

1-7-2012

Clinicopathological significance of psychotic experiences in non-psychotic young people: evidence from four population-based studies.

Ian Kelleher

Royal College of Surgeons in Ireland, iankelleher@rcsi.ie

Helen Keeley

National Suicide Research Foundation

Paul Corcoran

National Suicide Research Foundation

Fionnuala Lynch

Mater Misericordiae University Hospital

Carol Fitzpatrick

Mater Misericordiae University Hospital

See next page for additional authors

Citation

Kelleher I, Keeley H, Corcoran P, Devlin N, Molloy C, Roddy S, Clarke MC, Lynch F, Fitzpatrick C, Harley M, Arseneault L, Wasserman C, Carli V, Sarchiapone M, Hoven C, Wasserman D, Cannon M. Clinicopathological significance of psychotic experiences in non-psychotic young people: Evidence from 4 population-based studies. *British Journal of Psychiatry*. 2012; 201:26-32.

This Article is brought to you for free and open access by the Department of Psychiatry at e-publications@RCSI. It has been accepted for inclusion in Psychiatry Articles by an authorized administrator of e-publications@RCSI. For more information, please contact epubs@rcsi.ie.

Authors

Ian Kelleher, Helen Keeley, Paul Corcoran, Fionnuala Lynch, Carol Fitzpatrick, Nina Devlin, Charlene Molloy, Sarah Roddy, Mary C. Clarke, Michelle Harley, Louise Arseneault, Camilla Wasserman, Vladimir Carli, Marco Sarchiapone, Christina Hoven, Danuta Wasserman, and Mary Cannon

— Use Licence —



This work is licensed under a [Creative Commons Attribution-Noncommercial-Share Alike 4.0 License](https://creativecommons.org/licenses/by-nc-sa/4.0/).

What is the clinicopathological significance of psychotic symptoms in non-psychotic young people: Evidence from 4 population-based studies

Ian Kelleher¹, Helen Keeley², Paul Corcoran², Fionnuala Lynch⁷, Carol Fitzpatrick^{7,9}, Nina Devlin¹, Charlene Molloy¹, Sarah Roddy¹, Jennifer Murphy¹, Caroline Rawdon¹, Mary C. Clarke¹, Michelle Harley^{1,8}, Louise Arseneault, Camilla Wasserman³, Vladimir Carli⁵, Marco Sarchiapone⁴, Christina Hoven³, Danuta Wasserman⁵, Mary Cannon^{1,6}

¹Department of Psychiatry, Royal College of Surgeons in Ireland, Education and Research Centre, Beaumont Hospital, Dublin 9, Ireland

²National Suicide Research Foundation, Cork, Ireland

³Department of Child and Adolescent Psychiatry, New York State Psychiatric Institute, Columbia University, New York, USA

⁴Department of Health Sciences, University of Molise, Campobasso, Italy

⁵National Swedish Prevention of Suicide and Mental Ill-Health (NASP), Department of Public Health Sciences, Karolinska Institutet, Stockholm, Sweden

⁶Department of Psychiatry, Beaumont Hospital, Dublin 9, Ireland

⁷Child and Adolescent Mental Health Service, Mater Misericordiae University Hospital, Dublin 7, Ireland

⁸Department of Child and Adolescent Mental Health, St Vincent's Hospital, Fairview, Dublin 3, Ireland

⁹The Children's University Hospital, Temple Street, and University College Dublin, Ireland

¹⁰National University of Ireland, Maynooth, Co. Kildare, Ireland.

Correspondence to Ian Kelleher iankelleher@rcsi.ie and Mary Cannon marycannon@rcsi.ie, Department of Psychiatry, Royal College of Surgeons in Ireland, Education and Research Centre, Beaumont Hospital, Dublin 9, Ireland. Tel +353 1 8093855

Acknowledgements:

The Adolescent Brain Development Study was supported by an Essel NARSAD/Brain and Behavior Research Foundation Independent Investigator award and a Clinician Scientist Award (CSA/2004/1) from the Health Research Board (Ireland) to M. Cannon. The research leading to these results has received funding from the European Community's Seventh Framework Programme under grant agreement No. HEALTH-F2-2010-241909 (Project EU-GEI). EU-GEI is the acronym of the project 'European network of National Schizophrenia Networks Studying Gene-Environment Interactions'. We thank the Clinical Research Centre at Beaumont Hospital for use of research rooms.

The Challenging Times study was supported by Friends of the Children's University Hospital (Dublin), the American Foundation for Suicide Prevention, HSE Northern Area and the Mater Misericordiae University Hospital.

The Saving and Empowering Young Lives in Europe (SEYLE) project is supported through Coordination Theme 1 (Health) of the European Union Seventh Framework Program (FP7), Grant agreement number HEALTH-F2-2009-223091. The SEYLE project in Ireland was also supported by funding from the Health Service Executive National Office for Suicide Prevention.

The authors report no conflicts of interest.

Abstract

Background: Epidemiological research has shown that hallucinations and delusions, the classic symptoms of psychosis, are far more prevalent in the population than actual psychotic disorder. These symptoms are especially prevalent in childhood and adolescence. Longitudinal research has demonstrated that psychotic symptoms in adolescence increase risk for psychotic disorder in adulthood. There has been a lack of research, however, on the immediate clinicopathological significance of psychotic symptoms in adolescence.

Aims: To investigate the relationship between psychotic symptoms and non-psychotic psychopathology in community samples of adolescents in terms of prevalence, co-occurring disorders, comorbid (multiple) psychopathology, and variation across early versus middle adolescence.

Method: Data from four population studies were used: 2 early adolescence studies (ages 11 to 13 years) and two mid adolescence studies (ages 13 to 16 years). Studies 1 and 2 involved school-based surveys of 2,242 11-to 16-year olds for psychotic symptoms and for emotional and behavioural symptoms of psychopathology. Studies 3 and 4 involved in-depth diagnostic interview assessments of psychotic symptoms and lifetime psychiatric disorders in community samples of 423 11-to 15-year olds.

Results: Younger adolescents had a higher prevalence (21 to 23%) of psychotic symptoms than older adolescents (7%). In both age groups, the majority of adolescents who reported psychotic symptoms had at least one diagnosable non-psychotic psychiatric disorder, though associations with psychopathology increased with age: nearly 80% of

the mid-adolescence sample who reported psychotic symptoms had at least 1 diagnosis, compared to 57% of the early adolescence sample. Adolescents who reported psychotic symptoms were at particularly high risk of having multiple co-occurring diagnoses.

Conclusions: Psychotic symptoms are important risk markers for a wide range of non-psychotic psychopathology, in particular for severe psychopathology characterised by multiple co-occurring diagnoses. These symptoms should be carefully assessed in all patients.

Declaration of interest: None

Introduction

Hallucinations and delusions, the classic symptoms of psychosis, have recently been documented to occur at a much higher prevalence in the general population than clinically diagnosed psychotic disorder.¹ A meta-analysis of prevalence studies of psychotic symptoms in young people demonstrated a median prevalence of 17% in children aged 9 to 12 years and 7.5% in adolescents aged 13 to 18 years.² As the term suggests, psychotic symptoms have typically been considered to relate to psychotic disorder. Indeed, research has shown that members of the general population who report psychotic symptoms share a wide range of risk factors with schizophrenia patients³⁻⁸ (see⁹ for review) and young people who report psychotic symptoms have been found to be at increased risk of psychotic disorder in adulthood.^{10, 11}

More recently, several research groups have reported that individuals who report psychotic symptoms are also more likely to report symptoms of non-psychotic psychopathology, especially symptoms of depression.¹²⁻¹⁶ Yung et al., for example, reported that individuals who had a diagnosed depressive disorder endorsed an increased number of psychotic symptoms on the Community Assessment of Psychic Experiences (CAPE) questionnaire compared to controls.¹⁷ Bartels-Velthuis et al. found that young adolescents who disclosed psychotic symptoms were approximately 3 to 5 times more likely to score in the clinical psychopathology range on the parent-completed Child Behaviour Checklist.¹⁸ Community based studies to date, however, have relied mainly upon questionnaires to assess psychotic symptoms and have involved limited data on non-psychotic psychopathology. In addition, although research suggests that psychotic

symptoms are more common in younger compared to older children,² there is a lack of information on whether there are differences in the clinical significance of psychotic symptoms across different stages of adolescence. In an attempt to improve our understanding of the clinical significance of psychotic symptoms in the general population, we examined data from four population studies, including two large population surveys and two in-depth clinical interview studies of psychotic symptoms. The aims of this work were (i) to investigate whether psychotic symptoms predicted non-psychotic clinical diagnoses and, if so, which disorders (ii) to investigate whether psychotic symptoms predicted more clinically severe disorder, in terms of comorbid psychopathology (i.e., having more than 1 diagnosis) and (iii) to investigate whether the significance of psychotic symptoms varied as a function of age.

Survey studies

Methods

Study 1: Early adolescence survey study (Adolescent Brain Development study)

Sixteen schools in Dublin, Ireland and surrounding areas, took part in this study. Participants were aged 11 to 13 years and were in 5th and 6th class in school, the two most senior classes in the Irish primary school system. This was an ‘opt in’ study, with written parental consent required for adolescents to take part. In total 2190 consent forms were distributed and 1131 (52%) parents gave signed consent for their child to complete the survey in school. A total of 88.9% of participants were Irish-born participants (compared to 90.3% of 0 to 14 year olds nationally in the 2006 national census).

Survey Study 2: Mid adolescence survey study (Saving and Empowering Young Lives in Europe study)¹⁹

Seventeen schools in Cork and Kerry, Ireland, took part in this study. Participants were aged 13 to 16 years and were attending second-level education. This was an ‘opt out’ study, with pupils allowed to take part if their parents did not return the consent form to specifically opt out. In total, 1602 consent forms were distributed and approximately 70% (n=1112) completed the survey in school. A total of 82.2% of participants were Irish born.

Exposure and Outcome measures

Both studies had a common exposure and outcome measure. Using the Adolescent Psychotic Symptom Screener (APSS),²⁰ we have previously shown that a question on auditory hallucinations (“Have you ever heard voices or sounds that no one else can hear?”) demonstrates very good positive and negative predictive validity not just for clinical interview-verifiable auditory hallucinations but for psychotic symptoms in general. This question was used in both survey studies to assess for psychotic symptoms (exposure measure). The Strengths and Difficulties Questionnaire (SDQ) was used as the measure of general psychopathology in both samples.²¹ The SDQ is a well-validated brief screening instrument, which asks about 25 attributes divided into subscales. The emotional disorders section assesses for anxiety, depressive and obsessive compulsive disorders, the conduct disorders section assesses for conduct and oppositional defiant disorders, and the hyperkinetic disorders section assesses for attention deficit/hyperactivity disorders. A ‘total difficulties’ score is also generated by summing the psychopathology subscales, which predicts the presence of any psychiatric disorder. The SDQ has been validated both in terms of its ability to distinguish between clinic and community samples²² and as a screening device to detect children with a mental health disorder.²¹ More recently, the SDQ has been shown not only to predict psychopathology at the same point in time but also to predict disorder status three years later.²³

Clinical Interview Studies

Study 3: Early adolescence interview study (Adolescent Brain Development study)²⁴

Participants in this clinical interview study were drawn from the larger survey study reported above (Study 1). Of the 1131 adolescents who took part in the survey study, 656 (58%) indicated an interest in taking part in the interview study and a sample of 212 of these were brought for interview. A total of 88.9% of participants were Irish-born (compared to 90.3% of 0 – 14 year olds nationally). Adolescents who attended for interview were no more likely to have an abnormal or borderline-abnormal score on the SDQ²¹ ($\chi^2=1.22$ (df=1) $p=0.27$) and did not differ significantly in their scores on the APSS²⁰ compared to the non-interviewed sample (interviewed group mean=1.8 (SE=0.12), non-interviewed group mean=1.9 (SE=0.19); $t=0.26$, $df=1130$, $p=0.79$).

Study 4: Mid adolescence interview study (Challenging Times study)^{25, 26}

This study was established to investigate the prevalence of psychiatric disorders and suicidal behaviour among Irish adolescents aged 13 to 15 years. The study was carried out in the geographical catchment area of a Child and Adolescent Mental Health Team in North Dublin with a population of 137,000. The participating schools were selected using a stratified random sampling technique according to the approximate socioeconomic class of the school in order to approximate to the geographical area population. A total of 743 pupils in eight mainstream schools were screened for psychiatric symptoms using the SDQ,²¹ and with the Children's Depression Inventory,²⁷ which assesses cognitive, affective and behavioural signs of depression. Written informed consent was obtained from the parent or guardian of participants. One hundred and forty adolescents scored above threshold on these instruments, indicating high risk of having mental health problems, and all of these adolescents were invited to interview, of whom 117 (83.6%)

agreed to attend for full psychiatric interview. A comparison group of 173 adolescents, matched for gender and school were also invited to attend, of whom 94 (54%) agreed. A frequency weight was applied to participants in the CT study to account for enrichment for psychopathology so that reported rates represent the general population rather than a psychopathology-enriched sample. Data were not collected on participant nationalities.

Exposure and Outcome Measures

The interview instrument used was the Schedule for Affective Disorders and Schizophrenia for School-aged Children, Present and Lifetime versions (K-SADS-PL).²⁸ The K-SADS is a well-validated semi-structured research diagnostic interview for the assessment of all Axis-1 psychiatric disorders in children and adolescents. Children and parents were interviewed separately, both answering the same questions about the child. In the early adolescence study, interviews were conducted by two psychiatrists and four psychologists and in the mid adolescence study, interviews were conducted by one psychiatrist and two psychologists, all trained in the use of the K-SADS. Inter-rater reliability was >90% for both studies (kappa = 0.83 (Study 3) and 0.85 (Study 4)). The Psychosis section of the K-SADS was used to assess the participants' psychotic symptoms (hallucinations and delusions). All interviewers recorded extensive notes of potential psychotic phenomena in this section of the interview and a clinical consensus meeting was held following the interviews to classify these phenomena as psychotic symptoms (or not), blind to diagnoses and all other information on the participants. The exposure measure was the presence or absence of psychotic symptoms and the outcome measure was a diagnosable lifetime affective, anxiety or behavioural disorder.

Statistical Analyses

Survey Studies

Statistical analyses were conducted using STATA version 11.0 for Windows. First, we used analysis of variance to test the association between auditory hallucinations and SDQ total difficulties score. Second, we divided the samples into quartiles based on their SDQ total difficulties scores and used logistic regression to test the odds of reporting psychotic symptoms in each quartile of (increasing) psychopathology. To test for a statistically significant increase (or decrease) in the prevalence of psychotic symptoms across the quartiles of SDQ-rated psychopathology, we used the STATA command *nptrend*, which is an extension of the Wilcoxon rank-sum test and performs a nonparametric test for trend across ordered groups. We also used logistic regression to compare the prevalence of auditory hallucinations among the 5% who scored highest on the SDQ total difficulties, which is often taken as a ‘severe’ psychopathology group, with the 5% who scored lowest on the SDQ total difficulties. Finally, we stratified by the number of SDQ-rated disorder domains (emotional, conduct and hyperkinetic disorders) and used logistic regression to determine whether psychotic symptoms predicted comorbidity across these domains and, therein, more severe psychopathology.

Interview Studies

Statistical analyses were conducted using STATA version 11.0 for Windows. Univariate and multivariate regression analyses were used to measure the relationship between psychopathology and psychotic symptoms. First, we report the prevalence of psychotic

symptoms in diagnosable affective, behavioural and anxiety disorders and report odds ratios and 95% confidence intervals. Second, we stratify by comorbidity/multiple pathology (i.e., having 2 or more Axis-1 diagnoses) in order to determine the prevalence of psychotic symptoms in increasingly severe (comorbid) disorders and report odds ratios and 95% confidence intervals for the association with psychotic symptoms. To test for a statistically significant increase (or decrease) in the prevalence of auditory hallucinations in line with the number of diagnosable psychiatric disorders, we used the STATA command *nptrend*, which is an extension of the Wilcoxon rank-sum test and performs a nonparametric test for trend across ordered groups.

Ethical approval for Study 1 was received from the Beaumont Hospital Medical Ethics Committee; for Study 2 from the Clinical Research Ethics Committee of the Cork Teaching Hospitals; for Study 3 from the Beaumont Hospital Medical Ethics Committee; for Study 4 from the Mater Misericordiae University Hospital Medical Ethics Committee.

Results

Results of Survey Studies

Studies 1 and 2: Association between psychotic symptoms and psychopathology

Psychotic symptoms were reported by 21% (n=239) of the early adolescence sample (Study 1) and 7% (n=77) of the mid adolescence sample (Study 2). Increasing 'total difficulties' scores on the SDQ were associated with increasing odds of reporting psychotic symptoms (Study 1: $F=94.72$, $p<0.001$; Study 2: $F=104.81$, $p<0.001$). Adolescents who scored within the top quartile for SDQ-measured psychopathology in the early adolescence study were 6.5 times more likely to report psychotic symptoms compared to those in the lowest quartile (test for trend, $Z = 8.60$, $p<0.001$). Adolescents who scored within the top quartile for SDQ-measured psychopathology in the mid adolescence study were nearly 16 times more likely to report psychotic symptoms compared to those in the lowest quartile (test for trend, $Z = 7.32$, $p<0.001$) (see Table 1). In fact, in Study 1, among adolescents with the top 5% most severe SDQ total difficulties scores, 48.1% reported psychotic symptoms, in contrast to just 2.9% of adolescents with the lowest 5% SDQ total difficulties score ($OR=31.10$, $CI_{95}=6.91-140.02$, $p<0.001$). In Study 2, among adolescents with the top 5% most severe 'total difficulties' scores, 35% reported psychotic symptoms, in contrast to just 1.4% of adolescents with the lowest 5% 'total difficulties' scores ($OR=38.78$, $CI_{95}=4.95-304.02$, $p<0.001$). Psychotic symptoms were not confined to any one disorder – rather they were reported at an increased prevalence across each of the SDQ-rated emotional, conduct and hyperkinetic disorders (see Table 2).

Comparisons between Study 1 and Study 2:

The risk for psychopathology in adolescents with psychotic symptoms varied as a function of age, with participants less likely to endorse the auditory hallucinations question as age increased. However, psychotic symptoms became more closely associated with psychopathology as age increased, in that 49% of the early adolescent sample who endorsed the auditory hallucinations question scored in the clinical psychopathology range on at least one SDQ-rated disorder domain compared to 65% of the mid adolescence sample (see Figure 1).

Multiple psychopathology in Study 1 and Study 2:

In order to investigate whether psychotic symptoms were more prevalent in adolescents with more severe psychopathology, we calculated the prevalence of psychotic symptoms among adolescents who scored positive for psychopathology on 1, 2 or all 3 of the disorder domains compared to adolescents with no disorder. In the early adolescence sample (Study 1), 15% of participants with no SDQ-rated disorders reported psychotic symptoms, compared to 33% of adolescents who were abnormal on 1 SDQ disorder domain (OR=2.71, CI95=1.85-3.98, $p<0.001$), 43% of adolescents who were abnormal on 2 SDQ disorder domains (OR=4.85, CI95=2.69-8.74, $p<0.001$) and 54% of adolescents who were abnormal on all 3 SDQ disorder domains (OR=8.59, CI95=2.00-36.92, $p<0.001$) (test for trend: $Z = 7.83$, $p<0.001$). Among the mid adolescence sample (Study 2), the prevalence of psychotic symptoms among those who were not abnormal on any of the 3 SDQ disorder domains was less than 4%, but for psychopathology in 1 domain the prevalence of hallucinations was 11% (OR=3.33, CI95=1.91-5.80, $p<0.001$),

for psychopathology in 2 domains the prevalence of hallucinations was 24% (OR=8.00, CI95=4.02-15.92, $p<0.001$), and for psychopathology in all 3 domains the prevalence of hallucinations was 33% (OR=12.96, CI95=4.53-37.08, $p<0.001$) (test for trend, $Z = 7.33$, $p<0.001$).

Results of Interview Studies

Thirty one percent of the early adolescence interview study sample (Study 3) had a lifetime diagnosable affective, anxiety or behavioural disorder. The lifetime disorders included depressive disorders, including major depressive disorder (MDD) and adjustment disorder with depressed mood (15%); behavioural disorders, including attention deficit/hyperactivity disorder (ADHD), oppositional defiant disorder and conduct disorder (9%); and anxiety disorders, including, generalized anxiety disorder, social phobia, separation anxiety disorder and obsessive compulsive disorder (14%).

Thirty four percent of the mid adolescent interview study sample (Study 4) had a lifetime diagnosable affective, anxiety or behavioural disorder. The lifetime disorders included depressive disorders, including MDD and adjustment disorder with depressed mood (18%); behavioural disorders, including ADHD, oppositional defiant disorder and conduct disorder (9%); and anxiety disorders, including generalized anxiety disorder, social phobia, separation anxiety disorder, obsessive compulsive disorder and panic disorder (11%).

Study 3: Psychotic symptoms and association with psychopathology – early adolescence

In the early adolescence sample, 22.6% (n=53) reported psychotic symptoms, primarily auditory hallucinations (>90%). The prevalence of psychotic symptoms was higher among males ($\chi^2=7.03$, $p<0.01$). While participants were asked about lifetime psychotic symptoms, in almost all cases adolescents who reported psychotic symptoms had experienced these symptoms within the past year – only 3 participants from the entire sample who reported lifetime psychotic symptoms did not report experiencing these symptoms within the past year, indicating that a report of lifetime symptoms in reality almost always indicates recent (within previous 12 months) symptoms. Of all adolescents who reported psychotic symptoms, 57% had a lifetime diagnosable Axis-1 disorder (OR=3.73, CI95=1.97-7.07, $p<0.001$) and 30.2% had a current diagnosable Axis-1 disorder (OR=3.46, CI95=1.64-7.31, $p<0.01$). Adolescents with a lifetime diagnosable affective disorder were 5-times more likely to report psychotic symptoms compared to the rest of the sample, while adolescents with a lifetime diagnosable behavioural disorder were 3-times more likely to report psychotic symptoms (see Table 3)

Study 4: Psychotic symptoms and association with psychopathology – mid-adolescence

In the mid-adolescence sample, 7% of participants reported psychotic symptoms, primarily auditory hallucinations (>90%). There was a trend for psychotic symptoms to be more prevalent among males ($\chi^2=3.62$, $p=0.057$). Of all adolescents who reported psychotic symptoms, 79% had a lifetime diagnosable Axis-1 disorder (OR=11.94,

CI95=3.14-45.41, $p<0.01$) and 43% had a current diagnosable Axis-1 disorder (OR=4.27, CI95=1.38-13.21, $p=0.01$). Adolescents with a lifetime diagnosable affective disorder were more than 10-times more likely to report psychotic symptoms compared to the rest of the sample, while adolescents with a lifetime diagnosable behavioural disorder were 5-times more likely to report psychotic symptoms (see Table 3).

Interview Studies: Multiple psychopathology

Multiple psychopathology (i.e., the presence of more than 1 diagnosable disorder) was present in 15% ($n=35$) of the early adolescence sample (Study 3). We observed a dose-response relationship between the number of diagnoses the adolescent had and their risk of reporting psychotic symptoms (see Table 4 and Figure 1). Multiple psychopathology was present in 10% ($n=21$) of the mid-adolescence sample (Study 4). We also observed a dose-response relationship between the number of diagnoses the adolescent had and their risk of reporting psychotic symptoms in this sample (see Table 4 and Figure 1).

Discussion

Using two large population-based survey studies and two in-depth clinical interview studies, we have shown a number of important findings. (i) Psychotic symptoms are prevalent in a wide range of non-psychotic psychopathologies. (ii) While psychotic symptoms are not pathognomonic of illness, the majority of young people in the community who report psychotic symptoms do have a diagnosable psychiatric disorder. (iii) Psychotic symptoms index particularly high risk for multiple pathology, that is having more than 1 DSM diagnosis. (iv) Psychotic symptoms are reported more commonly in early compared to middle adolescence. (v) Psychotic symptoms become increasingly predictive of diagnosable psychopathology with increasing age.

While some research has shown that the majority of psychotic symptoms in childhood are transient, with symptoms that persist over time thought to be of more clinical significance,²⁹ in the current study the majority of adolescents who reported psychotic symptoms had at least one diagnosable psychiatric disorder, regardless of the issue of psychotic symptom persistence. Increased risk for psychopathology was not related to a particular diagnosis or even one group of disorders; rather, a variety of Axis-1 disorders were associated with psychotic symptoms. Interestingly, however, psychotic symptoms demonstrated a particularly strong relationship with more severe psychopathology, with prevalence of psychotic symptoms increasing in a dose-response fashion with the number of diagnosable disorders. In Study 4, for example, 40% of adolescents with three or more comorbid disorders reported psychotic symptoms, compared to just 8% of adolescents with only one disorder (see Table 3).

Psychotic symptoms were more common in early adolescence in both the surveyed and interviewed samples (21% to 23%) compared to middle adolescence (7% in both the surveyed and interviewed samples). This is in line with meta-analytic findings of a decline in prevalence of psychotic symptoms from childhood into adolescence.² However, associations between psychotic symptoms and diagnosable disorder were stronger in the older, compared to the younger, samples. While 57% of the early adolescence sample who reported psychotic symptoms had a diagnosable psychiatric disorder, nearly 80% of the mid adolescence sample who reported psychotic symptoms had at least 1 diagnosable disorder. In a study of younger children, aged 7 to 8, Bartels-Velthuis et al. found that auditory hallucinations were associated with only a minor increase in risk for parent-reported behavioural and emotional symptoms³⁰ but that at age 12 to 13 years psychotic symptoms predicted an approximately 3- to 5-fold increased risk of scoring in the clinical range of the Child Behaviour Checklist.¹⁸ Hallucinatory and delusional experiences, then, may fall within the normal spectrum of experience in childhood but might be expected to discontinue in the course of development. Psychotic symptoms in adolescence, the current findings suggest, become increasingly associated with psychopathology – in particular with severe, multiple diagnoses (see Figure 1).

There are a number of possible explanations as to how psychotic symptoms act as a marker for a wide range of psychopathology. One possibility is that the same risk factors may predispose to both psychotic symptoms and psychiatric illness. In fact, Breetvelt et al. have recently demonstrated that many risk factors that have typically been considered

risk factors for psychosis are risk factors for a wider range of (non-psychotic) psychopathology.³¹ It is also possible that psychological distress caused by psychotic symptoms contributes to, for example, depressive thoughts or behavioural symptoms. It may also be the case, however, that psychotic symptoms do not contribute to psychopathology per se but, rather, emerge in vulnerable individuals who experience non-psychotic psychopathology and therein act as a marker, rather than an aetiological factor, for non-psychotic psychopathology. From a biological perspective, Alemany et al. have recently published the first study documenting a molecular genetic association, showing an interaction between the BDNF val-met polymorphism and childhood trauma in increasing risk for psychotic symptoms.³² The limited structural and functional magnetic resonance imaging (MRI) research on psychotic symptoms to date suggests that adolescents with psychotic symptoms exhibit a profile of subtle neurodevelopmental differences that shares features with a number of psychiatric disorders.³³ A recent meta-analysis of brain volume abnormalities in major depressive disorder, for example, showed that the greatest changes occur in two regions important in emotion processing and stress regulation – the cingulum and orbitofrontal cortex,³⁴ both of which we have recently shown to be abnormal in adolescents with psychotic symptoms.³³ Using functional MRI and digital tractography, we have demonstrated reduced activity within the right frontal and bilateral temporal cortices during response inhibition tasks and overall reduced integrity of fronto-temporal pathways in adolescents with psychotic symptoms,³³ supporting a profile of a relative disinhibition/pro-impulsivity phenotype. These neurobiological findings mirror our clinical findings of increased affective and behavioural disorders. From a psychological perspective, psychotic symptoms in young

people have been linked to poorer theory of mind and an externalised locus of control,³⁵
³⁶ both of which have been shown to predict poorer mental health outcomes.^{37, 38}

The relevance of the current findings extends beyond adolescent mental health; the finding that psychotic symptoms are highly prevalent in a range of (non-psychotic) disorders raises questions about traditional diagnostic boundaries. While psychosis has conventionally been considered as separate to ‘neurotic’ disorders, a number of researchers have questioned the independence of the psychoses and non-psychotic psychopathology.³⁹⁻⁴¹ The findings of the current work, which show that psychotic symptoms are prevalent in a wide variety of non-psychotic disorders, suggest that divisions between the neuroses and psychoses are not clear cut.

There are a number of strengths to the current paper, most notably the use of four studies, each of which shows the same pattern of results. While the larger survey studies allowed us to test for relationships between psychotic symptoms and psychopathology in terms of a symptomatic continuum, the downside of this approach is that clinical implications, in the absence of actual diagnoses, can be hard to draw. However, the inclusion of two clinical interview studies allows us to draw clear clinical implications by exploring the relationship between psychotic symptoms and actual psychiatric diagnoses. The use of multiple studies also allowed us to examine the relationship between psychotic symptoms and psychopathology from early through middle adolescence. In addition, the use of community samples is particularly valuable because findings are generalisable to the population. A limitation is that the issue of temporality cannot be resolved in the current

study i.e., which came first: psychotic symptoms or psychopathology, or, indeed, did both arise together. However, this does not detract from the clinical utility of understanding the contemporaneous relationship between psychotic symptoms and non-psychotic psychopathology. Subgroup analyses within studies means that there are small groups and confidence intervals, as a result, are wide in some cases. However, the same pattern of results was found across all four studies showing that the findings are robust.

Conclusion

Hallucinations and delusions, while classically known as symptoms of psychosis, are common in a wide range of non-psychotic psychiatric disorders in young people. These symptoms become increasingly associated with diagnosable psychopathology with age. Psychotic symptoms demonstrated a particularly strong relationship with more severe psychopathology, indexing high risk for multiple disorders (i.e., the presence of 2 or more co-occurring diagnoses). The immediate clinical implications of these findings are that (i) psychotic symptoms, which are to a large extent seen as an ‘adult psychiatry’ issue, are in fact very prevalent in childhood and adolescence and should be carefully assessed in child and adolescent psychiatric clinics, and (ii) when psychotic symptoms are present, they index risk for severe psychopathology, in terms of the patient having more than one diagnosable disorder and, following from this, the potential importance of multiple therapeutic targets or approaches. For researchers, these findings highlight psychotic symptoms as a complex novel aspect in the study of the aetiology of severe mental illness, of which schizophrenia is only one. Research has only recently begun on neuro-genetics, imaging, electrophysiology and cognition among individuals with psychotic

symptoms.^{32, 33, 42-44} Much more work will be necessary to explore the role of psychotic symptoms – symptoms which, to date, have been largely considered features of psychotic illness – in the aetiology of a broad range of non-psychotic psychiatric disorders.

References

1. Kelleher I, Jenner JA, Cannon M. Psychotic symptoms in the general population - an evolutionary perspective. *Br J Psychiatry* 2010; **197**: 167-9.
2. Kelleher I, Connor D, Clarke MC, Devlin N, Harley M, Cannon M. Prevalence of psychotic symptoms in childhood and adolescence: a systematic review and meta-analysis of population-based studies. *Psychol Med* In Press.
3. Johns LC, Cannon M, Singleton N, Murray RM, Farrell M, Brugha T, et al. Prevalence and correlates of self-reported psychotic symptoms in the British population. *Br J Psychiatry* 2004; **185**: 298-305.
4. Laurens KR, West SA, Murray RM, Hodgins S. Psychotic-like experiences and other antecedents of schizophrenia in children aged 9-12 years: a comparison of ethnic and migrant groups in the United Kingdom. *Psychol Med* 2008; **38**: 1103-11.
5. Polanczyk G, Moffitt TE, Arseneault L, Cannon M, Ambler A, Keefe RS, et al. Etiological and clinical features of childhood psychotic symptoms: results from a birth cohort. *Arch Gen Psychiatry* 2010; **67**: 328-38.
6. Scott J, Welham J, Martin G, Najman J, O'Callaghan M, Williams G, et al. Demographic correlates of psychotic-like experience in young Australian adults. *Acta Psychiatr Scand* 2008; **118**: 230-7.
7. Kelleher I, Harley M, Lynch F, Arseneault L, Fitzpatrick C, Cannon M. Associations between childhood trauma, bullying and psychotic symptoms among a school-based adolescent sample. *Br J Psychiatry* 2008; **193**: 378-82.
8. Kuepper R, van Os J, Lieb R, Wittchen HU, Hofler M, Henquet C. Continued cannabis use and risk of incidence and persistence of psychotic symptoms: 10 year follow-up cohort study. *BMJ* 2011; **342**: d738.
9. Kelleher I, Cannon M. Psychotic-like experiences in the general population: characterizing a high-risk group for psychosis. *Psychol Med* 2011; **41**: 1-6.
10. Poulton R, Caspi A, Moffitt TE, Cannon M, Murray R, Harrington H. Children's self-reported psychotic symptoms and adult schizophreniform disorder: a 15-year longitudinal study. *Arch Gen Psychiatry* 2000; **57**: 1053-8.
11. Welham J, Scott J, Williams G, Najman J, Bor W, O'Callaghan M, et al. Emotional and behavioural antecedents of young adults who screen positive for non-affective psychosis: a 21-year birth cohort study. *Psychol Med* 2009; **39**: 625-34.
12. Wigman JT, Vollebergh WA, Raaijmakers QA, Iedema J, van Dorsselaer S, Ormel J, et al. The structure of the extended psychosis phenotype in early adolescence--a cross-sample replication. *Schizophr Bull* 2011; **37**: 850-60.
13. Nishida A, Tani H, Nishimura Y, Kajiki N, Inoue K, Okada M, et al. Associations between psychotic-like experiences and mental health status and other psychopathologies among Japanese early teens. *Schizophr Res* 2008; **99**: 125-33.
14. Scott J, Martin G, Welham J, Bor W, Najman J, O'Callaghan M, et al. Psychopathology during childhood and adolescence predicts delusional-like experiences in adults: a 21-year birth cohort study. *Am J Psychiatry* 2009; **166**: 567-74.
15. Varghese D, Scott J, Welham J, Bor W, Najman J, O'Callaghan M, et al. Psychotic-like experiences in major depression and anxiety disorders: a population-based survey in young adults. *Schizophr Bull* 2011; **37**: 389-93.

16. De Loore E, Gunther N, Drukker M, Feron F, Sabbe B, Deboutte D, et al. Persistence and outcome of auditory hallucinations in adolescence: a longitudinal general population study of 1800 individuals. *Schizophr Res* 2011; **127**: 252-6.
17. Yung AR, Buckby JA, Cosgrave EM, Killackey EJ, Baker K, Cotton SM, et al. Association between psychotic experiences and depression in a clinical sample over 6 months. *Schizophr Res* 2007; **91**: 246-53.
18. Bartels-Velthuis AA, van de Willige G, Jenner JA, van Os J, Wiersma D. Course of auditory vocal hallucinations in childhood: 5-year follow-up study. *Br J Psychiatry* 2011.
19. Wasserman D, Carli V, Wasserman C, Apter A, Balazs J, Bobes J, et al. Saving and empowering young lives in Europe (SEYLE): a randomized controlled trial. *BMC Public Health* 2010; **10**: 192.
20. Kelleher I, Harley M, Murtagh A, Cannon M. Are screening instruments valid for psychotic-like experiences? A validation study of screening questions for psychotic-like experiences using in-depth clinical interview. *Schizophr Bull* 2011; **37**: 362-9.
21. Goodman R, Ford T, Simmons H, Gatward R, Meltzer H. Using the Strengths and Difficulties Questionnaire (SDQ) to screen for child psychiatric disorders in a community sample. *Br J Psychiatry* 2000; **177**: 534-9.
22. Goodman R. The Strengths and Difficulties Questionnaire: a research note. *J Child Psychol Psychiatry* 1997; **38**: 581-6.
23. Goodman A, Goodman R. Strengths and Difficulties Questionnaire as a Dimensional Measure of Child Mental Health. *Journal of the American Academy of Child & Adolescent Psychiatry* 2009; **48**: 400-3.
24. Kelleher I, Murtagh A, Molloy C, Roddy S, Clarke MC, Harley M, et al. Identification and Characterization of Prodromal Risk Syndromes in Young Adolescents in the Community: A Population-Based Clinical Interview Study. *Schizophr Bull* 2011; doi: 10.1093/schbul/sbr164.
25. Lynch F, Mills C, Daly I, Fitzpatrick C. Challenging times: prevalence of psychiatric disorders and suicidal behaviours in Irish adolescents. *J Adolesc* 2006; **29**: 555-73.
26. Harley M, Kelleher I, Clarke M, Lynch F, Arseneault L, Connor D, et al. Cannabis use and childhood trauma interact additively to increase the risk of psychotic symptoms in adolescence. *Psychol Med* 2010; **40**: 1627-34.
27. Kovacs M. The Children's Depression, Inventory (CDI). *Psychopharmacol Bull* 1985; **21**: 995-8.
28. Kaufman J, Birmaher B, Brent D, Rao U, Ryan N. The schedule for affective disorders and schizophrenia for school aged children: present and lifetime version. University of Pittsburgh, Western Psychiatric Institute and Clinic. 1996.
29. 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**: 179-95.
30. Bartels-Velthuis AA, Jenner JA, van de Willige G, van Os J, Wiersma D. Prevalence and correlates of auditory vocal hallucinations in middle childhood. *Br J Psychiatry* 2010; **196**: 41-6.

31. Breetvelt EJ, Boks MP, Numans ME, Selten JP, Sommer IE, Grobbee DE, et al. Schizophrenia risk factors constitute general risk factors for psychiatric symptoms in the population. *Schizophr Res* 2010; **120**: 184-90.
32. Alemany S, Arias B, Aguilera M, Villa H, Moya J, Ibanez MI, et al. Childhood abuse, the BDNF-Val66Met polymorphism and adult psychotic-like experiences. *Br J Psychiatry* 2011; **199**: 38-42.
33. Jacobson S, Kelleher I, Harley M, Murtagh A, Clarke M, Blanchard M, et al. Structural and functional brain correlates of subclinical psychotic symptoms in 11-13 year old schoolchildren. *Neuroimage* 2010; **49**: 1875-85.
34. Koolschijn PC, van Haren NE, Lensvelt-Mulders GJ, Hulshoff Pol HE, Kahn RS. Brain volume abnormalities in major depressive disorder: a meta-analysis of magnetic resonance imaging studies. *Hum Brain Mapp* 2009; **30**: 3719-35.
35. Thompson A, Sullivan S, Lewis G, Zammit S, Heron J, Horwood J, et al. Association between locus of control in childhood and psychotic symptoms in early adolescence: results from a large birth cohort. *Cogn Neuropsychiatry* 2011; **16**: 385-402.
36. Bartels-Velthuis AA, Blijd-Hoogewys EM, van Os J. Better theory-of-mind skills in children hearing voices mitigate the risk of secondary delusion formation. *Acta Psychiatr Scand* 2011; **124**: 193-7.
37. Liu X, Kurita H, Uchiyama M, Okawa M, Liu L, Ma D. Life events, locus of control, and behavioral problems among Chinese adolescents. *Journal of Clinical Psychology* 2000; **56**: 1565-77.
38. Brune M, Brune-Cohrs U. Theory of mind--evolution, ontogeny, brain mechanisms and psychopathology. *Neuroscience and biobehavioral reviews* 2006; **30**: 437-55.
39. Garety PA, Kuipers E, Fowler D, Freeman D, Bebbington PE. A cognitive model of the positive symptoms of psychosis. *Psychol Med* 2001; **31**: 189-95.
40. Freeman D, Garety PA. Connecting neurosis and psychosis: the direct influence of emotion on delusions and hallucinations. *Behav Res Ther* 2003; **41**: 923-47.
41. Freeman D, Garety PA, Kuipers E, Fowler D, Bebbington PE. A cognitive model of persecutory delusions. *Br J Clin Psychol* 2002; **41**: 331-47.
42. Cullen AE, Dickson H, West SA, Morris RG, Mould GL, Hodgins S, et al. Neurocognitive performance in children aged 9-12 years who present putative antecedents of schizophrenia. *Schizophr Res* 2010; **121**: 15-23.
43. Laurens KR, Hodgins S, Mould GL, West SA, Schoenberg PL, Murray RM, et al. Error-related processing dysfunction in children aged 9 to 12 years presenting putative antecedents of schizophrenia. *Biol Psychiatry* 2010; **67**: 238-45.
44. Blanchard MM, Jacobson S, Clarke MC, Connor D, Kelleher I, Garavan H, et al. Language, motor and speed of processing deficits in adolescents with subclinical psychotic symptoms. *Schizophr Res* 2010; **123**: 71-6.

Table 1: Odds of experiencing psychotic symptoms according to SDQ psychopathology scores in quartiles (a) unadjusted and (b) adjusted for sex in Study 1 (early adolescence survey study) and Study 2 (mid adolescence survey study).

Quartile	N	% with psychotic symptoms	Early adolescence survey study		N	% with psychotic symptoms	Mid adolescence survey study	
			OR (CI95)				OR (CI95)	
			(a)	(b)			(a)	(b)
1	313	7.7%	1	1	278	1.4%	1	1
2	322	18%	2.31 (1.42-3.76)	1.91 (1.10-3.32)	234	3.4%	2.40 (0.71-8.07)	2.35 (0.69-7.90)
3	221	22.2%	3.00 (1.81-4.97)	2.59 (1.45-4.60)	250	5.7%	4.07 (1.32-12.55)	4.08 (1.32-12.59)
4	276	38.2%	6.50 (4.09-10.33)	5.50 (3.25-9.30)	235	19%	15.80 (5.58-44.71)	15.82 (5.57-44.94)
Test for trend across quartiles			Z=8.60, p<0.001				Z=7.32, p<0.001	

SDQ, Strengths and Difficulties Questionnaire

Table 2: Odds of experiencing psychotic symptoms among adolescents with SDQ-rated emotional, hyperkinetic and conduct disorders
 (a) unadjusted and (b) adjusted for sex in Study 1 (early adolescence survey study) and Study 2 (mid adolescence survey study).

	% with psychotic symptoms	Early adolescence survey study		% with psychotic symptoms	Mid adolescence survey study	
		OR (CI95)			OR (CI95)	
		(a)	(b)		(a)	(b)
Emotional disorders	44%	3.44 (2.33-5.10)	2.98 (1.89-4.69)	22%	4.79 (2.78-8.28)	5.19 (2.97-9.06)
Hyperkinetic disorders	35%	2.34 (1.62-3.37)	2.74 (1.80-4.18)	15%	3.06 (1.86-5.04)	3.00 (1.81-4.98)
Conduct disorders	36%	2.38 (1.63-3.48)	2.91 (1.85-4.58)	20%	4.60 (2.75-7.71)	4.68 (2.77-7.93)

SDQ, Strengths and Difficulties Questionnaire

Table 3: Odds of experiencing psychotic symptoms among adolescents with lifetime DSM IV Axis-1 diagnoses diagnosed by clinical interview (a) unadjusted and (b) adjusted for sex in Study 3 (early adolescence interview study) and Study 4 (mid adolescence interview study)

Diagnosis	% with psychotic symptoms	Early adolescence interview study OR (CI95)		% with psychotic symptoms	Mid adolescence interview study OR (CI95)	
		(a)	(b)		(a)	(b)
Any lifetime Axis-1 disorder	40%	3.73 (1.97-7.07)	3.57 (1.87-6.84)	19%	11.15 (2.99-41.65)	11.94 (3.14-45.41)
Affective disorders	51%	4.93 (2.31-10.51)	5.08 (2.33-11.07)	24%	10.67 (3.33-34.19)	12.33 (3.69-41.19)
Behavioural disorders	50%	3.95 (1.55-10.10)	3.23 (1.24-8.43)	22%	5.14 (1.43-18.51)	4.55 (1.23-16.75)
Anxiety disorders	23%	0.99 (0.48-2.06)	1.01 (0.48-2.12)	9%	1.45 (0.30-6.95)	1.67 (0.34-8.22)

Table 4: Odds of experiencing psychotic symptoms in adolescents with one, two or three or more comorbid DSM-IV Axis-1 disorders diagnosed by clinical interview, (a) unadjusted and (b) adjusted for sex, in Study 3 (early adolescence interview study) and Study 4 (mid adolescence interview study).

Diagnosis	% with psychotic symptoms	Early adolescence interview study		% with psychotic symptoms	Mid adolescence interview study	
		OR (CI95)			OR (CI95)	
		(a)	(b)		(a)	(b)
One disorder only	29%	2.25 (1.06-4.75)	2.27 (1.06-4.87)	8%	3.86 (0.83-17.88)	4.12 (0.88-19.38)
Two disorders only	38%	3.23 (1.27-8.27)	3.18 (1.22-8.29)	31%	20.15 (4.24-95.59)	18.33 (3.77-89.15)
Three or more disorders	55%	6.47 (1.82-22.98)	6.31 (1.73-23.05)	40%	29.56 (3.53-247.17)	36.18 (3.94-332.06)
Test for trend		Z = 3.67, p < 0.001			Z = 4.29, p < 0.001	

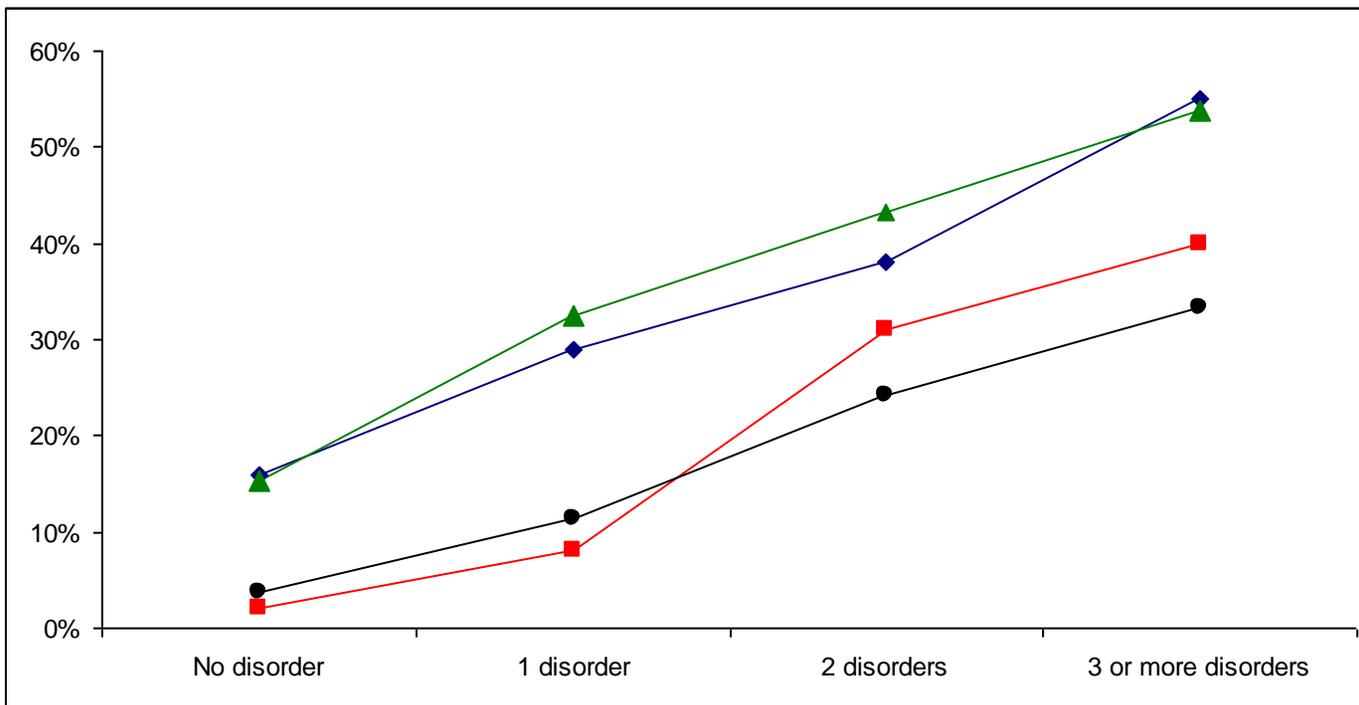


Figure 1: Prevalence of psychotic symptoms by comorbid diagnoses in the early adolescence survey sample (study 1: green line), early adolescence interview sample (study 3: blue line), mid adolescence survey sample (study 2: black line) and mid adolescence interview sample (study 4: red line)