, age of onset	High correlation between urban birth & urban exposure. Unable to test for incidence among people born in urban areas who moved to rural areas Similar pattern for affective psychoses
Marcelis et al[21] (1999) The Netherlands)	ICD-9 (narrow schizophrenia, broad schizophrenia)	Registers	N=1,351,637 (N= 338, Narrow schizophrenia; N=766, Broad schizophrenia)	Urban vs. rural (based on population density)	Birth & admission	People born in urban areas had highest risk of schizophrenia. People born in rural environment & admitted in urban ones were at no greater risk *cf.* people born & admitted in rural areas		Findings validate the hypothesis that being born & raised in urban environment affects risk of schizophrenia
Mortensen et al[23] (1999) Denmark	ICD-8 (schizophrenia)	Registers	N=1,750,000 (N= 2,699 with schizophrenia)	Degree of urbanization	Birth	Highest risk in those born in the capital *cf.* rural area, with gradient in risk by degree of urbanisation of birthplace	Age, sex, calendar month at diagnosis, maternal & paternal age at child's birth, family history of schizophrenia	

Study ID	Diagnostic criteria & outcome	Case ascertain-ment	Sample size	Definition of urban	Timing of urban	Findings	Confounders	Comments
Eaton et al[25] (2000) Denmark	ICD (schizophrenia, non-affective psychoses, affective psychosis, manic-depressive psychoses)	Registers	33,320 live births at 1 year occurred between 1973-1977 (10% random sample of all live births)	Degree of urbanization.	Birth	Highest odds of schizophrenia & non-affective psychoses with urban birth (capital *cf.* rural areas), with a marked gradient by degree of urbanisation. No differences by urban birth status for affective psychoses	Weight for age, gestational age, mother's age, parity, sex, birth year	Sample restricted to those under 21 years; only about 20% of people will have received diagnosis of a non-affective psychosis by then
Schelin et al[24] (2000) Denmark	ICD-8 schizophrenia	Register	2,441 first admissions 1978-82	Degree of urbanization	At diagnosis	Higher incidence (direct standardisation) in the capital & sub-urban areas *cf*. rural areas in males & females. [NB: not formally tested, but 95% CI do not overlap]	Age & sex	People in the capital had higher odds of being diagnosed at the first admissions in the capital, but not in suburban areas *cf.* rural areas.
Suvisaari et al[26] (2000) Finland	ICD-8, ICD-9 schizophrenia	Register (hospital + pension)	Sample = all people born 1950-69. Cases =15,892 patients hospitalised 1970-91	Urban vs. rural	Birth	Lower risk of schizophrenia in urban versus rural areas	Age, sex, month of birth, birth cohort	Only 15-20% of population lived in urban areas over the study period.
Agerbo et al[27] (2001) Denmark	ICD8, schizophrenia	Register	17,604 people. (191 cases admitted 1981-93 & 17,413 controls matched by gender & age)	Degree of urbanization.	Birth	Highest schizophrenia risk in people born in the capital *cf.* people born in rural areas, but no evidence of a gradient by degree of urbanisation	Crowding, family history of schizophrenia (parents & siblings), season of birth	Crowding not associated with schizophrenia, although there might be limitations in choice of measurement
Allardyce et al[28] (2001) Ireland	ICD9 – ICD10, schizophrenia	Register	439 cases diagnosed 1979-84 & 1992-97 (177 in Galloway, 262 in Camberwell)	Dumfries & Galloway, rural areas. Camberwell, inner city area.	At diagnosis	Higher incidence rate ratio in Camberwell *cf.* Dumfries & Galloway	Age, sex, time period	Timing of exposure at diagnosis does not rule out reverse causation
Haukka et al[29] (2001) Finland	ICD8 – ICD9, Schizophrenia	Register	Sample = all people born 1950–1969. Cases=14,828 patients hospitalised before 1992	Density of postal addresses	At birth	Higher schizophrenia risk in rural areas in 1950s, higher risk in urban areas in 1960s	Age, sex, birth year	
Pedersen et al[30] (2001) Denmark	ICD-10 (schizophrenia)	Register	Sample = 2.66 million Danish citizens born 1950-1993. Cases = 10,264 people with schizophrenia	Degree of urbanization.	Birth	Schizophrenia risk highest in the capital area *cf.* rural areas, with a gradient by degree of urbanization	Age, calendar year of diagnosis, history of mental illness in siblings, history of mental illness in parents	Same results found for different sub-groupings of population, by place & time of birth of mother

Study ID	Diagnostic criteria & outcome	Case ascertain-ment	Sample size	Definition of urban	Timing of urban	Findings	Confounders	Comments
Van Os et al[32] (2001) The Netherlands	DSM-III (any psychotic disorder, narrowly & broadly defined psychotic symptoms)	Survey, Diagnostic interview (CIDI)	Sample = 7,076 individuals aged 18-64 years. Cases = 107, any psychotic disorders. Psychotic symptoms = 295, narrow definition; 1,237 broad definition	Degree of urbanization.	At diagnosis	Odds of reporting any outcome were highest in the most urbanised areas, with evidence of a gradient across levels of urbanisation	Age, sex, education, country of birth of participant & parents	People born outside Finland excluded
Pedersen et al[31] (2001a) Denmark	ICD-8, ICD-10 (Schizophrenia)	Register	Sample = 1.89m Danish citizens born 1956-83. (807,000 born after 1971 for analyses on urbanicity during upbringing) Cases = 8,253 people with schizophrenia (1,553 born after 1971)	Degree of urbanization.	Birth & upbringing	People born in the capital had highest schizophrenia risk, with evidence of gradient by urbanisation. Living in a higher degree of urbanisation at age 5 than at birth was associated with higher schizophrenia risk *cf.* having always lived in rural areas. People living in a higher or lower degree of urbanization at age 10 *cf.* age 5 had higher or lower risks	Age, sex, calendar year, history of mental health in parents & siblings	When adjusting for urbanicity at birth & upbringing, the former was no longer significantly associated with schizophrenia risk, although the latter was
Harrison et al[33] (2003) Sweden	ICD-9, ICD-10 Schizophrenia, other non-affective psychoses	Register	Sample = 696,025 people born 1973-1980. Cases = 363 with schizophrenia, 590 with other non-affective psychoses.	Degree of urbanization.	Birth	Risk of non-affective psychoses, but not of schizophrenia was higher for people born in the main cities & their suburbs.	Birth weight, ponderal index, birth length, gestational age, season of birth, age of mother, APGAR score, parity, caesarean section, gender, mother's education	Short follow up means results are generalizable only to early onset cases.
Van Os et al[34] (2003) The Netherlands	DSM-III-R (psychotic disorder, broad & narrow psychosis)	Survey, Diagnostic interview (CIDI)	Sample = 7,076 people, cases = 915 with sub-clinical symptoms, 295 clinical symptoms,	Degree of urbanization.	At diagnosis	Urbanicity was associated with higher risk of psychotic disorder in the proband & a broadly or narrowly defined psychosis in the family	Age, sex, level of education & country of birth of proband, proband's mother, & proband's father & for parental history of delusions or hallucinations or diagnosis	The study found a significant interaction between urbanicity & family history in their effects on psychotic disorder in the proband.

Study ID	Diagnostic criteria & outcome	Case ascertain-ment	Sample size	Definition of urban	Timing of urban	Findings	Confounders	Comments
Byrne et al[46] (2004) Denmark	ICD-8, ICD-10 Schizophrenia	Registers	Sample = 200,294 Cases = 7,704	Degree of urbanization.	At birth	Higher incidence rate ratios of schizophrenia among people born in the capital, capital suburbs & provinces after adjusting for all covariates	Occupation, education, marital status. Father's age at birth, death of a parent prior to admission, number of siblings, reference to father at birth, history of family psychiatric illness	Socio-economic variables measured at time of diagnosis & not at birth
Sundquist et al[35] (2004) Sweden	ICD-9, ICD-10 (& DSM-IV) Psychosis	Registers	Sample = 4.4m Swedish people aged 25-64 years on 31/12/1999 (35,727 people excluded as they had a previous admission) Cases = 6,160	Quintiles of population density	At diagnosis	Psychosis risk highest for both men & women in most urbanised quintile, with some evidence of a dose response relationship	Marital status, education, immigrant status, age (stratified by gender)	Similar association found for depression, but not as strong
Allardyce et al[36] (2005) Scotland, UK	ICD-9 (schizophrenia)	Registers	Sample/cases = 5,838 cases with hospital admission 1989-1993	Degree of urbanization.	At diagnosis	No differences in schizophrenia risk by degree of urbanicity	Social fragmentation, material deprivation	Higher levels of social fragmentation were associated with higher risk of schizophrenia
Kirkbride et al[5] (2006) UK	DSM-IV	Population based case finding, 1997-9	Sample and cases = 568 (209 cases of schizophrenia)	Southeast London (Most Urban), Nottinghamshire & Bristol (Least Urban)	At diagnosis	Higher incidence of schizophrenia in London *cf.* Nottingham & Bristol	Age, sex, ethnicity	Similar distribution found for affective psychoses
Pedersen et al[37] (2006) Denmark	ICD-8, ICD-10 (schizophrenia)	Register	Sample = 711,897 people born 1956-86 alive at age 15; Cases = 2,720 with schizophrenia between 1970-2000	Degree of urbanization.	Birth, birth of sibling, age 15	People born in capital areas had higher schizophrenia risk *cf.* those born in rural areas, regardless of older sibling place of birth. Among people born in rural areas, some evidence that having an older sibling born in the capital increased schizophrenia	Age, sex, calendar year, parental age, history of mental health in parents or siblings	Study suggests that some of the causes of schizophrenia due to the environment are rooted in families
Pedersen & Mortensen[38] (2006a) Denmark	ICD-8, ICD-10 (schizophrenia)	Register	Sample = 1.89m people born 1956-83; Cases = 10,755 people with schizophrenia	Degree of urbanization.	Upbringing (15th birthday)	People living in the capital city had greatest risk of developing schizophrenia, with some evidence of a gradient across levels of urbanisation	Sex, calendar year, distance from main road & mental illness in parent or sibling	Distance from main road was no longer significant when model adjusted for degree of urbanisation

Study ID	Diagnostic criteria & outcome	Case ascertain-ment	Sample size	Definition of urban	Timing of urban	Findings	Confounders	Comments
Pedersen[39] (2006b) Denmark	ICD-8, ICD-10 (schizophrenia)	Register	Sample = 5.05m people born between 1910-86; cases = 23,051 cases diagnosed 1970-2001	Degree of urbanization.	Birth	Urbanisation associated with greater schizophrenia risk in the youngest, but not oldest age cohort	Age & sex	
Laursen et al[40] (2007) Denmark	ICD-8, ICD-10 (schizophrenia)	Register	Sample = 2 million people born 1955-1978; cases = 13,297 between 1973-2001	Degree of urbanization.	Birth	People born in urban areas had twice the schizophrenia risk than those born in rural areas		
Weiser et al[47] (2007) Israel	ICD-10 (schizophrenia)	Register	Sample = 371,603 conscripts age 16-17; Cases = 1,174	Degree of urbanization.	At military conscription	Increasing population density corresponded to increasing schizophrenia risk (linear trend)	Age, vulnerability & SES.	Male only sample. Effect more pronounced in "vulnerable" sample
Kelly et al[41] (2010) Ireland	DSM-III-R (schizophrenia, other psychotic illness)	Diagnostic interview (SCID)	Sample/cases= 324 schizophrenia	Urban vs. rural	At diagnosis	People living in Dublin had twice the risk of developing schizophrenia *cf.* people living in rural countries	Age, sex, SES, ethnicity	
Sorensen et al[42] (2014) Denmark	ICD-8, ICD-10 (schizophrenia)	Register	Sample = 2.49m people born 1955-93; Cases = 17,389 between 1970-2005	Degree of urbanization.	Birth	People living in the capital area had greatest schizophrenia risk, with some evidence of a gradient across levels of urbanisation	Age, sex, calendar year, parental history of mental illness, parental loss, immigration, parental age	
Szoke et al[43] (2014) France	DSM-IV (non-affective psychoses, affective psychoses)	Reported by public & private services	Sample = 246,773 (age 18-64 residing in catchment area & diagnosed with schizophrenia)	3 areas according to town size (smallest towns, medium towns, largest towns)	At diagnosis	People living in the largest towns had higher risk for both affective & non-affective psychoses	Age & sex	Risk for non-affective psychoses in largest towns was greater than that for affective psychoses.
Vassos et al[44] (2015) Denmark	ICD-10 (schizophrenia)	Register	Sample = 2,894,640 born 1995-2012 Cases = 13,702	Degree of urbanization.	Birth	Higher incidence of schizophrenia among people born in the capital *cf.* rural areas. Evidence of a dose-response	Calendar period, age & sex, parental age at birth, family history of mental illness	Higher incidence of affective psychoses among people born in the capital vs. rural areas, but no dose-response
Moreno-Kunster et al[45] (2016) Spain	ICD-10 (schizophrenia)	Register	Sample = 1,663 Cases = 1,052	Urban vs Rural	At diagnosis	Higher schizophrenia rates in urban areas	None	No confounders included in analyses

Study ID	Diagnostic criteria & outcome	Case ascertain-ment	Sample size	Definition of urban	Timing of urban	Findings	Confounders	Comments
LAMIC								
Ganguli[49] (2000) India	ICD & DSM (unspecified) Schizophrenia	Multiple*	Review of 15 studies across Indian regions	Urban vs rural	At diagnosis	Higher prevalence of schizophrenia in rural *cf.* urban areas	Multiple*	Differences between urban & rural prevalence not tested statistically
Vicente et al[50] (2006) Chile	DSM-III-R Non-affective psychosis	Survey, Diagnostic interview (CIDI)	Sample = 2,978 people	Urban vs rural	At diagnosis	Prevalence of non-affective psychoses lowest in area with greatest % rural population	Age, sex, education, marital status, income	Urban-rural areas not directly compared
Wei et al[51] (2008) Tibet	DSM-IV Schizophrenia	SCID-I	Sample = 5,145 Cases = N/A	Urban vs rural	At diagnosis	No significant differences between urban & rural areas	-	No multivariable analysis
Xiang et al[48] (2008) China	Schizophrenia	CIDI	Sample= 5,926 Cases = 0.49% of the sample	Urban vs rural	At diagnosis	Higher odds of schizophrenia in urban areas after adjustment for confounders	Age, sex, marital status, education, employment, income, smoking status, family history of schizophrenia	
Lundberg et al[52] (2009) Uganda	Psychotic symptoms	Interview (PDI-21)	Sample = 646	Urban, semi-urban, rural	Birth & upbringing	People born in urban areas had higher odds of having psychotic symptoms	Age, sex, education, marital status, SES, family history of psychiatric disorders	Small sample, findings could be due to chance
Phillips et al[53] (2009) China	DSM-IV Schizophrenia	Screening with GHQ followed up by SCID interview	Sample = 63,004 Cases = 2%	Urban vs rural	At diagnosis	No differences in odds of schizophrenia in urban & rural areas	Data were adjusted for design factors & clustering. Post-stratified to the sampling frame	No confounders included in analyses
Song et al[54] (2009) China	CCMD Schizophrenia	Screening (unspecified) followed by interview	Sample = 294,356 Age = 22 - 29	Urban vs rural	At diagnosis	Lower odds of schizophrenia in urban *cf.* rural populations	Sex, birth cohort (pre-during, post-famine)	Study refers to period of the famine of 1959-61. Generalisability to other contexts might be limited
Long et al[56] (2014) China	Schizophrenia	Multiple*	Meta-analysis of 52 studies	Urban vs rural	At diagnosis	Higher prevalence in urban *cf.* rural dwellers	Heterogeneous across studies	
Chan et al[55] (2015) China	Schizophrenia	Multiple*	Review of 42 prevalence studies	Urban vs rural	At diagnosis	Higher prevalence in urban *cf.* rural dwellers	Heterogeneous across studies	Differences between urban & rural prevalence not tested statistically

List of abbreviations: CIDI = CCMD = Chinese Classification of Mental Disorder; DSM = Diagnostic and Statistical Manual of mental disorders; GHQ = general health questionnaire; ICD = International Classification of Disease; SCAN = Schedules for Clinical Assessment in Neuropsychiatry; SCID = Structured Clinical Interview for DSM-IV Axis I Disorders (**SCID**-I); *cf.* = Compared with; SES: socioeconomic status

* The study is a literature review/meta-analysis therefore it is not possible to retrieve specific information for each study included.

India,[49] and the Chinese famine study,[54] where rural populations experienced greatest levels of malnutrition. Other studies, including those from Tibet,[51] Uganda[52] and China[53] have found equivocal prevalence between urban and rural populations. Of the eight studies which did not find observe higher schizophrenia rates in more urban areas, 5 were were conducted in LAMIC settings,[48,49,52–54] meaning only 4 of 9 LAMIC studies (44.4%) observed this phenomenon,[48,50,55,56] compared with 28 out of 31 (90.3%) studies in HIC settings; this difference was strongly statistically significant (Chi^2 [χ^2] test; p=0.002; Table 1). At present it is not possible to determine the reason for this difference; on the one hand the composition and risk profiles of people living in rural and urban settings in LAMIC settings may be very different to those in HICs, while on the other hand, methodological limitations of some studies from LAMIC settings (see below) may explain this difference. In general, these issues include the validity of definitions of urban exposure used,[50] small sample sizes,[52] absences in statistical testing[49,58] or failure to use appropriate regression models.[51] This may limit the validity and generalizability of these results, despite exceptions which have employed large sample sizes and robust statistical models to investigate urban-rural differences.[48,54]

2.2 Neighbourhoods

The majority of the studies which have investigated the spatial distribution of schizophrenia at finer-grained, small area "neighbourhood-levels" have been conducted in Europe[8,9,16,59–76] (9 in the UK,[8,9,59,60,62,65–67,70,71] four in The Netherlands,[61,63,68,75] three in Sweden,[64,69,76] two in Ireland,[73,74] one in Italy,[72] and one in Germany[16] with a minority undertaken in Israel,[77] South Africa[78] and the United States).[79] Most studies employed hospital or early intervention services registers to identify cases of schizophrenia,[8,9,16,59–64,69,70,74,76–78] or to identify a 'screened' population to further interview with clinical instruments,[65–68,71–73,75] and only one study employed a survey design.[79] Neighbourhood of residence was generally defined based upon administrative units at the time of diagnosis[8,9,16,59–68,70–75,77–79] or, more rarely, upbringing (Table 2).[69,76]

These ecological and multilevel studies have suggested that up to 12% of variance in the distribution of schizophrenia could be explained by neighbourhood characteristics,[61,64,66,69] although further work is required here; this pattern may vary by degree of urbanicity (higher in more urban areas[5,18,20–25,27,28,30–35,37–48,50,55,56]), and most studies, despite limited exceptions,[69,76] have not examined other potential causal levels such as the role of the family or school environment.

Indicators of area socioeconomic deprivation, such as overcrowding,[9] housing tenure,[61,73,79] unemployment[9,60,61,63,64,66–74,78,79] and social/welfare benefits[61,69,79] have extensively been used in the

Table 2: Summary of literature on neighbourhood differences in the distribution of schizophrenia (from 1990 onwards, chronologically ordered)

Study ID & Setting	Diagnostic Criteria & outcome	Case finding, age range, years	Sample size & cases	Definition of neighbourhood	Timing of exposure	Area-levels measures	Individual-level measures	Findings	Comments
High income countries									
Dauncey et al[59] (1993) UK	Schizophrenia	Psychiatric registers (age 15-54 years, 1978-80)	Cases = 67 schizophrenia	5 enumeration districts (Nottingham)	Birth, upbringing, diagnosis, follow up	Deprivation	Age, sex, ethnicity	Of 67 cases, 27 were borb in the inner city. 23 out of these 27 were born in council estates/deprived areas. Over half of the Nottingham-born were in deprived areas 5 years before & after diagnosis	Small sample limits validity of findings
Loffler et al[16] (1999) Germany	ICD-9 (Schizophrenia)	Psychiatric registers (age 12-59 years; 1987-89)	Cases = 276 incident schizophrenia	23 districts in Mannheim, 14 in Heidelberg	At diagnosis	Measure of segregation & population density	-	Highest admission rates in inner city areas with high population density & segregation	Ecological study could not separate role of area & individual
Croudace et al[60] (2000) UK	ICD-10 (admissions & first episode schizophrenia)	Hospital registers (ages 16-64 years, all admissions 1992-3, first episode 1992-4)	Cases = 1208 admissions; 168 first episode	104 Electoral wards (Nottingham)	At admissions	Social deprivation	Age & sex	Higher incidence & admissions for psychosis in areas with above-average social deprivation	Non-linear association
Van Os et al[61] (2000) The Netherlands	ICD-9 (Schizophrenia)	Psychiatric registers (all ages, 1986-97)	Sample= ~ 120,000 inhabitants Cases = 220	35 neighbourhoods in Maastricht (120,000 inhabitants). Traditional and sociological entities	At diagnosis	% men, % single/married, % under age 25. % of population: on rental support, non-voters, welfare dependent, foreign born, unemployed, mobility, new housing	Age, sex, marital status,	12% of variance in schizophrenia incidence at neighbourhood-level. % single/divorced men associated with higher schizophrenia risk. Higher risk of schizophrenia for single men living in areas with fewer single men	
Boydell et al[9] (2001) UK	ICD-9, ICD-10 (schizophrenia)	Psychiatric registers (all ages, 1988-97)	Sample= ~ 120,000 inhabitants Cases = 222	15 electoral wards in Camberwell, London	At diagnosis	% non-white ethnic minority, deprivation	Age, sex, ethnicity	Significant differences in incidence between neighbourhoods. Higher rates in non-white ethnic minorities as % non-white ethnic inhabitants decreased	
Silver et al[79] (2002) USA	DSM-III (schizophrenia)	Survey, Diagnostic interview (DIS) (age 18-96 years)	Sample = 11,686 survey respondents	261 census tracts across New Haven, CT, Baltimore, MD, St. Louis, MO, Durham, NC, and Los Angeles, CA	At diagnosis	Index consisting of several measures of poverty, social isolation & residential turnover	Age, sex, ethnicity, household income, years of education, marital status	Higher schizophrenia risk in women & with less education, lower income, single marital status & neighbourhoods with higher turnover & disadvantage; association disappeared after adjustment for SES	
Boydell et al[62] (2004) UK	Unspecified (schizophrenia)	Psychiatric registers (1988-97)	222 cases	15 electoral wards in Camberwell, London	At diagnosis	% non-white ethnic minorities, deprivation, inequality	Age, sex, individual ethnicity	Inequality only associated with higher rates of schizophrenia in most deprived areas	

Study ID & Setting	Diagnostic Criteria & outcome	Case finding, age range, years	Sample size & cases	Definition of neighbourhood	Timing of exposure	Area-levels measures	Individual-level measures	Findings	Comments
Drukker et al[63] (2006) The Netherlands	DSM-IV (schizophrenia)	Psychiatric registers (all ages, 1993-2002)	98 cases/3369 controls	36 districts in Maastricht	At diagnosis	Informal social control, social cohesion & trust, socioeconomic deprivation	Age, sex, education, SES, marital status, education, employment & living conditions	Low social cohesion & trust, high levels of residential instability associated with higher treated incidence of schizophrenia. Associations no longer significant after adjustment for SES	Social capital obtained from questionnaire sent to sample of residents in each district (48% response)
Lofors et al[64] (2007) Sweden	ICD-9 /ICD-10 (psychosis)	Psychiatric registers (incident cases) (age 25-64 years; 1997-9)	Sample = 4.5m Swedish citizens. Cases = 10,930	Clusters of small area units (~2,000 residents each in Stockholm, 1,000 in the rest of the country)	At diagnosis	Linking social capital (voting participation), neighbourhood deprivation	Sex, age, housing tenure, education, marital status, employment, country of birth	Low social capital & neighbourhood deprivation associated with high rates of psychoses, even after adjustment for individual level characteristics	Individual characteristics explain the whole association for depression
Kirkbride et al[66] (2007) UK	ICD-10 (schizophrenia, non-affective psychoses)	Clinical interview for cases identified in hospital registers [SCAN] (age 16-64 years, 1997-9)	Sample = 2001 census ward population Cases= 218 non affective psychosis	33 wards in South-East London (Lambeth and Southwark, ~6000 residents in each area)	At diagnosis	Population density, ethnic density, ethnic fragmentation, deprivation, voter turnout	Age, sex, ethnicity	Low social capital (measured by voting turnout) associated with higher rates of psychosis, even after adjusting for individual-level variables. Lower ethnic fragmentation associated with lower rates	
Kirkbride et al [65] (2007a) UK	ICD-10 (schizophrenia, non-affective psychoses)	Clinical interview for cases identified in hospital registers [SCAN] (age 16-64 years, 1997-9)	Sample = 2001 census ward population Cases = 294 (218 non-affective; 76 affective psychosis)	33 wards in South-East London (Lambeth and Southwark, ~6000 residents in each area)	At diagnosis		Age, sex, ethnicity	Incidence of broadly defined psychosis & non-affective psychosis followed non-random geographical distribution after accounting for individual-level variables. 12% of variance explained at neighbourhood level[80]	Pattern not observed for affective psychosis, but small sample
Kirkbride et al[67] (2008) UK	ICD-10 (schizophrenia)	Clinical interview for cases identified in hospital registers [SCAN] (1997-1999 age 16-64)	Sample = 2001 census ward population Cases = 148 schizophrenia	33 wards in South-East London (Lambeth and Southwark, ~6000 residents in each area)	At diagnosis	Social cohesion & trust, social disorganisation, ethnic density, ethnic fragmentation, socioeconomic deprivation	Age, sex, ethnicity	Evidence of non-linear (U-shaped) association between social cohesion & trust and incidence of schizophrenia. No evidence of role for social disorganisation. Lower ethnic fragmentation associated with lower rates	Social capital measured 5-9 years after admissions.
Werner et al[77] (2007) Israel	ICD-9 (schizophrenia)	Psychiatric registers (incident cases) (individuals born 1964-76; followed until 1997)	Sample = 68,794 people born & living in Jerusalem Cases = 520	24 areas (~2,900 residents in each area)	At diagnosis	Area-level SES index from multiple indicators	Age, sex, father's age & ethnicity, occupational prestige status, parental education,	Lower area-level SES associated with higher schizophrenia rates after adjustment for individual-level SES	

Study ID & Setting	Diagnostic Criteria & outcome	Case finding, age range, years	Sample size & cases	Definition of neighbourhood	Timing of exposure	Area-levels measures	Individual-level measures	Findings	Comments
Veiling et al[68] (2008) The Netherlands	DSM-IV (all psychotic disorders)	Clinical interview for cases identified in hospital registers (CASH) (age 15-54 years 1997-1999, 2000-2005)	Sample = whole population, Cases= 466	44 neighbourhoods in The Hague (max 38,000 inhabitant per neighbourhood)	At diagnosis	Socioeconomic deprivationethnic density	Ethnicity age, sex, marital status, ethnicity	Higher incidence of psychotic disorders in immigrants in low ethnic density neighbourhoods. No differences between native Dutch residents & immigrants in high ethnic density neighbourhoods	Outcome used might conceal differences between affective & non-affective psychoses
Zammit et al[69] (2010) Sweden	ICD-8, ICD-9, ICD-10 (schizophrenia, non-affective psychoses, affective psychoses)	Psychiatric registers (individuals born in Sweden born 1972-77 at age 16, followed up until 2003)	Sample = 169,910, Cases = 881 any non-affective psychoses; 355 affective psychoses	1,264 Schools, 284 municipalities, 24 counties in Sweden	Upbringing	School-level= average: foreign born, social fragmentation, low grade. Municipality = urbanicity, population density, index of social fragmentation (residential mobility, voting, % married/single households)	Sex, country of birth, parental history of psychosis, change of residence between 8/16 years, parental SES, education, family income, marital status, school grade	1) Higher risk of non-affective psychoses in urban *cf.* rural areas explained by school-level social fragmentation & population density 2) Only social fragmentation remained associated with non-affective psychosis risk after control for individual variables	2.2% of variance explained at neighbourhood level
Schofield et al[8] (2011) UK	Non-organic psychosis (excluding drug-induced ones)	Primary care database (age 16 to 74 years)	Sample = 185 827 patients Cases = 277 patients with FEP	Postcode areas	At Diagnosis	Area deprivation, ethnic density	Age, sex, ethnicity	FEP rates in people of black ethnicity increased in neighbourhoods with lower own-group ethnic density. Deprivation associated with greater FEP rates	Some evidence of a dose-response effect between ethnic density & FEP rates
Bhavsar et al[70] (2014) UK	OPCRIT ananlysis to obtain RDC first episode schizophrenia	Hospital records (age 16-35 years, 2000-2007)	Sample = 267,000 Lambeth residents Cases = 405	177 Super output areas (~1,100 – 1,700 residents)	At diagnosis	Deprivation, ethnic group density, population density	Age, sex, ethnicity, SES	Higher area-level deprivation associated with increase in schizophrenia incidence, after adjusting for all other factors	
Kirkbride et al[71] (2014) UK	DSM-IV (first episode non-affective and affective psychoses)	Clinical interview for cases identified in hospital registers [SCAN] (18-64 years, 1996-1998 City & Hackney; 1998-2000 in Newham and Tower Hamlet)	Sample = 2001 census population; cases = 484 first episode psychosis	56 neighbourhoods in East London boroughs of City & Hackney, Newham, and Tower Hamlets	At diagnosis	Deprivation, inequality, population density, own group ethnic density, own group ethnic separation, social fragmentation	Age at contact, ethnicity, social class	Deprivation, inequality and population density were independently associated with increased incidence of non-affective psychosis after adjustment for individual level variables. No interaction between inequality and deprivation.	Evidence of higher rates of schizophrenia in neighbourhoods with low ethnic density
Lasalvia et al,[72] (2014) Italy	ICD-10 (all psychoses, affective and non-affective)	SCAN to individuals age 15-54 screened positive for a possible FEP	Cases = 558 cases (441 non-affective, 117 affective psychosis)	198 municipalities in Region Veneto	At diagnosis	Population density, neighbourhood deprivation	Age, sex, immigration status	Non-affective incidence rates were twice as high in the most deprived areas vs. other areas; no differences by population density	No differences for affective psychoses

Study ID & Setting	Diagnostic Criteria & outcome	Case finding, age range, years	Sample size & cases	Definition of neighbourhood	Timing of exposure	Area-levels measures	Individual-level measures	Findings	Comments
Omer et al[73] (2014) Ireland	DSM-IV (first episode psychosis)	Clinical interview for cases identified in hospital registers (age 16+ years, 1995-2007)	Sample = 199,139 residents in 2002. Cases = 132 non-affective; 123 affective psychoses	155 electoral divisions in Cavan & Monaghan counties (Ireland)	At diagnosis	Material deprivation, social fragmentation, urbanicity	Age & sex	Association between deprivation & higher incidence of psychoses	Effect may have been in women only. First study in an entirely rural setting
Sariaslan et al[76] (2015) Sweden	ICD-9, ICD-10 (schizophrenia)	Register (people born 1967-1989 followed up from age 15 to 2009)	Sample = 2,361,585 in Sweden	Small area neighbourhood units, excluding <50 people (~1,000 residents each)	Upbringing	Population density, neighbourhood deprivation	Sex, birth year, birth order	Higher schizophrenia rates in areas with greater population density & deprivation. Partially mediated by unobserved familial characteristics; disappeared when investigating association within familial nuclei	
Veling et al[75] (2015) The Netherlands	DSM-IV (FEP)	Clinical interview for cases identified in hospital registers (CASH) (age 15-54 years, 1997-9, 2000-5)	Sample = 277,008 residents in 2005 Cases = 611	42 of 44 neighbourhoods in The Hague	At diagnosis	Social disorganisation domains = socio-economic level, residential mobility, ethnic diversity, % single person households, % voter turnout at local elections, population density, crime	Age, sex, ethnicity	All area level indicators showed association with schizophrenia incidence initially, but after mutual adjustment only association with crime level remained significant	
O'Donoghue et al[74] (2016) Ireland	DSM-IV (FEP)	SCID-I for DSM-IV in early intervention settings (between 2006-10, aged 16-65 years)	Cases = 292 FEP participants	139 electoral divisions (median 2,386 inhabitants per neighbourhood)	At diagnosis	Social Deprivation (using Haase-Pratschke index); unemployment; social fragmentation; social capital; population density	Age, sex, marital status, DUP, co-morbid substance use, functioning, family history of psychosis	FEP rate higher in neighbourhoods with greater social fragmentation & deprivation, and lower social capital. DUP greater in neighbourhoods with greater social fragmentation	
LAMIC									
Burns et al[78] (2008) South Africa	DSM-IV (first episode psychosis)	Psychiatric registers, (incident cases) (age 15-49, 2005)	Sample = 508,275 from 2001 census population; cases = 160	7 municipalities, in District Umgungundlovu	At diagnosis	Poverty & inequality indices, urbanicity (% urban population)	Age, sex, ethnicity, employment status	Positive correlation between inequality & FEP incidence after adjustment for individual-level characteristics. No significant correlation between poverty & FEP incidence	

List of abbreviations: CAS= Census Area Statistics; CASH= Comprehensive Assessment of Symptoms and History; DIS; DSM = Diagnostic and Statistical Manual of Mental Disorder; FEP = First Episode of Psychosis; ICD= International Classification of Disease; LSOA = Lower Super Output Area; OPCRIT = operational criteria; QMPA = Questionnaire for Adult Psychiatric Morbidity; SCAN = Schedules for Clinical Assessment in Neuropsychiatry; SCID = Structured Clinical Interview for DSM Disorders; *cf.* = compared with; SES = socioeconomic status; LAMIC = low and middle income country; DUP = duration of untreated psychosis

Literature, either individually[61] or in combined indices.[8,9,16,59,60,62–64,66–79] Although the plethora of measures used, and inclusion of different individual- and area-level variables, makes direct comparison of findings difficult, evidence of an association between measures of *absolute* deprivation at the neighbourhood level and higher risk of schizophrenia has been consistently observed.[59,60,62,68–70,72–74,77–79] Researchers have recently become increasingly interested in the role of *relative* deprivation, with higher schizophrenia rates reported in neighbourhoods with greater inequality.[62,71,78] As further discussed in Section 2.5, it has been hypothesised that exposure to deprivation and inequality may lead to psychosocial stresses arising from perceptions of exclusion, threat and mistrust, which in turn lead to the onset of psychotic symptoms.[70]

Subsequently, this has led researchers to investigate how neighbourhood-level social capital affects psychosis risk. Social capital refers to the amount of "resources […] embedded within an individual's social network"[81] (p. 911) (i.e. structural social capital), as well as social cohesion (i.e. cognitive social capital[81,82]), which taps into the presence of shared social norms, values and belonging within a community. Although developing routine measures to operationalise these potentially nebulus constructs within the field of psychiatric epidemiology remains a challenge, studies which have measured social cohesion have shown that higher levels are associated with positive mental health outcomes.[83] Studies which have investigated this directly in relation to psychotic disorders have used various proxy markers of social cohesion, including voter turnout,[61,64,66,69,75] the proportion of the population engaging in voluntary work,[74] and direct measures of social cohesion and trust via population surveys.[63,67] Evidence to support an association between social cohesion and schizophrenia is mixed, with positive findings from some studies,[64,66,74] but not others,[61,63,69,75] following adjustment for other individual- and area-level risk factors. One study reported a non-linear association between social cohesion and trust and schizophrenia rates,[67] with higher rates in areas with low or high levels of social cohesion (compared with areas with medium levels). Thus, although neighbourhood-level social capital may be associated with schizophrenia, further research is required to investigate this in more detail.

A related concept of social fragmentation, first tested by Faris and Dunham[11], has also been considered in relation to the incidence of psychotic disorders in urban areas. Social fragmentation has been heterogeneously operationalised in the literature, but can perhaps be thought of as indexing the absence of the social building blocks which would lead to the formation of social capital. Several neighbourhood-level markers of this broad construct have been investigated in relation to psychosis incidence, including the proportion of single persons,[61,69,71,75] proportion of rented households (as an

indicator of housing turnover and therefore transience)[71,79] and residential mobility.[61,69,71,75,79] These measures have been associated with greater schizophrenia rates, in some,[61,69] but not all studies,[71,75,79] with some evidence they may be driven by individual-level social isolation rather than its neighbourhood corollary.[75]

Ethnic density – the proportion of someone's own ethnic group in their neighbourhood – may represent a further ethnicity-specific construct of social fragmentation. Ethnic density may underpin a range of social processes, including the extent to which there are opportunities in your residential neighbourhood to develop ties and bonds with other people who may share similar migration histories, cultures, religious beliefs, values, norms, customs, conventions and modes of behaviour. The association between ethnic density and schizophrenia risk was first observed by Faris and Dunham,[11] and has subsequently been observed in various settings, where the relative risk for ethnic minority groups (compared with the majority population) is reduced as one's own-group ethnic density becomes greater at the neighbourhood level.[66–68,71] Further research from Kirkbride et al.[71] has extended this construct to consider the specific spatial patterning of ethnic groups within a community, which he has termed *ethnic fragmentation*. This research has revealed independent effects of both ethnic density and fragmentation on subsequent rates of non-affective psychotic disorders.[66,67,71] A recent systematic review concluded that ethnic density may be protective against several adverse mental health outcomes, not limited to schizophrenia.[84] The authors suggest ethnic density could act as a buffer towards negative social experiences (such as racism and discrimination) by promoting resilience. Living in socio-demographically and socio-economically homogeneous areas could also promote a stronger sense of identity and self-esteem in turn reducing experiences of conflict in social interactions.[84]

2.3 Strengths and limitations

Findings of higher rates of schizophrenia in urban areas and in some neighbourhoods compared with others are consistent in the schizophrenia literature across a number of study designs (e.g. longitudinal vs. cross-sectional, or register-based studies vs. surveys), populations (e.g., service users, general population), settings (including various European countries and the USA) and sample sizes, suggesting that these results are unlikely to have arisen by chance. The increasing number of studies measuring urbanicity at birth also provides evidence that urban exposures early in life could be a risk factor for schizophrenia.

Despite these considerable advantages, there are a number of limitations which research have yet to fully address. For instance, while cohort studies which use large – often national – population registers can provide powerful, longitudinal information on a large number of individuals, the breadth of data they can include is typically narrower, often restricted to routine administrative sources. Whilst these studies can account for several important socio-demographic indicators (e.g., age, gender, parental age, country of birth, income, education), measures of area deprivation, obstetric complications and history of family mental illness, data on other individual-level characteristics may not always be available, including ethnicity,[85–87] traumatic life events,[88–90] substance use[91,92] or markers of genetic vulnerability, although novel approaches are being developed.[76] Efforts to disentangle the possibility that associations between urban living and psychosis risk are due to other, unmeasured factors, including the role of genes, as well as neighbourhood studies employing residence at birth are still required.

2.4 A note on the affective psychoses

Curiously, the relationship between psychotic disorders and the urban environment appears to be specific to non-affective psychotic disorder, with no robust evidence that the affective psychoses, including bipolar disorder with psychotic features and psychotic depression, share such environmental correlates, despite a shared genetic predisposition.[93,94] The balance of evidence with respect to affective psychoses, including analyses of urban birth using national register data, suggests that there are few differences in incidence rates between urban and rural areas.[25,71,95–97] Only three studies have observed higher rates of affective psychoses in urban areas compared with rural ones,[5,22,43] and the magnitude of this association was smaller than observed for non-affective psychoses, while these studies only presented basic control for possible confounding factors (e.g., age, sex, ethnicity). Further research here is warranted, particularly as there is some evidence that non-psychotic affective disorders (such as depression) may vary by urban-rural environments (see Section 3). Finally, it is possible that the urban environment acts at the symptom- rather than disorder-level; in a study of people with ICD-10-confirmed first episode psychosis (including affective psychoses), Oher et al[98] observed that the urban environment was most strongly associated with positive symptoms (specifically hallucinations) and depressive symptoms.

2.5 Main Hypotheses

In this section we review the evidence in support of the main hypotheses concerning the association between urban residency and later risk of schizophrenia and other non-affective psychoses.

2.5.1 Individual (intra-generational) social drift

People who experience psychotic disorder usually have a lower socioeconomic status compared with their parents or peers who do not experience disorder. As proposed by Goldberg and Morrison,[99] this may result in the drift of people both socially and spatially into more deprived, urban or less socially desirable neighbourhoods, particularly into more deprived and fragmented parts of inner cities, for which there is some evidence.[100] Furthermore, studies which have investigated urban living close to the time of onset cannot exclude this possibility.[9,11,15–17,19,24,28,32,34–36,41,43,50,60,61,63,64,66–68,70,71,73,75,77–79,97] Nonetheless, the individual social drift hypothesis cannot explain the association between urban birth or upbringing and later psychosis risk.[18,20–23,25–27,29–33,37,39,40,42] Further, a recent study by Kirkbride et al[101] found that the spatial patterning of people classified as "At-Risk Mental States" for psychosis was more similar to that of first episode of psychosis (FEP) participants than of healthy controls, suggesting that those who go onto develop frank psychosis may be exposed to adverse social environments prior to a full psychotic episode. Confirmation of the existence of social and spatial drift would not preclude the possibility that aspects of the urban environment remain causally relevant to psychosis onset; indeed the two may coagulate to increase risk still further in the lead-up to disorder.

2.5.2 Intergenerational social drift

An interesting hypothesis to emerge more recently posits that drift could occur inter-generationally.[38,102] According to this idea, which encompasses the more formal notion of gene-environment correlation – families with an underlying vulnerability to psychosis may drift into lower socioeconomic positions and environments over time, even though frank psychosis may not reveal itself for several generations. Central to this hypothesis is that underlying genetic or environmental insults result in subclinical endophenotypes associated with non-affective psychoses, which compromise typical neurodevelopment or cognitive processes which subsequently inhibit people's upward social mobility relative to their peers across a range of domains including education, employment and social domains. While these traits may never lead to frank psychosis in a given generation, accumulated genetic and environmental insults may eventually trigger psychosis several generations later. Thus the apparent association between urban exposure and psychosis in the index case may be more readily explained by intergenerational drift, occurring via either gene- environment correlation or environment-environment correlation. It may be both an *active* and *passive* process. In the *active form* successive generations gradually drift into lower socioeconomic positions or more marginal neighbourhoods, whereas in the *passive form*, such groups remain in approximately the same social position, but unaffected families around them, over generations, exhibit a trend for upward social mobility. In a recent Swedish study, associations between population density,

neighbourhood deprivation and the incidence of schizophrenia were partially mediated by unobserved familiar risk factors and disappeared within nuclear families,[76] suggesting intergenerational drift may explain some of the association between risk and urban living. The current evidence, however, is limited and intergenerational social drift will be difficult to detect.

2.5.3 Antenatal & perinatal risk factors

These hypotheses propose that higher rates schizophrenia for people born in urban areas could arise from a set of biological influences confounded by urban birth, including exposure to infection in pregnancy and the perinatal period[103] or obstetric complications.[104–106] While these hypotheses are intuitively appealing, given that risk of infections, poorer prenatal nutrition or obstetric complications could more commonly occur in urban populations, evidence to support this is limited. Season of birth has been used as a proxy for infection during pregnancy (particularly with regard to influenza), but there is no evidence that this interacts with place of birth.[22,26] Further studies which have directly tested whether exposure to prenatal infections confound the association between urban birth and schizophrenia are required. Only two studies, to our knowledge, has investigated whether obstetric complications confound or mediate the association between urban birth and schizophrenia, with no apparent relationship.[25,33] The overall paucity of studies investigating this potential risk pathway marks this as an important topic for future research.

2.5.4 Social stressors

The possibility that urban environments create stressful environments which in turn disrupts key neurobiological pathways relevant to psychosis has received considerable lip-service.[107,108] Broadly, findings of higher rates of schizophrenia in neighbourhoods with greater levels of deprivation, population density and crime are consistent with the possibility that stress provides a mechanism to increase later psychosis risk.[18,20–25,27,28,30–35,37–43,45,47,48,50,52,55,57] Furthermore, neighbourhoods with low levels of protection from such risk factors, indexed by higher social fragmentation, lower levels of social cohesion[61,63,64,66,67,73,74,97] or a lack of ethnic density,[67,71] also appear to have increased rates. Nonetheless, studies which directly link exposure to urban environments with social stress, disrupted neurobiological process and psychosis are lacking, although new experimental data show that stressful social environments can increase paranoid ideation in healthy controls and people with existing psychosis.[109] Furthermore, another experimental study (limited to healthy subjects) found that urban residence and upbringing were associated with increased amygdala activity and affected the perigenual anterior cingulate cortex – an area of the brain which regulates negative affect and stress.[110] Specific hypotheses have also been advanced suggesting that experiences of social defeat or

social exclusion could mediate the association between urban exposure and neurobiological processes at the basis of vulnerability to psychosis,[111–113] though empirical evidence is still required. Alternatively, prolonged activation of the human stress response might suppress the Hypothalamic-pituitary-adrenocortical axis,[108] which, in turn, could result in dysfunctions of the immune system, predisposing some individuals to psychiatric illnesses.

2.5.5 Gene-environment interactions

An hypothesis that has increasingly gained attention is that environmental factors could combine with pre-existing genetic vulnerability to increase schizophrenia risk.[114] This possibility is supported by findings of independent associations between older sibling and individual's urban birth and the risk of schizophrenia, suggesting that risk might reside both in familial and environmental factors.[96] The lack of evidence to suggest that genetic risk differs between populations arranged along geographical or ethnic gradients, argues against a purely genetic explanation of higher rates of schizophrenia in urban populations and ethnic minorities, repsecitvely.[115] Instead, underlying genetic vulnerabilities to psychosis may mean that subsequent exposure to stressful life events, psychosical adverisites and hostile social environments has a more deleterious effect on key neurobiological pathways that affect psychosis risk. Unfortunately, at present direct evidence for gene-environment interactions implicating the urban environment are largely absent. Results from large, multisite gene-environment interaction studies in schizophrenia may reveal new directions for research including whether increased polygenic risk for psychosis exacerbates later risk of psychosis following exposure to adverse social environments.[116]

2.5.6 Differences in healthcare provision and socio-demographic characteristics

Two further hypotheses have been suggested to explain observed differences. First, it has been suggested that differences in the provision of healthcare between areas could account for the observed spatial heterogeneity in the distribution of schizophrenia. While differential access to mental health care between urban and rural settings and possible variation in duration of untreated psychosis remain important issues in their own right, there is little evidence to suggest such issues will explain urban-rural differences in risk,[117] given the use of population-based case ascertainment in studies which do not solely rely on routine case registers (i.e. see Kirkbride et al[5,65,67,71]).

Second, urban-rural differences in risk could be explained by differences in socio-demographic characteristics of individuals living in different areas (compositional effects). However, there is little evidence for this, although one study found that area-level differences disappeared after adjustment

for individual-level factors[63] (though most have not[9,61,64,66,67,69–71,73,75,77,78,97]). Advances in multilevel modelling techniques[65,71] have helped to partition variation in incidence rates between individual- and neighbourhood-level factors. Most studies have investigated this variance in relation to the neighbourhood, but school environments may be highly relevant at certain ages,[69] and the role of the family environment has largely been ignored, until very recently.[76]

3 Common mental disorders (depression and anxiety)

The annual prevalence of common mental disorders (CMD), defined as mood and anxiety disorders, has been recently estimated as 15.4% (95%CI: 12.8% - 18.6%),[118] with higher rates in women compared with men for both mood (women: 7.3%, 95%CI: 6.5%-8.1%; men: 4.0%, 95%CI: 3.5%-4.6%) and anxiety (women: 8.7%, 95%CI: 7.7%-9.8%; men: 4.3%, 95%CI: 3.7%-4.9%). Compared with schizophrenia (Section 2), evidence for non-random spatial variation of CMD is more mixed. Although this may reflect real, context-specific differences, a number methodological limitations could also account for these more heterogeneous findings. As opposed to the literature on schizophrenia, for instance, fewer epidemiological studies of CMD have used longitudinal, population-based study designs (i.e. cohort studies), or have measured incidence (*cf.* prevalence). Such studies are much harder to conduct for CMDs, given that a high proportion of people experiencing CMD may never present to mental health services. For this reason, cross-sectional surveys of the prevalence of CMDs in the general population or other settings have been more commonly used. Unfortunately, reliance on cross-sectional surveys and estimates of prevalence (which include both new and existing cases) makes it more difficult to separate cause from effect in respect to studying the role of the urban environment on risk of developing CMDs. Moreover, whilst ample literature exists, it has often been restricted to population sub-groups (e.g. adolescents, the elderly, ethnic minorities, or individuals with chronic disease), further limiting generalizability. Here, we review the strengths, weaknesses and overall level of evidence for spatial variation in CMDs.

3.1 Urban vs. rural settings

The majority of studies (Table 3) investigating the distribution of CMD between urban and rural settings have been conducted in Europe (three in the UK,[119–121] three in The Netherlands,[122–124] one in Sweden,[35] one in France[125] and one multi-country study across the UK, Spain, Finland, Ireland and Norway[126]). A number of studies have also been conducted in North America (four in Canada[127–130] and six in the USA[131–136]), one across European and North American settings (Canada, USA, Turkey,

Table 3: Summary of literature on rural/urban differences in the distribution of common mental disorders (from 1990 onwards, chronologically ordered)

Study ID	Outcome	Instrument	Sample size, age	Definition of urban	Timing of urban	Findings	Confounders	Comments
High Income Countries								
Lewis & Booth[119] (1994) UK	Psychiatric morbidity	GHQ	N= 6,456, Age 18 or over	Urban (no open access), urban (open access), rural	At time of survey	Participants living in urban areas had higher risk (odds) of experiencing psychiatric morbidity *cf.* those in rural areas, with access to open space associated with exact risk	Age, social class, marital status, employment, chronic illness & region of residence	Partial dose-response relationship observed.
Kessler et al[131] (1994) USA	Any anxiety disorder/ any mood disorder DSM-III-R (lifetime & 12-month prevalence)	CIDI	N = 8.098 Age 15-54	Degree of urbanisation	At time of survey	No difference in the distribution of anxiety & mood disorders between urban & non-urban areas	Age, sex, ethnicity, education, marital status, region	
Blazer et al (1994) USA [132]	Major depression DSM-III-R (1-month prevalence)	CIDI	N = 8.098 Age 15-54	Degree of urbanisation	At time of survey	No difference in distribution of major depression between urban & non-urban areas	Age, sex, ethnicity, education, marital status, region, income, employment, household composition, religion	
Parikh et al[127] (1996) Canada	Affective disorders DSM-III [1-month prevalence]	UM-CIDI	N=9,953, Age 15 – 64	Urban vs. rural	At time of survey	No differences between urban & rural areas	-	No adjustment for confounders
Paykel et al[120] (2000) UK	Mood & anxiety disorders DSM-III [1-week prevalence]	CIS-R	N=9,748 Age 16 – 64	Self-reported rating of urban, semi-rural, rural residence	At time of survey	Higher risk (odds) of psychiatric morbidity in urban *cf.* rural areas; no differences between semi-rural & rural.	Age, sex, social class, ethnicity, marital status, education, employment, housing type & tenure, life events in past year, social network, social support	
Andrews et al[137] (2001) Australia	Mood & anxiety disorders ICD-10, DSM-IV [12-month, 1-month prevalence]	MMSE	N = 10,641 Age: 16 – 64	Urban vs. rural	At time of survey	No differences in risk (odds) of mood & anxiety disorders between urban & rural areas in univariable models		No further testing in multivariable models

Study ID	Outcome	Instrument	Sample size, age	Definition of urban	Timing of urban	Findings	Confounders	Comments
Ayuso et al[126] (2001) Finland, Ireland, Norway, UK, Spain	Depressive disorder ICD-10 [1-month prevalence]	BDI + SCAN	N = 8,862 Age 18 – 64	Urban vs. rural	At time of survey	Higher prevalence of mood disorders in urban *cf.* rural areas. However, the difference was only statistically significant in UK & Ireland	Age & sex standardisation	Low response rates in UK & Ireland may have biased results. Differences expressed as means & 95%CI, no adjusted regression analyses
De Graaf et al[124] (2002) The Netherlands	Mood & anxiety disorders DSMIII incidence	CIDI	N=5,618 Age= 18-64	Urban vs. rural	At time of survey	No difference between urban & rural areas.	Age, sex, education, cohabitation status	
Andrade et al[138] (2003) Canada, Czech Rep, Germany, The Netherlands, Turkey, USA	Major depressive episode DSM-III-R in all countries (exc. Germany DSM-IV) [lifetime prevalence]	CIDI	Age varying acorss studies, overall from 14 years or over	Urban vs. rural	At time of survey	No difference between urban & rural areas, except in The Netherlands where risk (odds) were lower in rural areas	Other socio-demographc variables investigated, but not included in regression models	Response rate between 56% - 88% No multivariable adjustment for confounders
Kessler et al[133] (2003) USA	Major depression DSM-IV [lifetime and 12 month prevalence]	CIDI	N= 9,090 Age 18 or over	Degree of urbanisation	At time of survey	No difference between urban & rural areas.	None	
Sundquist et al[35] (2004) Sweden	Major Depression ICD-9, ICD-10 & DSM-IV Incidence	Registers	Sample = 4.4m Swedish people aged 25-64 years on 31/12/1999 (35,727 people excluded as they had a previous admission) Cases = 7,751	Degree of urbanisation	At diagnosis	Risk of depression highest for men & women in most urbanised quintile, but little evidence of dose-response	Marital status, education, immigrant status, age (stratified by sex)	
Wang et al, (2004) Canada[130]	Major depressive episode DSM-III-R [12-month prevalence]	CIDI	N=17,244 Age 12 or over	Urban vs. rural	At diagnosis	Higher risk (odds) of major depressive episode in urban areas after multivariable adjustment	Employment, marital status, ethnicity, immigration status	

Study ID	Outcome	Instrument	Sample size, age	Definition of urban	Timing of urban	Findings	Confounders	Comments
Kovess-Mafesty et al[125] (2005) France	Mood & anxiety disorders DSM-IV [lifetime, 6-month, 1-year prevalence]	CIDI-SF	N = 2,638 Age 18 – 102 years	Urban vs. rural	At time of survey	No differences between urban & rural settings after multivariable adjustment	Age, sex, education, employment status, marital status, country of birth, housing tenure & type	
Patten et al[129] (2006) Canada	Major depressive disorder/ episode classification not specified [1-year / point prevalence]	CIDI	N= 36,984 Age 15 or over	Unspecified	At time of survey	No differences between urban & rural settings	Age, sex, marital status, income, education, employment, chronic conditions	
Probst et al[134] (2006) USA	Depression Classification not specified (unspecified prevalence)	CIDI- SF	N= 30,801, Age 18 – 65	Urban vs. rural	At time of survey	Higher risk (odds) of depression in rural populations, but no differences once other health indicators were included	Age, sex, ethnicity, self-reported health, education, income, marital status, employment, limitation in daily activities, asthma, hypertension, diabetes, health status change	
Weich et al[121] (2006) UK	Common mental disorder (onset & maintenance) [Point prevalence]	GHQ	N=9518 wave 1 (onset) N = 7659 wave 2 (maintenance) Age = 17-64	Population density & Non-rural vs. rural	At time of survey	Population density associated with maintenance of CMD, but not onset. Higher risk (odds) of CMD in non-rural areas in univariable, but not multivariable models	Age, sex, marital status, education, employment, financial difficulties, physical health, income, housing tenure, type & problems, car access, overcrowding, social class	Non-rural areas do not necessarily correspond to urban areas Study is based on prevalence not incidence so 'onset' is a partial misnoma
Grant et al[135] (2009) USA	Generalised anxiety disorder (GAD) DSM-IV (Incidence & prevalence)	AUDADIS-IV	N=34,653	Urban vs. rural	At time of survey	No differences in risk (odds) of reporting GAD between urban & rural areas	Age, sex, ethnicity, income marital status, education, region	Only included GAD. Study also investigated major depressive disorder (MDD), not included in this review; no difference in urban-rural distribution of MDD
Romans et al[128] (2011) Canada	Mood & anxiety Disorders ICD-10, DSM-IV [12-month prevalence]	CIDI	N = 31,321 Age 15 or over	Degree of urbanisation	At time of survey	Weak evidence of difference in prevalence across the 4 geographical areas, with lower risk (odds) of depression in most rural area	Age, sex, marital status, income, income adequacy, employed, housing tenure, country of origin, health, ethnicity, education, community support	Anxiety as outcome was not investigated in multivariable models

Study ID	Outcome	Instrument	Sample size, age	Definition of urban	Timing of urban	Findings	Confounders	Comments
De Graaf et al[123] (2012) The Netherlands	Mood & anxiety Disorders ICD-10, DSM-IV [12-month prevalence]	CIDI	N = 6,646 Age: 18-64	Urban vs. rural & Degree of urbanisation	At time of survey	Lower risk (odds) of mood disorders in more urbanised areas. Highest risk of anxiety disorders in areas with very high degrees of urbanisation *cf.* the most rural areas.	Age & sex	
De Graaf et al[122] (2013) The Netherlands	Mood & anxiety disorders ICD-10, DSM-IV [Incidence]	CIDI	N=5303 (of the 6,646 eligible & invited)	Urban vs. rural	At time of survey	No difference in incidence rate ratio of mood & anxiety disorders between urban & rural areas	Age & sex	
Beyer et al[136] (2014) USA	Common Mental Disorders [Point prevalence]	DASS	N=2,479 Age: 21-74	Degree of urbanisation	At time of survey	Higher levels of depression & anxiety (though smaller coefficient & weaker association in the latter) in less urbanised areas but with no evidence of a linear relationship. Population density not associated with CMD	Age, sex, ethnicity, marital status, education, household income, occupational status, health insurance; green spaces, % tree canopy, urbanicity, population density, median household income below poverty, residential instability, % owner occupied households & unemployed, ethnic segregation	
LAMIC								
Mohammadi et al[139] (2005) Iran	Mood & anxiety disorders (DSM-IV) [Lifetime prevalence]	SADS	N = 25,180 Age 18 or over	Urban vs. rural	At time of survey	Higher risk (odds) of mood & anxiety disorders in urban *cf.* rural area	Unspecified	Unclear if odds ratios were from univariable or multivariable analyses
Vicente et al[50] (2006) Chile	Mood & anxiety disorders DSM-III-R [Lifetime, 12-month prevalence]	(CIDI)	N = 2,978 Age: 15 or over	Analyses grouped by 4 geographical regions, with different % of rural population	At time of survey	No differences across 4 regions in prevalence of disorders	Age, sex, education, marital status, income	Urban-rural areas not directly compared.

Study ID	Outcome	Instrument	Sample size, age	Definition of urban	Timing of urban	Findings	Confounders	Comments
Amoran et al[140] (2007) Nigeria	Common mental disorders [Point prevalence]	GHQ	N = 1,105 Age 15 or over	Urban vs. rural	At time of survey	Higher prevalence of depression in rural areas	-	No control for confounders, statistical tests only conducted for depression, not anxiety
Wei et al[51] (2008) Tibet	Depression DSM-IV Point prevalence	SCID-I	Sample = 5,145 Cases = N/A	City vs rural areas	At diagnosis	No significant differences between urban & rural areas	-	No multivariable analysis
Lundberg et al[52] (2009) Uganda	Depression & anxiety (classification not specified) [point prevalence]	HSCL–25	Sample = 646	Number of inhabitants Urban = Kampala Semi-urban = >25,000 inhabitants Rural ≤25,000 inhabitants	Birth & upbringing	People born in urban areas had higher risk (odds) of having depression & anxiety	Age, gender, education, marital status, SES, family history of psychiatric disorders	Small sample, type II error cannot be ruled out.

List of abbreviations: AUDADIS-IV= Alcohol Use Disorder and Associated Disabilities Interview Schedule DSM-IV Version; BDI= Beck Depression Inventory ; CIDI:= Composite International Diagnostic Interview; CIDI-SF= Composite International Diagnostic Interview short form; CIS-R= Clinical Interview Schedule Revised; DASS = Depression Anxiety Stress Scale ; GHQ= General Health Questionnaire; DSM = Diagnostic and Statistical Manual of mental disorders; HSCL = Hopkins Symptoms Checklist; ICD = International Classification of Disease; MMSE= Mini Mental State Examination; SADS= Somatic Anxiety Depressive Symptoms scale; SCAN= Schedules for Clinical Assessment in Neuropsychiatry; *cf.* = compared with.

Germany, The Netherlands, and Czech Republic),[138] one in South America (Chile[50]), one in Australia,[137] two in Africa (Nigeria[140] and Uganda[52]), and two in central Asia (Iran[139] and Tibet[51]).

All studies employed a cross-sectional design, with the exception of one longitudinal cohort[35] and two incidence-based studies.[122,124] Studies investigated CMD across a variety of ages, beginning in mid- to late-adolescence. Even though all investigations recorded place of residence concomitantly to the time of the survey, definitions of urbanicity varied considerably; while the majority of studies defined urbanicity according to degree of urbanisation[52,122,123,125,127,128,131–133,136,137,141] or population density,[35,121,124,130,135] others were based on combined metrics (population density and employment in rural occupations such as fishing, agriculture, etc),[126] housing type[119,125], self-report[120] or the percentage of survey respondents classified as from a rural district.[50] Six studies provided no criteria to define urbanicity.[51,129,135,138–140] All studies, with the exception of one (at birth),[52] measured urbanicity at time of diagnosis.

Most studies investigated urban-rural variation of mood and anxiety disorders together,[119–125,128,131,136,139,140,142] with eight studies restricted to mood (depressive) disorders only,[126,127,129,130,132–134,138] and one restricted to anxiety disorders.[135] A handful of other studies considered depression and anxiety alongside other psychiatric conditions.[35,50–52] Diagnostic criteria, however, varied greatly across studies; eight studies used DSM-III or DSM-III-R criteria,[50,120,124,127,130–132,138] four used DSM-IV,[51,125,133,135,139] one used ICD-10,[126] five used a combination of ICD-10 and DSM-IV [35,122,123,128,137] and the remainder reported general psychopathology scores without reference to specific diagnostic classifications.[119,121,129,134,136,140] A range of different instruments (CIDI,[50,122–125,127–133,138,141] DASS,[136] AUDADIS-IV,[135] GHQ,[119,121,140] SCID-I,[51] CIS-R,[120] BDI,[126] MMSE,[137] HSCL–25[52] and SADS[139]) were employed to diagnose incidence,[124,135] and point,[51,52,129,136,140] week,[120] month,[126,127,132,142] annual,[50,125,128,129,131,133,142] three-year[122] and lifetime CMD prevalence.[50,125,131,133,139] One study employed register data to measure incidence of depression.[35]

Perhaps unsurprisingly, results from these diverse study designs were highly heterogeneous. Eight studies found higher prevalence or risk (expressed as odds ratios) of CMD in urban areas,[35,52,119,120,126,128,130,139] two in rural settings,[136,140] while fourteen observed no differences.[50,51,121,122,124,125,127,129,131–133,135,141,142] One study reported a higher risk of depression in rural areas, but the opposite for anxiety disorders,[123] whereas another study found no rural-urban differences in five out of six countries (Canada, USA, Turkey, Germany, and Czech Republic).[138] Moreover, studies which used a categorical (i.e. non-binary) indicators of urbanisation, found little or

no evidence supporting the presence of a dose-response relationship between the degree of urbanisation and prevalence or risk of CMD.[35,120,122,127,128,131–133,136,142]

3.2 Neighbourhoods

A large literature has also investigated whether CMDs vary between small area neighbourhoods (Table 4), beyond variation which might exist between rural and urban populations (Section 3.1). Given the breadth of the available research, we have restricted our primary focus on general adult population studies, consistent with other sections of this chapter. As before, most studies have been conducted in Western Europe (twelve in UK,[143–154] two in The Netherlands,[155,156] two in Sweden,[64,157] one in France[158] and one across several cities[159]) and North America (twelve in the United States,[136,160–169] three in Canada[170–172]), with others undertaken in Australia, [173] Brazil[174] and South Africa.[175]

As for the urban-rural literature, the evidence for neighbourhood variation in CMD risk is more mixed than for schizophrenia. Whilst up to 12% of variance in schizophrenia might have been explained at the area-level, for CMD this proportion was much smaller, ranging from none to 4.4%.[64,145–147,153,154,156,158,172,176] Moreover, whilst many studies reported significant associations between CMD and at least one neighbourhood factor,[136,143,144,148,150,152–154,156,158–160,165,170,171,173–175,177–179] a considerable number found no associations.[144–147,149,151,155,160,161,163,167] Interestingly, whilst many studies did not find an overall main effect of neighbourhood factors on CMD risk, many studies reported subgroup effects,[145,148,150,154,159,160] which suggested that the role of neighbourhood factors such as deprivation were associated with CMD risk in particularly disadvantaged individuals. While more research is needed, this suggests that social adversities at the neighbourhood level many be particularly detrimental to the mental health of people who already face individual level social disadvantage. Deprivation was most commonly investigated,[64,136,145,147–149,151–154,156–158,162,163,167,168,170,172,173,177] followed by ethnic density,[150,160,170,178] social capital,[64,149,156,165,179] and features of the built environment (virtually absent in the schizophrenia literature), such as housing,[143,144] neighbourhood quality[143,159] or green space.[136,143,171]

With the exception of three observational studies employing longitudinal designs to examine either: maintenance of CMD symptoms[147,168]; social drift in individuals with CMD,[173] or; the association between the built environment and trajectories of depressive symptoms,[171] as well a randomised controlled trial,[164] all neighbourhood-level studies of CMD have employed cross-sectional designs. Place of residence has been exclusively measured at the time of data collection, although one longitudinal study was based on residence at multiple time-points.[173]

Table 4: Summary of literature on neighbourhood differences in the distribution of CMD (from 1990 onwards, chronologically ordered)

Study ID & Setting	Outcome & Instrument	Case finding, age range, years	Sample size	Definition of neighbourhood	Timing of exposure	Area-levels measures	Individual-level measures	Findings	Comments
Tweed[160] (1990) USA	Depressed mood (DIS) [6-month prevalence]	Survey Age 18+	N=3,481	Neighbourhoods in Baltimore	At time of Survey	Ethnic congruence	Age, sex, SES, ethnicity	Six-month prevalence was lower in neighbourhoods with highest ethnic congruence. Effect was greater for participants of black ethnicity	
Reijneveld & Schene[155] (1998) The Netherlands	Common Mental Disorders GHQ-12 [point prevalence]	Survey, Age: 16+	N=4,892	Boroughs in Amsterdam	At time of Survey	Area-level deprivation: registered income, household income below minimum, and unemployment rate	Age, sex, income, occupational status & educational level	Higher risk (odds) in more deprived neighbourhoods, but disappeared after adjustment	Similar results obtained when restricted to Dutch-born participants.
Yen & Kaplan[161] (1999) USA	Depressive symptoms 18-item depressive symptom scale	Survey Age: 20+ Years: 1965-1970	N=1,296	Census tracts	At time of survey	Neighbourhood SES: (% population with low income; living in substandard housing, low education, unskilled male labours, children in single parent homes)	Age, sex, ethnicity, income, chronic conditions, smoking, alcohol & BMI	No differences in depressive symptoms between low & high SES neighbourhoods	
Halpern & Nazroo[150] (2000) UK	Common Mental Disorders CIS-R [prevalent cases]	Survey Age: N/A	N=8,063	UK census enumeration district	At time of survey	Group density	Age, sex, ethnicity, economic hardship, fluency in English, age at migration, attacks on person & home	Lower group density associated with more depressive symptoms. After adjustement for individual-level variables, association was attenuated for white participants, strengthened for black ethnic minorities	
Ross et al[162] (2000) USA	Depression & anxiety (modified CES-D)	Survey Age: 18-92 Years: 1995	N=2,482	US census/postcode tracts	At time of survey	Neighbourhood SES; perceived neighbourhood disorder (physical & social)	Age gender, ethnicity, income education, marital, and parental status, employment and urban residence	Neighbourhood disorder associated with more symptoms of depression & anxiety in adjusted models, but not neighbourhood SES	
McCulloch[151] (2001) UK	Common Mental Disorders GHQ-12 [point prevalence]	Survey Age: 16 – 75 (year 1991-1998)	N=10,264	N/A	At time of survey	Area-level deprivation (Townsend index)	Region of residence, year, education, ethnicity, housing tenure, access to car, employment	No association between deprivation and CMD after adjustment for other confounders	Household-level characteristics not included in multilevel model

Study ID & Setting	Outcome & Instrument	Case finding, age range, years	Sample size	Definition of neighbourhood	Timing of exposure	Area-levels measures	Individual-level measures	Findings	Comments
Weich et al[144] (2002) UK	Depressive symptoms CES-D [prevalence]	Survey Age: 16-75	N = 1,887	86 housing areas (geographically bounded areas in which the majority of the housing was homogeneous in form and character) 2 Wards in North London	At time of survey	Built environment side survey checklist (BESSC)	Age, sex, marital status, employment, ethnicity, education. Household: tenure, level, structural problems	After adjusting for other characteristics, only living in areas with majority of buildings built after 1970s (vs pre-1940s) & with less than 25% of dwellings with private garden was associated with higher risk (odds) of depressive symptoms	
Stafford & Marmot[148] (2003) UK	Depression GHQ-28 [point prevalence]	Cohort study (wave 5)	N=5,539	Electoral wards	At time of survey	Neighbourhood deprivation (Townsend score, 1991 census); self-reported measure of neighbourhood safety	Age, sex, SES, financial problems, satisfaction with standard of living	Deprivation was associated with higher risk (odds) of depression. Some weak evidence that this was worse for people of low SES in such deprived areas	
Weich et al[145] (2003) UK	Common Mental Disorders GHQ-12 [point prevalence]	Survey Age: 16-74	N= 8,979	Electoral wards	At time of survey	Area-level deprivation (Cartairs index of socioeconomic deprivation), population density	Age, sex, marital status, ethnicity, employment status, number of current physical health problems. Household level: head of the household SES, structural housing problems, low income, access to a car & overcrowding	Negligible variance in CMD explained at area level , with no main effect for deprivation after adjusting for other characteristics. Possible subgroup effect of deprivation on CMD risk in the unemployed & economically inactive.	
Weich et al[146] (2003) UK	Common Mental Disorders GHQ-12 [point prevalence]	Survey e British Household Panel Survey (BHPS)	N= 8,979	Electoral wards (~2,400 adresses)	At time of survey	None (neighbourhood employed as unit in multilevel modelling)	Age, sex, marital status, ethnicity, education, employment status, financial strain & current physical health problems Household level: structural housing problems, household income, access to a car, tenure , SES, overcrowding, household type	CMD as binary outcome: No significant area-level variance. In adjusted models 94% of variance was explained at the individual level, 6% at area level GHQ score (continuous): 0.9% of variance at area level (significant) no longer significant in adjusted models, where 89% of variance was explained at individual level, 10% at household level	

Study ID & Setting	Outcome & Instrument	Case finding, age range, years	Sample size	Definition of neighbourhood	Timing of exposure	Area-levels measures	Individual-level measures	Findings	Comments
Leventhal & Brooks Gunn[164] (2004) USA	Depressive symptoms DMI Depressive mood inventory	RCT [treatment arm: moved to low poverty neighbourhoods + received voucher; comparison arm: voucher only; control arm: did not change residence]	N=550	Not defined	As assigned by RCT	Neighbourhood physical & social disorder measured by parental ratings of the size of problems. (parent & interviewer rated)	Neighbourhood satisfaction. Family randomised based on age, ethnicity, sex, education, marital status, employment	Parents in treatment arm were less likely to report depressive mood	69% response rate at follow up
Wainwright et al[152] (2004) UK	Mood disorder Health and Life Experiences Questionnaire (HLEQ) [current & lifetime prevalence]	Survey Age: 41–80 years	N=19,687	Electoral ward	At time of survey	Index of Multiple Deprivation	Age, sex, social class, marital status, employment status & educational level	Higher risk (odds) of reporting mood disorder for participants living in more deprived areas after accounting for individual-level characteristics. Non-significant 0.4% variation at area level once all individual level variables were included	
Greiner et al[165] (2004) USA	Depressive symptoms One (unspecified) option question [prevalence]	Survey Age 18 or over	N=4,601	Community as perceived by respondent	At time of survey	Community rating, community involvement, population density	Age, sex, race, education & identification of a personal health-care provider	Higher community ratings were associated with lower risk (odds) of reporting depressive symptoms	Self-rated measures of area could be affected by depressive symptom levels
Propper et al[176] (2005) UK	Common Mental Disorders GHQ-12 [point prevalence]	Survey (1991-2000)	N= 8184 (for prevalence) N= 7047 (5 year analyses)	Enumeration district (~500 people)	At time of survey	% unemployed, long term sick age 16-64, tenure type, central heating, no car, crowding, lone parent, one person (pensioner/non pensioner), black, Indian, Pakistani, Bangladeshi, migrant, working in agriculture, children, managerial	Individual: Age, sex, ethnicity & education. Household level: net household income, household size, tenure, employment	No statistically significant neigjhbourhood level variance in CMD (<1%), 3% at household-level	

Study ID & Setting	Outcome & Instrument	Case finding, age range, years	Sample size	Definition of neighbourhood	Timing of exposure	Area-levels measures	Individual-level measures	Findings	Comments
Weich et al[147] (2005) UK	Common Mental Disorders GHQ-12 [point prevalence]	Survey (1991-2) Age: 16-74 years	N= 5,809 (onset analyses) N=1850 (for episode maintenance analyses)	Electoral wards (~2000 people)	At time of survey	Socio-economic deprivation (Carstairs index)	Age, sex, marital status, ethnicity, education, employment status, financial strain & current physical health. Household level: structural housing problems, household income, car access, tenure, social class, overcrowding & household typ	No significant variance at area-level on onset or maintenance of CMD. No association with deprivation after adjusting for HH & individual-level variables	
Skapinakis et al[153] (2005) UK	Common Mental Disorders (SF-36) [point prevalence]	Survey Age: 18 years or over Years: 1998	N/A (circa 27,000)	Electoral division	At time of survey	Area-level deprivation	Age, sex, marital status, employment status, social class	1.5% variance explained at area level in null-model reduced to 0.6% in full model accounting for individual characteristics & regional deprivation. Both significant. Deprivation associated with greater risk of CMD after accounting for individual level variables	
Veenstra et al (2005) Canada[172]	Depressive symptoms 11-item questionnaire (Chronbach's alpha: 0.8)	Survey Age: 18+ Years: 2002	N=1,355	Census metropolitan areas	At time of survey	Internal & external built environment, social capital & neighbourhood SES	Age, sex, ethnicity, income, education, community trust, political trust, participation in voluntary association	More public spaces per capita was associated with higher scores on the depressive symptoms scale. 2.1% of variance (significant) explained at area level in null-model, 1.9% in multivariable model (significance not reported)	Community & political trust were associated with fewer symptoms
Galea et al (2005) USA[166]	Major depression NWS depression module (DSM-IV) [lifetime/6-month prevalence]	Survey Age: 18 or over Years: 2002	N= 1,355	59 community districts in New York City	At tiem of survey	Internal built environment, external built environment, neighbourhood income	Age, sex, ethnicity, income	In adjusted models, individuals living in neighbourhoods with poorer built environment were more likely to report six-month & lifetime prevalence of depression.	Survey conducted soon after 9/11 World Trade Centre terrorist attacks

Study ID & Setting	Outcome & Instrument	Case finding, age range, years	Sample size	Definition of neighbourhood	Timing of exposure	Area-levels measures	Individual-level measures	Findings	Comments
Lofors et al[157] (2006) Sweden	Anxiety (self-reported) [point prevalence]	Survey Age: 25-64 Years: 1995-2002	N=30,884	SAMS (small area market statistics ; ~2000 people in Stockholm, ~1000 people elsewhere)	At time of survey	% individuals with income lower than national average, neighbourhoods quartiles	Age, sex, marital status, immigrant status, employment, social network, housing tenure	Higher risk (odds) of anxiety when moving from least to most deprived neighbourhood, but not significant when adjusting for individual measures of SES.	
Fone & Dunstan[154] (2006) UK	Common Mental Disorders (SF-36) [point prevalence]	Survey Age: 14-74 years Years: 1998	N= 24,975	Electoral division	At time of survey	Townsend deprivation score	Age, sex, social class, economic inactivity, occupational status, marital status, whether the person is a carer, housing tenure	1.3% of CMD variance explained at area-level in the null-model. Adding compositional variables reduced variance to 0.5%, which remained significant. Both area-level & individual deprivation associated with poorer mental health, but greater effect in economically inactive individuals	
Matheson et al[170] (2006) Canada	Depression CES-D (short form) [point prevalence]	Survey Age: 18-74 Years: 2001-2001 & 2003-2004	N=56,428	Census tracts (range 2500-8000 people)	At time of survey	18 neighbourhood characteristics grouped into 4 factors: residential instability; material deprivation; dependency; ethnic diversity	Age, sex, marital status, education, visible ethnic minority	Material deprivation & residential stability associated with depression after adjustment for other characteristics	No control for household level characteristics
Guite et al[143] (2006) UK	Common Mental Disorders SF-36	Survey Age: 18 + Years: N/A	N=1,012	LSOA (lower super output area census tracts)	At time of survey	Quality of internal (heat, light, noise, damp & draughts) & external built environment, population density, long-term limiting illness, general health, crime level	Age, sex, ethnicity, residential stability, household size, housing type & tenure, housing benefit, rent arrears, requesting re-housing	Damp,; not liking residential area; noise; overcrowding; dissatisfaction with green spaces, community facilities & social facilities; feeling unsafe; presence of needles/syringes; lack of spaces where people can interact were all associated with higher CMD risk (odds) when entered individually in multivariable models	
Dupere & Perkins[167] (2007) USA	Depression (CES-D) [point prevalence] Anxiety (STAI) [point prevalence]	Survey Years: 1987	N=412	Empirically derived based on respondents' definitions	At time of survey	Fear of crime, civic participation, informal ties and % of people with characteristics measured at the individual level in neighbourhoods grouped in 5 categories: advantaged to disadvantaged	Age, sex, ethnicity, household income, education, unemployment, single parenthood, residential stability, personal stress, perceived social support	Depression: no associations found Anxiety: Lower in middle /middle-high advantage neighbourhoods & those with higher residential stability after multivariable adjustment	Multilevel models for depression not reported in text/table

Study ID & Setting	Outcome & Instrument	Case finding, age range, years	Sample size	Definition of neighbourhood	Timing of exposure	Area-levels measures	Individual-level measures	Findings	Comments
Galea et al[168] (2007) USA	Depression SCID-III incidence	Telephone survey in 2002 + follow up at 6 and 18 months age ≥18 years	N=1,570 / 1220 at FU	59 Community districts in NYC	At diagnosis	Area-level SES based on 2000 Census data	Age, sex, ethnicity, past 6-month depression, traumatic events exposure, income, education, marital status, social support, stressors	18-month cumulative incidence of depression was 19.4 vs. 10.5 per 100 persons in more *cf.* less disadvantaged neighbourhoods. Depression risk was doubled in disadvantaged neighbourhoods, after adjusting for individual-level confounders	Response rate 56% (Over-sampled residents close to World Trade Centre)
Lofors et al[64] (2007) Sweden	Depression Hospital Diagnosis ICD-9/ICD-10 Incidence	Psychiatric registers Age 25-64 years: 1997-1999)	Sample = 4.5m Swedish citizens. Cases = 10,930	Clusters of small area neighbourhood units	At diagnosis	Linking social capital (voting participation), neighbourhood deprivation	Age, sex, housing tenure, education, employment, country of birth, marital status	Between 1.7% (women) & 2.5% (men) of total variance explained at neighbourhood level. In multivariable models, deprivation, but not low levels of social capital associated with risk of depression	
Stockdale[163] (2007) USA	Common mental disorders (CIDI- short form) [point prevalence]	Survey Age: mean age 48 years Years:	N = 12,716	Census tract	At time of survey	Neighbourhood SES, density of outlets selling alcohol, density of mental health/ alcohol/ drug facilities, neighbourhood violent crime arrest rate, church density, average household occupancy	Age, sex, ethnicity. income, education, experience of witnessing violence in past year, residential stability	No evidence of area-level effect on risk (odds) of depressive symptoms	
Stafford et al[149] (2008) UK	Common Mental Disorder GHQ-12 [point prevalence]	Survey Age: Years: 1994-1995 & 1997-1999	N=9,082	Census ward (England) Postcode ward (Scotland)	At time of survey	Social capital (family ties, friendship ties, associational membership, integration in society, trust, attachment to neighbourhood, tolerance of others, reciprocity) & deprivation (Carstairs index)	Individual levels: age, gender, social class Household level: deprivation score.	No association between social capital measures & CMD in adjusted models. For people living in deprived areas, lower social capital was associated with higher CMD risk (odds)	
Ahern et al (2011) USA[179]	Major depression (unspecified prevalence) (PHQ-9)	Phone survey Age; 18 or over Years 2005	N=3,946	59 community districts in New York City	At time of survey	Neighbourhood collective efficacy, social cohesion, informal social control	Age, sex, marital status, ethnicity, birthplace, main language, income, education, length of time in neighbourhood, unemployment, illness, financial problems	Low neighbourhood collective efficacy associated with higher risk of depression after adjustment for other factors	49% response rate

Study ID & Setting	Outcome & Instrument	Case finding, age range, years	Sample size	Definition of neighbourhood	Timing of exposure	Area-levels measures	Individual-level measures	Findings	Comments
Vallée et al (2011) France[158]	Depression Current prevalence (MINI)	Years 2005	N=3,023	50 Census blocks in Paris and suburbs, and perceived neighbourhood	At time of survey	Activity space in neighbourhood, neighbourhood deprivation (self-reported, aggregate measure from respondents, actual deprivation) neighbourhood location (inner city, suburbs)	Age, sex, nationality, edication, occupational and employment status, marital status, functional limitation	People in deprived neighbourhoods were significantly more depressed than those in advantaged neighbourhoods, especially when activity spaces were limited Initial spatial variance in depression accounted for by neighbourhood factors	
Beyer et al[136] (2014) USA	Common Mental Disorders (unspecified prevalence) (DASS)	Survey Age: 21-74 Years: 2008-2011	N=2,479	Wisconsin Census Block groups [600-3000 people]	At time of survey	Green spaces, % tree canopy, urbanicity, population density, median household income below poverty, residential instability, % owner occupied households, % unemployed, ethnic segregation.	Age, sex, ethnicity, marital status, education, household income, occupational status, health insurance	Higher % green spaces associated with better mental health outcomes after adjustment for all other variables Other social & economic aspects of neighbourhood also associated with depression, anxiety & stress	
Jokela[173] (2014) Australia	Mental Health (unspecified prevalence) (mental health short form, SF-36)	Longitudinal Survey over 10 years Age: Years:	N=20,012	Statistical local areas (median population n=5,908)	Repeated measurements at baselines and follow ups.	Index of neighbourhood disadvantage; neighbourhood remoteness	Age, sex, country of birth, smoking, alcohol, physical activity, neighbourhood dissatisfaction & problems	Association between neighbourhood disadvantage & poorer mental health explained by individual-level characteristics. Neighbourhood remoteness was associated with better mental health	Participants moving to more disadvantaged areas had poorer mental health, supporting social drift hypothesis
Jones-Rounds et al[159] (2014) Multiple European cities	Psychological wellbeing Point prevalence (6 questions capturing symptoms of depression & anxiety)	Survey Age: N/A Years: 2002-2003	N=5,605	Not-specified	At time of survey	Neighbourhood quality	Individual level: SES, employment status, sex & marital status, housing quality Household level: size, composition, highest educational level of any member, number of people working full time, people over 60	Housing & neighbourhood quality predicted psychological well-being in adjusted models. Effect of neighbourhood quality less pronounced at higher levels of housing quality	

Study ID & Setting	Outcome & Instrument	Case finding, age range, years	Sample size	Definition of neighbourhood	Timing of exposure	Area-levels measures	Individual-level measures	Findings	Comments
Erdem et al[156] (2015) The Netherlands	Psychological distress Point prevalence (Kessler-10)	Survey Age: 16 or over Years: 2008	N= 18,173	City district (average 4000 people)	At time of survey	Neighbourhood SES (income, work and level of education), neighbourhood green space, urbanicity & home maintenance, social cohesion	Age, sex, ethnic background, marital status & years in current city, education, occupation & financial difficulties	In univariable model 2.87% of variance explained at neighbourhood level, but reduced to 0.25% when individual variables included Higher neighbourhood social cohesion associated with lower psychological distress after adjustment	
Gariepy et al[171] (2015) Canada	Episodes of depression Point prevalence (CIDI short form)	Survey Age: N/A (average 42 at baseline) Years: 2000-2011	N= 7,114	500m radius buffer around centre of postal code of each participant	At time of survey	Density of businesses, parks & recreational facilities	Age, sex, marital status, education income adequacy, family history of depression, chronic condition, childhood life events	Presence of parks, healthy food stores, fast food restaurants & health services associated with lower probability of depression episode among people in low depression trajectory. Parks were associated with lower probability of depression episode in people in the moderate depression trajectory	
LAMIC									
Dias Porto Chiavegatto Filho et al[174] (2013) Brazil	Depression & anxiety (CIDI) [point prevalence]	Survey Age: 18 + Years: 2004-2005	N= 3,542	Sao Paolo boroughs	At the time of survey	Income inequality (Gini Coefficient)	Age, sex, education, income, marital status	In multivariable analyses, living in areas with medium to high income inequality associated with higher risk (odds) of depression, but not anxiety.	
Tomita & Burns[175] (2013) South Africa	Depression (CES-D) [point prevalence]	Survey Age: 15+ Years: 2008	N = 13,469	Neighbourhoods (non-specified)	At the time of survey	Social capital (from 4 questions on (1) support network & reciprocity, (2) association activity, (3) collective norm & values, (4) safety)	Civic participation, social trust, age, sex, ethnicity, marital status, employment, education, self-reported health status, social class, neighbourhood attachment	In multivariable models lower social capital was associated with higher levels of depressive symptoms 2.61% of variance was attributable to neighbourhood level	

List of abbreviations: CES-D= Center for Epidemiological Studies Depression scale; CIDI:= Composite International Diagnostic Interview ; CIS-R = Clinical Interview Schedule Revised; DASS= Depression Anxiety Stress Scales ; DIS= Diagnostic Interview Schedule; DMI = Depressive Mood Inventory; GHQ= General Health Questionnaire; HLEQ= Health and Life Experiences Questionnaire; NWS = National Women Study; PHQ-9 = Patient Health Questionnaire; SF-36= Short Form 36; STAI = State Trait Anxiety Inventory

3.3 Strengths and limitations

Compared with studies of schizophrenia, sample sizes in CMD studies have generally been smaller, although these were generally adequately powered to detect any significant associations. Their reliance on cross-sectional survey based designs are well-suited to measuring prevalence in the general population, providing the sampling frame allows for adequate generalisation. These study designs also mean a large number of confounding factors can be measured at the time of the survey, offering an advantage over register-based investigations which may be limited to routinely-collected data. Such additional adjustment could explain the less pronounced association between urban environments and CMD than for schizophrenia, though further empirical work would be required in the schizophrenia literature to confirm this. Alternatively, studies of CMD typically use a broader variety of instruments to measure clinical disorder or general (often sub-clinical) psychopathology in their samples, which could lead to the observation of weaker associations overall, if exposure to social adversity was only causally important in the emergence of clinical disorders. Cross-sectional surveys have a number of inherent weaknesses; for example, people taking part in the surveys may be systematically different from those who do not, affecting (biasing) the results. In the studies we reviewed, participation rates varied from 54%[126] to 90.6%[180] in urban-rural studies and between 38%[143] and 86%[161] in neighbourhood studies, suggesting that selective participation could be an issue in some studies. A further limitation of cross-sectional studies is that exposures (i.e. urban living) and confounders are measured concomitantly with the outcome (CMD), making it impossible to infer causality from any observed association; as the adage goes, correlation does not imply causation. While cross-sectional surveys can obtain measures which happened in the past, via interview or questionnaire, the answers elicited from this type of study may be prone to recall bias. If the probability of (mis)remembering an exposure or confounder in the past is related to the participant's mental health status, this type of bias can be particularly problematic, since any observed associations may be under- or over-estimations of the true effect.

In summary, the evidence in favour of an association between contextual neighbourhood factors and CMD was weaker than for schizophrenia and other non-affective psychotic disorders. The overall variance in the distribution of CMDs was generally less than 2%, with some indication that observed associations were due to residual confounding or household-level characteristics. These results suggest that compositional rather than contextual characteristics are driving any small area-level variation in CMD. Notwithstanding, most studies of CMD included here were cross-sectional, making it impossible to exclude selection biases as an explanation for the inconsistent or null findings

observed. Further longitudinal research into the role of the neighbourhood on CMD risk would therefore appear warranted.

4 Suicide

Each year more than 800,000 people die by suicide, making it the second leading cause of death among young people globally.[181] Suicide therefore presents a major public health issue, particularly because a large amount of research suggests that rates are unequally distributed throughout the population. Thus, they vary by gender,[182–186] presence of an existing mental disorder,[187–189] chronic illness,[190] unemployment,[191] low social support and social capital[192,193] and exposure to violence, abuse or trauma.[194–198] While much of this research has focussed on the individual level, the distribution of these risk factors, as well as suicide rates, vary according to characteristics of geographic areas, communities, and neighbourhoods.

Investigation of the spatial distribution of suicide mortality dates back as far as the late 19th Century, with Durkheim's seminal monograph,[199] in which he first noted that suicide rates clustered geographically. He proposed that individual acts of suicide were due to forces outside of the individual, and that the geographical distribution of suicide rates could be explained by underlying patterns of social interaction and regulation. By contrast, Tarde (1903),[200] argued that such patterns could be understood by imitation, where behaviours and beliefs are shared within a population. Numerous studies have subsequently investigated the spatial distribution of suicide, demonstrating that suicide mortality varies geographically. Such research allows appropriate investment in public mental health and prevention strategies, and may give further insight into the aetiology of suicidal acts. In this section, we review the main studies on suicide risk in relation to both broad rural-urban variation and specific area-level or neighbourhood differences in risk. We briefly examine whether suicide methods differ between rural and urban settings, and summarise the main hypotheses put forward to explain geographical differences in patterns of risk.

4.1 Urban vs. rural settings

To study how suicide rates vary between rural and urban areas, research studies have often used centralized registries, coroners' reports and death certificates as a basis for investigation. Most studies have been conducted in High Income countries, including six from Australia,[201–206] four from the United States,[207–210] two from Austria,[211,212] three from the UK,[213–215] one from Canada[216] and one from New Zealand[217] (Table 5). More recently, a handful of studies have been conducted in LAMIC countries, including Taiwan,[218] India,[219] Belarus,[220] China[221] and South Korea.[222]

Table 5: Summary of literature on rural/urban differences in suicide rates (from 2000 onwards, chronologically ordered)

Study ID & setting	Diagnostic criteria & outcome	Case finding, age range, years	Sample size & no. of cases	Definition of spatial unit (rural/urban)	Timing of urban	Findings	Higher in	Confounders	Comments
Wilkinson & Gunnell[206] (2000) Australia	Suicide and undetermined deaths ICD-9 codes E950-9, E980-9 except E988.8	Australian Bureau of Statistics (ABS) Aged 15-34 years (1988-1997)		Nonmetropolitan classified as ≤20000 people; metropolitan >20000 people		Suicide rates in non-metropolitan areas higher for men aged 15–24 years, but lower for women aged 25-34 years old compared to their counterparts in metropolitan areas. No other differences	Rural (men 15-24), equivalent (men, 25-34; women 15-24), urban (women 25-34)		
Yip et al[225] (2000) China		China's Ministry of Health - Death certificates issued by physicians. (1991-2000)		Not specified	Not specified	Suicide rates consistently higher in rural *cf.* urban areas for men & women. Overall rates decreased over time, with an interplay of age, gender & region driving change	Rural	Age, sex, region	Authors suggest that rapid modernization has corresponded to decreased suicide rates in China, due in part to increased standards of living, education & medical care.
Singh & Siahpush[210] (2002) USA		County mortality data – National mortality data files. Aged 15+ years (1970-1997)		Counties categorized using US Department of Agriculture classification based on population size & proximity to metropolitan areas categorised into 10 levels	At death (county-specific annual suicide deaths) n=3,101 US counties	Male suicide rates were higher in rural areas. Gap increased over time & more pronounced in 15-24 men. For women, between 1970-1989, suicide rates were higher in urban areas, but this difference decreased over time & rates were higher in rural areas by 1995-7	Rural (men), urban (women, 1970-1989), rural (women, 1995-7)	Age-, sex- & county-specific deaths. Adjusted for county-level variation in ethnic composition & divorce rate (as indicator of social disintegration)	Classification of rurality/urbanicity was done in 1993 based on 1990 census. Criteria may not be appropriate across all time periods.
Middleton et al[215] (2003) England & Wales	Suicide & undetermined death – ICD-9 codes E950-E959 & E980-E989, excluding E988.8	Office for National Statistics (ONS) (1981-1998)		9264 electoral wards categorized by 2 indices: (1) population density (quartiles); (2) population potential (quartiles) – a measure of geographic remoteness from large settlements	Postcode of usual residence at time of death, linked to electoral wards based on 1981 boundaries	Among 15-44 year olds, suicides higher in remote areas. Rises in rates in rural areas were more related to population potential than population density.	Rural	Townsend socio-economic deprivation index & Congdon social fragmentation index	
Caldwell et al[201] (2004) Australia	ICD-10 codes X60-X84	Australian Bureau of Statistics (ABS) Aged 20+ years (1997-2000)	N=10,641	Metropolitan centres (≥100,000), rural centres (10000–99999) Population & rural areas (<10000 people)		Rates higher for men in rural compared with metropolitan areas. For women, only those aged 30-44 had higher rates in rural areas	Rural (men, women aged 30-44), equivalent (women, other ages)		Young men with mental health disorders in rural areas less likely to seek professional help

Study ID & setting	Diagnostic criteria & outcome	Case finding, age range, years	Sample size & no. of cases	Definition of spatial unit (rural/urban)	Timing of urban	Findings	Higher in	Confounders	Comments
Levin & Leyland[214] (2005) Scotland	Suicides & undetermined deaths. ICD-9 codes E950-959.0 & E980-988.9	General Register Office for Scotland (GROS) Ages 15+ years (1981-1999)		Four groups from the Scottish Household Survey rurality classification. (1) Urban >10,000 people; (2) Accessible Rural = settlements <10,000 & within 30min drive of settlement of ≥10,000; (3) Remote Towns = 3000–10,000 & >30min drive of a settlement of ≥10,000; (4) Remote Rural = <3000 population & >30min drive from settlement of ≥10,000	Residence at death	Highest rates in remote rural areas. Age- & deprivation-adjusted models showed significantly greater risk of male suicide in remote & rural areas relative to urban areas, but lower risk of female suicide in accessible rural areas	Rural (men)	Carstairs deprivation indicator using car ownership, low social class, male unemployment & overcrowding), age, sex	High divorce rates & population loss between 1990-2000 predicted suicide rates
Yip et al[221] (2005) Australia & China (Beijing)	ICD-9 codes E950-E959	Australia – Australian Bureau of Statistics - Coroner's report. Beijing – Death certificates & Public Security Office from the Ministry of Health (1991-6),	Not specified	Not specified	Not specified	In Beijing suicide rates in rural areas were nearly 3 times higher than urban areas, (~5 times higher for women aged 25-34). In Australia, rural male suicide rate was higher than urban rate, but pattern reversed for women	Rural (Beijing: men & women, Australia: men) Urban (Australia: women)	Age, sex, region	Authors noted that the male: female suicide ratio in China was less than 1:1, but in Australia it was 4:1. In Beijing, elderly suicide rates were 6 times higher than the general population, but were not as increased in Australia
Stark et al[213] (2007) Scotland	Suicide or undetermined cause ICD-9 codes E950-E959, ICD-10 codes X60-X84, E980-E989, Y10-Y34.	General Register Office for Scotland (1981-1999)		Postcode sector used as proxy for rurality. Population density divided into quartiles.	Death allocated to area of residence, rather than the area they died.	Higher rate ratios in most & least densely populated quartiles. Association in women varied by age – no association under 25 years, similar pattern to men in middle age, lower rural rates in older women	Various (see left)		
Page et al[204] (2007) Australia	Not specified	Australian Bureau of Statistics (ABU) Aged 15+ years (1979-2003)		Rural, remote & Metropolitan Area classification system: (1) metropolitan; (2) rural areas (large & small rural centres & other rural areas); (3) remote areas (remote centres & other remote areas)		Rural-urban differences reduced over the study period, but remained significant for men. Female suicide rates were lower in rural & remote areas, particularly for those aged 25-34	Rural (men), urban (women)	Sex, age, country-of-birth, area SES	
Pearce, Barnett & Jones[217] (2007) New Zealand		Ministry of Health Aged 15+ years (1980-2001)	N=9,054 suicide deaths	Census Area Unit (CAU) (~2300 people) classified according to Statistics New Zealand's Urban-Rural Profile Classification to create a binary urban-rural variable	Domicile code (linked to CAU) at death	Higher rates in urban areas (1980–1982), but equivocal by 1990s. Narrowing urban/ rural differential may be due to raised suicide rates in more rural communities over time	Urban (1980-82), equivalent (1990s)	Sex, residential domicile, age at death	
Kapusta et al[211] (2008) Austria	ICD-8, ICD-9, ICD-10	Statistics Austria – death certificates (1970-2005)	99 districts	Five population density categories		Ratio of rural to urban suicide rates continuously increased over last 30 years, indicating growing risk in rural areas	Rural	Age, sex, family status & suicide method	

Study ID & setting	Diagnostic criteria & outcome	Case finding, age range, years	Sample size & no. of cases	Definition of spatial unit (rural/urban)	Timing of urban	Findings	Higher in	Confounders	Comments
Razvodovsky & Stickley[220] (2009) Belarus		Belarus Ministry of Statistics Ages 15+ years (1990-2005)		Population density & structure of employment used. Classified as urban if >6000 inhabitants, or if >2/3 not employed in agriculture. All other settlements defined as 'rural'		Higher in rural areas, although for those ≥75 years, urban rates were higher until 2000, but this reversed by 2005.	Rural (men & women, except among oldest age groups by 2005)	Age, sex	Deteriorating social & economic situation may explain increasing suicide rates, with some rural-specific explanations, including increased social isolation & poor provision of medical services
Kapusta et al[212] (2010) Austria	Not specified	Statistics Austria for mortality database	Not specified	Continuous measure of population density	Population density in 2001	Lower rates in urban areas	Rural	Population density, religion, unemployment rate, income	Access to mental health care was also related to rural-urban differences, with fewer facilities in rural areas
Chang et al[218] (2011) Taiwan	Certified suicides, undetermined death, death by pesticide poisoning & suffocation: ICD-9 codes E950-E959, E980-E989, E863, & E913	1999-2007	N=37,326 suicides,	Deaths assigned to 358 districts according to registered address on death certificate.	Residence at death	Rates highest in rural, East Taiwan. No evidence of above-average rates in large cities. In Taipei, rates increased toward suburbs. Income, population density & lone parent households associated with risk. Spatial patterning strongest in young people	Rural		
Cheung et al[202] (2012) Australia	ICD-10 codes X60-X84 and/or with the 'intent' column registered as '2' (intentional self-harm).	National Coroners Information System (NCIS) (2004-2008)		Rural, Remote & Metropolitan classification (RRMA) & index of remoteness: (1) metropolitan zone with population ≥100,000 (RRMA 1-2); (2) Rural zones (RRMA 3-5); (3) remote zones (RRMA 6-7)	Post areas (PAs) (n=2507) assessed in 2006.	Counties with low population density had higher suicide risk than heavily-populated coastal cities. Rates higher for men in rural & remote areas. Spatial clusters identified in N. & W. areas. No rural-urban gradient for women	Rural (men), equivalent (women)	Age & sex standardized analyses	
Park & Lester[222] (2012) South Korea	Not specified	Korean Statistics Promotion Institute & census data Aged 15+ years (2005)	N=12,011 suicides (pop. n=38.1 m aged ≥15)	Korea's administrative districts. All townships without their own municipalities were classified as rural		Suicide rates higher in rural areas	Rural	Age, gender, marital status, month of suicide.	Authors noted a high rate of pesticide & chemical use as method of suicide.
Patel et al[219] (2012) India	ICD-10 codes X60-X84	Registrar General of India Aged 15+ years (2001-2003)	N=2,684 suicide deaths	6671 small areas, randomly selected	Not specified	Age-standardised suicide rates were about two times higher in rural than urban areas. Rates varied between states, generally higher in south India	Rural	Age, sex, region, marital status, occupation, alcohol use, household fuel type, education	Higher rate in rural India may be linked to availability of pesticides
Titelman et al[224] (2013) Nordic countries	Suicide & self-inflicted injury ICD-8 & ICD-9 codes E950-E959; ICD-10 codes X60-X84, Y87.0	Aged 15+ years (1980-2009)		No official definition. Rates in larger regions compared to each other		Rural areas in Norway, Finland, & Sweden had highest suicide rates, while capital cities had lower rates than national averages	Rural		

Study ID & setting	Diagnostic criteria & outcome	Case finding, age range, years	Sample size & no. of cases	Definition of spatial unit (rural/urban)	Timing of urban	Findings	Higher in	Confounders	Comments
Law, Snider & De Leo[203] (2014) Australia	Cases of "possible suicide" & "undetermined causes" were not included.	Queensland Suicide Register, aged 15+ years (2004-8)	2,803 suicides	Dichotomous categorization of 38 rural-urban areas		Deprivation associated with age-standardized suicide mortality, particularly in men aged 15-59. Deprivation factors had stronger association with suicide risk in urban areas, with non-significant or inverse effects in rural areas	Deprivation increased suicide rates, particularly in urban areas	22 socioeconomic variables indexing material & social conditions & relative socioeconomic disadvantage	Area-based indices of deprivation may produce inaccurate assessments of rural socioeconomic status
Ngui et al[223] (2014) Canada	ICD-10 codes X60-X84, Y87.	Register Aged 15+ years (2004-7)	N=2,951	406 postcode areas known as "Forward sortation areas"	Measured using postal code of place of death	Most likely clusters of suicide found in remote rural areas, lowest in metropolitan areas. Clusters likely driven by male rates; women more likely to die by suicide in urban areas	Rural (men), urban (women)	Age & sex	
Qi et al[205] (2014) Australia	ICD 9: 950.0-959.9 & ICD 10: X60-X84	ABS Ages 15+ years (1986-2005)	N = 45,293 suicide deaths	Statistical Local Area	Place of suicide occurrence	Suicide rates higher in rural areas	Rural		
Searles et al[209] (2014) USA (16 states)		Deaths categorized as suicide in National Violent Death Reporting System (2006-2008)		Based on population density, distance to metropolitan area & employment to create *urban, rural adjacent* & *rural nonadjacent* areas	County of residence	Demographic, socioeconomic & mental health risk factors differed amongst rural & urban cases; in rural areas cases were less likely to receive a psychiatric diagnosis & less likely to be in treatment for mental health problems. History of substance abuse, job & financial problems were more prevalent among urban dwellers	Did not compare rural-urban differences directly	Age, sex, Hispanic ethnicity, marital status, homeless-ness, urban–rural residence, veteran status, mental health history	Risk factors for suicide, including substance abuse & availability of mental health services differ by urban-rural location
Fontanella et al[207] (2015) USA	ICD-9 (Clinical Modification) codes E950-E959 and ICD-10 codes X60-X84, Y87.0 & U03	Aged 10-24 years (1996-2010)	N=66,595 suicide deaths	2003 Rural-Urban Continuum Codes from US Department of Agriculture, classifying 3141 US counties into 9 groups based on population size & adjacency to metropolitan areas		Rural suicide rates nearly double those in urban areas. Disparities persisted after controlling for confounders. Male rates declined in most urban areas over time, but remained stable in rural areas. Female rates increased in both rural & urban areas	Rural	Education, ethnicity, unemployment, poverty, female-headed households, unemployment, divorce, population density, health utilization, income	

Most studies have showed a consistently increased risk for suicide in rural compared with urban areas.[201,207,208,211,218,220] However, some studies have suggested that this effect may differ between men and women, as well as by age (Table 5), although such inconsistencies may be partly attributable to variation methodological approaches or differences over time. Variation in findings may also reflect the different characteristics of urban and rural places included in different studies, and how the distribution of resources, including mental health care, varies by country.

Increased suicide risk was most consistently found for rural men,[201,202,227] with some evidence of a null effect[202] or reversed trends for women.[204,223] It is currently unclear as to whether urban-rural differences in suicide rates are changing over time, with studies reporting that this mortality gap is both growing[207,210,211] and narrowing[204,217,220]; both are possible and may be context dependent, subject to a range of other social and economic determinants of health[209] (see Section 4.2). Further, as suicide rates in most countries are elevated among men (in some regions the rate is four times higher among men than women), the lower number of events for women may mean that some studies were underpowered to detect urban-rural variations in female suicide rates. Lower suicide rates in women, overall, may also be attributable to the fact that women are more likely to receive an open verdict than suicide on their death certificate,[228,229] highlighting the need for careful definition of the outcome measure used in an epidemiological enquiry into variation in suicide rates.

4.2 Neighbourhoods

In an attempt to move beyond basic rural-urban gradients in suicide mortality, several studies have used small area investigations to examine neighbourhood variation which may account for variation in suicide rates (Table 6), including social isolation and integration.[230] As before, this research has primarily been conducted in High Income countries, including Denmark,[231] Australia,[232] New Zealand,[233] the UK,[213,234–237] United States,[208,238] Canada,[216] Belguim,[230] Austria,[212] Netherlands,[193] Finland,[239] Taiwan,[218,241] Brazil,[242] Slovenia[243] and Japan.[244] Both social fragmentation,[223,230,236,237,243] and deprivation[193,203,230,233,236,239] have been associated with suicide mortality, as well as some evidence of a relationship with income inequality,[239] low social capital (in particular social trust),[193,208,240,244] and low population density.[208,213,230,232] Nonetheless, these relationships have not been uniformly observed, with for example, Chang et al.[218] finding that social fragmentation was not strongly or consistently associated with suicide rates in Taiwan. A limited number of studies have also investigated climatic factors,[238,241] including temperature, precipitation, sunshine, altitude and atmospheric pressure, finding they only explained a small amount of variance in suicide mortality, and were generally outweighed by socioeconomic factors.

Table 6: Summary of studies of suicide rates by area/neighbourhood (from 1999 onwards, chronologically ordered)

Study ID & setting	Diagnostic criteria & outcome	Case finding, age range, years	Definition of neighbourhood	Timing of exposure	Area-level measures	Individual-level measures	Findings	Comments
Neeleman & Wessely[235] (1999) UK	Suicide verdict, suicide note found, method unambiguously indicated suicide, and/or suicidal intent recorded	Office for National Statistics & coroner's reports. N=329 suicides in South London (population 902,008), 1991-3	109 electoral wards in London boroughs Lewisham, Lambeth, Southwark & Greenwich (mean pop. N=8274)	Postcodes linked to electoral wards	Small area ethnic densities & deprivation (Jarman index)	Age & sex	Minority suicide rates were higher in areas where minority groups were fewer. White suicide rates were higher in areas where more ethnic minorities live, independent of deprivation or age	Supports ethnic density hypothesis for completed suicide
Whitley et al[237] (1999) UK	Deaths coded as suicide or open verdict: ICD-9 codes E950-E959, E980-E989	1981-1992		633 parliamentary constituencies of Great Britain	Townsend deprivation score, Congdon's anomie index, mean abstention rates from general elections in 1979, 1983, 1987 & 1992		Higher suicide rates associated with higher abstention, social fragmentation & deprivation. Greatest for social fragmentation. Areas with greatest increases in social fragmentation over study period also had greatest increases in suicide	Ecological study unable to separate contextual from compositional effects
Martikainen, Maki & Blomgren[239] (2004) Finland	ICD-9 codes E950-E959B, E959X & ICD-10 codes X60-X84, X870	Statistics Finland Ages 15-99 (1991-2001)	Functional regions (n=85) were used, which are neighbouring municipalities grouped according to travel-to-work areas & patterns of cooperation among municipalities	Area characteristics measured in 1990, 1992, 1993	Socioeconomic structure & deprivation, income inequality, social cohesion	Age, sex, SES, household income, housing tenure, economic activity, marital status, family type, household size, mother tongue	Suicide mortality varied between regions; larger for men than women. High mortality observed in deprived areas & areas with low family cohesion & voter turnout. Relationships were attenuated, but not fully accounted for after adjustment for individual characteristics. Area characteristics did not mediate/modify effects of individual SES on suicide	Multilevel study
Hempstead[208] (2006) USA	ICD-9: E950-E959	Death certificates, medical examiner data 15 or older (1999-2001)	Municipality	Municipality of death (not residence) used	Population density, demographic structure, income, unemployment & crime rates		Low population density & high % single person households predicted suicide rates. More common in areas with declining population between 1990-2000 & where divorce rates were high	
Agerbo, Sterne & Gunnell[231] (2007) Denmark	ICD-8 codes E950-959 & ICD-10 codes X60-X84	Medical Register on Vital Statistics Ages 25-60 (1982-1997)	Municipalities in Denmark (N=276)	Year of suicide	% of people living alone, % employed individuals (based on male employment), median gross income (by male income)	Marital status, gross income, employment	When adjusted for individual measures, area-level associations were weak. Little evidence of cross-level interaction (that individual risk varied based on area characteristics)	Area-level associations explained by composition of high-risk individuals in some areas
Stark et al[213] (2007) Scotland	ICD-9 codes E950-E959. ICD-10 codes X60-X84, E980-E989 & Y10-Y34	General Register Office for Scotland 1981-1999	Postcode sector (used as proxy for rurality)	Death allocated to area of residency, not area at death.	Deprivation & population density		Deprivation was strongly associated with suicide rates in Scotland for all levels of population density for all ages	
O'Reilly et al[236] (2008) Northern Ireland	ICD-10 codes X60-X84, Y10-Y34, Y87.0	Northern Ireland Statistics & Research Agency linked all those in		Census super-output area level (a standard government	Material deprivation (%receiving social security benefits), population density, social fragmentation (% in rented	Marital status, household size, SES, economic activity,	Higher suicide rates in more deprived & fragmented areas disappeared after adjustment for individual & household factors. No relationship between	Area-level associations explained by composition of high-

Study ID & setting	Diagnostic criteria & outcome	Case finding, age range, years	Definition of neighbourhood	Timing of exposure	Area-level measures	Individual-level measures	Findings	Comments
		2001 census to deaths in the subsequent 5 years. n=1,116,748 (n=566 suicides) aged 16-74		administrative area, with average population size 1,894)	accommodation, unmarried, less than 65 living alone, population turnover in year preceding census)	self-reported health status	population density & suicide. Differences in rates of suicide between areas due to population composition than area-level factors.	risk individuals in some areas
Haws[238] (2009) USA	Not specified	Not specified (1990-1994)	States	Not specified	Elevation (i.e. altitude, of state capital city)	Age, race/ethnicity, sex	After adjustment, altitude of the state capital city was significantly correlated with suicide rates.	
Collings et al[233] (2009) New Zealand	ICD-9 codes E950–E959, E980–E989	2.8 million respondents in 1996 census, followed up for 3 years for mortality (n=1101 suicide deaths), Aged 20-74 years at follow-up. (1996-2000)	There were 1775 area units (approximately 2000 people in each area) with borders based on locally recognisable communities.		Index of Neighbourhood Social Fragmentation, Congdon index of fragmentation, neighbourhood deprivation	Age, sex, ethnicity, educational qualification, marital status	No linear association between neighbourhood fragmentation & suicide. However, a U-shaped association was suggested by Congdon index, indicating that living in the most or least fragmented decile of neighbourhoods was associated with increased suicide rates. Neighbourhood deprivation also predicted suicide rates. Authors concluded that neighbourhood SES is a risk factor for suicide independent of individual-level socioeconomic position	
Kelly et al[246] (2009) Europe		National suicide rates from World Health Organization (2002-2004)	Comparing 11 European nations	2003-4 variables measured in European Social Survey	Social trust, aage, sex, marriage rates, income & reported sadness	N/A	National suicide rates inversely related to social trust after controlling other factors	Ecological study
Kapusta et al[243] (2010) Austria		Statistics Austria for mortality database (1991-2005)	Districts (90 in Austria)		Population density, religion (% Roman Catholic), mean income, unemployment rate, number of general practitioners, psychiatrists & non-physician psychotherapists		Neither density of general practitioners or psychiatrists associated with suicide rates, but weak association of association with psychotherapist density.	Little variance in density of GPs in Austria may explain lack of association
Tsai[241] (2010) Taiwan		Population based mortality database from the Department of Health in Taiwan. (1998-2006)			Population characteristics (gender, age), socioeconomic status (marriage, unemployment, income) & climatic factors (temperature, atmospheric pressure, precipitation, duration of sunshine)	Not measured	Suicide was negativaely correlated with temperature & positively correlated with sunshine. Socioeconomic & climatic factors contributed 52.7% & 6.8% respectively to variance in suicide mortality	
Qi, Tong & Hu[232] (2010) Australia		Australian Bureau of Statistics (ABS) 1999-2003 N=2445 suicide deaths All ages		Statistical Local Area (SLA, n=452) & Local Governmental Area (LGA). Urban LGAs contained 2+ SLAs & rural/ remote areas	Geographical variation	Age, sex, year & month of suicide, country of birth, Statistical Local Area	Significant suicide clusters were discovered in NW & N Australia. These areas had very low population density.	Higher rates may be due to social isolation, lack of mental health services. Compositional effects included high % minority grousps & low SES

Study ID & setting	Diagnostic criteria & outcome	Case finding, age range, years	Definition of neighbourhood	Timing of exposure	Area-level measures	Individual-level measures	Findings	Comments
Chang et al[218] (2011) Taiwan	Certified suicides, undetermined death, accidental pesticide poisoning, suffocation. ICD-9 codes E950-E959, E980-E989, E863, E913.	(1999-2007)	358 districts – Districts are the administrative unit below the county/city level.	Residence assigned based on registered address on death certificate	Single-person households, people who moved to another district, marital status, lone-parent households, households not owner-occupied, non-employed adults, population aged 15-17 not at school, adults with college or higher education, median household income, population with limiting long term illnesses, indigenous people, agricultural workers, population density.		After controlling for other area characteristics, increasing suicide rates found in areas with high % lone-parent households, low household income & low population density. Indicators of social fragmentation (i.e. population mobility & % living alone / unmarried) were not strongly associated with suicide rates	
Hooghe & Vanhoutte[230] (2011) Belgium		Official death certificates (confirmed by a medical doctor) 1996-2005 N=12,000 registered cases of suicide		308 communities in Flanders region	Social integration (religious participation, rate of single households, internal migration rate, external migration rate, presence of non-European inhabitants), socioeconomic deprivation (average income), rural-urban divide (population density – inhabitants/km^2), age & sex		Community characteristics were significantly related to suicide rates. Measures of social integration were mixed: single person households & deprivation were associated with higher suicide rates; religious participation was unrelated; population density, immigration & presence of non-European inhabitants with lower suicide rates. Areas with older populations had higher suicide risks than expected	Ecological study Communities have an impact on suicidal behaviours, possibly via effects of social isolation
Bando et al[242] (2012) Brazil	ICD-10	Brazilian & São Paulo State Death Registry Databases Ages 15 or older 1996-2008 n=98904 deaths (Brazil), 21066 in São Paulo State, 5589 in São Paulo city	Deaths assigned to states (27 Brazilian states & 558 micro-regions), 645 counties of SP state &96 districts of SP city.		Average income	Sex	Higher suicide rates found in wealthier areas of Brazil, São Paulo city & poorer areas of São Paulo state. May reflect worldwide patterns, where direct associations with income are found in more equal areas, but inverse is found in areas with more inequality. Regional socioeconomic characteristics may moderate association between SES & suicide risk	Ecological study
Congdon[234] (2012) UK		Adult Psychiatric Morbidity Survey		Government office region (REG) & small area deprivation quintile (QIMD).	Age, ethnicity, social capital	Household income, education, marital status employment, owner occupied housing, receipt of income benefit, one person household, migrant in previous year	Neighbourhood perceptions associated with suicidal behaviours. However, area deprivation did not have a distinct significant influence, in contrast to a number of ecological studies. Deprivation may be partially mediated by social capital	
Zhang & Wang[248] (2012) China	Not specified	Part of a large psychological autopsy project ages 15-34 n=392 suicide, 416 controls			WHO Community Stress & Problems scale – social & structural stresses, community behavioural problems	Age, sex, education, income, marital status, physical illness, mental disorder & status in family.	Neighbourhood stresses & problems increase suicide risk in rural China. Health care, alcohol, job security, family disputes & transportation found to have important roles in increasing suicide risks	

Study ID & setting	Diagnostic criteria & outcome	Case finding, age range, years	Definition of neighbourhood	Timing of exposure	Area-level measures	Individual-level measures	Findings	Comments
Jagodic et al[243] (2013) Slovenia		Institute of Public Health of the Republic of Slovenia (mandatory registry of all deaths) (2000-2009)	Population divided into 12 statistical regions (administrative entities)	2000	GDP per capita, unemployment, marriages rates, divorces rates, mental health service availability (psychiatrists per 100,000, availability of psychological services & primary care doctors), prevalence of mental disorders, prescribed antiolytics & antidepressants, age & sex		Unemployment rate, marriage/divorce ratio , psychiatrist availability & quality of depressive disorder treatment predicted regional suicide rates	Ecological study
Kunst et al[193] (2013) Netherlands	ICD-9 codes E950-E959 & ICD-10 codes X60-X84	Mortality record & population data from Statistics Netherlands (CBS) n=6207 suicide deaths n=117,569 individuals 18+ years (1995-2000)	N=3507 neighbourhoods. Place of residence defined by meaningful socio-economic or geographical boundaries, corresponding to people's perceptions of their community.	Place of residence by postal code data on January 1, 1995	Area income, population density, religious orientation, social capital (WBO Housing Demand Survey in 1998) & complimentary measure of social fragmentation based on Congdon index	Age sex, marital status, country of origin	After controlling for individual factors, suicide rates were 60% higher in areas with lowest income compared with highest income. Variations in suicide rates according to population density & cultural/religious variables were smaller & non-linear. Suicide mortality rates were higher in areas with low social capital. Effect of social capital on suicide mortality more pronounced for some population subgroups (men, younger people & unmarried individuals)	Cross-sectional registry-based study
Okamoto et al[244] (2013) Japan		Data from previous survey, ages 20+ (2006-2007 for suicide & demographic variables, 2009 for social capital measures)	Administrative municipalities (n=20)		Social capital (organizational membership, social trust, fairness, helpfulness, confidence in organizations), sex, age, population density, unemployment, primary industry workers, % elderly, psychiatrist availability		Suicide rates inversely related to social trust for men, but not other indicators of social capital	Cross-sectional Ecological study
Ngui et al[223] (2014) Canada	ICD-10 codes X60-X84, & Y87.	Death Registry 15+ years (2004-7)	Forward sortation area (FSA) – first 3 letters of the postal code. (n=406)	Postal code of the place of death.	% renters, % population without a diploma, unemployment rate, % agricultural workers	Age & sex	Areas with highest % single person households more likely to contain a suicide cluster. Less likely in areas with high % 65+ years, single-parent families & % without a diploma. For women, % single-parent families & agricultural workers increased likelihood of suicide cluster, whereas % with a university education & % unemployed decreased risk	Not able to test for individual characteristics Unknown how long people had lived in recorded location
Zammit et al[247] (2014) Sweden	ICD-8 codes E950–E959, E980–E989, ICD-9, codes E950–E959, E980–E989, ICD-10 codes X60–X84, Y10–Y34	204 323 individuals born in Sweden in 1972-1977 up to age 26-31. (N=314 died by suicide)			School-level= average: foreign born, social fragmentation, low grade.Municipality = urbanicity, population density, index of social fragmentation (residential mobility, voting, % married/ single households)	Sex, country of birth, history of mental illness, change of xbetween 8/16 years, parental SES, education, family income, marital status, school grade	Little evidence that municipality-level measures associated with suicide risk. Several school-level measures were associated with suicide risk.. Suicide risk was higher for individuals who attended schools with higher % females. This applied equally to men & women. Finally, social/cultural distance may increase suicide risk	Municipalities are relatively large geographical areas which may not capture small-area level effects, which may be captured at school level

Despite investigating similar area-level measures, a number of methodological approaches were employed in neighbourhood-level enquiries of suicide risk (see Table 6), making direct comparisons challenging. For example, the spatial scale at which suicide rates were compared varied from locally recognizable communities to postcode areas, larger governmental administrative areas or political constituencies. In a systematic review of this literature, Rehkopf & Buka[245] found that studies conducted at smaller community levels were more likely to find lower suicide rates in higher socio-economic areas than studies which used larger areas of aggregation.[245] The authors recommend more attention to the size of region and measurement strategies in order to provide a clearer picture of how suicide rates vary by region.

Many studies were ecological – meaning that they only studied variance in rates between neighbourhoods, regionals or countries – and did not control for potentially relevant individual characteristics.[223,237,241,244] This approach, while useful for hypothesis generation and further enquiry, makes it impossible to determine whether variation in suicide rates were due to compositional or contextual effects.[236] To partially mitigate the risk of ecological fallacy, several multi-level studies (comibing both individual- and area-level risks) have been conducted. For example, following adjustment for a range of individual measures, Congdon et al.[234] found that area deprivation had no distinct influence on suicide rates, in contrast to other studies.[27,236,239] Nonetheless, simple control for individual factors also risks ignoring the complexity of how places make people, and how certain high risk individuals may be at more or less risk following exposure to further environmental factors (so-called cross-level interactions).[249]

Several studies have investigated such interactions; Neeleman & Wessley,[235] for example, have shown that suicide rates in different ethnic groups, including the white majority, were higher in areas with a smaller population of one's own ethnicity (i.e. an ethnic density effect), as consistently shown for schizophrenia (Section 2). Similarly, Kunst et al.[193] demonstrated that the effect of social capital on suicide mortality was more pronounced for certain population groups, including young people, unmarried individuals, and men. Finally, a systematic review conducted by Crawford, Kuforiji, Ghosh,[250] synthesizing data from 54 studies, found that established risk factors including unemployment, living alone, and ethnic minority status had less on suicide risk for individuals living in areas where these factors were more common.[250]

4.3 Variation in risk by suicide methods

There is strong evidence that the rural-urban gradient (higher rates in rural areas) for suicide mortality is strongly influenced by choice of method. Much of this literature points to the impact of accessibility

when it comes to highly lethal means, including firearms, pesticides, and fertilizers, although this also appears to vary by setting. In countries including the United States, Canada, UK and Australia, there is consistent evidence showing that use of firearms for suicide is strongly spatially patterned, being more prevalent in rural and remote areas.[205,207,209,211,223] Singh & Siahpush[210] have noted that firearms accounted for 75% of all rural suicides, but only half of such incidents in urban areas, and accessibility to firearms has been cited as a major contributory factor for rural-urban differences in several studies.[207,210,223,251,252] Further, the changing availability of firearms may account for some time trends in suicide rates. Fontanella et al.,[207] for example, have noted that firearm ownership has decreased in urban areas, but remains stable in rural areas, potentially widening the disparity in both the accessibility of method and suicide rates between rural and urban communities. In urban areas, methods including jumping, poisoning and hanging are more common.[223] Pesticide poisoning are more common in some rural areas, including in Taiwan[218] and South Korea,[222] with some evidence that hangings showed least geographic differences.[218]

These distinct geographic patterns of suicide methods appears to be driven by the ready availability of method,[210] although may also be shaped by cultural norms, localised patters (i.e. imitation, see[214]) and social expectations. Levin[214] also note that socioeconomic means may determine accessibility to certain more expensive methods, including the use of firearms or explosives. Changing attitudes towards firearms, increased regulations on storage and reduced access to firearms has been hown to reduce suicide rates.[206,253] Large & Nielssen[255] have used meta-analysis data to demonstrate that the decline in suicide in Australia coincided with a reduction in the availability of lethal means.

4.4 Main hypotheses explaining the spatial heterogeneity in suicide mortality

In addition to accessibility to methods and sociocultural influences, several other hypotheses have been proposed to explain the spatial patterning of suicide mortality, broadly organized into *compositional*, *contextual*, and *cross-level* explanations. We discuss each, in turn, below.

4.4.1 Compositional hypotheses

Compositional explanations posit that the individual characteristics of people within certain locales, including the social drift of high-risk individuals into certain areas,[231] account for the rural-urban and spatial differences in suicide (and other) rates. Low income and education, unemployment and social isolation are all strongly related to suicide risk,[27,236] and may be more prevalent in some communities as a result of both structural and cultural influences maintained over successive generations. In many rural areas, these compositional effects may be compounded by the “out-migration” of young,

educated individuals, which generates greater psychological distress or a sense of entrapment in those left behind.[251,256] It has been suggested that the subsequently increased levels of psychological distress may drive regional differences in suicide rates. However, there is no consistent evidence that differences in rates of psychiatric morbidity exist between areas with high and low suicide rates.[215,251] If compositional effects account for the majority of spatial variance in suicide risk, public mental health strategies to ameloriate this burden can focus on both indicated and selective prevention interventions which target high risk individuals or subgroups of the population.

4.4.2 Contextual hypotheses

Contextual effects refer to direct effects that characteristics of places have on suicide risk, which go beyond the totality of compositional effects. These contextual effects may operate either through increased likelihood of suicidal behaviour, or through low levels of social support.[231] Contextual explanations also include how the organization, accessibility, and availability of mental health care vary between different areas. The evidence for contextual effects for suicide (Table 6) generally indicates that areas characterized by greater social fragmentation, isolation and disintegration have higher mortality rates. This may reflect "differential changes over time in key social integration indicators,"[210] consistent with Durkheim's theory that "*anomie*" – low social integration – drives high suicide rates. Low levels of social integration may partly explain increased suicide rates in rural areas,[207,252] which may be confounded by changing demographic profiles in many rural and remote communities and deteriorating economic conditions.[215,251] It has been suggested, for example, that rurality *per se*, may be less important than the differential effects of global economic trends on local regions, with certain rural communities particularly affected by downturns in economic activity. Further nuanced investigation of such intricate spatial variation of suicide is warranted.[251]

Suicide rates may also be influenced by the availability and accessibility of mental health care services and other public amenities in a given area.[207,215,251,252] This may be compounded by issues of mental health literacy, less service utilization, concerns about stigma and discrimination, and lower willingness to seek help in some communities. Such barriers-to-care are often more common in rural communities, possibly due to cultural attitudes and shared norms.[210,215,251,257] Cultural factors and stigma can also present barriers to treatment, including the possible lack of anonymity in more rural, smaller communities.[207,252] In particular, community attitudes towards mental illness and help-seeking may contribute to elevated suicide rates, particularly amongst rural men.[251] Other authors have noted that dominant masculine hegemony, which may be more common in some rural communities, tends

to favour gendered expectations of stoicism and self-reliance, which may present a substantial barrier to help-seeking in the entire community.[251,256]

4.4.3 Cross-level hypotheses

Cross-level effects focus on how characteristics of geographic areas may have differential effects on individuals based on their particular characteristics. If prominent, these effects would make the debate about compositional *versus* contextual effects overly reductionist. Since few individual (i.e. compositional) risk factors are truly exogenous to the social environment, simple adjustment for these factors in the search for contextual mechanisms in suicide risk risks ignoring how the effects of place affect people's social and economic opportunities, including access to good education and high-income jobs. Much of the research reviewed above may thus have overlooked, or have been under-powered to detect, important cross-level interactions which may be vital for the development of putative prevention strategies in different contexts. Theoretical support for cross-level interactions can be traced back to Durkheim's proposal that greater dissonance between an individual and his/her social environment the greater their risk of suicide.[231] Likewise, Crawford and colleagues[250] argued that the impact of unemployment on suicide risk may be exacerbated if unemployed individuals lived in area of high employment, although universal support for this has not been found.[239] Combining the theoretical rational for cross-level interactions with empirical evidence is urgently warranted so we understand how "people make places and people make people,"[249] and permit appropriate public mental health responses in different populations, subgroups and settings.

5 Conclusion

We have reviewed the literature on the association between urban living and three major sets of mental health outcomes, namely psychotic disorders, common mental disorders and suicide. Our comprehensive review of the current evidence, its strengths and limitations and possible hypotheses to explain any variation should serve as a useful reference point for those working in epidemiology, public mental health and mental health care and provision. But what do these findings say in regard to possible preventive strategies to reduce the global burden of mental disorders? What conclusions can we draw at this stage to promote the design and maintenance of healthy environments which promote positive mental health?

The reader will probably concur with our view that no universal answer exists to these questions. Common mental disorders show no consistent direction of association with urban or rural living, which in part might be due to heterogeneous study designs, difficulties with case detection and other forms

of biases inherent to studying prevalent conditions for which people in the community may rarely seek help. Psychotic disorders and suicide showed stronger, more consistent associations with the environment, but in opposite directions; psychotic disorders being more common in urban populations, suicide generally being elevated in more rural communities. The extent to which these patterns were causally determined, that is due to the exposure rather than attributable to reverse causation, was considered, and for both outcomes there is reasonable evidence to implicate social and environmental determinants in the aetiology of these mental health outcomes. These may occur at a variety of levels, including as a result of individual attributes, such as poverty, unemployment and social class, as well as at household and neighbourhood levels.

For both psychotic disorders and suicide further research is required to investigate the extent to which social drift (of those with worse mental health into more deprived rural or urban communities) or upward social mobility (of those with better mental health away from such communities) may help to reveal whether patterns at the environmental level are purely compositional or at least partly contextual. Efforts to ameliorate exposure to advserse psychosocial adversities in the environment, including deprivation and social isolation may help reduce the occurrence of both schizophrenia and suicide, albeit that these efforts will need to be directed at different communities. For suicide the strong rural gradient associated with risk may be due in part to the availability of means, and more direct preventive strategies including tighter controls on firearms and pesticides may be worthwhile. For now, for all mental health outcomes, studies which can elucidate the multiple potential causal levels which drive increased risk of disorder are warranted, particularly those with a longitudinal element to their design which can tease out any sensitive windows to environmental factors over the life course.

Bibliography

1. Weich, S. Absence of spatial variation in rates of the common mental disorders. *J. Epidemiol. Community Health* **59,** 254–7 (2005).
2. Menezes, P. R. Commentary: epidemiological mental health research: contribution from low- and middle-income countries is essential. *Int. J. Epidemiol.* **43,** 301–3 (2014).
3. Saha, S., Chant, D., Welham, J. & McGrath, J. A systematic review of the prevalence of schizophrenia. *PLoS Med.* **2,** e141 (2005).
4. McGrath, J. *et al.* A systematic review of the incidence of schizophrenia: the distribution of rates and the influence of sex, urbanicity, migrant status and methodology. *BMC Med.* **2,** 13 (2004).
5. Kirkbride, J. B. *et al.* Heterogeneity in incidence rates of schizophrenia and other psychotic syndromes: findings from the 3-center AeSOP study. *Arch. Gen. Psychiatry* **63,** 250–8 (2006).
6. Kirkbride, J. B. *et al. Systematic Review of the Incidence and Prevalence of Schizophrenia and Other Psychoses in England*. (2012).
7. Bresnahan, M. *et al.* Race and risk of schizophrenia in a US birth cohort: another example of health disparity? *Int. J. Epidemiol.* **36,** 751–758 (2007).
8. Schofield, P., Ashworth, M. & Jones, R. Ethnic isolation and psychosis: re-examining the ethnic density effect. *Psychol. Med.* **41,** 1263–9 (2011).
9. Boydell, J. *et al.* Incidence of schizophrenia in ethnic minorities in London: ecological study into interactions with environment. *BMJ* **323,** 1336–1336 (2001).
10. Veling, W. *et al.* Incidence of schizophrenia among ethnic minorities in the Netherlands: a four-year first-contact study. *Schizophr. Res.* **86,** 189–93 (2006).
11. Faris, R. E. L. & Dunham, H. W. *Mental Disorders in urban areas.* (Chicago University Press, 1939).
12. Saha, S., Chant, D. C., Welham, J. L. & McGrath, J. J. The incidence and prevalence of schizophrenia varies with latitude. *Acta Psychiatr. Scand.* **114,** 36–39 (2006).
13. March, D. *et al.* Psychosis and place. *Epidemiol. Rev.* **30,** 84–100 (2008).
14. Heinz, A., Deserno, L. & Reininghaus, U. Urbanicity, social adversity and psychosis. *World Psychiatry* **12,** 187–97 (2013).
15. Hare, E. H. Family Setting and the Urban Distribution of Schizophrenia. *Br. J. Psychiatry* **102,** 753–760 (1956).
16. Löffler, W. & Häfner, H. Ecological pattern of first admitted schizophrenics in two German cities over 25 years. *Soc. Sci. Med.* **49,** 93–108 (1999).
17. Giggs, J. A. & Cooper, J. E. Ecological structure and the distribution of schizophrenia and affective psychoses in Nottingham. *Br. J. Psychiatry* **151,** 627–633 (1987).
18. Lewis, G., David, A., Andréasson, S. & Allebeck, P. Schizophrenia and city life. *Lancet (London, England)* **340,** 137–40 (1992).
19. Thornicroft, G., Bisoffi, G., De Salvia, D. & Tansella, M. Urban-rural differences in the associations between social deprivation and psychiatric service utilization in schizophrenia and all diagnoses: a case-register study in Northern Italy. *Psychol. Med.* **23,** 487–96 (1993).
20. Takei, N., Sham, P. C., O'Callaghan, E., Glover, G. & Murray, R. M. Schizophrenia: increased risk associated with winter and city birth--a case-control study in 12 regions within England and Wales. *J. Epidemiol. Community Health* **49,** 106–7 (1995).
21. Marcelis, M., Takei, N. & van Os, J. Urbanization and risk for schizophrenia: does the effect operate before or around the time of illness onset? *Psychol. Med.* **29,** 1197–203 (1999).
22. Marcelis, M., Navarro-Mateu, F., Murray, R., Selten, J. P. & Van Os, J. Urbanization and psychosis: a study of 1942-1978 birth cohorts in The Netherlands. *Psychol. Med.* **28,** 871–9 (1998).
23. Mortensen, P. B. *et al.* Effects of family history and place and season of birth on the risk of schizophrenia. *N. Engl. J. Med.* **340,** 603–8 (1999).
24. Schelin, E. M., Munk-Jørgensen, P., Olesen, A. V & Gerlach, J. Regional differences in

schizophrenia incidence in Denmark. *Acta Psychiatr. Scand.* **101,** 293–9 (2000).
25. Eaton, W. W., Mortensen, P. B. & Frydenberg, M. Obstetric factors, urbanization and psychosis. *Schizophr. Res.* **43,** 117–23 (2000).
26. Suvisaari, J. M., Haukka, J. K., Tanskanen, A. J. & Lönnqvist, J. K. Decreasing seasonal variation of births in schizophrenia. *Psychol. Med.* **30,** 315–24 (2000).
27. Agerbo, E., Torrey, E. F. & Mortensen, P. B. Household crowding in early adulthood and schizophrenia are unrelated in Denmark: a nested case-control study. *Schizophr. Res.* **47,** 243–6 (2001).
28. Allardyce, J. Comparison of the incidence of schizophrenia in rural Dumfries and Galloway and urban Camberwell. *Br. J. Psychiatry* **179,** 335–339 (2001).
29. Haukka, J., Suvisaari, J., Varilo, T. & Lönnqvist, J. Regional variation in the incidence of schizophrenia in Finland: a study of birth cohorts born from 1950 to 1969. *Psychol. Med.* **31,** 1045–53 (2001).
30. Pedersen, C. B. & Mortensen, P. B. Family history, place and season of birth as risk factors for schizophrenia in Denmark: a replication and reanalysis. *Br. J. Psychiatry* **179,** 46–52 (2001).
31. Pedersen, C. B. & Mortensen, P. B. Evidence of a dose-response relationship between urbanicity during upbringing and schizophrenia risk. *Arch. Gen. Psychiatry* **58,** 1039–46 (2001).
32. van Os, J., Hanssen, M., Bijl, R. V. & Vollebergh, W. Prevalence of Psychotic Disorder and Community Level of Psychotic Symptoms. *Arch. Gen. Psychiatry* **58,** 663 (2001).
33. Harrison, G. *et al.* Association between psychotic disorder and urban place of birth is not mediated by obstetric complications or childhood socio-economic position: a cohort study. *Psychol. Med.* **33,** 723–31 (2003).
34. van Os, J., Hanssen, M., Bak, M., Bijl, R. V & Vollebergh, W. Do urbanicity and familial liability coparticipate in causing psychosis? *Am. J. Psychiatry* **160,** 477–82 (2003).
35. Sundquist, K., Frank, G. & Sundquist, J. Urbanisation and incidence of psychosis and depression: follow-up study of 4.4 million women and men in Sweden. *Br. J. Psychiatry* **184,** 293–8 (2004).
36. Allardyce, J. *et al.* Social fragmentation, deprivation and urbanicity: relation to first-admission rates for psychoses. *Br. J. Psychiatry* **187,** 401–6 (2005).
37. Pedersen, C. B. & Mortensen, P. B. Are the cause(s) responsible for urban-rural differences in schizophrenia risk rooted in families or in individuals? *Am. J. Epidemiol.* **163,** 971–8 (2006).
38. Pedersen, C. B. & Mortensen, P. B. Urbanization and traffic related exposures as risk factors for schizophrenia. *BMC Psychiatry* **6,** 2 (2006).
39. Pedersen, C. B. No evidence of time trends in the urban-rural differences in schizophrenia risk among five million people born in Denmark from 1910 to 1986. *Psychol. Med.* **36,** 211–9 (2006).
40. Laursen, T. M., Munk-Olsen, T., Nordentoft, M. & Bo Mortensen, P. A comparison of selected risk factors for unipolar depressive disorder, bipolar affective disorder, schizoaffective disorder, and schizophrenia from a danish population-based cohort. *J. Clin. Psychiatry* **68,** 1673–81 (2007).
41. Kelly, B. D. *et al.* Schizophrenia and the city: A review of literature and prospective study of psychosis and urbanicity in Ireland. *Schizophr. Res.* **116,** 75–89 (2010).
42. Sørensen, H. J. *et al.* Population impact of familial and environmental risk factors for schizophrenia: a nationwide study. *Schizophr. Res.* **153,** 214–9 (2014).
43. Szöke, A. *et al.* Rural-urban variation in incidence of psychosis in France: a prospective epidemiologic study in two contrasted catchment areas. *BMC Psychiatry* **14,** 78 (2014).
44. Vassos, E., Agerbo, E., Mors, O. & Pedersen, C. B. Urban-rural differences in incidence rates of psychiatric disorders in Denmark. *Br. J. Psychiatry* bjp.bp.114.161091– (2015). doi:10.1192/bjp.bp.114.161091
45. Moreno-Küstner, B. *et al.* Prevalence of schizophrenia and related disorders in Malaga (Spain): results using multiple clinical databases. *Epidemiol. Psychiatr. Sci.* 1–11 (2014).
46. Byrne, M., Agerbo, E., Eaton, W. W. & Mortensen, P. B. Parental socio-economic status and risk of first admission with schizophrenia- a Danish national register based study. *Soc. Psychiatry*

Psychiatr. Epidemiol. **39,** 87–96 (2004).
47. Weiser, M. *et al.* Social and cognitive functioning, urbanicity and risk for schizophrenia. *Br. J. Psychiatry* **191,** 320–4 (2007).
48. Xiang, Y.-T. *et al.* Prevalence and socio-demographic correlates of schizophrenia in Beijing, China. *Schizophr. Res.* **102,** 270–7 (2008).
49. Ganguli, H. C. Epidemiological findings on prevalence of mental disorders in India. *Indian J. Psychiatry* **42,** 14–20 (2000).
50. Vicente, B. *et al.* Regional differences in psychiatric disorders in Chile. *Soc. Psychiatry Psychiatr. Epidemiol.* **41,** 935–942 (2006).
51. Wei, G. *et al.* The first epidemiological study of mental disorders of Tibetans. *World Cult. Psychiatr. Res. Rev.* 1–3 (2008).
52. Lundberg, P., Cantor-Graae, E., Rukundo, G., Ashaba, S. & Ostergren, P.-O. Urbanicity of place of birth and symptoms of psychosis, depression and anxiety in Uganda. *Br. J. Psychiatry* **195,** 156–62 (2009).
53. Phillips, M. R. *et al.* Prevalence, treatment, and associated disability of mental disorders in four provinces in China during 2001-05: an epidemiological survey. *Lancet (London, England)* **373,** 2041–53 (2009).
54. Song, S., Wang, W. & Hu, P. Famine, death, and madness: schizophrenia in early adulthood after prenatal exposure to the Chinese Great Leap Forward Famine. *Soc Sci Med* **68,** 1315–1321 (2009).
55. Chan, K. Y. *et al.* Prevalence of schizophrenia in China between 1990 and 2010. *J. Glob. Health* **5,** 010410 (2015).
56. Long, J. *et al.* The prevalence of schizophrenia in mainland China: evidence from epidemiological surveys. *Acta Psychiatr. Scand.* **130,** 244–56 (2014).
57. Vassos, E., Pedersen, C. B., Murray, R. M., Collier, D. A. & Lewis, C. M. Meta-analysis of the association of urbanicity with schizophrenia. *Schizophr. Bull.* **38,** 1118–23 (2012).
58. Chan, K. Y. *et al.* Urbanization and the prevalence of schizophrenia in China between 1990 and 2010. *World Psychiatry* **14,** 251–2 (2015).
59. Dauncey, K., Giggs, J., Baker, K. & Harrison, G. Schizophrenia in Nottingham: lifelong residential mobility of a cohort. *Br. J. Psychiatry* **163,** 613–619 (1993).
60. Croudace, T. J., Kayne, R., Jones, P. B. & Harrison, G. L. Non-linear relationship between an index of social deprivation, psychiatric admission prevalence and the incidence of psychosis. *Psychol. Med.* **30,** 177–85 (2000).
61. Van Os, J. Neighbourhood variation in incidence of schizophrenia: Evidence for person-environment interaction. *Br. J. Psychiatry* **176,** 243–248 (2000).
62. Boydell, J., van Os, J., McKenzie, K. & Murray, R. M. The association of inequality with the incidence of schizophrenia--an ecological study. *Soc. Psychiatry Psychiatr. Epidemiol.* **39,** 597–9 (2004).
63. Drukker, M., Krabbendam, L., Driessen, G. & van Os, J. Social disadvantage and schizophrenia. *Soc. Psychiatry Psychiatr. Epidemiol.* **41,** 595–604 (2006).
64. Lofors, J. & Sundquist, K. Low-linking social capital as a predictor of mental disorders: a cohort study of 4.5 million Swedes. *Soc. Sci. Med.* **64,** 21–34 (2007).
65. Kirkbride, J. B. *et al.* Neighbourhood variation in the incidence of psychotic disorders in Southeast London. *Soc. Psychiatry Psychiatr. Epidemiol.* **42,** 438–445 (2007).
66. Kirkbride, J. B. *et al.* Neighbourhood-level effects on psychoses: re-examining the role of context. *Psychol. Med.* **37,** 1413–25 (2007).
67. Kirkbride, J. B. *et al.* Testing the association between the incidence of schizophrenia and social capital in an urban area. *Psychol. Med.* **38,** 1083–94 (2008).
68. Veling, W. *et al.* Ethnic density of neighborhoods and incidence of psychotic disorders among immigrants. *Am. J. Psychiatry* **165,** 66–73 (2008).
69. Zammit, S. *et al.* Individuals, schools, and neighborhood: a multilevel longitudinal study of

variation in incidence of psychotic disorders. *Arch. Gen. Psychiatry* **67,** 914–22 (2010).
70. Bhavsar, V., Boydell, J., Murray, R. & Power, P. Identifying aspects of neighbourhood deprivation associated with increased incidence of schizophrenia. *Schizophr. Res.* **156,** 115–21 (2014).
71. Kirkbride, J. B., Jones, P. B., Ullrich, S. & Coid, J. W. Social deprivation, inequality, and the neighborhood-level incidence of psychotic syndromes in East London. *Schizophr. Bull.* **40,** 169–80 (2014).
72. Lasalvia, A. *et al.* First-contact incidence of psychosis in north-eastern Italy: influence of age, gender, immigration and socioeconomic deprivation. *Br. J. Psychiatry* **205,** 127–34 (2014).
73. Omer, S. *et al.* Neighbourhood-level socio-environmental factors and incidence of first episode psychosis by place at onset in rural Ireland: the Cavan-Monaghan First Episode Psychosis Study [CAMFEPS]. *Schizophr. Res.* **152,** 152–7 (2014).
74. B. O'Donoghue *et al.* Neighbourhood characteristics and the incidence of first-episode psychosis and duration of untreated psychosis. *Psychol. Med.* 1–12 doi:10.1017/S003329171500286X
75. Veling, W., Susser, E., Selten, J.-P. & Hoek, H. W. Social disorganization of neighborhoods and incidence of psychotic disorders: a 7-year first-contact incidence study. *Psychol. Med.* **45,** 1789–1798 (2015).
76. Sariaslan, A. *et al.* Does population density and neighborhood deprivation predict schizophrenia? A nationwide Swedish family-based study of 2.4 million individuals. *Schizophr. Bull.* **41,** 494–502 (2015).
77. Werner, S., Malaspina, D. & Rabinowitz, J. Socioeconomic Status at Birth Is Associated With Risk of Schizophrenia: Population-Based Multilevel Study. *Schizophr. Bull.* **33,** 1373–1378 (2006).
78. Burns, J. K. & Esterhuizen, T. Poverty, inequality and the treated incidence of first-episode psychosis: an ecological study from South Africa. *Soc. Psychiatry Psychiatr. Epidemiol.* **43,** 331–5 (2008).
79. Silver, E., Mulvey, E. P. & Swanson, J. W. Neighborhood structural characteristics and mental disorder: Faris and Dunham revisited. *Soc. Sci. Med.* **55,** 1457–70 (2002).
80. Kirkbride, J. B. *et al.* Addendum. *Psychol. Med.* **41,** 2462 (2011).
81. Kawachi, I. Commentary: social capital and health: making the connections one step at a time. *Int. J. Epidemiol.* **35,** 989–93 (2006).
82. Mckenzie, K. Urbanization, Social Capital and Mental Health. *Glob. Soc. Policy* **8,** 359–377 (2008).
83. De Silva, M. J., McKenzie, K., Harpham, T. & Huttly, S. R. A. Social capital and mental illness: a systematic review. *J. Epidemiol. Community Health* **59,** 619–27 (2005).
84. Shaw, R. J. *et al.* Impact of ethnic density on adult mental disorders: narrative review. *Br. J. Psychiatry* **201,** 11–9 (2012).
85. Veling, W., Hoek, H. W., Wiersma, D. & Mackenbach, J. P. Ethnic identity and the risk of schizophrenia in ethnic minorities: a case-control study. *Schizophr. Bull.* **36,** 1149–56 (2010).
86. Tortelli, A. *et al.* Schizophrenia and other psychotic disorders in Caribbean-born migrants and their descendants in England: systematic review and meta-analysis of incidence rates, 1950-2013. *Soc. Psychiatry Psychiatr. Epidemiol.* **50,** 1039–55 (2015).
87. Morgan, C., Charalambides, M., Hutchinson, G. & Murray, R. M. Migration, ethnicity, and psychosis: toward a sociodevelopmental model. *Schizophr. Bull.* **36,** 655–64 (2010).
88. Myin-Germeys, I., Krabbendam, L., Delespaul, P. A. E. G. & Van Os, J. Do life events have their effect on psychosis by influencing the emotional reactivity to daily life stress? *Psychol. Med.* **33,** 327–333 (2003).
89. Read, J., van Os, J., Morrison, A. P. & Ross, C. A. Childhood trauma, psychosis and schizophrenia: a literature review with theoretical and clinical implications. *Acta Psychiatr. Scand.* **112,** 330–50 (2005).

90. Norman, R. M. & Malla, A. K. Stressful life events and schizophrenia. I: A review of the research. *Br. J. Psychiatry* **162,** 161–166 (1993).
91. Løberg, E.-M. *et al.* The Cannabis Pathway to Non-Affective Psychosis may Reflect Less Neurobiological Vulnerability. *Front. psychiatry* **5,** 159 (2014).
92. D'Souza, D. C., Sewell, R. A. & Ranganathan, M. Cannabis and psychosis/schizophrenia: human studies. *Eur. Arch. Psychiatry Clin. Neurosci.* **259,** 413–31 (2009).
93. Craddock, N., O'Donovan, M. C. & Owen, M. J. The genetics of schizophrenia and bipolar disorder: dissecting psychosis. *J. Med. Genet.* **42,** 193–204 (2005).
94. Blackwood, D. H. R. *et al.* Are some genetic risk factors common to schizophrenia, bipolar disorder and depression? Evidence from DISC1, GRIK4 and NRG1. *Neurotox. Res.* **11,** 73–83 (2007).
95. Mortensen, P. B., Pedersen, C. B., Melbye, M., Mors, O. & Ewald, H. Individual and familial risk factors for bipolar affective disorders in Denmark. *Arch. Gen. Psychiatry* **60,** 1209–15 (2003).
96. Pedersen, C. B. & Mortensen, P. B. Urbanicity during upbringing and bipolar affective disorders in Denmark. *Bipolar Disord.* **8,** 242–7 (2006).
97. Kirkbride, J. B. *et al.* Neighbourhood variation in the incidence of psychotic disorders in Southeast London. *Soc. Psychiatry Psychiatr. Epidemiol.* **42,** 438–45 (2007).
98. Oher, F. J. *et al.* The effect of the environment on symptom dimensions in the first episode of psychosis: a multilevel study. *Psychol. Med.* **FirstView,** 1–12 (2014).
99. Goldberg, E. M. & Morrison, S. L. Schizophrenia and social class. *Br. J. Psychiatry* **109,** 785–802 (1963).
100. Ngamini Ngui, A. *et al.* Does elapsed time between first diagnosis of schizophrenia and migration between health territories vary by place of residence? A survival analysis approach. *Health Place* **20,** 66–74 (2013).
101. Kirkbride, J. B. *et al.* Social and spatial heterogeneity in psychosis proneness in a multilevel case–prodrome–control study. *Acta Psychiatr. Scand.* **132,** 283–292 (2015).
102. van Os, J., Krabbendam, L., Myin-Germeys, I. & Delespaul, P. The schizophrenia envirome. *Curr Opin Psychiatry* **18,** 141–145 (2005).
103. Bleuler, E. *Dementia praecox or the group of schizophrenias*. (1911).
104. Mednick, S. A. Breakdown in individuals at high risk for schizophrenia: Possible predispositional perinatal factors. *Ment. Hyg.* **54,** 50–63 (1970).
105. Lane, E. A. & Albee, G. W. Comparative Birth Weights of Schizophrenics and Their Siblings. *J. Psychol.* **64,** 227–231 (1966).
106. Lewis, S. W. & Murray, R. M. Obstetric complications, neurodevelopmental deviance, and risk of schizophrenia. *J. Psychiatr. Res.* **21,** 413–421 (1987).
107. Mizrahi, R. Social Stress and Psychosis Risk: Common Neurochemical Substrates? *Neuropsychopharmacology* **41,** 666–74 (2016).
108. Akdeniz, C., Tost, H. & Meyer-Lindenberg, A. The neurobiology of social environmental risk for schizophrenia: an evolving research field. *Soc. Psychiatry Psychiatr. Epidemiol.* **49,** 507–17 (2014).
109. Veling, W., Pot-Kolder, R., Counotte, J., van Os, J. & van der Gaag, M. Environmental Social Stress, Paranoia and Psychosis Liability: A Virtual Reality Study. *Schizophr. Bull.* sbw031–(2016). doi:10.1093/schbul/sbw031
110. Tost, H., Champagne, F. A. & Meyer-Lindenberg, A. Environmental influence in the brain, human welfare and mental health. *Nat. Neurosci.* **18,** 1421–31 (2015).
111. Selten, J.-P. & Cantor-Graae, E. Social defeat: risk factor for schizophrenia? *Br. J. Psychiatry* **187,** 101–2 (2005).
112. Selten, J.-P. & Cantor-Graae, E. Hypothesis: social defeat is a risk factor for schizophrenia? *Br. J. Psychiatry. Suppl.* **51,** s9–12 (2007).
113. Selten, J.-P., van der Ven, E., Rutten, B. P. F. & Cantor-Graae, E. The social defeat hypothesis of schizophrenia: an update. *Schizophr. Bull.* **39,** 1180–6 (2013).

114. van Os, J. & McGuffin, P. Can the social environment cause schizophrenia? *Br. J. Psychiatry* **182,** 291–292 (2003).
115. Kirkbride, J. B. & Jones, P. B. in *Migration and mental health* (eds. Bughra, D. & Gupta, S.) 15–31 (Cambridge University Press, 2011).
116. van Os, J. *et al.* Identifying gene-environment interactions in schizophrenia: contemporary challenges for integrated, large-scale investigations. *Schizophr. Bull.* **40,** 729–36 (2014).
117. Kirkbride, J. B. *et al.* Examining evidence for neighbourhood variation in the duration of untreated psychosis. *Health Place* **16,** 219–25 (2010).
118. Steel, Z. *et al.* The global prevalence of common mental disorders: a systematic review and meta-analysis 1980-2013. *Int. J. Epidemiol.* **43,** 476–93 (2014).
119. Lewis, G. & Booth, M. Are cities bad for your mental health? *Psychol. Med.* **24,** 913–915 (1994).
120. Paykel, E. S., Abbott, R., Jenkins, R., Brugha, T. S. & Meltzer, H. Urban-rural mental health differences in great Britain: findings from the national morbidity survey. *Psychol. Med.* **30,** 269–80 (2000).
121. Weich, S., Twigg, L. & Lewis, G. Rural/non-rural differences in rates of common mental disorders in Britain: prospective multilevel cohort study. *Br. J. Psychiatry* **188,** 51–7 (2006).
122. de Graaf, R., ten Have, M., Tuithof, M. & van Dorsselaer, S. First-incidence of DSM-IV mood, anxiety and substance use disorders and its determinants: Results from the Netherlands Mental Health Survey and Incidence Study-2. *J. Affect. Disord.* **149,** 100–107 (2013).
123. de Graaf, R., ten Have, M., van Gool, C. & van Dorsselaer, S. Prevalence of mental disorders and trends from 1996 to 2009. Results from the Netherlands Mental Health Survey and Incidence Study-2. *Soc. Psychiatry Psychiatr. Epidemiol.* **47,** 203–13 (2012).
124. de Graaf, R., Bijl, R. V., Ravelli, A., Smit, F. & Vollebergh, W. A. M. Predictors of first incidence of DSM-III-R psychiatric disorders in the general population: findings from the Netherlands Mental Health Survey and Incidence Study. *Acta Psychiatr. Scand.* **106,** 303–313 (2002).
125. Kovess-Masfety, V., Lecoutour, X. & Delavelle, S. Mood disorders and urban/rural settings: comparisons between two French regions. *Soc. Psychiatry Psychiatr. Epidemiol.* **40,** 613–8 (2005).
126. Ayuso-Mateos, J.-L. Depressive disorders in Europe: prevalence figures from the ODIN study. *Br. J. Psychiatry* **179,** 308–316 (2001).
127. Parikh, S. V., Wasylenki, D., Goering, P. & Wong, J. Mood disorders: rural/urban differences in prevalence, health care utilization, and disability in Ontario. *J. Affect. Disord.* **38,** 57–65 (1996).
128. Romans, S., Cohen, M. & Forte, T. Rates of depression and anxiety in urban and rural Canada. *Soc. Psychiatry Psychiatr. Epidemiol.* **46,** 567–75 (2011).
129. Patten, S. B. *et al.* Descriptive Epidemiology of Major Depression in Canada. *Can. J. Psychiatry.* **51,** 84–90 (2006).
130. Wang, J. L. Rural-urban differences in the prevalence of major depression and associated impairment. *Soc. Psychiatry Psychiatr. Epidemiol.* **39,** 19–25 (2004).
131. Kessler, R. C. *et al.* Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. Results from the National Comorbidity Survey. *Arch. Gen. Psychiatry* **51,** 8–19 (1994).
132. Blazer, D. G., Kessler, R. C., McGonagle, K. A. & Swartz, M. S. The prevalence and distribution of major depression in a national community sample: the National Comorbidity Survey. *Am. J. Psychiatry* **151,** 979–86 (1994).
133. Kessler, R. C. *et al.* The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). *JAMA* **289,** 3095–105 (2003).
134. Probst, J. C. *et al.* Rural-urban differences in depression prevalence: implications for family medicine. *Fam. Med.* **38,** 653–60 (2006).
135. Grant, B. F. *et al.* Sociodemographic and psychopathologic predictors of first incidence of DSM-IV substance use, mood and anxiety disorders: results from the Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions. *Mol. Psychiatry* **14,** 1051–66 (2009).

136. Beyer, K. M. M. *et al.* Exposure to neighborhood green space and mental health: evidence from the survey of the health of Wisconsin. *Int. J. Environ. Res. Public Health* **11,** 3453–72 (2014).
137. Andrews, G. Prevalence, comorbidity, disability and service utilisation: Overview of the Australian National Mental Health Survey. *Br. J. Psychiatry* **178,** 145–153 (2001).
138. Andrade, L. *et al.* The epidemiology of major depressive episodes: results from the International Consortium of Psychiatric Epidemiology (ICPE) surveys. *Int. J. Methods Psychiatr. Res.* **12,** 3–21 (2003).
139. Mohammadi, M.-R. *et al.* An epidemiological survey of psychiatric disorders in Iran. *Clin. Pract. Epidemiol. Ment. Health* **1,** 16 (2005).
140. Amoran, O., Lawoyin, T. & Lasebikan, V. Prevalence of depression among adults in Oyo State, Nigeria: a comparative study of rural and urban communities. *Aust. J. Rural Health* **15,** 211–5 (2007).
141. Probst, J. C. *et al.* Rural-urban differences in depression prevalence: implications for family medicine. *Fam. Med.* **38,** 653–60 (2006).
142. Andrews, G. Prevalence, comorbidity, disability and service utilisation: Overview of the Australian National Mental Health Survey. *Br. J. Psychiatry* **178,** 145–153 (2001).
143. Guite, H. F., Clark, C. & Ackrill, G. The impact of the physical and urban environment on mental well-being. *Public Health* **120,** 1117–26 (2006).
144. Weich, S. *et al.* Mental health and the built environment: cross-sectional survey of individual and contextual risk factors for depression. *Br. J. Psychiatry* **180,** 428–33 (2002).
145. Weich, S. Contextual risk factors for the common mental disorders in Britain: a multilevel investigation of the effects of place. *J. Epidemiol. Community Heal.* **57,** 616–621 (2003).
146. Weich, S. Geographic Variation in the Prevalence of Common Mental Disorders in Britain: A Multilevel Investigation. *Am. J. Epidemiol.* **157,** 730–737 (2003).
147. Weich, S., Twigg, L., Lewis, G. & Jones, K. Geographical variation in rates of common mental disorders in Britain: prospective cohort study. *Br. J. Psychiatry* **187,** 29–34 (2005).
148. Stafford, M. & Marmot, M. Neighbourhood deprivation and health: does it affect us all equally? *Int. J. Epidemiol.* **32,** 357–366 (2003).
149. Stafford, M., De Silva, M., Stansfeld, S. & Marmot, M. Neighbourhood social capital and common mental disorder: testing the link in a general population sample. *Health Place* **14,** 394–405 (2008).
150. Halpern, D. & Nazroo, J. The ethnic density effect: results from a national community survey of England and Wales. *Int. J. Soc. Psychiatry* **46,** 34–46 (2000).
151. McCulloch, A. Ward-Level Deprivation and Individual Social and Economic Outcomes in the British Household Panel Study. *Environ. Plan. A* **33,** 667–684 (2001).
152. Wainwright, N. W. J. & Surtees, P. G. Area and individual circumstances and mood disorder prevalence. *Br. J. Psychiatry* **185,** 227–32 (2004).
153. Skapinakis, P., Lewis, G., Araya, R., Jones, K. & Williams, G. Mental health inequalities in Wales, UK: multi-level investigation of the effect of area deprivation. *Br. J. Psychiatry* **186,** 417–22 (2005).
154. Fone, D. L. & Dunstan, F. Mental health, places and people: a multilevel analysis of economic inactivity and social deprivation. *Health Place* **12,** 332–44 (2006).
155. Reijneveld, S. A. & Schene, A. H. Higher prevalence of mental disorders in socioeconomically deprived urban areas in The Netherlands: community or personal disadvantage? *J. Epidemiol. Community Heal.* **52,** 2–7 (1998).
156. Erdem, Ö., Prins, R. G., Voorham, T. A. J. J., van Lenthe, F. J. & Burdorf, A. Structural neighbourhood conditions, social cohesion and psychological distress in the Netherlands. *Eur. J. Public Health* ckv120 (2015). doi:10.1093/eurpub/ckv120
157. Lofors, J., Ramírez-León, V. & Sundquist, K. Neighbourhood income and anxiety: a study based on random samples of the Swedish population. *Eur. J. Public Health* **16,** 633–9 (2006).
158. Vallée, J., Cadot, E., Roustit, C., Parizot, I. & Chauvin, P. The role of daily mobility in mental

health inequalities: the interactive influence of activity space and neighbourhood of residence on depression. *Soc. Sci. Med.* **73,** 1133–44 (2011).
159. Jones-Rounds, M. L., Evans, G. W. & Braubach, M. The interactive effects of housing and neighbourhood quality on psychological well-being. *J. Epidemiol. Community Health* **68,** 171–5 (2014).
160. Tweed, D. L. *et al.* Racial congruity as a contextual correlate of mental disorder. *Am. J. Orthopsychiatry* **60,** 392–403 (1990).
161. Yen, I. & Kaplan, G. Poverty area residence and changes in depression and perceived health status: evidence from the Alameda County Study. *Int. J. Epidemiol.* **28,** 90–94 (1999).
162. Ross, C. E., Reynolds, J. R. & Geis, K. J. The contingent meaning of neighborhood stability for residents' psychological well-being. *Am. Sociol. Rev.* **65,** 581–597 (2000).
163. Stockdale, S. E. *et al.* The importance of social context: neighborhood stressors, stress-buffering mechanisms, and alcohol, drug, and mental health disorders. *Soc. Sci. Med.* **65,** 1867–81 (2007).
164. Leventhal, T. & Brooks-Gunn, J. Moving to opportunity: an experimental study of neighborhood effects on mental health. *Am. J. Public Health* **93,** 1576–82 (2003).
165. Greiner, K. A., Li, C., Kawachi, I., Hunt, D. C. & Ahluwalia, J. S. The relationships of social participation and community ratings to health and health behaviors in areas with high and low population density. *Soc. Sci. Med.* **59,** 2303–12 (2004).
166. Galea, S., Ahern, J., Rudenstine, S., Wallace, Z. & Vlahov, D. Urban built environment and depression: a multilevel analysis. *J Epidemiol Community Heal.* **59,** 822–827 (2005).
167. Dupéré, V. & Perkins, D. D. Community types and mental health: a multilevel study of local environmental stress and coping. *Am. J. Community Psychol.* **39,** 107–19 (2007).
168. Galea, S. *et al.* Urban neighborhood poverty and the incidence of depression in a population-based cohort study. *Ann. Epidemiol.* **17,** 171–9 (2007).
169. Ahern, J. & Galea, S. Collective efficacy and major depression in urban neighborhoods. *Am. J. Epidemiol.* **173,** 1453–62 (2011).
170. Matheson, F. I. *et al.* Urban neighborhoods, chronic stress, gender and depression. *Soc. Sci. Med.* **63,** 2604–16 (2006).
171. Gariepy, G. *et al.* The Neighbourhood Built Environment and Trajectories of Depression Symptom Episodes in Adults: A Latent Class Growth Analysis. *PLoS One* **10,** e0133603 (2015).
172. Veenstra, G. Location, location, location: contextual and compositional health effects of social capital in British Columbia, Canada. *Soc. Sci. Med.* **60,** 2059–71 (2005).
173. Jokela, M. Are neighborhood health associations causal? A 10-year prospective cohort study with repeated measurements. *Am. J. Epidemiol.* **180,** 776–84 (2014).
174. Chiavegatto Filho, A. D. P., Kawachi, I., Wang, Y. P., Viana, M. C. & Andrade, L. H. S. G. Does income inequality get under the skin? A multilevel analysis of depression, anxiety and mental disorders in Sao Paulo, Brazil. *J. Epidemiol. Community Health* **67,** 966–72 (2013).
175. Tomita, A. & Burns, J. K. A multilevel analysis of association between neighborhood social capital and depression: evidence from the first South African National Income Dynamics Study. *J. Affect. Disord.* **144,** 101–5 (2013).
176. Propper, C. *et al.* Local neighbourhood and mental health: evidence from the UK. *Soc. Sci. Med.* **61,** 2065–83 (2005).
177. Galea, S., Ahern, J., Rudenstine, S., Wallace, Z. & Vlahov, D. Urban built environment and depression: a multilevel analysis. *J. Epidemiol. Community Health* **59,** 822–7 (2005).
178. Das-Munshi, J., Becares, L., Dewey, M. E., Stansfeld, S. A. & Prince, M. J. Understanding the effect of ethnic density on mental health: multi-level investigation of survey data from England. *BMJ* **341,** c5367 (2010).
179. Ahern, J. & Galea, S. Collective efficacy and major depression in urban neighborhoods. *Am. J. Epidemiol.* **173,** 1453–62 (2011).
180. Amoran, O., Lawoyin, T. & Lasebikan, V. Prevalence of depression among adults in Oyo State,

Nigeria: a comparative study of rural and urban communities. *Aust. J. Rural Health* **15,** 211–5 (2007).
181. World Health Organization. *Preventing suicide: A global imperative*. (2014).
182. Shiner, M., Scourfield, J., Fincham, B. & Langer, S. When things fall apart: Gender and suicide across the life-course. *Soc. Sci. Med.* **69,** 738–46 (2009).
183. Langhinrichsen-Rohling, J., Friend, J. & Powell, A. Adolescent suicide, gender, and culture: A rate and risk factor analysis. *Aggress. Violent Behav.* **14,** 402–414 (2009).
184. von Borczyskowski, A., Lindblad, F., Vinnerljung, B. & Hjern, A. Gender differences in risk factors for suicide: findings from a Swedish national cohort study. *Can. J. Psychiatry.* **55,** 108–11 (2010).
185. Gibb, S. J., Beautrais, A. L. & Fergusson, D. M. Mortality and further suicidal behaviour after an index suicide attempt: a 10-year study. *Aust. N. Z. J. Psychiatry* **39,** 95–100 (2004).
186. Hawton, K. Sex and suicide. Gender differences in suicidal behaviour. *Br. J. Psychiatry* **177,** 484–5 (2000).
187. Beautrais, A. Risk factors for suicide and attempted suicide among young people. *Aust. N. Z. J. Psychiatry* **34,** 420–436 (2000).
188. Arsenault-Lapierre, G., Kim, C. & Turecki, G. Psychiatric diagnoses in 3275 suicides: a meta-analysis. *BMC Psychiatry* **4,** 37 (2004).
189. Beskow, J. Suicide in mental disorder in Swedish men. *Acta Psychiatr. Scand.* **277,** (1979).
190. Qin, P., Hawton, K., Mortensen, P. B. & Webb, R. Combined effects of physical illness and comorbid psychiatric disorder on risk of suicide in a national population study. *Br. J. Psychiatry* (2014). doi:10.1192/bjp.bp.113.128785
191. Page, A., Milner, A., Morrell, S. & Taylor, R. The role of under-employment and unemployment in recent birth cohort effects in Australian suicide. *Soc. Sci. Med.* **93,** 155–62 (2013).
192. Winfree Jr, T. & Jiang, S. Youthful Suicide and Social Support: Exploring the Social Dynamics of Suicide-Related Behavior and Attitudes Within a National Sample of US Adolescents. *Youth Violence Juv. Justice* **8,** 19–37 (2010).
193. Kunst, A. E., van Hooijdonk, C., Droomers, M. & Mackenbach, J. P. Community social capital and suicide mortality in the Netherlands: a cross-sectional registry-based study. *BMC Public Health* **13,** 969 (2013).
194. Fergusson, D. M., Horwood, L. J., Ridder, E. M. & Beautrais, A. L. Suicidal behaviour in adolescence and subsequent mental health outcomes in young adulthood. *Psychol. Med.* **35,** 983–993 (2005).
195. Fergusson, D. M. & Lynskey, M. T. Suicide attempts and suicidal ideation in a birth cohort of 16-year-old New Zealanders. *J. Am. Acad. Child Adolesc. Psychiatry* **34,** 1308–17 (1995).
196. Zapata, L. B. *et al.* Orphaned and abused youth are vulnerable to pregnancy and suicide risk. *Child Abuse Negl.* **37,** 310–9 (2013).
197. Rajalin, M., Hirvikoski, T. & Jokinen, J. Family history of suicide and exposure to interpersonal violence in childhood predict suicide in male suicide attempters. *J. Affect. Disord.* **148,** 92–7 (2013).
198. Pompili, M. *et al.* Substance abuse, temperament and suicide risk: evidence from a case-control study. *J. Addict. Dis.* **28,** 13–20 (2009).
199. Durkheim, E. *On suicide*. (Penguin Books, 1897).
200. Tarde, G. *The laws of imitation*. (Henry Holt, 1903).
201. Caldwell, T. M., Jorm, A. F. & Dear, K. B. G. Suicide and mental health in rural, remote and metropolitan areas in Australia. *Med. J. Aust.* **181,** 10–14 (2004).
202. Tak, Y. *et al.* Spatial analysis of suicide mortality in Australia : Investigation of metropolitan-rural-remote differentials of suicide risk across states/territories. *Soc. Sci. Med.* **75,** 1460–1468 (2012).
203. Snider, C. L. A. & Leo, D. De. The influence of deprivation on suicide mortality in urban and rural Queensland : an ecological analysis. 1919–1928 (2014). doi:10.1007/s00127-014-0905-1
204. Page, A., Morrell, S., Taylor, R., Dudley, M. & Carter, G. Further increases in rural suicide in

young Australian adults: secular trends, 1979-2003. *Soc. Sci. Med.* **65,** 442–453 (2007).
205. Qi, X., Hu, W., Page, A. & Tong, S. Dynamic pattern of suicide in Australia, 1986-2005: a descriptive-analytic study. *BMJ Open* **4,** e005311 (2014).
206. Wilkinson, D. & Gunnell, D. Youth suicide trends in Australian metropolitan and non-metropolitan areas, 1988-1997. *Aust. N. Z. J. Psychiatry* **34,** 822–828 (2000).
207. Fontanella, C. A. *et al.* Widening Rural-Urban Disparities in Youth Suicides, United States, 1996-2010. *JAMA Pediatr.* **169,** 466 (2015).
208. Hempstead, K. The geography of self-injury: Spatial patterns in attempted and completed suicide. *Soc. Sci. Med.* **62,** 3186–3196 (2006).
209. Searles, V. B., Valley, M. a, Hedegaard, H. & Betz, M. E. Suicides in urban and rural counties in the United States, 2006-2008. *Crisis* **35,** 18–26 (2014).
210. Singh, G. K. & Siahpush, M. Increasing Rural–Urban Gradients in US Suicide Mortality, 1970–1997. *Am. J. Public Health* **92,** 1161–1167 (2002).
211. Kapusta, N. D. *et al.* Rural-urban differences in Austrian suicides. *Soc. Psychiatry Psychiatr. Epidemiol.* **43,** 311–318 (2008).
212. Kapusta, N. D. *et al.* Availability of mental health service providers and suicide rates in Austria: a nationwide study. *Psychiatr. Serv.* **61,** 1198–1203 (2010).
213. Stark, C., Hopkins, P., Gibbs, D., Belbin, A. & Hay, A. Population density and suicide in Scotland. *Rural Remote Health* **7,** (2007).
214. Levin, K. A. & Leyland, A. H. Urban/rural inequalities in suicide in Scotland, 1981-1999. *Soc. Sci. Med.* **60,** 2877–2890 (2005).
215. Middleton, N., Gunnell, D., Frankel, S., Whitley, E. & Dorling, D. Urban–rural differences in suicide trends in young adults: England and Wales, 1981–1998. *Soc. Sci. Med.* **57,** 1183–1194 (2003).
216. Ngamini Ngui, A. *et al.* Disentangling the influence of neighborhood and individual characteristics on early residential mobility among newly diagnosed patients with schizophrenia: a multilevel analysis. *Soc. Psychiatry Psychiatr. Epidemiol.* **49,** 1569–78 (2014).
217. Pearce, J., Barnett, R. & Jones, I. Have urban/rural inequalities in suicide in New Zealand grown during the period 1980-2001? *Soc. Sci. Med.* **65,** 1807–1819 (2007).
218. Chang, S. S. *et al.* Geography of suicide in Taiwan: spatial patterning and socioeconomic correlates. *Health Place* **17,** 641–650 (2011).
219. Patel, V. *et al.* Suicide mortality in India: A nationally representative survey. *Lancet* **379,** 2343–2351 (2012).
220. Razvodovsky, Y. & Stickley, A. Suicide in urban and rural regions of Belarus, 1990-2005. *Public Health* **123,** 27–31 (2009).
221. Yip, P. S. F., Callanan, C. & Yuen, H. P. Urban/rural and gender differentials in suicide rates: East and West. *J. Affect. Disord.* **57,** 99–106 (2000).
222. Park, B. & Lester, D. Rural and urban suicide in South Korea. *Psychol. Rep.* **111,** 495–497 (2012).
223. Ngamini Ngui, A., Apparicio, P., Moltchanova, E. & Vasiliadis, H.-M. Spatial analysis of suicide mortality in Québec: spatial clustering and area factor correlates. *Psychiatry Res.* **220,** 20–30 (2014).
224. Titelman, D. *et al.* Suicide mortality trends in the Nordic countries 1980-2009. *Nord. J. Psychiatry* **67,** 414–23 (2013).
225. Yip, P. S. F., Liu, K. Y., Hu, J. & Song, X. M. Suicide rates in China during a decade of rapid social changes. *Soc. Psychiatry Psychiatr. Epidemiol.* **40,** 792–798 (2005).
226. Middleton, N., Sterne, J. A. C. & Gunnell, D. J. An atlas of suicide mortality: England and Wales, 1988-1994. *Heal. Place* **14,** 492–506 (2008).
227. Taylor, R., Page, A., Morrell, S., Harrison, J. & Carter, G. Social and Psychiatric Influences on Urban-Rural Differentials in Australian Suicide. *Suicide Life-Threatening Behav.* **35,** 277–290 (2005).
228. Linsley, K. R., Schapira, K. & Kelly, T. P. Open verdict v. suicide - Importance to research. *Br. J.*

Psychiatry **178,** 465–468 (2001).
229. Palmer, B. S. *et al.* Factors influencing coroners' verdicts: An analysis of verdicts given in 12 coroners' districts to researcher-defined suicides in England in 2005. *J. Public Heal. (United Kingdom)* **37,** 157–165 (2015).
230. Hooghe, M. & Vanhoutte, B. An ecological study of community-level correlates of suicide mortality rates in the Flemish region of Belgium, 1996-2005. *Suicide Life. Threat. Behav.* **41,** 453–64 (2011).
231. Agerbo, E., Sterne, J. a C. & Gunnell, D. J. Combining individual and ecological data to determine compositional and contextual socio-economic risk factors for suicide. *Soc. Sci. Med.* **64,** 451–61 (2007).
232. Qi, X., Tong, S. & Hu, W. Spatial distribution of suicide in Queensland, Australia. *BMC Psychiatry* **10,** 106 (2010).
233. Collings, S., Ivory, V., Blakely, T. & Atkinson, J. Are neighbourhood social fragmentation and suicide associated in New Zealand? A national multilevel cohort study. *J. Epidemiol. Community Health* **63,** 1035–1042 (2009).
234. Congdon, P. Latent variable model for suicide risk in relation to social capital and socio-economic status. *Soc. Psychiatry Psychiatr. Epidemiol.* **47,** 1205–19 (2012).
235. Neeleman, J. & Wessely, S. Ethnic minority suicide: a small area geographical study in south London. *Psychol. Med.* **29,** 429–36 (1999).
236. O'Reilly, D. O., Rosato, M., Connolly, S. & Cardwell, C. Area factors and suicide: 5-year follow-up of the Northern Ireland population. *Br. J. Psychiatry* **192,** 106–11 (2008).
237. Whitley, E., Gunnell, D., Dorling, D. & Smith, G. D. Ecological study of social fragmentation, poverty, and suicide. *BMJ* **319,** 1034–7 (1999).
238. Haws, C. A. *et al.* The possible effect of altitude on regional variation in suicide rates. *Med. Hypotheses* **73,** 587–590 (2009).
239. Martikainen, P., Mäki, N. & Blomgren, J. The Effects of Area and Individual Social Characteristics on Suicide Risk : A Multilevel Study of Relative Contribution and Effect Modification. *Eur. J. Popul.* **20,** 323–350 (2004).
240. Kelly, B. D. & Davoren, Æ. M. Social capital and suicide in 11 European countries : an ecological analysis. 971–977 (2009). doi:10.1007/s00127-009-0018-4
241. Tsai, J. F. Socioeconomic factors outweigh climate in the regional difference of suicide death rate in Taiwan. *Psychiatry Res.* **179,** 212–216 (2010).
242. Bando, D. H., Brunoni, A. R., Benseñor, I. M. & Lotufo, P. a. Suicide rates and income in São Paulo and Brazil: a temporal and spatial epidemiologic analysis from 1996 to 2008. *BMC Psychiatry* **12,** 127 (2012).
243. Jagodic, H. K., Rokavec, T., Agius, M. & Pregelij, P. Availability of mental health service providers and suicide rates in Slovenia: A nationwide ecological study. *Croat Med J* **54,** 1198–1203 (2013).
244. Okamoto, M., Kawakami, N., Kido, Y. & Sakurai, K. Social capital and suicide: An ecological study in Tokyo, Japan. *Environ. Health Prev. Med.* **18,** 306–312 (2013).
245. Rehkopf, D. H. & Buka, S. L. The association between suicide and the socio-economic characteristics of geographical areas: a systematic review. *Psychol. Med.* **36,** 145 (2005).
246. Kelly, B. D., Davoren, M., Mhaoláin, A. N., Breen, E. G. & Casey, P. Social capital and suicide in 11 European countries: an ecological analysis. *Soc. Psychiatry Psychiatr. Epidemiol.* **44,** 971–7 (2009).
247. Zammit, S. *et al.* Individual- and area-level influence on suicide risk: a multilevel longitudinal study of Swedish schoolchildren. *Psychol. Med.* **44,** 267–77 (2014).
248. Zhang, J. & Wang, C. Factors in the neighborhood as risks of suicide in rural China: a multilevel analysis. *Community Ment. Health J.* **48,** 627–33 (2012).
249. Macintyre, S. & Ellaway, A. in *Neighbourhoods and health* (eds. Kawachi, I. & Berkman, L.) 20–43 (Oxford University Press, 2003).
250. Crawford, M. J., Kuforiji, B. & Ghosh, P. The impact of social context on socio-demographic risk

factors for suicide: a synthesis of data from case-control studies. *J. Epidemiol. Community Health* **64,** 530–4 (2010).
251. Judd, F., Cooper, A. M., Fraser, C. & Davis, J. Rural suicide - People or place effects? *Aust. N. Z. J. Psychiatry* **40,** 208–216 (2006).
252. Hirsch, J. K. & Cukrowicz, K. C. Suicide in rural areas: An updated review of the literature. *J. Rural Ment. Heal.* **38,** 65–78 (2014).
253. Rodríguez Andrés, A. & Hempstead, K. Gun control and suicide: the impact of state firearm regulations in the United States, 1995-2004. *Health Policy* **101,** 95–103 (2011).
254. Park, S. *et al.* Increased use of lethal methods and annual increase of suicide rates in Korean adolescents: Comparison with adolescents in the United States. *J. Child Psychol. Psychiatry Allied Discip.* **55,** 258–263 (2014).
255. Large, M. M. & Nielssen, O. B. Suicide in Australia: Meta-analysis of rates and methods of suicide between 1988 and 2007. *Med. J. Aust.* **192,** 432–437 (2010).
256. Alston, M. Rural male suicide in Australia. *Soc. Sci. Med.* **74,** 515–522 (2012).
257. Hirsch, J. K. A review of the literature on rural suicide: risk and protective factors, incidence, and prevention. *Crisis* **27,** 189–199 (2006).