

This electronic thesis or dissertation has been downloaded from the King's Research Portal at <https://kclpure.kcl.ac.uk/portal/>



Multilevel investigation of the role of urbanicity in psychotic phenomena during childhood and adolescence

Newbury, Joanne Barbara

Awarding institution:
King's College London

The copyright of this thesis rests with the author and no quotation from it or information derived from it may be published without proper acknowledgement.

END USER LICENCE AGREEMENT



Unless another licence is stated on the immediately following page this work is licensed

under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International

licence. <https://creativecommons.org/licenses/by-nc-nd/4.0/>

You are free to copy, distribute and transmit the work

Under the following conditions:

- Attribution: You must attribute the work in the manner specified by the author (but not in any way that suggests that they endorse you or your use of the work).
- Non Commercial: You may not use this work for commercial purposes.
- No Derivative Works - You may not alter, transform, or build upon this work.

Any of these conditions can be waived if you receive permission from the author. Your fair dealings and other rights are in no way affected by the above.

Take down policy

If you believe that this document breaches copyright please contact librarypure@kcl.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.

**Multilevel investigation of the role of urbanicity in
psychotic phenomena during childhood and adolescence**

Joanne Newbury

Social, Genetic and Developmental Psychiatry Centre

Institute of Psychiatry, Psychology and Neuroscience

King's College London, UK

Submitted for the degree of Doctor of Philosophy

Abstract

City-living is one of the most consistently identified factors associated with psychosis. Individuals who are born and raised in urban (versus rural) settings have around a two-fold adulthood risk for psychotic disorder. However, very little is currently known about the potential role of the urban environment in subclinical psychotic phenomena among children and adolescents. These symptoms, such as auditory hallucinations and delusions, are thought to lie on a phenotypic and aetiological continuum with psychotic disorders, and therefore constitute a prime target for early-intervention as well as a useful paradigm to investigate the pathogenesis of psychosis. This thesis comprises three studies investigating the potential neighbourhood- and individual-level pathways linking urban upbringing to early psychotic phenomena during childhood and adolescence. Analyses use data from the Environmental-Risk (E-Risk) Longitudinal Twin Study, a birth cohort of 2,232 twin children born in 1994 and 1995. The first study explores the association between urban upbringing and childhood psychotic symptoms, and tests the extent that adverse neighbourhood social conditions such as low levels of social cohesion and high levels of crime and disorder mediate the association between urban upbringing and childhood psychotic symptoms. The second study investigates the cumulative association of neighbourhood social adversity and personal crime victimisation with adolescent psychotic experiences. The third study uses longitudinal and genetically informed methods to explore the association between personal perceptions of neighbourhood adversity and adolescent psychotic experiences. In each study, psychotic phenomena are shown to be significantly more common among children and adolescents raised in urban settings. Analyses highlight several potential pathways linking the urban environment to the emergence of early psychotic phenomena, including adverse neighbourhood social

conditions, direct victimisation by violent crime during adolescence, and adolescents' personal perceptions of threatening neighbourhood conditions. The findings in this thesis suggest that wider environmental factors should be explored as targets in future preventative intervention efforts for early psychotic phenomena.

Table of Contents

Abstract	2
List of tables	8
List of figures	10
Acknowledgments.....	11
Declaration of authorship	13
Chapter 1: Introduction	14
1.1 Background	14
1.2 Definition of research terms	15
1.2.1 Psychosis	15
1.2.2 Urbanicity.....	20
1.3 Urbanicity and psychosis.....	23
1.4 Neighbourhood characteristics and psychosis.....	26
1.5 Potential mechanisms linking the wider social environment to psychosis ...	29
1.6 Thesis outline	34
Chapter 2: Literature Review	38
2.1 Method.....	39
2.1.1 Literature search strategy	39
2.1.2 Inclusion criteria.....	39
2.1.3 Exclusion criteria.....	40
2.2 Results	40
2.2.1 Study selection and demographics	40
2.2.2 Measurement of urbanicity or neighbourhood characteristics	41
2.2.3 Assessment of subclinical psychotic phenomena.....	42

2.2.4 Association of urbanicity/neighbourhood characteristics with subclinical psychotic phenomena	43
2.2.5 Findings by study design and by participant age	44
2.3 Discussion	65
2.3.1 Gaps in the existing literature.....	66
2.3.2 Methodological considerations	68
2.3.3 Conclusions	68
2.4 Aims and hypotheses.....	69
2.5 Distinct and original contribution to the field	72
Chapter 3: Methodology.....	74
3.1 Environmental Risk (E-Risk) Longitudinal Twin Study.....	74
3.2 Psychotic phenomena	76
3.2.1 Psychotic symptoms	77
3.2.2 Psychotic experiences	79
3.3 Urbanicity	80
3.3.1 Urbanicity from the resident survey	81
3.3.2 Urbanicity from the Office of National Statistics	83
3.4 Neighbourhood variables	84
3.4.1 Social processes.....	85
3.4.2 Neighbourhood-level socioeconomic status.....	88
3.4.3 Official neighbourhood levels of crime.....	89
3.5 Personal crime victimisation	90
3.6 Other childhood and adolescent mental health outcomes	92
3.6.1 Childhood mental health outcomes	92
3.6.2 Adolescent mental health outcomes	93

3.7 Family-level covariates	94
3.8 Statistical analyses.....	95
3.8.1 The classical twin design.....	96
3.8.2 The co-twin control design.....	99
3.8.3 The non-independence of twin observations.....	100
Chapter 4: Why are children in urban neighbourhoods at increased risk for psychotic symptoms? Findings from a UK longitudinal cohort study.....	102
4.1 Supplementary materials	115
4.1.1 Comparison of “CLUSTER” command and multilevel modelling in STATA	115
4.1.2 Replication of main analyses using the ONS urbanicity measure	117
Chapter 5: Cumulative effects of neighbourhood social adversity and personal crime victimisation on adolescent psychotic experiences.....	120
5.1 Supplementary materials	132
Chapter 6: In the eye of the beholder: Perceptions of neighbourhood adversity and psychotic experiences in adolescence	136
Chapter 7: Discussion.....	152
7.1 Summary of findings from empirical chapters.....	152
7.1.1 Why are children in urban neighbourhoods at increased risk for psychotic symptoms?	152
7.1.2 Cumulative effects of neighbourhood social adversity and personal crime victimisation on adolescent psychotic experiences.....	153
7.1.3 Perceptions of neighbourhood adversity and psychotic experiences in adolescence.....	154
7.2 Discussion of main findings	157

7.2.1 Urban upbringing and early psychotic phenomena.....	157
7.2.2 Neighbourhood social adversity and early psychotic phenomena	157
7.2.3 Crime victimisation and early psychotic phenomena	159
7.2.4 Wider social environment, social stress, and early psychotic phenomena	159
7.3 Limitations and methodological considerations.....	162
7.3.1 Findings could be due to social drift	162
7.3.2 Western perspective on urbanicity	163
7.3.3 Timing and duration of neighbourhood exposures	165
7.3.4 Shared method variance	166
7.3.5 Adolescent psychotic experiences were self-report	167
7.3.6 Subclinical psychotic phenomena are not psychotic disorders	168
7.3.7 Twins could differ from singletons	169
7.3.8 Missing data	170
7.3.9 Effect sizes and significance thresholds.....	171
7.4 Future directions.....	171
7.5 Implications.....	174
7.6 Conclusion.....	176
References	177
Appendix I.....	211
Appendix II	219
Appendix III.....	225
Appendix IV.....	227

List of tables

Table 2.1. Studies investigating the association between urbanicity/ neighbourhood characteristics and subclinical psychotic phenomena.....	47
Table 4.1. Bivariate association between urbanicity and neighbourhood-level social processes.....	108
Table 4.2. Bivariate associations between neighbourhood-level social processes and childhood psychotic symptoms.....	108
Table 4.3. Association between urbanicity and childhood psychotic symptoms, split into the total effects, and direct and indirect pathways via neighbourhood- level social processes.....	109
Supplementary Table 4.1. Main logistic regression analyses performed using both the “cluster” command and multilevel modelling in STATA.....	116
Supplementary Table 4.2. Association between age-5 ONS urbanicity and childhood psychotic symptoms, split into total effects, and direct and indirect pathways via neighbourhood-level social process mediators	117
Table 5.1. Association between childhood urbanicity and adolescent psychotic experiences.....	125
Table 5.2. Association between neighbourhood characteristics and adolescent psychotic experiences with neighbourhood characteristics categorised at various thresholds.....	126
Table 5.3. The cumulative effects of neighbourhood social adversity and personal crime victimisation on adolescent psychotic experiences.....	127
Supplementary Table 5.1. Levels of social cohesion and neighbourhood disorder according to level of urbanicity.....	133

Supplementary Table 5.2. Association between childhood urbanicity and adolescent psychotic symptoms.....	134
Supplementary Table 5.3. The cumulative effect of neighbourhood social adversity and personal crime victimization on adolescent psychotic symptoms.....	135
Table 6.1. Perceptions of neighbourhood disorder according to level of urbanicity.....	143
Table 6.2. The unadjusted and adjusted association of perceptions of neighbourhood disorder with adolescent psychotic experiences.....	144
Table 6.3. The longitudinal associations of perceptions of neighbourhood safety and psychotic symptoms at age 12 with subsequent psychotic experiences perceptions of neighbourhood disorder at age 18.....	145
Table 6.4. Cross-trait, cross-twin, and cross-twin cross-trait phenotypic correlations of and between adolescent psychotic experiences and perceptions of neighbourhood disorder.....	146
Table 6.5. Fit statistics of submodels (ACE, AE, CE, E) compared to the saturated univariate model for adolescent psychotic experiences and perceptions of neighbourhood disorder.....	146

List of figures

Figure 2.1. Flowchart of selection process for articles included in this review.....	46
Figure 3.1. Location of families in the E-Risk study who were living in England and Wales and participated in the age 12 assessment.....	76
Figure 4.1. Conceptualised pathways between urbanicity and childhood psychotic symptoms.....	105
Figure 6.1. ACE estimates and ACE correlations from cross-twin cross-trait (bivariate) model.....	147

Acknowledgments

I have been incredibly lucky to use data from the E-Risk Twin Study, which represents decades of work funded by the Medical Research Council as well as the Jacobs Foundation, National Institute of Child Health and Human Development, and British Academy. E-Risk was designed, created, and maintained by PI Professor Louise Arseneault and E-Risk founders Professors Terrie Moffitt and Avshalom Caspi. Their forward planning and drive has led to countless new discoveries and insights into early-life determinants of health.

Each study phase has depended on the hard work and dedication of many E-Risk research workers, data managers, and team members, to whom I am enormously grateful. The continued participation of the E-Risk children and their families makes the E-Risk study possible. Special thanks to data managers and general E-Risk legends, Dr Tim Matthews and Tony Ambler, for their patience and kindness over the past four years. It has been a privilege to be part of such a fantastic team and use such highly coveted data. Thank you, Louise, for making it so fun to be an E-Risker.

My PhD was funded by the Economic and Social Research Council and SGDP Centre, both of which have provided me with every opportunity for personal development that I could wish for, including an institutional visit to colleagues at Duke University. Thank you, Grey House team, for making the trip so enjoyable. The SGDP Centre has been the most supportive and inspiring environment I could hope for my PhD journey. I am extremely grateful for the years of support from all my friends at the SGDP, including Laurie, Flo, Elle, Tim, Sophie, Niamh, and my number one office and travel buddy, Jessie.

All my thanks to my parents, Sue and Bob, uncle Keely, and my beloved chief of grammar police, Simon, for their love and support, and for giving me food for

thought when I contemplate the subtleties of human madness. Thank you, Simon, for bearing with me and always finding my research interesting.

I would like to express immense gratitude to my wonderful supervisors and mentors. Professor Candice Odgers has been instrumental in providing her invaluable insights and expertise on neighbourhood research. Thank you so much, Candice, for giving up your time to mentor me at Duke. I am also extremely grateful to Dr Helena Zavos for her indispensable support in navigating the tricky world of twin modelling. Finally, I could not have hoped for a better primary supervisor than Dr Helen Fisher. Helen has tirelessly guided me through the ups and downs of the PhD, and has been my number one source of advice, encouragement, and motivation throughout. Helen, I will be eternally grateful for and inspired by your patience, kindness, wisdom, dedication, and optimism.

Declaration of authorship

I certify that the conceptualising, planning, data analysis and writing in this thesis is my own original work. The empirical chapters (Chapters 4, 5, and 6) are published papers, and the contribution of co-authors to these papers has been acknowledged in the appropriate manner. Specifically, the final drafts of papers in this thesis were circulated to E-Risk co-authors and principal investigators prior to submitting to academic journals. Co-authors provided suggestions for amendments or additional analyses, and I conducted these amendments where appropriate. All co-authors are acknowledged as such on the papers' title pages. The data used in this thesis has been collected by trained research workers over many years, and this is also acknowledged within the empirical chapters. In addition, data checks and variable construction for most of the variables used in this thesis have been undertaken by E-Risk co-investigators and data managers, and relevant E-Risk references are cited where appropriate. This thesis has not been submitted elsewhere towards any other degree.

Chapter 1: Introduction

1.1 Background

For much of the 20th century, the relative roles of nature versus nurture in the aetiology of psychotic disorders such as schizophrenia remained equivocal (Farmer, McGuffin, & Williams, 2002). We now know that both nature (i.e., genes) and nurture (i.e., the environment) contribute to complex illnesses such as psychosis. Molecular and quantitative genetic analyses estimate genes to account for between 20% (molecular) and 80% (quantitative) of risk for psychotic disorders (Cardno & Gottesman, 2000; Lee et al., 2012; Sullivan, Kendler, & Neale, 2003), indicating that at least a fifth of the population-level variance in risk for psychotic disorders is attributable to environmental influences (Plomin, DeFries, Knopik, & Neiderhiser, 2013). Indeed, an extensive range of prenatal, early-life, and adulthood environmental factors are now implicated in the aetiology of psychosis (van Os, Kenis, & Rutten, 2010). Crucially, identifying environmental factors associated with psychosis could help to design interventions to prevent the onset and progression of illness. Over the past few decades, psychosis research and theory have also been shaped by the discovery that attenuated expressions of psychosis, such as hearing voices, having visions, and being extremely paranoid, occur in the general population at a far higher frequency than the clinical manifestations of psychosis (Johns et al., 2004; Kelleher et al., 2012a; van Os, Hanssen, Bijl, & Vollebergh, 2001). These subclinical psychotic symptoms share similar social and developmental risk factors and correlates to psychotic disorders (Kelleher & Cannon, 2011; Polanczyk et al., 2010; van Os, Linscott, Myin-Germeys, Delespaul, & Krabbendam, 2009; Verdoux & van Os, 2002). Thus, rather than categorically distinct and unavoidable illnesses, psychotic disorders are now suggested

to represent the clinical extreme of a phenotypic and aetiological continuum in the general population (van Os, Hanssen, Bijl, & Ravelli, 2000; van Os et al., 2009). Subclinical psychotic phenomena therefore constitute a prime target for early-intervention as well as a useful paradigm to investigate the role of the environment in psychosis using larger, non-clinical samples. Urban birth, upbringing, and living are among the most consistently identified putative environmental risk factors associated with psychotic disorders (Krabbendam & Van Os, 2005; Vassos, Pedersen, Murray, Collier, & Lewis, 2012), but the basis of this association (e.g., mechanisms, developmental timing) is not fully understood. This thesis seeks to address some equivocal areas in the field by examining the role of urbanicity and neighbourhood conditions in early subclinical psychotic phenomena occurring during childhood and adolescence. The following sections briefly define the main research terms that will be used throughout the thesis (psychosis, subclinical psychotic phenomena, urbanicity, and neighbourhood characteristics). The literature on the association between urbanicity and adult psychotic disorder is then discussed, followed by an overview of the contents of this thesis.

1.2 Definition of research terms

1.2.1 Psychosis

Psychosis is a broad term describing a heterogeneous range of symptoms and diagnosable psychiatric disorders. The latest version of the World Health Organization's (WHO) International Classification of Diseases (ICD-10) includes eight diagnoses under the umbrella of primary psychotic disorders: schizophrenia; schizoaffective disorder; schizotypal disorder; delusional disorder; shared psychotic disorder; brief psychotic disorder; other psychotic disorder not due to a substance or

known physiological condition; and unspecified psychosis not due to a substance or known physiological condition (World Health Organization, 1992). Diagnostic criteria vary between these disorders, but they are unified by an involvement of altered perceptions of reality (Kapur, 2003), such as persistent hallucinations (e.g., hearing or seeing things that others cannot), delusions (e.g., extreme paranoia), and thought disorder (e.g., confused speech), which are collectively described as the “positive” symptoms of psychosis. In the case of schizophrenia, these positive symptoms often co-occur with “negative” symptoms, such as apathy and anhedonia (i.e., inability to feel pleasure from normally pleasurable activities). A distinction is also made between “nonaffective” psychotic disorders (e.g., schizophrenia), in which emotional disturbance does not play a key role in the diagnosis; and “affective” psychotic disorders (e.g., depressive psychosis, bipolar disorder with psychotic features), in which emotional disturbance (e.g., depression, mania, mood swings) plays a primary role in the diagnosis.

Psychotic disorders are relatively rare. Schizophrenia is diagnosed in less than 1% of the population, and the combined prevalence of all psychotic disorders is around 3% (van Os et al., 2001). Psychotic disorders typically first emerge and reach clinical significance in late adolescence and early adulthood (Häfner, Maurer, Löffler, & Fätkenheuer, 1994), at a time when most young people become independent, embark on their careers, and build social networks. However, both the positive and negative symptoms of psychosis can severely impact mood and functioning (Fervaha, Foussias, Agid, & Remington, 2014a; Fervaha et al., 2014b; Mohamed et al., 2008) and thereby cause a range of difficulties in relationships, education, and employment. Furthermore, psychotic disorders are associated with a whole host of other health conditions including smoking (de Leon & Diaz, 2005), substance abuse (Regier et al., 1990),

metabolic and cardiovascular problems (Mitchell et al., 2011), and suicide (Harris & Barraclough, 1997). A first-episode of psychosis increases risk of death within a year by over 20-fold (Schoenbaum et al., 2017). Psychotic disorders therefore place a huge emotional, functional, and economic burden on individuals, families, and society more broadly. Treatment strategies for psychotic disorders typically include a combination of pharmacological and psychological therapies. However, psychotic disorders are associated with high rates of relapse as well as clinical deterioration over time (Robinson et al., 1999). It is now recognised that early intervention – in the very first stages of illness if not before – offers the best hope for improving outcomes in psychosis (Millan et al., 2016).

Research over the past few decades has shown that attenuated expressions of psychosis also occur in the general population at a far higher frequency than the clinical manifestations of psychosis (Hanssen, Bak, Bijl, Vollebergh, & van Os, 2005; Kelleher & Cannon, 2011; Kelleher et al., 2012a; van Os et al., 2000). These subclinical symptoms are generally defined by the presence of psychosis-like phenomena – usually positive symptoms such as hallucinations, delusions and thought disorder – in the absence of a psychosis diagnosis and clinical need (van Os et al., 2009). Various terms have been used in the literature to describe these phenomena, such as psychotic symptoms, psychotic experiences, psychotic-like experiences and schizotypal traits. A distinction is sometimes made between “psychotic symptoms”, describing a rarer and more clinically-pertinent phenotype conveying some potential impairment; and “psychotic experiences” describing a broader, transient, and more prevalent phenotype which may have little or no impact on functioning (van Os et al., 2009), though recent evidence suggests that psychotic experiences may also be associated with disability (Navarro-Mateu et al., 2017). In this thesis, the term

“psychotic phenomena” is used to refer collectively to subclinical psychotic symptoms and experiences. The estimated lifetime prevalence of subclinical psychotic phenomena varies considerably between studies depending on measurement, ranging from around 6% (McGrath et al., 2015) to up to 30% of general population adults (Kendler, Gallagher, Abelson, & Kessler, 1996). In a meta-analysis of 47 studies, van Os et al. (2009) reported a median prevalence of 5.3% and a median incidence of 3.1% of psychotic phenomena in the general population, though the median prevalence of broader psychotic experiences was higher, at 8.4%. Rates of subclinical psychotic phenomena are even higher among young people. In a meta-analysis of 19 population-based studies of children and adolescents, Kelleher et al. (2012a) reported a median prevalence of psychotic symptoms of 17% among children (aged 9–12) and 7.5% among adolescents (aged 13–18).

Several lines of evidence have led to the suggestion that subclinical psychotic phenomena lie on a phenotypic and aetiological continuum with clinical psychotic disorders. Aside from the symptomatic overlap, subclinical psychotic phenomena are heritable (Lataster, Myin-Germeys, Derom, Thiery, & van Os, 2009) and exhibit familial clustering with psychotic disorders (Polanczyk et al., 2010). Both share a similar range of risk factors including childhood trauma, low socioeconomic status (SES), family psychiatric history, and cannabis use (Kelleher & Cannon, 2011; Polanczyk et al., 2010; van Os et al., 2000). Moreover, children and adolescents who report psychotic phenomena have a significantly elevated adulthood risk for psychotic disorder (Dominguez, Wichers, Lieb, Wittchen, & van Os, 2011; Fisher et al., 2013; Linscott & van Os, 2013; Poulton et al., 2000). For example, Poulton et al. (2000) showed in a longitudinal cohort of over 700 participants that odds for adult psychotic disorder were over 16-times greater for individuals with versus without psychotic

symptoms at age 11. The relatively high prevalence of psychotic experiences during childhood and adolescence has led to the suggestion that early psychotic phenomena represent the “normal developmental expression” of psychosis, which abates for most individuals, but persists, progresses and eventually results in impairment for a small minority (Cougnard et al., 2007; Dominguez et al., 2011; van Os et al., 2009). For example, brain maturation processes such as synaptic pruning and enhancement of the prefrontal cortex (Blakemore & Choudhury, 2006) could make children and adolescents particularly prone to experiencing psychotic phenomena (Millan et al., 2016). However, there is evidence that early psychotic phenomena are more likely to emerge, persist and reach clinical significance when young people are exposed to environmental factors such as trauma (Spauwen, Krabbendam, Lieb, Wittchen, & Van Os, 2006a), cannabis use (Kuepper et al., 2011b), and urbanicity (Spauwen, Krabbendam, Lieb, Wittchen, & van Os, 2006b). Moreover, likelihood of persistence follows a dose-response pattern with cumulative environmental risk (Cougnard et al., 2007). Early psychotic phenomena are also associated with a range of other serious adulthood conditions including depression, post-traumatic stress disorder, substance abuse, and suicidal behaviour (Fisher et al., 2013; Kelleher et al., 2012c; Poulton et al., 2000). This phenotype therefore represents an early indicator of risk for adult psychopathology more broadly, and should not be viewed as a homotypic precursor of psychotic disorder. Nevertheless, it is crucial to improve our understanding of the aetiology of subclinical psychotic phenomena. Investigating the role of environmental factors in the emergence of psychotic phenomena during childhood and adolescence could highlight new avenues for interventions to prevent the onset and persistence of these symptoms. This thesis will therefore focus on the aetiology of early psychotic

phenomena among a large representative cohort of children and adolescents in the general population.

1.2.2 Urbanicity

Urbanicity describes the quality and degree of a geographic area being manmade and populated by humans (alternative terms include urbanism and urbanisation). Characteristics that contribute to levels of urbanicity include population density, building density, infrastructure (e.g., transport routes, hospitals, schools), industrialisation (e.g., trade, factories) as well as proximity to and density of natural/green space. Urbanicity follows a spectrum, ranging from mostly rural areas that are sparsely populated and have few buildings and manmade features (e.g., forests, countryside, farmland, villages); to intermediate urban settings, with denser populations, more buildings and infrastructure, and some green space (e.g., small towns, suburbs); to the most urban settings, characterised by high population densities, mostly manmade environments, and little or no natural or green space (e.g., cities, conurbations).

Urbanicity is therefore a complex construct, containing numerous physical and social facets. This raises difficulties in quantifying degree of urbanisation (Cohen, 2006; Dahly & Adair, 2007). Urbanicity has been measured in various ways for research and administrative purposes. Common methods include absolute population size, population density, and building density. Population and building density have the advantage of providing quasi-continuous data, allowing several levels of urbanicity to be compared. However, the most common measurement technique has been to use administrative definitions to categorise levels of urbanicity (e.g., capital city versus surrounding areas) (Dahly & Adair, 2007). While readily available, this dichotomy treats specific cities and other areas as homogeneous entities and therefore

loses considerably more information than measures derived from population density. Developments in geospatial technologies and satellite imagery (e.g., Google Aerial View) provide new opportunities to estimate levels of urbanicity via demographic data and birds-eye observations of land-use (Odgers, Caspi, Bates, Sampson, & Moffitt, 2012a).

We are an increasingly urban-dwelling species. Two-hundred years ago only 10% of Europeans lived in towns and cities; today, 70% of people in Europe inhabit urban areas. Globally, half the world's population currently live in urban areas, and this will reach 70% by 2050 (Dye, 2008). Major urbanisation is a process that started in the West, and is now occurring worldwide. However, there are many socioeconomic and infrastructural differences between present day cities in high-income versus low- and middle-income countries (Cohen, 2006; World Health Organization, 2008). This thesis necessarily takes a Western perspective on urbanicity, and the implications of this approach are discussed in Chapter 7. The temporal trend in urbanicity is partly explained by the expansion of human settlements. Taking London as an example, Roman Londinium covered an area of only one square mile, whereas Greater London today covers an area of 600 square miles. In addition to the expansion of urban areas, global populations have increased exponentially, and more and more people have migrated to cities (Cohen, 2006; Porter, 1998). For example, medieval London was inhabited by around 600,000 people. This increased to 2 million people during the industrial revolution, and Greater London is now inhabited by over 8 million people. For much of human history, individuals lived in small groups of familiar group members (Dunbar, 1998). Thus, in evolutionary terms, humans have become an urban species in the blink of an eye. It is therefore crucial to understand the potential benefits and risks of city-living on human health and wellbeing.

With more job opportunities, better access to schools and hospitals, and greater investment in infrastructure, contemporary cities in developed countries provide a range of potential advantages over rural areas (Dahly & Adair, 2007; Dye, 2008). On the other hand, cities also contain numerous less desirable characteristics, including pollution, overcrowding, and stark contrasts in affluence and poverty (Beevers et al., 2016; Dye, 2008; Gracey, 2002; World Health Organization, 2008). A great deal of heterogeneity exists between as well as within cities and other settlement types, and this raises difficulties for studies seeking to understand the potential impact of urban environments on mental health. Sociological theory provides a useful framework to understand the relationship between neighbourhood environments and health. It is suggested that the effects of structural features (i.e., relatively static built and economic factors such as urbanicity and neighbourhood-level deprivation) on human health outcomes are mediated via social processes (i.e., the dynamic and modifiable ways in which individuals and groups interact and form patterns of behaviour in the context of their environment) (Sampson, 2001; Sampson, Morenoff, & Gannon-Rowley, 2002). The overcrowding and inequality found in cities might clearly contribute to different patterns of behaviour among urban versus rural inhabitants. For example, the prevalence of crime victimisation in the UK is over twice as high in urban versus rural areas (Home Office Statistical Bulletin, 2010). A related construct is neighbourhood disorder (or disorganization) (Sampson & Raudenbush, 1999), describing physical and social signs of threat and danger in the neighbourhood, such as graffiti, vandalism, gang activity, drug activity, muggings, burglaries, and antisocial neighbours. Again, people residing in urban (Goldman-Mellor, Margerison-Zilko, Allen, & Cerdá, 2016; Sampson & Raudenbush, 1999) and deprived (Polling, Khondoker, Hatch, Hotopf, & SELCoH study team, 2014) areas tend to perceive

higher levels of neighbourhood disorder. Another construct of interest is social cohesion (and related constructs such as collective efficacy, social capital, informal social control, and social fragmentation) (Sampson, Raudenbush, & Earls, 1997). This describes the quality and quantity of interactions between residents in a community, such as trust, shared values, social networks, supportiveness, and civic participation: the “glue that keeps societies together” (McKenzie, Whitley, & Weich, 2002). Again, there is some evidence that urban communities tend to be less socially cohesive than rural communities (Coulthard, Walker, & Morgan, 2002).

This thesis draws from the sociological framework of structural features and social processes to investigate the neighbourhood- and individual-level mechanisms by which urbanicity might be associated with the emergence of psychotic phenomena in young people. The research in this thesis utilises detailed measures of the structural and social environment which are accurate to the level of the street or postcode. The following sections describe the literature on the association of urbanicity and neighbourhood characteristics with *adult* psychotic disorder, to illustrate the rationale for investigating the role of urbanicity in *early* psychotic phenomena.

1.3 Urbanicity and psychosis

Area-level variation in psychosis incidence was first reported in 1939 by Faris and Dunham, who showed that the prevalence of schizophrenia in inner city Chicago exceeded that of the city outskirts by over six-fold (Faris & Dunham, 1939). Since this ecological study, significantly elevated rates of psychotic disorders in urban (versus rural/less urban) areas have been documented by numerous studies of different designs in counties including the United States (Kendler et al., 1996), China (Chan et al., 2015), Finland (Haukka, Suvisaari, Varilo, & Lönnqvist, 2001), the Netherlands (Dragt et al., 2011; Marcelis, Navarro-Mateu, Murray, Selten, & Van Os, 1998;

Marcelis, Takei, & Van Os, 1999; van Os et al., 2001), Sweden (Harrison et al., 2003; Lewis, Davis, Andreasson, & Allebeck, 1992; Sundquist, Frank, & Sundquist, 2004; Zammit et al., 2010), Denmark (Mortensen et al., 1999; Pedersen & Mortensen, 2001; Pedersen & Mortensen, 2006b; van Os, Pedersen, & Mortensen, 2004; Vassos, Agerbo, Mors, & Pedersen, 2015), Germany (Spauwen, Krabbendam, Lieb, Wittchen, & van Os, 2004; Spauwen et al., 2006b), France (Szöke et al., 2014), Ireland (Kelly et al., 2010), and the United Kingdom (Allardyce et al., 2001; Kirkbride et al., 2006). For example, Sundquist et al. (2004) showed in a Swedish cohort of over 4 million people that individuals living in the most (versus least) urban setting were 77% more likely to have a first episode of psychosis (hazard ratio=1.77, 95% CI=1.56-1.99). Similarly, Allardyce et al. (2001) showed in a UK-based catchment study of nearly 300,000 people that the incidence of schizophrenia was 63% higher in the urban versus nonurban catchment area (incident rate ratio [IRR]=1.63, 95% CI=1.35-1.98). Meta-analytic estimates from this body of research indicate that odds for psychotic disorder are around two-times greater for individuals raised in urban versus rural settings (Krabbendam & Van Os, 2005; Vassos et al., 2012).

Several aspects of the association between urbanicity and psychotic disorder suggest causal underpinnings (Kirkbride, Jones, Ullrich, & Coid, 2014; Krabbendam & Van Os, 2005). First, the urban exposure appears to be most potent from birth to adolescence (Marcelis et al., 1999; Pedersen & Mortensen, 2001). For example, Pedersen and Mortensen (2001) showed that up to the age of 15, risk for schizophrenia increased and decreased, respectively, by moving to more and less urban settings. Consistent with the neurodevelopmental model of psychosis (Rapoport, Addington, Frangou, & Psych, 2005), this suggests that the main effect of urbanicity on psychosis outcome is transmitted when brain development is most active and vulnerable.

Second, the association between urbanicity and psychosis persists after considering a wide range of potential factors that might otherwise explain the association, including parental age (Mortensen et al., 1999), obstetric complications (Eaton, Mortensen, & Frydenberg, 2000; Harrison et al., 2003), ethnicity (Kirkbride et al., 2006; Marcelis et al., 1998; Marcelis et al., 1999), migrant and marital status (Sundquist et al., 2004), and season of birth (Mortensen et al., 1999), among others. Third, though urban living is associated with a range of mental health problems (Peen, Schoevers, Beekman, & Dekker, 2010), urban upbringing demonstrates a degree of specificity with psychosis. That is, urban upbringing is more strongly associated with nonaffective psychotic disorders than with affective psychotic and mood disorders (Pedersen & Mortensen, 2006a; Sundquist et al., 2004; Vassos et al., 2015), suggesting that aspects of the urban environment are particularly relevant to the aetiology of psychosis. Fourth, not only the prevalence, but the incidence of psychosis is elevated in urban areas. This suggests that the association between urbanicity and psychosis is not solely attributable to individuals migrating into urban settings after the onset of psychosis. Fifth, there is a dose-response association between degree of urbanisation and length of exposure on the one hand, and risk for psychosis on the other hand, suggesting the presence of a biological gradient between exposure and outcome (Pedersen & Mortensen, 2001). Sixth, there is evidence that the association between urbanicity and psychosis is stronger in more recent generations (Chan et al., 2015; Haukka et al., 2001; Marcelis et al., 1998), which indicates that the factor(s) contained in urbanicity are becoming progressively more toxic. Furthermore, much of the evidence linking urbanicity with psychosis comes from record-linkage analyses of millions of individuals (Dragt et al., 2011; Harrison et al., 2003; Lewis et al., 1992; Marcelis et al., 1998; Marcelis et al., 1999; Mortensen et al., 1999; Pedersen & Mortensen, 2001; Sundquist et al., 2004;

Vassos et al., 2015; Zammit et al., 2010), thus studies have generally been adequately powered to detect small effects on relatively rare psychiatric outcomes.

However, three comprehensive reviews of the urbanicity-psychosis literature conclude that, while the effect of urbanicity on clinical psychosis outcomes appears to have a causal underpinning, a higher resolution focus is now needed to identify the pathogenic factor(s) contained within this macro-level exposure (Heinz, Deserno, & Reininghaus, 2013; Krabbendam & Van Os, 2005; March et al., 2008). Cities are complex and heterogeneous environments, containing numerous potential physical and social features that might plausibly contribute to the aetiology of psychosis. These features cannot be estimated via population density or administrative data alone. Efforts are needed to dissect the proxy risk factor “urbanicity” into its risk subcomponents, in order to shed light on potential mechanisms linking exposure to illness (Tost, Champagne, & Meyer-Lindenberg, 2015). More recently, attention has turned to specific neighbourhood-level features that might characterise urban settings and contribute to the heightened rates of psychosis.

1.4 Neighbourhood characteristics and psychosis

Developments in epidemiological and statistical approaches such as multilevel analyses have enabled neighbourhood-level effects to be more robustly isolated from the potential confounding by individual-level compositional effects (e.g., SES and ethnicity). In the past two decades, associations have been documented between psychotic disorder and a range of neighbourhood-level characteristics, including structural features such as poverty and inequality; and social processes such as social fragmentation, disorganization, and crime. As with the literature on urbanicity and psychosis, most of this evidence comes from high-income countries.

Neighbourhood-level deprivation (often operationalised using area-level data on unemployment, income, health inequalities, crime, housing, and education (Department for Communities and Local Government, 2015)) has been repeatedly implicated in psychosis (Allardyce et al., 2005; Bhavsar, Boydell, Murray, & Power, 2014; Kirkbride et al., 2014; Omer et al., 2014; Zammit et al., 2010). Kirkbride et al. (2014) showed that the heightened incidence of psychosis in areas of London with higher income deprivation (relative risk [RR]=1.28, 95% CI=1.08-1.51) and income inequality (RR=1.25, 95% CI=1.04-1.49) was not attributable to individual-level factors including social class, age, sex, or ethnicity. Allardyce et al. (2005) documented a greater than 5-fold odds for psychotic disorder incidence among individuals residing in the most materially deprived (versus affluent) settings (odds ratio [OR]=5.29, 95% CI=1.49-18.75). Furthermore, a significant association between income inequality and schizophrenia incidence was demonstrated by Allardyce et al. (2001) after considering age, sex, absolute deprivation, and ethnicity, but only in deprived neighbourhood settings (IRR=3.79, 95% CI=1.25-11.49). However, other studies have demonstrated that the apparent effect of neighbourhood deprivation on psychosis outcome is explained by individual-level compositional factors and neighbourhood-level social processes. For example, Zammit et al. (2010) reported an attenuated and non-significant association between neighbourhood deprivation and psychosis after considering a battery of individual-level factors such as family psychiatric history, unemployment and family income. Similarly, Kirkbride et al. (2007) showed that the association between neighbourhood deprivation and first-episode psychosis became non-significant after considering individual-level factors and other neighbourhood-level factors including population density, ethnic density, ethnic fragmentation, and social capital. In contrast, a 1% reduction in ethnic

fragmentation (IRR=0.95, 95% CI=0.92-0.99) and 1% increase in social capital (IRR=0.95, 95% CI=0.92-0.99) still significantly predicted lower schizophrenia incidence after considering individual-level and neighbourhood-level factors including deprivation (Kirkbride et al., 2007).

Other studies have shown similarly robust associations between neighbourhood-level social processes and psychotic disorder. Allardyce et al. (2005) identified a strong association between high (versus low) social fragmentation and psychosis incidence (OR=12.84, 95% CI=5.71-28.88), which was independent of the effects of neighbourhood deprivation. Silver, Mulvey, and Swanson (2002) documented a significant association between residential mobility (as a proxy for social fragmentation) and schizophrenia prevalence after considering age, gender, race, income, education, and marital status. Furthermore, using resident survey data, Kirkbride et al. (2008) identified a non-linear association between neighbourhood levels of social cohesion and trust and schizophrenia incidence. Incidence was significantly higher in areas with lower (IRR=2.0, 95% CI=1.2-3.3) but also higher (IRR=2.5, 95% CI=1.3-4.8) versus medial levels of social cohesion and trust, independent of sex, age, ethnicity, and neighbourhood deprivation, ethnic density, and fragmentation (Kirkbride et al., 2008). In an incident-catchment study, Veling, Susser, Selten, and Hoek (2015) documented an almost two-fold incidence of psychotic disorder in neighbourhoods with the highest versus lowest levels of social disorganization (IRR=1.95, 95% CI=1.38–2.75). Similarly, Bhavsar et al. (2014) showed that the association between area-level deprivation and schizophrenia incidence was explained by the deprivation subcategory of crime (IRR=1.28, 95% CI=1.06-1.56), after considering potential individual-level and neighbourhood-level confounders. Recent research also implicates these kinds of adverse neighbourhood-

level factors in higher rates of psychosis-proneness and ultra-high-risk (Kirkbride et al., 2015; O'Donoghue et al., 2015), which highlights that neighbourhood social conditions might exert effects across the full spectrum of psychosis phenotypes.

The evidence on neighbourhood social features and psychosis therefore covers several interrelated domains describing the quality and quantity of interactions between neighbours and supportiveness of communities (e.g., social cohesion, social capital, social fragmentation, trust), and the levels of threat and potential subordination faced by individuals within neighbourhoods (e.g., neighbourhood disorder, ethnic fragmentation, crime, disorganization). Findings from this literature and the broader literature on urbanicity provide some insights into potential mechanisms that might underlie the association of urbanicity and neighbourhood characteristics (herein collectively referred to as the wider social environment) with psychotic disorders, which are briefly explored below.

1.5 Potential mechanisms linking the wider social environment to psychosis

Given the apparent developmental timing of the association between urban upbringing and adult psychotic disorder (Marcelis et al., 1999; Pedersen & Mortensen, 2001), several pre- and perinatal mechanisms have been examined. For example, urban pregnancy and birth could increase risk for infection and other obstetric factors, and thereby affect brain development. However, Eaton et al. (2000) found that obstetric complications did not account for the association between urban birth and adult psychotic disorder. Similarly, Harrison et al. (2003) found that winter birth (as a proxy for viral infection) did not modify the effect of urban birth on psychotic disorder. It is also possible that urban residents have a greater developmental exposure to pollutants such as nitrogen oxide, lead, and carbon monoxide as well as light and noise pollution, which could increase risk for psychopathology by triggering neuroinflammation

(Calderón-Garcidueñas et al., 2008). This has only been investigated by two studies (Gao, Xu, Guo, Fan, & Zhu, 2017; Pedersen & Mortensen, 2006b), which used either proxy or low-resolution measures of air pollution to examine associations with schizophrenia. Further research using more precise measures is therefore needed to examine the potential role of pollutants and other physical exposures in the development of psychosis.

In contrast, the association between neighbourhood-level social processes and psychotic disorder is not entirely explained by the composition of individuals in adverse neighbourhoods (described above). There is a growing suggestion that the complex, ambiguous, and potentially threatening social environment of urban neighbourhoods increases residents' exposure to social stress (Heinz et al., 2013; Kirkbride et al., 2007; Lederbogen, Haddad, & Meyer-Lindenberg, 2013; Meyer-Lindenberg & Tost, 2012; Selten, van der Ven, Rutten, & Cantor-Graae, 2013). Psychosocial cognitive processing places heavy demands on the hypothalamic-pituitary adrenal (HPA) axis, the neuroendocrinological system for processing stress and eliciting the biological stress response (van Winkel, Stefanis, & Myin-Germeys, 2008). Elevated exposure to social stress, particularly during development, might then increase risk for psychosis by dysregulating the HPA axis, the dopaminergic system (the leading neurobiological mechanism implicated in the positive symptoms of psychosis), and brain maturation processes (Tarullo & Gunnar, 2006; van Winkel et al., 2008; Walker, Mittal, & Tessner, 2008). In addition, a psychological pathway could exist, whereby specific social exposures in cities (e.g., threatening and ambiguous interactions with strangers) promote or exacerbate psychotic phenomena. There is some experimental evidence to support a role of social stress and social neural processing in the association between urbanicity and psychosis. For example, healthy

adults with urban (versus rural) upbringing show heightened activity in the perigenual anterior cingulate cortex (a key brain region for regulating amygdala activity and the stress response) during social evaluative stress tasks (Lederbogen et al., 2011). Other studies have also documented associations between urban upbringing and reduced grey matter volume, particularly in the frontal cortex (Besteher, Gaser, Spalthoff, & Nenadić, 2017; Haddad et al., 2015), though null findings have also been shown (Frissen et al., 2017). Furthermore, levels of stress, paranoia, hallucinations and negative schema among adults with psychosis are immediately exacerbated by brief exposure to an urban environment (Freeman et al., 2014), demonstrating a symptomatic link between the urban environment and psychotic experiences. However, most evidence linking neighbourhood social environments to psychotic disorder has been cross-sectional and obtained in adulthood. Research using prospective designs and young samples is needed to further investigate the potential developmental role of neighbourhood social conditions in the association between the urban environment and psychosis.

Additionally, there is evidence that the urban environment might modify (or be modified by) other putative environmental risk factors for psychosis. For example, the associations of cannabis use (Kuepper, Van Os, Lieb, Wittchen, & Henquet, 2011a) and childhood victimisation (Frissen et al., 2015) with psychotic disorder is stronger in more urban settings. Consistent with cumulative stress models of psychosis (Morgan et al., 2014), this could suggest that urban and adverse neighbourhood conditions convey an enduring vulnerability and impaired resilience to subsequent stressors. However, very little is currently known about the potential interactive relationship between urbanicity and crime victimisation. A large body of research suggests that early-life exposure to victimisation is associated with the

development of subclinical psychotic phenomena through to psychotic disorders (Trotta, Murray, & Fisher, 2015; Varese et al., 2012). Given that crime victimisation (e.g., muggings, assaults, verbal harassment) is twice as common in cities than rural settings (Home Office Statistical Bulletin, 2010), the potential cumulative and interactive effects of urbanicity and victimisation on psychosis outcome warrants investigation.

Risk for psychosis is of course dependent on both genes and the environment. Several studies have shown that the association between urbanicity (and related neighbourhood features) and psychosis outcome is stronger for individuals with a family history of psychosis (as a proxy for genetic liability) (Binbay et al., 2012; Van Os, Hanssen, Bak, Bijl, & Vollebergh, 2003; van Os et al., 2004; Wicks, Hjern, & Dalman, 2010). Recent research using virtual reality paradigms also suggests that individuals with higher psychosis liability experience more social distress and paranoia from crowded and hostile virtual reality social environments (Veling, Couston, Pot-Kolder, van Os, & van der Gaag, 2016a; Veling, Pot-Kolder, Couston, van Os, & van der Gaag, 2016b). Taken together, this research could indicate that genetic risk for psychosis is associated with an increased sensitivity to social stressors in the urban environment, which is consistent with a wider literature documenting a link between genetic risk for psychosis and stress-sensitivity (Collip et al., 2011; Myin-Germeys, Delespaul, & Van Os, 2005; Myin-Germeys, van Os, Schwartz, Stone, & Delespaul, 2001). However, there is currently no research on the potential role of personal appraisals and perceptions of adverse neighbourhood conditions in the emergence of psychotic phenomena. Given that social stress is suggested to underpin the association between adverse neighbourhood conditions and psychosis outcomes (described above), we might predict that young people's own perceptions

of their neighbourhoods would play a fundamental role. Moreover, given the phenotypic correlation between psychosis and stress-sensitivity (Myin-Germeys et al., 2005; Myin-Germeys et al., 2001), it is plausible that overlapping genetic influences might simultaneously contribute to psychotic phenomena and perceptions of the neighbourhood. No studies have yet used genetically informed methods to explore the association between psychotic phenomena and perceptions of neighbourhood adversity.

Each of the potential mechanisms described above assume that the association between urbanicity and psychotic disorder has a causal underpinning. However, non-causal mechanisms are possible. The “social drift” hypothesis proposes that the association between urbanicity and psychotic disorder arises due to the downward social mobility of individuals migrating into cities after the onset of psychotic illness (Ødegård, 1956). It is possible, for example, that individuals with psychotic disorder are less able to “buy their way out” of crowded and deprived urban environments because of the functional impairment associated with illness. While this mechanism has previously gained little traction in the literature, emerging research using polygenic risk score (PRS) data suggests that a degree of drift might in fact be present. Two studies from Denmark (Paksarian et al., 2018) and Australia (Colodro-Conde et al., 2017) recently showed that individuals with higher schizophrenia PRS were more likely to live in densely populated areas. However, only one of these studies investigated the association of schizophrenia PRS and urbanicity at birth, and found that this did not explain the association between urbanicity and adult psychotic disorder in the sample (Paksarian et al., 2018). Findings from these studies are therefore consistent with a mechanism whereby individuals drift into adverse neighbourhood settings because of their illness (or subclinical traits due to genetic

risk), but they do not fully explain the association of urban birth and upbringing with subsequent psychosis risk. Again, research focussing on the wider social environment and subclinical psychotic phenomena in younger samples could shed light on the developmental timing and direction of the association between urbanicity, neighbourhood characteristics and psychosis.

1.6 Thesis outline

This thesis investigates the role of urbanicity and neighbourhood conditions in the emergence of psychotic phenomena during childhood and adolescence by: first, conducting a literature review of existing studies that have investigated the association between urbanicity/neighbourhood conditions and subclinical psychotic phenomena in the general population; and second, by undertaking three empirical studies using data from the Environmental Risk (E-Risk) Longitudinal Twin Study, a cohort of over 2,000 individuals born in England and Wales who have been followed from birth to age 18. The three results chapters are published articles and have been presented in published format. References from these results chapters are shown in the articles only, and are not repeated in the main reference list at the end of the thesis. If applicable, supplementary materials for each study are presented at the end of results chapters. An outline of the subsequent chapters is provided below.

Chapter 2: Chapter 2 presents a literature review of studies that have investigated the association of urbanicity and/or neighbourhood-level characteristics with subclinical psychotic phenomena in the general population. This is conducted to collate the main methods, findings, and remaining research gaps in the literature. The research aims and hypotheses of this thesis are outlined at the end of Chapter 2.

Chapter 3: All results chapters comprise a methods and statistical analysis section for that study. However, Chapter 3 provides more detail on the methods and

variables used throughout the thesis, including a more comprehensive description of the E-Risk study design and sample, further detail on the main measures used in the three results chapters (e.g., psychotic phenomena, urbanicity, neighbourhood characteristics), and a description of analytic approaches for handling data from twin samples.

Chapter 4: Chapter 4 presents an investigation of the association between urban upbringing and childhood psychotic symptoms at age 12 (Newbury et al., 2016). Drawing from sociological theory (described above), this study also tests whether certain neighbourhood-level social processes (social cohesion, social control, neighbourhood disorder, neighbourhood crime) mediate the association between urban upbringing and childhood psychotic symptoms. Analyses control for proxy genetic and environmental confounding factors by adjusting for family SES, family psychiatric history, and maternal psychotic symptoms. Given evidence that urbanicity may be specifically associated with adult psychotic disorder, the associations between urbanicity and other age-12 mental health outcomes were calculated to check specificity.

Chapter 5: Chapter 5 presents an investigation of the association between childhood urbanicity and adolescent psychotic experiences (Newbury et al., 2017a). Again, the potential mediatory effects of adverse neighbourhood-level social conditions (low social cohesion and high neighbourhood disorder) are examined. Based on evidence that the association between urbanicity, neighbourhood adversity and psychosis might be partly conditional on individual-level exposures (described above) – as well as the fact that youth in cities have an elevated risk of crime victimisation – this study investigates the potential cumulative and interactive effects of neighbourhood social adversity and personal victimisation by violent crime on

adolescent psychotic experiences. That is, analyses investigate whether the effect of violent crime victimisation on psychotic experiences is substantially greater in adverse neighbourhood contexts. Again, analyses control for key proxy measures of genetic and environmental risk, including family SES, family psychiatric history, maternal psychotic symptoms, adolescent substance problems, as well as earlier psychotic symptoms. In addition, the sensitivity of findings is examined by repeating analyses using clinically-verified psychotic symptoms.

Chapter 6: Chapter 6 presents a multilevel investigation of the role of adolescents' *personal* perceptions of threatening neighbourhood conditions (neighbourhood disorder) in adolescent psychotic experiences (Newbury et al., 2017b). Given that elevated social stress is one leading theory for how adverse neighbourhood conditions increase risk for psychosis, and psychotic phenomena involve altered perceptions of reality such as threat detection bias, we might predict personal appraisals of threatening neighbourhood conditions to play an important role. To disentangle the nature of the association between perceptions of neighbourhood adversity and adolescent psychotic experiences, this study utilises the longitudinal design of the E-Risk study to investigate temporality. Given evidence that individuals with higher genetic liability for psychosis may be more sensitive to stressful social situations, this study also uses the twin sample to investigate the genetic and environmental sources of variance and covariance between perceptions of neighbourhood adversity and adolescent psychotic experiences.

Chapter 7: Chapter 7 summarises the main findings from each of the results chapters, before discussing the findings in the context of the wider literature. The limitations of this thesis are also addressed, and areas for future research are explored. Finally, the implications of the findings of this thesis are discussed.

Chapter 2: Literature Review

A consistent body of research demonstrates that individuals who are born and raised in cities (versus rural settings) have around a two-fold adulthood risk for developing a psychotic disorder (Allardyce et al., 2001; Lewis et al., 1992; Marcelis et al., 1998; Marcelis et al., 1999; Mortensen et al., 1999; Pedersen & Mortensen, 2001; Sundquist et al., 2004; Vassos et al., 2012). However, a continued focus on urbanicity may be of limited use for understanding the potential pathways linking the urban environment to psychosis (Heinz et al., 2013; Krabbendam & Van Os, 2005; March et al., 2008). A higher resolution focus on specific neighbourhood-level factors has revealed associations between psychosis and deprivation (Allardyce et al., 2005; Bhavsar et al., 2014; Kirkbride et al., 2014; Omer et al., 2014), crime (Bhavsar et al., 2014), inequality (Boydell, Van Os, McKenzie, & Murray, 2004; Kirkbride et al., 2014), and ethnic (Kirkbride et al., 2007) and social (Allardyce et al., 2005; Kirkbride et al., 2008; Omer et al., 2014) fragmentation, offering clues to the potential mechanisms underpinning the urbanicity-psychosis association (described above in Chapter 1). Recent research also documents higher rates of ultra-high risk and psychosis-proneness among young adults residing in these kinds of adverse neighbourhood conditions (Kirkbride et al., 2015; O'Donoghue et al., 2015), providing further evidence for a developmental role of wider environmental exposures in the pathogenesis of psychosis.

However, very little is currently known about the potential role of these types of wider environmental exposures in the aetiology of subclinical psychotic phenomena, which include auditory hallucinations, delusions, and other unusual thoughts and beliefs in the absence of clinical need. Attenuated psychotic experiences are common in the general population (Johns et al., 2004; Kelleher et al., 2012a; van

Os et al., 2001) and are thought to lie on a phenotypic and aetiological continuum with clinical psychotic disorders (Polanczyk et al., 2010; van Os et al., 2000; van Os et al., 2009; Verdoux & van Os, 2002). This provides a useful paradigm to investigate environmental risk factors for psychosis. Furthermore, there is a growing consensus that targeted early-intervention – before the onset of clinical psychosis and ideally in adolescence – is necessary to improve outcomes among individuals at risk for psychosis (Davidson, Grigorenko, Boivin, Rapa, & Stein, 2015; Millan et al., 2016). The purpose of this review of the empirical literature is to identify studies that have examined the association of urbanicity and/or neighbourhood characteristics with subclinical psychotic phenomena in the general population. This review seeks to characterise the predominant methods and findings from relevant studies, and also to identify areas of this emerging topic which remain unaddressed.

2.1 Method

2.1.1 Literature search strategy

Advanced searches of the databases Medline (PubMed), Embase, and PsycINFO were used to identify relevant studies published between 1930 and 6th December 2017. Using Boolean operator terms, the outcome-related keywords (“psychotic symptoms” OR “psychotic experiences” OR schizoid OR schizotyp* OR paranoi* OR hallucina* OR suspicious OR “voice hearing” OR delusion OR “psychosis proneness”) were combined using AND with the exposure-related keywords (urban* OR city OR neighbourhood OR neighborhood OR “area-level” OR spatial). Reference lists from included studies were also examined for relevant studies.

2.1.2 Inclusion criteria

For papers to be included they had to meet the following criteria:

- (i) Investigations of urbanicity and/or neighbourhood-level characteristics as a predictor variable, and subclinical psychotic phenomena as at least one outcome variable
- (ii) General population samples
- (iii) Child, adolescent or adult samples
- (iv) Cross-sectional survey or prospective cohort designs

2.1.3 Exclusion criteria

Papers were excluded for the following reasons:

- (v) Clinical / help-seeking / extreme samples
- (vi) Not general population
- (vii) Between-group comparison not possible
- (viii) Reviews, meta-analyses, conference abstracts
- (ix) Not available in English
- (x) No methods information provided on the predictor or outcome variables
- (xi) No data on the bivariate association between the urbanicity or neighbourhood characteristics and psychotic phenomena variables (e.g., neighbourhood variable treated as a confounder)

2.2 Results

2.2.1 Study selection and demographics

The database search yielded 3707 articles (Figure 2.1). After title and abstract screening, 3686 articles were excluded leaving 21 potentially relevant studies. After full text screening, two further articles were excluded based on the above exclusion criteria. The present literature review therefore includes 19 studies, and a summary of

each is provided in Table 2.1. Of these studies, 14 provided information on both the number of cases of individuals with subclinical psychotic phenomena (n) and the total sample size (N). One study (Solmi, Colman, Weeks, Lewis, & Kirkbride, 2017) provided information for two time-points, and therefore the later n/N information was extracted to calculate the prevalence of subclinical psychotic phenomena. Out of a total sample size of 59,395 individuals, there were 6,427 individuals with subclinical psychotic phenomena, yielding an overall prevalence of 10.8%. The age of participants ranged from 8 to 86 years. Five studies focussed on child and adolescent samples (≤ 18 years). Studies were all published since 2000, and originated from eight different countries.

2.2.2 Measurement of urbanicity or neighbourhood characteristics

Of the 19 studies, 14 studies investigated urbanicity as an exposure variable (Bartels-Velthuis, Jenner, van de Willige, van Os, & Wiersma, 2010; Kuepper et al., 2011a; Lundberg, Cantor-Graae, Rukundo, Ashaba, & Östergren, 2009; Mimarakis, Roumeliotaki, Roussos, Giakoumaki, & Bitsios, 2018; Polanczyk et al., 2010; Scott, Chant, Andrews, & McGrath, 2006; Shevlin et al., 2011; Singh, Winsper, Wolke, & Bryson, 2014; Spauwen et al., 2004, 2006b; Stefanis et al., 2004; van der Werf, van Winkel, van Boxtel, & van Os, 2010; van Os et al., 2001; van Os, Hanssen, de Graaf, & Vollebergh, 2002). Seven of these studies contrasted urban with rural/nonurban populations (e.g., a major city versus surrounding areas), six studies estimated urbanicity from population density, and one study estimated urbanicity from a resident survey. Of the 19 studies, five studies investigated neighbourhood characteristics as an exposure variable (Binbay et al., 2012; Das-Munshi et al., 2012; Saha, Scott, Varghese, & McGrath, 2013; Solmi et al., 2017; Wickham, Taylor, Shevlin, & Bentall, 2014). These five studies investigated a range of neighbourhood characteristics

including social control, social cohesion, social disorganization, neighbourhood discord, neighbourhood stress, unemployment rate, deprivation and ethnic density. Three studies derived neighbourhood measures from census data, one study derived neighbourhood measures from responses to questionnaires completed by the participants' mothers, and one study used a combination of census data and survey responses to construct the neighbourhood measures. The geographic resolution of neighbourhood characteristic measures varied between studies, ranging from low (e.g., an area encompassing 7200 inhabitants) to high (e.g., an area covering only the immediate neighbourhood surrounding each participant).

2.2.3 Assessment of subclinical psychotic phenomena

All 19 studies investigated positive psychotic phenomena (e.g., auditory/visual hallucinations, delusions, and/or other unusual thoughts and experiences), with only three studies additionally investigating schizotypal traits (e.g., odd or eccentric behaviour) or negative psychotic symptoms (e.g., anhedonia, apathy). Thirteen of the 19 studies measured psychotic phenomena via interviews with the participants, either during longitudinal follow-ups or cross-sectional surveys. The remaining six studies measured psychotic phenomena via self-report questionnaires. The most common instrument used to assess psychotic phenomena was the World Health Organization's Composite International Diagnostic Interview (CIDI) which was used by nine studies and includes approximately 10-20 items (depending on which version is used), though several studies used only a subset of items from this instrument. Three studies measured psychotic phenomena with only two or three items (Saha et al., 2013; Scott et al., 2006; Shevlin et al., 2011).

2.2.4 Association of urbanicity/neighbourhood characteristics with subclinical psychotic phenomena

Of the 14 studies that investigated urbanicity, ten found urbanicity to be significantly positively associated with subclinical psychotic phenomena. That is, psychotic phenomena were significantly more common among individuals who resided (Mimarakis et al., 2018; Polanczyk et al., 2010; Scott et al., 2006; Spauwen et al., 2004, 2006b; Stefanis et al., 2004; van Os et al., 2001; van Os et al., 2002) or had been born (Lundberg et al., 2009; Singh et al., 2014) in urban versus rural settings, with odds ratios ranging between 1.12 and 2.51. Three studies did not find a significant association between urbanicity and psychotic phenomena (Kuepper et al., 2011a; Shevlin et al., 2011; van der Werf et al., 2010). However, two of these studies found that urban residency increased the association of other exposures including cannabis use (Kuepper et al., 2011a) and hearing impairment (van der Werf et al., 2010) with psychotic phenomena. In addition, one study found auditory hallucinations to be significantly more common among children in *rural* versus urban environments (Bartels-Velthuis et al., 2010). However, this study also showed that the intensity, persistence and interference associated with voice hearing was worse for children living in urban settings.

All five studies that investigated neighbourhood characteristics found significant positive associations between various neighbourhood-level features and psychotic phenomena. Specifically, psychotic phenomena were significantly more common among individuals living in deprived neighbourhoods (Binbay et al., 2012; Saha et al., 2013; Wickham et al., 2014), as well as neighbourhoods with high levels of unemployment (Binbay et al., 2012), ethnic fragmentation (Das-Munshi et al., 2012), and stress and discord (Solmi et al., 2017).

Therefore, out of 19 studies examining the association between wider social environmental factors and psychotic phenomena, 15 found significant positive associations (Binbay et al., 2012; Das-Munshi et al., 2012; Lundberg et al., 2009; Mimarakis et al., 2018; Polanczyk et al., 2010; Saha et al., 2013; Scott et al., 2006; Singh et al., 2014; Solmi et al., 2017; Spauwen et al., 2004, 2006b; Stefanis et al., 2004; van Os et al., 2001; van Os et al., 2002; Wickham et al., 2014). Furthermore, all but one (Polanczyk et al., 2010) of these 15 studies controlled for various potential individual-level confounders that might otherwise explain the association, including age, sex, verbal/spatial memory, ethnicity, marital status, SES, family psychiatric history, unemployment, education, alcohol/drug dependence, migrant status, residential/school mobility, bullying, peer difficulties, parental age, depression, and stressful life events.

2.2.5 Findings by study design and by participant age

Of the 19 studies, 13 had cross-sectional designs and six had prospective designs. Associations did not appear to vary by study design. For example, ten out of 13 (76.9%) cross-sectional studies versus five out of six (83.3%) prospective studies reported statistically significant associations between wider social environmental factors and subclinical psychotic phenomena. In addition, only three out of the 19 studies utilised higher resolution methods to derive neighbourhood measures (e.g., resident surveys, participant interviews), with the remaining 16 studies deriving urbanicity and neighbourhood characteristic measures from lower resolution data (e.g., census and administrative data). All of the three (100%) higher resolution studies reported significant associations between wider social environmental factors and subclinical psychotic phenomena. In contrast, twelve out of the 16 (75%) census/administrative-data studies reported significant associations between wider

social environmental factors and subclinical psychotic phenomena. Thus, there was tentative evidence that studies using higher resolution measures were more able to capture associations with subclinical psychotic phenomena, with the obvious limitation that there were only three studies that used higher resolution measures.

Of the 19 studies, 14 focussed on adult samples (or all ages) and five focussed on child and adolescent samples (≤ 18 years). Again, associations did not appear to vary by participant age. For example, eleven out of 14 (78.6%) studies that focussed on adult (or all age) participants reported significant associations between wider social environmental factors and subclinical psychotic phenomena. Similarly, four out of five (80%) studies that focussed on child and adolescent samples reported significant associations between wider social environmental factors and subclinical psychotic phenomena. Furthermore, the effect sizes of associations between wider social environmental factors and subclinical psychotic phenomena did not appear to vary by study design or participant age (i.e., the range of effect sizes was spread between different study designs and participant ages). Thus, for the studies included in this literature review, findings do not appear to vary by study design or participant age. Nevertheless, there is a dearth of studies that have used a prospective design, high-resolution neighbourhood measures, and young samples, and such methods are likely to provide insights into the developmental timing and nature of the association between the wider social environment and subclinical psychotic phenomena.

Figure 2.1. Flowchart of selection process for articles included in this review

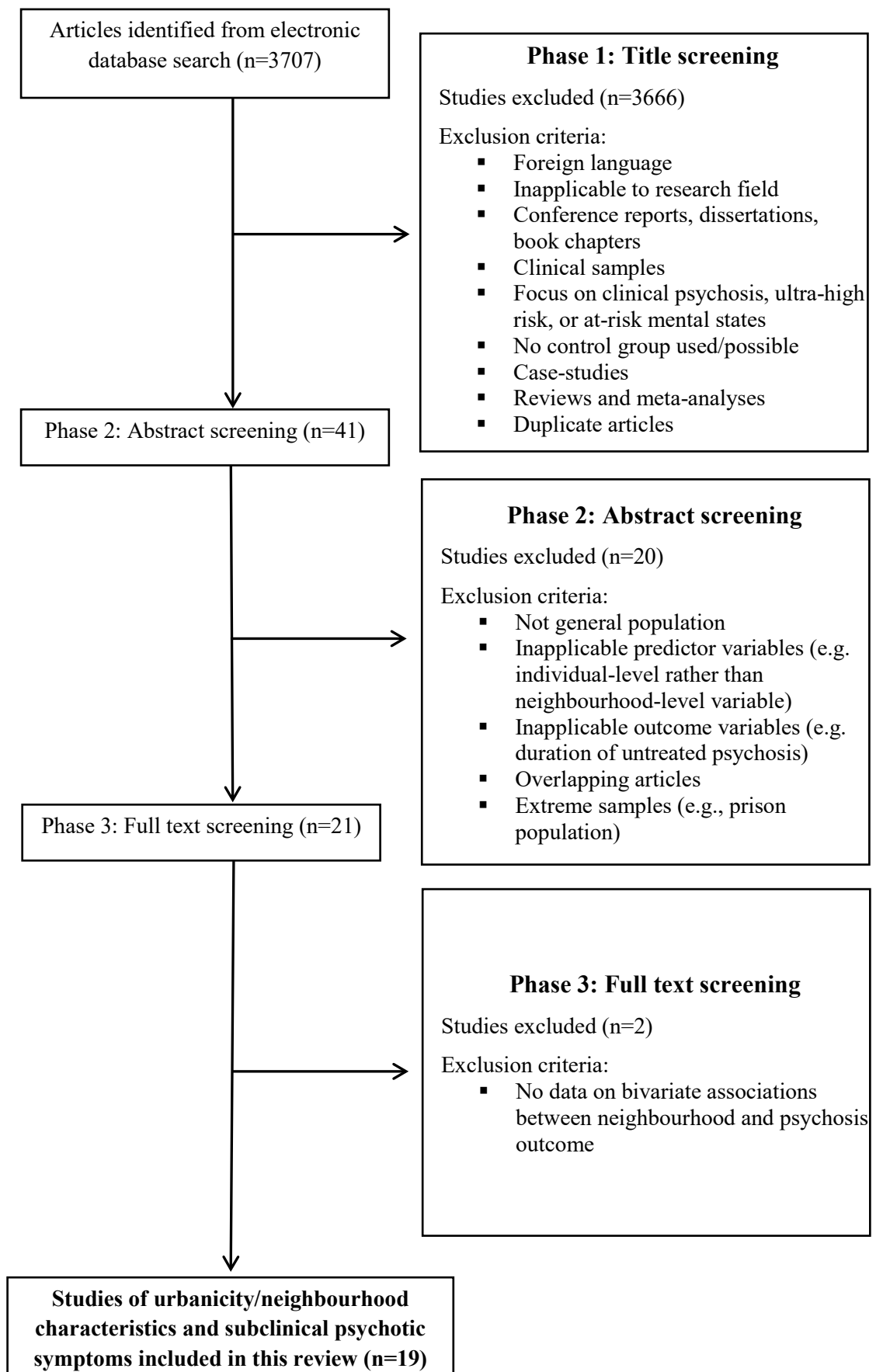


Table 2.1. Studies investigating the association between urbanicity/neighbourhood characteristics and subclinical psychotic phenomena

Study (Year) (country)	Study Design	Sample (n/N) (age)	Urbanicity/neighbourhood measure		Psychotic phenomena measure	Main Findings
			(U/N)	Method		
<i>Bartels-Velthuis et al. (2010)</i> (The Netherlands)	Cross-sectional population-based survey	Case/sample (347/3870) (7-8 years)	U	Urban vs. rural (two-level) derived from density of letter boxes per square kilometre.	Auditory vocal hallucinations were measured using the 11-item Auditory Vocal Hallucinations Rating Scale (AVHRS; Jenner and Van de Willige (2002)).	Auditory vocal hallucinations were significantly more common among children living in the rural (vs. urban) setting (OR=3.74, 95% CI=2.39-5.87). However, children living in urban (vs. rural settings) were significantly more likely to report two or more voices ($\chi^2=8.77$, $p=0.01$), hear simultaneous voices ($\chi^2=12.21$, $p=0.002$), hear more prolonged voices ($\chi^2=9.61$, $p=0.008$), experience more thought interference ($\chi^2=13.01$, $p=0.001$), and attribute voices to an external source ($\chi^2=12.14$, $p=0.002$).

Study (Year) (country)	Study Design	Sample (n/N) (age)	Urbanicity/neighbourhood measure		Psychotic phenomena measure	Main Findings
			(U/N)	Method		
<i>Binbay et al. (2012)</i> (Turkey)	Cross-sectional population-based interview	Case/sample (1031/4011) (15-64 years)	N	Informal social control and social disorganization were derived from resident surveys. Unemployment and poverty rate were both derived from census data.	Psychotic symptoms were measured using the 14-item Composite International Diagnostic Interview (CIDI; Robins et al. (1988)).	After controlling for gender, age, marital status, ethnicity, socioeconomic status (SES), individual-level unemployment and family psychiatric history, neighbourhood unemployment ($B=0.07$, 95% CI=0.03-0.10, $p<0.001$) and neighbourhood poverty rate ($B=0.06$, 95% CI=0.03-0.10, $p<0.001$) were significantly associated with psychotic symptoms. Social disorganization was negatively associated with psychotic symptoms ($B=-0.04$, 95% CI=-0.07—0.01, $p=0.019$).

Study (Year) (country)	Study Design	Sample (n/N) (age)	Urbanicity/neighbourhood measure		Psychotic phenomena measure	Main Findings
			(U/N)	Method		
<i>Das-Munshi et al.</i> (2012) (United Kingdom)	Cross-sectional representative population-based survey	Case/sample (351/4281) (16-74 years)	N	Ethnic density was derived from the percentage of minority ethnic people living within each middle super output-area (an administrative area containing an average of 7200 people).	Positive psychotic symptoms were measured using the Psychosis Screening Questionnaire (PSQ; Bebbington and Nayani (1995)), which covers mania/hypomania, thought control, paranoia, strange experiences, and auditory verbal hallucinations.	After adjusting for area-level deprivation, social class, education, marital status, age and gender, ethnic density was found to be significantly associated with psychotic experiences. For the whole sample, for every 10% reduction in own-group ethnic density, odds for psychotic experiences increased: OR=1.07, 95% CI=1.01-1.14, 0=0.03). This significant effect was strongest for the Indian ethnic group: OR=1.38, 95% CI=1.02-1.86, p=0.03.

Study (Year) (country)	Study Design	Sample (n/N) (age)	Urbanicity/neighbourhood measure		Psychotic phenomena measure	Main Findings
			(U/N)	Method		
<i>Kuepper et al.</i> (2011) (Germany)	Prospective longitudinal representative cohort	Case/sample (231/1923) (22-32 years at follow-up)	U	Urban vs. rural (two-level) residence defined as Munich (1562 persons per square kilometre) vs. surrounding areas (213 persons per square kilometre).	Positive psychotic symptoms were measured with 20- items from the Munich-Composite International Diagnostic Interview (DIA-X/M-CIDI; Wittchen, Lachner, Wunderlich, and Pfister (1998)).	After adjusting for age, sex, SES, baseline cannabis use, childhood trauma and other drug use, urbanicity was not significantly associated with psychotic symptoms (OR=1.16, 95% CI=0.77- 1.76, p=0.497). However, the association between cannabis use and psychotic symptoms was significantly stronger among individuals living in the urban setting (adjusted risk difference=6.8%, 95% CI=1.0-12.5, p=0.021), suggesting an interaction between these two exposures.

Study (Year) (country)	Study Design	Sample (n/N) (age)	Urbanicity/neighbourhood measure		Psychotic phenomena measure	Main Findings
			(U/N)	Method		
<i>Lundberg et al.</i> (2009) (Uganda)	Cross- sectional general population probability sample	Sample (646) (18-30 years)	U	Three-level urbanicity based on residential location in a particular city (only city in Uganda), particular town, and a collection of villages from same district. Both place of birth and place of current residence were investigated.	Delusional experiences measured with Peters et al. Delusions Inventory (PDI-21; Peters et al., 1999) which includes 21 items across 11 domains. Other positive psychotic symptoms (e.g., hallucinations) measured with the Symptoms Checklist 90-item version (SCL- 90; Derogatis, Lipman, and Covi (1973)).	Psychotic symptoms were significantly more common among individuals with urban compared to rural birth (OR=2.1, 95% CI=1.2-3.7) after adjusting for age, gender, and education. This association was not shown for semi-urban (town) place of birth (OR=1.2, 95% CI=0.8- 1.9).

Study (Year) (country)	Study Design	Sample (n/N) (age)	Urbanicity/neighbourhood measure		Psychotic phenomena measure	Main Findings
			(U/N)	Method		
<i>Mimarakis et al.</i> (2018) (Greece)	Cross- sectional population- based survey	Sample (445) (17-22 years)	U	Four-level urbanicity based on population density, ranging from <5000 persons per square kilometre to >50,000 persons per square kilometre.	Schizotypal traits measured using the 37-item Schizotypal Traits Questionnaire (Cyhlarova et al., 2005). Items cover magical thinking, paranoid ideation, and unusual experiences.	After considering confounders including season of birth, immigrant status, family SES, family psychiatric history, health behaviours, and co-occurring psychiatric problems, magical thinking was significantly predicted by living in the higher versus baseline urbanicity categories, but only among women (e.g., 10001-50,000 person/km ² : B=1.67, 95% CI=0.01-3.32, p=0.049).

Study (Year) (country)	Study Design	Sample (n/N) (age)	Urbanicity/neighbourhood measure		Psychotic phenomena measure	Main Findings
			(U/N)	Method		
<i>Polanczyk et al.</i> (2010) (United Kingdom)	Prospective longitudinal representative cohort	Case/sample (125/2127) (12 years at follow-up)	U	Urban vs. nonurban (two-level) urbanicity derived from responses to a community-level survey of neighbours living alongside participants.	Positive psychotic symptoms were ascertained via private interviews with research workers, and responses were verified by mental health professionals. The seven items pertained to delusions and hallucinations. Items were guided by the ALSPAC and Dunedin longitudinal cohorts.	Children with urban residency at age 12 had significantly greater odds of reporting psychotic symptoms (OR=1.8, 95% CI=1.2-2.7) compared to children with non-urban residency.

Study (Year) (country)	Study Design	Sample (n/N) (age)	Urbanicity/neighbourhood measure		Psychotic phenomena measure	Main Findings
			(U/N)	Method		
<i>Saha et al. (2013)</i> (Australia)	Cross-sectional population-based probability-sample survey	Case/sample (776/8773) (16-85 years)	N	Area-level socioeconomic disadvantage was derived from of census data information on income, education, employment status, and accommodation status. The variable resolution applied to approximately 225 households.	Delusional-like experiences were measured using 3 items from the Composite International Diagnostic Interview version 1.1 (CIDI; Robins et al. (1988); Smeets and Dingemans (1993)).	Compared to individuals living in the least socioeconomically deprived neighbourhoods, individuals living in more deprived neighbourhoods had elevated odds for delusional-like experiences. Even after considering age, sex, alcohol abuse/dependence, other drug use/dependence, anxiety/depressive disorders, marital status, migrant status, and individual-level deprivation, individuals living in neighbourhoods with high levels of deprivation were more likely to have delusions (OR=1.58, 95% CI=1.06-2.35, p<0.001).

Study (Year) (country)	Study Design	Sample (n/N) (age)	Urbanicity/neighbourhood measure		Psychotic phenomena measure	Main Findings
			(U/N)	Method		
<i>Scott et al. (2006)</i> (Australia)	Cross-sectional population-based probability-sample survey	Case/sample (1245/ 10641) (18-65 years)	U	Urban vs. rural (two-level) urbanicity defined as living in a city/metropolitan area vs. rural or nonurban area.	Delusional-like experiences were measured using 3 items from the Composite International Diagnostic Interview version 1.1 (CIDI; Robins et al. (1988); Smeets and Dingemans (1993)).	After adjusting for age and sex, individuals living in rural/nonurban (vs. urban) settings were significantly less likely to have delusional-like experiences (OR=0.89, 95% CI=0.79- 0.99, p<0.05).
<i>Shevlin et al. (2011)</i> (United States of America)	Cross-sectional population-based survey	Case/sample (247/2353) (M=44.35 years, SD=17.27)	U	Urban vs. nonurban (two-level) urbanicity defined as living in a metropolitan area vs. nonurban area.	Hallucinations measured with 2 items from the Composite International Diagnostic Interview version 3.0 (CIDI; Kessler and Üstün (2004)).	Urban residency was not significantly associated with visual (OR=0.75, 95% CI=0.45-1.24) or auditory hallucinations (OR=1.01, 95% CI=0.54-1.90).

Study (Year) (country)	Study Design	Sample (n/N) (age)	Urbanicity/neighbourhood measure		Psychotic phenomena measure	Main Findings
			(U/N)	Method		
<i>Singh et al. (2014)</i> (United Kingdom)	Prospective longitudinal cohort	Case/sample (Age 13: 883/6448)	U	Urban vs. rural (two-level) urbanicity defined at birth as living in an urban area/town vs. living in a village/hamlet.	Probable/definite positive psychotic symptoms were measured at age 13 using the 12-item Psychotic-Like Symptoms Interview (PLIKSI), a semi- structured interview.	After adjusting for family adversity, ethnicity, residential mobility, school mobility, peer difficulties, bullying involvement, and negative friendships, children with urban birth were significantly more likely to have psychotic experiences (OR=2.31, 95% CI=1.45-3.67, p<0.05).

Study (Year) (country)	Study Design	Sample (n/N) (age)	Urbanicity/neighbourhood measure		Psychotic phenomena measure	Main Findings
			(U/N)	Method		
<i>Solmi et al. (2017)</i> (United Kingdom)	Prospective longitudinal cohort	Case/sample (Age 13: 736/6455) (Age 18: 342/4426)	N	Neighbourhood measures were derived from questionnaire responses from the participants' mothers. Social cohesion estimated trust, amicability and support between neighbours. Neighbourhood discord estimated arguments etc. between neighbours. Neighbourhood stress estimated problems and crime in the neighbourhood.	Positive psychotic symptoms were measured at ages 13 and 18 using the 12- item Psychotic-Like Symptoms Interview (PLIKSI), a semi- structured interview.	After considering parental age, maternal education, marital status, social class, depression, residential mobility, flu during pregnancy, child's ethnicity, gender, stressful life events, and area deprivation, high (versus low) neighbourhood stress was significantly associated with psychotic symptoms at age 13 (OR=1.77, 95% CI=1.30-2.41, p≤0.05), and high (versus low) neighbourhood discord was significantly associated with psychotic symptoms at age 18 (OR=1.50, 95% CI=1.10-2.07, p≤0.05). Low social cohesion and high neighbourhood stress were also significantly associated with depression at age 18.

Study (Year) (country)	Study Design	Sample (n/N) (age)	Urbanicity/neighbourhood measure		Psychotic phenomena measure	Main Findings
			(U/N)	Method		
<i>Spauwen et al.</i> (2004) (Germany)	Prospective longitudinal representative sample	Case/cohort (441/ 2548) (17-28 years at follow-up)	U	Urban vs. rural (two-level) urbanicity defined as central Munich (4061 persons per square kilometre) versus surrounding areas (553 persons per square kilometre).	Subclinical psychotic experiences were measured using the Munich-Composite International Diagnostic Interview (M-CIDI; Wittchen et al. (1998)), which includes 11 delusional items and 4 hallucinatory items.	The prevalence of psychotic experiences was higher in the urban (18.5%) compared to the rural (14.6%) setting, yielding a significant association between urbanicity and psychotic symptoms after adjusting for gender, SES, drug use, family history of psychosis, and any psychiatric diagnosis in adolescence (OR=1.31 (95% CI=1.03- 1.66).

Study (Year) (country)	Study Design	Sample (n/N) (age)	Urbanicity/neighbourhood measure		Psychotic phenomena measure	Main Findings
			(U/N)	Method		
<i>Spauwen et al.</i> (2006) (Germany)	Prospective longitudinal representative sample	Case/sample (143/918) (14-17 years)	U	Urban vs. rural (two-level) urbanicity defined as central Munich (4061 persons per square kilometre) versus surrounding areas (553 persons per square kilometre).	Baseline psychotic symptoms were measured using the self-report Symptom Checklist-90-R (SCL- 90; Derogatis et al. (1973)), which includes items on psychoticism (10 items) and paranoia (6 items). Follow-up subclinical psychotic symptoms were measured using the Munich-Composite International Diagnostic Interview (M-CIDI; Wittchen, 1998), which includes 11 delusional items and 4 hallucinatory items.	For low psychotic symptoms score at baseline, urban residency was not associated with psychotic symptoms at follow-up (OR=0.83, 95% CI=0.52- 1.33). For high psychotic symptoms score at baseline rural residence was neutral (OR=1.05, 95% CI=0.50-2.23) whereas urban residence was a risk for psychotic symptoms at one-year follow- up (OR=2.46, 95% CI=1.46-4.14). Analyses were adjusted for gender, SES, drug use, family history of psychosis. These results suggest that the outcome for young people with early expressions of psychosis is worse in urban environments.

Study (Year) (country)	Study Design	Sample (n/N) (age)	Urbanicity/neighbourhood measure		Psychotic phenomena measure	Main Findings
			(U/N)	Method		
<i>Stefanis et al. (2004)</i> (Greece)	Cross-sectional representative sample of male conscripts	Sample (943) (18-24 years)	U	Urban vs. rural (two-level) urbanicity derived from population density.	Schizotypal traits were measured with the 74- item self-report questionnaire, the Schizotypal Personality Questionnaire (SPQ; Raine (1991)), which measures ideas of reference, social anxiety, odd beliefs/magical thinking, unusual experiences, odd behaviour/speech, and suspiciousness.	After adjusting for co-occurring symptoms, age, education, IQ, spatial and verbal memory, and attention, individuals with urban (vs. rural) residency were significantly more likely to have odd beliefs/magical thinking (OR=2.31, 95% CI=1.53-3.50, p<0.001). In contrast, individuals with urban residency were significantly less likely to have excessive social anxiety (OR=0.64, 95% CI=0.48-0.85, p=0.002) and no close friends (OR=0.60, 95% CI=0.40-0.90, p=0.014).

Study (Year) (country)	Study Design	Sample (n/N) (age)	Urbanicity/neighbourhood measure		Psychotic phenomena measure	Main Findings
			(U/N)	Method		
<i>van der Werf et al.</i> (2010) (The Netherlands)	Representative population- based survey	Sample (1823) (24-86 years)	U	Five-level urbanicity based on population density, ranging from <500 addresses per square kilometre to 2500+ addresses per square kilometre.	Baseline psychotic symptoms were measured using the self-report Symptom Checklist-90-R (SCL- 90; Derogatis et al. (1973)), which includes items on psychoticism (10 items) and paranoia (6 items).	Urbanicity was not significantly associated with psychotic symptoms (B=0.05, 95% CI=-0.21-0.31, p=0.72). However, the association between hearing impairment and psychotic symptoms was only present among individuals living in the most urban setting (B=2.56, 95% CI=0.47-4.65, p=0.016), suggesting that the effect of hearing impairment on psychotic symptoms was conditional on the complexity of the social environment.

Study (Year) (country)	Study Design	Sample (n/N) (age)	Urbanicity/neighbourhood measure		Psychotic phenomena measure	Main Findings
			(U/N)	Method		
<i>van Os et al. (2001)</i> (The Netherlands)	Cross-sectional analysis on prospective random sample	Case/sample (295/7076) (18-64 years)	U	Five-level urbanicity of place of residence based on population density, ranging from <500 to >2500 addresses per square kilometre.	Psychotic symptoms were measured using the 17-item Composite International Diagnostic Interview version 1.1 (CIDI; Robins et al. (1988); Smeets and Dingemans (1993)). Items pertained to delusions and hallucinations. Positive responses indicated clinical significance were followed up via telephone by a trainee psychiatrist.	Psychotic symptom prevalence increased linearly with increased level of urbanicity. For narrowly defined psychotic symptoms, individuals living in the highest (versus lowest) level of urbanicity had a significantly elevated odds of reporting psychotic symptoms (OR=2.51, 95% CI=1.61-3.91) compared to people at the bottom-level urbanicity. Odds for psychotic symptoms increased in a dose-response pattern with increasing level of urbanicity. Results were adjusted for age, sex, education, and country of birth.

Study (Year) (country)	Study Design	Sample (n/N) (age)	Urbanicity/neighbourhood measure		Psychotic phenomena measure	Main Findings
			(U/N)	Method		
<i>van Os et al. (2002)</i> (The Netherlands)	Cross-sectional analysis on prospective random sample	Sample (7076) (18-64 years)	U	Five-level urbanicity of place of residence based on population density, ranging from <500 to >2500 address per square kilometre.	Negative and positive psychotic symptoms were measured using the 17-item Composite International Diagnostic Interview version 1.1 (CIDI; Robins et al. (1988); Smeets and Dingemans (1993)). Items pertained to delusions and hallucinations. Positive responses were followed up via telephone by a trainee psychiatrist.	After adjusting for age, sex, ethnic group, marital status, unemployment, education, and the corresponding symptom dimension (positive/negative), urbanicity was significantly associated with both negative psychotic symptoms (linear trend OR=1.32, 95% CI=1.03-1.68, p<0.05) and positive psychotic symptoms (linear trend OR=1.13, 95% CI=1.06-1.19, p<0.05).

Study (Year) (country)	Study Design	Sample (n/N) (age)	Urbanicity/neighbourhood measure		Psychotic phenomena measure	Main Findings
			(U/N)	Method		
<i>Wickham et al.</i> (2014) (United Kingdom)	Cross-sectional population-based probability-sample survey	Sample (7353) (16 years and above)	N	Neighbourhood deprivation was estimated using the index of multiple deprivation (IMD) which utilises census data. The IMD covers several aspects of deprivation including income, employment, health, education, skills, housing, living environment, and crime.	Positive psychotic symptoms were measured using the Psychosis Screening Questionnaire (PSQ; Bebbington and Nayani (1995)), which covers mania/hypomania, thought control, paranoia, strange experiences, and auditory verbal hallucinations.	After adjusting for age, sex, ethnicity, education, and drug use, neighbourhood deprivation was significantly associated with probable psychosis (OR=1.5, 95% CI=1.1-1.9, p<0.001) and paranoia (OR=1.2, 95% CI=1.1-1.5, p<0.001), as well as definite psychosis (OR=1.8, 95% CI=1.2-2.6, p<0.01) and depression (OR=1.2, 95% CI=1.2, 95% CI=1.1-1.4, p<0.001).

Note: B, beta coefficient; *B*, standardised beta coefficient; CI, confidence interval; N, neighbourhood; OR, odds ratio; U, urbanicity; χ^2 , chi-square

2.3 Discussion

The aim of this systematic review was to collate the main methods and results from studies that have investigated the association of urbanicity or neighbourhood characteristics with subclinical psychotic phenomena in the general population. Nineteen relevant studies were identified. Most studies investigated urbanicity, with only five studies investigating neighbourhood characteristics. The methods used to estimate urbanicity and neighbourhood characteristics varied between studies, with most studies utilising census data linked to broad geostatistical units, and only two studies utilising higher resolution data (e.g., survey data linked to postcodes). The instruments used to measure subclinical psychotic phenomena were generally thorough. Of the 19 studies, 13 had cross-sectional designs and six had prospective designs. In addition, only three out of 19 studies utilised higher resolution data to estimate neighbourhood conditions (e.g., resident surveys). Five studies focussed on child and adolescent samples. The overall prevalence of psychotic phenomena from available data was 10.8%, which is in keeping with meta-analytic estimates for adults (van Os et al., 2009) and children and adolescents (Kelleher et al., 2012a) in the general population. Urban residents were consistently found to have elevated odds for psychotic phenomena, with significant odds ratios ranging between 1.12 and 2.51. In addition, individuals living in adverse neighbourhood conditions characterised by deprivation, fragmentation, stress and problems were consistently found to have an elevated risk for psychotic phenomena. This is again consistent with research implicating adverse neighbourhood conditions in adult psychotic disorders and the occurrence of ultra-high risk for psychosis (Allardyce et al., 2005; Bhavsar et al., 2014; Boydell et al., 2004; Kirkbride et al., 2015; Kirkbride et al., 2008; Kirkbride et al., 2014; Kirkbride et al., 2007; O'Donoghue et al., 2015; Omer et al., 2014). However, four studies reported

negative or reversed associations between urbanicity and psychotic phenomena. It is nevertheless interesting that in two of these studies, the associations between other exposures and psychotic phenomena were significantly stronger in urban settings, suggesting that the urban environment might modify the effect of other putative risk factors for psychotic phenomena. In addition, most studies adjusted for a range of potential individual-level confounders, suggesting that the documented associations between urbanicity/neighbourhood characteristics and subclinical psychotic phenomena in the general population were not due solely to the composition of individuals living in urban or adverse neighbourhood settings.

2.3.1 Gaps in the existing literature

This review revealed some methodological weaknesses and gaps in the existing literature. First, evidence on the role of urbanicity and neighbourhood conditions in early psychotic phenomena remains scarce. Only five studies focussed on child and adolescent samples, and only two of these incorporated higher resolution data to construct the urbanicity/neighbourhood variables. As outlined in Chapter 1 there is a pressing need to understand the aetiology of early psychotic symptoms to design and target preventative interventions. A related issue is that cross-sectional investigations of neighbourhood environments and the prevalence of psychotic phenomena during adulthood do not rule out the possibility that adults move to urban or adverse neighbourhoods after or because of the onset of psychotic symptoms. Therefore, studies are required that can ascertain the temporal order of exposure and emergence of psychotic phenomena and this is likely to be easiest in prospective studies of children and adolescents. Second, cities are complex and heterogeneous environments containing numerous potential exposures (Heinz et al., 2013; Krabbendam & Van Os, 2005; March et al., 2008). Investigations of specific neighbourhood characteristics are

likely to be more informative, as they could help to dissect urbanicity into its risk subcomponents. Furthermore, identifying specific features of the urban environment which are associated with psychosis could help to design and target early intervention strategies. However, there are only a handful of studies on the role of neighbourhood conditions in subclinical psychotic phenomena, and there is currently no research on whether neighbourhood-level social processes mediate the effect of urbanicity on psychotic phenomena, as suggested by sociological theory (described in Chapter 1). Additionally, very few studies have investigated the potential interactive relationship between urban/adverse neighbourhood environments and other putative risk factors for psychotic phenomena, such as victimisation. Violent crime victimisation is a common exposure among youth in cities (Home Office Statistical Bulletin, 2010). Combined exposure to adverse neighbourhood conditions and violence could therefore be associated with a cumulative increase in risk for psychotic symptoms. Lastly, the resolution of studies to date has generally been low. Most investigations of urbanicity have used dichotomous urban-rural variables derived from administrative data, and most investigations of neighbourhood conditions have relied on census data applied to broad geostatistical areas. These designs do not indicate the extent that study subjects were truly exposed to the neighbourhood conditions examined. Higher resolution measurement, ideally at the address level, will provide a more accurate estimate of exposure. Moreover, there is currently no research on the potential role of individuals' own personal evaluations and perceptions of neighbourhood conditions in psychotic phenomena. This is likely to be important because delusions and hallucinations involve altered perceptions of reality, which are potentially developed due to hostile attributions of others' intentions and other biases (Garety et al., 2001). Thus, we might expect personal perceptions of the neighbourhood (e.g., "*my neighbourhood is dangerous*") to play a crucial role in the development of psychotic experiences.

2.3.2 Methodological considerations

This review entailed some limitations. Only studies written in English were included, which may have excluded some relevant research. Furthermore, the scope of this review meant that only studies investigating subclinical psychotic phenomena in the general population were included. Emerging evidence implicates urbanicity in biological and behavioural traits linked to psychosis, such as reduced cortical thickness of the parahippocampal region and heightened neurocognitive reactivity to social stress (Besteher et al., 2017; Haddad et al., 2015; Lederbogen et al., 2011). Thus, this review excluded some emerging evidence of potential mechanisms linking neighbourhood conditions with psychotic phenomena. In addition, this review included only published articles. As such, article selection could have been influenced by publication bias, whereby negative findings are less likely to be accepted for publication in academic journals and books, leading to an over-reporting and over-estimation of positive findings. To address this, I could have conducted searches of the “grey literature”, such as unpublished research findings using OpenGrey, research theses using WorldCat, and government, academic and business documents using the Health Management Information Consortium database. In addition, I could have used a funnel plot, which plots study precision against effect size to examine publication bias. These additional methods would be crucial steps for a systematic review and meta-analysis, but are beyond the scope of the present literature review.

2.3.3 Conclusions

A growing body of evidence suggests that subclinical psychotic phenomena are more common among individuals residing in urban settings. A handful of studies suggest that these symptoms are also more common among people living in deprived, fragmented,

and stressful neighbourhood conditions. However, the nature of this association remains equivocal.

Several lines of research are now necessary to shed light on the mechanisms linking the wider social environment to subclinical psychotic phenomena. Focussing on child and adolescent samples could provide insights into the developmental timing of the association of urbanicity and neighbourhood conditions with psychotic phenomena, and potentially inform preventative intervention strategies which are needed to reduce the persistence and progression of psychotic symptoms in young people. Since children and adolescents have minimal choice in where they live, a focus on early psychotic phenomena and neighbourhood conditions in early-life also pre-empts the possibility of individuals moving into certain environments *because* of their symptoms. Furthermore, higher resolution neighbourhood measures (ideally at the address-level), combining objective census data, independent reports by residents, and subjective appraisals by participants themselves will ensure that the individuals under study are truly embedded in – and perceive – the environmental milieu represented by their neighbourhood scores. Additionally, a multilevel approach – spanning the wider social environment, family-level factors, and individual-level influences such as crime victimisation and genetic influences – is needed to examine the interplay between neighbourhood-level exposures and other potential risk factors as well as account for potential confounding factors that might otherwise explain the association of urbanicity and neighbourhood characteristics with psychotic phenomena. This thesis aims to address these gaps in this area of research. The specific aims and hypotheses of this thesis are outlined below.

2.4 Aims and hypotheses

The aim of the research presented in this thesis is to investigate the role of urbanicity in early psychotic phenomena during childhood and adolescence, exploring both

neighbourhood- and individual-level exposures and mechanisms. The specific aims are:

1. To examine whether children who grow up in urban neighbourhoods are more likely to have psychotic symptoms, and if so, whether adverse neighbourhood social characteristics might explain the association (Chapter 4).
2. To investigate whether there is an accumulation of risk for psychotic phenomena among adolescents who are raised in urban and adverse neighbourhood conditions, and are subsequently victimised by a violent crime (Chapter 5).
3. Using longitudinal and genetically informed methods, to explore the role of young people's personal perceptions of adverse neighbourhood conditions in the development of adolescent psychotic phenomena (Chapter 6).

Based on these aims, it is hypothesised that:

- 1.1 Psychotic symptoms will be more common among children raised in urban (versus nonurban) settings.
- 1.2 This association will demonstrate a degree of specificity to childhood psychotic symptoms (i.e., associations will be weaker or absent for other childhood mental health outcomes).
- 1.3 Adverse neighbourhood social conditions, such as higher levels of disorder and lower levels of cohesion between neighbours, will partly explain the association between urban upbringing and childhood psychotic symptoms.
- 2.1 Psychotic experiences will be more common among adolescents raised in urban settings. That is, the association between urbanicity and psychotic experiences will continue into adolescence.
- 2.2 This association will again be partly explained by adverse neighbourhood social characteristics.

- 2.3 The cumulative effects of neighbourhood social adversity and personal victimisation by violent crime on adolescent psychotic experiences will be significantly greater than the individual exposures alone, such that adolescents with combined exposure to both will have the greatest risk for psychotic phenomena.
- 2.4 Main findings (hypotheses 2.1-2.3) will replicate for clinically-verified adolescent psychotic symptoms.
- 3.1 Adolescents living in urban (versus rural/intermediate) settings will themselves perceive higher levels of disorder (i.e., physical and social signs of threat) in their neighbourhoods.
- 3.2 Adolescents who perceive higher levels of neighbourhood disorder will be significantly more likely to report psychotic phenomena, even when controlling for independent measures of neighbourhood disorder.
- 3.3 The association between adolescents' perceptions of neighbourhood disorder and psychotic phenomena will not be explained by a range of potential neighbourhood-, family-, and individual-level confounding factors.
- 3.4 A bidirectional relationship will be found in longitudinal models, such that perceptions of danger in the neighbourhood in childhood will predict psychotic phenomena in adolescence; and childhood psychotic symptoms will predict perceptions of neighbourhood disorder in adolescence.
- 3.5 The phenotypic overlap between perceptions of neighbourhood disorder and adolescent psychotic phenomena will be partly explained by overlapping genetic influences shared between these traits.

2.5 Distinct and original contribution to the field

The research presented in this thesis addresses several gaps in the literature. First, analyses will focus solely on child and adolescent psychotic phenomena. Second, analyses use data from a prospective longitudinal cohort of children, which will both enable temporal sequencing of exposure and outcome, and allow adjustment for a range of potential individual- and family-level factors which have been measured throughout the study. Third, analyses will move beyond urbanicity, utilising a range of neighbourhood characteristics spanning both structural features (e.g., deprivation) and social processes (e.g., social cohesion and crime). In addition, the neighbourhood measures used in this thesis achieve a high level of geographic resolution for this field: neighbourhood characteristics are accurate to the postcode- or street-level, meaning that participants were truly embedded in the neighbourhood milieu represented by the measures. Furthermore, the analytic framework in this thesis is informed by sociological theory, wherein social processes (e.g., neighbourhood levels of social cohesion and crime) are suggested to mediate the effects of structural features (e.g., urbanicity) on health outcomes (Sampson, 2001; Sampson et al., 2002). This provides a framework to explore the pathways by which the macro-level exposure “urbanicity” might transmit effects on early psychotic phenomena. Fourth, the research in this thesis will be the first to investigate the role of personal perceptions of neighbourhood adversity in the aetiology of early psychotic phenomena. The effects of urban and adverse neighbourhood conditions have been suggested to increase psychotic phenotypes via a social stress pathway (described in Chapter 1), meaning that personal attitudes and appraisals of neighbourhood conditions could play a crucial role in the association. However, this has not yet been tested. Indeed, few datasets other than E-Risk have the necessary design (e.g., repeated measures, large sample size, objective neighbourhood measures) to examine the role neighbourhood perceptions while considering potential

confounding factors and mechanisms. Fifth, the research in this thesis is based on a twin sample. Analyses will be the first to use genetically informed methods to examine the potential overlapping genetic and environmental contributions between perceptions of neighbourhood conditions and early psychotic phenomena. This will highlight whether genetic influences on psychotic phenomena also contribute to perceptions of neighbourhood adversity.

Chapter 3: Methodology

3.1 Environmental Risk (E-Risk) Longitudinal Twin Study

Participants are members of the Environmental Risk (E-Risk) Longitudinal Twin Study, which investigates how genetic and environmental factors shape children's development. The sampling frame from which the E-Risk families were drawn was two consecutive birth cohorts (1994 and 1995) in a birth register of twins born in England and Wales (Trouton, Spinath, & Plomin, 2002). Of the 15,906 twin pairs born in these two years, 71% joined the register.

The E-Risk Study probability sample was drawn using a high-risk stratification strategy. High-risk families were those in which the mother had her first birth when she was 20 years of age or younger. This sampling frame was used (1) to replace high risk families who were selectively lost to the register via non-response and (2) to ensure sufficient base rates of environmental risk factors. Age at first childbearing was used as the risk-stratification variable because it was present for virtually all families in the register, it is relatively free of measurement error, and early childbearing is associated with a host of other difficulties and is a known risk factor for children's problem behaviours (Maynard, 1997; Moffitt & The E-Risk Study Team, 2002). The high-risk sampling strategy resulted in a final sample in which one-third of Study mothers constitute a 160% oversample of mothers who were at high risk based on their young age at first birth (13–20 years), while the other two-thirds of Study mothers accurately represent all mothers in the general population (13–48 years) in England and Wales in 1994–95 (estimates derived from the General Household Survey; Bennett, Jarvis, Rowlands, Singleton, and Haselden (1996)).

The Study sought a sample size of 1,100 families to allow for attrition in future years of the longitudinal study while retaining statistical power. An initial list of

families who had same-sex twins was drawn from the register to target for home-visits, with a 10% oversample to allow for nonparticipation. Same-sex twin pairs were selected to simplify twin analyses. Of the 1,203 families from the initial list who were eligible for inclusion, 1,116 (93%) participated in home-visit assessments when the twins were age 5 years, forming the base sample for the study (2,232 children): 4% of families refused, and 3% were lost to tracing or could not be reached after many attempts. With parent's permission, questionnaires were posted to the children's teachers, and teachers returned questionnaires for 94% of cohort children. Zygosity was determined using a standard zygosity questionnaire, which has been shown to have 95% accuracy (Price et al., 2000). Ambiguous cases were zygosity-typed using DNA. Subsequently, all participants who provided a DNA sample at any point across the study phases (97%) have been genotyped and had their zygosity checked. The sample includes 56% monozygotic (MZ) and 44% dizygotic (DZ) twin pairs. Sex is evenly distributed within zygosity (49% male). All families are English speaking, and the majority (93.7%) are White. Figure 3.1 below shows the distribution of E-Risk families who participated at age 12 across England and Wales.

Attrition has been minimal, and data has been successfully collected from 98% (at age 7 years), 96% (at age 10 years), 96% (at age 12 years), and most recently in 2012–2014, 93% of the original sample (at age 18 years). Home-visits at ages 5, 7, 10, and 12 years included face-to-face assessments with participants as well as their mother (or primary caregiver); the home-visit at age 18 included interviews only with the participants, and questionnaires completed by co-informants (caregivers and other family members). Each twin participant was assessed by a different interviewer. The Joint South London and Maudsley and the Institute of Psychiatry Research Ethics Committee approved each phase of the study. Parents gave informed consent at ages 5–12. Participants gave assent at ages 5–12 and informed consent at age 18.



Figure 3.1 Location of families in the E-Risk study who were living in England and Wales and participated in the age 12 assessment. Adapted from Odgers et al. (2012).

3.2 Psychotic phenomena

The research presented in this thesis utilises two measures of early psychotic phenomena that were obtained at two time-points – age 12 (childhood) and age 18 (adolescence). At ages 12 and 18, the prevalence of psychotic *symptoms* was measured via face-to-face structured interviews that were verified by clinicians to obtain an estimate of more clinically pertinent psychotic phenomena. At age 18, psychotic *experiences* were additionally measured, using responses to the face-to-face structured interview, but without clinical verification. This broader estimate of self-reported psychotic phenomena reflects the methodology used by many groups in the psychosis prodrome research field (Loewy, Pearson, Vinogradov, Bearden, & Cannon, 2011) and therefore increases the comparability of this research with that from other groups. In

addition, previous research has shown that such self-report screening measures, particularly of delusions and hallucinations, have reasonable predictive value for identifying adolescents who meet clinical interview criteria for definite psychotic phenomena (Kelleher, Harley, Murtagh, & Cannon, 2011). Further detail about these two measures is provided below, and the relevant booklet sections for the structured interviews are shown in Appendix I.

3.2.1 Psychotic symptoms

E-Risk families were visited by mental health trainees or professionals when children were aged 12. Interviewers had no prior knowledge about the child. Different staff members interviewed the child's parents. Each child was privately interviewed about seven psychotic symptoms they may have experienced throughout childhood, with items pertaining to delusions and hallucinations including:

- Have other people ever read your thoughts?
- Have you ever believed that you were being sent special messages through the television or radio, or that a programme has been arranged just for you alone?
- Have you ever thought you were being followed or spied on?
- Have you ever heard voices that other people cannot hear?
- Have you ever felt like you were under the control of some special power?
- Have you ever known what another person was thinking, like you could read their mind?
- Have you ever seen something or someone that other people could not see?

This interview has been described in detail previously (Polanczyk et al., 2010). The item choice was guided by the Dunedin Study's age-11 interview protocol (Poulton et al., 2000) and an instrument prepared for the Avon Longitudinal Study of Parents and Children (Schreier et al., 2009). Interviewers coded each experience 0, 1, 2 indicating respectively “not present”, “probably present”, and “definitely present”. A conservative approach was taken in designating a child's report as a symptom. First, the interviewer probed using standard prompts designed to discriminate between experiences that were plausible (e.g., “I was followed by a man after school”) and potential symptoms (e.g., “I was followed by an angel who guards my spirit”), and wrote down the child's narrative description of the experience. Second, items and interviewer notes were assessed by a psychiatrist expert in schizophrenia, a psychologist expert in interviewing children, and a child and adolescent psychiatrist to verify the validity of the symptoms (but without consulting other data sources about the child or family). Third, because children were twins, experiences limited to the twin relationship (e.g., “My twin and I often know what each other are thinking”) were coded as “not a symptom”. Children were only designated as experiencing psychotic symptoms if they reported at least one definite, clinically-verified symptom. At age 12, 5.9% (N=125) of children reported experiencing psychotic symptoms (referred to as *childhood psychotic symptoms* in this thesis).

The same items and clinical verification procedure was used when participants were interviewed at age 18, this time enquiring about psychotic symptoms they may have experienced *since age 12*. At age 18, 2.9% (N=59) of participants reported experiencing psychotic symptoms since age 12 (referred to as *adolescent psychotic symptoms* in this thesis). These rates are similar to those reported for community samples of children and adolescents in other studies using clinical verification procedures (Dhossche, Ferdinand, van der Ende, Hofstra, & Verhulst, 2002; Horwood

et al., 2008). The comparatively low prevalence of psychotic symptoms at age 18 versus age 12 is also consistent with findings from other studies showing an attenuating rate of psychotic symptoms from childhood to adulthood (Kelleher et al., 2012b; Zammit et al., 2013). Furthermore, psychotic symptoms in this cohort have previously been shown to have good construct validity, sharing many of the same genetic, social, neurodevelopmental, and behavioural risk factors and correlates as adult psychotic disorders (Polanczyk et al., 2010).

3.2.2 *Psychotic experiences*

During the age 18 interviews, participants were asked six items about unusual feelings and thoughts *in addition* to the seven hallucination/delusion items. These items drew on item pools since formalised in prodromal psychosis screening instruments including the Prevention through Risk Identification, Management and Education (PRIME)-screen (Miller, Cicchetti, Markovich, McGlashan, & Woods, 2004) and the Structured Interview for Psychosis-Risk Syndromes (SIPS) (Miller et al., 2003). These additional items included:

- I have become more sensitive to lights or sounds
- I feel as though I can't trust anyone
- I worry that my food may be poisoned
- People or places I know seem different
- I believe I have special abilities or powers beyond my natural talents
- My thinking is unusual or frightening

Interviewers coded each of the 13 items 0, 1, 2, indicating respectively “not present”, “probably present” and “definitely present”. Responses to each of the 13 items (none, probable, definite) were summed to create a psychotic experiences scale (potential range=0–26, actual range=0–18, $M=1.19$, $SD=2.58$). The psychotic experiences

measure did not involve clinical verification, meaning that this is a self-report measure capturing a broader range of mild, moderate and potentially clinically pertinent hallucinations, delusions, and other unusual feelings and thoughts (referred to as *adolescent psychotic experiences* in this thesis). Since there were low numbers of adolescents with high psychotic experiences scores (e.g., only 1.0% [N=21] of participants reported 13 or more psychotic experiences), scores were placed into an ordinal scale to tackle the skewed distribution while retaining more information than a binary score. Just over 30% of participants had at least one psychotic experience between ages 12 and 18: 69.8% reported no psychotic experiences (coded 0; N=1,440), 15.5% reported 1 or 2 psychotic experiences (coded 1; N=319), 8.1% reported 3–5 psychotic experiences (coded 2; N=166), and 6.7% reported 6 or more psychotic experiences (coded 3; N=138). This 30.2% prevalence is similar to the prevalence of self-reported psychotic experiences in other community samples of teenagers and young adults (Spauwen et al., 2004; Yoshizumi, Murase, Honjo, Kaneko, & Murakami, 2004; Yung et al., 2009). In Chapter 6, categories 2 (3–5 psychotic experiences) and 3 (6 or more psychotic experiences) are collapsed because there were no DZ twin pairs concordant for 6 or more psychotic experiences, and empty matrix cells prevent twin analysis of ordinal data.

3.3 Urbanicity

The research in this thesis uses two measures of urbanicity. In Chapter 4, urbanicity is derived from responses to a resident survey completed by immediate neighbours of the E-Risk families when children were aged 12. In Chapters 5 and 6, urbanicity is derived from data from the UK's Office of National Statistics (ONS). The ONS urbanicity data provides a more precise and objective means of measuring urbanicity compared to the resident reports. However, this data was geocoded and linked to E-Risk families'

addresses during the course of this PhD, and was not available at the time the analysis was conducted for the research presented in Chapter 4. However, the two measures are consistent in terms of urbanicity estimates. For example, 72% of the neighbourhoods reported as rural by residents are coded as rural according to the ONS measure; 94% of the neighbourhoods reported as urban by residents are coded as urban according to the ONS measure. In addition, sensitivity analyses were conducted by repeating main analyses in Chapter 4 using the ONS measure of urbanicity, and these results are presented in supplementary materials at the end of Chapter 4. In short, findings are similar regardless of which urbanicity measure is used. Further detail about both measures of urbanicity is provided below.

3.3.1 Urbanicity from the resident survey

Classification of E-Risk families' neighbourhoods as within an urban versus nonurban setting was based on responses from a postal survey sent in 2008 to residents living alongside E-Risk families when children were aged 12 (Odgers et al., 2012a; Odgers et al., 2009). This questionnaire is provided in Appendix II. In Britain, a postcode area typically contains 15 households, with at most 100 households (e.g., large apartment block). This type of postcode-level resolution represents a marked advantage over many existing neighbourhood studies in which much larger census tract or census block units of analysis are used. Our objective was to obtain multiple reporters (e.g., 2 or more) for each family's neighbourhood (here defined to the street or apartment block level). Considering that the typical response rate for neighbourhood surveys is approximately 30% (Messner, Baumer, & Rosenfeld, 2004), questionnaires were sent to every household in the same postcode as the E-Risk families, excluding the E-Risk families themselves (addresses were identified from electoral roll records). The number of surveys sent per postcode ranged from 15 to 50 residences per neighbourhood

(Average=18.96, SE=0.21). Excluding undelivered surveys (N=600), the overall response rate was 28.1% (5601/19926), similar to that previously found (Messner et al., 2004). Survey respondents typically lived on the same street or within the same apartment block as the children in our study. Surveys were returned by an average of 5.18 (SD=2.73) respondents per neighbourhood (range=0–18 respondents). There were at least three responses for 80% of neighbourhoods and at least two responses from 95% of the neighbourhoods (N=5,601 respondents) (Odgers et al., 2012a). Most respondents had lived in the neighbourhood for more than 5 years (83%), and only 1% of respondents had lived in the neighbourhood for less than 1 year. Residents reported whether their neighbourhood was in “a city”, “a town”, “a suburb”, “a small village” or “the countryside” (Polanczyk et al., 2010). There was high agreement between residents in the same neighbourhood, with only 50 neighbourhoods returning discordant responses (i.e., neighbourhoods where residents differed in their urbanicity responses). Degree of urbanicity for these 50 ambiguous neighbourhoods was clarified by a British researcher using Google Aerial View and an online population density map, based on features such as population density, building density, proximity to the countryside or city/town centre, land-use (e.g., agriculture, transportation, industry, etc.) and the official definition of the settlement. Given the low numbers of participants within some urbanicity categories (e.g., only 2.1% of children lived in the countryside), urbanicity was dichotomised as urban (1: city/town) versus nonurban (0: suburb/small village/countryside). At age 12, the sample was split evenly between urban and nonurban neighbourhoods, with 51.9% (N=1,066) of children living in urban neighbourhoods and the remaining 988 children living in nonurban neighbourhoods.

Urbanicity for the children’s addresses at age 5 was also derived from these resident reports, to investigate the temporal sequencing of urbanicity and psychotic symptoms in Chapter 4. This was possible because, while the resident reports were

obtained when children were aged 12, full address information is known for each child from age 5. Over half (57%) of children did not move address between ages 5 and 12, therefore urbanicity at age 5 is known for these children (provided that the level of urbanicity of neighbourhoods did not substantially change over this time). The neighbourhoods for the remaining 43% of children who moved address at least once between ages 5 and 12 were visually inspected by a British researcher using Google Aerial View and an online population density map (using the same method described above for clarifying the 50 ambiguous addresses at age 12), and coded according to level of urbanicity. At age 5, 55.1% (N=1117) of children with available data lived in urban neighbourhoods with the remaining children living in nonurban neighbourhoods.

3.3.2 Urbanicity from the Office of National Statistics

Urbanicity was also derived from the ONS's Rural-Urban Definition for Small Area Geographies (RUC2011) classifications (Office for National Statistics, 2013). The ONS classifications utilised 2011 census data, and were designed for application to small geostatistical units (e.g. Output Areas). Detailed information on how the ONS created the RUC2011 classifications of urbanicity is available on the ONS webpages (https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/239477/RUC11methodologypaperaug_28_Aug.pdf). Briefly, RUC2011 was created by laying a grid of hectare cells (100m²) over England and Wales. Postcode addresses were assigned to cells, and residential densities were then calculated for increasing radii around each cell, providing each residential property with a density profile. This was combined with Output Area and contextual data, allowing each settlement to be assigned to one of ten urbanicity categories (Rural categories: sparse/non-sparse hamlets and isolated dwellings, sparse/non-sparse villages, sparse/non-sparse rural town and fringe; Urban categories: sparse/non-sparse city and town, and minor/major

conurbations [conurbations are densely populated, large urban regions resulting from the expansion and coalescence of adjacent cities and towns]). ONS urbanicity scores were then assigned to every E-Risk family via the family's postcode when children were aged 5, 7, 10, 12 and 18. Given the low numbers within some rural categories, urbanicity was collapsed into three levels (1: "rural" = all rural categories [19.9% of children at age 12]; 2: "intermediate" = urban cities and towns [47.9% of children at age 12]; and 3: "urban" = minor/major conurbations [32.2% of children at age 12]). E-Risk families are nationally-representative in terms of ONS urbanicity classifications; 32.2% of E-Risk children lived in urban settings at age 12 compared to 36.1% nationwide; 47.9% versus 45.0% lived in intermediate settings; and 19.9% versus 18.9% lived in rural settings.

3.4 Neighbourhood variables

This thesis uses several objective and subjective measures of the neighbourhood environments that E-Risk participants grew up in. Most neighbourhood measures are accurate to the level of the postcode or street, because previous research using accelerometers and global positioning technology in England has found that the majority of children's activities take place within ten minutes (or 800 metres/0.5 miles) from their home (Jones, Coombes, Griffin, & van Sluijs, 2009). The primary focus of analyses in this thesis is neighbourhood social processes, describing the quality, quantity and nature of interactions between residents in the neighbourhood (defined in Chapter 1), such as the levels of crime and disorder in neighbourhoods and cohesion and support between neighbours. Objective neighbourhood measures including neighbourhood socioeconomic status (SES) and official crime levels are also used as control variables in this thesis to examine the independent associations of urbanicity

and neighbourhood social processes with psychotic phenomena. The neighbourhood variables used in this thesis are described below.

3.4.1 Social processes

Social processes include social cohesion, social control, neighbourhood disorder, and neighbourhood crime. These were measured in three ways at three time-points. At age 5, the children's mothers (or primary caregivers) reported on their immediate neighbourhood during the face-to-face interviews. At age 12, residents living alongside the E-Risk children reported on their neighbourhoods during the resident survey. At age 18, participants themselves reported on their immediate neighbourhoods during the age-18 face-to-face interviews. Previous E-Risk data checks have demonstrated high reliability and intraclass correlations for the mother-reported and resident-reported social processes scales (Odgers et al., 2009).

Mothers' reports of neighbourhood social processes are used in Chapter 4. The relevant section of the age-5 interview used to obtain mothers' reports of social processes is shown in Appendix III. Social cohesion (Sampson et al., 1997) (5 items; items NB28-NB32 in Appendix III) was assessed by asking mothers whether their neighbourhood was close-knit, whether neighbours shared values, and whether neighbours trusted and got along with each other, etc. Social control (Sampson et al., 1997) (5 items; items NB23-NB27 in Appendix III) was assessed by asking mothers to judge whether people in their neighbourhoods would take action against different types of undesirable activities (e.g., children skipping school, fights in public places). For neighbourhood disorder (13 items; items NB7-NB19 in Appendix III) (Sampson & Raudenbush, 1999) mothers were asked whether thirteen problems affected their neighbourhood, including noisy neighbours, arguments or loud parties, vandalism, graffiti or deliberate damage to property, and cars broken into. Crime victimisation (3

items; items NB20-NB22 in Appendix III) was assessed by asking mothers whether they or their family had been victimised by a violent crime (e.g., mugging, assault), a burglary, or a theft in the neighbourhood. Items for each social process were coded 0 (e.g., never/not true) to 2 (e.g., often/very true) and scores within each social process scale were summed for each mother (social cohesion: $M=7.61$, $SD=2.74$; social control: $M=7.45$, $SD=2.71$; neighbourhood disorder: $M=3.97$; $SD=3.82$; neighbourhood crime victimisation; $M=0.92$, $SD=1.31$). Because social processes were measured on different scales, each was standardised to have a mean of 0 and a standard deviation of 1 to facilitate comparability of the results.

Resident reports of social processes are used in Chapters 4, 5 and 6. The resident survey questionnaire is provided in Appendix II and the full methodology for the resident survey is described above in the urbanicity methods. Residents were asked the same (or very similar) questions regarding social cohesion (5 items, coded 0–4; items E1-E5 in Appendix II), social control (5 items, coded 0–4; items D1-D5 in Appendix II), neighbourhood disorder (14 items, coded 0–2; items C1-C7, C14-C17 and C20-C22 in Appendix II), and neighbourhood crime (3 items, coded 0–1/2; items J1-J3 in Appendix II) as used for the mothers' reports. Social process scales from the resident surveys were created in two steps. First, items belonging to each social process were averaged to create a summary score for each of the 5601 respondents. Second, scores for each E-Risk family were created by averaging the social process scores of respondents within that family's neighbourhood (social cohesion: $M=2.23$, $SD=0.50$; social control: $M=2.20$, $SD=0.53$; neighbourhood disorder: $M=0.49$; $SD=0.34$; neighbourhood crime; $M=0.19$, $SD=0.22$). Because social processes were measured on different scales, each was standardised to have a mean of 0 and a standard deviation of 1.

The participants' personal reports of neighbourhood social processes are used in Chapter 6. These personal perceptions of the neighbourhood were obtained during the face-to-face interviews at age 18, and the relevant parts of the interview booklet are shown in Appendix IV. Analyses in Chapter 6 focus specifically on perceptions of neighbourhood disorder for two reasons. First, of all the social processes examined, neighbourhood disorder has the most objective and longitudinal equivalent variables collected throughout the study (e.g., official neighbourhood crime levels, resident reports of neighbourhood disorder, childhood perceptions of neighbourhood safety at age 12), allowing temporality to be examined and the association between perceived neighbourhood disorder and psychotic phenomena to be controlled for objective levels of threat and crime in the neighbourhood. Second, given that psychosis often involves altered perceptions of reality such as threat detection bias and hypervigilance (Freeman, Garety, Kuipers, Fowler, & Bebbington, 2002; Garety, Kuipers, Fowler, Freeman, & Bebbington, 2001), adolescents' *personal perceptions* of threat and danger in the neighbourhood could be particularly relevant to psychotic phenomena. Participants were asked about whether six problems affected their neighbourhood (items NB13a-NB13f in Appendix IV), including: litter, broken glass, and rubbish in public places; run-down buildings, abandoned cars, wasteland or vacant shop fronts; people being drunk or unruly in public; people selling or using drugs; groups of young people hanging out and causing trouble; and homes getting broken into or burgled (each coded 0, 1, 2, indicating respectively "not true", "sometimes true", and "often true"). Item responses were averaged for each participant ($M=0.52$, $SD=0.49$, range=0–2).

Chapter 6 also uses children's reports of neighbourhood safety to examine the temporal sequence of perceived neighbourhood conditions and psychotic phenomena. As part of a computer-based self-report stress questionnaire conducted at age 12, children indicated whether the statement "You feel unsafe in your neighbourhood" was

true or false. At age 12, 12.3% (N=260) of children reported that they felt their neighbourhood was unsafe.

3.4.2 Neighbourhood-level socioeconomic status

Chapters 4, 5 and 6 include neighbourhood-level SES in analyses to control for poverty. Neighbourhood SES is treated as a confounder in this way because area-level deprivation has been repeatedly implicated in adult psychosis (see Chapter 1). The focus of this thesis is the potential neighbourhood social processes linking the urban environment to early psychotic phenomena, therefore analyses adjust for neighbourhood-level SES to check if any association between urbanicity/neighbourhood social conditions and early psychotic phenomena is explained by poverty levels in urban versus rural neighbourhoods.

Neighbourhood-level SES was assessed using a geodemographic discriminator developed by a consumer marketing group, CACI Ltd (<http://www.caci.co.uk/>), for commercial use in Great Britain: A Classification of Residential Neighbourhoods (ACORN) (Caspi, Taylor, Moffitt, & Plomin, 2000; Odgers et al., 2012b; Odgers et al., 2009). CACI utilised over 400 variables from 2001 census data for Great Britain and an extensive consumer research database (e.g., educational qualifications, unemployment, housing tenure) to give a comprehensive picture of socioeconomic differences between different areas. The ACORN classifications are provided at the Enumeration District (ED) level (~150 households), the smallest area at which census data are made available by the ONS. Hierarchical cluster analysis was used to group EDs into 56 neighbourhood types and five distinct and homogeneous ordinal groups ranging from “Wealthy Achievers” (category 1) with high incomes, large single family houses and access to many amenities to “Hard Pressed” neighbourhoods (category 5) dominated by government-subsidised housing estates, low incomes, high unemployment and single

parents. ACORN classifications are typically sold to businesses and local health authorities for marketing and planning purposes, but the ratings were shared with our research team by CACI Ltd for educational and research purposes. Neighbourhood-level SES scores for the E-Risk families were then created by geocode matching the ACORN classifications to the E-Risk families' postcodes when children were aged 5, 7, 10, 12 and 18. E-Risk families are representative of UK households across the spectrum of neighbourhood-level SES: for example, when children were aged 12, 25.6% of E-Risk families live in "wealthy achiever" neighbourhoods compared to 25.3% of households nation-wide; 5.3% vs. 11.6% live in "urban prosperity" neighbourhoods; 29.6% vs. 26.9% live in "comfortably off" neighbourhoods; 13.4% vs. 13.9% live in "moderate means" neighbourhoods; and 26.1% vs. 20.7% live in "hard-pressed" neighbourhoods. E-Risk underrepresents "urban prosperity" neighbourhoods because such households are likely to be childless.

3.4.3 Official neighbourhood levels of crime

Official levels of crime in the E-Risk families' neighbourhoods are used in Chapter 6. This measure was used to estimate the independent associations of perceived threat (adolescents' perceptions of neighbourhood disorder) versus objectively measured threat in the neighbourhood with adolescent psychotic experiences. Street-level crime data, including information on the type of crime, date of occurrence, and approximate location, were accessed online as part of an open data sharing effort about crime and policing in England and Wales. Data covers various forms of crime, including violent offences, sexual offences, robberies, burglaries, theft, arson, and vandalism. Street-level crime data was extracted for each of the geospatial coordinates marking the family's home. Further information about how the levels of crime were estimated and made available for research is provided on the police data sharing webpage

(<https://data.police.uk/about/#location-anonymisation>). Neighbourhood crime rates were calculated by mapping a one mile radius around each E-Risk Study participant's home and tallying the total number of crimes that occurred in the area each month (M=247, SD=274, range=1–1868). Scores were computed for 2011 (the year prior to age 18 assessments), which was the first year for which full street-level data was available. These scores were then collapsed into quartiles.

3.5 Personal crime victimisation

The participants' personal experiences of crime victimisation are used in Chapter 5 to investigate the potential cumulative and interactive effects of adverse neighbourhood conditions and more direct victimisation experiences. Personal experiences of violent crime victimisation were assessed during the age-18 interviews using the Juvenile Victimization Questionnaire 2nd revision (JVQ-R2) (Finkelhor, Hamby, Turner, & ORMOD, 2011) adapted as a clinical interview. Full details about the victimisation interview are described by Fisher et al. (2015). Participants were interviewed face-to-face with the modified version of the JVQ-R2 about exposure to a range of adverse experiences that might have occurred during adolescence. JVQ crime victimisation comprised nine items, each enquiring about the period "since you were 12":

- Did anyone use force to take something away from you that you were carrying or wearing?
- Did anyone steal something from you and never give it back? Things like a bag, money, watch, clothing, bike, iPod, or anything else?
- Did anyone break or ruin any of your things on purpose?
- Did anyone hit or attack you on purpose with an object or weapon like a stick, rock, gun, knife or anything that hurt? Somewhere like: at home, at school, in a shop, a car, on the street, or anywhere else?

- Did anyone hit or attack you without using an object or weapon?
- Did someone start to attack you, but for some reason, it didn't happen?
For example, someone helped you or you got away?
- Did someone threaten to hurt you when you thought that they might really do it?
- Did anyone try to kidnap you? By this I mean you were made to go somewhere, like into a car, by someone who you thought might hurt you.

Participants responded “yes” or “no” as to whether each type of victimisation had occurred, and follow-up questions were asked concerning details of the worst event the participant had experienced. All information from the modified JVQ-R2 interview was compiled into victimisation dossiers and rated by an expert in victimology (Dr Helen Fisher) and three other trained E-Risk team members. Ratings were made using a 6-point scale: 0=not exposed, then 1–5 for increasing levels of severity, adapted from the standardised coding system used for the Childhood Experience of Care and Abuse interview (CECA) (Bifulco, Brown, Neubauer, Moran, & Harris, 1994a; Bifulco, Brown, & Harris, 1994b). High levels of interrater reliability were achieved for the crime victimisation severity ratings (intraclass correlation coefficient=0.89, $p<0.001$). The severity of crime victimisation reflected the level of physical harm that had occurred. In the present study, crime victimisation was dichotomised to represent very violent forms of crime, with adolescents who reported the top two levels of JVQ crime victimisation (levels 4/5; injury or threat to life likely) designated as having experienced *personal crime victimisation*. At age 18, 19.3% of participants (N=398) reported that they had experienced personal crime victimisation since age 12.

3.6 Other childhood and adolescent mental health outcomes

Analyses in Chapters 4, 5 and 6 use other childhood (age 12) and adolescent (age 18) mental health outcomes (e.g., depression, anxiety, substance problems) to check the specificity of the associations of neighbourhood variables with psychotic phenomena, or to control for potential co-occurring problems.

3.6.1 Childhood mental health outcomes

Chapter 4 assesses specificity by calculating the association between urbanicity and age 12 anxiety, depression, and antisocial behaviour. Anxiety was assessed when children were aged 12, via private interviews using the 10-item version of the Multidimensional Anxiety Scale for Children (MASC) (March, Parker, Sullivan, Stallings, & Conners, 1997). This self-report scale measures a wide spectrum of anxiety symptoms, corresponding with diagnostic criteria for social phobia, separation anxiety, selective mutism, and generalised anxiety disorder. Each of the 10 items were graded in severity (0–2), with a total score range of 0 to 18 ($M=7.62$, $SD=3.04$) in this sample. The internal consistency reliability of this scale was 0.63 (Bowes et al., 2013). Children scoring at or above the 95th centile (raw score of 13 or more) constitute the childhood anxiety group ($N=129$, 6.1%) in this thesis. Depression symptoms were assessed at age 12 during the private interviews using the Children’s Depression Inventory (CDI) (Kovacs, 1992). The CDI is a 27-item scale assessing several aspects of depression including negative mood, negative self-esteem, anhedonia, ineffectiveness, and interpersonal problems. Children who scored 20 or more (Rivera, Bernal, & Rosello, 2005) were deemed to have clinically significant depressive symptoms ($N=74$, 3.5%) and constitute the childhood depression group in this thesis. Antisocial behaviour was assessed at age 12 using the Achenbach’s family instrument (Achenbach, 1991), the most widely used and well-validated assessment scheme for assessing antisocial behaviour problems

among children and adolescents. Both mothers' and teachers' reports of the children's delinquent and aggressive behaviours were combined by summing items from each rater (scored 0–2). An extreme antisocial behaviour group was formed with children who scored at or above the 95th centile (N=110, 5.1%) (Odgers, Donley, Caspi, Bates, & Moffitt, 2015).

3.6.2 Adolescent mental health outcomes

Chapter 5 adjusts analyses for adolescent cannabis and alcohol dependence, and checks specificity by investigating the association of urbanicity with adolescent major depression (referred to as depression). Chapter 6 adjusts analyses for adolescent cannabis dependence, alcohol dependence, generalised anxiety disorder (referred to as anxiety), and depression. Adolescent cannabis dependence, alcohol dependence, anxiety and depression were each assessed during the age-18 face-to-face interviews according to DSM-IV criteria (American Psychiatric Association, 1994), using the Diagnostic Interview Schedule (DIS) (Robins, Cottler, Bucholz, & Compton, 1995). Alcohol dependence was assessed with 27 items enquiring about a range of past-year alcohol-related behaviours such as frequency of drinking alcohol, frequency of binge drinking, addictive behaviour, and alcohol-related problems. At age 18, 12.8% (N=263) of participants met DSM-IV criteria for past-year alcohol dependence. Cannabis dependence was assessed with 23 items enquiring about past-year cannabis-related behaviours such as frequency of use, interference, and addiction. At age 18, 4.3% (N=89) of participants met DSM-IV criteria for cannabis dependence. Anxiety was assessed with 41 items enquiring about a range of past-year anxiety symptoms and behaviours such as frequency and severity of worrying and nervousness, avoidance behaviours, restlessness, sleep problems, physical symptoms (e.g., sweating, heart palpitations, chest pains), and interference. At age 18, 7.4% (N=153) of participants met

DSM-IV criteria for anxiety. Depression was assessed with 30 items enquiring about a range of past-year depressive symptoms and behaviours such as frequency and severity of sadness and tearfulness, anhedonia, hopelessness, sleep problems, weight changes, feelings of guilt, and interference. At age 18, 20.1% (N=414) of participants met DSM-IV criteria for depression. These rates of adolescent substance and affective problems are similar to those documented in other general population samples of adolescents and young adults (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Hankin et al., 1998; Merikangas et al., 2010).

3.7 Family-level covariates

Analyses in Chapters 4, 5 and 6 adjust for key family-level factors that might simultaneously influence both the selection of families into certain types of neighbourhood conditions and the children's likelihood of developing psychotic phenomena, including family SES, family psychiatric history, and maternal psychotic symptoms. Family SES was measured at age 5 via a composite of parental income, parental education, and parental occupation: parental income was measured as the entire income of the household; parental education was the highest level of education achieved by either the mother or father (highest value taken), ranging from 1 (CSE [1], O Level [A-C], GCSE [A-C]) to 7 (postgraduate degree); parental occupation was the highest level of parental occupation of either parent, ranging from 1 (both parents unemployed [coded 2 if single unemployed mother]) to 9 (professional). The three SES indicators were highly correlated (r 's=0.57–0.67, all p 's<0.05) and loaded significantly onto one latent factor (M =2.00, SD = 0.82; factor loadings=0.80, 0.70 and 0.83 for parental income, education and occupation, respectively). These variables were then standardised and summed, before categorising into tertiles at the 33.33rd and 66.66th centile (low-, medium-, and high-SES) (Trzesniewski, Moffitt, Caspi, Taylor, &

Maughan, 2006). Family psychiatric history was measured when children were aged 12 during the face-to-face interviews with the children's mothers. The mother reported on her own mental health history and the mental health history of her biological mother, father, sisters, brothers, as well as the twins' biological father (Milne et al., 2008; Weissman et al., 2000). This was converted to the proportion of family members with a history of any psychiatric disorder (coded 0–1.0; $M=0.37$, $SD=0.27$). For maternal psychotic symptoms, mothers were interviewed when children were aged 12 using the Diagnostic Interview Schedule (DIS) (Robins et al., 1995) for DSM-IV (American Psychiatric Association, 1994) which provides a symptom count for characteristic symptoms of schizophrenia (e.g. hallucinations, delusions, anhedonia). The goal was not to diagnose clinical schizophrenia but to identify women who endorsed impairing psychotic-like experiences and beliefs: 16.6% of mothers had at least one symptom of schizophrenia.

3.8 Statistical analyses

Chapters 4, 5 and 6 each contain a section on the statistical analyses used in that study. In terms of missing data, E-Risk has very low rates of attrition (93% of the original sample participated at age 18), and the age 18 sample is representative of the original sample in terms of family SES ($\chi^2=0.86$, $p=0.65$), age-5 IQ scores ($t=0.98$, $p=0.33$), and age-5 internalizing and externalizing behaviour problems ($t=0.40$, $p=0.69$ and $t=0.41$, $p=0.68$, respectively). Thus, E-Risk data does not appear to be confounded by selective attrition. In addition, E-Risk interviews and supplementary information (e.g., resident surveys, co-informant questionnaires) were carefully designed to maximise response rates. All interviews were undertaken in privacy by trained research workers, and participants (or caregivers) were assured of confidentiality. Further, for the resident surveys, an excess of surveys was mailed to allow for non-response and ensure multiple

responses for each neighbourhood. Nevertheless, there was a small amount of missing data for key variables used in this thesis. At age 12, 95.7% (N=2,054) of the participants who were interviewed had complete data on psychotic symptoms and urbanicity (from the resident survey data). Again, at age 18, 95.7% (N=1,978) of the participants who were interviewed had complete data on psychotic experiences and urbanicity (from the ONS data). For other key variables used in this thesis such as neighbourhood social processes and crime victimisation, again under 5% of data was missing for active participants (e.g., for the resident-reported social process variables, 3.4% of participants [N=73] had missing data). Since there was very little missing data, analyses were performed using listwise deletion (i.e., analyses were only performed on cases with complete data for the model specification). The implications of this approach as well as alternative approaches for handling missing data are discussed in Chapter 7.

The following sections provide further detail on two methods for analysing twin data which are used in Chapter 6 – the classical twin design and the twin differences design. The strategy used in this thesis to account for the non-independence of the twin observations when treating the twins as individual children is then described.

3.8.1 The classical twin design

Twin studies provide the opportunity to examine the relative contributions of genetic and environmental influences to individual differences in a phenotype (such as psychotic symptoms). This is because monozygotic (MZ) twins share ~100% of their segregating DNA, whereas dizygotic (DZ) twins share on average 50% of their segregating DNA. In contrast, MZ and DZ reared-together twin pairs are assumed not to differ in the extent that they share environmental exposures. This “equal environment assumption” could be violated, for example, if parents treat MZ twin offspring more similarly than they treat DZ twin offspring (Plomin et al., 2013). However, studies of

twin pairs whose zygosity was misidentified at birth suggest that “perceived” zygosity does not substantially influence the similarity between twin pairs’ environments (Kendler, Neale, Kessler, Heath, & Eaves, 1993). Thus, the classical twin design compares the phenotypic correlation between MZ twin pairs to that between DZ twin pairs. This allows the variation in observed traits to be partitioned into three latent explanatory factors: additive genetic (A), common environmental (C), and unique environmental (E) components. Additive genetic influences are the summed effects of all individual alleles that influence the trait. This equates to the heritability of a trait. Common environmental influences are the environmental exposures shared between all siblings in a family, which make them more similar to each other (e.g., socioeconomic status, neighbourhood conditions). Unique environmental influences are the environmental exposures that are unique to each sibling in a family, which make them different to each other (e.g., victimisation, accidents). However, the twin design does not reveal which specific genetic and environmental factors contribute to the ACE proportions.

In univariate analyses, genetic influences on a trait are inferred if MZ correlations are greater than DZ correlations, as this increased similarity between MZ twin pairs can only be accounted for by their increased genetic resemblance. Within-pair similarity that is not due to genetic factors is attributed to common environmental influences. Common environmental influences are implicated if DZ correlations are greater than half that of MZ correlations for a given trait, as this excess similarity can only be accounted for by environmental factors shared between twin pairs. Unique environmental influences are estimated from within-pair differences between MZ twins, as E is the only influence that makes MZ twins different from one another (Neale & Cardon, 2013). Measurement error is also included in E. The twin design can also be used to examine the genetic, common environmental, and unique environmental sources

of covariance between two phenotypes (e.g., psychotic experiences and perceptions of neighbourhood adversity), by investigating the phenotypic correlation between one trait in one twin and a second trait in the second twin (the cross-twin cross-trait design). In this bivariate analysis, higher cross-twin cross-trait correlations between MZ twin pairs versus DZ twin pairs suggests genetic sources of correlation between two traits (i.e., overlapping genetic influences on two traits).

Phenotypic correlation between MZ twin pairs (r_{MZ}) is the sum of all genetic and common environmental influences: $r_{MZ} = A + C$. Phenotypic correlation between DZ twin pairs (r_{DZ}) is the sum of all common environmental influences plus 50% of genetic influences: $r_{DZ} = 0.5A + C$. The relative contributions of A, C and E to a phenotype can therefore be calculated as follows using Falconer's formula (Falconer, 1965):

$$A = 2 \times (r_{MZ} - r_{DZ})$$

$$C = r_{MZ} - A$$

$$E = 1 - r_{MZ}$$

In this thesis, twin analyses are conducted using structural equation modelling (SEM) in the statistical package OpenMx. SEM fixes the within-pair correlation between genetic factors to 1 for MZ twins and 0.5 for DZ twins, and fixes the correlation between common environmental factors to 1 for both MZ and DZ twins. Maximum likelihood estimation in OpenMx estimates ACE parameters with associated confidence intervals given the data, and handles missing data. In addition, maximum likelihood estimation provides goodness-of-fit statistics for the full ACE model compared to the saturated model which describes the data perfectly, as well as for the AE, CE, and E sub-models compared to the ACE model. The most parsimonious model is selected based on fit statistics including Akaike's Information Criterion (AIC) and -2 times log-likelihood ($-2LL$) which follows a chi-square distribution (χ^2). A non-significant χ^2 value suggests

that the model (ACE, AE, CE, or E) provides a good fit to the data. The AIC fit statistic reflects the trade-off between increasing the fit of the model and increasing the uncertainty in model prediction (error) by adding model parameters. Lower AIC values indicate a better fitting model. SEM has the additional advantages of allowing multivariate analyses to be conducted (e.g., cross-twin cross-trait analyses), as well as allowing categorical traits to be modelled according to the liability-threshold model (Rijsdijk & Sham, 2002).

3.8.2 The co-twin control design

Whereas the classical twin design estimates the relative contribution of genetic and environmental influences on traits, the co-twin control design (also called the twin differences design) uses the same principles to control robustly for additive genetic and common environmental influences. The co-twin control design also controls for passive and evocative gene-environment correlations which arise when the genotype that influences an individual's outcome (e.g., psychotic symptoms) also influences the individual's exposure to certain environments (Plomin et al., 2013). Passive gene-environment correlation refers to the association between the genotype which an individual inherits from its parents (e.g., genes for psychosis) and the environment that an individual is raised in, which is also influenced by the parents' genotypes (e.g., parental unemployment). Evocative gene-environment correlation refers to the association between an individual's genetically influenced behaviour (e.g., behavioural problems) and the reactions that this behaviour induces in others (e.g., harsh parenting) (Jaffee & Price, 2008). Gene-environment correlations can lead to associations between environmental factors and mental health outcomes being incorrectly interpreted as causal, when the association is in fact confounded by genes. The twin difference method

gives an indication of the extent that the association between two variables is environmentally mediated.

The method follows several steps. First, residual scores are created by subtracting the score of one twin for a trait (e.g., psychotic symptoms) from the co-twin's score for that trait. Second, the score of one twin for an exposure (e.g., perceptions of neighbourhood adversity) is also subtracted from the co-twin's score for that exposure. The resulting residual scores reveal the difference between twins for both the exposure and the outcome. As described above, differences between MZ twins are only attributable to unique environmental influences. Differences between DZ twins are attributable to unique environmental influences as well as some genetic influences. Third, the residual score for the outcome is correlated with the residual score for the exposure. In combined samples of MZ and DZ twins, this analysis controls completely for common environmental influences and partly for genetic influences. A significant association between the residual exposure and outcome scores provides evidence of an environmentally mediated association. Chapter 6 uses the co-twin control design as an additional control step to account for unmeasured genetic and environmental sources of confounding of the association between perceptions of neighbourhood adversity and adolescent psychotic experiences as well as to hold neighbourhood environments constant by design.

3.8.3 The non-independence of twin observations

Since the E-Risk cohort is a twin sample, it is necessary to adjust all regression analyses for the within-twin pair correlated nature of the data. That is, observations are correlated between twin siblings, and this violates the assumption of independent residuals. This is accounted for by using the “CLUSTER” command in STATA, followed by the family (twin pair) identifier variable. This procedure is derived from the Huber-White variance

estimator and provides robust standard errors adjusted for within-cluster correlated data (Rogers, 1994). Within-pair correlation can also be handled via multilevel modelling approaches, by treating twin pairs as random effects. In Chapter 4, Supplementary Table 4.1 presents results from analyses using the “CLUSTER” command compared to multilevel approaches in STATA. Findings are similar regardless of which procedure is used. In neighbourhood research, it is often appropriate to use multilevel modelling techniques to control for the clustering of individuals within neighbourhoods (as described in Chapter 1). For example, participants (level 1) might be drawn from several schools (level 2) in several regions (level 3), and this non-independency must be modelled in order to obtain more stringent point estimates. In E-Risk, all neighbourhood measures apply to the postcode- or street-level, and there are no sets of E-Risk families that occupy the same neighbourhoods at this level. As such, the adjustment for family-level (twin) clustering, using the “CLUSTER” command, in effect also controls for neighbourhood-level clustering.

Chapter 4: Why are children in urban neighbourhoods at increased risk for psychotic symptoms? Findings from a UK longitudinal cohort study

This chapter is presented in the published format from the following publication:

Newbury, J., Arseneault, L., Caspi, A., Moffitt, T. E., Odgers, C. L., & Fisher, H. L. (2016). Why are children in urban neighbourhoods at increased risk for psychotic symptoms? Findings from a UK longitudinal cohort study. *Schizophrenia Bulletin*, 42(6), 1372-1383, doi.org/10.1093/schbul/sbw052

Why Are Children in Urban Neighborhoods at Increased Risk for Psychotic Symptoms? Findings From a UK Longitudinal Cohort Study

Joanne Newbury¹, Louise Arseneault¹, Avshalom Caspi^{1,2}, Terrie E. Moffitt^{1,2}, Candice L. Odgers^{3,4}, and Helen L. Fisher^{*,1,4}

¹MRC Social, Genetic & Developmental Psychiatry Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK; ²Departments of Psychology and Neuroscience, Psychiatry and Behavioral Sciences, and Centre for Genomic and Computational Biology, Duke University, Durham, NC; ³Center for Child and Family Policy and the Sanford School of Public Policy, Duke University, Durham, NC

⁴These authors are joint senior authors.

*To whom correspondence should be addressed; MRC Social, Genetic & Developmental Psychiatry Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, 16 De Crespigny Park, London SE5 8AF, UK; tel: +44-(0)207-848-5430, fax: +44-(0)207-848-0866, e-mail: helen.2.fisher@kcl.ac.uk

Background: Urban upbringing is associated with a 2-fold adulthood psychosis risk, and this association replicates for childhood psychotic symptoms. No study has investigated whether specific features of urban neighborhoods increase children's risk for psychotic symptoms, despite these early psychotic phenomena elevating risk for schizophrenia and other psychiatric disorders in adulthood. **Methods:** Analyses were conducted on over 2000 children from the Environmental Risk (E-Risk) Longitudinal Twin Study, a nationally-representative cohort of UK-born twins. Neighborhood-level characteristics were assessed for each family via: a geodemographic discriminator indexing neighborhood-level deprivation, postal surveys of over 5000 residents living alongside the children, and in-home interviews with the children's mothers. Children were interviewed about psychotic symptoms at age 12. Analyses were adjusted for important family-level confounders including socioeconomic status (SES), psychiatric history, and maternal psychosis. **Results:** Urban residency at age-5 (OR = 1.80, 95% CI = 1.16–2.77) and age-12 (OR = 1.76, 95% CI = 1.15–2.69) were both significantly associated with childhood psychotic symptoms, but not with age-12 anxiety, depression, or antisocial behavior. The association was not attributable to family SES, family psychiatric history, or maternal psychosis, each implicated in childhood mental health. Low social cohesion, together with crime victimization in the neighborhood explained nearly a quarter of the association between urbanicity and childhood psychotic symptoms after considering family-level confounders. **Conclusions:** Low social cohesion and crime victimization in the neighborhood

partly explain why children in cities have an elevated risk of developing psychotic symptoms. Greater understanding of the mechanisms leading from neighborhood-level exposures to psychotic symptoms could help target interventions for emerging childhood psychotic symptoms.

Key words: childhood psychotic symptoms/neighborhood characteristics/social cohesion/psychosis/urbanicity

Introduction

Urban vs rural upbringing doubles a child's odds of developing schizophrenia in adulthood.¹ The association between urbanicity and psychosis has been frequently replicated,^{2–10} shows a degree of specificity to non-affective psychoses,^{4,7,11,12} and is not explained by a range of potential confounding factors^{2,13–15} including migration of individuals with schizophrenia into cities.¹⁶ These converging lines of evidence suggest that the association between urbanicity and psychosis has genuine aetiological underpinnings,^{16–19} though the mechanisms driving the association are currently unknown. Urbanicity is therefore a key area for psychosis research, considering that over two-thirds of the world's population are predicted to live in cities by 2050.^{20,21}

The vast majority of urbanicity-psychosis research has focused on adult psychosis. Yet urban residency from birth to adolescence, rather than during adulthood, appears to be more strongly associated with adult

psychosis.^{6,10,13} Consistent with the neurodevelopmental model of schizophrenia, this suggests that the processes leading from urban exposure to psychosis begin in adolescence, childhood, or earlier. Notably, positive psychotic symptoms, such as hallucinations and delusions, are surprisingly prevalent among children in the general population.^{22–26} These early psychotic phenomena share familial and environmental risk factors with psychotic disorders,^{27–29} and whilst they are usually transitory,^{22,23,30} children who experience psychotic symptoms have a significantly elevated risk for schizophrenia and other psychoses in adulthood.^{31,32} Additionally, childhood psychotic symptoms have broad psychiatric relevance as they significantly heighten risk for other subsequent mental health difficulties including substance abuse,²⁶ depression,²⁶ PTSD,³² and suicidal behavior.^{32,33} Childhood psychotic symptoms are therefore a useful marker of early-life risk indicators for psychosis and general psychopathology. Childhood psychotic symptoms could also shed light on the urbanicity-psychosis association: a handful of studies have shown that these symptoms occur more frequently²⁹ and are more likely to persist into adulthood among youth living in urban vs nonurban settings.^{34,35} However, no studies have tested whether specific aspects of the urban environment increase risk for psychotic symptoms among children.

Indeed, urbanicity is only a proxy for the currently unknown operative risk factor(s) for psychosis.^{18,36} More recently, attention has turned to potential urban characteristics³⁷ operating at the neighborhood-level. Neighborhood-level deprivation has been frequently implicated in adult psychosis.^{17,38–43} However, modern urban neighborhoods are very mixed in terms of poverty and affluence,⁴⁴ whilst adult psychosis risk increases incrementally through increasing levels of urbanicity.^{2,3,6,13} Furthermore, the association between urbanicity and psychosis appears stronger in more recent generations,^{9,45} despite urban populations becoming generally wealthier. Thus, the association is difficult to explain through neighborhood-level deprivation alone. Cumulative evidence also supports the importance of neighborhood-level social processes such as crime,^{40,46} disorganization^{46,47} and social fragmentation^{37,39,41,48} in adult psychosis (thoroughly reviewed by March et al³⁶), which are purported to increase adult psychosis risk by heightening childhood exposure to social stressors.^{18,19,49,50} Intriguingly, prodromal status among young adults has been shown to follow spatial patterning in accordance with these kinds of neighborhood-level psychosocial characteristics.⁵¹ However, the longitudinal associations between neighborhood-level social processes and childhood psychotic symptoms are currently unknown. Ultimately, such research could help target social and clinical interventions for early psychotic symptoms.

Here we draw from sociological theory and evidence illustrating that neighborhood-level social processes

mediate the effect of neighborhood structural features (eg, urbanicity) on a range of health outcomes.^{52–54} Guided by this theory and adult psychosis findings, the current study focuses on 4 neighborhood-level social processes: (1) social cohesion, describing the cohesiveness and supportiveness of relationships between neighbors⁵²; (2) social control, describing the likelihood that neighbors would intervene in problems in the neighborhood⁵²; (3) neighborhood disorder, describing physical and social evidence of disorder/threat within the neighborhood⁵³; and (4) crime victimization, representing more direct experiences of victimization in the neighborhood (eg, mugging). The current study investigates the pathways leading from urbanicity to childhood psychotic symptoms, whilst differentiating the effects of specific neighborhood-level social processes from family-level effects. We utilized a cohort of 2232 nationally-representative British twin children who have been followed from birth to age 12 and interviewed for psychotic symptoms at age 12. Our longitudinal neighborhood-level measures were obtained from multiple sources, and neighborhood scores were allocated with fine geographic resolution (ie, postcode-level). With these measures, we asked: (1) Are children in urban vs nonurban neighborhoods at increased risk for psychotic symptoms? (2) Is this association specific to childhood psychotic symptoms? (3) Is the association between urbanicity and childhood psychotic symptoms explained by background characteristics of families living in cities? (4) Are urban neighborhoods more likely to lack social cohesion and social control and be characterized by disorder and crime? (5) Finally, does the level of social cohesion, social control, neighborhood disorder, and crime victimization operating within neighborhoods mediate the effect of urban residency on childhood psychotic symptoms? We hypothesized that the effect of urbanicity on childhood psychotic symptoms would be specific to this phenotype, and mediated via exposure to low social cohesion and social control, and high disorder and crime victimization in the neighborhood (proposed pathways shown in [figure 1](#)).

Methods

Study Cohort

Participants were members of the Environmental Risk (E-Risk) Longitudinal Twin Study, which tracks the development of a nationally-representative birth cohort of 2232 British twin children. The sample was drawn from a larger cohort of twins born in England and Wales in 1994–1995.⁵⁵ Full details about the sample are reported elsewhere.⁵⁶ Briefly, the E-Risk sample was constructed in 1999–2000, when 1116 families with same-sex 5-year-old twins (93% of those eligible) participated in home-visit assessments. Families were recruited to represent the UK population of families with newborns in the 1990s, based on residential location throughout England and Wales and mothers' age

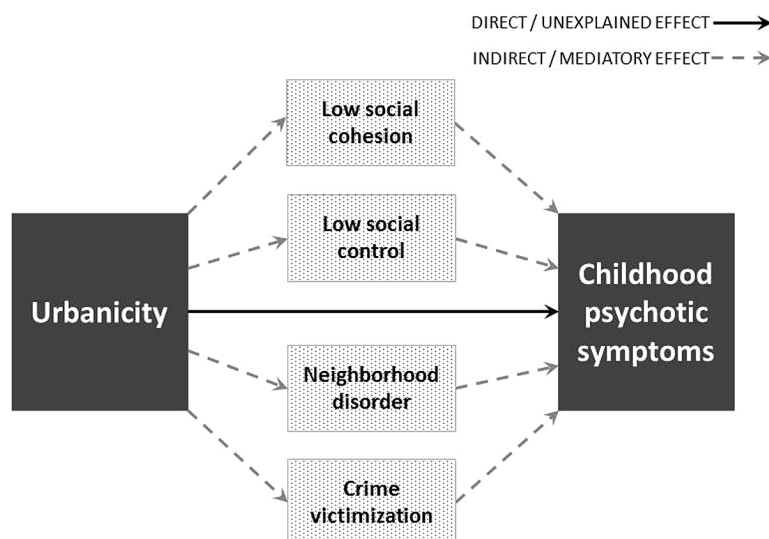


Fig. 1. Conceptualized pathways between urbanicity and childhood psychotic symptoms, with the total effects transmitting both directly (solid line), and indirectly (dashed lines) via neighborhood-level social process mediators (low social cohesion, low social control, high neighborhood disorder, and high crime victimization).

(teenaged mothers with twins were over-selected to replace high-risk families who were selectively lost to the register through non-response. Older mothers having twins via assisted reproduction were under-selected to avoid an excess of well-educated older mothers). E-Risk families are representative of UK households across the spectrum of neighborhood-level deprivation: 25.6% of E-Risk families live in “wealthy achiever” neighborhoods compared to 25.3% of households nation-wide; 5.3% vs 11.6% live in “urban prosperity” neighborhoods; 29.6% vs 26.9% live in “comfortably off” neighborhoods; 13.4% vs 13.9% live in “moderate means” neighborhoods; and 26.1% vs 20.7% live in “hard-pressed” neighborhoods.^{57,58} E-Risk families under-represent “urban prosperity” neighborhoods because such households are likely to be childless. Sex was evenly distributed in the resulting sample (49% male). All families were English speaking, and the majority (93.7%) were White. Follow-up home-visits were conducted when children were aged 7, 10, and 12 (participation rates were 98%, 96%, and 96%, respectively). At age 12, the E-Risk sample comprised 2146 twin children, and the majority of these children had complete data on both psychotic symptoms and urbanicity at age 12 (95.7%; $N = 2054$). Over half of children (56.7%, $N = 1180$) never moved house at all between ages 5 and 12, and of those who did nearly two-thirds (65.0%) moved less than 500 meters. The Joint South London and Maudsley and the Institute of Psychiatry Research Ethics Committee approved each phase of the study. Parents gave informed consent and children gave assent.

Measures

Childhood Psychotic Symptoms. E-Risk families were visited by mental health trainees or professionals when

children were aged 12.²⁹ Each child was privately interviewed about 7 psychotic symptoms pertaining to delusions and hallucinations, with items including “have other people ever read your thoughts?”, “have you ever thought you were being followed or spied on?”, and “have you ever heard voices that other people cannot hear?”. This interview has been described in detail previously.²⁹ The item choice was guided by the Dunedin Study’s age-11 interview protocol³¹ and an instrument prepared for the Avon Longitudinal Study of Parents and Children.⁵⁹ Interviewers coded each experience 0, 1, 2 indicating respectively “not a symptom,” “probable symptom,” and “definite symptom.” A conservative approach was taken in designating a child’s report as a symptom. First, the interviewer probed using standard prompts designed to discriminate between experiences that were plausible (eg, “I was followed by a man after school”) and potential symptoms (eg, “I was followed by an angel who guards my spirit”), and wrote down the child’s narrative description of the experience. Second, items and interviewer notes were assessed by a psychiatrist expert in schizophrenia, a psychologist expert in interviewing children, and a child and adolescent psychiatrist to verify the validity of the symptoms. Third, because children were twins, experiences limited to the twin relationship (eg, “My twin and I often know what each other are thinking”) were coded as “not a symptom”. Children were only designated as experiencing psychotic symptoms if they reported at least one definite symptom. At age 12, 5.9% ($N = 125$) of children reported experiencing psychotic symptoms. This is similar to the prevalence of psychotic symptoms in other community samples of children and adolescents.^{22–26} Furthermore, we previously showed that childhood psychotic symptoms in this cohort have good

construct validity, sharing many of the genetic, social, neurodevelopmental, and behavioral risk factors and correlates as adult schizophrenia.²⁹ Additionally, as we focused on psychotic symptoms rather than diagnoses, the present study design avoids confounding by psychiatric service utilization.

Urbanicity. Urban/nonurban classification of E-Risk families' neighborhoods was based on responses from a postal survey sent to residents living alongside E-Risk families when children were aged 12.^{60,61} Questionnaires were sent to every household in the same postcode as the E-Risk families, excluding the E-Risk families themselves (addresses were identified from electoral roll records). The number of surveys sent ranged from 15 to 50 residences per neighborhood (Average = 18.96, SE = 0.21). Excluding undelivered surveys ($N = 600$), the overall response rate was 28.1% (5601/19 926). Survey respondents typically lived on the same street or within the same apartment block as the children in our study. Surveys were returned by an average of 5.18 (SD = 2.73) respondents per neighborhood (range = 0–18 respondents), and there were at least 2 responses from 95% of the neighborhoods ($N = 5601$ respondents).⁶¹ Residents reported whether their neighborhood was in “a city,” “a town,” “a suburb,” “a small village,” or “the countryside.”²⁹ There was high agreement between residents in the same neighborhood, with only 50 neighborhoods returning discordant responses (ie, neighborhoods where residents differed in their urbanicity responses). These 50 ambiguous neighborhoods were clarified by a British researcher (blind to any phenotypic/identifying data) using the children's full postcode, Google Aerial view and the Office of National Statistics' population density map (http://www.neighbourhood.statistics.gov.uk/HTMLDocs/PopulationDensity_2010.html, last accessed April 28, 2016), based on a combination of features including population density, building density, proximity to the countryside or city/town centre, land-use (eg, agriculture, transportation, industry, etc.), and the official definition of the settlement. This same method was used to estimate urbanicity at age-5 for the 35% of children who had moved over 500 metres between ages 5 and 12. For ease of interpretation and to increase analytic power, urbanicity is herein dichotomized as urban (1: city/town) vs non-urban (0: suburb/small village/countryside). At age 12, the sample was split evenly between urban and nonurban neighborhoods, with 51.9% ($N = 1066$) of children living in urban neighborhoods and the remaining 988 children living in nonurban neighborhoods. Similarly, 55.1% ($N = 1117$) lived in urban neighborhoods at age 5.

Neighborhood-Level Deprivation. Neighborhood-level deprivation was constructed using A Classification of Residential Neighbourhoods (ACORN), a geodemographic discriminator developed by CACI Information

Services (<http://www.caci.co.uk/>, last accessed April 28, 2016).⁵⁷ Detailed information about ACORN's classification of neighborhood-level socioeconomic-status (SES) has been provided previously.^{58,60,62} Briefly, CACI utilized over 400 variables from 2001 census data for Great Britain (eg, educational qualifications, unemployment, housing tenure) and CACI's consumer lifestyle database. Following hierarchical-cluster-analysis, 5 distinct and homogeneous ordinal groups were created ranging from “Wealthy Achiever” (coded 1) to “Hard Pressed” (coded 5) neighborhoods. Each family in our sample was matched to the ACORN code for its neighborhood via its postcode (age 5 or age 12 postcode, where relevant).⁵⁸

Neighborhood-Level Social Processes. Social processes included social cohesion, social control, neighborhood disorder and crime victimization, and were measured in both early and late childhood. Social processes were first measured at age 5 via in-home interviews with the children's mothers.⁶³ Social cohesion⁵² (5 items) was assessed by asking mothers whether their neighborhood was close-knit, whether neighbors shared values, and whether neighbors trusted and got along with each other, etc. Higher scores indicate greater social cohesion. Social control⁵² (5 items) was assessed by asking mothers to judge whether people in their neighborhoods would take action against different types of undesirable activities (eg, children skipping school, fights in public places). Higher scores indicate greater social control. For neighborhood disorder,⁵³ mothers were asked whether 13 problems affected their neighborhood, including noisy neighbors, arguments or loud parties, vandalism, graffiti or deliberate damage to property, and cars broken into. Higher scores indicate greater neighborhood disorder. Crime victimization was assessed by asking mothers whether they or their family had been victimized by violent crime (eg, mugging, assault), a burglary, or a theft in the neighborhood. Higher scores indicate greater crime victimization. Items (each coded 0–2) within each social process scale were summed for each mother. Social processes were also measured when children were aged 12 via the resident surveys^{60,61} (survey methodology described in detail under urbanicity heading). Residents were asked the same questions regarding these 4 neighborhood-level social processes. For the resident reports, the social process scales were created in 2 steps. First, items belonging to each social process scale were averaged to create summary scores for each of the 5601 respondents. Second, scores for each E-Risk family were created by averaging the social process scores of respondents within that neighborhood.

Thus, neighborhood-level social processes were estimated both before and contemporaneously to childhood psychotic symptoms, enabling us to triangulate a prospective design with objective neighborhood appraisals. At age 5, mothers' views of the neighborhood were used as mothers are considered more reliable reporters

than children at this age and because their perceptions are likely to influence their children's amount of exposure and experiences in the neighborhood.^{64,65} At age 12, resident reports were used to gain more objective and comprehensive assessments of the neighborhood. As children themselves reported on their own psychotic symptoms at age 12, both our age-5 (mother-reported) and age-12 (resident-reported) assessments of neighborhood-level social processes are obtained from independent sources.

Other Age-12 Outcomes. Anxiety was assessed when children were aged 12, via private interviews using the 10-item version of the Multidimensional Anxiety Scale for Children (MASC).⁶⁶ An extreme anxiety group was formed with children who scored at or above the 95th percentile ($N = 129$, 6.1%). Depression symptoms were assessed at age 12 using the Children's Depression Inventory (CDI).⁶⁷ Children who scored 20 or more⁶⁸ were deemed to have clinically significant depressive symptoms ($N = 74$, 3.5%). Antisocial behavior was assessed using the Achenbach system of empirically-based assessment.⁶⁹ An extreme antisocial behavior group was formed with children who scored at or above the 95th percentile ($N = 110$, 5.1%), based on combined mother and teacher reports at age 12.⁷⁰

Family-Level Confounders. Family SES was measured via a composite of parental income (total household), education (highest mother/father), and occupation (highest mother/father) when children were aged 5, and was categorized into tertiles (ie, low-, medium-, and high-SES). Family psychiatric history and maternal psychosis were both assessed when children were aged 12. In private interviews, mothers reported on family history of DSM disorders,⁷¹ which was converted to a proportion (0–1.0) of family members with a history of psychiatric disorder. For maternal psychosis, mothers were interviewed using the Diagnostic Interview Schedule⁷² for DSM-IV⁷³ which provides a symptom count for characteristic symptoms of schizophrenia (eg, hallucinations, delusions, anhedonia).

Statistical Analysis. Analyses were conducted in STATA 11.2 (Stata-Corp). Firstly, linear regression was used to investigate the association between urbanicity and neighborhood-level social processes (table 1). Secondly, logistic regression was used to investigate the associations between neighborhood-level social processes and childhood psychotic symptoms (table 2). Thirdly, our mediation analyses utilized KHB pathway decomposition (table 3).⁷⁴ This procedure partitions the total effect of one variable (urbanicity) on another variable (childhood psychotic symptoms) into the direct effect (which also includes the effects of unknown/unspecified mediators and measurement error), and indirect effects explained by specified mediators (neighborhood-level social processes). Age-5 urbanicity is used when age-5

social processes are analyzed; age-12 urbanicity is used when age-12 social processes are analyzed. As the scales differed between the age-5 (mother-reported) and age-12 (resident-reported) social process variables, social process variables in steps 2 and 3 were standardized with a mean of 0 and a SD of 1 (subtraction of the mean then division by the SD) to facilitate comparability of the results. Where appropriate, analyses accounted for the non-independence of observations using the "CLUSTER" command because the sample comprised twins. This procedure is derived from the Huber-White variance estimator, and provides robust standard errors adjusted for within-cluster correlated data⁷⁵ (Note: within-pair twin correlations can also be corrected using multi-level approaches. [Supplementary table 1](#) shows that our main logistic regression analyses are highly robust to alternative estimation procedures.).

Results

Are Children in Urban vs Nonurban Neighborhoods at Increased Risk for Psychotic Symptoms?

There was a significant cross-sectional association between age-12 urban residency and childhood psychotic symptoms ($OR = 1.76$, 95% $CI = 1.15–2.69$, $P = .009$). Around 7.4% ($N = 79$) of urban-dwelling children compared to 4.4% ($N = 43$) of nonurban-dwelling children experienced at least one definite psychotic symptom at age 12. The association between urbanicity and psychotic symptoms held when analyses were restricted to the 56.6% of children who never moved house between ages 5 and 12 ($OR = 2.01$, 95% $CI = 1.14–3.58$, $P = .017$), and when controlling for residential mobility during this period ($OR = 1.71$, 95% $CI = 1.12–2.61$, $P = .014$). The association also held for the 93.7% of children who were ethnically White ($OR = 1.85$, 95% $CI = 1.21–2.84$, $P = .005$). Although in our sample there was a tendency for urban neighborhoods to be more deprived ($OR = 2.57$, 95% $CI = 1.99–3.32$, $P < .001$), half of urban neighborhoods were relatively affluent (ACORN categories 1–3; 50.3%), and over a quarter of nonurban neighborhoods were considered deprived (ACORN categories 4 and 5; 27.8%). Moreover, when urbanicity and neighborhood deprivation were included in a logistic regression model together, they were both significantly associated with childhood psychotic symptoms ($OR = 1.62$, 95% $CI = 1.03–2.56$, $P = .039$; $OR = 1.62$, 95% $CI = 1.05–2.50$, $P = .029$, respectively), demonstrating that urbanicity is associated with childhood psychotic symptoms largely independently of neighborhood-level deprivation in this sample. Additionally, the association between urbanicity and childhood psychotic symptoms held when earlier urbanicity at age 5 was examined ($OR = 1.80$, 95% $CI = 1.16–2.77$, $P = .008$). Therefore, the remaining analyses in this article will focus on tracing the effects of urbanicity (age-5 or age-12, where appropriate) on childhood psychotic symptoms.

Table 1. Bivariate Associations Between Urbanicity and Neighborhood-Level Social Processes

Neighborhood-Level Social Processes	Range	Urban	Nonurban	Standardized Association Between Urbanicity and Social Processes	
		<i>M</i> (SD)	<i>M</i> (SD)	<i>B</i> ^a	<i>P</i> Value
Age-5 (mother reports) ^b					
Social cohesion	0–10	7.11 (2.95)	8.18 (2.32)	–.19	<.001
Social control	0–10	7.04 (2.88)	7.91 (2.41)	–.16	<.001
Neighborhood disorder	0–22	4.40 (4.15)	3.46 (3.24)	.12	<.001
Crime victimization	0–6	1.06 (1.39)	0.75 (1.18)	.12	<.001
Age-12 (resident reports) ^c					
Social cohesion	0–4	2.11 (0.50)	2.36 (0.47)	–.25	<.001
Social control	0–4	2.09 (0.53)	2.33 (0.51)	–.22	<.001
Neighborhood disorder	0–2	0.56 (0.35)	0.40 (0.32)	.23	<.001
Crime victimization	0–2	0.22 (0.24)	0.15 (0.19)	.16	<.001

Note: *B*, standardized beta coefficient; *M*, mean. Social cohesion and social control consistently have negative beta coefficients, demonstrating that urban neighborhoods had lower levels of social cohesion and social control compared to nonurban neighborhoods. In contrast, neighborhood disorder and crime victimization consistently have positive beta coefficients, demonstrating that urban neighborhoods had higher levels of disorder and crime victimization compared to nonurban neighborhoods. All analyses account for the nonindependence of twin observations.

^aThe standardized (*B*) beta coefficients indicate the unit SD change in each social process given 1 unit SD change in urbanicity, and allow comparison between each social process. Standardized betas provide exactly the same point estimates as correlation coefficients and may be interpreted as correlations, with a score of –1.0 indicating a 100% negative correlation and a score of +1.0 indicating a 100% positive correlation.

^bAge-5 urbanicity is used for the bivariate associations between urbanicity and age-5 mother-reported social processes.

^cAge-12 urbanicity is used for the bivariate associations between urbanicity and age-12 resident-reported social processes. Age-12 resident-reported social process scores were imputed for 2 children with missing data.

Table 2. Bivariate Associations Between Neighborhood-Level Social Processes and Childhood Psychotic Symptoms

Neighborhood-Level Social Processes	OR	95% CI	<i>P</i> Value
Age-5 (mother reports)			
Social cohesion	0.68	[0.58, 0.82]	<.001
Social control	0.75	[0.62, 0.91]	.003
Neighborhood disorder	1.26	[1.06, 1.51]	.010
Crime victimization	1.40	[1.19, 1.65]	<.001
Age-12 (resident reports) ^a			
Social cohesion	0.76	[0.65, 0.89]	.001
Social control	0.83	[0.69, 1.00]	.050
Neighborhood disorder	1.27	[1.07, 1.52]	.007
Crime victimization	1.17	[0.96, 1.42]	.123

Note: Social cohesion and social control are consistently associated with odds lower than 1 for childhood psychotic symptoms, demonstrating that children were less likely to experience psychotic symptoms in neighborhoods with higher levels of social cohesion and social control. In contrast, neighborhood disorder and crime victimization are consistently associated with odds greater than 1 for childhood psychotic symptoms, demonstrating that children were more likely to experience psychotic symptoms in neighborhoods with higher levels of neighborhood disorder and crime victimization. All analyses account for the nonindependence of twin observations. All social process variables have been standardized with a mean of 0 and a SD of 1.

^aAge-12 resident-reported social process scores were imputed for 2 children with missing data.

Is Urbanicity Specifically Associated With Childhood Psychotic Symptoms?

Our assumption of specificity to psychotic symptoms was tentatively supported, as associations between age-12 urbanicity and age-12 depression (OR = 1.16, 95% CI = 0.69–1.96, *P* = .571), anxiety (OR = 1.42, 95% CI = 0.95–2.12, *P* = .091) and antisocial behavior (OR = 0.93, 95% CI = 0.59–1.47, *P* = .753) were each nonsignificant, with smaller effect sizes than demonstrated for psychotic symptoms. However, given that the CIs for both depression and anxiety included the point estimate for the association between age-12 urbanicity and childhood psychotic symptoms (OR = 1.76), we cannot be sure that these associations differed significantly. Nevertheless, after simultaneous adjustment for age-12 depression, anxiety and antisocial behavior, urbanicity remained significantly associated with childhood psychotic symptoms (OR = 1.74, 95% CI = 1.15–2.65, *P* = .009), suggesting that urbanicity was independently associated with childhood psychotic symptoms in this sample. Furthermore, the associations between urbanicity and these 3 additional age-12 outcomes remained nonsignificant when they were recategorized at a lower threshold (80th percentile), suggesting that the negative findings were not due to inadequate power (results available upon request).

Table 3. Association Between Urbanicity and Childhood Psychotic Symptoms, Split Into Total Effects, and Direct and Indirect Pathways via Neighborhood-Level Social Process Mediators

Potential Neighborhood-Level Social Process Mediators	Mediation Model 1				Mediation Model 2 ^a					
	Sample Size	Total OR [95% CI]	Direct OR [95% CI]	Indirect OR [95% CI]	% Mediated ^b	Sample Size	Total OR [95% CI]	Direct OR [95% CI]	Indirect OR [95% CI]	% Mediated ^b
Age-5 (mother reports) ^c										
Social cohesion	2014	1.71* [1.10, 2.64]	1.49† [0.95, 2.35]	1.15** [1.05, 1.25]	25	2005	1.58* [1.00, 2.49]	1.46 [0.92, 2.33]	1.08* [1.02, 1.16]	17
Social control	1998	1.74* [1.13, 2.70]	1.62* [1.04, 2.54]	1.07* [1.00, 1.15]	13	1989	1.62* [1.03, 2.55]	1.57† [0.99, 2.48]	1.04 [0.99, 1.09]	8
Neighborhood disorder	2022	1.72* [1.11, 2.66]	1.65* [1.06, 2.57]	1.04 [0.99, 1.09]	7	2013	1.58* [1.01, 2.49]	1.57† [0.99, 2.47]	1.01 [0.98, 1.04]	2
Crime victimization	2022	1.71* [1.11, 2.65]	1.59* [1.02, 2.48]	1.07* [1.02, 1.13]	13	2013	1.57† [1.00, 2.47]	1.50† [0.95, 2.37]	1.05 [1.00, 1.10]	11
Age-12 (resident reports) ^d										
Social cohesion	2054	1.76** [1.15, 2.69]	1.58* [1.03, 2.43]	1.11* [1.02, 1.21]	19	2045	1.61* [1.03, 2.50]	1.53† [0.98, 2.40]	1.05 [0.97, 1.13]	10
Social control	2054	1.76** [1.15, 2.69]	1.66* [1.07, 2.57]	1.06 [0.97, 1.16]	11	2045	1.61* [1.03, 2.51]	1.58* [1.00, 2.50]	1.02 [0.94, 1.10]	4
Neighborhood disorder	2054	1.76** [1.15, 2.69]	1.60* [1.01, 2.53]	1.10† [1.00, 1.21]	16	2045	1.61* [1.03, 2.51]	1.55† [0.97, 2.49]	1.04 [0.96, 1.12]	7

Note: The sample sizes and total effect ORs vary slightly for the age-5 mother reports of social processes, due to small numbers of children missing data on neighborhood-level social processes and/or family-level covariates. These sample size differences also account for the difference between the main effect OR (1.80) and the total effect ORs for mother reports in Mediation model 1. Social processes can still be compared for the percentage that they mediate the total effect of urbanicity. We also conducted mediation analyses using Full Information Maximum Likelihood (FIML) in Mplus to include all available cases at age 5 ($N = 2232$ for all Models reported) and found no differences in the size, direction or pattern of effects. Total effect = overall association between urbanicity and childhood psychotic symptoms; direct effect = the part of the overall association that is not explained by the mediator/covariates in the model; and indirect effect = the part of the overall association that is explained by the social process mediator in the model. Bold text denotes significant indirect (mediation) pathways at $P < .05$. All analyses account for the nonindependence of twin observations. All social process variables have been standardized with a mean of 0 and a SD of 1.

^aThe total, direct and indirect ORs in mediation model 2 are adjusted for family-level confounders: family socioeconomic status, family psychiatric history, and maternal psychosis.

^bPercentages rounded to whole numbers.

^cAge-5 urbanicity is used for the mediation analysis of urbanicity and childhood psychotic symptoms via age-5 mother-reported social processes.

^dAge-12 urbanicity is used for the mediation analysis of urbanicity and childhood psychotic symptoms via age-12 resident-reported social processes. Age-12 resident-reported social process scores were imputed for 2 children with missing data.

* $P < .05$, ** $P < .01$, †Nominally significant $P > .05$ and $P < .1$.

Is the Association Between Urbanicity and Childhood Psychotic Symptoms Explained by Background Characteristics of Families Living in Cities?

The association between age-12 urbanicity and childhood psychotic symptoms did not appear to be explained by 3 key potential family-level confounders, namely family SES, family psychiatric history and maternal psychosis. Simultaneous adjustment for these proxy indicators of genetic and environmental risk only slightly attenuated the association between age-12 urbanicity and childhood psychotic symptoms (OR = 1.61, 95% CI = 1.04–2.51, $P = .035$).

Are Urban Neighborhoods More Likely to Lack Social Cohesion and Social Control and Be Characterized by Disorder and Crime?

Associations of urbanicity with neighborhood-level social processes are shown in [table 1](#). At age 5, urban neighborhoods had (ie, mothers reported) significantly lower social cohesion and social control, and significantly higher neighborhood disorder and crime victimization than nonurban neighborhoods (all P s < .001). Similar bivariate associations were found between urbanicity and social processes for age-12 neighborhoods (residents' reports) (all P s < .001; [table 1](#)).

Associations of neighborhood-level social processes with childhood psychotic symptoms are shown in [table 2](#). Children were significantly less likely to experience psychotic symptoms at age 12 if, at age 5, they lived in neighborhoods with higher social cohesion ($P < .001$) and higher social control ($P = .003$). In contrast, children were significantly more likely to experience psychotic symptoms at age 12 if their age-5 neighborhood was characterized by higher neighborhood disorder ($P = .010$) and higher crime victimization ($P < .001$). A comparable cross-sectional pattern was found for the associations between age-12 neighborhood-level social processes and childhood psychotic symptoms, though social control was borderline statistically significant ($P = .050$) and neighborhood-level crime victimization failed to reach conventional levels of statistical significance ($P = .123$; [table 2](#)).

Do Neighborhood-Level Social Processes Mediate the Effect of Urban Residency on Childhood Psychotic Symptoms?

We investigated the extent that neighborhood-level social processes mediated the effect of urban residency on childhood psychotic symptoms ([figure 1](#)). Social processes were only included if they were significantly associated with both urbanicity and childhood psychotic symptoms (ie, age-12 neighborhood-level crime victimization was excluded as it was not associated with childhood psychotic symptoms at $P < .05$). [Table 3](#) shows results as odds ratios with 95% CIs for the total (overall association), direct

(the part of the overall association that is not explained by the mediator/covariates in the model) and indirect (the part of the overall association that is explained by the social process mediator in the model) effects of urbanicity on childhood psychotic symptoms. A model in which the indirect OR is equal to the total OR would indicate that the effect of the predictor on the outcome is entirely (100%) mediated by the specified mediator. Mediation model 1 is unadjusted, and Mediation model 2 is adjusted for family-level confounders (family SES, family psychiatric history, maternal psychosis) (Note: sample size and total effect ORs vary slightly within [table 3](#) due to small numbers of children missing data on age-5 neighborhood-level social processes and/or family-level confounders. Further detail is provided in [Table 3's](#) footnote.). Mediation model 1 shows that neighborhood-level low social cohesion at age 5 significantly mediated the effect of age-5 urbanicity on age-12 psychotic symptoms, explaining 25% of the association. Low social control and high crime victimization in the neighborhood also significantly mediated the effect of age-5 urbanicity on childhood psychotic symptoms, each explaining 13% of the association. These prospective models were somewhat supported by our cross-sectional analysis of age-12 urbanicity and age-12 social processes, in that low social cohesion once again significantly explained the largest proportion of the association between urbanicity and childhood psychotic symptoms (19%). These mediatory effects were slightly attenuated after considering family-level confounders (Mediation model 2, [table 3](#)). Nonetheless, following adjustment, neighborhood-level low social cohesion and high crime victimization at age 5 still significantly mediated the effect of age-5 urbanicity on childhood psychotic symptoms (explaining 17% and 11%, respectively). When age-5 social cohesion and crime victimization were simultaneously modeled, together they explained nearly a quarter of the effect of age-5 urbanicity on age-12 psychotic symptoms (24%: OR = 1.11, 95% CI = 1.03–1.20, $P = .004$).

Discussion

This is the first study to investigate whether specific psychosocial features of the urban environment increase children's risk for psychotic symptoms. Our findings add to existing knowledge in at least 3 ways. First, children living in urban neighborhoods were ~80% more likely to experience psychotic symptoms at age 12 compared to children living in nonurban neighborhoods. This association held in both prospective and cross-sectional models, and was not explained by the socioeconomic or psychiatric composition of urban families. Second, psychotic symptoms were more common among children living in neighborhoods characterized by low social cohesion, low social control, high neighborhood disorder, and where the family had been directly victimized by a crime. Our findings

highlight that these neighborhood-level social processes, which are implicated in adult psychosis,^{17,37,39,40,46–48} may also be relevant to positive psychotic symptoms in childhood. Third, low social cohesion explained the largest proportion of the effect of urbanicity on childhood psychotic symptoms, regardless of reporter (17% for mother reports, 10% for resident reports), and independently of the potential family-level confounders measured in this study. Furthermore, social cohesion together with crime victimization at age-5 explained almost a quarter of the effect of age-5 urbanicity on childhood psychotic symptoms. Though we have investigated childhood psychotic symptoms as the main outcome measure, our findings regarding social cohesion and crime victimization are consistent with previous studies implicating area-level social fragmentation^{39,41,47} (or related constructs) and crime^{40,46} in adult psychosis.

A significant minority of children experience persistent psychotic symptoms and eventual clinical diagnosis.^{31,32} Furthermore, urban upbringing is highly correlated with urban adult residency.⁶ Taken together, ours and previous findings are consistent with the proposal that early-life exposure to neighborhood-level social stressors contributes to the heightened psychosis rates found in cities.^{17–19,49,50} From a child's perspective, growing up in a crowded neighborhood characterized by insecure/nonexistent social support networks, unfriendly/unpredictable interactions between neighbors, and fear of exposure to crime could promote psychotic symptoms in various mutually compatible ways. Prolonged exposure to neighborhood-level social stressors could dysregulate the hypothalamic–pituitary–adrenal axis,⁷⁶ dopaminergic system,⁵⁰ and/or neurodevelopment,²¹ increasing risk for psychotic symptoms particularly among children with genetic predisposition.⁷⁷ A cognitive mechanism, with specific adverse neighborhood-level experiences exacerbating or providing content to emerging delusions and hallucinations⁷⁸ could also explain why urbanicity was associated with positive psychotic symptoms but not significantly with anxiety or depression.⁷⁹ These neighborhood effects could also be transmitted indirectly by heightening children's exposure to family-level stress or even maltreatment. Indeed, low neighborhood-level social cohesion appears to undermine positive parenting practices.⁸⁰ The individual-level factors and potential mechanisms leading from neighborhood-level adverse exposures to childhood psychotic symptoms now require attention. For example, children raised in urban vs non-urban neighborhoods could differ in their neurocognitive reactivity to social stress, as recently demonstrated among healthy adults.^{81,82}

Limitations

Five limitations deserve mention. First, causal inference is limited as families were not randomly selected

into neighborhoods. Whilst we adjusted for a number of important proxy measures of genetic and environmental risk, various non/reverse-causal explanations remain possible. Future research with larger samples, and ideally quasi-experimental designs, are required to more persuasively rule out social selection as an explanation for these findings. The role of gene-environment correlation (eg, individuals with higher genetic risk for psychosis “drifting” into urban neighborhoods) can also now be estimated via emerging methods such as polygenic risk score analysis. Second, childhood psychotic symptoms are relatively rare, with only ~6% of children reporting symptoms in the E-Risk cohort at age 12. Our findings would benefit from replication. Third, this low base-rate also made it necessary to dichotomize urbanicity to increase power. This potentially simplified our findings, particularly given previous evidence for a dose-response urbanicity-psychosis association through the range of urbanicity. Fourth, although childhood psychotic symptoms are thought to lie on a continuum with schizophrenia,⁸³ they are also associated with other psychiatric disorders in adulthood^{26,32,33} and therefore the current findings may extend beyond schizophrenia to risk for serious adult psychopathology in general. Finally, the E-Risk cohort is a twin sample, and whether findings from twin studies generalize to singletons is sometimes contested. However, the children in our study are representative of singletons for the prevalence of psychotic symptoms,^{22–26} and representative of UK families in terms of geographic and socioeconomic distribution.^{57,58}

Importantly, neighborhood-level social processes did not completely explain the effect of urbanicity in our analyses. Future investigations should consider a wider range of potential social and physical neighborhood-level characteristics when testing for environmental contributions to childhood psychotic symptoms. Neighborhood-level physical exposures such as noise, light, and air pollution, as well as exposure to viral infections warrant research in relation to early psychotic symptoms. The modest mediation could also be partly attributable to measurement error entailed in the neighborhood-level social process measures. Additionally, it is possible that up to age 12 the children in our study were relatively sheltered from certain threats in their neighborhoods. Cumulative neighborhood-level exposures, from childhood, through adolescence and into adulthood, may each contribute in different ways or combine to increase risk for psychotic symptoms. It will therefore be important to investigate the contribution of neighborhood-level social processes to the emergence of psychotic symptoms in late adolescence, when many children will have experienced more direct exposure to adversity in their neighborhood.

Conclusion

In this study, the increased risk for childhood psychotic symptoms in urban neighborhoods was explained, in

part, by lower levels of social cohesion and higher levels of crime victimization operating within these neighborhoods. If these novel findings are replicated, they could support the role of exposure to neighborhood-level social stressors in the aetiology of childhood psychotic symptoms.^{17,18,46} Populations are becoming increasingly urban, and child and adolescent psychopathology represents a growing proportion of the global burden of disease.⁸⁴ The present findings therefore underscore the emerging need to identify the social, psychological, and biological pathways leading from neighborhood-level exposures to childhood psychotic symptoms.

Supplementary Material

Supplementary material is available at <http://schizophreniabulletin.oxfordjournals.org>.

Funding

The E-Risk study is funded by the UK Medical Research Council (G1002190, G9806489). This work was supported by the Economic and Social Research Council (RES-177-25-0013, and a Multidisciplinary Studentship to J.N.); National Institute of Child Health and Development (HD061298); MQ: Transforming Mental Health (MQ14F40); Google Streetview; British Academy (SQ140024); William T. Grant Foundation; and Jacobs Foundation. C.L.O. is a Jacobs Foundation Advanced Research Fellow.

Acknowledgments

We are grateful to the study mothers and fathers, the twins, and the twins' teachers for their participation. Our thanks to members of the E-Risk team for their dedication, hard work, and insights, and to CACI Inc. for use of their consumer lifestyle databases. We also thank Emma Hedman, Jill Collins and Paul Langston for their geocoding assistance. The authors have declared that there are no conflicts of interest in relation to the subject of this study.

References

1. Vassos E, Pedersen CB, Murray RM, Collier DA, Lewis CM. Meta-analysis of the association of urbanicity with schizophrenia. *Schizophr Bull.* 2012;38:1118–1123.
2. Lewis G, David A, Andréasson S, Allebeck P. Schizophrenia and city life. *Lancet.* 1992;340:137–140.
3. van Os J, Hanssen M, Bijl RV, Vollebergh W. Prevalence of psychotic disorder and community level of psychotic symptoms: an urban-rural comparison. *Arch Gen Psychiatry.* 2001;58:663–668.
4. 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.* 2004;184:293–298.
5. Allardyce J, Boydell J, Van Os J, et al. Comparison of the incidence of schizophrenia in rural Dumfries and Galloway and urban Camberwell. *Br J Psychiatry.* 2001;179:335–339.
6. Pedersen CB, Mortensen PB. Evidence of a dose-response relationship between urbanicity during upbringing and schizophrenia risk. *Arch Gen Psychiatry.* 2001;58:1039–1046.
7. Kelly BD, O'Callaghan E, Waddington JL, et al. Schizophrenia and the city: a review of literature and prospective study of psychosis and urbanicity in Ireland. *Schizophr Res.* 2010;116:75–89.
8. Lundberg P, Cantor-Graae E, Rukundo G, Ashaba S, Ostergren PO. Urbanicity of place of birth and symptoms of psychosis, depression and anxiety in Uganda. *Br J Psychiatry.* 2009;195:156–162.
9. Marcelis M, Navarro-Mateu F, Murray R, Selten JP, Van Os J. Urbanization and psychosis: a study of 1942–1978 birth cohorts in The Netherlands. *Psychol Med.* 1998;28:871–879.
10. 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.* 1999;29:1197–1203.
11. Pedersen CB, Mortensen PB. Urbanicity during upbringing and bipolar affective disorders in Denmark. *Bipolar Disord.* 2006;8:242–247.
12. Vassos E, Agerbo E, Mors O, Pedersen CB. Urban–rural differences in incidence rates of psychiatric disorders in Denmark [published online ahead of print December 17, 2015]. *Br J Psychiatry.* doi:10.1192/bjp.bp.114.161091.
13. Mortensen PB, Pedersen CB, Westergaard T, et al. Effects of family history and place and season of birth on the risk of schizophrenia. *N Engl J Med.* 1999;340:603–608.
14. van Os J, Hanssen M, Bak M, Bijl RV, Vollebergh W. Do urbanicity and familial liability coparticipate in causing psychosis? *Am J Psychiatry.* 2003;160:477–482.
15. Harrison G, Fouskakis D, Rasmussen F, 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.* 2003;33:723–731.
16. Pedersen CB. Persons with schizophrenia migrate towards urban areas due to the development of their disorder or its prodromata. *Schizophr Res.* 2015;168:204–208.
17. Kirkbride JB, Jones PB, Ullrich S, Coid JW. Social deprivation, inequality, and the neighborhood-level incidence of psychotic syndromes in East London. *Schizophr Bull.* 2014;40:169–180.
18. Krabbendam L, van Os J. Schizophrenia and urbanicity: a major environmental influence—conditional on genetic risk. *Schizophr Bull.* 2005;31:795–799.
19. Heinz A, Deserno L, Reininghaus U. Urbanicity, social adversity and psychosis. *World Psychiatry.* 2013;12:187–197.
20. Dye C. Health and urban living. *Science.* 2008;319:766–769.
21. Lederbogen F, Kirsch P, Haddad L, et al. City living and urban upbringing affect neural social stress processing in humans. *Nature.* 2011;474:498–501.
22. Kelleher I, Connor D, Clarke MC, et al. Prevalence of psychotic symptoms in childhood and adolescence: a systematic review and meta-analysis of population-based studies. *Psychol Med.* 2012;42:1857–1863.
23. Scott J, Chant D, Andrews G, McGrath J. Psychotic-like experiences in the general community: the correlates of CIDI psychosis screen items in an Australian sample. *Psychol Med.* 2006;36:231–238.
24. Yoshizumi T, Murase S, Honjo S, Kaneko H, Murakami T. Hallucinatory experiences in a community sample of

- Japanese children. *J Am Acad Child Adolesc Psychiatry*. 2004;43:1030–1036.
25. Horwood J, Salvi G, Thomas K, et al. IQ and non-clinical psychotic symptoms in 12-year-olds: results from the ALSPAC birth cohort. *Br J Psychiatry*. 2008;193:185–191.
26. Dhossche D, Ferdinand R, Van der Ende J, Hofstra MB, Verhulst F. Diagnostic outcome of self-reported hallucinations in a community sample of adolescents. *Psychol Med*. 2002;32:619–627.
27. Kelleher I, Cannon M. Psychotic-like experiences in the general population: characterizing a high-risk group for psychosis. *Psychol Med*. 2011;41:1–6.
28. van Os J, Linscott RJ, Myin-Germeys I, Delespaul P, Krabbendam L. A systematic review and meta-analysis of the psychosis continuum: evidence for a psychosis proneness-persistence-impairment model of psychotic disorder. *Psychol Med*. 2009;39:179–195.
29. Polanczyk G, Moffitt TE, Arseneault L, et al. Etiological and clinical features of childhood psychotic symptoms: results from a birth cohort. *Arch Gen Psychiatry*. 2010;67:328–338.
30. Kelleher I, Keeley H, Corcoran P, et al. Clinicopathological significance of psychotic experiences in non-psychotic young people: evidence from four population-based studies. *Br J Psychiatry*. 2012;201:26–32.
31. Poulton R, Caspi A, Moffitt TE, et al. Children's self-reported psychotic symptoms and adult schizophreniform disorder: a 15-year longitudinal study. *Arch Gen Psychiatry*. 2000;57:1053–1058.
32. Fisher HL, Caspi A, Poulton R, et al. Specificity of childhood psychotic symptoms for predicting schizophrenia by 38 years of age: a birth cohort study. *Psychol Med*. 2013;43:2077–2086.
33. Kelleher I, Lynch F, Harley M, et al. Psychotic symptoms in adolescence index risk for suicidal behavior: findings from 2 population-based case-control clinical interview studies. *Arch Gen Psychiatry*. 2012;69:1277–1283.
34. Dragt S, Nieman DH, Veltman D, et al. Environmental factors and social adjustment as predictors of a first psychosis in subjects at ultra high risk. *Schizophr Res*. 2011;125:69–76.
35. Spauwen J, Krabbendam L, Lieb R, Wittchen HU, van Os J. Evidence that the outcome of developmental expression of psychosis is worse for adolescents growing up in an urban environment. *Psychol Med*. 2006;36:407–415.
36. March D, Hatch SL, Morgan C, et al. Psychosis and place. *Epidemiol Rev*. 2008;30:84–100.
37. Zammit S, Lewis G, Rasbash J, et al. Individual, schools, and neighbourhood. *Arch Gen Psychiatry*. 2010;67:914–922.
38. Silver E, Mulvey EP, Swanson JW. Neighborhood structural characteristics and mental disorder: Faris and Dunham revisited. *Soc Sci Med*. 2002;55:1457–1470.
39. Allardyce J, Gilmour H, Atkinson J, et al. Social fragmentation, deprivation and urbanicity: relation to first-admission rates for psychoses. *Br J Psychiatry*. 2005;187:401–406.
40. Bhavsar V, Boydell J, Murray R, Power P. Identifying aspects of neighbourhood deprivation associated with increased incidence of schizophrenia. *Schizophr Res*. 2014;156:115–121.
41. Omer S, Kirkbride JB, Pringle DG, 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*. 2014;152:152–157.
42. Koppel S, McGuffin P. Socio-economic factors that predict psychiatric admissions at a local level. *Psychol Med*. 1999;29:1235–1241.
43. Goldsmith HF, Holzer CE, Manderscheid RW. Neighborhood characteristics and mental illness. *Eval Program Plann*. 1998;21:211–225.
44. Massey DS. The age of extremes: concentrated affluence and poverty in the twenty-first century. *Demography*. 1996;33:395–412.
45. Chan KY, Zhao FF, Meng S, et al. Urbanization and the prevalence of schizophrenia in China between 1990 and 2010. *World Psychiatry*. 2015;14:251–252.
46. Lögdberg B, Nilsson LL, Levander MT, Levander S. Schizophrenia, neighbourhood, and crime. *Acta Psychiatr Scand*. 2004;110:92–97.
47. Veling W, Susser E, Selten JP, Hoek HW. Social disorganization of neighborhoods and incidence of psychotic disorders: a 7-year first-contact incidence study. *Psychol Med*. 2015;45:1789–1798.
48. Kirkbride JB, Boydell J, Ploubidis GB, et al. Testing the association between the incidence of schizophrenia and social capital in an urban area. *Psychol Med*. 2008;38:1083–1094.
49. Lederbogen F, Haddad L, Meyer-Lindenberg A. Urban social stress–risk factor for mental disorders. The case of schizophrenia. *Environ Pollut*. 2013;183:2–6.
50. Selten JP, van der Ven E, Rutten BP, Cantor-Graae E. The social defeat hypothesis of schizophrenia: an update. *Schizophr Bull*. 2013;39:1180–1186.
51. Kirkbride JB, Stochl J, Zimbrón J, et al. Social and spatial heterogeneity in psychosis proneness in a multilevel case-prodrome-control study. *Acta Psychiatr Scand*. 2015;132:283–292.
52. Sampson RJ, Raudenbush SW, Earls F. Neighborhoods and violent crime: a multilevel study of collective efficacy. *Science*. 1997;277:918–924.
53. Sampson RJ, Raudenbush SW. Systematic social observation of public spaces: a new look at disorder in urban Neighborhoods I. *Am J Sociol*. 1999;105:603–651.
54. Sampson RJ, Morenoff JD, Gannon-Rowley T. Assessing “neighborhood effects”: Social processes and new directions in research. *Annu Rev Sociol*. 2002;28:443–478.
55. Trouton A, Spinath FM, Plomin R. Twins early development study (TEDS): a multivariate, longitudinal genetic investigation of language, cognition and behavior problems in childhood. *Twin Res*. 2002;5:444–448.
56. Moffitt TE; E-Risk Study Team. Teen-aged mothers in contemporary Britain. *J Child Psychol Psychiatry*. 2002;43:727–742.
57. CACI Information Services. *ACORN User Guide*. London, UK: CACI; 2006.
58. Caspi A, Taylor A, Moffitt TE, Plomin R. Neighborhood deprivation affects children's mental health: environmental risks identified in a genetic design. *Psychol Sci*. 2000;11:338–342.
59. Schreier A, Wolke D, Thomas K, et al. Prospective study of peer victimization in childhood and psychotic symptoms in a nonclinical population at age 12 years. *Arch Gen Psychiatry*. 2009;66:527–536.
60. Odgers CL, Moffitt TE, Tach LM, et al. The protective effects of neighborhood collective efficacy on British children growing up in deprivation: a developmental analysis. *Dev Psychol*. 2009;45:942–957.
61. Odgers CL, Caspi A, Bates CJ, Sampson RJ, Moffitt TE. Systematic social observation of children's neighborhoods using Google Street View: a reliable and cost-effective method. *J Child Psychol Psychiatry*. 2012;53:1009–1017.
62. Odgers CL, Caspi A, Russell MA, et al. Supportive parenting mediates neighborhood socioeconomic disparities in children's

- antisocial behavior from ages 5 to 12. *Dev Psychopathol.* 2012;24:705–721.
63. Jaffee SR, Caspi A, Moffitt TE, Polo-Tomás M, Taylor A. Individual, family, and neighborhood factors distinguish resilient from non-resilient maltreated children: a cumulative stressors model. *Child Abuse Negl.* 2007;31:231–253.
 64. Veitch J, Bagley S, Ball K, Salmon J. Where do children usually play? A qualitative study of parents' perceptions of influences on children's active free-play. *Health Place.* 2006;12:383–393.
 65. Kohen DE, Leventhal T, Dahinten VS, McIntosh CN. Neighborhood disadvantage: pathways of effects for young children. *Child Dev.* 2008;79:156–169.
 66. March JS, Parker JD, Sullivan K, Stallings P, Conners CK. The Multidimensional Anxiety Scale for Children (MASC): factor structure, reliability, and validity. *J Am Acad Child Adolesc Psychiatry.* 1997;36:554–565.
 67. Kovacs M. *Children's Depression Inventory: Manual.* North Tonawanda, NY: Multi-Health Systems; 1992.
 68. Rivera CL, Bernal G, Rosello J. The Children Depression Inventory (CDI) and the Beck Depression Inventory (BDI): their validity as screening measures for major depression in a group of Puerto Rican adolescents. *Int J Clin Health Psychol.* 2005;5:485.
 69. Achenbach T. *Manual for the Child Behavior Checklist and 1991 Profile.* Burlington, VT: University of Vermont Department of Psychiatry; 1991.
 70. Odgers CL, Donley S, Caspi A, Bates CJ, Moffitt TE. Living alongside more affluent neighbors predicts greater involvement in antisocial behavior among low-income boys. *J Child Psychol Psychiatry.* 2015;56:1055–1064.
 71. Milne BJ, Caspi A, Crump R, et al. The validity of the family history screen for assessing family history of mental disorders. *Am J Med Genet B Neuropsychiatr Genet.* 2009;150B:41–49.
 72. Robins L, Cottler L, Bucholz K, Compton W. *Diagnostic Interview Schedule for DSM-IV (DIS-IV).* St Louis, MO: Washington University School of Medicine; 1995.
 73. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders.* 4th ed. Washington, DC: American Psychiatric Association; 1994.
 74. Breen R, Karlson KB, Holm A. Total, direct, and indirect effects in logit and probit models. *Sociol Methods Res.* 2013;42:164–191.
 75. Rogers W. Regression standard errors in clustered samples. *STB.* 1994;3:19–23.
 76. van Winkel R, Stefanis NC, Myin-Germeys I. Psychosocial stress and psychosis. A review of the neurobiological mechanisms and the evidence for gene-stress interaction. *Schizophr Bull.* 2008;34:1095–1105.
 77. van Os J, Pedersen CB, Mortensen PB. Confirmation of synergy between urbanicity and familial liability in the causation of psychosis. *Am J Psychiatry.* 2004;161:2312–2314.
 78. Garety PA, Kuipers E, Fowler D, Freeman D, Bebbington PE. A cognitive model of the positive symptoms of psychosis. *Psychol Med.* 2001;31:189–195.
 79. Oher FJ, Demjaha A, Jackson D, et al. The effect of the environment on symptom dimensions in the first episode of psychosis: a multilevel study. *Psychol Med.* 2014;44:2419–2430.
 80. Chung HL, Steinberg L. Relations between neighborhood factors, parenting behaviors, peer deviance, and delinquency among serious juvenile offenders. *Dev Psychol.* 2006;42:319–331.
 81. Lederbogen F, Kirsch P, Haddad L, et al. City living and urban upbringing affect neural social stress processing in humans. *Nature.* 2011;474:498–501.
 82. Haddad L, Schäfer A, Streit F, et al. Brain structure correlates of urban upbringing, an environmental risk factor for schizophrenia. *Schizophr Bull.* 2015;41:115–122.
 83. van Os J, Linscott RJ, Myin-Germeys I, Delespaul P, Krabbendam L. A systematic review and meta-analysis of the psychosis continuum: evidence for a psychosis proneness-persistence-impairment model of psychotic disorder. *Psychol Med.* 2009;39:179–195.
 84. Costello EJ, Mustillo S, Erkanli A, Keeler G, Angold A. Prevalence and development of psychiatric disorders in childhood and adolescence. *Arch Gen Psychiatry.* 2003;60:837–844.

4.1 Supplementary materials

4.1.1 Comparison of “CLUSTER” command and multilevel modelling in STATA

Main analyses in Chapter 4 were repeated using multilevel modelling techniques in STATA. Multilevel mixed models were estimated in STATA using the XTMELOGIT command. For odds ratios (Supplementary Table 4.1), we specified the fixed portion of the model as a binominal distribution, and specified random intercepts with an unstructured covariance matrix to account for the clustering of twins within families.

Supplementary Table 4.1. Main logistic regression analyses performed using both the “cluster” command and multilevel modelling in STATA

Predictor variable <i>Outcome variable</i>	Cluster analysis			Multilevel analysis		
	OR	95% CI	<i>p</i>	OR	95% CI	<i>p</i>
Age-12 urbanicity						
<i>Childhood psychotic symptoms</i>	1.76	[1.15, 2.68]	0.009	2.12	[1.22, 3.70]	0.008
<i>Childhood psychotic symptoms*</i>	1.61	[1.04, 2.51]	0.035	1.89	[1.09, 3.30]	0.024
<i>Depression</i>	1.16	[0.69, 1.96]	0.571	1.28	[0.65, 2.51]	0.472
<i>Anxiety</i>	1.42	[0.95, 2.12]	0.091	1.57	[0.94, 2.62]	0.085
Age-5 social cohesion						
<i>Childhood psychotic symptoms</i>	0.68	[0.58, 0.82]	<0.001	0.62	[0.49, 0.78]	<0.001
Age-5 social control						
<i>Childhood psychotic symptoms</i>	0.75	[0.62, 0.91]	0.003	0.69	[0.55, 0.88]	0.003
Age-5 neighbourhood disorder						
<i>Childhood psychotic symptoms</i>	1.26	[1.06, 1.51]	0.010	1.33	[1.05, 1.68]	0.017
Age-5 crime victimisation						
<i>Childhood psychotic symptom</i>	1.40	[1.19, 1.65]	<0.001	1.54	[1.22, 1.95]	<0.001
Age-12 social cohesion						
<i>Childhood psychotic symptoms</i>	0.77	[0.65, 0.90]	0.001	0.69	[0.52, 0.90]	0.007
Age-12 social control						
<i>Childhood psychotic symptoms</i>	0.83	[0.69, 1.00]	0.056	0.77	[0.59, 1.02]	0.064
Age-12 neighbourhood disorder						
<i>Childhood psychotic symptoms</i>	1.27	[1.06, 1.52]	0.008	1.39	[1.07, 1.81]	0.013
Age-12 crime victimisation						
<i>Childhood psychotic symptoms</i>	1.17	[0.95, 1.42]	0.133	1.21	[0.95, 1.55]	0.119

CI, confidence interval. OR, odds ratio. *Adjusted for family socioeconomic status, family psychiatric history and maternal psychosis.

4.1.2 Replication of main analyses using the ONS urbanicity measure

Main analyses from Chapter 4 were repeated using the ONS's measure of urbanicity. Because of the low numbers of children reporting psychotic symptoms, the ONS urban categories (categories 2 and 3: major/minor conurbations and urban cities/towns) were collapsed and compared to the ONS rural category (category 1).

Are psychotic symptoms more common among children raised in urban neighbourhoods?

Among children who had lived in urban settings at age 5 (ONS categories 2 or 3), 6.4% of children reported psychotic symptoms at age 12. In contrast, 3.8% of children who had lived in rural settings at age 5 (ONS category 1) subsequently reported psychotic symptoms at age 12. This resulted in an association between age-5 urbanicity and age-12 psychotic symptoms (OR=1.75, 95% CI=0.98-3.14) which was nominally significant at the $p=0.06$ level. However, there was not a significant cross-sectional association between age-12 ONS urbanicity and childhood psychotic symptoms (OR=1.47, 95% CI=0.84-2.57, $p=0.182$).

Is urbanicity specifically associated with childhood psychotic symptoms?

Specificity analyses revealed that age-5 ONS urbanicity was not significantly associated with age-12 anxiety (OR=1.30, 95% CI=0.79–2.12, $p=0.297$), depression (OR=0.98, 95% CI= 0.52–1.86, $p=0.959$), or antisocial behaviour (OR=1.48, 95% CI=0.75–2.93, $p=0.257$).

Do neighbourhood-level social processes mediate the association between urban residency and childhood psychotic symptoms?

Supplementary Table 4.2 below shows mediation models of the association between age-5 ONS urbanicity and age-12 childhood psychotic symptoms, split into the total

(overall association), direct (association not explained by mediators) and indirect pathways (association explained by mediators). Mothers' reports of social cohesion, social control, neighbourhood disorder and neighbourhood crime each significantly explained part of the effect of urbanicity on childhood psychotic symptoms (mediation range = 15–35%). There was no significant direct effect of urbanicity on childhood psychotic symptoms. When all social processes were simultaneously modelled, together they explained 51% of the effect of urbanicity on childhood psychotic symptoms ($p < 0.001$).

Main findings using the ONS measure of urbanicity are therefore similar to the prospective associations identified using the resident reports of urbanicity. For example, the main effect of age-5 urbanicity on childhood psychotic symptoms was $OR = 1.75$ according to the ONS measure and $OR = 1.80$ according to resident reports.

Supplementary Table 4.2. Association between age-5 ONS urbanicity and childhood psychotic symptoms, split into total effects, and direct and indirect pathways via neighbourhood-level social process mediators

Social process mediators	Mediation model				
	N	Total OR (95% CI)	Direct OR (95% CI)	Indirect OR (95% CI)	% Mediated ^a
Age-5 mother reports					
Social cohesion	1999	1.66 [†] [0.92, 2.98]	1.39 [0.76, 2.53]	1.19** [1.08, 1.32]	35
Social control	1981	1.67 [†] [0.93, 3.00]	1.49 [0.82, 2.69]	1.12* [1.02, 1.24]	23
Neighbourhood disorder	2007	1.68 [†] [0.94, 3.02]	1.56 [0.86, 2.80]	1.08* [1.01, 1.16]	15
Crime victimisation	2007	1.67 [†] [0.93, 3.00]	1.49 [0.82, 2.69]	1.12* [1.04, 1.21]	23

Note: CI = confidence interval; OR = odds ratio. * $p < 0.05$ ** $p < 0.01$ [†]nominally significant $p > 0.05$ & < 0.1 . ^a Percentages rounded to whole numbers. Total effect = overall association between urbanicity and childhood psychotic symptoms; direct effect = the part of the overall association that is not explained by the mediator in the model; and indirect effect = the part of the overall association that is explained by the social process mediator in the model. Bold text denotes significant indirect (mediation) pathways at $p < 0.05$. Small sample size differences account for the slight differences between the main effect OR (1.75) in binary logistic model and the total effect ORs in Mediation models. All analyses account for the non-independence of twin observations. All social process variables have been standardised with a mean of 0 and a standard deviation of 1.

Chapter 5: Cumulative effects of neighbourhood social adversity and personal crime victimisation on adolescent psychotic experiences

This chapter is presented in the published format from the following publication:

Newbury, J., Arseneault, L., Caspi, A., Moffitt, T. E., Odgers, C. L., & Fisher, H. L. (2017). Cumulative effects of neighbourhood social adversity and personal crime victimization on adolescent psychotic experiences. *Schizophrenia Bulletin*, doi.org/10.1093/schbul/sbx060

Cumulative Effects of Neighborhood Social Adversity and Personal Crime Victimization on Adolescent Psychotic Experiences

Joanne Newbury¹, Louise Arseneault¹, Avshalom Caspi^{1,2}, Terrie E. Moffitt^{1,2}, Candice L. Odgers^{3,4}, and Helen L. Fisher^{*,1,4}

¹MRC Social, Genetic & Developmental Psychiatry Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK; ²Departments of Psychology and Neuroscience, Psychiatry and Behavioral Sciences, and Centre for Genomic and Computational Biology, Duke University, Durham, NC; ³Center for Child and Family Policy and the Sanford School of Public Policy, Duke University, Durham, NC

⁴These authors are joint senior authors.

*To whom correspondence should be addressed; MRC Social, Genetic & Developmental Psychiatry Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, 16 De Crespigny Park, London SE5 8AF, UK; tel: +442078485430, fax: +442078480866, e-mail: helen.2.fisher@kcl.ac.uk

Background: Little is known about the impact of urbanicity, adverse neighborhood conditions and violent crime victimization on the emergence of adolescent psychotic experiences. **Methods:** Participants were from the Environmental Risk (E-Risk) Longitudinal Twin Study, a nationally-representative cohort of 2232 British twins who were interviewed about adolescent psychotic experiences at age 18. Urbanicity, neighborhood characteristics, and personal victimization by violent crime were measured during childhood and adolescence via geocoded census data, surveys of over 5000 immediate neighbors of the E-Risk participants, and interviews with participants themselves. **Results:** Adolescents raised in urban vs rural neighborhoods were significantly more likely to have psychotic experiences (OR = 1.67, 95% CI = 1.21–2.30, $P = .002$). This association remained significant after considering potential confounders including family socioeconomic status, family psychiatric history, and adolescent substance problems (OR = 1.43, 95% CI = 1.01–2.03, $P = .042$), but became nonsignificant after considering adverse social conditions in urban neighborhoods such as low social cohesion and high neighborhood disorder (OR = 1.35, 95% CI = 0.94–1.92, $P = .102$). The combined association of adverse neighborhood social conditions and personal crime victimization with adolescent psychotic experiences (adjusted OR = 4.86, 95% CI = 3.28–7.20, $P < .001$) was substantially greater than for either exposure alone, highlighting a potential interaction between neighborhood conditions and crime victimization (interaction contrast ratio = 1.81, 95% CI = –0.03 to 3.65) that was significant at the $P = .054$ level. **Conclusions:** Cumulative effects of adverse neighborhood social conditions and personal victimization by violent crime during upbringing partly explain why

adolescents in urban settings are more likely to report psychotic experiences. Early intervention efforts for psychosis could be targeted towards victimized youth living in urban and socially adverse neighborhoods.

Key words: adolescence/assault/neighborhood characteristics/psychosis/trauma/urbanicity

Background

Up to 1 in 3 adolescents in the general population at some point experience subclinical psychotic phenomena such as attenuated forms of auditory hallucinations and paranoid delusions.^{1–4} Though relatively common, early psychotic experiences are associated with a greater adulthood risk for psychotic disorders and other psychiatric problems including substance abuse, depression, and suicidal behavior.^{5–7} Because early intervention offers the best hope for improving outcomes in psychosis⁸ and adult psychopathology more generally,⁹ it is crucial to understand how the wider structural and social environment may influence psychotic experiences among young people in order to design and effectively target preventive interventions.

To date, most prior research on the emergence of adolescent psychotic experiences has focused on individual-level risk factors¹⁰ and little is currently known about the potential impact of macro-level structures such as urbanicity and neighborhood-level social processes like social fragmentation and crime. These common forms of wider environmental exposures have been implicated in adult psychotic disorder,^{11–21} and adult psychosis shares similar social and behavioral risk factors as early psychotic

phenomena.^{10,22} Early expressions of psychosis are more likely to persist and reach clinical significance among urban vs nonurban youth,^{23,24} but the reasons for this are unclear. We previously showed that adverse neighborhood social conditions in early childhood, such as low social cohesion and high crime, explained one quarter of the association between urbanicity and *childhood* psychotic symptoms.²⁵ Elucidating the role of macro- and neighborhood-level exposures in *adolescent* psychotic experiences could be particularly informative for early-intervention efforts, because the clinical relevance of psychotic phenomena increases later in adolescence.²⁶

Cities (vs rural settings) have higher rates of violent crime^{27,28} and tend to be more threatening²⁶ and less socially cohesive.^{25,29} Additionally, 16–24 year-olds in the United Kingdom are 3 times more likely than other age groups to be victimized by a violent crime.³⁰ Therefore, many adolescents raised in cities are not only embedded in more socially adverse neighborhoods, but are also more likely to be personally victimized by crime compared to other age groups and peers living in rural neighborhoods. Given that cumulative trauma (ie, an accumulation of stressful exposures such as social adversity and victimization) is implicated in risk for psychosis,^{31–34} we hypothesized that one of the reasons that young people in urban settings are at increased risk for psychotic phenomena is that they experience a greater accumulation of neighborhood-level social adversity and personal experiences of violence during upbringing. No study has yet explored the potential cumulative effects of adverse neighborhood social conditions and personal crime victimization on the emergence of psychotic experiences during adolescence.

The present study addresses this topic with data from a nationally-representative cohort of over 2000 British adolescents, who have been interviewed repeatedly up to age 18, with comprehensive assessments of victimization and psychotic experiences and high-resolution measures of the built and social environment. We asked: (1) Are psychotic experiences more common among adolescents raised in urban vs rural settings? And does this association hold after controlling for neighborhood-level deprivation (ie, poverty), as well as individual- and family-level factors, that might otherwise explain the relationship? (2) Can the association between urban upbringing and adolescent psychotic experiences be explained by urban neighborhoods having lower levels of social cohesion and higher levels of neighborhood disorder (subsequently defined as exposure to *neighborhood social adversity*)? (3) Are psychotic experiences more common among adolescents who have been personally victimized by a violent crime? And (4) Is there a cumulative effect of neighborhood social adversity and personal crime victimization on adolescent psychotic experiences? In addition, the present study conducted sensitivity analyses using adolescent psychotic *symptoms* as the outcome (which are psychotic experiences verified by clinicians).

Methods

Study Cohort

Participants were members of the Environmental Risk (E-Risk) Longitudinal Twin Study, which tracks the development of a nationally-representative birth cohort of 2232 British twin children born in 1994–1995 and initially assessed in home visits at age 5. Follow-up home-visits were conducted when participants were aged 7, 10, 12, and 18 (participation rates were 98%, 96%, 96%, and 93%, respectively). At age 18, the E-Risk sample comprised 2066 participants. All but 3 participants completed the psychotic experiences interview at age 18. The final sample for this study was therefore 2063 individuals, comprising 55% monozygotic twin pairs and 48% males. There were no differences between those who did and did not take part at age 18 in terms of age-5 socioeconomic status (SES) ($\chi^2 = 0.86$, $P = .65$), age-5 IQ scores ($t = 0.98$, $P = .33$), or age-5 internalizing or externalizing behavior problems ($t = 0.40$, $P = .69$ and $t = 0.41$, $P = .68$, respectively). The Joint South London and Maudsley and the Institute of Psychiatry Research Ethics Committee approved each phase of the study. Parents gave informed consent, and participants gave assent at ages 5–12 and informed consent at age 18. Full details about the sample are reported elsewhere,³⁵ and in the supplementary materials.

Measures

Adolescent Psychotic Phenomena. The present study uses 2 measures of psychotic phenomena which were both obtained from private interviews when participants were aged 18.

Our primary outcome was a self-report measure of adolescent psychotic experiences which reflects the methodology used by many groups in the psychosis prodrome research field.³⁶ At age 18, each E-Risk participant was privately interviewed by a research worker about 13 psychotic experiences occurring since age 12. Seven items pertained to delusions and hallucinations and this interview has been described in detail previously²² and in the supplementary materials. Six items pertained to unusual experiences which drew on item pools since formalized in prodromal psychosis instruments including the PRIME-screen and SIPS.³⁶ These included “I worry that my food may be poisoned” and “My thinking is unusual or frightening.” Interviewers coded each item 0, 1, 2 indicating respectively “not present,” “probably present” and “definitely present.” All 13 items were summed to create a psychotic experiences scale (range = 0–18, $M = 1.19$, $SD = 2.58$). Scores were placed into an ordinal scale. Just over 30% of participants had at least 1 psychotic experience between ages 12 and 18: 69.8% reported no psychotic experiences (coded 0; $n = 1440$), 15.5% reported 1 or 2 psychotic experiences (coded 1; $n = 319$), 8.1% reported 3 to 5 psychotic experiences (coded 2; $n = 166$),

and 6.7% reported 6 or more psychotic experiences (coded 3; $n = 138$). This is similar to the prevalence of self-reported psychotic experiences in other community samples of teenagers and young adults.¹⁻⁴

We additionally examined clinically-verified adolescent psychotic symptoms as a secondary outcome, using the same methodology as used at age 12.²² Responses to the 7 hallucination/delusion items were verified by a team of clinicians, including child and adolescent psychiatrists, to capture more clinically pertinent psychotic symptoms. Full details on the verification procedure for adolescent psychotic symptoms are provided in the supplementary materials. At age 18, 2.9% ($N = 59$) of participants were designated as having experienced at least 1 definite psychotic symptom.

Urbanicity. Urbanicity was defined based on data from the Office of National Statistics (ONS) Rural-Urban Definition for Small Area Geographies (RUC2011) classifications.³⁷ The ONS classifications utilized 2011 census data. Detailed information on ONS's creation of RUC2011 is available on the ONS webpages (https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/239477/RUC11methodologypaperaug_28_Aug.pdf; this link was working on April 20, 2017) and in the supplementary materials. ONS urbanicity scores (range 1–10) were assigned to every E-Risk family via the family's postcode when participants were aged 12. Given the low numbers within some rural categories, urbanicity was collapsed into 3 levels (1 = rural: all rural settings; 2 = intermediate: urban cities and towns; and 3 = urban: major and minor conurbations [conurbations are densely populated, large urban regions resulting from the expansion and coalescence of adjacent cities and towns]). E-Risk families are nationally-representative in terms of ONS urbanicity classifications; 32.2% of E-Risk children lived in urban settings at age 12 compared to 36.1% nationwide; 47.9% vs 45.0% lived in intermediate settings; and 19.9% vs 18.9% lived in rural settings.

Neighborhood Characteristics. Social conditions (ie, social processes) in the participants' neighborhoods were estimated via a postal survey sent to residents living alongside E-Risk families when participants were aged 13–14.^{38,39} Survey respondents, who were typically living on the same street or within the same apartment block as the participants in our study, reported on various characteristics of their immediate neighborhood, including levels of *social cohesion* and *neighborhood disorder*.^{40,41} Surveys were returned by an average of 5.18 (SD = 2.73) respondents per neighborhood, and there were at least 2 responses for 95% of neighborhoods ($N = 5601$ respondents). We were interested in social cohesion and neighborhood disorder because they collectively capture neighborhood characteristics that could plausibly influence risk for psychotic phenomena, such as trust and

support between neighbors and physical and social signs of threat in the neighborhood. Social cohesion (5 items, each coded 0–4) was assessed by asking residents whether their neighbors shared values and trusted and got along with each other, etc. Neighborhood disorder (14 items, each coded 0–2) was assessed by asking residents whether certain problems affected their neighborhood, including muggings, assaults, vandalism, graffiti and deliberate damage to property, etc. Items within each neighborhood characteristic scale were averaged to create summary scores from each of the 5601 resident respondents. Neighborhood characteristic scores for each E-Risk family were then created by averaging the summary scores of respondents within that family's neighborhood. The resulting variables approach normal distribution across the full potential range (Social cohesion: $M = 2.23$, $SD = 0.50$, range = 0–3.71; Neighborhood disorder: $M = 0.49$, $SD = 0.34$, range = 0–1.93). Supplementary table 1 demonstrates that urban neighborhoods were characterized by significantly lower levels of social cohesion and significantly higher levels of neighborhood disorder. Additionally, we indexed the most socially adverse neighborhoods by combining social cohesion with neighborhood disorder. Participants who had lived in neighborhoods that were simultaneously characterized by lower than average social cohesion and higher than average neighborhood disorder were designated as having experienced neighborhood social adversity (coded 1: 35.9% of participants, $N = 772$).

Personal Crime Victimization. Personal experiences of violent crime victimization were assessed in private interviews with the participants at age 18 via the Juvenile Victimization Questionnaire 2nd revision (JVQ-R2)⁴² adapted as a clinical interview (see Fisher et al⁴³ and supplementary materials for full details). JVQ crime victimization comprised 9 items, each enquiring about the period “since you were 12” (eg, “Did anyone hit or attack you on purpose with an object or weapon like a stick, rock, gun, knife or anything that hurt?”). The worst experience (according to the participant) was rated using a 6-point scale: 0 = not exposed, then 1–5 for increasing levels of severity, reflecting the level of physical harm that had occurred. In the present study, crime victimization was dichotomized to represent the most violent forms of crime where injury or threat to life was likely, with participants who reported the top 2 levels of JVQ crime victimization (levels 4/5) designated as having experienced *personal crime victimization* (coded 1: 19.3% of participants, $N = 398$).

Neighborhood-Level Deprivation. Neighborhood-level deprivation was constructed using A Classification of Residential Neighborhoods (ACORN), a geodemographic discriminator developed by CACI Information Services (<http://www.caci.co.uk/>; this link was working on April 20, 2017). Detailed information about

ACORN's classification of neighborhood-level deprivation has been provided previously.^{38,44,46} Briefly, CACI utilized over 400 variables from 2001 census data for Great Britain (eg, educational qualifications, unemployment, housing tenure) and CACI's consumer lifestyle database. Following hierarchical-cluster-analysis, CACI created 5 distinct and homogeneous ordinal groups ranging from "Wealthy Achiever" (coded 1) to "Hard Pressed" (coded 5) neighborhoods. Neighborhood-level deprivation scores for the E-Risk families were then created by identifying the ACORN classification for that family's postcode when children were aged 12. E-Risk families are representative of UK households across the spectrum of neighborhood-level deprivation: 25.6% of E-Risk families live in "wealthy achiever" neighborhoods compared to 25.3% of households nation-wide; 5.3% vs 11.6% live in "urban prosperity" neighborhoods; 29.6% vs 26.9% live in "comfortably off" neighborhoods; 13.4% vs 13.9% live in "moderate means" neighborhoods; and 26.1% vs 20.7% live in "hard-pressed" neighborhoods.^{45,46}

Family- and Individual-Level Covariates. Family SES was measured via a composite of parental income, education, and occupation when participants were aged 5. The latent variable was categorized into tertiles (ie, low-, medium-, and high-SES). Family psychiatric history and maternal psychosis were both considered as proxy indicators of genetic and environmental risks, to control for potential social drift whereby individuals with mental illness may be more likely to move to adverse neighborhoods. Both were assessed when participants were aged 12. In private interviews, mothers reported on family history of DSM disorders,^{47,48} which was converted to a proportion (0–1.0) of family members with a history of psychiatric disorder. For maternal psychosis, mothers were interviewed using the Diagnostic Interview Schedule⁴⁹ for DSM-IV⁵⁰ which provides a symptom count for characteristic symptoms of schizophrenia (eg, hallucinations, delusions, anhedonia). Alcohol and cannabis dependence were considered because alcohol and cannabis are conceivably more available in cities, and abuse of these substances is associated with psychotic symptoms.^{51,52} We interviewed participants when they were aged 18 for the presence of alcohol/cannabis dependence according to DSM-IV criteria. Assessments were conducted in face-to-face interviews using the DIS.⁵¹ The rates were 12.8% ($N = 263$) and 4.3% ($N = 89$), respectively. Childhood psychotic symptoms at age 12 (described previously²²) were included as a potential confound in models involving crime victimization because early psychotic phenomena have been associated with the likelihood of experiencing victimization. At age 12, 5.9% ($N = 125$) of children reported psychotic symptoms. Further details on the covariates are provided in the supplementary materials.

Adolescent Major Depression. Specificity analyses were conducted with adolescent depression as the outcome,

because psychotic experiences and depression commonly co-occur and share similar aetiology.⁵³ Adolescent major depression was assessed at age 18 following DSM-IV criteria in face-to-face interviews using the DIS.⁵¹ By age 18, 20.1% ($N = 414$) of adolescents had met DSM-IV criteria for a major depressive episode.

Statistical Analysis

We conducted analyses following 5 steps. First, logistic regression was used to test whether psychotic experiences (between ages 12 and 18) were more common among adolescents raised in urban neighborhoods. We controlled for family- and individual-level factors and for neighborhood-level deprivation to check that the association was not explained by these characteristics which could potentially differ between urban vs rural residents. We also examined the association between urbanicity and adolescent major depression to check for specificity of the previous findings. Second, because urban neighborhoods are characterized by lower levels of social cohesion and higher levels of neighborhood disorder (supplementary table 1) we tested whether levels of these neighborhood characteristics accounted for the association between urbanicity and adolescent psychotic experiences, and we also estimated the separate associations of social cohesion and neighborhood disorder with adolescent psychotic experiences. Third, using logistic regression we checked whether adolescents who had lived in the most socially adverse neighborhoods (neighborhood characterized by both low social cohesion and high neighborhood disorder) were more likely to be personally victimized by violent crime and, in turn, whether psychotic experiences were more common among adolescents who had been victimized. Fourth, using interaction contrast ratio analysis we investigated potential cumulative and interactive effects of adverse neighborhood social conditions and personal victimization by violent crime on adolescent psychotic experiences. Four exposure categories were created for this analysis by combining *neighborhood social adversity* with *personal crime victimization* (0 = not exposed to either; 1 = lived in the most adverse neighborhoods but not personally victimized by violent crime; 2 = personally victimized by violent crime but did not live in the most adverse neighborhoods; and 3 = exposed to both the most socially adverse neighborhood conditions and also personally victimized by violent crime). Finally, sensitivity analyses were conducted using the clinically-verified adolescent psychotic symptoms as the outcome measure. All analyses were conducted in STATA 14.2 (Stata-Corp), and accounted for the nonindependence of twin observations using the "CLUSTER" command. This procedure is derived from the Huber-White variance estimator, and provides robust standard errors adjusted for within-cluster correlated data.⁵⁴ Note: ordinal logistic regression

was used in analyses where adolescent psychotic experiences was the dependent variable, because this was on an ordinal (rather than binary) scale.

Results

Are Psychotic Experiences More Common Among Adolescents Raised in Urban vs Rural Neighborhoods?

Model 1 in [table 1](#) shows that as the level of childhood urbanicity increased from rurality, odds for adolescent psychotic experiences also increased (intermediate urbanicity: OR = 1.37, 95% CI = 1.01–1.86, $P = .042$; highest urbanicity: OR = 1.67, 95% CI = 1.21–2.30, $P = .002$). Crucially, model 2 in [table 1](#) highlights that the association between the most urban setting and adolescent psychotic experiences remained significant after considering a range of potential family- and individual-level confounders (family SES, family psychiatric history, maternal psychosis, and adolescent alcohol/cannabis dependence) and neighborhood-level deprivation (OR = 1.43, 95% CI = 1.01–2.03, $P = .042$), indicating that the association

in that urban residency was not significantly associated with adolescent depression (unadjusted OR = 0.94, 95% CI = 0.68–1.31, $P = .736$).

Can the Association Between Growing Up in an Urban (vs Rural) Setting and Adolescent Psychotic Experiences be Explained by Social Conditions of Urban Neighborhoods?

Model 3 in [table 1](#) shows that after considering resident-reported neighborhood social conditions, the association between living in the most urban setting and adolescent psychotic experiences was attenuated to below conventional levels of significance (OR = 1.35, 95% CI = 0.94–1.92, $P = .103$). That is, almost half of the effect of urbanicity on adolescent psychotic experiences (mediatory estimates are supported by pathway analyses⁵⁵) was explained by the levels of social cohesion and neighborhood disorder in urban vs rural neighborhoods. In [table 2](#) we additionally show the independent effects of social cohesion and neighborhood disorder on adolescent psy-

Table 1. Association Between Childhood Urbanicity and Adolescent Psychotic Experiences

Model Specification	Level of Urbanicity ^a	Covariates	Association Between Childhood Urbanicity and Adolescent Psychotic Experiences ^b		
			OR	95% CI	<i>P</i> Value
Model 1	Rural		[Reference]	—	—
	Intermediate		1.37	1.01–1.86	.042
	Urban		1.67	1.21–2.30	.002
Model 2	Rural		[Reference]	—	—
	Intermediate		1.11	0.81–1.54	.513
	Urban		1.43	1.01–2.03	.042
		Family socioeconomic status	1.20	1.02–1.41	.029
		Family psychiatric history	1.99	1.30–3.06	.002
		Maternal psychotic symptoms	1.09	0.96–1.23	.187
		Adolescent alcohol dependence	2.20	1.66–2.92	<.001
		Adolescent cannabis dependence	4.21	2.60–6.82	<.001
Model 3		Neighborhood-level deprivation	1.10	1.00–1.20	.044
	Rural		[Reference]	—	—
	Intermediate		1.17	0.85–1.62	.329
	Urban		1.35	0.94–1.92	.103
		Neighborhood social conditions	1.28	1.11–1.48	.001

Note: OR, odds ratio from ordinal logistic regression.

^a3-level urbanicity at age 12: Rural = rural towns and fringes, villages, hamlets, isolated dwellings; Intermediate = urban cities and towns; Urban = major and minor conurbations.

^bThe association of childhood urbanicity (and other covariates) with adolescent psychotic experiences was calculated with ordinal logistic regression because adolescent psychotic experiences are on an ordinal (0–3) rather than binary scale. Model 1—the unadjusted association between childhood urbanicity and adolescent psychotic experiences (sample size = 1978 participants). Model 2—adjusted for family-level characteristics (family socioeconomic status, family psychiatric history, maternal psychotic symptoms), individual-level characteristics (adolescent alcohol dependence and adolescent cannabis dependence), and neighborhood-level deprivation at age 12 (sample size = 1900 participants). Model 3—adjusted for neighborhood social conditions (social cohesion and neighborhood disorder) at age 12 (sample size = 1956 participants). Sample sizes vary slightly between models due to small numbers of participants missing data on independent variables. All analyses account for the nonindependence of twin observations.

was not likely due to compositional effects. Moreover, the association also demonstrated a degree of specificity

chotic experiences, with the neighborhood characteristic measures categorized at various thresholds. In short,

psychotic experiences were more common among adolescents who had lived in neighborhoods with lower levels of social cohesion and higher levels of neighborhood disorder, and these associations were very similar regardless of the threshold used.

Are Psychotic Experiences More Common Among Adolescents Who Have Been Personally Victimized by a Violent Crime?

Among adolescents who had lived in the most socially adverse neighborhoods (neighborhoods that were simultaneously characterized by low social cohesion and high neighborhood disorder), 24.0% had been personally victimized by a violent crime compared to 15.1% of adolescents who had lived in more favorable neighborhood conditions (OR = 1.78, 95% CI = 1.32–2.41, $P < .001$). Furthermore, adolescents who had been victimized by violent crime had over 3 times greater odds of having psychotic experiences than non-victimized adolescents (OR = 3.76, 95% CI = 3.00–4.72, $P < .001$), and this association was not explained by the set of potential confounders reported in [table 3](#) (OR = 2.90, 95% CI = 2.28–3.69, $P < .001$).

Is There a Cumulative Effect of Neighborhood Social Adversity and Personal Crime Victimization on Adolescent Psychotic Experiences?

Given previous evidence that risk for psychosis increases incrementally following an accumulation of stressful exposures, we tested for cumulative and interactive effects of adverse neighborhood social conditions and personal crime victimization during upbringing on adolescent psychotic experiences. [Table 3](#) shows that both neighborhood social adversity and personal crime victimization each

had significant independent associations with adolescent psychotic experiences. However, focusing on model 2, which adjusts for all potential confounders, the combined effect of neighborhood social adversity and personal crime victimization on adolescent psychotic experiences was much greater than either exposure alone, at nearly 5 times the odds compared to unexposed adolescents (OR = 4.86, 95% CI = 3.28–7.20, $P < .001$). The interaction between neighborhood social adversity and personal crime victimization (ICR = 1.81, 95% CI = -0.03–3.65) was significant at the $P = .054$ level. That is, the odds for adolescent psychotic experiences among individuals who were exposed to both neighborhood social adversity and crime victimization was 1.81 points higher than the summed effects of the individual exposures (model 2 in [table 3](#)).

Sensitivity Check: Are Urbanicity, Neighborhood Social Conditions, and Crime Victimization Also Associated With Adolescent Psychotic Symptoms (vs Experiences)?

Only 2.9% ($n = 59$) of adolescents met criteria for the clinically-verified psychotic symptoms. Adjusted model 2 in supplementary table 2 shows that participants raised in urban (vs rural) settings appeared to be at elevated risk for experiencing adolescent psychotic symptoms, though this association was nonsignificant (OR = 1.40, 95% CI = 0.57–3.41, $P = .460$). While the point estimate was very similar to that produced for adolescent psychotic experiences (OR = 1.43, 95% CI = 1.01–2.03, $P = .042$), the low base rate of verified symptoms in the current sample restricted our power to detect associations at this level. In addition, model 3 in supplementary table 2 revealed that neighborhood social adversity explained a similar proportion of the

Table 2. Association Between Neighborhood Characteristics and Adolescent Psychotic Experiences With Neighborhood Characteristics Categorized at Various Thresholds

Neighborhood Characteristic	Association Between Neighborhood Characteristics and Adolescent Psychotic Experiences								
	Full-Scale Neighborhood Characteristics ^a			Neighborhood Characteristics Dichotomized at the Mean ^b			Neighborhood Characteristics Dichotomized at the Tertile ^c		
	OR	95% CI	P Value	OR	95% CI	P Value	OR	95% CI	P Value
Low social cohesion	1.57	1.26–1.95	<.001	1.53	1.24–1.89	<.001	1.54	1.23–1.93	<.001
High neighborhood disorder	2.07	1.52–2.81	<.001	1.73	1.40–2.14	<.001	1.53	1.23–1.91	<.001

Note: E-Risk, Environmental Risk; OR, odds ratio from ordinal logistic regression.
^aAnalyses were conducted using the full-scale neighborhood characteristic variables. That is, the average of resident-rated neighborhood characteristic scores for each E-Risk neighborhood. Social cohesion was reverse scored to facilitate comparison with neighborhood disorder.
^bThe full-scale neighborhood characteristic variables were dichotomized at the mean, so that low social cohesion was a score lower than the mean, and high neighborhood disorder was a score higher than the mean.
^cThe full-scale neighborhood characteristic variables were dichotomized at the tertile, so that low social cohesion was a score lower than the 33rd centile, and high neighborhood disorder was a score higher than the 66th centile. All analyses account for the nonindependence of twin observations.

Table 3. The Cumulative Effect of Neighborhood Social Adversity and Personal Crime Victimization on Adolescent Psychotic Experiences

Exposure to Neighborhood Social Adversity and/or Personal Crime Victimization ^a	Association of Cumulative Exposure to Neighborhood Social Adversity and Personal Crime Victimization With Adolescent Psychotic Experiences ^b					
	Model 1			Model 2		
	OR	95% CI	P Value	OR	95% CI	P Value
0—Neither exposure	[Reference]	—	—	[Reference]	—	—
1—Neighborhood social adversity only	1.52	1.18–1.97	.001	1.33	1.00–1.78	.052
2—Personal crime victimization only	3.35	2.46–4.55	<.001	2.72	1.96–3.77	<.001
3—Neighborhood social adversity and personal crime victimization	6.79	4.81–9.60	<.001	4.86	3.28–7.20	<.001
Interaction between neighborhood social adversity and personal crime victimization	ICR 2.92, 95% CI = 0.63–5.22, $P = .013$			ICR = 1.81, 95% CI = -0.03–3.65, $P = .054$		

Note: ICR, interaction contrast ratio; OR, odds ratio from ordinal logistic regression.

^aThese 4 exposure categories were created by combining neighborhood social adversity (neighborhood was simultaneously characterized by low social cohesion and high neighborhood disorder) with personal crime victimization: 0 = not exposed to either; 1 = lived in the most socially adverse neighborhood but not personally victimized by violent crime; 2 = personally victimized by violent crime but did not live in the most socially adverse neighborhood; and 3 = exposed to both the most socially adverse neighborhood conditions and also personally victimized by violent crime.

^bThe association of cumulative exposures to neighborhood social adversity and personal crime victimization with adolescent psychotic experiences was calculated with ordinal logistic regression because adolescent psychotic experiences are on an ordinal (0–3) rather than binary scale. Model 1—the unadjusted associations of neighborhood social adversity and personal crime victimization with adolescent psychotic experiences. Model 2—adjusted simultaneously for childhood psychotic symptoms, family-level characteristics (family socioeconomic status, family psychiatric history, maternal psychotic symptoms), individual-level characteristics (adolescent alcohol dependence and adolescent cannabis dependence), and neighborhood-level deprivation at age 12. All analyses account for the nonindependence of twin observations.

effect of the most urban residency on adolescent psychotic symptoms to that found for adolescent psychotic experiences. Finally, supplementary table 3 yielded very similar point estimates for the cumulative exposures categories, though some associations failed to reach statistical significance.

Discussion

This study investigated the role of urbanicity, neighborhood social conditions, and personal crime victimization in adolescent psychotic experiences and revealed 3 initial findings. First, the association between growing up in an urban environment and adolescent psychotic experiences remained after considering a range of potential confounders including family SES, family psychiatric history, maternal psychosis, adolescent substance problems, and neighborhood-level deprivation. This association between urbanicity and psychotic experiences was explained, in part, by 2 features of the neighborhood social environment, namely lower levels of social cohesion and higher levels of neighborhood disorder. Second, personal victimization by violent crime was nearly twice as common among adolescents in the most socially adverse neighborhoods, and adolescents who had experienced such victimization had over 3 times greater odds of having psychotic experiences. Third, the cumulative effect of neighborhood social adversity and personal crime victimization on adolescent psychotic experiences was substantially greater than either exposure alone, highlighting a potential interaction between these exposures. That is, adolescents who had lived in the most adverse neighborhood conditions and been personally victimized were at the greatest risk for psychotic experiences during adolescence.

The present findings extend previous evidence from this cohort implicating childhood urbanicity and neighborhood characteristics in the occurrence of childhood psychotic symptoms.²⁵ Here we show that the effects of urban and socially adverse neighborhood conditions on psychotic experiences are not limited to childhood, but continue into adolescence when psychotic phenomena become more clinically relevant.²⁶ These findings support previous evidence demonstrating higher rates of psychosis-proneness and prodromal status among adolescents and young adults in urban,¹ threatening,⁵⁶ and socially fragmented neighborhoods.⁵⁷ Late adolescence heralds the peak age at which psychotic disorders are typically diagnosed.⁵⁸ If a degree of aetiological continuity truly exists between adolescent psychotic experiences and adult psychotic disorder, ours and other recent findings tentatively support a mechanism linking adverse neighborhood conditions during upbringing with psychosis in adulthood.

In our study, the combined effect of adverse neighborhood social conditions and personal victimization by

violent crime was greater than the independent effects of each. This is consistent with cumulative stress models and previous studies showing that risk for psychosis phenotypes increases as the frequency and severity of stressful exposures increase.^{31–34,59,60} Several biological and psychological mechanisms could explain why adolescents who were exposed to neighborhood social adversity and violent crime during upbringing were more prone to psychotic experiences. Prolonged and acute early-life stress is purported to dysregulate the biological stress response^{61–63} and lead to dopaminergic sensitization, which is the leading hypothesized neurochemical pathway for the positive symptoms of psychosis.^{61,64} In addition, adolescents who grow up in threatening neighborhoods with weak or absent community networks could develop psychosis-like cognitive schemas such as paranoia, hypervigilance, and negative attributional styles.^{65,66} A cognitive pathway (rather than a nonspecific stress mechanism alone) could explain why effects were apparent for psychotic experiences but not major depression. Our findings tentatively suggest a mechanism whereby childhood exposure to neighborhood social adversity sensitizes individuals to subsequent stressful experiences such as crime victimization. This hypothesized mechanism is supported by recent evidence of neurological differences in social stress reactivity between adults with urban vs rural upbringing.^{67,68} Further research into the influence of neighborhood exposures on childhood neurocognitive development could shed light on this hypothesized mechanism.

Limitations

Several limitations should be considered. First, causality of findings from this observational study cannot be assumed. Noncausal mechanisms, such as the selection of genetically high-risk families into urban and adverse neighborhoods, remain possible,⁶⁹ though our findings were not explained by proxy indicators of genetic and familial risk. Second, neighborhood conditions were measured approximately 5 years before adolescent psychotic experiences were assessed. However, the vast majority of adolescents (71.4%, $n = 1475$) reported that they did not move house between ages 12 and 18. Third, though crime victimization was more common in adverse neighborhoods, we do not know the extent to which these victimization experiences occurred outside the home. Perpetrators of physical violence are often family members,⁷⁰ suggesting that our measure of violent crime captured victimization inside as well as outside the home. Fourth, psychotic experiences are associated with adult psychosis but also with other serious psychiatric conditions⁵; while a degree of specificity was suggested in that the effect of urbanicity on psychotic experiences was not replicated for adolescent depression and was not explained by adolescent substance problems, it is probable that the mental health implications of growing up in

an urban setting extend beyond psychosis.⁷¹ In addition, associations arising for the clinically-verified psychotic symptoms were often nonsignificant. It is possible that the low prevalence of psychotic symptoms in this sample restricted our power to detect associations. However, it is also possible that the self-report measure of adolescent psychotic experiences captured genuine experiences (eg, being followed by a stranger) as well as psychotic phenomena (eg, being followed by a detective). This may have inflated the associations arising for adolescent psychotic experiences, though it is reassuring that point estimates were fairly similar to those produced for psychotic symptoms. Finally, our findings come from a sample of twins which potentially differ from singletons. However, E-Risk families closely match the distribution of UK families across the spectrum of urbanicity³⁸ and neighborhood-level deprivation.⁴⁶ Furthermore, the prevalence of adolescent psychotic experiences among E-Risk participants is similar to non-twin samples of adolescents and young adults.¹⁻⁴

Conclusions

Our findings provide initial evidence that adverse neighborhood social conditions and violent crime victimization, which are relatively common exposures particularly among urban youth, increase risk for adolescent psychotic experiences. From a public health perspective, ours and other recent findings on geospatial correlates of early psychosis phenotypes^{56,57} suggest that preventative early intervention strategies for psychosis might capture particularly high-risk groups if targeted towards youth living in urban and socially adverse neighborhoods. As increasing numbers of youth around the world are living in cities,⁷² there is a growing need to improve our understanding of how both built and social features of urban settings are supporting and challenging young people's mental health.

Supplementary Material

Supplementary material is available at *Schizophrenia Bulletin* online.

Funding

The E-Risk Study is funded by the Medical Research Council (G1002190). Additional support was provided by National Institute of Child Health and Human Development (HD077482); Google Streetview; British Academy (SQ140024); and the Jacobs Foundation. J.N. received a Multidisciplinary Studentship from the Economic and Social Research Council (ESRC). L.A. is the Mental Health Leadership Fellow for the UK ESRC. H.L.F. is supported by an MQ Fellows Award (MQ14F40). C.L.O. is a Jacobs Foundation Advanced

Research Fellow and a Canadian Institute for Advanced Research Fellow.

Acknowledgments

We are extremely grateful to the study mothers and fathers, the twins, and the twins' teachers for their participation. Our thanks to members of the E-Risk team for their dedication, hard work and insights, and to CACI Inc. for use of their consumer lifestyle databases. We also thank Emma Hedman, Jill Collins and Paul Langston for their geo-coding assistance. The authors have declared that there are no conflicts of interest in relation to the subject of this study.

References

1. Spauwen J, Krabbendam L, Lieb R, Wittchen HU, van Os J. Does urbanicity shift the population expression of psychosis? *J Psychiatr Res*. 2004;38:613–618.
2. Kelleher I, Connor D, Clarke MC, et al. Prevalence of psychotic symptoms in childhood and adolescence: a systematic review and meta-analysis of population-based studies. *Psychol Med*. 2012;42:1857–1863.
3. Yoshizumi T, Murase S, Honjo S, Kaneko H, Murakami T. Hallucinatory experiences in a community sample of Japanese children. *J Am Acad Child Adolesc Psychiatry*. 2004;43:1030–1036.
4. Horwood J, Salvi G, Thomas K, et al. IQ and non-clinical psychotic symptoms in 12-year-olds: results from the ALSPAC birth cohort. *Br J Psychiatry*. 2008;193:185–191.
5. Fisher HL, Caspi A, Poulton R, et al. Specificity of childhood psychotic symptoms for predicting schizophrenia by 38 years of age: a birth cohort study. *Psychol Med*. 2013;43:2077–2086.
6. Poulton R, Caspi A, Moffitt TE, et al. Children's self-reported psychotic symptoms and adult schizophreniform disorder: a 15-year longitudinal study. *Arch Gen Psychiatry*. 2000;57:1053–1058.
7. Kelleher I, Lynch F, Harley M, et al. Psychotic symptoms in adolescence index risk for suicidal behavior: findings from 2 population-based case-control clinical interview studies. *Arch Gen Psychiatry*. 2012;69:1277–1283.
8. Millan MJ, Andrieux A, Bartzokis G, et al. Altering the course of schizophrenia: progress and perspectives. *Nat Rev Drug Discov*. 2016;15:485–515.
9. Davidson LL, Grigorenko EL, Boivin MJ, Rapa E, Stein A. A focus on adolescence to reduce neurological, mental health and substance-use disability. *Nature*. 2015;527:S161–S166.
10. Kelleher I, Cannon M. Psychotic-like experiences in the general population: characterizing a high-risk group for psychosis. *Psychol Med*. 2011;41:1–6.
11. Vassos E, Pedersen CB, Murray RM, Collier DA, Lewis CM. Meta-analysis of the association of urbanicity with schizophrenia. *Schizophr Bull*. 2012;38:1118–1123.
12. Krabbendam L, van Os J. Schizophrenia and urbanicity: a major environmental influence—conditional on genetic risk. *Schizophr Bull*. 2005;31:795–799.
13. Pedersen CB, Mortensen PB. Evidence of a dose-response relationship between urbanicity during upbringing and schizophrenia risk. *Arch Gen Psychiatry*. 2001;58:1039–1046.

14. Marcelis M, Navarro-Mateu F, Murray R, Selten JP, Van Os J. Urbanization and psychosis: a study of 1942-1978 birth cohorts in The Netherlands. *Psychol Med*. 1998;28:871-879.
15. Lewis G, Davis A, Andreasson S, Allebeck P. Schizophrenia and city life. *The Lancet*. 1992;340:137-140.
16. Allardyce J, Boydell J, Van Os J, et al. Comparison of the incidence of schizophrenia in rural Dumfries and Galloway and urban Camberwell. *Br J Psychiatry*. 2001;179:335-339.
17. Lögdberg B, Nilsson LL, Levander MT, Levander S. Schizophrenia, neighbourhood, and crime. *Acta Psychiatr Scand*. 2004;110:92-97.
18. Allardyce J, Gilmour H, Atkinson J, et al. Social fragmentation, deprivation and urbanicity: relation to first-admission rates for psychoses. *Br J Psychiatry*. 2005;187:401-406.
19. Kirkbride JB, Boydell J, Ploubidis GB, et al. Testing the association between the incidence of schizophrenia and social capital in an urban area. *Psychol Med*. 2008;38:1083-1094.
20. Zammit S, Lewis G, Rasbash J, et al. Individual, schools, and neighborhood. *Arch Gen Psychiatry*. 2010;67:914-922.
21. Veling W, Susser E, Selten JP, Hoek HW. Social disorganization of neighborhoods and incidence of psychotic disorders: a 7-year first-contact incidence study. *Psychol Med*. 2015;45:1789-1798.
22. Polanczyk G, Moffitt TE, Arseneault L, et al. Etiological and clinical features of childhood psychotic symptoms: results from a birth cohort. *Arch Gen Psychiatry*. 2010;67:328-338.
23. Dragt S, Nieman DH, Veltman D, et al. Environmental factors and social adjustment as predictors of a first psychosis in subjects at ultra high risk. *Schizophr Res*. 2011;125:69-76.
24. Spauwen J, Krabbendam L, Lieb R, Wittchen HU, van Os J. Evidence that the outcome of developmental expression of psychosis is worse for adolescents growing up in an urban environment. *Psychol Med*. 2006;36:407-415.
25. Newbury J, Arseneault L, Caspi A, et al. Why are children in urban neighborhoods at increased risk for psychotic symptoms? Findings from a UK longitudinal cohort study. *Schizophr Bull*. 2016;42:1372-1383.
26. Kelleher I, Keeley H, Corcoran P, et al. Clinicopathological significance of psychotic experiences in non-psychotic young people: evidence from four population-based studies. *Br J Psychiatry*. 2012;201:26-32.
27. Home Office Statistical Bulletin. *Crime in England and Wales 2009/10: Findings from the British Crime Survey and Police Recorded Crime (Third Edition)*. London, UK: Home Office; 2010.
28. Federal Bureau of Investigation. *Crime in the United States, 2015: Uniform Crime Report*. Clarksburg, WV: FBI Criminal Justice Information Services Division; 2015.
29. Kirkbride JB, Jones PB, Ullrich S, Coid JW. Social deprivation, inequality, and the neighborhood-level incidence of psychotic syndromes in East London. *Schizophr Bull*. 2014;40:169-180.
30. Office for National Statistics. *The Likelihood of Becoming a Victim of Crime: Crime Statistics, Period Ending March 2012*. London, UK: Office for National Statistics; 2012.
31. Turner RJ, Lloyd DA. Lifetime traumas and mental health: the significance of cumulative adversity. *J Health Soc Behav*. 1995;36:360-376.
32. Shevlin M, Houston JE, Dorahy MJ, Adamson G. Cumulative traumas and psychosis: an analysis of the national comorbidity survey and the British Psychiatric Morbidity Survey. *Schizophr Bull*. 2008;34:193-199.
33. Lataster J, Myin-Germeys I, Lieb R, Wittchen HU, van Os J. Adversity and psychosis: a 10-year prospective study investigating synergism between early and recent adversity in psychosis. *Acta Psychiatr Scand*. 2012;125:388-399.
34. Morgan C, Reininghaus U, Reichenberg A, et al. Adversity, cannabis use and psychotic experiences: evidence of cumulative and synergistic effects. *Br J Psychiatry*. 2014;204:346-353.
35. Moffitt TE; E-Risk Study Team. Teen-aged mothers in contemporary Britain. *J Child Psychol Psychiatry*. 2002;43:727-742.
36. Loewy RL, Pearson R, Vinogradov S, Bearden CE, Cannon TD. Psychosis risk screening with the Prodromal Questionnaire-brief version (PQ-B). *Schizophr Res*. 2011;129:42-46.
37. Office for National Statistics. *Urban and Rural Area Definitions for Policy Purposes in England and Wales: Methodology (v1.0)*. London, UK: Office of National Statistics; 2013.
38. Odgers CL, Moffitt TE, Tach LM, et al. The protective effects of neighborhood collective efficacy on British children growing up in deprivation: a developmental analysis. *Dev Psychol*. 2009;45:942-957.
39. Odgers CL, Caspi A, Bates CJ, Sampson RJ, Moffitt TE. Systematic social observation of children's neighborhoods using Google Street View: a reliable and cost-effective method. *J Child Psychol Psychiatry*. 2012;53:1009-1017.
40. Sampson RJ, Raudenbush SW, Earls F. Neighborhoods and violent crime: a multilevel study of collective efficacy. *Science*. 1997;277:918-924.
41. Sampson RJ, Raudenbush SW. Systematic social observation of public spaces: a new look at disorder in urban neighborhoods. *Am J Sociol*. 1999;105:603-651.
42. Finkelhor D, Hamby S, Turner H, Ormrod R. *The Juvenile Victimization Questionnaire: 2nd Revision (JVQ-R2)*. Durham, NC: Crimes Against Children Research Center; 2011.
43. Fisher HL, Caspi A, Moffitt TE, et al. Measuring adolescents' exposure to victimization: the Environmental Risk (E-Risk) Longitudinal Twin Study. *Dev Psychopathol*. 2015;27:1399-1416.
44. Odgers CL, Caspi A, Russell MA, et al. Supportive parenting mediates neighborhood socioeconomic disparities in children's antisocial behavior from ages 5 to 12. *Dev Psychopathol*. 2012;24:705-721.
45. CACI Information Services. *ACORN User Guide*. London, UK: CACI; 2006.
46. Caspi A, Taylor A, Moffitt TE, Plomin R. Neighborhood deprivation affects children's mental health: environmental risks identified in a genetic design. *Psychol Sci*. 2000;11:338-342.
47. Milne BJ, Moffitt TE, Crump R, et al. How should we construct psychiatric family history scores? A comparison of alternative approaches from the Dunedin Family Health History Study. *Psychol Med*. 2008;38:1793-1802.
48. Weissman MM, Wickramaratne P, Adams P, et al. Neighborhood deprivation affects children's mental health: environmental risks identified in a genetic design. *Arch Gen Psychiatry*. 2000;57:675-682.
49. Robins L, Cottler L, Bucholz K, Compton W. *Diagnostic Interview Schedule for DSM-IV (DIS-IV)*. St Louis, MO: Washington University School of Medicine; 1995.
50. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. Washington, DC: American Psychiatric Association; 1994.
51. Henquet C, Krabbendam L, Spauwen J, et al. Prospective cohort study of cannabis use, predisposition for psychosis, and psychotic symptoms in young people. *BMJ*. 2005;330:11.

52. Johns LC, Cannon M, Singleton N, et al. Prevalence and correlates of self-reported psychotic symptoms in the British population. *Br J Psychiatry*. 2004;185:298–305.
53. Zavos HM, Eley TC, McGuire P, et al. Shared etiology of psychotic experiences and depressive symptoms in adolescence: a Longitudinal Twin Study. *Schizophr Bull*. 2016;42:1197–1206.
54. Rogers W. Regression standard errors in clustered samples. *STB*. 1994;3:19–23.
55. Breen R, Karlson KB, Holm A. Total, direct, and indirect effects in logit and probit models. *Sociol Methods Res*. 2013;42:164–191.
56. Wilson C, Smith ME, Thompson E, et al. Context matters: the impact of neighborhood crime and paranoid symptoms on psychosis risk assessment. *Schizophr Res*. 2016;171:56–61.
57. Kirkbride JB, Stochl J, Zimbrón J, et al. Social and spatial heterogeneity in psychosis proneness in a multilevel case-prodrome-control study. *Acta Psychiatr Scand*. 2015;132:283–292.
58. Häfner H, Maurer K, Löffler W, Fätkenheuer B. The epidemiology of early schizophrenia. Influence of age and gender on onset and early course. *Br J Psychiatry*. 1994;164:29–38.
59. Morgan C, Reininghaus U, Fearon P, et al. Modelling the interplay between childhood and adult adversity in pathways to psychosis: initial evidence from the AESOP study. *Psychol Med*. 2014;44:407–419.
60. Arseneault L, Cannon M, Fisher HL, et al. Childhood trauma and children's emerging psychotic symptoms: a genetically sensitive longitudinal cohort study. *Am J Psychiatry*. 2011;168:65–72.
61. van Winkel R, Stefanis NC, Myin-Germeys I. Psychosocial stress and psychosis. A review of the neurobiological mechanisms and the evidence for gene-stress interaction. *Schizophr Bull*. 2008;34:1095–1105.
62. Walker E, Mittal V, Tessner K. Stress and the hypothalamic pituitary adrenal axis in the developmental course of schizophrenia. *Annu Rev Clin Psychol*. 2008;4:189–216.
63. Tarullo AR, Gunnar MR. Child maltreatment and the developing HPA axis. *Horm Behav*. 2006;50:632–639.
64. Selten JP, van der Ven E, Rutten BP, Cantor-Graae E. The social defeat hypothesis of schizophrenia: an update. *Schizophr Bull*. 2013;39:1180–1186.
65. Garety PA, Kuipers E, Fowler D, Freeman D, Bebbington PE. A cognitive model of the positive symptoms of psychosis. *Psychol Med*. 2001;31:189–195.
66. Freeman D, Garety PA, Kuipers E, Fowler D, Bebbington PE. A cognitive model of persecutory delusions. *Br J Clin Psychol*. 2002;41:331–347.
67. Lederbogen F, Kirsch P, Haddad L, et al. City living and urban upbringing affect neural social stress processing in humans. *Nature*. 2011;474:498–501.
68. Haddad L, Schäfer A, Streit F, et al. Brain structure correlates of urban upbringing, an environmental risk factor for schizophrenia. *Schizophr Bull*. 2015;41:115–122.
69. Sariaslan A, Fazel S, D'Onofrio BM, et al. Schizophrenia and subsequent neighborhood deprivation: revisiting the social drift hypothesis using population, twin and molecular genetic data. *Transl Psychiatry*. 2016;6:e796.
70. Finkelhor D, Ormrod R, Turner H, Hamby SL. The victimization of children and youth: a comprehensive, national survey. *Child Maltreat*. 2005;10:5–25.
71. Vassos E, Agerbo E, Mors O, Pedersen CB. Urban-rural differences in incidence rates of psychiatric disorders in Denmark. *Br J Psychiatry*. 2016;208:435–440.
72. UNICEF. *Children in an urban world*. New York, NY: United Nations Children's Fund; 2012.

5.1 Supplementary materials

The following supplementary tables present results from additional analyses in Chapter 5, which calculated the levels of social cohesion and neighbourhood disorder according to level of urbanicity, and tested the sensitivity of findings by repeating analyses using the clinically-verified measure of adolescent psychotic symptoms.

Supplementary Table 5.1. Levels of social cohesion and neighbourhood disorder according to level of urbanicity

Level of urbanicity	Levels of social cohesion and neighbourhood disorder according to level of urbanicity			
	Social cohesion		Neighbourhood disorder	
	M	SD	M	SD
Rural	2.58	0.42	0.27	0.22
Intermediate	2.19	0.45	0.49	0.32
Urban	2.07	0.52	0.62	0.37
Association between urbanicity and neighbourhood characteristics	B = -0.24, (95% CI = -0.28 – -0.20), $p < 0.001$, $B = -0.34$		B = 0.17, (95% CI = 0.14 – 0.19), $p < 0.001$, $B = 0.35$	

Note: B, unstandardised beta coefficient; B , standardised beta coefficient; CI, confidence; M mean; SD, standard deviation. ^aThree-level urbanicity at age 12: Rural = rural towns and fringes, villages, hamlets, isolated dwellings; Intermediate = urban cities and towns; Urban = major and minor conurbations. The standardised (B) beta coefficients indicate the unit standard deviation change in each neighbourhood characteristic given one unit standard deviation change in urbanicity, and allow comparison between social cohesion and neighbourhood disorder which are on different scales. Standardised betas provide the same point estimates as correlation coefficients and may be interpreted as correlations, with a score of +1.0 indicating a 100% positive correlation. Unstandardised beta (B) coefficients account for the non-independence of twin observations.

Supplementary Table 5.2. Association between childhood urbanicity and adolescent psychotic symptoms

Model	Level of urbanicity ^a	Covariates	Association between childhood urbanicity and adolescent psychotic symptoms		
			OR	95% CI	P value
Model 1	Rural		[reference]	-	-
	Intermediate		1.44	0.64 – 3.22	0.373
	Urban		1.68	0.73 – 3.85	0.218
Model 2	Rural		[reference]	-	-
	Intermediate		1.06	0.43 – 2.58	0.905
	Urban		1.40	0.57 – 3.41	0.460
		Family socioeconomic status	1.08	0.70 – 1.65	0.734
		Family psychiatric history	2.51	0.73 – 8.66	0.146
		Maternal psychotic symptoms	1.22	0.95 – 1.58	0.124
		Adolescent alcohol dependence	2.14	1.11 – 4.14	0.023
		Adolescent cannabis dependence	2.06	0.79 – 5.34	0.137
		Neighbourhood-level deprivation	1.14	0.88 – 1.47	0.312
Model 3	Rural		[reference]	-	-
	Intermediate		1.33	0.56 – 3.16	0.516
	Urban		1.41	0.58 – 3.44	0.446
		Neighbourhood social conditions	1.34	0.99 – 1.80	0.055

Note: CI, confidence interval; OR, odds ratio from logistic regression. ^a Three-level urbanicity at age 12: Rural = rural towns and fringes, villages, hamlets, isolated dwellings; Intermediate = urban cities and towns; Urban = major and minor conurbations. Model 1 – the unadjusted association between childhood urbanicity and adolescent psychotic symptoms (Sample size = 1978). Model 2 – adjusted for family-level characteristics (family socioeconomic status, family psychiatric history, maternal psychotic symptoms), individual-level characteristics (adolescent alcohol dependence and adolescent cannabis dependence), and neighbourhood-level deprivation at age 12 (sample size = 1900 participants). Model 3 – adjusted for neighbourhood social conditions (social cohesion and neighbourhood disorder) at age 12 (sample size = 1956 participants). Sample sizes vary slightly between models due to small numbers of participants missing data on independent variables. All analyses account for the non-independence of twin observations.

Supplementary Table 5.3. The cumulative effect of neighbourhood social adversity and personal crime victimization on adolescent psychotic symptoms

Exposure to neighbourhood social adversity and/or personal crime victimization ^a	Association of cumulative exposure to neighbourhood social adversity and personal crime victimization with adolescent psychotic symptoms					
	Model 1			Model 2		
	OR	95% CI	P value	OR	95% CI	P value
0 – Neither exposure	[reference]	-	-	[reference]	-	-
1 – Neighbourhood social adversity only	1.46	0.72 – 2.96	0.300	1.29	0.60 – 2.79	0.509
2 – Personal crime victimization only	2.95	1.38 – 6.28	0.005	2.11	0.90 – 4.92	0.084
3 – Neighbourhood social adversity and personal crime victimization	4.52	2.18 – 9.36	<0.001	3.19	1.34 – 7.57	0.009
Interaction between neighbourhood social adversity and personal crime victimization	ICR = 1.12, 95% CI = -1.96 – 4.19, p = 0.477			ICR = 0.79, 95% CI = -1.74 - 3.31, p = 0.541		

Note: CI, confidence interval; ICR, interaction contrast ratio; OR, odds ratio from logistic regression. ^a These four exposure categories were created by combining neighbourhood social adversity (neighbourhood was simultaneously characterized by low social cohesion and high neighbourhood disorder) with personal crime victimization: 0=not exposed to either; 1=lived in the most socially adverse neighbourhood but not personally victimized by violent crime; 2=personally victimized by violent crime but did not live in the most socially adverse neighbourhood conditions; and 3=exposed to both the most socially adverse neighbourhood conditions and also personally victimized by violent crime. Model 1 – the unadjusted associations of neighbourhood social adversity and personal crime victimization with adolescent psychotic symptoms. Model 2 – adjusted simultaneously for childhood psychotic symptoms, family SES, family psychiatric history, maternal psychosis, adolescent cannabis dependence, adolescent alcohol dependence, and neighbourhood-level deprivation. All analyses account for the non-independence of twin observations.

Chapter 6: In the eye of the beholder: Perceptions of neighbourhood adversity and psychotic experiences in adolescence

This chapter is presented in the published format from the following publication:

Newbury, J, B., Arseneault, L., Caspi, A., Moffitt, T, E., Odgers, C, L., Baldwin, J, R., Zavos, H, M, S., Fisher, H, L. (2017). In the eye of the beholder: Perceptions of neighbourhood adversity and psychotic experiences in adolescence. *Development and Psychopathology*, 29, 1823–1837. doi.org/10.1017/S0954579417001420

In the eye of the beholder: Perceptions of neighborhood adversity and psychotic experiences in adolescence

JOANNE B. NEWBURY,^a LOUISE ARSENEAULT,^a AVSHALOM CASPI,^{a,b} TERRIE E. MOFFITT,^{a,b}
CANDICE L. ODGERS,^b JESSIE R. BALDWIN,^a HELENA M. S. ZAVOS,^a AND HELEN L. FISHER^a
^aKing's College London; and ^bDuke University

Abstract

Adolescent psychotic experiences increase risk for schizophrenia and other severe psychopathology in adulthood. Converging evidence implicates urban and adverse neighborhood conditions in the etiology of adolescent psychotic experiences, but the role of young people's personal perceptions of disorder (i.e., physical and social signs of threat) in their neighborhood is unknown. This was examined using data from the Environmental Risk Longitudinal Twin Study, a nationally representative birth cohort of 2,232 British twins. Participants were interviewed at age 18 about psychotic phenomena and perceptions of disorder in the neighborhood. Multilevel, longitudinal, and genetically sensitive analyses investigated the association between perceptions of neighborhood disorder and adolescent psychotic experiences. Adolescents who perceived higher levels of neighborhood disorder were significantly more likely to have psychotic experiences, even after accounting for objectively/independently measured levels of crime and disorder, neighborhood- and family-level socioeconomic status, family psychiatric history, adolescent substance and mood problems, and childhood psychotic symptoms: odds ratio = 1.62, 95% confidence interval [1.27, 2.05], $p < .001$. The phenotypic overlap between adolescent psychotic experiences and perceptions of neighborhood disorder was explained by overlapping common environmental influences, $rC = .88$, 95% confidence interval [0.26, 1.00]. Findings suggest that early psychological interventions to prevent adolescent psychotic experiences should explore the role of young people's (potentially modifiable) perceptions of threatening neighborhood conditions.

Up to one-third of youth in the general population report sub-clinical psychotic experiences such as hearing voices, having visions, being extremely paranoid, and other unusual thoughts and beliefs (Horwood et al., 2008; Kelleher, Connor, et al., 2012; Newbury, Arseneault, Caspi, et al., 2017; Spauwen, Krabbendam, Lieb, Wittchen, & van Os, 2004; Yoshizumi, Muase, Honjo, Kanesko, & Murakami, 2004). Though early psychotic phenomena are usually transitory (Kelleher, Connor, et al., 2012; Scott, Chant, Andrews, & McGrath, 2006), adolescents who report these experiences have a significantly elevated adulthood risk for schizophrenia

(Fisher et al., 2013; Poulton et al., 2000) and other serious psychiatric problems such as depression, substance dependence, and suicide attempts (Dhossche, Ferdinand, van der Ende, Hofstra, & Verhulst, 2002; Fisher et al., 2013; Kelleher, Lynch, et al., 2012). Late adolescence heralds the peak age of risk for a first episode of psychosis (Häfner, Maurer, Löffler, & Fätkenheuer, 1994), a diagnosis that increases young people's risk of death within a year by over 20-fold (Schoenbaum et al., 2017). Subclinical psychotic experiences during this period have also been shown to be more clinically relevant than at earlier ages (Kelleher, Keeley, et al., 2012). It is therefore crucial to improve our understanding of the mechanisms leading to psychotic experiences during adolescence, from genetic influences through to the wider built and social environment, in order to develop more targeted and effective preventative interventions (Millan et al., 2016).

Adolescent psychotic experiences share similar familial and social risk factors to adult psychosis, such as family history of mental illness, marijuana use, and low socioeconomic status (SES; Kelleher & Cannon, 2011; Polanczyk et al., 2010). Emerging research now implicates adverse wider environmental factors in the etiology of subclinical psychotic phenomena and clinical psychosis. Compared to youth living in rural settings, young people in cities are exposed to higher neighborhood levels of fragmentation, crime, and disorder (Goldman-Mellor, Margerison-Zilko, Allen, & Cerdá, 2016; Newbury, Arseneault, Caspi, et al., 2017; Office for National Statistics, 2012). Neighborhood disorder is a sociological con-

We are grateful to the study mothers and fathers, the twins, and the twins' teachers for their participation. Our thanks to members of the E-Risk team for their dedication, hard work, and insights, and to CACI Inc. for use of their consumer lifestyle databases. We also thank Emma Hedman for geocoding assistance. The Environmental Risk (E-Risk) Longitudinal Twin Study is funded by the Medical Research Council (G1002190). Additional support was provided by National Institute of Child Health and Human Development (HD077482); the British Academy (SQ140024); and the Jacobs Foundation. Support was also provided through Multidisciplinary Studentships from the Economic and Social Research Council (ESRC; to J.B.N. and J.R.B.); a Mental Health Leadership Fellowship for the UK ESRC (to L.A.); MQ Fellows Award MQ14F40 (to H.L.F.); and a Jacobs Foundation and Canadian Institute for Advanced Research Fellowship (to C.L.O.). The last two authors are joint senior authors.

Address correspondence and reprint requests to: Helen L. Fisher, MRC SGDP Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, 16 De Crespigny Park, London SE5 8AF, UK; E-mail: helen.2.fisher@kcl.ac.uk.

struct that refers to physical and social signs of threat and danger in the neighborhood, such as vandalism, gang activity, and burglaries (Sampson & Raudenbush, 1999). Youth and young adults who live in these kinds of urban, fragmented, and threatening settings are more likely to have prodromal symptoms, persistent psychotic experiences, and a first episode of psychosis (Bhavsar, Boydell, Murray, & Power, 2014; Kirkbride et al., 2015; Spauwen, Krabbendam, Lieb, Wittchen, & van Os, 2006; Wilson et al., 2016), and there is evidence that symptom severity among adults with clinical psychosis is exacerbated after brief exposure to a densely populated urban environment (Ellett, Freeman, & Garety, 2008; Freeman et al., 2014). Furthermore, we recently identified higher rates of psychotic phenomena among children and adolescents living in cities in the United Kingdom (Newbury et al., 2016; Newbury, Arseneault, Caspi, et al., 2017). Our analyses showed that threatening and adverse neighborhood social conditions, as reported by mothers and residents, explained up to half of this association between urbanicity and early psychotic phenomena (Newbury et al., 2016; Newbury, Arseneault, Caspi, et al., 2017). There is now a growing consensus that urban and adverse neighborhood conditions increase risk for psychotic phenomena by elevating background and acute sources of social stress, particularly during upbringing (Heinz, Deserno, & Reininhaus, 2013; Lederbogen, Haddad, & Meyer-Lindenberg, 2013; Selten, van der Ven, Rutten, & Cantor-Graae, 2013). This proposed mechanism requires that young people in cities and adverse neighborhood settings are themselves perceiving their neighborhoods as stressful and threatening.

Existing studies of neighborhood conditions and psychosis (both subclinical and clinical phenotypes) have typically derived neighborhood measures from official data assigned to broad geostatistical units. While being objective, these types of measures do not establish the extent to which the neighborhood feature(s) in question was personally experienced or perceived by the individuals under study (the ecological fallacy). Individuals can and do differ in how they perceive the same environment or experience, but we currently know very little about the potential role of young people's personal perceptions of threat in their immediate neighborhood in the etiology of early psychotic phenomena. That is, it is unknown whether personal perceptions of neighborhood conditions are important over and above objectively measured neighborhood conditions. Considering that urban and adverse neighborhood conditions putatively increase risk for psychotic phenomena via a social stress pathway, and delusions and hallucinations involve altered perceptions of reality, we might expect personal perceptions of the neighborhood (e.g., "my neighborhood is dangerous") to play a crucial role in the association between adverse neighborhood conditions and psychotic experiences. Recent research has shown that perceptions of neighborhood disorder are associated with common mental health problems and psychological distress among youth, above and beyond the effects of official levels of crime (Goldman-Mellor et al., 2016; Polling, Khondoker, Hatch, Hotopf, & South East London Community

Health Study Team, 2014). These findings also parallel a body of research documenting stronger associations between childhood trauma and psychiatric problems when childhood trauma is retrospectively self-reported rather than obtained from objective or independent sources (Brown, Berenson, & Cohen, 2005; Newbury, Arseneault, Moffitt, et al., 2017; Reuben et al., 2016; Widom & Morris, 1997; Widom, Weiler, & Cottler, 1999). Examining the role of young people's personal perceptions of threatening neighborhood conditions in early psychotic experiences could not only elucidate the mechanisms underlying previous findings on neighborhood adversity and psychotic experiences but also highlight potential new avenues for interventions. For example, targeted cognitive behavioral interventions have been shown to alleviate the paranoia and distress caused by busy urban settings among patients with clinical psychosis (Freeman et al., 2015).

A number of potential methodological issues must be considered when examining the role of perceived neighborhood conditions in early psychotic phenomena. Similarly to self-report measures of childhood trauma (Hardt & Rutter, 2004), self-report measures of adverse neighborhood conditions could be subject to shared method and mood-congruent recall biases, whereby an individual's contemporaneous mental health influences their perception and memory. It is particularly important to consider this potential confounding mechanism when investigating psychotic experiences, which involve altered perceptions of reality, such as paranoia and threat detection bias (Freeman, Garety, Kuipers, Fowler, & Bebbington, 2002; Garety, Kuiper, Fowler, Freeman, & Bebbington, 2001). It is therefore useful to establish the construct validity of personal perceptions of neighborhood adversity by comparing self-reports to objective and independent measures of the neighborhood. Moreover, given the potential bidirectional relationship between psychotic experiences and perceptions of the neighborhood, longitudinal designs are needed to examine the temporality of the association. It is also crucial to consider a range of factors that might simultaneously influence both adolescents' perceptions of neighborhood adversity and their psychotic experiences, such as family SES, substance use, earlier psychotic symptoms in childhood, and genetic influences. Emerging behavioral genetics research suggests that overlapping genes may partly explain the correlation between psychotic phenomena and certain putatively environmental exposures, such as stressful life events (Shakoor et al., 2016) and neighborhood-level deprivation (Sariaslan et al., 2016). It is plausible that shared genetic influences might also contribute to covariance between psychotic phenomena and perceptions of neighborhood adversity. The classical twin design allows the covariance between two variables to be partitioned into genetic and environmental sources, thus providing an ideal technique for exploring this issue.

Using data from a longitudinal cohort of over 2,000 British twin children, the present study adopts a multilevel approach (spanning the wider built and social environment, family-level characteristics, and individual-level factors including genetic influences) to investigate the role of personal percep-

tions of threatening neighborhood conditions in the development of adolescent psychotic experiences. A comprehensive battery of data has been collected at several time points across early development. Psychotic phenomena were measured in both childhood (age 12) and adolescence (age 18). Urbanicity, neighborhood-level SES, and neighborhood crime rates were obtained from detailed geodemographic and official data sources. Resident surveys of over 5,000 immediate neighbors of Environmental Risk (E-Risk) Longitudinal Twin Study participants provided an independent measure of neighborhood disorder. Personal perceptions of neighborhood disorder were self-reported by the participants themselves in private interviews at age 18. All neighborhood measures had high resolution (i.e., street level or postcode level). The twin sample afforded us the opportunity to estimate the genetic versus environmental sources of covariance between perceptions of neighborhood disorder and adolescent psychotic experiences. With these measures, we investigated the construct validity of adolescents' personal perceptions of neighborhood disorder by correlating these self-reports with objective/independent measures of neighborhood adversity. We then asked the following:

1. Do higher perceived levels of neighborhood disorder among adolescents in urban (versus rural) settings explain the association between urbanicity and adolescent psychotic experiences?
2. a. Is the association between perceptions of neighborhood disorder and adolescent psychotic experiences robust to neighborhood-, family-, and individual-level confounders (official neighborhood crime rates, resident-reported neighborhood disorder, neighborhood-level SES, family SES, family psychiatric history, maternal psychotic symptoms, adolescent marijuana dependence, alcohol dependence, anxiety, depression, and childhood psychotic symptoms)?
b. Are twins who perceive higher levels of neighborhood disorder than their co-twin also more likely to have psychotic experiences (this within-family co-twin control analysis holds neighborhoods constant and accounts more robustly for unmeasured genetic and environmental factors shared between twins)?
3. Do childhood perceptions of neighborhood safety predict adolescent psychotic experiences after considering childhood psychotic symptoms, and do childhood psychotic symptoms predict adolescent perceptions of neighborhood disorder after considering childhood perceptions of neighborhood safety? (i.e., what is the temporality of the association between perceptions of neighborhood disorder and early psychotic phenomena?)
4. a. To what extent do genetic versus environmental factors contribute to perceptions of neighborhood disorder and adolescent psychotic experiences?
b. To what extent do *overlapping* genetic versus environmental factors contribute to the covariance between perceptions of neighborhood disorder and adolescent psychotic experiences?

Method

Study cohort

Participants were members of the E-Risk Longitudinal Twin Study, which tracks the development of a nationally representative birth cohort of 2,232 British twin children. The sample was drawn from a larger cohort of twins born in England and Wales in 1994–1995 (Trouton, Spinath, & Plomin, 2002). Full details about the sample are reported elsewhere (Moffitt & E-Risk Study Team, 2002). Briefly, the E-Risk sample was constructed in 1999–2000, when 1,116 families with same-sex 5-year-old twins (93% of those eligible) participated in home-visit assessments. This sample comprised 56% monozygotic (MZ) and 44% dizygotic (DZ) twin pairs; sex was evenly distributed within zygosity (49% male). Families were recruited to represent the UK population of families with newborns in the 1990s, based on residential location throughout England and Wales and mothers' age (teenaged mothers with twins were overselected to replace high-risk families who were selectively lost to the register through nonresponse; older mothers having twins via assisted reproduction were underselected to avoid an excess of well-educated older mothers). All families were English speaking, and the majority (93.7%) were White. Follow-up home visits were conducted when children were aged 7, 10, 12, and 18 (participation rates were 98%, 96%, 96%, and 93%, respectively). Home visits at ages 5, 7, 10, and 12 years included assessments with participants as well as their mother (or primary caretaker); the home visit at age 18 included interviews only with the participants. Each twin participant was assessed by a different interviewer. The average age of the twins at the time of the age 18 assessment was 18.4 years ($SD = 0.36$); all interviews were conducted after the 18th birthday. At age 18, the E-Risk sample comprised 2,066 participants. There were no differences between those who did and did not take part at age 18 in terms of age 5 SES ($\chi^2 = 0.86$, $p = .65$, age 5 IQ scores, $t = 0.98$, $p = .33$) or age 5 internalizing or externalizing behavior problems ($t = 0.40$, $p = .69$ and $t = 0.41$, $p = .68$, respectively). The Joint South London and Maudsley and the Institute of Psychiatry Research Ethics Committee approved each phase of the study. Parents gave informed consent, and participants gave assent at ages 5–12 and informed consent at age 18.

Measures

Adolescent psychotic experiences. At age 18, E-Risk participants were privately interviewed by a research worker about 13 psychotic experiences occurring since age 12. Seven items pertained to delusions and hallucinations, with items including "Have other people ever read your thoughts?" "Have you ever thought you were being followed or spied on?" and "Have you ever heard voices that other people cannot hear?" Six items pertained to unusual experiences that drew on item pools since formalized in prodromal psychosis instruments including the Prevention Through Risk Identification, Management, and Education Screen and the Structured Inter-

view for Prodromal Symptoms (Loewy, Pearson, Vinogradov, Bearden, & Cannon, 2011). These included “I worry that my food may be poisoned” and “My thinking is unusual or frightening.” Interviewers coded each item 0, 1, or 2 indicating, respectively, *not present*, *probably present*, and *definitely present*. All 13 items were summed to create a psychotic experiences scale (range = 0–18, $M = 1.19$, $SD = 2.58$). Scores were placed into an ordinal scale. All but three participants completed the psychotic experiences interview at age 18 ($N = 2,063$). Just over 30% of participants had at least one psychotic experience between ages 12 and 18: 69.8% reported no psychotic experiences (coded 0; $N = 1,440$), 15.5% reported one or two psychotic experiences (coded 1; $n = 319$), and 14.7% reported three or more psychotic experiences (coded 2; $n = 304$). This 30% prevalence is similar to the prevalence of self-reported psychotic experiences in other community samples of teenagers and young adults (Horwood et al., 2008; Kelleher, Connor, et al., 2012; Spauwen et al., 2004; Yoshizumi et al., 2004).

Childhood psychotic symptoms. Childhood psychotic symptoms were used as a control and to investigate the temporality of the association between psychotic phenomena and perceptions of neighborhood conditions. This interview has been described in detail previously (Polanczyk et al., 2010). Briefly, E-Risk families were visited by mental health trainees or professionals when children were aged 12. Each child was privately interviewed about seven psychotic symptoms pertaining to delusions and hallucinations (these same delusion/hallucination items were used at age 18 as described above). The item choice was guided by the Dunedin Study’s age 11 interview protocol (Poulton et al., 2000) and an instrument prepared for the Avon Longitudinal Study of Parents and Children (Schreier et al., 2009). Interviewers coded each experience 0, 1, or 2, indicating, respectively, *not a symptom*, *probable symptom*, and *definite symptom*. A conservative approach was taken in designating a child’s report as a symptom. First, the interviewer probed using standard prompts designed to discriminate between experiences that were plausible (e.g., “I was followed by a man after school”) and potential symptoms (e.g., “I was followed by an angel who guards my spirit”), and wrote down the child’s narrative description of the experience. Second, items and interviewer notes were assessed by a psychiatrist expert in schizophrenia, a psychologist expert in interviewing children, and a child and adolescent psychiatrist to verify the validity of the symptoms. Third, because children were twins, experiences limited to the twin relationship (e.g., “My twin and I often know what each other are thinking”) were coded as *not a symptom*. Children were only designated as experiencing psychotic symptoms if they reported at least one definite symptom. At age 12, 5.9% ($N = 125$) of children reported at least one clinically verified psychotic symptom.

Personal perceptions of neighborhood disorder. During the age 18 interviews, participants reported on social characteristics of their immediate neighborhoods, including neighbor-

hood disorder (Sampson & Raudenbush, 1999). We were interested in perceptions of neighborhood disorder based on previous research linking residents’ independent assessments of neighborhood disorder with psychotic phenomena in both childhood and adolescence (Newbury et al., 2016; Newbury, Arseneault, Caspi, et al., 2017), and because adolescents’ personal perceptions of threat and danger could plausibly influence (or be influenced by) psychotic phenomena. Neighborhood disorder was assessed by asking participants about whether six problems affected their neighborhood, including litter, broken glass, and rubbish in public places; run-down buildings, abandoned cars, wasteland, or vacant shop fronts; people being drunk or unruly in public; people selling or using drugs; groups of young people hanging out and causing trouble; and homes getting broken into or burgled (coded 0 = *not true*, 1 = *sometimes true*, and 2 = *often true*). Item responses were averaged for each participant ($M = 0.52$, $SD = 0.49$, range = 0–2).

At age 12, participants also reported on neighborhood safety as part of a computer-based self-report stress questionnaire. Children indicated whether the statement “You feel unsafe in your neighborhood” was true or false. At age 12, 12.3% ($N = 260$) of children reported that they felt their neighborhood was unsafe.

Urbanicity. Our measure of urbanicity was derived from the Office of National Statistics’ (ONS) Rural-Urban Definition for Small Area Geographies (RUC2011) classifications. The ONS RUC2011 rural–urban classification utilized 2011 census data and was designed for application to small statistical units (e.g., output areas, superoutput areas, and wards). Detailed information on the creation of RUC2011 is available on the ONS website (https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/239477/RUC11methodologypaperaug_28_Aug.pdf). Briefly, RUC2011 was created by laying a grid of hectare cells (100 m²) over England and Wales. Postcode addresses were assigned to cells, providing an indication of residential density surrounding every individual residential property. Residential densities were then calculated for increasing radii around each cell, providing each residential property with a “density profile.” This measure was combined with Output Area and contextual data, allowing each settlement to be assigned to 1 of 10 categories of increasing urbanicity (rural categories: sparse/nonsparse hamlets and isolated dwellings, sparse/nonsparse villages, sparse/nonsparse rural towns and fringes; urban categories: sparse/nonsparse cities and towns, and minor/major conurbations). Urbanicity scores for the E-Risk participants were then created by identifying the ONS RUC2011 classification for each participant’s postcode at age 18. Given the low numbers within some rural categories, urbanicity was collapsed into three levels: 1 = *rural*: all rural settings; 2 = *intermediate*: urban cities and towns; and 3 = *urban*: major and minor conurbations (conurbations are densely populated, large urban regions resulting from the expansion and coalescence of adjacent cities and towns). E-Risk families are nationally representative in terms of level of urbanicity. For example, 31.9% of E-Risk participants lived in the most highly

urbanized settings at age 18 compared to 36.1% nationwide; 48.4% versus 45.0% lived in intermediate settings; and 19.7% versus 18.9% lived in rural settings (Office for National Statistics, 2013).

Official neighborhood crime rates. Associations between perceptions of neighborhood disorder and adolescent psychotic experiences were adjusted for official rates of crime in the neighborhood to isolate the associations arising from perceived versus objectively measured threat in the neighborhood. Street-level crime data, including information on the type of crime, date of occurrence, and approximate location, were accessed online as part of an open data-sharing effort about crime and policing in England and Wales. An application program interface was used to extract street-level crime data for each of the geospatial coordinates marking the family's home (for a full description, see <https://data.police.uk/about/#location-anonymisation>). Neighborhood crime rates were calculated by mapping a 1-mile radius around each E-Risk Study participant's home and tallying the total number of crimes that occurred in the area each month ($M = 247$, $SD = 274$, range = 1–1,868). Scores were computed for 2011 (the year prior to age 18 assessments), the first year for which full street-level data was available. These scores were then collapsed into quartiles. This measure covers various forms of crime, including violent offenses (e.g., assaults), sexual offenses (e.g., rape), robberies, burglaries, theft, arson, and vandalism.

Resident-reported neighborhood disorder. Associations between participants' perceptions of neighborhood disorder and adolescent psychotic experiences were also adjusted for independently rated neighborhood conditions as reported by immediate neighbors of the E-Risk participants, to further isolate the effects of adolescent's personal perceptions of neighborhood disorder. Neighborhood conditions were estimated via a postal survey sent to residents living alongside E-Risk families in 2008 (Odgers, Caspi, Bates, Sampson, & Moffitt, 2012; Odgers et al., 2009). Survey respondents, who were typically living on the same street or within the same apartment block as the participants in our study, reported on various characteristics of their immediate neighborhood, including levels of neighborhood disorder. Surveys were returned by an average of 5.18 ($SD = 2.73$) respondents per neighborhood, and there were at least two responses for 95% of neighborhoods ($N = 5,601$ respondents). For neighborhood disorder, residents were asked whether 14 problems affected their neighborhood (e.g., muggings, assaults, vandalism, graffiti, and deliberate damage to property), which were each coded 0–2 (the same or very similar items were included in the 6 items used at age 18 to measure E-Risk participants' perceptions of neighborhood disorder). Items were averaged to create summary scores for each of the 5,601 resident respondents. Neighborhood disorder scores for each E-Risk family were then created by averaging the summary scores of respondents within that family's neighborhood. The resulting variable approached normal distribution across the full potential range ($M = 0.49$, $SD = 0.34$, range = 0–1.93).

Neighborhood-level SES. Associations between perceptions of neighborhood disorder and adolescent psychotic experiences were also adjusted for neighborhood-level SES to check that associations were not explained simply by poverty. Neighborhood-level SES was constructed using A Classification of Residential Neighborhoods (ACORN), a geodemographic discriminator developed by CACI Information Services (<http://www.caci.co.uk/>). Detailed information about ACORN's classification of neighborhood-level SES has been provided previously (Caspi, Taylor, Moffitt, & Plomin, 2000; Odgers, Caspi, Russell, et al., 2012; Odgers et al., 2009). Briefly, CACI utilized over 400 variables from 2001 census data for Great Britain (e.g., educational qualifications, unemployment, and housing tenure) and CACI's consumer lifestyle database. Following hierarchical cluster analysis, CACI created five distinct and homogeneous ordinal groups ranging from "wealthy achiever" (coded 1) to "hard pressed" (coded 5) neighborhoods. Neighborhood-level SES scores for the E-Risk families were then created by identifying the ACORN classifications for the E-Risk families' postcodes when children were aged 12. E-Risk families are representative of UK households across the spectrum of neighborhood-level SES: 25.6% of E-Risk families live in wealthy achiever neighborhoods compared to 25.3% of households nationwide; 5.3% versus 11.6% live in "urban prosperity" neighborhoods; 29.6% versus 26.9% live in "comfortably off" neighborhoods; 13.4% versus 13.9% live in "moderate means" neighborhoods; and 26.1% versus 20.7% live in hard-pressed neighborhoods (CACI Information Services, 2006; Caspi et al., 2000). E-Risk underrepresents urban prosperity neighborhoods because such households are likely to be childless.

Family- and individual-level covariates. Analyses were also adjusted for a range of family- and individual-level characteristics to account for potential compositional effects and biases due to co-occurring substance and mood problems. Family SES was measured via a composite of parental income, education, and occupation when participants were aged 5. The latent variable was categorized into tertiles (i.e., low-, medium-, and high-SES; Trzesniewski, Moffitt, Caspi, Taylor, & Maughan, 2006). Family psychiatric history and maternal psychotic symptoms were both assessed when participants were aged 12. In private interviews, the mother reported on her own mental health history and the mental health history of her biological mother, father, sisters, and brothers, as well as the twins' biological father (Milne et al., 2008; Weissman et al., 2000). This was converted to the proportion of family members with a history of any psychiatric disorder (coded 0–1.0; $M = 0.37$, $SD = 0.27$). For maternal psychotic symptoms, mothers were interviewed using the Diagnostic Interview Schedule (Robins, Cottler, Bucholz, & Compton, 1995) for DSM-IV (American Psychiatric Association, 1994), which provides a symptom count for characteristic symptoms of schizophrenia (e.g., hallucinations, delusions, and anhedonia): 16.6% of mothers had at least one symptom of schizophrenia. We interviewed participants when they were aged 18 for the presence of marijuana depen-

dence, alcohol dependence, generalized anxiety disorder, and major depressive episode, according to DSM-IV criteria. Assessments were conducted in face-to-face interviews using the Diagnostic Interview Schedule (Robins et al., 1995). At age 18, 4.3% ($N = 89$) of participants met criteria for marijuana dependence, 12.8% ($N = 263$) met criteria for alcohol dependence, 7.4% ($N = 153$) met criteria for anxiety, and 20.1% ($N = 414$) met criteria for depression. Longitudinal analyses were adjusted for potential confounders measured at age 12 or earlier including resident-reports of neighborhood disorder, neighborhood-level SES, family-level confounders (SES, psychiatric history, and maternal psychotic symptoms), and also for childhood anxiety and depression at age 12. Childhood anxiety was assessed via private interviews using the 10-item version of the Multidimensional Anxiety Scale for Children (March, Parker, Sullivan, Stallings, & Conners, 1997). An extreme anxiety group was formed with children who scored at or above the 95th percentile ($N = 129$, 6.1%). Childhood depression was also assessed at age 12 using the Children's Depression Inventory (Kovacs, 1992). Children who scored 20 or more (Rivera, Bernal, & Rosello, 2005) were deemed to have clinically significant depressive symptoms ($N = 74$, 3.5%).

The twin design

The classical twin design compares the phenotypic correlation between MZ twin pairs to that between DZ twin pairs, and allows the variation/covariation in observed traits to be partitioned into additive genetic (A), common environmental (C), and unique environmental (E) components. This is because MZ twins share ~100% of their segregating DNA, whereas DZ twins share on average 50% of their segregating DNA. In contrast, MZ and DZ reared-together twin pairs both share 100% of their common environmental influences. The twin design methodology depends on the equal environment assumption, which assumes that MZ twin pairs and DZ twin pairs do not differ in the extent that they share environmental factors (Plomin, DeFries, Knopik, & Neiderhiser, 2013). In univariate analyses (variance in one trait), genetic influences on a trait are inferred if MZ correlations are greater than DZ correlations as this increased similarity between MZ twin pairs can only be accounted for by their increased genetic resemblance. Within-pair similarity that is not due to genetic factors is attributed to common environmental influences and would be implicated if the DZ correlation is greater than half that of the MZ correlation for a given trait. Unique environment accounts for individual-specific environmental factors that create differences among siblings from the same family. These are estimated from within-pair differences between MZ twins as E is the only influence that makes MZ twins different from one another. Measurement error is also included in E. Similarly, in bivariate analyses (covariance between two traits), higher cross-twin cross-trait correlations between MZ twin pairs versus DZ twin pairs suggests genetic sources of correlation between two traits (i.e., overlapping genetic influences on two traits). Maximum-likelihood estimation in

OpenMx handles missing data and provides confidence intervals in addition to parameter estimates. Structural equation model fitting is used to estimate A, C, and E sources of phenotypic correlation and select the most parsimonious model (ACE, AE, CE, or E compared to the saturated model, which describes the data perfectly) according to fit statistics, including -2 log likelihood and the Akaike information criterion.

Statistical analysis

Analyses were conducted using STATA 14.2 and OpenMx. First, we investigated the construct validity of participants' perceptions of neighborhood disorder by calculating the correlations of their personal perceptions with objectively/independently measured neighborhood conditions, including official neighborhood crime rates, resident-reports of neighborhood disorder, and neighborhood-level SES. Second, we calculated the mean levels of perceived neighborhood disorder among adolescents in urban, intermediate, and rural settings, and used KHB pathway decomposition (Breen, Karlson, & Holm, 2013) to test whether perceptions of neighborhood disorder mediated the effect of urbanicity on adolescent psychotic experiences. Third, we used ordinal logistic regression to test whether participants' perceptions of neighborhood disorder were associated with adolescent psychotic experiences. Regression models were adjusted for official crime rates, resident-reports of neighborhood disorder, neighborhood-level SES, family-level factors (family SES, family psychiatric history, and maternal psychotic symptoms), adolescent substance and mood problems (marijuana dependence, alcohol dependence, anxiety, and depression), childhood psychotic symptoms, and for all potential confounders simultaneously. As an additional control step, we conducted co-twin control analyses to compare twin pairs in the same family and neighborhood who differed in their perceptions of neighborhood disorder. For this analysis, we used all complete twin pairs and calculated the differences between twins (i.e., Twin 1 perceived neighborhood disorder–Twin 2 perceived neighborhood disorder; Twin 1 psychotic experiences–Twin 2 psychotic experiences). Using ordinal logistic regression, we then regressed twin differences in adolescent psychotic experiences on twin differences in perceptions of neighborhood disorder. Fourth, we used ordinal logistic regression to test whether participants who perceived their neighborhoods as unsafe at age 12 were more likely to subsequently report psychotic experiences at age 18, after considering childhood psychotic symptoms at age 12 and perceptions of neighborhood disorder at age 18; and whether participants who reported psychotic symptoms at age 12 were subsequently more likely to perceive their neighborhoods as disordered at age 18, after considering perceptions of neighborhood unsafety at age 12 and adolescent psychotic experiences at age 18. This step was conducted to investigate the temporality of the association between early psychotic phenomena and perceptions of neighborhood conditions. Steps 2 to 4 accounted for the nonindependence of twin observations using the CLUSTER command in STATA. Fifth, cross-trait (the within-individual corre-

lations between Trait 1 and Trait 2), cross-twin (the within-trait correlations between Twin 1 and Twin 2), and cross-twin cross-trait (the correlations between Trait 1 in Twin 1 and Trait 2 in Twin 2) phenotypic correlations for and between adolescent psychotic experiences and perceptions of neighborhood disorder were calculated in OpenMx (note: analyses were restricted to the 80.3% of participants who lived with their co-twin at age 18 to ensure that twin pairs were reporting on the same neighborhood). Univariate (cross-twin) and bivariate (cross-twin, cross-trait) ACE models were fitted and compared to the saturated model to estimate the extent that variation/covariation in adolescent psychotic experiences and perceptions of neighborhood disorder was attributable to A, C, and E influences. For adolescent psychotic experiences, a liability-threshold ACE model was fitted because this variable was on an ordinal scale. Because adolescent psychotic experiences were on an ordinal scale whereas perceptions of neighborhood disorder were on a quasi-continuous scale, bivariate ACE models were conducted using a combined continuous-ordinal approach. As is common practice in behavioral genetics analysis, sex was regressed out of variables and model fitting was conducted using the standardized residuals.

Results

Are participants' personal perceptions of neighborhood disorder consistent with objective/independent measures of neighborhood adversity?

Correlations between participants' personal perceptions of neighborhood disorder and objectively/independently measured neighborhood conditions were computed to investigate the construct validity of self-reports of neighborhood disorder. Personal perceptions of neighborhood disorder were significantly positively correlated (all p s < .001) with official neighborhood crime rates ($r = .18$), resident-reported neighborhood disorder ($r = .33$), and neighborhood-level SES ($r = .35$). Thus, participants' perceptions of neighborhood disorder were consistent with more objective measures of neighborhood disorder and crime.

Do higher perceived levels of neighborhood disorder among adolescents in urban (vs. rural) settings explain the association between urbanicity and adolescent psychotic experiences?

Table 1 shows the mean levels of perceived neighborhood disorder in urban, intermediate, and rural settings. Consistent with previous research, participants living in urban and intermediate (vs. rural) settings perceived significantly higher levels of neighborhood disorder, $B = 0.13$, 95% CI [0.10, 0.17], $p < .001$. In keeping with previous analyses in this cohort using independent reports of neighborhood disorder (Newbury et al., 2016; Newbury, Arseneault, Caspi, et al., 2017), mediation analysis showed that participants' personal perceptions of neighborhood disorder explained 42% of the

Table 1. Perceptions of neighborhood disorder according to level of urbanicity

Level of Urbanicity	Perceptions of Neighborhood Disorder	
	<i>M</i>	<i>SD</i>
Rural	0.35	0.41
Intermediate	0.52	0.49
Urban	0.63	0.51
Association between urbanicity and perceptions of neighborhood disorder	$B = 0.13$, 95% CI [0.10, 0.17], $p < .001$; $B = 0.19$	

Note: B, unstandardized beta coefficient; B , standardized beta coefficient, which indicates the unit standard deviation change in perceptions of neighborhood disorder given 1 *SD* change in urbanicity. Standardized betas provide exactly the same point estimates as correlation coefficients and may be interpreted as correlations, with a score of +1.0 indicating a 100% positive correlation. Beta (B) regression coefficients account for the nonindependence of twin observations.

effect of the most urban residency at age 18 on adolescent psychotic experiences: total effect of urbanicity on adolescent psychotic experiences, odds ratio (OR) = 1.81, 95% CI [1.29–2.53], $p = .001$; direct effect of urbanicity, $OR = 1.41$, 95% CI [1.00, 1.98], $p = .049$; indirect effect of urbanicity mediated via perceptions of neighborhood disorder, $OR = 1.28$, 95% CI [1.16, 1.42], $p < .001$.

Is the association between perceptions of neighborhood disorder and adolescent psychotic experiences robust to neighborhood-, family-, and individual-level confounders?

Model 1 in Table 2 shows that psychotic experiences were significantly more common among adolescents who perceived higher levels of neighborhood disorder (i.e., physical and social signs of threat, such as vandalism, gang activity and burglaries) in their immediate neighborhood, $OR = 2.52$, 95% CI [2.07, 3.06], $p < .001$. This association was slightly attenuated but remained highly significant (all p s < .001) after considering official neighborhood crime rates (Model 2); resident-reported neighborhood disorder (Model 3); neighborhood-level SES (Model 4); family-level characteristics including SES, psychiatric history, and maternal psychotic symptoms (Model 5); adolescent substance and mood problems, including marijuana dependence, alcohol dependence, anxiety, and depression (Model 6); childhood psychotic symptoms at age 12 (Model 7); as well as after considering all potential confounders simultaneously (Model 8), $OR = 1.62$, 95% CI [1.27, 2.05], $p < .001$.

As an additional control step, we investigated whether participants who perceived higher levels of neighborhood disorder than their co-twin were also more likely to score higher for adolescent psychotic experiences. The co-twin control design controls both the predictor and the outcome for within-

Table 2. *The unadjusted and adjusted association of perceptions of neighborhood disorder with adolescent psychotic experiences*

Model Specification	OR	95% CI	p
Model 1 unadjusted	2.52	[2.07, 3.06]	<.001
Model 2 adjusted for official neighborhood crime rates	2.39	[1.96, 2.91]	<.001
Model 3 adjusted for resident-reported neighborhood disorder	2.43	[1.98, 2.98]	<.001
Model 4 adjusted for neighborhood-level SES	2.31	[1.87, 2.86]	<.001
Model 5 adjusted for family-level characteristics	2.20	[1.79, 2.70]	<.001
Model 6 adjusted for adolescent substance and mood problems	1.94	[1.57, 2.39]	<.001
Model 7 adjusted for childhood psychotic symptoms	2.43	[2.00, 2.96]	<.001
Model 8 adjusted for all covariates simultaneously	1.62	[1.27, 2.05]	<.001
Official neighborhood crime rates	1.13	[1.01, 1.26]	.035
Resident-reported neighborhood disorder	1.08	[0.73, 1.61]	.700
Neighborhood-level SES	1.02	[0.92, 1.12]	.715
Family socioeconomic status	1.17	[0.99, 1.39]	.072
Family psychiatric history	1.27	[0.81, 1.99]	.299
Maternal psychotic symptoms	1.06	[0.92, 1.21]	.448
Adolescent marijuana dependence	3.29	[2.01, 5.36]	<.001
Adolescent alcohol dependence	1.58	[1.16, 2.15]	.004
Adolescent anxiety	2.56	[1.74, 3.76]	<.001
Adolescent depression	3.05	[2.33, 3.99]	<.001
Childhood psychotic symptoms	2.20	[1.38, 3.49]	.001

Note: OR, odds ratio from ordinal logistic regression; SES, socioeconomic status. Model 1 is the unadjusted association between adolescents' perceptions of neighborhood disorder and adolescent psychotic experiences. Model 2 is the adjusted for official neighborhood crime rates. Model 3 is adjusted for resident-reported neighborhood disorder. Model 4 is adjusted for neighborhood-level SES. Model 5 is adjusted for family-level characteristics (family SES, family psychiatric history, and maternal psychotic symptoms). Model 6 is adjusted for adolescent substance and mood problems (marijuana dependence, alcohol dependence, anxiety, and depression). Model 7 is adjusted for childhood psychotic symptoms at age 12. Model 8 is adjusted simultaneously for all covariates. All analyses account for the nonindependence of twin observations.

family environmental influences and partially for genetic influences. By restricting analyses to the 80.3% of twin pairs who lived together at age 18, this analysis also holds the actual neighborhood conditions constant by design, thus providing a more stringent test of whether perceived levels of neighborhood disorder are independently associated with adolescent psychotic experiences. Among twin pairs living together, twins who perceived a higher level of neighborhood disorder than their co-twin were also significantly more likely to report more psychotic experiences than their co-twin, $OR = 1.34$, 95% CI [1.05, 1.82], $p = .036$. This effect is smaller than that yielded for the entire sample from regression models of the association between perceived neighborhood disorder and adolescent psychotic experiences, adjusted $OR = 1.62$, 95% CI [1.27, 2.05], $p < .001$. Nevertheless, the statistically significant associations in both the regression and co-twin control models demonstrates that perceptions of neighborhood disorder were independently associated with adolescent psychotic experiences, net of a range of measured and unmeasured genetic, individual-level, and family-level potential confounders.

What is the temporality of the association between early psychotic phenomena and perceptions of neighborhood disorder?

Consistent with the association between perceptions of neighborhood disorder and adolescent psychotic experiences at age

18, children's own perceptions that their neighborhoods were unsafe were significantly associated with childhood psychotic symptoms at age 12, unadjusted $OR = 2.88$, 95% CI [1.88, 4.44], $p < .001$. These earlier age 12 measures of psychotic symptoms and perceived neighborhood conditions were used to investigate the temporality of the association between early psychotic phenomena and perceptions of neighborhood disorder.

Model 1 in Table 3 shows that participants who had perceived their neighborhoods as unsafe at age 12 were significantly more likely to report adolescent psychotic experiences at age 18, even after taking into account earlier childhood psychotic symptoms at age 12, $OR = 2.02$, 95% CI [1.51, 2.71], $p < .001$. The association between children's perceptions of neighborhood unsafety and adolescent psychotic experiences remained significant after considering perceptions of neighborhood disorder at age 18 (Model 2), as well as after considering other potential confounders listed under Table 3 (Model 3). Model 1 in Table 3 also shows that participants who reported childhood psychotic symptoms at age 12 were significantly more likely to perceive their neighborhood as disordered at age 18, even after considering earlier perceptions of neighborhood unsafety at age 12, $OR = 1.59$, 95% CI [1.16, 2.18], $p = .004$. However, the association between childhood psychotic symptoms at age 12 and perceptions of neighborhood disorder at age 18 was attenuated to below conventional levels of significance after considering adolescent

Table 3. The longitudinal associations of perceptions of neighborhood safety and psychotic symptoms at age 12 with subsequent psychotic experiences and perceptions of neighborhood disorder at age 18

Age 12 Measures	Model 1			Model 2			Model 3		
	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
Adolescent Psychotic Experiences at Age 18 ^a									
Perceptions of neighborhood as unsafe	2.02	[1.51, 2.71]	<.001	1.72	[1.27, 2.32]	<.001	1.45	[1.06, 1.99]	.021
Perceptions of Neighborhood Disorder at Age 18 ^b									
Childhood psychotic symptoms	1.59	[1.16, 2.18]	.004	1.31	[0.93, 1.84]	.125	1.19	[0.83, 1.70]	.338

Note: OR, odds ratio from ordinal logistic regression; SES, socioeconomic status. Model 1, the association of childhood perceptions of neighborhood unsafety with adolescent psychotic experiences, was adjusted for childhood psychotic symptoms. The association of childhood psychotic symptoms with perceptions of neighborhood disorder was adjusted for childhood perceptions of neighborhood unsafety. Model 2, the association between perceptions of neighborhood unsafety and adolescent psychotic experiences, was additionally adjusted for perceptions of neighborhood disorder at age 18. The association between childhood psychotic symptoms and perceptions of neighborhood disorder was also adjusted for adolescent psychotic experiences. Model 3 contains both regression models that were also adjusted for resident reports of neighborhood disorder, neighborhood-level SES, family SES, family psychiatric history, maternal psychotic symptoms, and childhood anxiety and depression. All analyses account for the nonindependence of twin observations.

^aThe association of childhood perceptions of neighborhood unsafety at age 12 with adolescent psychotic experiences at age 18.

^bThe association of childhood psychotic symptoms at age 12 with perceptions of neighborhood disorder at age 18.

psychotic experiences at age 18 (Model 2) and other potential confounders (Model 3).

To what extent do genetic versus environmental factors contribute to perceptions of neighborhood disorder and adolescent psychotic experiences?

Using the classical twin design and maximum-likelihood estimation in OpenMx, we further examined the genetic and environmental contributions to adolescent psychotic experiences and participants' perceptions of neighborhood disorder at age 18 (note: analyses were again restricted to the 80.3% of participants who lived with their co-twin at age 18, to ensure that twins were reporting on the same neighborhoods and therefore only perceptions of neighborhoods varied between twin pairs). Table 4 shows the cross-trait, cross-twin, and cross-twin cross-trait phenotypic correlations of adolescent psychotic experiences and perceptions of neighborhood disorder, stratified by zygosity. Consistent with the logistic regression results for the entire sample in Table 2, Table 4 shows that there was a significant cross-trait correlation between adolescent psychotic experiences and perceptions of neighborhood disorder for the 80.3% of participants who lived with their co-twin, $r = .27$, 95% CI [0.21, 0.33].

Cross-twin phenotypic correlations for adolescent psychotic experiences suggested some genetic contributions because MZ twin correlations ($r = .46$) were slightly larger than DZ twin correlations ($r = .36$); common environmental contributions (C) were also indicated because DZ correlations were greater than half that of MZ correlations; and unique environmental contributions were also indicated because MZ correlations were less than unity (Table 4). For perceptions of neighborhood disorder, cross-twin phenotypic corre-

lations again suggested genetic contributions because MZ correlations ($r = .48$) were slightly greater than DZ correlations ($r = .39$); common environmental contributions (C) were indicated because DZ correlations were greater than half that of MZ correlations; and unique environmental contributions were indicated because MZ correlations were less than unity (cross-twin phenotypic correlations did not vary substantially between males and females; see Table 4 footnotes); therefore, subsequent analyses were conducted on both sexes together).

ACE estimates from univariate model fitting were consistent with the cross-twin correlations. For adolescent psychotic experiences, observed variance was mostly explained by unique environmental (55%) and common environmental (28%) factors, with genetic factors explaining a small proportion of the observed variance (17%). For perceptions of neighborhood disorder, observed variance was explained by unique environmental (50%), common environmental (24%), as well as genetic (26%) factors. Table 5 displays the fit statistics for the ACE model and nested models (AE, CE, and E). Given that the full ACE model was the best fitting model for perceptions of neighborhood disorder, we present the results from the full ACE bivariate model.

To what extent do overlapping genetic versus environmental factors contribute to the covariance between adolescent psychotic experiences and perceptions of neighborhood disorder?

The cross-twin cross-trait correlations in Table 4 give an indication of the genetic, common environmental, and unique environmental sources of phenotypic correlation between adolescent psychotic experiences and perceptions of neighborhood

Table 4. Cross-trait, cross-twin, and cross-twin cross-trait phenotypic correlations of and between adolescent psychotic experiences and perceptions neighborhood disorder

Cross-Trait Phenotypic Correlations ^b	MZ and DZ Twins Together ^a			
	Correlation		CI	
Adolescent psychotic experiences, perceptions of neighborhood disorder	.27		[0.21, 0.33]	
Cross-Twin Phenotypic Correlations ^c	MZ		DZ	
	Correlation	CI	Correlation	CI
Adolescent psychotic experiences	.46	[0.33, 0.58]	.36	[0.21, 0.50]
Perceptions of neighborhood disorder	.48	[0.41, 0.55]	.39	[0.30, 0.48]
Cross-Twin Cross-Trait Phenotypic Correlations ^d	MZ		DZ	
	Correlation	CI	Correlation	CI
Adolescent psychotic experiences, perceptions of neighborhood disorder	.22	[0.14, 0.29]	.22	[0.14, 0.30]

Note: MZ, monozygotic (identical) twins; DZ, dizygotic (fraternal) twins.

^aAll phenotypic correlation analyses in Table 4 were conducted on the subsample of twins who lived together with their co-twin at age 18 (80.3%).

^bThe phenotypic correlation in the entire analysis sample between adolescent psychotic experiences and adolescents' perceptions of neighborhood disorder in the immediate neighborhood.

^cThe phenotypic correlation between twins for adolescent psychotic experiences and perceptions of neighborhood disorder among MZ versus DZ twins. Cross-twin phenotypic correlations were also calculated for MZ males (MZm), DZ males (DZm), MZ females (MZf), and DZ females (DZf) separately to check for potential sex differences. (These cross-twin phenotypic correlations were calculated in STATA 14.2 without confidence intervals because of low numbers of female twin pairs concordant for three or more psychotic experiences when stratified by sex.) Phenotypic correlations (all $ps < .05$) did not differ substantially by sex. For neighborhood disorder: MZm = 0.47, DZm = 0.43, MZf = 0.48, and DZf = 0.35; for adolescent psychotic experiences: MZm = 0.41, DZm = 0.27, MZf = 0.52, and DZf = 0.46.

^dThe correlation of Trait 1 in Twin 1 with Trait 2 in Twin 2 among MZ versus DZ twins.

disorder. Modest positive cross-twin cross-trait correlations between adolescent psychotic experiences and perceptions of neighborhood disorder were apparent. Correlations did not differ by zygosity, giving an initial indication that overlapping genes did not account for the phenotypic correlations.

This was supported by results from the cross-twin cross-trait bivariate model, which is presented in a pathway diagram in Figure 1. (Note that ACE estimates for perceptions of neighborhood disorder from the bivariate model, i.e., $A = 0.25$, $C = 0.25$, differ slightly from those described above from the univariate model, i.e., $A = 0.26$, $C = 0.24$, because the bivariate model

Table 5. Fit statistics of submodels (ACE, AE, CE, E) compared to the saturated univariate model for adolescent psychotic experiences and perceptions of neighborhood disorder

Trait	Model	EP	-2LL	df	AIC	Diff. LL	Diff. df	p
Adolescent psychotic experiences	Saturated	10	2514.245	1630	-745.756	NA	NA	NA
	ACE	5	2520.850	1636	-751.150	6.610	6	.359
	AE	4	2523.643	1637	-750.357	2.793	1	.095
	CE ^a	4	2521.600	1637	-752.400	0.750	1	.386
	E	3	2583.039	1638	-692.961	62.189	2	3.133-14
Perceptions of neighborhood disorder	Saturated	10	2048.567	1616	-1183.433	NA	NA	NA
	ACE ^a	4	2058.314	1622	-1185.686	9.747	6	.135
	AE	3	2064.804	1623	-1181.196	6.490	1	.011
	CE	3	2064.418	1623	-1181.582	6.104	1	.013
	E	2	2236.698	1624	-1011.302	178.384	2	1.848 e-39

Note: ACE, full model testing genetic, common, and unique environmental influences compared to the saturated model; AE, model testing genetic and unique environmental influences compared to the ACE model; CE, model testing common and unique environmental influences compared to the ACE model; E, model testing unique environmental influences compared to the ACE model; EP, estimated parameters; -2LL, -2 log likelihood; AIC, Akaike information criterion (lower values indicate a better fitting model); Diff., difference; NA, not applicable.

^aBest fitting model.

contains more information. However, confidence intervals for these estimates overlap.) The phenotypic correlation between adolescent psychotic experiences and perceptions of neighborhood disorder was mostly explained by a large significant correlation between common environmental influences ($r_C = .88$), whereas A and E influences were not significantly correlated between traits. That is, a large proportion of the environmental influences that made twin siblings more similar in terms of their perceptions of neighborhood disorder also made twin siblings more similar in terms of their psychotic experiences.

Discussion

This study used a multilevel, longitudinal, and genetically sensitive design to investigate the association between individuals' own perceptions of threatening neighborhood conditions and psychotic experiences during adolescence. Analyses revealed three main findings. First, adolescents' personal perceptions of neighborhood disorder statistically explained 42% of the effect of the most urban residency on adolescent psychotic experiences. Second, adolescents who perceived higher levels of disorder in their immediate neighborhoods at age 18 (such as vandalism, gang activity, and burglaries) were over 60% more likely to report psychotic experiences compared to individuals who perceived their neighborhoods to be safer and less threatening, even after considering a wide range of potential neighborhood-, family-, and individual-level confounders. Third, the phenotypic correlation between adolescent psychotic experiences and perceptions of neighborhood disorder at age 18 was mostly explained by overlapping common environmental factors.

The present study's mediation findings are consistent with previous analyses in this cohort showing that threatening and adverse neighborhood conditions (as independently rated by mothers and residents) statistically explain up to half of the effect of urbanicity during upbringing on psychotic phenomena

in childhood and adolescence (Newbury et al., 2016; Newbury, Arseneault, Caspi, et al., 2017). Our findings are also in keeping with those from recent studies documenting higher rates of psychotic phenomena, psychosis proneness, and psychotic disorder among children, adolescents, and young adults living in regions with higher fragmentation, disorder, and crime as rated by independent or objective sources (Bhavsar et al., 2014; Kirkbride et al., 2015; Newbury et al., 2016; Newbury, Arseneault, Caspi, et al., 2017; Wilson et al., 2016). Here we identify a potential role for personal perceptions of threatening neighborhood conditions in early psychotic phenomena. That is, the association between adverse neighborhood conditions and early expressions of psychosis is detectable at the level of the eye of the beholder. This is consistent with psychological theories and empirical studies of psychosis etiology that emphasize the key role played by negative beliefs about the world and other people, hostile attributions of the intentions of others, and threat anticipation (An et al., 2010; Appiah-Kusi et al., 2017; Fowler et al., 2006; Freeman, 2016; Garety, Bebbington, Fowler, Freeman, & Kuipers, 2007; Noone et al., 2015) in the development of psychotic experiences, such as paranoia; together with a broader literature suggesting that subjective perceptions of early life adversity are associated with mental health problems over and above more objective reports of adversity exposure (Brown et al., 2005; Reuben et al., 2016; Widom & Morris, 1997; Widom et al., 1999).

Our adjustment for a range of potential confounders indicated that the association between personal perceptions of neighborhood disorder and adolescent psychotic experiences was (a) above and beyond the effect of objectively/independently measured levels of threat in the neighborhood (associations were not explained by official neighborhood crime rates or resident-reports of neighborhood disorder); (b) not due to poverty (associations were not explained by neighborhood-level SES); (c) not explained by the composition of families living in

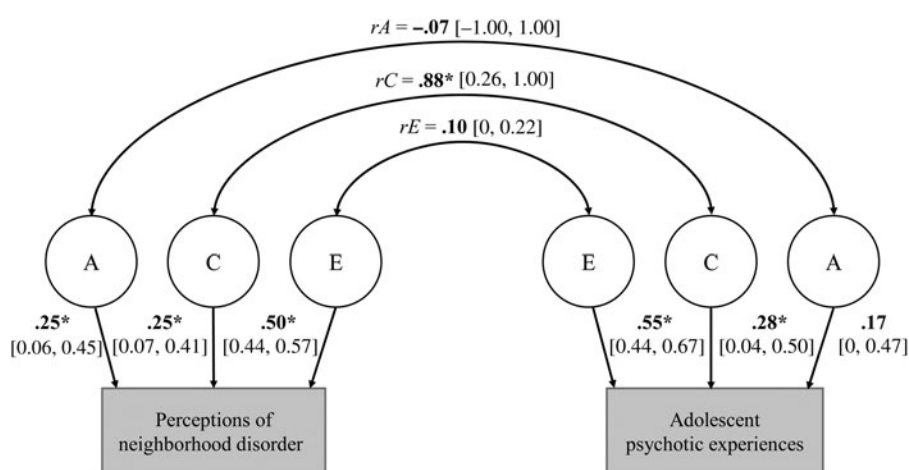


Figure 1. ACE estimates and ACE correlations from cross-twin cross-trait (bivariate) model. A, additive genetic influences; E, unique environmental influences; r_A , r_C , and r_E , genetic, common environmental, and unique environmental sources of correlation between phenotypes. The common (C) environmental contributions to variance in perception of neighborhood disorder, $C = 0.25$, CI [0.07, 0.41], were significantly correlated with the common environmental contributions to variance in adolescent psychotic experiences, $C = 0.28$, CI [0.04, 0.50], yielding a large significant environmental correlation between perceptions of neighborhood disorder and adolescent psychotic experiences of 0.88, CI [0.26, 1.00]. * $p < .05$.

disordered neighborhoods (associations were not explained by family SES or family history of psychiatric problems); (d) not attributable solely to substance intoxication or mood-congruent recall bias (associations were not explained by adolescent marijuana dependence, alcohol dependence, anxiety or depression); and (e) not explained by earlier childhood psychotic symptoms that might simultaneously influence participants' subsequent perceptions of neighborhood disorder and their risk for adolescent psychotic experiences. Therefore, this association was impressively robust to a wide range of factors that typically confound such relationships. Co-twin control analyses demonstrated that the association between perceived neighborhood disorder and adolescent psychotic experiences was attenuated but remained significant after holding the family environment and neighborhood conditions (and partially genetic influences) constant by design. This approach provides strong evidence that personal perceptions of neighborhood disorder were associated with adolescent psychotic experiences above and beyond variation in the actual neighborhood conditions.

In addition, there was tentative evidence of a bidirectional relationship between perceptions of threatening neighborhood conditions and early psychotic phenomena. Individuals who had perceived their neighborhood as unsafe during childhood were subsequently more likely to have psychotic experiences during adolescence: this was not due to earlier psychotic symptoms in childhood, contemporaneous perceptions of neighborhood disorder at age 18, or a range of other potential neighborhood-, family-, and individual-level confounders. Individuals who reported psychotic symptoms at age 12 were also more likely to subsequently perceive their neighborhoods as more disordered at age 18, though this appeared to be explained by adolescent psychotic experiences at age 18 and other confounders. We could speculate that personal perceptions of threat in the neighborhood tend to precede the onset of early psychotic phenomena, rather than vice versa. However, given that psychotic experiences involve altered perceptions of reality such as threat detection biases and persecutory delusions (Freeman et al., 2002; Garety et al., 2001), it is likely that the true relationship between adolescent psychotic experiences and perceptions of neighborhood conditions is bidirectional. Psychotic experiences might intensify perceptions of neighborhood disorder, and perceptions of neighborhood disorder might exacerbate psychotic experiences.

We hypothesized that the overlap between adolescent psychotic experiences and perceptions of neighborhood disorder could be due to shared genetic factors. That is, some of the same genetic contributions to psychotic experiences could also contribute to perceptions of threatening neighborhood conditions. This hypothesis was not supported. Genetic contributions to adolescent psychotic experiences did not appear to contribute to perceptions of neighborhood disorder in this sample. Instead, common environmental factors were implicated. These environmental factors contributed to increased similarity between twin siblings in terms of both their perceptions of neighborhood disorder and their psychotic experiences. This contrasts with emerging research showing that putative

environmental risk factors for psychotic experiences, such as stressful life events (Shakoor et al., 2016) and neighborhood-level deprivation (Sariaslan et al., 2016), are associated with psychotic experiences due partly to overlapping genetic influences. One obvious environmental exposure shared between twin pairs, which could influence both adolescent psychotic experiences and perceptions of neighborhood disorder, is actual levels of neighborhood disorder. That is, threatening conditions such as vandalism, gang activity, and burglaries in the neighborhood could simultaneously influence adolescents' perceptions of neighborhood disorder and their experience of psychotic phenomena. However, a number of alternative candidates for the overlapping common environmental influences are possible. For example, parental attitudes or family environments characterized by suspicion and fearfulness could simultaneously promote psychotic experiences and perceptions of high neighborhood disorder among offspring, though in this sample the phenotypic and longitudinal associations were not explained by family psychiatric history or maternal psychotic symptoms. In addition, findings from the co-twin control analysis (which yielded a smaller though significant association compared to the full sample) highlight that family-wide and neighborhood-level influences did not completely explain the effect of perceived neighborhood disorder on adolescent psychotic experiences. Taken together, these findings suggest that both actual (i.e., family-level) and perceived (i.e., individual-level) neighborhood conditions contributed to risk for adolescent psychotic experiences.

Considering all the findings together: that perceptions of threatening neighborhood conditions explained part of the effect of urbanicity on adolescent psychotic experiences; were not confounded by numerous potential neighborhood-, family-, and individual-level factors; and overlapped with psychotic experiences due to environmental (rather than genetic) influences, the present study provides initial evidence implicating perceptions of disordered neighborhood conditions in the etiology of adolescent psychotic experiences. These findings are consistent with leading aetiological models of psychosis. Growing evidence implicates psychosocial stress in the emergence of psychotic phenomena, whereby chronic, acute, and daily-life stressors (e.g., urban living, crime victimization, and noisy neighbors) might promote and exacerbate psychotic phenomena. Biological and psychological mechanisms have been suggested. Chronic and acute stressors during upbringing are thought to disrupt the biological stress response (Tarullo & Gunnar, 2006; Walker, Mittal, & Tessner, 2008), and in turn disrupt dopaminergic activity (van Winkel, Stefanis, & Myin-Germeys, 2008). The dopaminergic system plays a key role in the brain's attribution of salience to stimuli, and excess dopamine activity is currently the strongest biological explanation for the positive symptoms of psychosis (Howes, McCutcheon, Owen, & Murray, 2017; Kapur, 2003; van Winkel et al., 2008). From an adolescent's perspective, residing in and navigating a threatening neighborhood environment could also promote or reinforce maladaptive cognitive styles such as paranoia and threat detection biases. This proposed mechanism is consistent with studies

showing that the severity of persecutory delusions, anxiety, paranoia, and hallucinations among adults with schizophrenia is immediately exacerbated after brief exposure to crowded urban environments (Ellett et al., 2008; Freeman et al., 2014). The potential bidirectional relationship between perceptions of adverse neighborhood conditions and adolescent psychotic experiences is also consistent with the phenotypic overlap documented between psychosis and stress sensitivity and stress reactivity (Collip et al., 2011; Myin-Germeys, Delespaul, & van Os, 2005; Myin-Germeys, van Os, Schwartz, Stone, & Delespaul, 2001). It is reasonable to assume that adolescents who are experiencing psychotic phenomena might be more sensitive to stressful or threatening exposures in the neighborhood.

Strengths and limitations

Combining multilevel, longitudinal and genetically sensitive methods, this study was able to examine the association between perceptions of neighborhood adversity and adolescent psychotic experiences while considering a range of potential confounders including genetic influences. Nonetheless, we acknowledge several limitations. First, our self-report measure of adolescent psychotic experiences reflected the methodology widely used in the psychosis-prodrome research field. It is possible, however, that this self-report measure captured genuine experiences (e.g., being followed by a stranger) as well as psychotic phenomena (e.g., being followed by a spy). This may have led to the fairly low additive genetic estimate for adolescent psychotic experiences in this sample (17%), which is lower than that typically reported from twin analyses of more strictly defined early psychotic phenomena (Polanczyk et al., 2010; Ronald, 2015; Zavos et al., 2014). Second, the absence of overlapping genetic influences between psychotic experiences and perceptions of neighborhood disorder could also be due to the young age of the E-Risk participants. At age 18, the study individuals would have had minimal choice in the type of the neighborhood they lived in compared to later in adulthood. It will be important to investigate the genetic and environmental contributions to the association between perceived neighborhood conditions and psychotic experiences later in adulthood, when individuals become more active in choosing their neighborhood environments. Furthermore, studies of adult twins living apart could investigate the genetic and environmental contributions to actual (i.e., objectively measured) neighborhood conditions as well. Third, we must interpret the longitudinal associations between perceptions of neighborhood conditions and psychotic phenomena with caution, because the age 12 measures were on binary scales measuring only neighborhood safety and the presence of at least one psychotic symptom so did not capture as much variance as the age 18 measures. Thus, we tentatively suggest that the association between perceived neighborhood adversity and psychotic phenomena is likely to be bidirectional.

Looking forward, multidisciplinary research examining the interplay between neighborhood conditions, genetic and environmental risk, and neurological and cognitive biomarkers

during development is needed to establish the nature of the association between perceived neighborhood conditions and adolescent psychotic experiences. There is evidence, for example, that adults with urban versus rural upbringing differ in their neurocognitive reactivity to social stress (Haddad et al., 2015; Lederbogen et al., 2011), though little is known about the potential effects of adverse neighborhood conditions on the adolescent brain. Furthermore, future research is needed to establish whether the association between perceptions of threat and psychotic experiences is specific to neighborhood conditions, or whether this association extends to other domains such as school and work environments and social interactions.

Conclusions

Notwithstanding its limitations, the present study has clinical and public health implications. Our findings add to growing evidence that threatening and adverse neighborhood conditions during upbringing increase risk for early psychotic phenomena. This highlights potential opportunities for preventative interventions. On the one hand, our findings suggest that early interventions for psychosis (and mental health problems more generally) could reach particularly high-risk groups if targeted toward adolescents living in threatening and adverse neighborhood conditions. Given the potential bidirectional relationship between psychotic experiences and perceptions of threatening neighborhood conditions, psychological therapies could incorporate strategies to help young people understand whether their perceptions of threat in the neighborhood are rational, or whether these perceptions are contributing unnecessarily to a cycle of stress, fear, and psychotic experiences. On the other hand, recent findings from this team (Newbury et al., 2016; Newbury, Arseneault, Caspi, et al., 2017; Odgers, Donley, Caspi, Bates, & Moffitt, 2015) and others (Bhavsar et al., 2014; Goldman-Mellor et al., 2016; Kirkbride et al., 2015; Polling et al., 2014; Wilson et al., 2016) suggest a need to address whether wider physical and social environmental conditions can be improved for the benefit of young people's mental health. Within two or three decades, 70% of the world's population will live in cities (Dye, 2008). This figure already exceeds 80% in many developed nations, including Great Britain. It is therefore likely that, as communities become more crowded and societies become more unequal (UNICEF, 2012), the neighborhoods in which young people are born and raised will become more adverse and more fragmented. We suggest that public health and urban planning initiatives aimed at increasing the safety and supportiveness (both actual and perceived) of urban communities could benefit the mental health of young people and improve mental health trajectories for a large section of society over the life course.

Supplementary Material

To view the supplementary material for this article, please visit <https://doi.org/10.1017/S0954579417001420>.

References

- American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: Author.
- An, S. K., Kang, J. I., Park, J. Y., Kim, K. R., Lee, S. Y., & Lee, E. (2010). Attribution bias in ultra-high risk for psychosis and first-episode schizophrenia. *Schizophrenia Research*, 118, 54–61.
- Appiah-Kusi, E., Fisher, H. L., Petros, N., Wilson, R., Mondelli, V., Garety, P., . . . Bhattacharyya, S. (2017). Do cognitive schema mediate the association between childhood trauma and being at ultra-high risk for psychosis? *Journal of Psychiatric Research*, 88, 89–96.
- Bhavsar, V., Boydell, J., Murray, R., & Power, P. (2014). Identifying aspects of neighbourhood deprivation associated with increased incidence of schizophrenia. *Schizophrenia Research*, 156, 115–121.
- Breen, R., Karlson, K. B., & Holm, A. (2013). Total, direct, and indirect effects in logit and probit models. *Sociological Methods & Research*, 42, 164–191.
- Brown, J., Berenson, K., & Cohen, P. (2005). Documented and self-reported child abuse and adult pain in a community sample. *Clinical Journal of Pain*, 21, 374–377.
- CACI Information Services. (2006). *ACORN user guide*. London: Author.
- Caspi, A., Taylor, A., Moffitt, T. E., & Plomin, R. (2000). Neighborhood deprivation affects children's mental health: Environmental risks identified in a genetic design. *Psychological Science*, 11, 338–342.
- Collip, D., Nicolson, N., Lardinois, M., Lataster, T., van Os, J., & Myin-Germeys, I. (2011). Daily cortisol, stress reactivity and psychotic experiences in individuals at above average genetic risk for psychosis. *Psychological Medicine*, 41, 2305–2315.
- Dhossche, D., Ferdinand, R., van der Ende, J., Hofstra, M., & Verhulst, F. (2002). Diagnostic outcome of self-reported hallucinations in a community sample of adolescents. *Psychological Medicine*, 32, 619–627.
- Dye, C. (2008). Health and urban living. *Science*, 319, 766–769.
- Ellett, L., Freeman, D., & Garety, P. A. (2008). The psychological effect of an urban environment on individuals with persecutory delusions: The Camberwell walk study. *Schizophrenia Research*, 99, 77–84.
- Fisher, H. L., Caspi, A., Poulton, R., Meier, M. H., Houts, R., Harrington, H., . . . Moffitt, T. E. (2013). Specificity of childhood psychotic symptoms for predicting schizophrenia by 38 years of age: A birth cohort study. *Psychological Medicine*, 43, 2077–2086.
- Fowler, D., Freeman, D., Smith, B., Kuipers, E., Bebbington, P., Bashforth, H., . . . Dunn, G. (2006). The Brief Core Schema Scales (BCSS): Psychometric properties and associations with paranoia and grandiosity in non-clinical and psychosis samples. *Psychological Medicine*, 36, 749–759.
- Freeman, D. (2016). Persecutory delusions: A cognitive perspective on understanding and treatment. *Lancet Psychiatry*, 3, 685–692.
- Freeman, D., Emsley, R., Dunn, G., Fowler, D., Bebbington, P., Kuipers, E., . . . Garety, P. (2014). The stress of the street for patients with persecutory delusions: A test of the symptomatic and psychological effects of going outside into a busy urban area. *Schizophrenia Bulletin*, 41, 971–979.
- Freeman, D., Garety, P. A., Kuipers, E., Fowler, D., & Bebbington, P. E. (2002). A cognitive model of persecutory delusions. *British Journal of Clinical Psychology*, 41, 331–347.
- Freeman, D., Waller, H., Harpur-Lewis, R. A., Moore, R., Garety, P., Bebbington, P., . . . Fowler, D. (2015). Urbanicity, persecutory delusions, and clinical intervention: The development of a brief CBT module for helping patients with persecutory delusions enter social urban environments. *Behavioural and Cognitive Psychotherapy*, 43, 42–51.
- Garety, P. A., Bebbington, P., Fowler, D., Freeman, D., & Kuipers, E. (2007). Implications for neurobiological research of cognitive models of psychosis: A theoretical paper. *Psychological Medicine*, 37, 1377.
- Garety, P., Kuipers, E., Fowler, D., Freeman, D., & Bebbington, P. (2001). A cognitive model of the positive symptoms of psychosis. *Psychological Medicine*, 31, 189–196.
- Goldman-Mellor, S., Margerison-Zilko, C., Allen, K., & Cerdá, M. (2016). Perceived and objectively-measured neighborhood violence and adolescent psychological distress. *Journal of Urban Health*, 93, 758–769.
- Haddad, L., Schäfer, A., Streit, F., Lederbogen, F., Grimm, O., Wüst, S., . . . Meyer-Lindenberg, A. (2015). Brain structure correlates of urban upbringing, an environmental risk factor for schizophrenia. *Schizophrenia Bulletin*, 41, 115–122.
- Häfner, H., Maurer, K., Löffler, W., & Fätkenheuer, B. (1994). The epidemiology of early schizophrenia: Influence of age and gender on onset and early course. *British Journal of Psychiatry*, 164, 29–38.
- Hardt, J., & Rutter, M. (2004). Validity of adult retrospective reports of adverse childhood experiences: Review of the evidence. *Journal of Child Psychology and Psychiatry*, 45, 260–273.
- Heinz, A., Deserno, L., & Reininghaus, U. (2013). Urbanicity, social adversity and psychosis. *World Psychiatry*, 12, 187–197.
- Horwood, J., Salvi, G., Thomas, K., Duffy, L., Gunnell, D., Hollis, C., . . . Wolke, D. (2008). IQ and non-clinical psychotic symptoms in 12-year-olds: Results from the ALSPAC birth cohort. *British Journal of Psychiatry*, 193, 185–191.
- Howes, O. D., McCutcheon, R., Owen, M. J., & Murray, R. M. (2017). The role of genes, stress, and dopamine in the development of schizophrenia. *Biological Psychiatry*, 81, 9–20.
- Kapur, S. (2003). Psychosis as a state of aberrant salience: A framework linking biology, phenomenology, and pharmacology in schizophrenia. *American Journal of Psychiatry*, 160, 13–23.
- Kelleher, I., & Cannon, M. (2011). Psychotic-like experiences in the general population: Characterizing a high-risk group for psychosis. *Psychological Medicine*, 41, 1–6.
- Kelleher, I., Connor, D., Clarke, M. C., Devlin, N., Harley, M., & Cannon, M. (2012). Prevalence of psychotic symptoms in childhood and adolescence: A systematic review and meta-analysis of population-based studies. *Psychological Medicine*, 42, 1857–1863.
- Kelleher, I., Keeley, H., Corcoran, P., Lynch, F., Devlin, N., Molloy, C., . . . Cannon, M. (2012). Clinicopathological significance of psychotic experiences in non-psychotic young people: Evidence from four population-based studies. *British Journal of Psychiatry*, 201, 26–32.
- Kelleher, I., Lynch, F., Harley, M., Molloy, C., Roddy, S., Fitzpatrick, C., & Cannon, M. (2012). Psychotic symptoms in adolescence index risk for suicidal behavior: Findings from 2 population-based case-control clinical interview studies. *Archives of General Psychiatry*, 69, 1277–1283.
- Kirkbride, J., Stochl, J., Zimbron, J., Crane, C., Metastasio, A., Aguilar, E., . . . Jones, P. (2015). Social and spatial heterogeneity in psychosis proneness in a multilevel case-prodrome-control study. *Acta Psychiatrica Scandinavica*, 132, 283–292.
- Kovacs, M. (1992). *Children's Depression Inventory: Manual*. North Tonawanda, NY: Multi-Health Systems.
- Lederbogen, F., Haddad, L., & Meyer-Lindenberg, A. (2013). Urban social stress—Risk factor for mental disorders. The case of schizophrenia. *Environmental Pollution*, 183, 2–6.
- Lederbogen, F., Kirsch, P., Haddad, L., Streit, F., Tost, H., Schuch, P., . . . Meyer-Lindenberg, A. (2011). City living and urban upbringing affect neural social stress processing in humans. *Nature*, 474, 498–501.
- Loewy, R. L., Pearson, R., Vinogradov, S., Bearden, C. E., & Cannon, T. D. (2011). Psychosis risk screening with the Prodromal Questionnaire—Brief version (PQ-B). *Schizophrenia Research*, 129, 42–46.
- March, J. S., Parker, J. D., Sullivan, K., Stallings, P., & Conners, C. K. (1997). The Multidimensional Anxiety Scale for Children (MASC): Factor structure, reliability, and validity. *Journal of the American Academy of Child & Adolescent Psychiatry*, 36, 554–565.
- Millan, M. J., Andrieux, A., Bartzokis, G., Cadenhead, K., Dazzan, P., Fusar-Poli, P., . . . Weinberger, D. (2016). Altering the course of schizophrenia: Progress and perspectives. *Nature Reviews Drug Discovery*, 15, 485–515.
- Milne, B., Moffitt, T., Crump, R., Poulton, R., Rutter, M., Sears, M., . . . Caspi, A. (2008). How should we construct psychiatric family history scores? A comparison of alternative approaches from the Dunedin Family Health History Study. *Psychological Medicine*, 38, 1793–1802.
- Moffitt, T. E., & E-Risk Study Team. (2002). Teen-aged mothers in contemporary Britain. *Journal of Child Psychology and Psychiatry*, 43, 727–742.
- Myin-Germeys, I., Delespaul, P., & van Os, J. (2005). Behavioural sensitization to daily life stress in psychosis. *Psychological Medicine*, 35, 733–741.
- Myin-Germeys, I., van Os, J., Schwartz, J. E., Stone, A. A., & Delespaul, P. A. (2001). Emotional reactivity to daily life stress in psychosis. *Archives of General Psychiatry*, 58, 1137–1144.
- Newbury, J., Arseneault, L., Caspi, A., Moffitt, T. E., Odgers, C. L., & Fisher, H. L. (2016). Why are children in urban neighborhoods at increased risk for psychotic symptoms? Findings from a UK longitudinal cohort study. *Schizophrenia Bulletin*, 42, 1372–1383.
- Newbury, J., Arseneault, L., Caspi, A., Moffitt, T. E., Odgers, C. L., & Fisher, H. L. (2017). Cumulative effects of neighborhood social adversity and personal crime victimization on adolescent psychotic experiences. *Schizophrenia Bulletin*. Advance online publication. doi:10.1093/schbul/sbx060
- Newbury, J. B., Arseneault, L., Moffitt, T. E., Caspi, A., Danese, A., Baldwin, J. R., & Fisher, H. L. (2017). Measuring childhood maltreat-

- ment to predict early-adult psychopathology: Comparison of prospective informant-reports and retrospective self-reports. *Journal of Psychiatric Research*. Advance online publication. doi:10.1016/j.jpsychires.2017.09.020
- Noone, D., Ames, C., Hassanali, N., Browning, S., Bracegirdle, K., Corrigan, R., ... Maddox, L. (2015). A preliminary investigation of schematic beliefs and unusual experiences in children. *European Psychiatry*, 30, 569–575.
- Odgers, C. L., Caspi, A., Bates, C. J., Sampson, R. J., & Moffitt, T. E. (2012). Systematic social observation of children's neighborhoods using Google Street View: A reliable and cost-effective method. *Journal of Child Psychology and Psychiatry*, 53, 1009–1017.
- Odgers, C. L., Caspi, A., Russell, M. A., Sampson, R. J., Arseneault, L., & Moffitt, T. E. (2012). Supportive parenting mediates neighborhood socioeconomic disparities in children's antisocial behavior from ages 5 to 12. *Development and Psychopathology*, 24, 705–721.
- Odgers, C. L., Donley, S., Caspi, A., Bates, C. J., & Moffitt, T. E. (2015). Living alongside more affluent neighbors predicts greater involvement in antisocial behavior among low-income boys. *Journal of Child Psychology and Psychiatry*, 56, 1055–1064.
- Odgers, C. L., Moffitt, T. E., Tach, L. M., Sampson, R. J., Taylor, A., Matthews, C. L., & Caspi, A. (2009). The protective effects of neighborhood collective efficacy on British children growing up in deprivation: A developmental analysis. *Developmental Psychology*, 45, 942.
- Office for National Statistics. (2012). *The likelihood of becoming a victim of crime: Crime statistics, period ending March 2012*. London: Author.
- Office for National Statistics. (2013). *Urban and rural area definitions for policy purposes in England and Wales: Methodology (v1.0)*. London: Author.
- Plomin, R., DeFries, J. C., Knopik, V. S., & Neiderhiser, J. M. (2013). *Behavioral genetics*. New York: Worth.
- Polanczyk, G., Moffitt, T. E., Arseneault, L., Cannon, M., Ambler, A., Keefe, S. E. R., ... Caspi, A. (2010). Etiological and clinical features of childhood psychotic symptoms: Results from a birth cohort. *Archives of General Psychiatry*, 67, 328–338.
- Polling, C., Khondoker, M., Hatch, S., Hotopf, M., & South East London Community Health Study Team. (2014). Influence of perceived and actual neighbourhood disorder on common mental illness. *Social Psychiatry and Psychiatric Epidemiology*, 49, 889–901.
- Poulton, R., Caspi, A., Moffitt, T. E., Cannon, M., Murray, R. M., & Harrington, H. (2000). Children's self-reported psychotic symptoms and adult schizophreniform disorder: A 15-year longitudinal study. *Archives of General Psychiatry*, 57, 1053–1058.
- Reuben, A., Moffitt, T. E., Caspi, A., Belsky, D. W., Harrington, H., Schroeder, F., ... Danese, A. (2016). Lest we forget: Comparing retrospective and prospective assessments of adverse childhood experiences in the prediction of adult health. *Journal of Child Psychology and Psychiatry*, 57, 1103–1112.
- Rivera, C. L., Bernal, G., & Rosello, J. (2005). The Children Depression Inventory (CDI) and the Beck Depression Inventory (BDI): Their validity as screening measures for major depression in a group of Puerto Rican adolescents. *International Journal of Clinical and Health Psychology*, 5, 485.
- Robins, L., Cottler, L., Buchholz, K., & Compton, W. (1995). *Diagnostic Interview Schedule for DSM-IV (DIS-IV)*. St Louis, MO: Washington University School of Medicine.
- Ronald, A. (2015). Recent quantitative genetic research on psychotic experiences: New approaches to old questions. *Current Opinion in Behavioral Sciences*, 2, 81–88.
- Sampson, R. J., & Raudenbush, S. W. (1999). Systematic social observation of public spaces: A new look at disorder in urban neighborhoods. *American Journal of Sociology*, 105, 603–651.
- Sariaslan, A., Fazel, S., D'Onofrio, B., Långström, N., Larsson, H., Bergen, S., ... Lichtenstein, P. (2016). Schizophrenia and subsequent neighborhood deprivation: Revisiting the social drift hypothesis using population, twin and molecular genetic data. *Translational Psychiatry*, 6, e796.
- Schoenbaum, M., Sutherland, J. M., Chappel, A., Azrin, S., Goldstein, A. B., Rupp, A., & Heinssen, R. K. (2017). Twelve-month health care use and mortality in commercially insured young people with incident psychosis in the United States. *Schizophrenia Bulletin*. Advance online publication. doi:10.1093/schbul/sbx009
- Schreier, A., Wolke, D., Thomas, K., Horwood, J., Hollis, C., Gunnell, D., ... Duffy, L. (2009). Prospective study of peer victimization in childhood and psychotic symptoms in a nonclinical population at age 12 years. *Archives of General Psychiatry*, 66, 527–536.
- Scott, J., Chant, D., Andrews, G., & McGrath, J. (2006). Psychotic-like experiences in the general community: The correlates of CIDI psychosis screen items in an Australian sample. *Psychological Medicine*, 36, 231–238.
- Selten, J.-P., van der Ven, E., Rutten, B. P., & Cantor-Graae, E. (2013). The social defeat hypothesis of schizophrenia: An update. *Schizophrenia Bulletin*, 39, 1180–1186.
- Shakoor, S., Zavos, H. M., Haworth, C. M., McGuire, P., Cardno, A. G., Freeman, D., & Ronald, A. (2016). Association between stressful life events and psychotic experiences in adolescence: Evidence for gene-environment correlations. *British Journal of Psychiatry*, 208, 532–538.
- Spauwen, J., Krabbendam, L., Lieb, R., Wittchen, H. U., & van Os, J. (2004). Does urbanicity shift the population expression of psychosis? *Journal of Psychiatric Research*, 38, 613–618.
- Spauwen, J., Krabbendam, L., Lieb, R., Wittchen, H. U., & van Os, J. (2006). Evidence that the outcome of developmental expression of psychosis is worse for adolescents growing up in an urban environment. *Psychological Medicine*, 36, 407–415.
- Tarullo, A. R., & Gunnar, M. R. (2006). Child maltreatment and the developing HPA axis. *Hormones and Behavior*, 50, 632–639.
- Trouton, A., Spinath, F. M., & Plomin, R. (2002). Twins early development study (TEDS): A multivariate, longitudinal genetic investigation of language, cognition and behavior problems in childhood. *Twin Research*, 5, 444–448.
- Trzesniewski, K. H., Moffitt, T. E., Caspi, A., Taylor, A., & Maughan, B. (2006). Revisiting the association between reading achievement and antisocial behavior: New evidence of an environmental explanation from a twin study. *Child Development*, 77, 72–88.
- UNICEF. (2012). *Children in an urban world*. New York: Author.
- van Winkel, R., Stefanis, N. C., & Myin-Germeys, I. (2008). Psychosocial stress and psychosis: A review of the neurobiological mechanisms and the evidence for gene-stress interaction. *Schizophrenia Bulletin*, 34, 1095–1105.
- Walker, E., Mittal, V., & Tessner, K. (2008). Stress and the hypothalamic-pituitary-adrenal axis in the developmental course of schizophrenia. *Annual Review of Clinical Psychology*, 4, 189–216.
- Weissman, M. M., Wickramaratne, P., Adams, P., Wolk, S., Verdelli, H., & Olfson, M. (2000). Brief screening for family psychiatric history: The family history screen. *Archives of General Psychiatry*, 57, 675–682.
- Widom, C. S., & Morris, S. (1997). Accuracy of adult recollections of childhood victimization: Part 2. Childhood sexual abuse. *Psychological Assessment*, 9, 34–46.
- Widom, C. S., Weiler, B. L., & Cottler, L. B. (1999). Childhood victimization and drug abuse: A comparison of prospective and retrospective findings. *Journal of Consulting and Clinical Psychology*, 67, 867–880.
- Wilson, C., Smith, M. E., Thompson, E., Demro, C., Kline, E., Bussell, K., ... Schiffman, J. (2016). Context matters: The impact of neighborhood crime and paranoid symptoms on psychosis risk assessment. *Schizophrenia Research*, 171, 56–61.
- Yoshizumi, T., Murase, S., Honjo, S., Kaneko, H., & Murakami, T. (2004). Hallucinatory experiences in a community sample of Japanese children. *Journal of the American Academy of Child & Adolescent Psychiatry*, 43, 1030–1036.
- Zavos, H. M., Freeman, D., Haworth, C. M., McGuire, P., Plomin, R., Cardno, A. G., & Ronald, A. (2014). Consistent etiology of severe, frequent psychotic experiences and milder, less frequent manifestations: A twin study of specific psychotic experiences in adolescence. *JAMA Psychiatry*, 71, 1049–1057.

Chapter 7: Discussion

This thesis investigated potential neighbourhood- and individual-level pathways linking urban upbringing to the emergence of psychotic phenomena among children and adolescents. The main aims were 1) to examine whether children who grow up in urban neighbourhoods are more likely to have psychotic symptoms, and if so, whether adverse neighbourhood social characteristics might explain the association; 2) to investigate whether there is an accumulation of risk for psychotic phenomena among adolescents who are raised in urban and adverse neighbourhood conditions, and are subsequently victimised by a violent crime; 3) to explore the role of young people's personal perceptions of adverse neighbourhood conditions in the development of adolescent psychotic phenomena. Findings from each of the empirical chapters are summarised below, with particular attention paid to the longitudinal, genetically informed findings in Chapter 6 since these entailed several levels of analyses. Key findings, methodological considerations, future directions, and implications of this thesis are then discussed.

7.1 Summary of findings from empirical chapters

7.1.1 Why are children in urban neighbourhoods at increased risk for psychotic symptoms?

Chapter 4 demonstrated that children were around 80% more likely to report psychotic symptoms at age 12 if they had been raised in urban versus nonurban settings. Urbanicity was not significantly associated with other age-12 mental health problems including anxiety, depression, and antisocial behaviour. The association between urban upbringing and childhood psychotic symptoms was not fully explained by key family-level factors including family SES, family psychiatric history, and maternal psychosis.

In addition, the association between urbanicity and childhood psychotic symptoms was independent of neighbourhood-level SES. However, neighbourhood-level social processes explained part of the association between urban upbringing and childhood psychotic symptoms. After considering family-level confounders, low social cohesion and high crime in the neighbourhood (as reported by the children's mothers) together statistically explained 25% of the association between urbanicity at age 5 and childhood psychotic symptoms at age 12. Therefore, each of the three hypotheses outlined in Chapter 2 were supported.

7.1.2 Cumulative effects of neighbourhood social adversity and personal crime victimisation on adolescent psychotic experiences

Chapter 5 demonstrated that adolescents were around 70% more likely to report psychotic experiences if they had lived in the most urban versus rural settings at age 12. Again, this association was not fully explained by key potential confounders including neighbourhood-level SES, family SES, family psychiatric history, maternal psychosis, and adolescent substance problems. In contrast, adverse neighbourhood social conditions (low social cohesion and high neighbourhood disorder, as reported by residents) together statistically explained almost half of the association between urban residency and adolescent psychotic experiences. Additionally, adolescents who had been victimised by violent crime were over three-times more likely to report psychotic experiences. The combined association of neighbourhood social adversity and personal crime victimisation with psychotic experiences was greater still. After considering confounders, adolescents who had been raised in adverse neighbourhoods *and* had been victimised by violent crime were almost five-times more likely to report psychotic experiences, compared to unexposed adolescents. However, specificity analyses using the clinically-verified measure of adolescent psychotic symptoms yielded mostly non-

significant associations – though point estimates were similar to those yielded for adolescent psychotic experiences. Therefore, three of the four hypotheses outlined in Chapter 2 were supported, but there was only tentative evidence that findings replicated for adolescent psychotic symptoms.

7.1.3 Perceptions of neighbourhood adversity and psychotic experiences in adolescence

Chapter 6 demonstrated that adolescents residing in the most urban (versus rural) settings at age 18 were around 80% more likely to report psychotic experiences. Adolescents' personal perceptions of neighbourhood disorder were significantly, though only modestly (r 's=0.18–0.35, all p 's<0.001), correlated with objective/independent measures of neighbourhood adversity such as official levels of crime, resident reports of neighbourhood disorder, and neighbourhood SES. This provided initial evidence that the adolescents' own personal perceptions of neighbourhood disorder captured additional though complementary information about the neighbourhoods to that captured by the objective/independent measures. Adolescents in urban and intermediate (versus rural) settings perceived higher levels of disorder (physical and social signs of threat) in their immediate neighbourhoods, and these perceptions of disorder statistically explained over 40% of the association between urban residency and adolescent psychotic experiences. Adolescents who perceived higher levels of neighbourhood disorder were over 60% more likely to report psychotic experiences, after considering objective/independent measures of neighbourhood crime and adversity, family-level factors, adolescent substance and mood problems, and childhood psychotic symptoms. Several approaches were used to disentangle the nature of the association between adolescent psychotic experiences and perceptions of neighbourhood disorder, which were both obtained from the same informants and at the same time.

In longitudinal models, children who perceived their neighbourhood to be unsafe at age 12 were 45% more likely to report psychotic experiences in adolescence, net of childhood psychotic symptoms, adolescent perceptions of neighbourhood disorder, and other potential confounders. In contrast, the initially significant longitudinal association between childhood psychotic symptoms and perceptions of neighbourhood disorder at age 18 became non-significant after considering childhood perceptions of neighbourhood safety, adolescent psychotic experiences and other potential confounders. However, it is important to highlight that longitudinal models controlled for adolescent psychotic experiences at age 18 to isolate the independent associations arising from early childhood psychotic symptoms with adolescent perceptions of neighbourhood disorder (as well as controlling for adolescent perceptions of neighbourhood disorder to isolate the independent associations arising from earlier perceptions of neighbourhood safety with adolescent psychotic experiences). This could mean that longitudinal models were controlled for factors on a causal pathway. In addition, the age 18 psychotic phenomena and neighbourhood perceptions variables were on ordinal scales and thus captured more variance than the age 12 equivalent (binary) variables. As such, the adjusted longitudinal models may have over-controlled for covariates, and therefore the findings from the longitudinal analyses must be interpreted with caution.

In co-twin control analyses (the twin differences design, which controls completely for common environmental and partly for genetic influences), adolescents who perceived higher levels of neighbourhood disorder than their co-twin were significantly more likely to report psychotic experiences than their co-twin. This association was smaller than the association between perceptions of neighbourhood disorder and adolescent psychotic experiences in the entire sample, suggesting that part of the association was indeed attributable to overlapping common environmental factors

and/or genetic factors. Nevertheless, the significant association from co-twin control analyses provides further evidence that individual *perceptions* of neighbourhood disorder were associated with adolescent psychotic experiences, after holding actual neighbourhood conditions constant, and controlling for unmeasured genetic and common environmental confounding factors.

Twin model analyses highlighted that while perceptions of neighbourhood disorder were partly attributable to additive genetic influences, the correlation between adolescent psychotic experiences and perceptions of neighbourhood disorder was mostly explained by overlapping common environmental influences ($r_C=0.88$). Consistent with results from the co-twin control analysis, there was also a small unique environmental source of covariance between perceptions of neighbourhood disorder and adolescent psychotic experiences ($r_E=0.10$), though confidence intervals included zero.

Taken together, findings from co-twin and twin model analyses indicate that the association between perceptions of neighbourhood disorder and adolescent psychotic experiences was largely environmentally mediated. Since both common (shared between twins) and unique (specific to each twin) environmental factors were implicated, findings suggest that both objective levels and individual perceptions of neighbourhood adversity contributed to psychotic phenomena. That is, the findings support a mechanism whereby the actual neighbourhood conditions contributed to the overall association between perceptions of neighbourhood disorder and psychotic experiences; but even after holding neighbourhood conditions constant by design, the adolescents' personal perceptions of disorder were associated with psychotic experiences above and beyond variation in neighbourhood conditions.

Therefore, three out of the five hypotheses described in Chapter 2 were supported. However, longitudinal models provided only tentative evidence of a

bidirectional relationship between adolescent psychotic experiences and perceptions of neighbourhood disorder. Further, twin models did not reveal shared genetic influences between adolescent psychotic experiences and perceptions of neighbourhood disorder.

7.2 Discussion of main findings

7.2.1 Urban upbringing and early psychotic phenomena

The most consistent finding in this thesis was that psychotic phenomena were more common among youth raised in urban settings. Unadjusted point estimates were similar, regardless of the age of participants, regardless of how psychotic phenomena were measured, and regardless of how urbanicity was defined. The present findings are consistent with the wider literature on urbanicity and adult psychotic disorder (Krabbendam & Van Os, 2005; Vassos et al., 2012), as well as previous reports on the association between urbanicity and subclinical psychotic phenomena (Polanczyk et al., 2010; Scott et al., 2006; Spauwen et al., 2004, 2006b; Stefanis et al., 2004; van Os et al., 2001; van Os et al., 2002). Taken together, this body of research suggests that children and adolescents raised in urban settings are up to twice as likely to experience subclinical psychotic phenomena such as hallucinations, delusions, and other unusual thoughts and beliefs. By focussing on a longitudinal cohort of children and adolescents, the research in this thesis demonstrated that the association between urbanicity and psychosis is detectable even in the earliest subclinical expressions of psychosis.

7.2.2 Neighbourhood social adversity and early psychotic phenomena

The association between urbanicity and early psychotic phenomena was not explained by a range of potential individual- and family-level confounders. In contrast, adverse social conditions including low social cohesion and high levels of crime and disorder in the participants' immediate neighbourhoods explained up to half of the association

between urbanicity and psychotic phenomena. Mediatory effects were present regardless of age period and regardless of how neighbourhood social processes were measured (e.g., mother reports, resident reports, self-reports). Findings are in keeping with the wider literature on neighbourhood characteristics and psychosis, which documents higher rates of psychotic disorder, ultra-high-risk, and subclinical psychotic phenomena among adults and youth living in areas with high levels of crime, fragmentation, stress, and disorder (Allardyce et al., 2005; Bhavsar et al., 2014; Binbay et al., 2012; Das-Munshi et al., 2012; Kirkbride et al., 2015; Kirkbride et al., 2008; Silver et al., 2002; Solmi et al., 2017; Veling et al., 2015). Drawing from sociological theory (Sampson, 2001; Sampson et al., 2002; Sampson & Raudenbush, 1999) and using high resolution measures of neighbourhood social conditions, the research in this thesis traced a potential pathway leading from urban upbringing, through neighbourhood-level social conditions, to early psychotic phenomena.

In addition, the association between neighbourhood social adversity and psychotic phenomena was detectable at the level of the eye of the beholder. The association between participants' perceptions of neighbourhood adversity and psychotic phenomena was apparent in longitudinal models, had environmental rather than genetic underpinnings, and occurred above and beyond variation in actual neighbourhood conditions. The present findings build on those from recent studies reporting associations between perceptions of neighbourhood disorder in common mental health problems among youth (Goldman-Mellor et al., 2016; Polling et al., 2014). Adopting a longitudinal and genetically informed design, the research in this thesis isolated the effects of perceived neighbourhood adversity from a range of confounding mechanisms and background factors. Taken together, findings indicate that both objective levels and perceptions of neighbourhood social adversity contributed to the higher rates of psychotic phenomena among young people in cities.

7.2.3 Crime victimisation and early psychotic phenomena

Of all exposures examined in this thesis, combined exposure to neighbourhood social adversity plus violent crime victimisation during adolescence was associated with the greatest odds for psychotic experiences. In addition, there was tentative evidence of an additive interaction between neighbourhood social adversity and crime victimisation, such that the association between crime victimisation and psychotic experiences was stronger in the most adverse neighbourhood contexts. These findings are in keeping with an extensive body of research implicating early-life victimisation and trauma in risk for subclinical (Trotta et al., 2015) and clinical (Varese et al., 2012) expressions of psychosis. Given that cities have higher rates of violent crime (Federal Bureau of Investigation, 2015; Home Office Statistical Bulletin, 2010), and teenagers and young adults have the highest risk of being victimised by violent crime (Office for National Statistics, 2012), the present findings suggest a role of adolescent exposure to crime victimisation in the association between urbanicity and early psychotic experiences.

7.2.4 Wider social environment, social stress, and early psychotic phenomena

Being raised in a neighbourhood characterised by few or poor quality social networks and threatening exposures such as disorder and crime might clearly be stressful for a child. The findings in this thesis are consistent with leading aetiological models of psychosis, which emphasise a key role played by psychosocial stressors in the emergence of psychotic phenomena (van Winkel et al., 2008). Both biological and psychological mechanisms are mutually possible.

For example, chronic and acute early-life stress could increase risk for psychosis by dysregulating the hypothalamic-pituitary adrenal (HPA) axis and disrupting the dopaminergic system (Tarullo & Gunnar, 2006; van Winkel et al., 2008; Walker et al., 2008). The HPA axis is a major neuroendocrine system involved in the body's response

to stress (Herman & Cullinan, 1997). When activated (e.g., when a person perceives a threat), the HPA axis releases cortisol, which interacts with multiple tissues throughout the brain and body, and contributes to bodily resources being reallocated away from repair and growth processes and to the skeletal muscles (Pariante & Lightman, 2008). This response is an adaptive process to increase the likelihood of surviving a threat. However, chronic or acute stressors (e.g., living in a threatening, violent neighbourhood) are thought to lead to lasting changes in how the HPA axis responds to stress (van Winkel et al., 2008). For example, the HPA axis might become either too sluggish or too vigilant, and base levels of cortisol might be abnormally low or high. Such dysregulation of the HPA axis has been frequently postulated to contribute to the aetiology of depression and anxiety (Pariante & Lightman, 2008). Dysregulation of the HPA axis could also contribute to the aetiology of psychosis (and psychotic phenomena) via several mechanisms. For instance, converging evidence suggests that persistently elevated cortisol is neurotoxic, inhibiting neurogenesis and neuronal survival (Walker et al., 2008). Thus, chronic or acute stress during upbringing could contribute to the aetiology of psychosis and psychotic phenomena by inhibiting the development of certain brain regions such as the hippocampus – reduced volume of which has been associated with psychotic disorder (Velakoulis et al., 2006). In addition, there is evidence that the HPA axis and the dopaminergic system operate in a synergistic fashion. For example, cortisol secretion increases dopamine activity in the brain (Walker et al., 2008). The dopaminergic system plays a key role in how the brain ascribes salience to stimuli, and abnormal dopamine activity is currently the leading neurobiological model for the positive symptoms of psychosis (Howes, McCutcheon, Owen, & Murray, 2017; Kapur, 2003; van Winkel et al., 2008). Thus, chronic or acute stress during upbringing could also contribute to the aetiology of psychotic phenomena by leading to lasting changes to the dopaminergic system.

The combined, interactive effect of neighbourhood adversity and violent crime on adolescent psychotic experiences could suggest that adolescents living in adverse neighbourhood conditions were more susceptible to the deleterious effects of victimisation. This is in keeping with a broader literature showing that risk for psychotic symptoms and disorders increases as lifetime stressors accumulate (Cougnard et al., 2007; Morgan et al., 2014; Shevlin, Houston, Dorahy, & Adamson, 2008), as well as with studies showing that the effects of key risk factors for psychosis such as childhood trauma (Frissen et al., 2015) and cannabis use (Kuepper et al., 2011a) are stronger in urban settings. Taken together, this research could suggest that being raised in adverse, urban settings leads to biological/behavioural sensitisation and undermines young people's resilience to subsequent stressors. However, it is important to acknowledge that the E-Risk measure of violent crime victimisation is on a severity scale, and does not indicate frequency. Given that violent crime was more prevalent among youth in adverse neighbourhood settings, it is likely that it was also more frequent, and this could have contributed to the cumulative effects of neighbourhood adversity and violent crime.

In addition, early-life exposure to threatening and ambiguous social interactions could promote or exacerbate specific psychotic phenomena such as persecutory delusions. This psychological mechanism could explain why, in this sample, urban upbringing was specifically associated with psychotic phenomena and not with other mental health problems such as depression. Furthermore, the association between perceived neighbourhood disorder and adolescent psychotic experiences is consistent with cognitive theories of psychotic phenomena, which emphasise the role of negative beliefs about the world, hostile attributions of others' intentions, and threat anticipation in the emergence of paranoia and hallucinations (An et al., 2010; Appiah-Kusi et al., 2017; Fowler et al., 2006; Freeman, 2016; Garety, Bebbington, Fowler, Freeman, &

Kuipers, 2007). Findings on the directionality of this association were inconclusive. However, given that psychotic phenomena involve altered perceptions of reality such as persecutory delusions and negative attribution bias (Freeman et al., 2002; Garety et al., 2001), it is likely that a bidirectional relationship exists between adolescent psychotic experiences and perceptions of neighbourhood adversity. As such, there may be a “double hit” from the urban environment. Young people in urban, adverse neighbourhoods may be more likely to experience psychotic phenomena due to their heightened exposure to stress. In addition, young people with psychotic phenomena may be more likely to perceive their neighbourhoods as threatening, which further exacerbates their symptoms. This proposed mechanism is supported by empirical work showing that the paranoia, voice-hearing, anxiety, and negative beliefs about the self and others among adults with psychotic disorder is immediately exacerbated after brief exposure to a busy urban environment (Freeman et al., 2014).

7.3 Limitations and methodological considerations

The results chapters each include a brief overview of the main limitations relevant to that study. In the following section I describe in more detail the limitations and methodological considerations that apply to research throughout this thesis.

7.3.1 Findings could be due to social drift

Given that children and adolescents have minimal control over where they grow up, it is implausible that the association between urban upbringing and early psychotic phenomena in this sample was due to participants drifting into urban neighbourhoods because of their symptoms. Analyses were also adjusted for proxy indicators of genetic risk including family psychiatric history and maternal psychosis, suggesting that findings were not solely attributable to urban-rural differences in genetic risk for

psychosis. However, family psychiatric history captures only the diagnosed fraction of the spectrum of genetic risk for psychopathology (Yang, Visscher, & Wray, 2010). Findings could still be attributable to social drift rather than causation. That is, it remains possible that families with higher genetic risk for psychosis were more likely to live in urban settings *because* of this heightened risk. For example, cognitive impairments associated with genetic risk could reduce the employment prospects of parents, and thereby reduce their financial means to move out of crowded and deprived areas (though findings were not explained by family SES). Children would then inherit both genetic risk and the urban environment from their parents, and therefore the association between urban upbringing and early psychotic symptoms would be confounded by genes. The advent of polygenic risk score (PRS) data offers new opportunities to examine the spatial distribution of genetic risk for psychosis. Indeed, one recent study documented an association between schizophrenia PRS and urban residency at age 15, though notably, schizophrenia PRS was not associated with urban birth (Paksarian et al., 2018). This suggests that future research into the association between urban upbringing and psychosis should consider spatial variation in genetic risk as a confounding factor. However, PRS data has only recently been generated for the E-Risk study, and was not available when the analyses in this thesis were conducted.

7.3.2 Western perspective on urbanicity

Using data from a UK sample, this thesis takes a Western perspective in terms of defining and analysing the urban environment. However, social and physical characteristics of cities in wealthy countries differ considerably from those of cities in low- and middle-income countries. For example, absolute poverty levels and overcrowding in cities in low- and middle-income countries typically far exceed that found in higher income counties (United Nations Human Settlements Programme,

2006). On the other hand, sociocultural factors in low- and middle-income countries – such as the Indian extended family system – could bolster the cohesiveness of urban communities and thereby buffer children from psychosocial stressors in cities. As such, the findings in this thesis might not generalise to low- and middle-income countries. Only a handful of studies have investigated urban-rural contrasts in psychosis in lower income countries (Chan et al., 2015; Lundberg et al., 2009) (although the literature search strategy in this thesis included only articles written in English, and therefore relevant studies from low- and middle-income countries may have been excluded). Intriguingly, the prevalence of psychotic disorder among urban residents has doubled in China since the 1980s – in parallel with the most rapid industrialisation of any country in history – whereas psychosis prevalence in rural China has not changed (Chan et al., 2015). Given that most of the projected urban population growth will occur in low- and middle-income countries (Cohen, 2006; United Nations, 2004) – particularly through the expansion of city slums – research that examines the mental health consequences of urbanisation in developing countries is strongly needed.

A related issue is that this thesis has focussed solely on neighbourhood-level *social* factors that might characterise urban areas and pose a risk to children's mental health. As outlined in Chapter 1, cities are complex environments, containing numerous potential social and physical benefits and risks. Analyses indicated that neighbourhood social factors accounted for part – but not all – of the association between urban upbringing and early psychotic phenomena. This suggests that part of the association was explained by factors that were not examined in this thesis. Moreover, recent research demonstrates that adverse neighbourhood social conditions such as deprivation and ethnic fragmentation are also associated with psychosis incidence in rural areas (Richardson, Hameed, Perez, Jones, & Kirkbride, 2017). Thus, neighbourhood social adversity is by no means an exclusively urban problem. There remains a pressing need

to examine other potential exposures within cities which might be relevant to children's mental health, such as green space and pollution (discussed in more detail below). However, pollution data has only recently been linked to E-Risk addresses, and was not available at the time the analyses in this thesis were conducted.

7.3.3 Timing and duration of neighbourhood exposures

The neighbourhood measures used in this thesis were obtained at several time points from age 5 to age 18. Longitudinal associations were identified between age 5 neighbourhood conditions and age 12 psychotic symptoms, as well as between age 12 neighbourhood conditions and age 18 psychotic experiences. Findings therefore suggested that neighbourhood conditions throughout childhood and adolescence contributed to the emergence of psychotic phenomena. However, detailed neighbourhood measures were not available at birth, and therefore I was not able to examine the potential role of perinatal neighbourhood conditions in early psychotic phenomena. Additionally, neighbourhood conditions were highly correlated throughout childhood and adolescence. For example, among the 53% of children who moved house at least once by age 18, 84% of children who had lived in the most urban settings at age 5 also lived in the most urban settings at age 18. As such, analyses were not adequately powered to test whether neighbourhood conditions during specific age periods (e.g., early childhood versus adolescence) were more strongly associated with psychotic phenomena; nor whether duration of exposure modified the effect of neighbourhood conditions. Research that combines larger samples or quasi-experimental designs with high resolution neighbourhood data is needed to answer these questions.

7.3.4 Shared method variance

For most analyses in this thesis, neighbourhood measures and psychotic experiences were obtained from different sources, and therefore findings were not confounded by shared method variance. In addition, analyses in Chapter 6 purposely explored the nature of the association between the adolescents' psychotic experiences and their perceptions of neighbourhood conditions. However, in Chapter 5's investigation of the potential role of violent crime victimisation in psychotic experiences, both measures were obtained from the same informants during the same private interviews at age 18. As such, the associations between crime victimisation and psychotic experiences could have been confounded by shared method variance. A more concerning issue is the possibility that adolescents with concurrent mental problems were more likely to recall unpleasant experiences such as crime victimisation because of their mood, leading to mood-congruent recall bias (Hardt & Rutter, 2004). This could have inflated the association between violent crime victimisation and adolescent psychotic experiences in this sample. Indeed previous research from this cohort (Newbury et al., 2018) and others (Reuben et al., 2016) suggests that associations between childhood adversities and psychopathology are stronger when adversities are self-reported rather than objectively or independently measured. This limitation is inherent to victimology research, and it nevertheless remains preferable to measure victimisation via self-reports since victimised individuals rarely meet the attention of professionals and therefore official estimates capture a very small minority of cases (Gilbert et al., 2009). In addition, the E-Risk crime victimisation measure is derived from detailed responses to the JVQ, which were then rated by a team of trained researchers following anchor points from the Childhood Experience of Care and Neglect (CECA) instrument (Bifulco et al., 1994b). The CECA anchor points are designed to improve the objectivity of ratings by basing them on the coder's impressions and concrete descriptions, rather than relying

on the participant's judgement and emotional responses (Fisher et al., 2015). However, future research in this cohort could explore whether official sources such as hospital records could be used to supplement the JVQ measure of crime victimisation.

7.3.5 Adolescent psychotic experiences were self-report

Though obtained during private face-to-face interviews, the adolescent psychotic *experiences* measure was nevertheless a self-report measure in that responses (none/probable/definite) were not verified by a team of clinicians. Just under a third of participants self-reported having psychotic experiences between age 12 and 18. This prevalence is on the upper end of that typically reported in the literature for this age group, which varies considerably depending on method. For example, in a meta-analysis of population-based studies that had used either previously validated items (Kelleher et al., 2011) or clinically-verified interviews, Kelleher et al. (2012a) reported a 7.5% prevalence of psychotic symptoms during adolescence. In contrast, endorsement of self-report screen items among adolescents is much higher, ranging from around 10% (have you ever heard voices talking to each other when you were alone?) to 90% (have you ever felt as if some people are not what they seem to be?) depending on item (Yung et al., 2009). It is therefore probable that the adolescent psychotic experiences measure used in this thesis captured some false-positives. For example, genuine experiences (e.g., a real incident of being followed by a stranger) could have been recorded as psychotic experiences, and this could have inflated the association between urban/adverse neighbourhood conditions and psychotic experiences. While sensitivity analyses in Chapter 5 revealed comparable point estimates for the association between neighbourhood measures and adolescent psychotic symptoms (which were verified by clinicians and experts), the findings in this thesis would benefit from replication in a larger sample using a clinically-verified measure of adolescent psychotic phenomena.

In addition, genetic influences were found to account for only 17% of the variance in psychotic experiences. This is lower than typically reported for subclinical psychotic phenomena for this age group, with estimates usually ranging between 30% and 50% (Ericson, Tuvblad, Raine, Young-Wolff, & Baker, 2011; Hur, Cherny, & Sham, 2012; Lin et al., 2007). The comparatively low heritability estimate in this thesis could also be due the adolescent psychotic experiences measure capturing false-positives. Ideally, twin model analyses would have been repeated using the clinically-verified measure of psychotic symptoms. However, the low prevalence of these symptoms in adolescence (2.9%) meant that this sensitivity check was not possible. It is important to highlight, however, that heritability estimates vary depending on method and symptom. In the largest twin study of adolescent psychotic phenomena, the heritability of hallucinations (15%) was much lower than the heritability of paranoia (52%) (Zavos et al., 2014), suggesting that environmental influences may be differentially associated with specific psychotic phenomena. Future research using larger samples could explore the genetic versus environmental contributions to specific psychotic experiences, as well as whether urban and adverse neighbourhood conditions are differentially associated with certain psychotic experiences. However, the low base rates of individual psychotic symptoms in the E-Risk sample restricted power to explore this properly in the present thesis.

7.3.6 Subclinical psychotic phenomena are not psychotic disorders

Subclinical psychotic phenomena differ considerably from psychotic disorders, and therefore the present findings might not generalise to adult psychotic disorders. For instance, the psychotic phenomena measures in this thesis included only positive symptoms. Diagnoses of psychotic disorders are based on a range of positive, negative and cognitive symptoms (World Health Organization, 1992). Only one study has

investigated the association between urbanicity and negative psychotic symptoms among general population adults, and reported the same dose-response association as found for positive psychotic symptoms (van Os et al., 2002). Research that examines the relevance of neighbourhood conditions to early negative and cognitive psychotic symptoms among youth is needed, particularly given that these symptoms are typically hardest to treat and convey the most functional impairment (Carbon & Correll, 2014). In addition, though early psychotic phenomena are associated with a heightened adulthood risk for psychotic disorder (Dominguez et al., 2011; Fisher et al., 2013; Linscott & van Os, 2013; Poulton et al., 2000), for most young people these symptoms are transient and developmentally limited (Kelleher et al., 2012a; Scott et al., 2006). This is evidenced by the fact that the prevalence of clinically-verified psychotic symptoms in E-Risk halved between age 12 and age 18. However, early psychotic phenomena are also implicated in a range of other serious adult psychiatric problems, including depression, post-traumatic stress disorder, substance abuse and suicidal behaviour (Fisher et al., 2013; Kelleher et al., 2012c; Poulton et al., 2000). As such, the present findings are not directly generalisable to the wider literature on urbanicity and adult psychosis, but instead suggest a role of urban and adverse neighbourhood conditions during upbringing in the development of a range of mental health conditions (or at least in vulnerability for psychopathology more broadly).

7.3.7 Twins could differ from singletons

A key concern with using twin data is that twin siblings could differ from singletons for exposures and outcomes. For example, the conspicuousness of identical twins could increase their risk of being victimised by peers and strangers. Indeed, the prevalence of violent crime victimisation during adolescence in E-Risk (19.3%) is higher than reported for this age group by the ONS (11.7%) (Office for National Statistics, 2012),

though this could be due to the E-Risk measure being obtained via structured face-to-face interviews rather than a survey. Importantly, E-Risk is representative of the UK population in terms urbanicity (Office for National Statistics, 2013), and the prevalence of psychotic experiences and symptoms is within the range reported in similar age non-twin samples (Spauwen et al., 2004; Yoshizumi et al., 2004; Yung et al., 2009). Moreover, the findings in this thesis are in keeping with previous studies based on non-twin samples, reviewed in Chapter 2.

7.3.8 Missing data

Since E-Risk has very little missing data, analyses were conducted using listwise deletion. That is, only cases with data on all variables included in the model specification were included in analyses. It is important to acknowledge that listwise deletion can produce biased results if missing data are not missing completely at random (Sterne et al., 2009). That is, if missingness is linked in some way to the data, point estimates of associations could be biased. An increasingly valued approach for handling missing data is full information maximum likelihood estimation (FIML), which uses all available information to handle the missing data within the models. Reassuringly, mediation analyses in Chapter 4 were repeated using FIML in Mplus to include all available cases at age 5 (N=2,232), and point estimates were the same (described in notes under Table 4.3). In addition, listwise deletion in the present thesis only slightly reduced sample sizes, even for fully specified models. Taking Chapter 4's fully adjusted mediation results in Table 4.3 (Model 2) as an example, full data were available for between 92.7% and 95.3% (N=1989-2045) of the age-12 sample.

7.3.9 Effect sizes and significance thresholds

This thesis follows scientific convention by using a $p < 0.05$ significance (alpha) threshold to reject the null hypothesis and judge the statistical significance of associations. Trend level associations (i.e., $p > 0.05$ and < 0.10) are also acknowledged as such. This significance threshold is of course arbitrary (Hackshaw & Kirkwood, 2011). There have been growing calls for researchers to focus on effect sizes and confidence intervals when interpreting results. In this thesis, the conventional threshold was used to judge statistical significance, but due attention was also paid to effect sizes and confidence intervals, for example when specificity was examined by repeating main analyses using other mental health outcomes.

7.4 Future directions

Within the E-Risk cohort, it will be important to track the associations of wider socioenvironmental factors with psychotic phenomena and disorders into adulthood. This will highlight whether adverse neighbourhood social conditions are associated with the persistence and progression of early symptoms into clinically-relevant mental health problems. In addition, by this point participants will have more choice in where they live and spend their time, and most twin pairs will have left home and be living separately from each other. It will then become possible, using the twin design and PRS data, to investigate the genetic and environmental contributions to participants' actual (as well as perceived) neighbourhood conditions. This will highlight whether social drift plays a role in the association between neighbourhood conditions and psychotic phenomena, providing insights into the basis of previous and future findings on urbanicity and psychosis. Moreover, mapping the spatial distribution of genetic risk for psychosis could help to target early-intervention services with greater precision.

Future research should examine the mental health implications of a wider range of social and physical factors within cities. Pollution is a worldwide health issue (Health Effects Institute, 2010; World Health Organization, 2013), but is a particular problem in highly urban areas where levels of air pollutants such as nitrogen dioxide and particulate matter consistently exceed limits set by WHO and the European Union (Beevers et al., 2016; Cohen, 2006). Post-mortem studies have revealed air pollutants in brain tissue (Calderón-Garcidueñas et al., 2008). Once in the brain, air pollutants could increase risk for psychopathology by triggering neuroinflammation (Block & Calderón-Garcidueñas, 2009), with infants and children potentially being most vulnerable due to the young brain's rapid development. In addition, noise pollution from road and air traffic could impact child development by increasing stress levels and disrupting sleep (Stansfeld & Matheson, 2003). A handful of studies have used high-resolution measures to investigate the potential role of pollution in psychopathology, with associations documented for anxiety (Power et al., 2015), depression (Szyszkowicz, Rowe, & Colman, 2009), and suicidality (Bakian et al., 2015). Only two studies have investigated the association of air pollution with psychotic disorder (Gao et al., 2017; Pedersen & Mortensen, 2006b), and these studies used proxy or fairly low-resolution measures of air pollution (e.g., distance to major roads). As such, future research using high-resolution measures of air and noise pollution is needed to examine whether elevated early-life exposure to pollutants contributes to the heightened rates of psychotic phenomena among youth in cities. In addition, this thesis examined only two potential individual-level mechanisms (neighbourhood perceptions and crime victimisation) linking adverse neighbourhood settings to early psychotic phenomena. Previous studies have demonstrated that family-level factors such as parenting styles and dysfunction mediate the effects of neighbourhood conditions on childhood outcomes (Kohen, Leventhal, Dahinten, & McIntosh, 2008; Odgers et al., 2012b).

Future research should examine a wider range of potential individual- and family-level factors that might lie on the pathway between neighbourhood conditions and early psychotic phenomena.

The findings in this thesis are consistent with a mechanism involving early-life stress and mutually-compatible biological (e.g., HPA axis) and psychological (e.g., cognitive biases) processes. However, key components of this proposed aetiological pathway are poorly characterised. Little is currently known about the potential effects of wider socioenvironmental stressors on childhood biomarkers, such as brain activity, inflammation, and cortisol levels (the main hormonal output from the HPA axis). In addition, potential urban-rural differences among children in terms of subjective stress levels and cognitive styles have not yet been explored. Converging evidence implicates acute, proximal early-life adversities such as maltreatment in maladaptive biological sequelae (Danese & Baldwin, 2017). Experimental research using experiencing sampling methods (Rauschenberg et al., 2017) and virtual reality tasks (Veling et al., 2016a) has also been used to demonstrate links between childhood trauma and stress-sensitivity and cognitive styles among young adults. An emerging body of evidence now implicates wider environmental adversities such as neighbourhood disadvantage and disorder in abnormal cortisol activity among infants and children (Dulin-Keita, Casazza, Fernandez, Goran, & Gower, 2010; Finegood, Rarick, Blair, & The Family Life Project Investigators, 2017; Rudolph et al., 2014). Research that combines experience sampling techniques and virtual reality tasks with biological and cognitive measures in young samples could be used to explore potential biopsychological mechanisms linking distal, wider environmental stressors to early psychotic phenomena.

7.5 Implications

From a research perspective, the findings in this thesis provide further evidence that the association of urbanicity and neighbourhood-level exposures with psychosis is detectable in the earliest subclinical expressions of psychosis. Assuming a degree of aetiological continuity between early psychotic phenomena and adult psychotic disorder (as has been previously shown in this sample: Polanczyk et al. (2010)), this supports the theory that elevated early-life exposure to social stressors contributes to the heightened rates of psychotic disorders among adults in cities (Heinz et al., 2013; Kirkbride et al., 2007; Lederbogen et al., 2013; Meyer-Lindenberg & Tost, 2012; Selten et al., 2013).

From a clinical perspective, this highlights potential areas for intervention. It is now accepted that early-intervention offers the best hope for improving outcomes in psychosis (Davidson et al., 2015; Millan et al., 2016). This has been recognised in the development of targeted youth mental health services in high-income countries, such as “Headspace” in Australia (McGorry, Goldstone, Parker, Rickwood, & Hickie, 2014) and “OASIS” in South London (Fusar-Poli, Byrne, Badger, Valmaggia, & McGuire, 2013). In addition, there is a growing interest in the instrumental role that schools could play by adopting mental health screening programmes to identify at-risk children and adolescents who might benefit from psychological intervention (Fazel, Hoagwood, Stephan, & Ford, 2014). In the context of severe shortfalls in mental health funding (NHS Providers, 2016), the UK government has announced plans for targeted investment in youth mental health services including training for staff in a third of secondary schools. The present findings suggest that child and adolescent mental health services and school-based mental health screening programmes for psychotic phenomena could be particularly valuable in urban, adverse areas. Furthermore, given that personal perceptions of neighbourhood adversity were associated with adolescent

psychotic phenomena, clinicians could explore whether psychological therapies are enhanced by including content on young people's (potentially modifiable) attitudes towards their neighbourhoods. That is, negative attitudes towards one's neighbourhood – even if justified – could contribute to a cycle of stress and psychotic phenomena. Indeed, targeted cognitive behavioural programmes have been successfully used to help adults with psychosis to cope with the stress of crowded urban settings (Freeman et al., 2015).

The present findings are also relevant to public health and policy. Youth in cities have the highest risk of being victimised by violent crime (Office for National Statistics, 2012), and the ONS recently reported an increase in violent crime in the UK for the first time in 10 years (Office of National Statistics, 2017). The present findings suggest that greater investment and targeted policies to reduce crime victimisation among youth could also reduce young people's risk for psychotic phenomena. Indeed, research from the wider literature on victimisation and early psychotic phenomena suggests that adolescent psychotic experiences abate when bullying victimisation stops (Kelleher et al., 2013). Additionally, given that adverse neighbourhood social conditions were consistently found to mediate the association between urban upbringing and early psychotic phenomena, the findings in this thesis suggest that public health policy should consider neighbourhood social conditions as modifiable factors to target to reduce the population-level risk for psychotic phenomena. Urban planners and architects have long known the importance of urban design for contributing to the safety and supportiveness of communities. For example, crime rates can be reduced by increasing the diversity and accessibility of neighbourhoods, because increased pedestrian traffic creates a natural surveillance system to monitor criminal activity (Giles-Corti et al., 2016). Furthermore, access to public spaces and amenities such as parks is clearly an essential resource for civic participation and community cohesion, and there is growing evidence

of the buffering effect of green space for numerous physical and mental health outcomes (Maas, Verheij, Groenewegen, De Vries, & Spreeuwenberg, 2006). Closer collaboration between local government, urban planners, and public health practitioners is vital to respond to the challenge of an increasingly urban world (Northridge, Sclar, & Biswas, 2003; World Health Organization, 2011). Future urban planning initiatives should aim to bolster the cohesiveness and safety of urban communities to support the mental health of young people living in cities and improve mental health trajectories over the lifespan.

7.6 Conclusion

Understanding the mechanisms linking the urban environment to psychosis is an increasingly urgent public health priority. This thesis contributes to the existing literature by focussing on early psychotic phenomena, using high resolution measures of neighbourhood social conditions, and adopting longitudinal and genetically informed methods. Consistent with the broader literature on adult psychosis, the present findings highlight a role of urbanicity, neighbourhood-level social adversity, and violent crime victimisation in psychotic phenomena among children and adolescents. Multidisciplinary research should consider these pervasive wider environmental exposures in future efforts to understand the aetiology of early psychotic phenomena. Such research has the potential to improve outcomes in psychosis by helping to design and target early-intervention efforts to prevent the onset, persistence and progression of early expressions of psychosis.

References

- Achenbach, T. (1991). *Manual for the child behavior checklist and 1991 profile*. Burlington, VT: University of Vermont Department of Psychiatry.
- Allardyce, J., Boydell, J., Van Os, J., Morrison, G., Castle, D., Murray, R., & McCreadie, R. (2001). Comparison of the incidence of schizophrenia in rural Dumfries and Galloway and urban Camberwell. *The British Journal of Psychiatry*, 179(4), 335-339.
- Allardyce, J., Gilmour, H., Atkinson, J., Rapson, T., Bishop, J., & McCreadie, R. (2005). Social fragmentation, deprivation and urbanicity: Relation to first-admission rates for psychoses. *The British Journal of Psychiatry*, 187(5), 401-406.
- American Psychiatric Association. (1994). *Diagnostic and Statistical Manual of Mental Disorders*. Washington, DC: American Psychiatric Association.
- An, S. K., Kang, J. I., Park, J. Y., Kim, K. R., Lee, S. Y., & Lee, E. (2010). Attribution bias in ultra-high risk for psychosis and first-episode schizophrenia. *Schizophrenia Research*, 118(1), 54-61.
- Appiah-Kusi, E., Fisher, H., Petros, N., Wilson, R., Mondelli, V., Garety, P., McGuire, P., & Bhattacharyya, S. (2017). Do cognitive schema mediate the association between childhood trauma and being at ultra-high risk for psychosis? *Journal of Psychiatric Research*, 88, 89-96.
- Bakian, A. V., Huber, R. S., Coon, H., Gray, D., Wilson, P., McMahon, W. M., & Renshaw, P. F. (2015). Acute air pollution exposure and risk of suicide completion. *American Journal of Epidemiology*, 181(5), 295-303.

- Bartels-Velthuis, A. A., Jenner, J. A., van de Willige, G., van Os, J., & Wiersma, D. (2010). Prevalence and correlates of auditory vocal hallucinations in middle childhood. *The British Journal of Psychiatry*, 196(1), 41-46.
- Bebbington, P., & Nayani, T. (1995). The psychosis screening questionnaire. *International Journal of Methods in Psychiatric Research*, 5(1), 11-19.
- Beevers, S. D., Carslaw, D. C., Dajnak, D., Stewart, G. B., Williams, M. L., Fussell, J. C., & Kelly, F. J. (2016). Traffic management strategies for emissions reduction: recent experience in London. *Energy and Emission Control Technologies*, 4, 27-39.
- Bennett, N., Jarvis, L., Rowlands, O., Singleton, N., & Haselden, L. (1996). *Living in Britain: Results from the 1994 general household survey*. London: HMSO.
- Besteher, B., Gaser, C., Spalthoff, R., & Nenadić, I. (2017). Associations between urban upbringing and cortical thickness and gyrification. *Journal of Psychiatric Research*, 95, 114-120.
- Bhavsar, V., Boydell, J., Murray, R., & Power, P. (2014). Identifying aspects of neighbourhood deprivation associated with increased incidence of schizophrenia. *Schizophrenia Research*, 156(1), 115-121.
- Bifulco, A., Brown, G., Neubauer, A., Moran, P., & Harris, T. (1994a). *Childhood Experience of Care and Abuse (CECA): Training Manual*. London.
- Bifulco, A., Brown, G. W., & Harris, T. O. (1994b). Childhood Experience of Care and Abuse (CECA): A retrospective interview measure. *Journal of Child Psychology and Psychiatry*, 35(8), 1419-1435.
- Binbay, T., Drukker, M., Alptekin, K., Elbi, H., Tanık, F. A., Özkınay, F., Onay, H., Zağlı, N., & van Os, J. (2012). Evidence that the wider social environment moderates the association between familial liability and psychosis spectrum outcome. *Psychological Medicine*, 42(12), 2499-2510.

- Blakemore, S. J., & Choudhury, S. (2006). Development of the adolescent brain: implications for executive function and social cognition. *Journal of Child Psychology and Psychiatry*, 47(3-4), 296-312.
- Block, M. L., & Calderón-Garcidueñas, L. (2009). Air pollution: Mechanisms of neuroinflammation and CNS disease. *Trends in Neurosciences*, 32(9), 506-516.
- Bowes, L., Maughan, B., Ball, H., Shakoor, S., Ouellet-Morin, I., Caspi, A., Moffitt, T. E., & Arseneault, L. (2013). Chronic bullying victimization across school transitions: The role of genetic and environmental influences. *Development and Psychopathology*, 25(2), 333-346.
- Boydell, J., Van Os, J., McKenzie, K., & Murray, R. (2004). The association of inequality with the incidence of schizophrenia. *Social Psychiatry and Psychiatric Epidemiology*, 39(8), 597-599.
- Calderón-Garcidueñas, L., Solt, A. C., Henríquez-Roldán, C., Torres-Jardón, R., Nuse, B., Herritt, L., Villarreal-Calderón, R., Osnaya, N., Stone, I., & García, R. (2008). Long-term air pollution exposure is associated with neuroinflammation, an altered innate immune response, disruption of the blood-brain barrier, ultrafine particulate deposition, and accumulation of amyloid β -42 and α -synuclein in children and young adults. *Toxicologic Pathology*, 36(2), 289-310.
- Carbon, M., & Correll, C. U. (2014). Thinking and acting beyond the positive: The role of the cognitive and negative symptoms in schizophrenia. *CNS Spectrums*, 19(S1), 35-53.
- Cardno, A. G., & Gottesman, I. I. (2000). Twin studies of schizophrenia: From bow-and-arrow concordances to star wars Mx and functional genomics. *American Journal of Medical Genetics Part A*, 97(1), 12-17.

- Caspi, A., Taylor, A., Moffitt, T. E., & Plomin, R. (2000). Neighborhood deprivation affects children's mental health: Environmental risks identified in a genetic design. *Psychological Science, 11*(4), 338-342.
- Chan, K. Y., Zhao, F. f., Meng, S., Demaio, A. R., Reed, C., Theodoratou, E., Campbell, H., Wang, W., & Rudan, I. (2015). Urbanization and the prevalence of schizophrenia in China between 1990 and 2010. *World Psychiatry, 14*(2), 251-252.
- Cohen, B. (2006). Urbanization in developing countries: Current trends, future projections, and key challenges for sustainability. *Technology in Society, 28*(1), 63-80.
- Collip, D., Nicolson, N., Lardinois, M., Lataster, T., Van Os, J., & Myin-Germeys, I. (2011). Daily cortisol, stress reactivity and psychotic experiences in individuals at above average genetic risk for psychosis. *Psychological Medicine, 41*(11), 2305-2315.
- Colodro-Conde, L., Couvy-Duchesne, B., Whitfield, J. B., Streit, F., Gordon, S., Rietschel, M., McGrath, J., Medland, S. E., & Martin, N. G. (2017). Higher genetic risk for schizophrenia is associated with living in urban and populated areas. *bioRxiv, 179432*.
- Costello, E. J., Mustillo, S., Erkanli, A., Keeler, G., & Angold, A. (2003). Prevalence and development of psychiatric disorders in childhood and adolescence. *Archives of General Psychiatry, 60*(8), 837-844.
- Cougnard, A., Marcelis, M., Myin-Germeys, I., De Graaf, R., Vollebergh, W., Krabbendam, L., Lieb, R., Wittchen, H.-U., Henquet, C., & Spauwen, J. (2007). Does normal developmental expression of psychosis combine with environmental risk to cause persistence of psychosis? A psychosis proneness–persistence model. *Psychological Medicine, 37*(4), 513-527.

- Coulthard, M., Walker, A., & Morgan, A. (2002). *People's perceptions of their neighbourhood and community involvement: Results from the social capital module of the General Household Survey 2000* (Vol. 1). London: Office of National Statistics.
- Dahly, D. L., & Adair, L. S. (2007). Quantifying the urban environment: A scale measure of urbanicity outperforms the urban–rural dichotomy. *Social Science & Medicine*, 64(7), 1407-1419.
- Danese, A., & Baldwin, J. R. (2017). Hidden wounds? Inflammatory links between childhood trauma and psychopathology. *Annual Review of Psychology*, 68(1), 517-544.
- Das-Munshi, J., Bécaries, L., Boydell, J. E., Dewey, M. E., Morgan, C., Stansfeld, S. A., & Prince, M. J. (2012). Ethnic density as a buffer for psychotic experiences: Findings from a national survey (EMPIRIC). *The British Journal of Psychiatry*, 201(4), 282-290.
- Davidson, L. L., Grigorenko, E. L., Boivin, M. J., Rapa, E., & Stein, A. (2015). A focus on adolescence to reduce neurological, mental health and substance-use disability. *Nature*, 527(7578), S161-S166.
- de Leon, J., & Diaz, F. J. (2005). A meta-analysis of worldwide studies demonstrates an association between schizophrenia and tobacco smoking behaviors. *Schizophrenia Research*, 76(2), 135-157.
- Department for Communities and Local Government. (2015). *The English Indices of Deprivation: 2015*. London: Department for Communities and Local Government.
- Derogatis, L., Lipman, R., & Covi, I. (1973). The SCL-90: An outpatient psychiatric rating scale. *Psychopharmacology Bulletin*, 9, 13-28.

Dhossche, D., Ferdinand, R., van der Ende, J., Hofstra, M., & Verhulst, F. (2002).

Diagnostic outcome of self-reported hallucinations in a community sample of adolescents. *Psychological Medicine*, 32(4), 619-627.

Dominguez, M., Wichers, M., Lieb, R., Wittchen, H.-U., & van Os, J. (2011).

Evidence that onset of clinical psychosis is an outcome of progressively more persistent subclinical psychotic experiences: An 8-year cohort study.

Schizophrenia Bulletin, 37(1), 84-93.

Dragt, S., Nieman, D. H., Veltman, D., Becker, H. E., van de Fliert, R., de Haan, L., &

Linszen, D. H. (2011). Environmental factors and social adjustment as predictors of a first psychosis in subjects at ultra high risk. *Schizophrenia Research*, 125(1), 69-76.

Dulin-Keita, A., Casazza, K., Fernandez, J. R., Goran, M. I., & Gower, B. (2010). Do

neighbourhoods matter? Neighbourhood disorder and long-term trends in serum cortisol levels. *Journal of Epidemiology & Community Health*, 66, 24-29.

Dunbar, R. I. (1998). The social brain hypothesis. *Evolutionary Anthropology*, 6, 178-190.

Dye, C. (2008). Health and urban living. *Science*, 319(5864), 766-769.

Eaton, W. W., Mortensen, P. B., & Frydenberg, M. (2000). Obstetric factors,

urbanization and psychosis. *Schizophrenia Research*, 43(2), 117-123.

Ericson, M., Tuvblad, C., Raine, A., Young-Wolff, K., & Baker, L. A. (2011).

Heritability and longitudinal stability of schizotypal traits during adolescence. *Behavior Genetics*, 41(4), 499-511.

Falconer, D. S. (1965). The inheritance of liability to certain diseases estimated from

the incidence among relatives. *Annals of Human Genetics*, 29, 51-76.

- Faris, R. E. L., & Dunham, H. W. (1939). *Mental disorders in urban areas: An ecological study of schizophrenia and other psychoses*. Oxford, England: Chicago Press.
- Farmer, A., McGuffin, P., & Williams, J. (2002). *Measuring Psychopathology*. Oxford, England: Oxford University Press.
- Fazel, M., Hoagwood, K., Stephan, S., & Ford, T. (2014). Mental health interventions in schools in high-income countries. *The Lancet Psychiatry*, 1(5), 377-387.
- Federal Bureau of Investigation. (2015). *Crime in the United States: Violent Crime*. West Virginia: FBI Criminal Justice Information Services Division.
- Fervaha, G., Foussias, G., Agid, O., & Remington, G. (2014a). Motivational and neurocognitive deficits are central to the prediction of longitudinal functional outcome in schizophrenia. *Acta Psychiatrica Scandinavica*, 130(4), 290-299.
- Fervaha, G., Zakzanis, K. K., Foussias, G., Graff-Guerrero, A., Agid, O., & Remington, G. (2014b). Motivational deficits and cognitive test performance in schizophrenia. *JAMA Psychiatry*, 71(9), 1058-1065.
- Finegood, E. D., Rarick, J. R. D., Blair, C., & The Family Life Project Investigators. (2017). Exploring longitudinal associations between neighborhood disadvantage and cortisol levels in early childhood. *Development and Psychopathology*, 29(5), 1649-1662.
- Finkelhor, D., Hamby, S., Turner, H., & ORMOD, R. (2011). *The Juvenile Victimization Questionnaire: 2nd Revision (JVQ-R2)*. Durham, NC: Crimes Against Children Research Center.
- Fisher, H. L., Caspi, A., Moffitt, T. E., Wertz, J., Gray, R., Newbury, J., Ambler, A., Zavos, H., Danese, A., Mill, J., Odgers, C. L., Pariante, C., Wong, C., C, Y., & Arseneault, L. (2015). Measuring adolescents' exposure to victimization: The

- Environmental Risk (E-Risk) Longitudinal Twin Study. *Development and Psychopathology*, 27(4pt2), 1399-1416.
- Fisher, H. L., Caspi, A., Poulton, R., Meier, M. H., Houts, R., Harrington, H., Arseneault, L., & Moffitt, T. E. (2013). Specificity of childhood psychotic symptoms for predicting schizophrenia by 38 years of age: A birth cohort study. *Psychological Medicine*, 43(10), 2077-2086.
- Fowler, D., Freeman, D., Smith, B., Kuipers, E., Bebbington, P., Bashforth, H., Coker, S., Hodgekins, J., Gracie, A., & Dunn, G. (2006). The Brief Core Schema Scales (BCSS): Psychometric properties and associations with paranoia and grandiosity in non-clinical and psychosis samples. *Psychological Medicine*, 36(06), 749-759.
- Freeman, D. (2016). Persecutory delusions: A cognitive perspective on understanding and treatment. *The Lancet Psychiatry*, 3(7), 685-692.
- Freeman, D., Emsley, R., Dunn, G., Fowler, D., Bebbington, P., Kuipers, E., Jolley, S., Waller, H., Hardy, A., & Garety, P. (2014). The stress of the street for patients with persecutory delusions: A test of the symptomatic and psychological effects of going outside into a busy urban area. *Schizophrenia Bulletin*, 41(4), 971-979.
- Freeman, D., Garety, P. A., Kuipers, E., Fowler, D., & Bebbington, P. E. (2002). A cognitive model of persecutory delusions. *British Journal of Clinical Psychology*, 41(4), 331-347.
- Freeman, D., Waller, H., Harpur-Lewis, R. A., Moore, R., Garety, P., Bebbington, P., Kuipers, E., Emsley, R., Dunn, G., & Fowler, D. (2015). Urbanicity, persecutory delusions, and clinical intervention: The development of a brief CBT module for helping patients with persecutory delusions enter social urban environments. *Behavioural and Cognitive Psychotherapy*, 43(1), 42-51.

- Frissen, A., Lieveise, R., Drukker, M., van Winkel, R., Delespaul, P., & Genetic Risk and Outcome in Psychosis (GROUP). (2015). Childhood trauma and childhood urbanicity in relation to psychotic disorder. *Social Psychiatry and Psychiatric Epidemiology*, 50(10), 1481-1488.
- Frissen, A., van Os, J., Habets, P., Gronenschild, E., Marcelis, M., & Genetic Risk and Outcome in Psychosis (GROUP). (2017). No evidence of association between childhood urban environment and cortical thinning in psychotic disorder. *PloS One*, 12(5), e0178312.
- Fusar-Poli, P., Byrne, M., Badger, S., Valmaggia, L., & McGuire, P. (2013). Outreach and support in south London (OASIS), 2001–2011: Ten years of early diagnosis and treatment for young individuals at high clinical risk for psychosis. *European Psychiatry*, 28(5), 315-326.
- Gao, Q., Xu, Q., Guo, X., Fan, H., & Zhu, H. (2017). Particulate matter air pollution associated with hospital admissions for mental disorders: A time-series study in Beijing, China. *European Psychiatry*, 44, 68-75.
- Garety, P., Kuipers, E., Fowler, D., Freeman, D., & Bebbington, P. (2001). A cognitive model of the positive symptoms of psychosis. *Psychological Medicine*, 31(2), 189-196.
- Garety, P. A., Bebbington, P., Fowler, D., Freeman, D., & Kuipers, E. (2007). Implications for neurobiological research of cognitive models of psychosis: A theoretical paper. *Psychological Medicine*, 37(10), 1377-1391.
- Gilbert, R., Widom, C. S., Browne, K., Fergusson, D., Webb, E., & Janson, S. (2009). Burden and consequences of child maltreatment in high-income countries. *The Lancet*, 373(9657), 68-81.
- Giles-Corti, B., Vernez-Moudon, A., Reis, R., Turrell, G., Dannenberg, A. L., Badland, H., Foster, S., Lowe, M., Sallis, J. F., & Stevenson, M. (2016). City

- planning and population health: A global challenge. *The Lancet*, 388(10062), 2912-2924.
- Goldman-Mellor, S., Margerison-Zilko, C., Allen, K., & Cerdá, M. (2016). Perceived and objectively-measured neighborhood violence and adolescent psychological distress. *Journal of Urban Health*, 93(5), 758-769.
- Gracey, M. (2002). Child health in an urbanizing world. *Acta Paediatrica*, 91(1), 1-8.
- Hackshaw, A., & Kirkwood, A. (2011). Interpreting and reporting clinical trials with results of borderline significance. *BMJ*, 343, d3340.
- Haddad, L., Schäfer, A., Streit, F., Lederbogen, F., Grimm, O., Wüst, S., Deuschle, M., Kirsch, P., Tost, H., & Meyer-Lindenberg, A. (2015). Brain structure correlates of urban upbringing, an environmental risk factor for schizophrenia. *Schizophrenia Bulletin*, 41(1), 115-122.
- Häfner, H., Maurer, K., Löffler, W., & Fätkenheuer, B. (1994). The epidemiology of early schizophrenia. Influence of age and gender on onset and early course. *The British Journal of Psychiatry*, 164(23), 29-38.
- Hankin, B. L., Abramson, L. Y., Moffitt, T. E., Silva, P. A., McGee, R., & Angell, K. E. (1998). Development of depression from preadolescence to young adulthood: Emerging gender differences in a 10-year longitudinal study. *Journal of Abnormal Psychology*, 107(1), 128.
- Hanssen, M., Bak, M., Bijl, R., Vollebergh, W., & van Os, J. (2005). The incidence and outcome of subclinical psychotic experiences in the general population. *British Journal of Clinical Psychology*, 44(Pt 2), 181-191.
- Hardt, J., & Rutter, M. (2004). Validity of adult retrospective reports of adverse childhood experiences: review of the evidence. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, 45(2), 260-273.

- Harris, E. C., & Barraclough, B. (1997). Suicide as an outcome for mental disorders. A meta-analysis. *The British Journal of Psychiatry*, 170(3), 205-228.
- Harrison, G., Fouskakis, D., Rasmussen, F., Tynelius, P., Sipos, A., & Gunnell, D. (2003). Association between psychotic disorder and urban place of birth is not mediated by obstetric complications or childhood socio-economic position: A cohort study. *Psychological Medicine*, 33(4), 723-731.
- Haukka, J., Suvisaari, J., Varilo, T., & Lönnqvist, J. (2001). Regional variation in the incidence of schizophrenia in Finland: A study of birth cohorts born from 1950 to 1969. *Psychological Medicine*, 31(6), 1045-1053.
- Health Effects Institute. (2010). *Traffic-Related Air Pollution: A Critical Review of the Literature on Emissions, Exposure, and Health Effects. HEI Special Report 17*. Boston, MA: Health Effects Institute.
- Heinz, A., Deserno, L., & Reininghaus, U. (2013). Urbanicity, social adversity and psychosis. *World Psychiatry*, 12(3), 187-197.
- Herman, J. P., & Cullinan, W. E. (1997). Neurocircuitry of stress: central control of the hypothalamo–pituitary–adrenocortical axis. *Trends in Neurosciences*, 20(2), 78-84.
- Home Office Statistical Bulletin. (2010). *Crime in England and Wales 2009/10: Findings from the British Crime Survey and police recorded crime (Third Edition)*. London: Home Office.
- Horwood, J., Salvi, G., Thomas, K., Duffy, L., Gunnell, D., Hollis, C., Lewis, G., Menezes, P., Thompson, A., & Wolke, D. (2008). IQ and non-clinical psychotic symptoms in 12-year-olds: Results from the ALSPAC birth cohort. *The British Journal of Psychiatry*, 193(3), 185-191.

- Howes, O. D., McCutcheon, R., Owen, M. J., & Murray, R. M. (2017). The role of genes, stress, and dopamine in the development of schizophrenia. *Biological Psychiatry*, 81(1), 9-20.
- Hur, Y.-M., Cherny, S. S., & Sham, P. C. (2012). Heritability of hallucinations in adolescent twins. *Psychiatry Research*, 199(2), 98-101.
- Jaffee, S. R., & Price, T. S. (2008). Genotype–environment correlations: implications for determining the relationship between environmental exposures and psychiatric illness. *Psychiatry*, 7(12), 496-499.
- Jenner, J., & Van de Willige, G. (2002). *The auditory vocal hallucination rating scale (AVHRS)*. Groningen, the Netherlands: University Medical Center Groningen.
- Johns, L. C., Cannon, M., Singleton, N., Murray, R. M., Farrell, M., Brugha, T., Bebbington, P., Jenkins, R., & Meltzer, H. (2004). Prevalence and correlates of self-reported psychotic symptoms in the British population. *The British Journal of Psychiatry*, 185(4), 298-305.
- Jones, A. P., Coombes, E. G., Griffin, S. J., & van Sluijs, E. M. (2009). Environmental supportiveness for physical activity in English schoolchildren: A study using Global Positioning Systems. *International Journal of Behavioral Nutrition and Physical Activity*, 6, 42.
- Kapur, S. (2003). Psychosis as a state of aberrant salience: A framework linking biology, phenomenology, and pharmacology in schizophrenia. *American Journal of Psychiatry*, 160(1), 13-23.
- Kelleher, I., & Cannon, M. (2011). Psychotic-like experiences in the general population: Characterizing a high-risk group for psychosis. *Psychological Medicine*, 41(1), 1-6.
- Kelleher, I., Connor, D., Clarke, M. C., Devlin, N., Harley, M., & Cannon, M. (2012a). Prevalence of psychotic symptoms in childhood and adolescence: A

systematic review and meta-analysis of population-based studies.

Psychological Medicine, 42(9), 1857-1863.

Kelleher, I., Harley, M., Murtagh, A., & Cannon, M. (2011). Are screening instruments valid for psychotic-like experiences? A validation study of screening questions for psychotic-like experiences using in-depth clinical interview. *Schizophrenia Bulletin*, 37(2), 362-369.

Kelleher, I., Keeley, H., Corcoran, P., Lynch, F., Fitzpatrick, C., Devlin, N., Molloy, C., Roddy, S., Clarke, M. C., & Harley, M. (2012b). Clinicopathological significance of psychotic experiences in non-psychotic young people: Evidence from four population-based studies. *The British Journal of Psychiatry*, 201(1), 26-32.

Kelleher, I., Keeley, H., Corcoran, P., Ramsay, H., Wasserman, C., Carli, V., Sarchiapone, M., Hoven, C., Wasserman, D., & Cannon, M. (2013). Childhood trauma and psychosis in a prospective cohort study: cause, effect, and directionality. *American Journal of Psychiatry*, 170(7), 734-741.

Kelleher, I., Lynch, F., Harley, M., Molloy, C., Roddy, S., Fitzpatrick, C., & Cannon, M. (2012c). Psychotic symptoms in adolescence index risk for suicidal behavior: Findings from 2 population-based case-control clinical interview studies. *Archives of General Psychiatry*, 69(12), 1277-1283.

Kelly, B. D., O'Callaghan, E., Waddington, J. L., Feeney, L., Browne, S., Scully, P. J., Clarke, M., Quinn, J. F., McTigue, O., & Morgan, M. G. (2010). Schizophrenia and the city: A review of literature and prospective study of psychosis and urbanicity in Ireland. *Schizophrenia Research*, 116(1), 75-89.

Kendler, K. S., Gallagher, T. J., Abelson, J. M., & Kessler, R. C. (1996). Lifetime prevalence, demographic risk factors, and diagnostic validity of nonaffective

- psychosis as assessed in a US community sample: The National Comorbidity Survey. *Archives of General Psychiatry*, 53(11), 1022-1031.
- Kendler, K. S., Neale, M. C., Kessler, R. C., Heath, A. C., & Eaves, L. J. (1993). A test of the equal-environment assumption in twin studies of psychiatric illness. *Behavior Genetics*, 23(1), 21-27.
- Kessler, R. C., & Üstün, T. B. (2004). The world mental health (WMH) survey initiative version of the world health organization (WHO) composite international diagnostic interview (CIDI). *International Journal of Methods in Psychiatric Research*, 13(2), 93-121.
- Kirkbride, J., Stochl, J., Zimbron, J., Crane, C., Metastasio, A., Aguilar, E., Webster, R., Theegala, S., Kabacs, N., & Jones, P. (2015). Social and spatial heterogeneity in psychosis proneness in a multilevel case–prodrome–control study. *Acta Psychiatrica Scandinavica*, 132(4), 283-292.
- Kirkbride, J. B., Boydell, J., Ploubidis, G., Morgan, C., Dazzan, P., McKenzie, K., Murray, R. M., & Jones, P. B. (2008). Testing the association between the incidence of schizophrenia and social capital in an urban area. *Psychological Medicine*, 38(8), 1083-1094.
- Kirkbride, J. B., Fearon, P., Morgan, C., Dazzan, P., Morgan, K., Tarrant, J., Lloyd, T., Holloway, J., Hutchinson, G., & Leff, J. P. (2006). Heterogeneity in incidence rates of schizophrenia and other psychotic syndromes: Findings from the 3-center AeSOP study. *Archives of General Psychiatry*, 63(3), 250-258.
- Kirkbride, J. B., Jones, P. B., Ullrich, S., & Coid, J. W. (2014). Social deprivation, inequality, and the neighborhood-level incidence of psychotic syndromes in East London. *Schizophrenia Bulletin*, 40(1), 169-180.

- Kirkbride, J. B., Morgan, C., Fearon, P., Dazzan, P., Murray, R. M., & Jones, P. B. (2007). Neighbourhood-level effects on psychoses: Re-examining the role of context. *Psychological Medicine*, 37(10), 1413-1425.
- Kohen, D. E., Leventhal, T., Dahinten, V. S., & McIntosh, C. N. (2008). Neighborhood disadvantage: Pathways of effects for young children. *Child Development*, 79(1), 156-169.
- Kovacs, M. (1992). *Children's Depression Inventory: Manual*. Toronto: Multi-Health Systems.
- Krabbendam, L., & Van Os, J. (2005). Schizophrenia and urbanicity: A major environmental influence—conditional on genetic risk. *Schizophrenia Bulletin*, 31(4), 795-799.
- Kuepper, R., Van Os, J., Lieb, R., Wittchen, H.-U., & Henquet, C. (2011a). Do cannabis and urbanicity co-participate in causing psychosis? Evidence from a 10-year follow-up cohort study. *Psychological Medicine*, 41(10), 2121-2129.
- Kuepper, R., van Os, J., Lieb, R., Wittchen, H.-U., Höfler, M., & Henquet, C. (2011b). Continued cannabis use and risk of incidence and persistence of psychotic symptoms: 10 year follow-up cohort study. *British Medical Journal*, 342, d738.
- Lataster, T., Myin-Germeys, I., Derom, C., Thiery, E., & van Os, J. (2009). Evidence that self-reported psychotic experiences represent the transitory developmental expression of genetic liability to psychosis in the general population. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics*, 150B(8), 1078-1084.
- Lederbogen, F., Haddad, L., & Meyer-Lindenberg, A. (2013). Urban social stress - Risk factor for mental disorders. The case of schizophrenia. *Environmental Pollution*, 183, 2-6.

- Lederbogen, F., Kirsch, P., Haddad, L., Streit, F., Tost, H., Schuch, P., Wust, S., Pruessner, J. C., Rietschel, M., Deuschle, M., & Meyer-Lindenberg, A. (2011). City living and urban upbringing affect neural social stress processing in humans. *Nature*, 474(7352), 498-501.
- Lee, S. H., DeCandia, T. R., Ripke, S., Yang, J., Sullivan, P. F., Goddard, M. E., Keller, M. C., Visscher, P. M., Wray, N. R., & Consortium, S. P. G.-W. A. S. (2012). Estimating the proportion of variation in susceptibility to schizophrenia captured by common SNPs. *Nature Genetics*, 44(3), 247-250.
- Lewis, G., Davis, A., Andreasson, S., & Allebeck, P. (1992). Schizophrenia and city life. *The Lancet*, 340(8812), 137-140.
- Lin, C. C., Su, C.-H., Kuo, P.-H., Hsiao, C. K., Soong, W.-T., & Chen, W. J. (2007). Genetic and environmental influences on schizotypy among adolescents in Taiwan: A multivariate twin/sibling analysis. *Behavior Genetics*, 37(2), 334-344.
- Linscott, R., & van Os, J. (2013). An updated and conservative systematic review and meta-analysis of epidemiological evidence on psychotic experiences in children and adults: On the pathway from proneness to persistence to dimensional expression across mental disorders. *Psychological Medicine*, 43(6), 1133-1149.
- Loewy, R. L., Pearson, R., Vinogradov, S., Bearden, C. E., & Cannon, T. D. (2011). Psychosis risk screening with the Prodromal Questionnaire—brief version (PQ-B). *Schizophrenia Research*, 129(1), 42-46.
- Lundberg, P., Cantor-Graae, E., Rukundo, G., Ashaba, S., & Östergren, P.-O. (2009). Urbanicity of place of birth and symptoms of psychosis, depression and anxiety in Uganda. *The British Journal of Psychiatry*, 195(2), 156-162.

- Maas, J., Verheij, R. A., Groenewegen, P. P., De Vries, S., & Spreeuwenberg, P. (2006). Green space, urbanity, and health: How strong is the relation? *Journal of Epidemiology & Community Health*, 60(7), 587-592.
- Marcelis, M., Navarro-Mateu, F., Murray, R., Selten, J.-P., & Van Os, J. (1998). Urbanization and psychosis: A study of 1942–1978 birth cohorts in The Netherlands. *Psychological Medicine*, 28(4), 871-879.
- Marcelis, M., Takei, N., & Van Os, J. (1999). Urbanization and risk for schizophrenia: Does the effect operate before or around the time of illness onset. *Psychological Medicine*, 29(5), 1197-1203.
- March, D., Hatch, S. L., Morgan, C., Kirkbride, J. B., Bresnahan, M., Fearon, P., & Susser, E. (2008). Psychosis and place. *Epidemiologic Reviews*, 30(1), 84-100.
- March, J. S., Parker, J. D., Sullivan, K., Stallings, P., & Conners, C. K. (1997). The Multidimensional Anxiety Scale for Children (MASC): Factor structure, reliability, and validity. *Journal of the American Academy of Child & Adolescent Psychiatry*, 36(4), 554-565.
- Maynard, R. A. (1997). *Kids having kids: Economic costs & social consequences of teen pregnancy*. Washington, DC: The Urban Institute.
- McGorry, P. D., Goldstone, S. D., Parker, A. G., Rickwood, D. J., & Hickie, I. B. (2014). Cultures for mental health care of young people: An Australian blueprint for reform. *The Lancet Psychiatry*, 1(7), 559-568.
- McGrath, J. J., Saha, S., Al-Hamzawi, A., Alonso, J., Bromet, E. J., Bruffaerts, R., Caldas-de-Almeida, J. M., Chiu, W. T., de Jonge, P., & Fayyad, J. (2015). Psychotic experiences in the general population: A cross-national analysis based on 31261 respondents from 18 countries. *JAMA Psychiatry*, 72(7), 697-705.

- McKenzie, K., Whitley, R., & Weich, S. (2002). Social capital and mental health. *The British Journal of Psychiatry*, 181(4), 280-283.
- Merikangas, K. R., He, J.-p., Burstein, M., Swanson, S. A., Avenevoli, S., Cui, L., Benjet, C., Georgiades, K., & Swendsen, J. (2010). Lifetime prevalence of mental disorders in US adolescents: Results from the National Comorbidity Survey Replication–Adolescent Supplement (NCS-A). *Journal of the American Academy of Child & Adolescent Psychiatry*, 49(10), 980-989.
- Messner, S. F., Baumer, E. P., & Rosenfeld, R. (2004). Dimensions of social capital and rates of criminal homicide. *American Sociological Review*, 69(6), 882-903.
- Meyer-Lindenberg, A., & Tost, H. (2012). Neural mechanisms of social risk for psychiatric disorders. *Nature Neuroscience*, 15(5), 663-668.
- Millan, M. J., Andrieux, A., Bartzokis, G., Cadenhead, K., Dazzan, P., Fusar-Poli, P., Gallinat, J., Giedd, J., Grayson, D. R., Heinrichs, M., Kahn, R., Krebs, M.-O., Leboyer, M., Lewis, D., Marin, O., Marin, P., Meyer-Lindenberg, A., McGorry, P., McGuire, P., Owen, M. J., Patterson, P., Sawa, A., Spedding, M., Uhlhaas, P., Vaccarino, F., Wahlestedt, C., & Weinberger, D. (2016). Altering the course of schizophrenia: Progress and perspectives. *Nature Reviews Drug Discovery*, 15(7), 485-515.
- Miller, T. J., Cicchetti, D., Markovich, P. J., McGlashan, T. H., & Woods, S. W. (2004). The SIPS-Screen: a brief self-report screen to detect the schizophrenia prodrome. *Schizophrenia Research*, 70 (suppl1), 78.
- Miller, T. J., McGlashan, T. H., Rosen, J. L., Cadenhead, K., Ventura, J., McFarlane, W., Perkins, D. O., Pearlson, G. D., & Woods, S. W. (2003). Prodromal assessment with the structured interview for prodromal syndromes and the

- scale of prodromal symptoms: predictive validity, interrater reliability, and training to reliability. *Schizophrenia Bulletin*, 29(4), 703.
- Milne, B., Moffitt, T., Crump, R., Poulton, R., Rutter, M., Sears, M., Taylor, A., & Caspi, A. (2008). How should we construct psychiatric family history scores? A comparison of alternative approaches from the Dunedin Family Health History Study. *Psychological Medicine*, 38(12), 1793-1802.
- Mimarakis, D., Roumeliotaki, T., Roussos, P., Giakoumaki, S., & Bitsios, P. (2018). Winter birth, urbanicity and immigrant status predict psychometric schizotypy dimensions in adolescents. *European Psychiatry*, 47, 9-18.
- Mitchell, A. J., Vancampfort, D., Sweers, K., van Winkel, R., Yu, W., & De Hert, M. (2011). Prevalence of metabolic syndrome and metabolic abnormalities in schizophrenia and related disorders—a systematic review and meta-analysis. *Schizophrenia Bulletin*, 39(2), 306-318.
- Moffitt, T. E., & The E-Risk Study Team. (2002). Teen-aged mothers in contemporary Britain. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, 43(6), 727-742.
- Mohamed, S., Rosenheck, R., Swartz, M., Stroup, S., Lieberman, J. A., & Keefe, R. S. (2008). Relationship of cognition and psychopathology to functional impairment in schizophrenia. *American Journal of Psychiatry*, 165(8), 978-987.
- Morgan, C., Reininghaus, U., Reichenberg, A., Frissa, S., Hotopf, M., & Hatch, S. L. (2014). Adversity, cannabis use and psychotic experiences: Evidence of cumulative and synergistic effects. *The British Journal of Psychiatry*, 204(5), 346-353.
- Mortensen, P. B., Pedersen, C. B., Westergaard, T., Wohlfahrt, J., Ewald, H., Mors, O., Andersen, P. K., & Melbye, M. (1999). Effects of family history and place

- and season of birth on the risk of schizophrenia. *New England Journal of Medicine*, 340(8), 603-608.
- Myin-Germeys, I., Delespaul, P., & Van Os, J. (2005). Behavioural sensitization to daily life stress in psychosis. *Psychological Medicine*, 35(5), 733-741.
- Myin-Germeys, I., van Os, J., Schwartz, J. E., Stone, A. A., & Delespaul, P. A. (2001). Emotional reactivity to daily life stress in psychosis. *Archives of General Psychiatry*, 58(12), 1137-1144.
- Navarro-Mateu, F., Alonso, J., Lim, C., Saha, S., Aguilar-Gaxiola, S., Al-Hamzawi, A., Andrade, L., Bromet, E., Bruffaerts, R., & Chatterji, S. (2017). The association between psychotic experiences and disability: Results from the WHO World Mental Health Surveys. *Acta Psychiatrica Scandinavica*, 136(1), 74-84.
- Neale, M., & Cardon, L. (2013). *Methodology for genetic studies of twins and families* (Vol. 67): Springer Science & Business Media.
- Newbury, J., Arseneault, L., Caspi, A., Moffitt, T. E., Odgers, C. L., & Fisher, H. L. (2016). Why are children in urban neighborhoods at increased risk for psychotic symptoms? Findings from a UK longitudinal cohort study. *Schizophrenia Bulletin*, 42(6), 1372-1383.
- Newbury, J., Arseneault, L., Caspi, A., Moffitt, T. E., Odgers, C. L., & Fisher, H. L. (2017a). Cumulative effects of neighborhood social adversity and personal crime victimization on adolescent psychotic experiences. *Schizophrenia Bulletin*, 44(2), 348-358.
- Newbury, J. B., Arseneault, L., Caspi, A., Moffitt, T. E., Odgers, C. L., Baldwin, J. R., Zavos, H. M., & Fisher, H. L. (2017b). In the eye of the beholder: Perceptions of neighborhood adversity and psychotic experiences in adolescence. *Development and Psychopathology*, 29(5), 1823-1837.

- Newbury, J. B., Arseneault, L., Moffitt, T. E., Caspi, A., Danese, A., Baldwin, J. R., & Fisher, H. L. (2018). Measuring childhood maltreatment to predict early-adult psychopathology: Comparison of prospective informant-reports and retrospective self-reports. *Journal of Psychiatric Research*, 96, 57-64.
- NHS Providers. (2016). *Funding mental health at local level: Unpicking the variation*. London: Foundation Trust Network.
- Northridge, M. E., Sclar, E. D., & Biswas, P. (2003). Sorting out the connections between the built environment and health: A conceptual framework for navigating pathways and planning healthy cities. *Journal of Urban Health*, 80(4), 556-568.
- O'Donoghue, B., Yung, A. R., Wood, S., Thompson, A., Lin, A., McGorry, P., & Nelson, B. (2015). Neighbourhood characteristics and the rate of identification of young people at ultra-high risk for psychosis. *Schizophrenia Research*, 169(1-3), 214-216.
- Ødegaard, Ø. (1956). The incidence of psychoses in various occupations. *International Journal of Social Psychiatry*, 2(2), 85-104.
- Odgers, C. L., Caspi, A., Bates, C. J., Sampson, R. J., & Moffitt, T. E. (2012a). Systematic social observation of children's neighborhoods using Google Street View: A reliable and cost-effective method. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, 53(10), 1009-1017.
- Odgers, C. L., Caspi, A., Russell, M. A., Sampson, R. J., Arseneault, L., & Moffitt, T. E. (2012b). Supportive parenting mediates neighborhood socioeconomic disparities in children's antisocial behavior from ages 5 to 12. *Development and Psychopathology*, 24(3), 705-721.
- Odgers, C. L., Donley, S., Caspi, A., Bates, C. J., & Moffitt, T. E. (2015). Living alongside more affluent neighbors predicts greater involvement in antisocial

- behavior among low-income boys. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, 56(10), 1055-1064.
- Odgers, C. L., Moffitt, T. E., Tach, L. M., Sampson, R. J., Taylor, A., Matthews, C. L., & Caspi, A. (2009). The protective effects of neighborhood collective efficacy on British children growing up in deprivation: A developmental analysis. *Developmental Psychology*, 45(4), 942-957.
- Office for National Statistics. (2012). *The likelihood of becoming a victim of crime: Crime statistics, period ending March 2012*. London: Office for National Statistics.
- Office for National Statistics. (2013). *Urban and rural area definitions for policy purposes in England and Wales: Methodology (v1.0)*. London: Office of National Statistics.
- Office of National Statistics. (2017). *Crime in England and Wales: Year ending June 2017*. London: Office of National Statistics.
- Omer, S., Kirkbride, J. B., Pringle, D. G., Russell, V., O'Callaghan, E., & Waddington, J. L. (2014). 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]. *Schizophrenia Research*, 152(1), 152-157.
- Paksarian, D., Trabjerg, B., Merikangas, K., Mors, O., Børglum, A., Hougaard, D., McGrath, J., Pedersen, C., Mortensen, P., & Agerbo, E. (2018). The role of genetic liability in the association of urbanicity at birth and during upbringing with schizophrenia in Denmark. *Psychological Medicine*, 48(2), 305-314.
- Pariante, C. M., & Lightman, S. L. (2008). The HPA axis in major depression: classical theories and new developments. *Trends in Neurosciences*, 31(9), 464-468.

- Pedersen, C. B., & Mortensen, P. B. (2001). Evidence of a dose-response relationship between urbanicity during upbringing and schizophrenia risk. *Archives of General Psychiatry*, 58(11), 1039-1046.
- Pedersen, C. B., & Mortensen, P. B. (2006a). Urbanicity during upbringing and bipolar affective disorders in Denmark. *Bipolar Disorders*, 8(3), 242-247.
- Pedersen, C. B., & Mortensen, P. B. (2006b). Urbanization and traffic related exposures as risk factors for schizophrenia. *BMC Psychiatry*, 6, 2.
- Peen, J., Schoevers, R. A., Beekman, A. T., & Dekker, J. (2010). The current status of urban-rural differences in psychiatric disorders. *Acta Psychiatrica Scandinavica*, 121(2), 84-93.
- Peters, E. R., Joseph, S. A., & Garety, P. A. (1999). Measurement of delusional ideation in the normal population: Introducing the PDI (Peters et al. Delusions Inventory). *Schizophrenia Bulletin*, 25(3), 553-576.
- Plomin, R., DeFries, J. C., Knopik, V. S., & Neiderhiser, J. M. (2013). *Behavioral Genetics* (6 ed.). New York: Worth Publishers.
- Polanczyk, G., Moffitt, T. E., Arseneault, L., Cannon, M., Ambler, A., Keefe, S. E. R., Houts, R. M., Odgers, C. L., & Caspi, A. (2010). Etiological and clinical features of childhood psychotic symptoms: Results from a birth cohort. *Archives of General Psychiatry*, 67(4), 328-338.
- Polling, C., Khondoker, M., Hatch, S., Hotopf, M., & SELCoH study team. (2014). Influence of perceived and actual neighbourhood disorder on common mental illness. *Social Psychiatry and Psychiatric Epidemiology*, 49(6), 889-901.
- Porter, R. (1998). *London: A social history*: Harvard University Press.
- Poulton, R., Caspi, A., Moffitt, T. E., Cannon, M., Murray, R., & Harrington, H. (2000). Children's self-reported psychotic symptoms and adult

- schizophreniform disorder: A 15-year longitudinal study. *Archives of General Psychiatry*, 57(11), 1053-1058.
- Power, M. C., Kioumourtzoglou, M.-A., Hart, J. E., Okereke, O. I., Laden, F., & Weiskopf, M. G. (2015). The relation between past exposure to fine particulate air pollution and prevalent anxiety: Observational cohort study. *BMJ*, 350, h1111.
- Price, T. S., Freeman, B., Craig, I., Petrill, S. A., Ebersole, L., & Plomin, R. (2000). Infant zygosity can be assigned by parental report questionnaire data. *Twin Research and Human Genetics*, 3(3), 129-133.
- Raine, A. (1991). The SPQ: A scale for the assessment of schizotypal personality based on DSM-III-R criteria. *Schizophrenia Bulletin*, 17(4), 555-564.
- Rapoport, J. L., Addington, A. M., Frangou, S., & Psych, M. (2005). The neurodevelopmental model of schizophrenia: Update 2005. *Molecular Psychiatry*, 10(5), 434-449.
- Rauschenberg, C., Os, J., Cremers, D., Goedhart, M., Schievel, J., & Reininghaus, U. (2017). Stress sensitivity as a putative mechanism linking childhood trauma and psychopathology in youth's daily life. *Acta Psychiatrica Scandinavica*, 136(4), 373-388.
- Regier, D. A., Farmer, M. E., Rae, D. S., Locke, B. Z., Keith, S. J., Judd, L. L., & Goodwin, F. K. (1990). Comorbidity of mental disorders with alcohol and other drug abuse: results from the Epidemiologic Catchment Area (ECA) study. *JAMA*, 264(19), 2511-2518.
- Reuben, A., Moffitt, T. E., Caspi, A., Belsky, D. W., Harrington, H., Schroeder, F., Hogan, S., Ramrakha, S., Poulton, R., & Danese, A. (2016). Lest we forget: Comparing retrospective and prospective assessments of adverse childhood

- experiences in the prediction of adult health. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, 57(10), 1103-1112.
- Richardson, L., Hameed, Y., Perez, J., Jones, P. B., & Kirkbride, J. B. (2017). Association of environment with the risk of developing a psychotic disorder in rural populations: Findings from the Social Epidemiology of Psychoses in East Anglia Study. *JAMA Psychiatry*, doi:10.1001/jamapsychiatry.2017.3582.
- Rijsdijk, F. V., & Sham, P. C. (2002). Analytic approaches to twin data using structural equation models. *Briefings in Bioinformatics*, 3(2), 119-133.
- Rivera, C. L., Bernal, G., & Rosello, J. (2005). The Children Depression Inventory (CDI) and the Beck Depression Inventory (BDI): Their validity as screening measures for major depression in a group of Puerto Rican adolescents. *International Journal of Clinical and Health Psychology*, 5(3), 485-498.
- Robins, L., Cottler, L., Bucholz, K., & Compton, W. (1995). *Diagnostic Interview Schedule for DSM-IV (DIS-IV)*. St Louis, MO: Washington University School of Medicine.
- Robins, L. N., Wing, J., Wittchen, H. U., Helzer, J. E., Babor, T. F., Burke, J., Farmer, A., Jablenski, A., Pickens, R., & Regier, D. A. (1988). The Composite International Diagnostic Interview: An epidemiologic instrument suitable for use in conjunction with different diagnostic systems and in different cultures. *Archives of General Psychiatry*, 45(12), 1069-1077.
- Robinson, D., Woerner, M. G., Alvir, J. M. J., Bilder, R., Goldman, R., Geisler, S., Koreen, A., Sheitman, B., Chakos, M., & Mayerhoff, D. (1999). Predictors of relapse following response from a first episode of schizophrenia or schizoaffective disorder. *Archives of General Psychiatry*, 56(3), 241-247.
- Rogers, W. (1994). Regression standard errors in clustered samples. *Stata Technical Bulletin*, 3(13), 19-23.

- Rudolph, K. E., Stuart, E. A., Glass, T. A., Marques, A. H., Duncko, R., & Merikangas, K. R. (2014). The association between cortisol and neighborhood disadvantage in a US population-based sample of adolescents. *Health & Place*, 25, 68-77.
- Saha, S., Scott, J., Varghese, D., & McGrath, J. (2013). Socio-economic disadvantage and delusional-like experiences: A nationwide population-based study. *European Psychiatry*, 28(1), 59-63.
- Sampson, R. J. (2001). How do communities undergird or undermine human development? Relevant contexts and social mechanisms. In A. Booth & A. C. Crouter (Eds.), *Does it take a village? Community effects on children, adolescents, and families* (pp. 3-30). Mahwah, NJ: Lawrence Erlbaum Associates.
- Sampson, R. J., Morenoff, J. D., & Gannon-Rowley, T. (2002). Assessing "neighborhood effects": Social processes and new directions in research. *Annual Review of Sociology*, 28, 443-478.
- Sampson, R. J., & Raudenbush, S. W. (1999). Systematic social observation of public spaces: A new look at disorder in urban neighborhoods. *American Journal of Sociology*, 105(3), 603-651.
- Sampson, R. J., Raudenbush, S. W., & Earls, F. (1997). Neighborhoods and violent crime: A multilevel study of collective efficacy. *Science*, 277(5328), 918-924.
- Schoenbaum, M., Sutherland, J. M., Chappel, A., Azrin, S., Goldstein, A. B., Rupp, A., & Heinssen, R. K. (2017). Twelve-month health care use and mortality in commercially insured young people with incident psychosis in the United States. *Schizophrenia Bulletin*, 43(6), 1262-1272.
- Schreier, A., Wolke, D., Thomas, K., Horwood, J., Hollis, C., Gunnell, D., Lewis, G., Thompson, A., Zammit, S., & Duffy, L. (2009). Prospective study of peer

- victimization in childhood and psychotic symptoms in a nonclinical population at age 12 years. *Archives of General Psychiatry*, 66(5), 527-536.
- Scott, J., Chant, D., Andrews, G., & McGrath, J. (2006). Psychotic-like experiences in the general community: the correlates of CIDI psychosis screen items in an Australian sample. *Psychological Medicine*, 36(2), 231-238.
- Selten, J.-P., van der Ven, E., Rutten, B. P., & Cantor-Graae, E. (2013). The social defeat hypothesis of schizophrenia: An update. *Schizophrenia Bulletin*, 39(6), 1180-1186.
- Shevlin, M., Houston, J. E., Dorahy, M. J., & Adamson, G. (2008). Cumulative traumas and psychosis: An analysis of the national comorbidity survey and the British Psychiatric Morbidity Survey. *Schizophrenia Bulletin*, 34(1), 193-199.
- Shevlin, M., Murphy, J., Read, J., Mallett, J., Adamson, G., & Houston, J. E. (2011). Childhood adversity and hallucinations: A community-based study using the National Comorbidity Survey Replication. *Social Psychiatry and Psychiatric Epidemiology*, 46(12), 1203-1210.
- Silver, E., Mulvey, E. P., & Swanson, J. W. (2002). Neighborhood structural characteristics and mental disorder: Faris and Dunham revisited. *Social Science and Medicine*, 55(8), 1457-1470.
- Singh, S. P., Winsper, C., Wolke, D., & Bryson, A. (2014). School mobility and prospective pathways to psychotic-like symptoms in early adolescence: A prospective birth cohort study. *Journal of the American Academy of Child & Adolescent Psychiatry*, 53(5), 518-527.e511.
- Smeets, R., & Dingemans, P. (1993). *Composite International Diagnostic Interview (CIDI), Version 1.1*. Amsterdam/Geneva: World Health Organization.
- Solmi, F., Colman, I., Weeks, M., Lewis, G., & Kirkbride, J. B. (2017). Trajectories of Neighborhood Cohesion in Childhood, and Psychotic and Depressive

Symptoms at Age 13 and 18 Years. *Journal of the American Academy of Child & Adolescent Psychiatry*, 56(7), 570-577.

Spauwen, J., Krabbendam, L., Lieb, R., Wittchen, H.-U., & Van Os, J. (2006a).

Impact of psychological trauma on the development of psychotic symptoms: relationship with psychosis proneness. *The British Journal of Psychiatry*, 188(6), 527-533.

Spauwen, J., Krabbendam, L., Lieb, R., Wittchen, H. U., & van Os, J. (2004). Does urbanicity shift the population expression of psychosis? *Journal of Psychiatric Research*, 38(6), 613-618.

Spauwen, J., Krabbendam, L., Lieb, R., Wittchen, H. U., & van Os, J. (2006b).

Evidence that the outcome of developmental expression of psychosis is worse for adolescents growing up in an urban environment. *Psychological Medicine*, 36(3), 407-415.

Stansfeld, S. A., & Matheson, M. P. (2003). Noise pollution: Non-auditory effects on health. *British Medical Bulletin*, 68(1), 243-257.

Stefanis, N., Delespaul, P., Smyrnis, N., Lembesi, A., Avramopoulos, D.,

Evdokimidis, I., Stefanis, C., & Van Os, J. (2004). Is the excess risk of psychosis-like experiences in urban areas attributable to altered cognitive development? *Social Psychiatry and Psychiatric Epidemiology*, 39(5), 364-368.

Sterne, J. A., White, I. R., Carlin, J. B., Spratt, M., Royston, P., Kenward, M. G.,

Wood, A. M., & Carpenter, J. R. (2009). Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *BMJ*, 338, b2393.

- Sullivan, P. F., Kendler, K. S., & Neale, M. C. (2003). Schizophrenia as a complex trait: Evidence from a meta-analysis of twin studies. *Archives of General Psychiatry*, 60(12), 1187-1192.
- Sundquist, K., Frank, G., & Sundquist, J. (2004). Urbanisation and incidence of psychosis and depression: Follow-up study of 4.4 million women and men in Sweden. *The British Journal of Psychiatry*, 184(4), 293-298.
- Szöke, A., Charpeaud, T., Galliot, A.-M., Vilain, J., Richard, J.-R., Leboyer, M., Llorca, P.-M., & Schürhoff, F. (2014). Rural-urban variation in incidence of psychosis in France a prospective epidemiologic study in two contrasted catchment areas. *BMC Psychiatry*, 14(1), 78.
- Szyszkowicz, M., Rowe, B., & Colman, I. (2009). Air pollution and daily emergency department visits for depression. *International Journal of Occupational Medicine and Environmental Health*, 22(4), 355-362.
- Tarullo, A. R., & Gunnar, M. R. (2006). Child maltreatment and the developing HPA axis. *Hormones and Behavior*, 50(4), 632-639.
- Tost, H., Champagne, F. A., & Meyer-Lindenberg, A. (2015). Environmental influence in the brain, human welfare and mental health. *Nature Neuroscience*, 18(10), 1421-1431.
- Trotta, A., Murray, R., & Fisher, H. (2015). The impact of childhood adversity on the persistence of psychotic symptoms: A systematic review and meta-analysis. *Psychological Medicine*, 45(12), 2481-2498.
- Trouton, A., Spinath, F. M., & Plomin, R. (2002). Twins early development study (TEDS): A multivariate, longitudinal genetic investigation of language, cognition and behavior problems in childhood. *Twin Research*, 5(5), 444-448.
- Trzesniewski, K. H., Moffitt, T. E., Caspi, A., Taylor, A., & Maughan, B. (2006). Revisiting the association between reading achievement and antisocial

- behavior: New evidence of an environmental explanation from a twin study. *Child Development*, 77(1), 72-88.
- United Nations. (2004). *World Urbanization Prospects: The 2003 Revision*. New York: United Nations Publications.
- United Nations Human Settlements Programme. (2006). *State of the world's cities: 2006/7*. London, UK: Earthscan.
- van der Werf, M., van Winkel, R., van Boxtel, M., & van Os, J. (2010). Evidence that the impact of hearing impairment on psychosis risk is moderated by the level of complexity of the social environment. *Schizophrenia Research*, 122(1), 193-198.
- Van Os, J., Hanssen, M., Bak, M., Bijl, R. V., & Vollebergh, W. (2003). Do urbanicity and familial liability coparticipate in causing psychosis? *American Journal of Psychiatry*, 160(3), 477-482.
- van Os, J., Hanssen, M., Bijl, R. V., & Ravelli, A. (2000). Strauss (1969) revisited: A psychosis continuum in the general population? *Schizophrenia Research*, 45(1-2), 11-20.
- van Os, J., Hanssen, M., Bijl, R. V., & Vollebergh, W. (2001). Prevalence of psychotic disorder and community level of psychotic symptoms: an urban-rural comparison. *Archives of General Psychiatry*, 58(7), 663-668.
- van Os, J., Hanssen, M., de Graaf, R., & Vollebergh, W. (2002). Does the urban environment independently increase the risk for both negative and positive features of psychosis? *Social Psychiatry and Psychiatric Epidemiology*, 37(10), 460-464.
- van Os, J., Kenis, G., & Rutten, B. P. (2010). The environment and schizophrenia. *Nature*, 468(7321), 203-212.

- van Os, J., Linscott, R. J., Myin-Germeys, I., Delespaul, P., & Krabbendam, L. (2009). A systematic review and meta-analysis of the psychosis continuum: Evidence for a psychosis proneness-persistence-impairment model of psychotic disorder. *Psychological Medicine*, 39(2), 179-195.
doi:10.1017/S0033291708003814
- van Os, J., Pedersen, C. B., & Mortensen, P. B. (2004). Confirmation of synergy between urbanicity and familial liability in the causation of psychosis. *American Journal of Psychiatry*, 161(12), 2312-2314.
- van Winkel, R., Stefanis, N. C., & Myin-Germeys, I. (2008). Psychosocial stress and psychosis. A review of the neurobiological mechanisms and the evidence for gene-stress interaction. *Schizophrenia Bulletin*, 34(6), 1095-1105.
- Varese, F., Smeets, F., Drukker, M., Lieveise, R., Lataster, T., Viechtbauer, W., Read, J., van Os, J., & Bentall, R. P. (2012). Childhood adversities increase the risk of psychosis: A meta-analysis of patient-control, prospective- and cross-sectional cohort studies. *Schizophrenia Bulletin*, 38(4), 661-671.
- Vassos, E., Agerbo, E., Mors, O., & Pedersen, C. B. (2015). Urban–rural differences in incidence rates of psychiatric disorders in Denmark. *The British Journal of Psychiatry*, 208(5), 435-440.
- Vassos, E., Pedersen, C. B., Murray, R. M., Collier, D. A., & Lewis, C. M. (2012). Meta-analysis of the association of urbanicity with schizophrenia. *Schizophrenia Bulletin*, 38(6), 1118-1123.
- Velakoulis, D., Wood, S. J., Wong, M. T., McGorry, P. D., Yung, A., Phillips, L., Smith, D., Brewer, W., Proffitt, T., & Desmond, P. (2006). Hippocampal and amygdala volumes according to psychosis stage and diagnosis: A magnetic resonance imaging study of chronic schizophrenia, first-episode psychosis, and ultra–high-risk individuals. *Archives of General Psychiatry*, 63(2), 139-149.

- Veling, W., Counotte, J., Pot-Kolder, R., van Os, J., & van der Gaag, M. (2016a). Childhood trauma, psychosis liability and social stress reactivity: A virtual reality study. *Psychological Medicine*, 46(16), 3339-3348.
- Veling, W., Pot-Kolder, R., Counotte, J., van Os, J., & van der Gaag, M. (2016b). Environmental social stress, paranoia and psychosis liability: A virtual reality study. *Schizophrenia Bulletin*, 42(6), 1363-1371.
- Veling, W., Susser, E., Selten, J.-P., & Hoek, H. (2015). Social disorganization of neighborhoods and incidence of psychotic disorders: A 7-year first-contact incidence study. *Psychological Medicine*, 45(9), 1789-1798.
- Verdoux, H., & van Os, J. (2002). Psychotic symptoms in non-clinical populations and the continuum of psychosis. *Schizophrenia Research*, 54(1-2), 59-65.
- Walker, E., Mittal, V., & Tessner, K. (2008). Stress and the hypothalamic pituitary adrenal axis in the developmental course of schizophrenia. *Annual Reviews of Clinical Psychology*, 4, 189-216.
- Weissman, M. M., Wickramaratne, P., Adams, P., Wolk, S., Verdeli, H., & Olfson, M. (2000). Brief screening for family psychiatric history: The family history screen. *Archives of General Psychiatry*, 57(7), 675-682.
- Wickham, S., Taylor, P., Shevlin, M., & Bentall, R. P. (2014). The impact of social deprivation on paranoia, hallucinations, mania and depression: The role of discrimination social support, stress and trust. *PLoS One*, 9(8), e105140.
- Wicks, S., Hjern, A., & Dalman, C. (2010). Social risk or genetic liability for psychosis? A study of children born in Sweden and reared by adoptive parents. *American Journal of Psychiatry*, 167(10), 1240-1246.
- Wittchen, H.-U., Lachner, G., Wunderlich, U., & Pfister, H. (1998). Test-retest reliability of the computerized DSM-IV version of the Munich-Composite

- International Diagnostic Interview (M-CIDI). *Social Psychiatry and Psychiatric Epidemiology*, 33(11), 568-578.
- World Health Organization. (1992). *The ICD-10 classification of mental and behavioural disorders: Clinical descriptions and diagnostic guidelines*. Geneva: World Health Organization.
- World Health Organization. (2008). *Closing the gap in a generation: health equity through action on the social determinants of health: Commission on Social Determinants of Health final report*. Geneva: WHO Commission on Social Determinants of Health.
- World Health Organization. (2011). *Addressing the social determinants of health: The urban dimension and the role of local government*. Copenhagen: World Health Organization.
- World Health Organization. (2013). *Review of Evidence on Health Aspects of Air Pollution - REVIHAAP Project: Final Technical Report*. Copenhagen: WHO Regional Office for Europe.
- Yang, J., Visscher, P. M., & Wray, N. R. (2010). Sporadic cases are the norm for complex disease. *European Journal of Human Genetics*, 18(9), 1039-1043.
- Yoshizumi, T., Murase, S., Honjo, S., Kaneko, H., & Murakami, T. (2004). Hallucinatory experiences in a community sample of Japanese children. *Journal of the American Academy of Child and Adolescent Psychiatry*, 43(8), 1030-1036.
- Yung, A. R., Nelson, B., Baker, K., Buckby, J. A., Baksheev, G., & Cosgrave, E. M. (2009). Psychotic-like experiences in a community sample of adolescents: Implications for the continuum model of psychosis and prediction of schizophrenia. *Australian and New Zealand Journal of Psychiatry*, 43(2), 118-128.

- Zammit, S., Kounali, D., Cannon, M., David, A. S., Gunnell, D., Heron, J., Jones, P. B., Lewis, S., Sullivan, S., & Wolke, D. (2013). Psychotic experiences and psychotic disorders at age 18 in relation to psychotic experiences at age 12 in a longitudinal population-based cohort study. *American Journal of Psychiatry*, 170(7), 742-750.
- Zammit, S., Lewis, G., Rasbash, J., Dalman, C., Gustafsson, J.-E., & Allebeck, P. (2010). Individuals, schools, and neighbourhoods: A Multilevel longitudinal study of variation in incidence of psychotic disorders. *Archives of General Psychiatry*, 67(9), 914-922.
- Zavos, H. M., Freeman, D., Haworth, C. M., McGuire, P., Plomin, R., Cardno, A. G., & Ronald, A. (2014). Consistent etiology of severe, frequent psychotic experiences and milder, less frequent manifestations: a twin study of specific psychotic experiences in adolescence. *JAMA Psychiatry*, 71(9), 1049-1057.

Appendix I

Interview items for assessing psychotic symptoms and experiences

Page 49

UNUSUAL FEELINGS

Sometimes we get unusual feelings or thoughts. I'd like to ask some questions about these. You might recognise these from last time we visited. I am interested in whether you've had any of these feelings or thoughts since you were 12.

Use the LHC to orient the twin to the period since age 12, secondary school till now.

FF1 Some people believe that their thoughts can be read by another person. I don't mean they could guess what you were thinking because of the look on your face or because they knew you really well. I mean they could actually read your mind. Since you turned 12, have other people ever read your thoughts?

No	Maybe	Yes	DK/Ref
☐	☐	☐	☐
↓	↘	↙	
Skip to FF3 (next page)		Continue below	

FF1i *If yes, prompt: "Was that your twin?"*

No	Maybe	Yes	DK/Ref
☐	☐	☐	☐

FF1a How do they read your thoughts? Do you think they used special powers?

FF1p Did anyone read your mind in the past year?

No	Maybe	Yes	DK/Ref
☐	☐	☐	☐

FF2 *(Interviewer) Do you believe this is a symptom?*

No	Unsure	Yes
☐	☐	☐

Adapted from ALSPAC "Funny Feelings" questionnaire

+

+

FF3 Since you turned 12, have you ever believed that you were being sent special messages through television or radio, or that a programme has been arranged just for you alone?

No	Maybe	Yes	DK/Ref
☐	☐	☐	☐
↓	↘	↙	
Skip to FF5 (next page)		Continue below	

FF3a Who do you think these messages come from?

FF3b Can you give me an example of one of these messages?

FF3c Why do you think you were getting these messages?

FF3p Were you sent special messages in the past year?

No	Maybe	Yes	DK/Ref
☐	☐	☐	☐

FF4 (Interviewer) Do you believe this is a symptom?

No	Unsure	Yes
☐	☐	☐

+

+

FF5 Since you turned 12, have you ever thought you were being watched, followed or spied on?

No	Maybe	Yes	DK/Ref
☐	☐	☐	☐
↓	↙	↘	
<i>Skip to FF7 (next page)</i>	<i>Continue below</i>		

FF5a Who was doing this?

FF5b Why do you think they were doing this?

FF5p Have you been watched or spied on in the past year?

No	Maybe	Yes	DK/Ref
☐	☐	☐	☐

FF6 (Interviewer) Do you believe this is a symptom?

No	Unsure	Yes
☐	☐	☐

+

+

FF7 Since you turned 12, have you ever heard voices that other people cannot hear?

No	Maybe	Yes	DK/Ref
☐	☐	☐	☐
↓	↘	↘	
Skip to FF9 (next page)		Continue below	

FF7a Did the voices say something about what you were doing or thinking?

FF7b Can you give me an example of what these voices say?

FF7c Did you ever hear two or more of these voices that nobody else could hear?

FF7d Were they talking about you? What were they saying?

FF7e Did this only happen when you were ill with a high temperature?

FF7f Did this only happen after taking some drugs or medicine?

FF7p Have you heard voices in the past year?

No	Maybe	Yes	DK/Ref
☐	☐	☐	☐

FF8 (Interviewer) Do you believe this is a symptom?

No	Unsure	Yes
☐	☐	☐

+

+

FF9 Since you turned 12, have you ever felt like you were under the control of some special power?

No	Maybe	Yes	DK/Ref
☐	☐	☐	☐
↓	↙	↘	
Skip to FF11 (next page)	Continue below		

FF9a Who was controlling you?

FF9b (If religious) Do other members of your religion believe this also?

FF9c Did it control what you were doing or thinking? Did you feel that you were forced to say or do things that you didn't want to?

FF9d Can you give me an example?

FF9p Have you felt under the control of a special power in the past year?

No	Maybe	Yes	DK/Ref
☐	☐	☐	☐

FF10 (Interviewer) Do you believe this is a symptom?

No	Unsure	Yes
☐	☐	☐

+

+

FF11 Since you turned 12, have you ever known what another person was thinking, even though the person wasn't speaking? I don't mean you could guess what they were thinking because of the look on their face or because you knew them really well. I mean you have a special power and you could actually read their mind. Has that happened since you were 12?

No	Maybe	Yes	DK/Ref
☐	☐	☐	☐
↓	↘	↘	
Skip to FF13 (next page)		Continue below	

FF11a Whose thoughts did you read?

FF11i (Interviewer to complete): Score YES if it was their twin

No	Maybe	Yes	DK/Ref
☐	☐	☐	☐

FF11b How did you read these thoughts?

FF11p Have you read someone's mind in the past year?

No	Maybe	Yes	DK/Ref
☐	☐	☐	☐

FF12 (Interviewer) Do you believe this is a symptom?

No	Unsure	Yes
☐	☐	☐

+

+

FF13 Since you turned 12, have you ever seen something or someone that other people could not see?

No	Maybe	Yes	DK/Ref
☐	☐	☐	☐
↓	↘	↘	
Skip to FF15 (next page)	Continue below		

FF13a Who or what did you see? Did it seem real?

FF13b Were you completely awake when you saw these things?

FF13c Did this only happen when you were ill with a high temperature?

FF13d Did this only happen after taking some drugs or medicine?

FF13p Have you seen something others could not see in the past year?

No	Maybe	Yes	DK/Ref
☐	☐	☐	☐

FF14 (Interviewer) Do you believe this is a symptom?

No	Unsure	Yes
☐	☐	☐

+

+

Remember, we are talking about unusual feelings and thoughts. Do any of the following apply to you, since you turned 12?

		No	Maybe	Yes	DK/Ref
FF15	I have become more sensitive to lights or sounds	☐	☐	☐	☐
FF16	I feel as though I can't trust anyone	☐	☐	☐	☐
FF17	I worry that my food may be poisoned	☐	☐	☐	☐
FF18	People or places I know seem different	☐	☐	☐	☐
FF19	I believe I have special abilities or powers beyond my natural talents	☐	☐	☐	☐
FF20	My thinking is unusual or frightening	☐	☐	☐	☐

GATE: → If YES to any symptoms from FF1 onwards, continue
 → If not, skip to next module (next page)

FF21 You have described having unusual feelings or thoughts. On a scale of 1 to 5, how much have problems like these interfered with your family, friends, work or everyday activities?

Show card INTERFERENCE

Very little					Very much	DK/Ref
1	2	3	4	5		
☐	☐	☐	☐	☐		☐

FF22	Was there any time when you wanted to talk to a doctor or other professional about these feelings and thoughts?	No	Maybe	Yes	DK/Ref
		☐	☐	☐	☐
FF23	Did you do so?	No	Maybe	Yes	DK/Ref
		☐	☐	☐	☐

FFCOM Unusual Feelings notes: *(Record twin's and RW's comments)*

+

+

Appendix II

Resident survey of urbanicity and neighbourhood conditions

Postcode

A SURVEY ABOUT YOUR LOCAL NEIGHBOURHOOD

COL 1-8

People in Britain are becoming more and more concerned about what goes on in their neighbourhoods. This survey is designed to find out what kinds of neighbourhood problems are causing concern and even stress. We also want to find out what kinds of good things your neighbourhood may have to offer. We are sending this survey to over 20,000 people all over Britain.

Your response is important. For every completed questionnaire we will donate 50p to the Young Minds Charity. If every one returns their questionnaire we will be donating over £10,000!
<http://www.youngminds.org.uk/>

Why did we write to you? You have been randomly selected to represent your post-code area in this survey. We hope you will take part so that your neighbourhood is represented.

How long will this take? About 15 minutes.

Your response is strictly confidential. After this envelope was mailed to you, we do not any longer have your name. Your survey form is identified only by your postcode at the top right corner. It cannot be traced back to you.

Who are we? We work at King's College, London. The team leader is Professor Terrie Moffitt. We will report the results of the survey to the government.

Please indicate your answers with a tick ☒ BLACK ink is best. If you make a mistake shade it out and tick the appropriate box e.g. ☒ ☐ ☐ ☐ ☒

First we would like to ask you a few questions about yourself.

SCIIA1 A1. Are you male or female?	Male	☐	Female	☐	
A2. What is your age?	Under 25	☐	25-49	☐	
	50-65	☐	Over 65	☐	
A3. Do any children live with you?	Yes	☐	No	☐	
If yes, what are the age(s) of your children (check all that apply):					
	birth - 6 yrs	☐	7 yrs - 15 yrs	☐	16 yrs -19 yrs ☐
SCIIA3A	SCIIA3B	SCIIA3C			

To begin, we would like to ask you to think about the local area close around your home. We will call this place your NEIGHBOURHOOD. We need to know what kind of place you have in mind when you answer the questions.

A4. How long have you lived in this neighbourhood?

Less than a year	☐	1 to 5 years	☐	
6 to 20 years	☐	More than 20 years	☐	

SCIIA5 A5. Is your neighbourhood....				
Inside a large city?	☐	In a small village?	☐	
In a suburb outside or near a city?	☐	In the countryside?	☐	
In a town?	☐	Somewhere else, such as a military base?	☐	

Next, we would like to ask you whether the following facilities and services exist in your neighbourhood.

Do any of the following facilities exist in your neighbourhood?

	Yes	No	Don't know	
SCIIB1 B1. Playground or park?	☒	☒	☒	17
B2. Area for teenagers to play sport (e.g., football pitch)?	☐	☐	☐	18
B3. Day Care Centre?	☐	☐	☐	19
B4. Recreation Centre or Swimming pool?	☐	☐	☐	20
B5. Supermarket?	☐	☐	☐	21
B6. Fast Food Restaurants?	☐	☐	☐	22
B7. Convenience Store or Corner Shop?	☐	☐	☐	23
B8. GP Surgery?	☐	☐	☐	24
B9. Dental Surgery?	☐	☐	☐	25
B10. Chemist?	☐	☐	☐	26
B11. Post Office?	☐	☐	☐	27
B12. Laundrette?	☐	☐	☐	28
B13. Local Pub?	☐	☐	☐	29
B14. Bank?	☐	☐	☐	30
B15. Primary or Secondary School?	☐	☐	☐	31
B16. Library?	☐	☐	☐	32
B17. Youth Centre?	☐	☐	☐	33
B18. Family Planning Clinic?	☐	☐	☐	34
B19. Drug Treatment Program?	☐	☐	☐	35
SCIIB20 B20. Mental Health Centre?	☒	☒	☒	36

Next, we would like to ask you some questions about problems that may or may not exist in your neighbourhood.

Are these things a problem in the neighbourhood where you live?

	Yes, a big problem	Yes, somewhat of problem	No, not a problem	
SCIIC1 C1. Noisy neighbours, arguments, or loud parties?	☒	☒	☒	37
C2. Vandals who do things like damage phone boxes, smash street lamps, break windows, or paint graffiti on walls?	☐	☐	☐	38
C3. Litter, broken glass, rubbish in public places?	☐	☐	☐	39
C4. Run down buildings, abandoned cars, wastelands or vacant shop fronts?	☐	☐	☐	40
SCIIC5 C5. People being drunk and unruly in public?	☒	☒	☒	41

		Yes, a big problem	Yes, somewhat of problem	No, not a problem	
SCIIC6	C6. People selling or using drugs?	☒ 2	☒ 1	☒ 0	42
	C7. Groups of young people hanging out and causing trouble?	☐	☐	☐	43
	C8. Noisy traffic?	☐	☐	☐	44
	C9. Bad smells from factories, farms, sewage or rubbish dump?	☐	☐	☐	45
	C10. Things such as ugly buildings or signs that make the area look unattractive?	☐	☐	☐	46
	C11. Poor public transport service?	☐	☐	☐	47
	C12. Not enough local shops?	☐	☐	☐	48
	C13. Schools for children are too far away, or not good quality?	☐	☐	☐	49
	C14. Women and girls risk being harassed if they go out by themselves after dark?	☐	☐	☐	50
	C15. Muggings, robberies or assaults on people?	☐	☐	☐	51
	C16. Cars or trucks getting stolen or broken into?	☐	☐	☐	52
	C17. Homes getting broken into or burgled?	☐	☐	☐	53
	C18. Air pollution, petrol exhaust, or factory fumes?	☐	☐	☐	54
	C19. Pesticides, chemicals, water pollution, or toxic wastes?	☐	☐	☐	55
	C20. Gang activity?	☐	☐	☐	56
	C21. Children or teenagers involved in gangs or gang activity?	☐	☐	☐	57
	C22. People being attacked or harassed because of their skin colour, ethnic origin or religion?	☐	☐	☐	58
SCIIC23	C23. Anything else?	☒ 2	☒ 1	☒ 0	59

Please say if it is likely or unlikely that people in your neighbourhood would act in the following ways.

		Very Unlikely	Neither likely nor unlikely	Unlikely	Likely	Very likely	
SCIID1	D1. If a group of neighbourhood children were playing truant and hanging around, how likely is it that your neighbours would do something about it?	☒ 0	☒ 1	☒ 2	☒ 3	☒ 4	60
	D2. If some children were spray-painting graffiti on a local building, how likely is it that your neighbours would do something about it?	☐	☐	☐	☐	☐	61
	D3. If there was a fight in a public place in your community and someone was being beaten or threatened, how likely is it that your neighbours would break it up?	☐	☐	☐	☐	☐	62
SCIID4	D4. If a child was showing disrespect to an adult, how likely is it that people in your neighbourhood would scold that child?	☒ 0	☒ 1	☒ 2	☒ 3	☒ 4	63

SCIID5	D5.	Suppose that because of budget cuts the fire station closest to your home was going to be closed down by the council. How likely is it that neighbourhood residents would organise to try to do something to keep the fire station open?	Very unlikely	Neither likely nor unlikely	Unlikely	Likely	Very likely	64
			0	1	2	3	4	
	D6.	If an adult was smacking a child on the street, how likely is it that people in your neighbourhood would do something about it?	☐	☐	☐	☐	☐	65
	D7.	If customers were being rude or abusive to the owner of a local shop, how likely is it that people in your neighbourhood would do something about it?	☐	☐	☐	☐	☐	66
SCIID8	D8.	If a child wandered off by him/herself, how likely is it that people in your neighbourhood would go after the child and do something about it?	0	1	2	3	4	67

For each of these statements, please say whether you agree or disagree:

		Strongly Agree	Agree	Neither Agree or Disagree	Disagree	Strongly Disagree	
SCIIE1	E1. People around here are willing to help their neighbours.	4	3	2	1	0	68
	E2. This is a close-knit community.						69
	E3. People in this neighbourhood can be trusted.						70
	E4. People in this neighbourhood generally get along with each other.						71
	E5. People in this neighbourhood share the same values.						72
	E6. People in this neighbourhood do things together						73
SCIIE7	E7. People in this neighbourhood mostly go their own way	4	3	2	1	0	74

For each of these statements, please say whether you agree or disagree:

		Strongly Agree	Agree	Neither Agree or Disagree	Disagree	Strongly Disagree	
SCIIF1	F1. Adults in this neighbourhood know who the local children and teenagers are.	4	3	2	1	0	75
	F2. There are adults in the neighbourhood that young people can look up to.	☐	☐	☐	☐	☐	76
	F3. Young people in this neighbourhood have no place to play or hang out but in the street.	☐	☐	☐	☐	☐	77
	F4. You can count on adults in this neighbourhood to watch out that young people are safe and do not get into trouble.	☐	☐	☐	☐	☐	78
	F5. Young people in this neighbourhood might yell or swear at someone who verbally corrects their behaviour.	☐	☐	☐	☐	☐	79
	F6. Young people might physically assault a neighbour who verbally corrects their behaviour.	☐	☐	☐	☐	☐	80
SCIIF7	F7. People in this neighbourhood are afraid to intervene when they see young people misbehaving.	4	3	2	1	0	81

Next, a few questions about how well people get on with each other in your neighbourhood.

SCIIG1	G1. Do you have any <i>close friends</i> that live in your neighbourhood?	Yes, several friends 2	Yes, one friend 1	No 0	82
	G2. Do you <i>meet with people from the neighbourhood</i> anywhere outside your home, such as down at the pub, in a local hall, or at church or school events?	Yes, often 2	Yes, sometimes 1	No 0	83
	G3. Would you generally be happy to <i>lend your tools to a neighbour</i> if they asked you to (for example, your vacuum-cleaner hoover or your power drill)?	2	1	0	84
	G4. Would you be happy to <i>leave your keys with a neighbour</i> if you went away on holiday?	☐	☐	☐	85
	G5. If any of your neighbours disturbed you by <i>playing loud music</i> would you feel that you could speak to them about it?	☐	☐	☐	86
	G6. If any of your <i>neighbours' children did anything that upset you</i> would you feel that you could speak to their parents about it?	☐	☐	☐	87
	G7. If you met someone from the neighbourhood, <i>would you stop and greet</i> each other	☐	☐	☐	88
SCIIG8	G8. If you lost your purse/wallet containing your address details and it was found in the street by someone living in this neighbourhood, would it be returned to you with nothing missing?	2	1	0	89

Next, a few questions about how much you like your neighbourhood.

		Yes, definitely	Yes, probably	No, probably not	No, definitely not	
SCIIH1	H1. Would you recommend to a close friend to <i>move into</i> your neighbourhood?	3	2	1	0	90
	H2. Would you regard your neighbourhood as a <i>good place for children</i> to grow up?	☐	☐	☐	☐	91
	H3. Would you regard your neighbourhood as a <i>good place for teenagers</i> to grow up?	☐	☐	☐	☐	92
	H4. Would you say that your neighbourhood generally is a <i>safe place</i> ?	☐	☐	☐	☐	93
	H5. Would you say that your neighbourhood is a place where people from different backgrounds get on well together	☐	☐	☐	☐	94
SCIIH6	H6. Overall, are you <i>happy</i> to live in your neighbourhood?	3	2	1	0	95

Next, a few questions about how your neighbourhood may have changed during the last 5 years

		Better	Same	Worse	Don't know	
SCIII1	I1. Has personal safety in your neighbourhood gotten better, stayed about the same, or gotten worse?	2	1	0	9	96
	I2. How about the way the neighbourhood looks? has this gotten better, stayed about the same, or gotten worse?	☐	☐	☐	☐	97
	I3. Would you say that the people moving into the neighbourhood are making the neighbourhood better, about the same or worse?	☐	☐	☐	☐	98
SCIII4	I4. How about crime by <i>young people</i> in your neighbourhood? has this gotten better, stayed about the same, or gotten worse?	2	1	0	9	99

Now a few questions about your feelings of safety in your neighbourhood

SCIIJ1	J1. Are there any particular people who live in your neighbourhood that you fear?	Yes (several).	Yes, (one)	No	100
		2	1	0	
	J2. Are there any particular places in your neighbourhood that you would not go after dark by yourself?	2	1	0	101
SCIIJ3	J3. Do you feel safe when you are by yourself in your own home	Yes		No	102
		1		0	

Next, a few questions about the welfare of adults in your neighbourhood.

SCIIK1	K1. Are there people in your neighbourhood who do not have enough money to buy food?	Yes	Possibly	No	103
		2	1	0	
	K2. Do <i>adults in your home</i> ever cut the size of meals or skip meals because there isn't enough money for food?	☐	☐	☐	104
SCIIK3	K3. Are there any families in this neighbourhood whose food doesn't last, and they don't have money to get more?	2	1	0	105

Next, a few questions about whether or not you have been victimised by crime in your neighbourhood this year.

SCII L1	L1. During the <u>last year</u> , has someone <i>broken into your home</i> and stolen or damaged your property?	Yes, more than once.	Yes, once	No	106
		2	1	0	
	L2. In the <u>last year</u> , have you had <i>anything damaged or stolen on the outside of your home</i> , from your garden, garage, shed, or elsewhere, including your cars or bikes parked in the street?	☐	☐	☐	107
SCII L3	L3. In the <u>last year</u> , has <i>anyone ever used violence against you or any member of your household</i> anywhere in this neighbourhood? By this we mean someone in your family has been mugged, robbed, raped, hit, or assaulted in your neighbourhood this year.	2	1	0	108

Finally, a quick question about your overall health.

SCIIM1	M1. Would you say that your health in general is:	Excellent	Very good	Good	Fair	Poor	109
		4	3	2	1	0	

Thank you very much for completing this survey! Remember, your response is anonymous. Your survey cannot be linked back to you. Please post it back to us in the freepost envelope we provided.

Post your survey as soon as you can, so your views can be counted.

Sometimes people want to take part in a survey, but they just forget to post it in. A reminder letter can help. In a few weeks, people who got this survey will also automatically get a reminder letter. If you get a reminder letter after you send us your survey, please forgive us. Because we cannot link your survey to your name, we are not able to stop the reminder going out to you.

If you have any questions about this survey, please feel free to phone us at 0800 996 1471. Or you may write to us at this address: The E-Risk Study, PO80, De Crespigny Park, London, SE5 8AF.

Appendix III

Interview items for mothers' reports of neighbourhood conditions

[Record 10]

Page 51

This part of the interview is about what it's like to live in your neighbourhood. By neighbourhood, we mean the area around where you live. It may include places you shop, religious or public institutions, or a local business district.

How often do the following things bother you about the area you live in?

<i>Show response card 23</i>		Never	Occas- ionally	Often	dk/Ref	
NB7	Noisy neighbours, arguments or loud parties NB7M5	☐ 0	☐ 1	☐ 2	☐ 9	15
NB8	Teenagers hanging around NB8M5	☐ 0	☐ 1	☐ 2	☐ 9	16
NB9	Drunks or tramps NB9M5	☐ 0	☐ 1	☐ 2	☐ 9	17
NB10	Homes and gardens in bad condition NB10M5	☐ 0	☐ 1	☐ 2	☐ 9	18
NB11	Vandalism, graffiti or deliberate damage to property NB11M5	☐ 0	☐ 1	☐ 2	☐ 9	19
NB12	Homes broken into NB12M5	☐ 0	☐ 1	☐ 2	☐ 9	20
NB13	Cars broken into or stolen NB13M5	☐ 0	☐ 1	☐ 2	☐ 9	21
NB14	Animals running loose NB14M5	☐ 0	☐ 1	☐ 2	☐ 9	22
NB15	Dump/sewage smells NB15M5	☐ 0	☐ 1	☐ 2	☐ 9	23
NB16	Inadequate public transportation NB16M5	☐ 0	☐ 1	☐ 2	☐ 9	24
NB17	Not enough local shops NB17M5	☐ 0	☐ 1	☐ 2	☐ 9	25
NB18	Quality of available schooling NB18M5	☐ 0	☐ 1	☐ 2	☐ 9	26
NB19	Noisy traffic NB19M5	☐ 0	☐ 1	☐ 2	☐ 9	27

I'm going to read you some statements about things that people in your neighbourhood may or may not do. For each of the following statements, please tell me whether it is very true, sometimes or maybe true, or not true.

		NO, not true	Sometimes true	YES, very true	dk/Ref
Show response card 24					
NB20	While you have lived in this neighbourhood, has anyone ever used violence, such as in a mugging, fight, or assault, against <u>you</u> or <u>any member of your household</u> anywhere in your neighbourhood? NB20M5 . . .	0	1	2	9 28
NB21	While you have lived in this neighbourhood, has your home ever been broken into? NB21M5	0	1	2	9 29
NB22	While you have lived in this neighbourhood, have you had anything damaged or stolen from your garden, garage or elsewhere outside your home (including vehicles parked in the street)? NB22M5	0	1	2	9 30
NB23	If a group of neighbourhood children were skipping school and hanging around, would your neighbours do something about it? NB23M5	0	1	2	9 31
NB24	If some children were spray-painting graffiti on a local building, would your neighbours do something about it? NB24M5	0	1	2	9 32
NB25	If a child was showing disrespect to an adult, would people in your neighbourhood scold that child? NB25M5	0	1	2	9 33
NB26	If there was a fight in a public place in your community and someone was being beaten or threatened, would your neighbours break it up? NB26M5	0	1	2	9 34
NB27	If because of budget cuts the fire station closest to your home was going to be closed down by the council, would neighbourhood residents organise to try to do something to keep the fire station open? NB27M5	0	1	2	9 35
NB28	Is this a close-knit neighbourhood? NB28M5	0	1	2	9 36
NB29	Are people around here willing to help their neighbours? NB29M5	0	1	2	9 37
NB30	Do you think people in this neighbourhood can be trusted? NB30M5	0	1	2	9 38
NB31	Do you think people in this neighbourhood generally get along with each other? NB31M5	0	1	2	9 39
NB32	Do you think people in this neighbourhood share the same values? NB32M5	0	1	2	9 40

Appendix IV

Interview items for adolescents' perceptions of neighbourhood conditions

Page 30

NEIGHBOURHOOD

Now I'm going to ask you a few questions about where you spend your time and what your area is like.

NB1 During a typical week, where do you spend the majority of your time? (List up to 3 places)

	Place	Location		Check up to 3 locations
		Street and city?	Nearest crossstreet?	
NB1a	Home			☐
NB1b	School			☐
NB1c	Work			☐
NB1d	Shops			☐
NB1e				☐
NB1f				☐
NB1g				☐

Now I would like to ask you some questions about your neighbourhood. For these questions, "neighbourhood" includes the street you live on and several streets in each direction. Please keep this in mind when answering these questions.

Please say how likely it is that people in your neighbourhood would act in the following ways:

Show response card NEIGHBOURHOOD1

		Very likely	Likely	Neither likely nor unlikely	Unlikely	Very unlikely	DK/Ref
NB2	If a group of neighbourhood children were playing truant and hanging around, how likely is it that your neighbours would do something about it?	☐	☐	☐	☐	☐	☐
NB3	If children were spray-painting graffiti on a local building, how likely is it that your neighbours would do something about it?	☐	☐	☐	☐	☐	☐
NB4	If there was a fight in a public place in your community and someone was being beaten or threatened, how likely is it that your neighbours would break it up?	☐	☐	☐	☐	☐	☐

+

+

		Very likely	Likely	Neither likely nor unlikely	Unlikely	Very unlikely	DK/Ref
NB5	If a child was showing disrespect to an adult, how likely is it that people in your neighbourhood would scold that child?	☐	☐	☐	☐	☐	☐
NB6	If because of budget cuts the fire station closest to your home was going to be closed down by the council, how likely is it that neighbourhood residents would organise to try to do something to keep the fire station open?	☐	☐	☐	☐	☐	☐

For each of the following statements, please indicate how much you agree or disagree:

Show response card NEIGHBOURHOOD2

		Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	DK/Ref
NB7	People around my area are willing to help their neighbours	☐	☐	☐	☐	☐	☐
NB8	Mine is a close-knit neighbourhood	☐	☐	☐	☐	☐	☐
NB9	People in my neighbourhood can be trusted ...	☐	☐	☐	☐	☐	☐
NB10	People in my neighbourhood generally get along with each other	☐	☐	☐	☐	☐	☐
NB11	People in my neighbourhood share the same values	☐	☐	☐	☐	☐	☐

For each of the following statements, please tell me whether it is not true, sometimes true or often true:

Show response card NEIGHBOURHOOD3

		Not True	Sometimes True	Often True	DK/Ref
NB12	Would you say that your neighbourhood generally is a safe place?	☐	☐	☐	☐
	Are these things a problem in the area where you live?				
NB13a	Litter, broken glass, rubbish in public places?	☐	☐	☐	☐
NB13b	Run-down buildings, abandoned cars, wastelands or vacant shop fronts?	☐	☐	☐	☐
NB13c	People being drunk and unruly in public?	☐	☐	☐	☐
NB13d	People selling or using drugs?	☐	☐	☐	☐
NB13e	Groups of young people hanging out and causing trouble? ...	☐	☐	☐	☐
NB13f	Homes getting broken into or burgled?	☐	☐	☐	☐

+

+