

# Precursors and correlates of transient and persistent longitudinal profiles of psychotic experiences from late childhood through early adulthood

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## Background

Psychotic experiences are reported by 5–10% of young people, although only a minority persist and develop into psychotic disorders. It is unclear what characteristics differentiate those with transient psychotic experiences from those with persistent psychotic experiences that are more likely to be of clinical relevance.

## Aims

To investigate how longitudinal profiles of psychotic experiences, created from assessments at three different time points, are influenced by early life and co-occurring factors.

## Method

Using data from 8045 individuals from a birth cohort study, longitudinal profiles of psychotic experiences based on semi-structured interviews conducted at 12, 18 and 24 years were defined. Environmental, cognitive, psychopathological and genetic determinants of these profiles were investigated, along with concurrent changes in psychopathology and cognition.

## Results

Following multiple imputations, the distribution of longitudinal profiles of psychotic experiences was none (65.7%), transient (24.1%), low-frequency persistent (8.4%) and high-frequency

persistent (1.7%). Individuals with high-frequency persistent psychotic experiences were more likely to report traumatic experiences, other psychopathology, a more externalised locus of control, reduced emotional stability and conscientious personality traits in childhood, compared with those with transient psychotic experiences. These characteristics also differed between those who had any psychotic experiences and those who did not.

## Conclusions

These findings indicate that the same risk factors are associated with incidence as with persistence of psychotic experiences. Thus, it might be that the severity of exposure, rather than the presence of specific disease-modifying factors, is most likely to determine whether psychotic experiences are transient or persist, and potentially develop into a clinical disorder over time.

## Keywords

Risk factors; schizophrenia; childhood experience; Avon Longitudinal Study of Parents and Children; psychotic disorders.

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Psychotic experiences are not uncommon, with at least 5–10% of individuals experiencing a psychotic experience during their lifetime.<sup>1,2</sup> Although most experiences occur outside the context of a psychotic disorder, the risk of developing a psychotic disorder such as schizophrenia in adulthood is increased in those reporting psychotic experiences during childhood and adolescence.<sup>2,3</sup>

Psychotic experiences can be highly distressing and are associated with adverse outcomes such as impaired social and occupational functioning and suicidal thoughts.<sup>4–8</sup> However, in most cases psychotic experiences are transient, only ever occurring on a few instances.<sup>1,9,10</sup> Studying such transient experiences is likely to be less informative for understanding the aetiology or prediction of later psychiatric disorder compared with studying persistent or frequently recurring psychotic experiences.<sup>2,9,11,12</sup> Longitudinal studies with repeated measures of psychotic experiences allow researchers to study trajectories of psychotic experiences over time, while minimising misclassification error from single time-point assessments.<sup>13</sup> The few studies that have been able to quantify longitudinal profiles of psychotic experiences have shown that substance use, other psychopathology, and victimisation are more common in those with increasing or persistently high probabilities of having psychotic experiences across time.<sup>6,14–18</sup> However, as the baseline class in these studies combined individuals with either no or low levels of psychotic experiences, they do not provide information on factors that differentiate between incidence and persistence

of psychotic experiences. Additionally, these studies<sup>15–18</sup> have relied on self-reported measures of psychotic experiences that overestimate the presence of psychotic experiences compared with semi-structured interview measures,<sup>11,19</sup> potentially leading to biased (most likely underestimated) estimates of association.

## Aim

To address these limitations, we aimed to (a) define temporal longitudinal profiles of psychotic experiences, using semi-structured interviews assessed at three time points over a 12-year period in the population-based Avon Longitudinal Study of Parents and Children (ALSPAC) birth cohort; (b) investigate environmental, cognitive, psychopathological and genetic precursors of these longitudinal profiles; and (c) describe concurrent changes in other psychopathology, cognition and social functioning over this 12-year period.

## Method

### Sample

The ALSPAC cohort initially comprised offspring of pregnant women resident in Avon, UK, with expected delivery dates between 1 April 1991 and 31 December 1992 ( $N = 14\,541$ ; 13 988 infants were alive at 1 year). Further recruitment of eligible cases

resulted in a sample of 15 454 pregnancies, of which 14 901 infants were alive at 1 year of age. For information about data available see <http://www.bris.ac.uk/alspac/researchers/data-access/data-dictionary/>. Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. Informed consent for the use of data collected via questionnaires and clinics was obtained from participants, following the recommendations of the ALSPAC Ethics and Law Committee at the time. Study data after 2014 were collected with REDCap (Research Electronic Data CAPture tools); a secure web application for online data collection, hosted at the University of Bristol (<https://catalyst.harvard.edu/redcap/>).<sup>20,21</sup>

The sample used for this study comprised 8045 individuals who participated in at least one Psychosis-Like Symptoms (PLIKS) interview (see below) from the assessments at 12 ( $n = 6822$ ), 18 ( $n = 5213$ ) and 24 ( $n = 3862$ ) years of age. Although the original cohort was representative of the target population,<sup>22–24</sup> individuals included in this sample differed from the original cohort in that they were more likely to be female and have slightly higher verbal and performance IQ (Supplementary Table 1 available at <https://doi.org/10.1192/bjp.2021.145>).

## Outcome measures

Longitudinal profiles of psychotic experiences

The semi-structured PLIKS interview was used at ages 12 (mean 12.8, s.d. 0.23), 18 (mean 17.8, s.d. 0.46) and 24 (mean 24.1, s.d. 0.85) years, to assess current (past 6 months) psychotic experiences.<sup>2,11,25</sup> The PLIKS interview assesses 12 key psychotic experiences, including hallucinations, delusions and experiences of thought interference. Structured stem questions are followed by cross-questioning to establish whether the experience was psychotic or not, and to establish the frequency of these experiences over the previous 6 months. Coding of psychotic experiences followed glossary definitions and rating rules for the Schedules for Clinical Assessment in Neuropsychiatry.<sup>26</sup> Interviewers rated psychotic experiences as not present, suspected or definitely present (see Supplementary material for more detail).

We used an empirical approach rather than a latent model approach to derive our profiles of psychotic experiences over time, as latent models were unstable and underlying assumptions could not be met. To generate psychotic experience longitudinal profiles, a measure at each time point was constructed that reflected the current (average over past 6 months) frequency of the most frequently occurring suspected or definite psychotic experience (0: 'no psychotic experiences'; 1: 'low-frequency psychotic experiences', defined as psychotic experiences occurring less than once per week; 2: 'high-frequency psychotic experiences', defined as psychotic experiences occurring weekly or daily). These were then used to create four longitudinal profiles (based on the balance between the number of groups that could be meaningfully examined and greatest discrimination of patterns over time) that summarised the psychotic experience data across the three time points, and maximised the use of the available information:

- No psychotic experiences: individuals without a psychotic experience at any time point.
- Transient psychotic experiences: individuals with a psychotic experience rated at only one time point, regardless of frequency (reference group for primary analyses comparing persistent and transient profiles).
- Low-frequency persistent psychotic experiences: individuals with a low-frequency psychotic experience at two or more time points, or with a low-frequency rating at one time point and a high-frequency rating at another.

- High-frequency persistent psychotic experiences: individuals with a high-frequency psychotic experience rated at two or more time points.

As a secondary analysis, we also examined age 12–18 years profiles and age 18–24 years profiles, to see whether predictors of persistence differed across developmental stages (see Supplementary material).

## Precursors

Family psychiatric history

We collected data on the presence of depression or schizophrenia in the parents and grandparents of participants.

Genetic data

We obtained polygenic risk scores (at discovery sample  $P$ -value thresholds of 0.05<sup>27</sup>) for schizophrenia,<sup>28</sup> major depression<sup>29</sup> and neuroticism.<sup>30</sup>

Sociodemographic characteristics

Data on gender, maternal social class (higher versus lower), and maternal education (one or more O-level versus lower) were collected from parental questionnaires administered around the time of birth.

Pregnancy and birth measures

These included binary measures of self-reported maternal cigarette smoking during pregnancy, self-reported maternal infection during third trimester of pregnancy, and hypoxia at birth (obstetric records).

Cognitive, psychopathology and trauma measures

All measures were continuous and standardised unless otherwise stated. Verbal IQ and performance IQ were assessed at 8 years of age, using the Wechsler Intelligence Scale for Children.<sup>31</sup> External locus of control was assessed at 8 years of age, using the 12-item Children's Nowicki Strickland Internal-External Control Scale.<sup>32</sup> Emotional and behavioural difficulties were assessed with the Strengths and Difficulties Questionnaire total score,<sup>33</sup> and depression was assessed with the Short Moods and Feelings Questionnaire,<sup>34</sup> both administered at 11 years of age. Borderline personality disorder traits covering the nine DSM-IV criteria for disorder were assessed at 11 years of age, and a binary variable was derived, using a cut-off of five or more criteria to define those at highest risk of having a disorder.<sup>35</sup> The Big Five personality domains (extraversion, agreeableness, conscientiousness, emotional stability and intellect/openness) were assessed at 14 years (hence measured after the start of the profiles, but included here as they are trait measures, so likely reflecting pre-psychotic experience characteristics), using the International Personality Item Pool.<sup>36</sup> A categorical measure reflecting the number of types (0–4) of childhood trauma exposure (ages 0–10 years) was derived with data from assessments completed by the parents or self-reported by the participants.<sup>37</sup> Self-harm (binary measure of child reporting whether they had 'hurt him/herself on purpose') was assessed at 11 years of age. The existence of nightmares or night terrors (binary measure) was assessed during a semi-structured interview at 12 years of age.

## Concurrent measures

Additional measures assessed concurrently to the psychotic experience measures (i.e. between ages 12 and 24 years) were examined to

relate patterns of these over time to the psychotic experience profiles: tobacco use (at least weekly compared with non-weekly smoking at ages 10, 12, 15 and 24 years); cannabis use (at least weekly compared with non-weekly use at ages 12, 15, 17 and 24 years); negative symptoms (assessed with the Community Assessment of Psychic Experience questionnaire,<sup>38</sup> administered at ages 16 (past month), 23 (past year) and 24 (past year) years); past-year self-harm (at ages 16, 18, 21, 24 and 25 years); depression and generalised anxiety disorder (current, assessed with the CIS-R,<sup>39</sup> administered at ages 18 and 24 years); vocabulary and digit symbol scores (assessed as part of the Wechsler Intelligence Scale for Children<sup>31</sup> at ages 8, 15 (digit symbol score only) and 24 years); and friendship quality (using the item 'I talk with my friends about my problems' from the Cambridge Friendship Questionnaire,<sup>40</sup> administered at ages 8, 14, 17 and 24 years).

**Missing data**

The number of individuals participating in one, two or all three of the PLIKS interviews was 2931, 2371 and 2743, respectively. The proportion of people with missing data on the precursors/concurrent measures ranged from 0 to 44.6% (see Supplementary Table 2 for more detail). We used multiple imputation to minimise the selection bias likely from using a complete-case approach.

**Statistical analysis**

Statistical analyses were undertaken with R version 3.6.0 for Windows or Stata version 15.1 for Windows. We performed multiple imputation, using the R package 'mice', to impute values (and uncertainty around these) for all missing data up to the sample who had participated in at least one PLIKS interview (*n* = 8045). All precursor, concurrent and outcome variables described

above were used to impute any missing data. Additionally, when imputing psychotic experience data, we also used self-reported measures of psychotic-like experiences assessed with the PLIKS questionnaires<sup>16</sup> at ages 11, 13, 14, 16 and 22 years, to make the missing at random assumption more plausible (see Supplementary material for more details). The psychotic experience profiles were passively imputed with the underlying composite frequency variables actively imputed in each instance.

The associations between the precursors and psychotic experience profiles were examined with univariable multinomial logistic regressions separately in each of the imputed data-sets, with Rubin's rules<sup>41</sup> used to create pooled estimates (effects in results referred to as odds ratios for clarity). Prevalence/means of concurrent measures at each age are plotted as figures, stratified by psychotic experience profiles.

**Results**

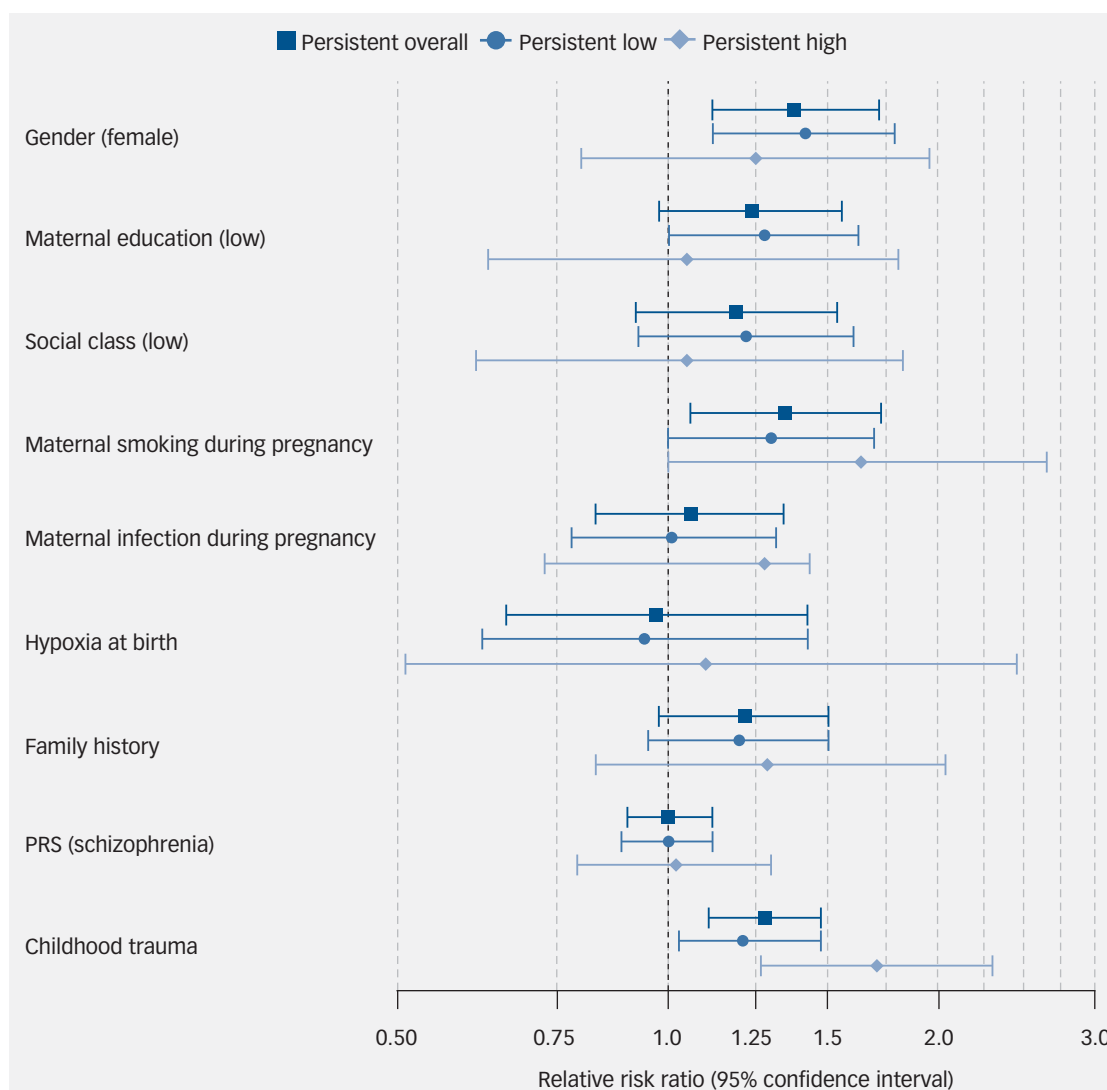
**Longitudinal profiles of psychotic experiences**

The proportions of participants in the imputed sample who were classified within each of the longitudinal profiles were as follows: no psychotic experiences (*n* = 5259, 65.4%), transient psychotic experiences (*n* = 1959, 24.3%), low-frequency persistent psychotic experiences (*n* = 687, 8.5%) and high-frequency persistent psychotic experiences (*n* = 140, 1.7%). There was a higher proportion of individuals with transient, low-frequency persistent and high-frequency persistent psychotic experiences in the imputed compared with the complete-case data, whereas the opposite was observed for the no psychotic experiences profile (Table 1; see also Supplementary Table 3 for more details on the complete-case sample).

**Table 1** Proportion or mean (s.d.) of demographic, genetic cognitive and psychopathological characteristics stratified by psychotic experience profile in the imputed sample (*n* = 8045)

Variable	Psychotic experiences				
	None	Transient	Persistent low	Persistent high	Persistent (any)
Female, %	52.6	51.2	59.8	56.7	59.3
Low maternal education, %	20.2	27.8	32.9	29.2	32.3
Low social class, %	16.3	21.7	25.4	22.8	25
Maternal smoking during pregnancy, %	16.3	22.7	27.8	32.7	28.6
Maternal infection during pregnancy, %	22.8	25.2	25.5	30.3	26.3
Hypoxia at birth, %	9.5	9.3	8.9	10.5	9.5
Family history of mental health problems, %	39.5	42	46.4	48.4	46.7
PRS (schizophrenia), mean (s.d.)	-0.05 (1)	0.01 (1)	0.01 (1)	0.02 (1)	0.03 (1)
PRS (depression), mean (s.d.)	-0.03 (1)	0.06 (1)	0.1 (1)	0.08 (1)	0.13 (1)
PRS (neuroticism), mean (s.d.)	-0.03 (1)	-0.02 (1)	0.04 (1)	0.07 (1)	0.04 (1)
Verbal IQ, mean (s.d.)	108.4 (19)	106.1(20)	105.1 (20)	103.7 (21.5)	104.9 (20)
Performance IQ, mean (s.d.)	101.5 (17)	99.8(17.3)	98.9 (17.1)	99 (17.8)	99 (17.3)
SDQ, mean (s.d.)	6.1 (4.7)	7.2 (5.1)	7.9 (5.5)	8.8 (5.6)	8 (5.5)
Locus of control, mean (s.d.)	5.8 (2.1)	6.2 (2)	6.5 (2.1)	6.7 (2.1)	6.55 (2.1)
MFQ, mean (s.d.)	2.1 (2.9)	2.7 (3.5)	3.3 (3.9)	3.6(4.1)	3.3 (4)
Extraversion, mean (s.d.)	35.1 (6.8)	35.3 (7)	35.8 (7.1)	34.8 (7.8)	35.6 (7.2)
Agreeableness, mean (s.d.)	37.8 (5.2)	37.5(5.4)	37.7 (5.5)	38 (6)	37.8 (5.6)
Conscientiousness, mean (s.d.)	32.2 (5.8)	31.2 (5.9)	30.3 (5.8)	29.4 (6.3)	30.2 (5.9)
Emotional stability, mean (s.d.)	32.1 (6.4)	30.4(6.6)	29 (6.7)	27.6(6.9)	28.8 (6.8)
Intellect/openness, mean (s.d.)	35.6 (6.0)	35.5(5.8)	35.9 (5.8)	36.1 (6.5)	35.9 (6)
Trauma types, mean (s.d.)	0.6 (0.9)	0.9 (1)	1 (1)	1.3 (1.1)	1.1 (1.1)
BPD diagnosis (%)	1.8	4.4	9.3	15.3	10.3
Nightmares/terrors (%)	25.2	36.2	49.8	51.7	50.1
Complete-case, <i>n</i> (%)	1982 (72.2)	545 (19.9)	188 (6.9)	28 (1)	216 (7.9)
Imputed, <i>n</i> (%)	5259 (65.4)	1959 (24.3)	687 (8.5)	140 (1.7)	827 (10.2)

Profiles were based on current psychotic experiences (past 6 months at ages 18 and 24 years; average past 8 months at age 12 years). Transient indicates transient or episodic psychotic experiences; persistent low indicates persistent or recurrent psychotic experiences with a frequency of less than once per week; persistent high indicates persistent or recurrent psychotic experiences with a frequency of weekly or daily; persistent (all) indicates persistent or recurrent psychotic experiences regardless of frequency. Complete-case refers to everyone with psychotic experience data at all three time points, whereas imputed refers to everyone with psychotic experience data on at least one time point. PRS, polygenic risk score; SDQ, Strengths and Difficulties Questionnaire; MFQ, Moods and Feelings Questionnaire; BPD, borderline personality disorder.



**Fig. 1** Univariable multinomial logistic regressions of persistent versus transient psychotic experiences (reference): sociodemographic characteristics, family history and childhood trauma. PRS, polygenic risk score.

### Precursors of psychotic experience profiles

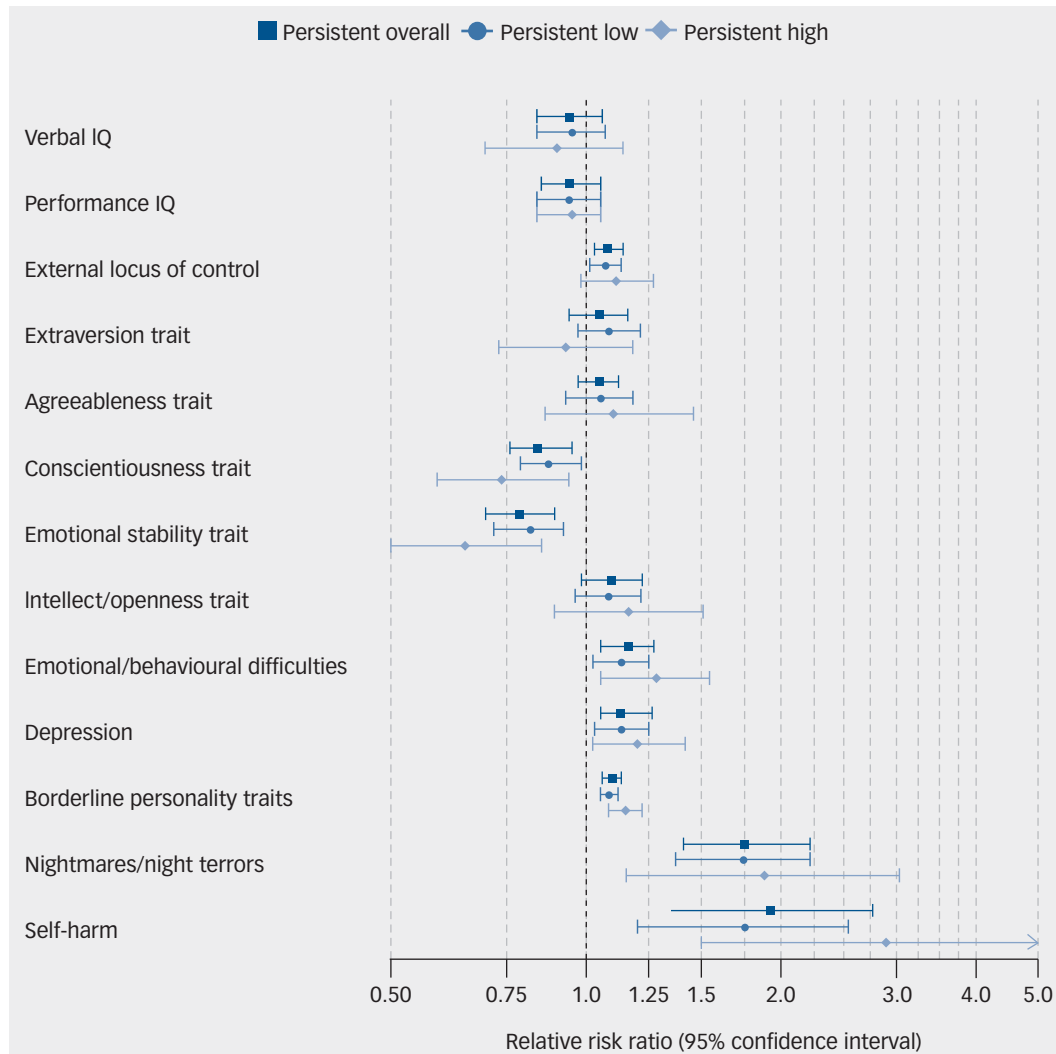
The demographic and childhood psychopathological and cognitive characteristics for the four profiles are summarised in Table 1, and comparisons between the transient and persistent profiles are presented in Figs 1 and 2, as well as Supplementary Table 4.

Compared with those with an outcome of transient psychotic experiences, there was evidence that individuals with an outcome of persistent psychotic experiences (low- and high-frequency combined) were more likely to be female (odds ratio 1.38, 95% CI 1.12–1.72) and have mothers who smoked during pregnancy (odds ratio 1.35, 95% CI 1.06–1.73). Additionally, they were more likely to have childhood emotional and behavioural problems (odds ratio 1.16, 95% CI 1.05–1.27), depression (odds ratio 1.13, 95% CI 1.05–1.26), borderline personality disorder traits (odds ratio 1.10, 95% CI 1.06–1.13), self-harming behaviours (odds ratio 1.93, 95% CI 1.35–2.76), nightmares (odds ratio 1.76, 95% CI 1.41–2.21), an externalised locus of control (odds ratio 1.08, 95% CI 1.02–1.14) and to have experienced traumatic events (odds ratio 1.28, 95% CI 1.11–1.48), compared with individuals with transient psychotic experiences. Individuals with

persistent psychotic experiences also differed on two of the personality traits, scoring lower on conscientiousness (odds ratio 0.84, 95% CI 0.75–0.94) and emotional stability (odds ratio 0.79, 95% CI 0.71–0.88).

For all of these characteristics, with the exception of female gender and maternal education, the effect estimates for the high-frequency persistent profiles were more extreme (i.e. further away from the transient profile average value) than those for the low-frequency persistent profile, although the confidence intervals for these two profiles overlapped (see Figs 1 and 2, and Supplementary Table 4).

There was weaker evidence that lower social class (odds ratio 1.19, 95% CI 0.92–1.54), maternal education (odds ratio 1.24, 95% CI 0.98–1.56) and family history of mental health problems (odds ratio 1.22, 95% CI 0.98–1.51) were more common in those with persistent compared with transient psychotic experiences, and little evidence that polygenic risk scores, maternal infection during pregnancy, birth hypoxia or IQ indices differed between the transient and persistent psychotic experience profiles. There was little evidence that predictors of persistence differed across developmental stages (see Supplementary Table 9).



**Fig. 2** Univariable multinomial logistic regressions of persistent versus transient psychotic experiences (reference): psychopathology and cognition.

Comparison with no psychotic experiences

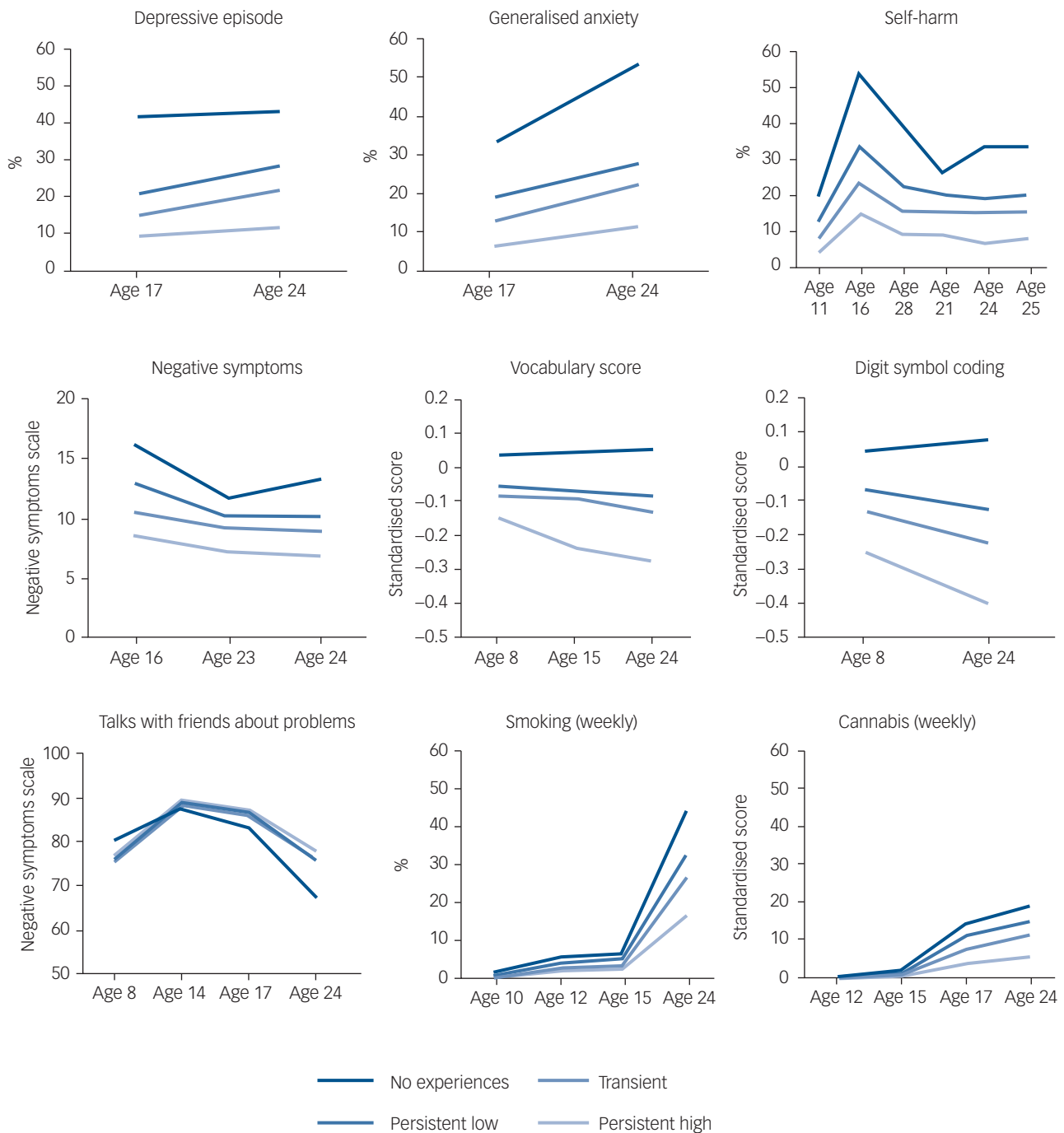
Most of the characteristics that differed between persistent and transient psychotic experience profiles also differed between those with and those without psychotic experiences at any time point over the 12-year period (Supplementary Figs 1 and 2, and Supplementary Table 5). In other words, there were no characteristics that appeared to be related only to the persistence of psychotic experiences rather than to both the incidence and subsequent persistence of these experiences. There was stronger evidence, however, that poorer performance for both verbal and performance IQ in childhood was associated with the presence of any psychotic experiences in adolescence/adulthood, despite there being little evidence that IQ distinguished between transient and persistent psychotic experience profiles. Risk for transient experiences lay somewhere between that for no psychotic experiences and persistent psychotic experiences for all precursors examined, apart from birth hypoxia and schizophrenia polygenic risk score.

**Concurrent correlates of psychotic experience profiles**

Individuals with high-frequency persistent psychotic experiences had more negative symptoms, current self-harm, depressive episodes and generalised anxiety at all ages, and showed a clear

separation from the transient psychotic experiences group, which was itself separate from the no psychotic experiences profile (Fig. 3 and Supplementary Tables 6 and 7). Although 27% of individuals with no psychotic experiences had developed anxiety or depression at some point in their life, that proportion was 44.4% in the transient, 53.3% in the low-frequency persistent and 79.8% in the high-frequency persistent psychotic experiences profiles. Additionally, the cumulative risk of self-harm by 24 years of age followed a similar pattern, ranging from 31.5% in those with no psychotic experiences to 79.3% in those with high-frequency persistent psychotic experiences (Supplementary Table 8).

A reverse pattern was present in relation to the vocabulary and digit symbol coding tests between ages 8 and 24 years, with those in the high-frequency persistent profile scoring consistently lower on these measures than those in the other three profiles, and with these differences seemingly increasing with age. For weekly tobacco and cannabis use, there were no discernible differences until 15 years of age, when there was a sharper rise in the use of both in individuals with high-frequency persistent psychotic experiences compared with the rest of the profiles. There was generally little evidence of any differences in friendship quality, although there was weak evidence that this was deteriorating in the high-frequency persistent profile compared with the other profiles.



**Fig. 3** Trajectories of temporal correlates of psychotic experiences. All ages are shown in years. Negative symptoms scale assessed using the Community Assessment of Psychic Experience questionnaire.

### Discussion

The aim of our study was to investigate environmental, cognitive and genetic antecedents and co-occurring traits that discriminate between transient and persistent longitudinal profiles of psychotic experiences. To achieve that, we utilised longitudinal data from a birth cohort to create temporal profiles of psychotic experiences from late childhood through to early adulthood. We found that the main childhood characteristics that distinguished between transient and persistent psychotic experience profiles were that the latter were characterised by having greater general psychopathology (borderline personality traits, emotional and behavioural difficulties,

depression, self-harm, parasomnia-related disturbances); fewer emotional stability and conscientiousness personality traits; more traumatic events and a more externalised locus of control. These differences were more pronounced when individuals with transient psychotic experiences were compared with those with high-frequency persistent psychotic experiences. Although female gender and markers of lower socioeconomic status were also associated with persistent psychotic experiences, these characteristics were more common in individuals with low-frequency compared with high-frequency persistent psychotic experiences. Finally, there was weak evidence that persistence of psychotic experiences was greater in those with a family psychiatric history, but no evidence

that this was because of excess schizophrenia polygenic loading in those with persistent psychotic experiences.

When relating psychotic experience profiles to concurrent characteristics across adolescence and early adulthood, there was a greater proportion of substance use and comorbid psychopathology (anxiety, depression, negative symptoms, self-harm) among individuals with persistent psychotic experiences compared with those with transient psychotic experiences and no psychotic experiences. The proportion of individuals with these traits increased over time, and this was especially true for anxiety disorders in those with high-frequency persistent psychotic experiences. The only exception to this pattern was for negative symptoms, although these were still consistently more common in those with persistent compared with transient psychotic experiences profiles.

Additionally, individuals with high-frequency persistent psychotic experiences scored lower in both cognitive tasks compared with the other groups, and this difference again seemed to increase with age, particularly compared with the no psychotic experiences group (where performance remained relatively stable). However, there was little evidence to support a difference between the transient and persistent psychotic experiences groups (Supplementary Tables 6 and 7).

## Implications

All precursors that were associated with persistence in our study were also associated with incidence of psychotic experience, whereas for almost all precursors examined, risk for transient experiences lay somewhere between that for no psychotic experiences and persistent psychotic experiences. Our findings provide little evidence to support the presence of specific disease-modifying factors, i.e. characteristics that have little impact on aetiology, but primarily affect severity after onset. Insights gained into aetiology and prevention strategies are therefore likely to be very similar, whether we want to prevent the onset of psychotic experiences or impede the persistence of these and subsequent transition to psychotic disorder over time. It is possible, however, that other measures not included in our study, such as proteomic, lipidomic or other biomarkers, might affect only persistence or severity rather than onset of psychotic phenomena, as has been described, albeit rarely, in other areas of medicine.<sup>42</sup>

Our results, if reflecting causal effects, suggest there might be multiple avenues for prevention of onset and persistence of psychotic experience, including treating childhood psychopathology and parasomnias, improving cognitive skills and emotional stability, and reducing exposure to trauma (for example, through parenting or bullying-reduction programmes<sup>43,44</sup>) or addressing post-traumatic symptoms (for example, through trauma-focused therapies<sup>45</sup>). These highlight the importance of current initiatives aimed at early identification and treatment of mental health problems in children and young people. Furthermore, the constellation of characteristics (borderline traits, emotional instability, self-harm, nightmares and trauma history) associated with the high-frequency persistent psychotic experiences group indicates similarity to complex post-traumatic stress disorder, consistent with conceptualisations of psychotic disorders as complex manifestations of post-traumatic psychological mechanisms.<sup>46</sup>

In our study, over 75% of those with high-frequency persistent psychotic experiences met the ICD-10 criteria for an anxiety disorder or for moderate or severe depression at either age 18 or 24 years, compared with 44% of those with transient experiences, and the cumulative risk of these disorders is likely to have been even higher if we had measures of depression and anxiety that spanned the whole period from adolescence to early adulthood. Similarly, approximately 80 and 60%, respectively, of those with high-frequency and low-frequency persistent psychotic experiences

had self-harmed by 24 years of age, highlighting that individuals with recurrent or persistent psychotic experiences represent a group of young people with a substantial need for clinical intervention or support.

It was not possible to determine the temporal relationship between the psychotic experience profiles and other psychopathology over the same time period, which may have facilitated inference of causality, although the strength of support for causal effects of most exposures that we examine here on psychotic experiences has previously been documented.<sup>19,47</sup> Nevertheless, our findings suggest that the vast majority of those with high-frequency persistent psychotic experiences will have required help for other mental health problems at some stage, and thus there are likely to be opportunities for identifying and monitoring those who are at highest risk of developing a clinical psychotic disorder.<sup>2,9,11,12</sup>

## Strengths and limitations





This study has a number of strengths, including the use of prospectively assessed and often repeated measures of precursors and correlates of psychotic experience profiles, allowing for a more comprehensive examination of characteristics that discriminate between persistent and non-persistent experiences than previous studies. Ours is also the first study to use semi-structured interview measures to assess psychotic experiences, thus minimising information bias. Additionally, although previous studies (with one exception<sup>6</sup>) examined trajectories over relatively short periods of time (2–6 years), our study is able to provide information on longer-term persistence of psychotic experiences over a timespan of more than 12 years, with our findings being similar when examining profiles at different developmental stages (ages 12–18 years and 18–24 years). Nevertheless, the findings described here must also be interpreted in the context of a number of limitations.

First, as with most other large cohort studies that span long periods of time, there was a substantial amount of missing data. To address this we used multiple imputation and included a large number of covariates to make the missing at random assumption more plausible; nevertheless, it remains possible that our results are affected by selection bias. Second, for variables included in our repeat-measure correlates, we were unable to tease out the direction of effect in relation to the psychotic experience profiles. However, the aim of our study was not to determine whether the associations we observed are likely to be causal or not, but to identify markers that characterise persistence of psychotic experiences once they occur, and which could potentially inform future studies of prediction of psychotic disorder. Third, although we examined a broad range of measures encompassing markers of sociodemographic status, genetic risk, psychopathology, cognition and behaviours in relation to psychotic experience profiles, we did not examine all cognitive or psychological constructs, or other biological or neuroimaging data.

Finally, we used an empirical approach rather than a latent model approach to derive our profiles of psychotic experiences over time, as, because of the small numbers in the non-zero classes, no latent model was sufficiently stable despite the size of our study. We utilised information on frequency and persistence of experiences to help create profiles to represent psychotic experience trajectories that were guided by our research questions; nevertheless, there may be some misclassification of individuals. Additionally, it would have been of interest to include information on distress in the derivation of the psychotic experience profiles as distress, as both distress and frequency are likely to index psychotic experience severity,<sup>48</sup> but unfortunately this was not available at all assessments.

## Summary

In this study, we identified a number of characteristics that differentiated between longitudinal profiles of psychotic experiences across adolescence and early adulthood, including other psychopathology, substance use, cognitive deficits and biases, personality traits and childhood trauma. There was little evidence, however, that any of these characteristics affected only the course rather than the onset of psychotic experiences, suggesting that it is the severity of exposure rather than specific disease-modifying factors that most strongly determines whether psychotic experiences are transient or persist over time.

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## Supplementary material

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## Data availability

Scripts used for the analyses conducted in this study are available on request from the corresponding author, A.R. The data that support the findings of this study are available from ALSPAC (see <http://www.bristol.ac.uk/alspac/researchers/access/>)

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## Author contributions

G.L., P.B.J., M.C., A.T., D.W., S.Z. contributed to data acquisition, all co-authors contributed at analysis or interpretation of the data. A.R., J.H. and S.Z. drafted the manuscript which was critically revised for important intellectual content by all co-authors.

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## Declaration of interest

M.C. is part of the editorial board for the *British Journal of Psychiatry*, but did not take part in the review or decision-making process of this paper. The authors declare no other conflicts of interest.

## References

- McGrath JJ, Saha S, Al-Hamzawi A, Alonso J, Bromet EJ, Bruffaerts R, et al. Psychotic experiences in the general population: a cross-national analysis based on 31,261 respondents from 18 countries. *JAMA Psychiatry* 2015; **72**(7): 697–705.
- Sullivan SA, Kounali D, Cannon M, David AS, Fletcher PC, Holmans P, et al. A population-based cohort study examining the incidence and impact of psychotic experiences from childhood to adulthood, and prediction of psychotic disorder. *Am J Psychiatry* 2020; **177**(4): 308–17.
- Poulton R, Caspi A, Moffitt TE, Cannon M, Murray R, Harrington H. Children's self-reported psychotic symptoms and adult schizophrenia disorder: a 15-year longitudinal study. *Arch Gen Psychiatry* 2000; **57**(11): 1053–8.
- Asher L, Zammit S, Sullivan S, Dorrington S, Heron J, Lewis G. The relationship between psychotic symptoms and social functioning in a non-clinical population of 12-year olds. *Schizophr Res* 2013; **150**(2–3): 404–9.
- Davies J, Sullivan S, Zammit S. Adverse life outcomes associated with adolescent psychotic experiences and depressive symptoms. *Soc Psychiatry Psychiatr Epidemiol* 2018; **53**(5): 497–507.
- Rossler W, Riecher-Rossler A, Angst J, Murray R, Gamma A, Eich D, et al. Psychotic experiences in the general population: a twenty-year prospective community study. *Schizophr Res* 2007; **92**(1–3): 1–14.
- Kelleher I, Lynch F, Harley M, Molloy C, Roddy S, Fitzpatrick C, 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**(12): 1277–83.
- Sullivan SA, Lewis G, Gunnell D, Cannon M, Mars B, Zammit S. The longitudinal association between psychotic experiences, depression and suicidal behaviour in a population sample of adolescents. *Soc Psychiatry Psychiatr Epidemiol* 2015; **50**(12): 1809–17.
- Dominguez MD, Wichers M, Lieb R, Wittchen HU, van Os J. Evidence that onset of clinical psychosis is an outcome of progressively more persistent subclinical psychotic experiences: an 8-year cohort study. *Schizophr Bull* 2011; **37**(1): 84–93.
- Bartels-Velthuis AA, Wigman JT, Jenner JA, Bruggeman R, van Os J. Course of auditory vocal hallucinations in childhood: 11-year follow-up study. *Acta Psychiatr Scand* 2016; **134**(1): 6–15.
- Zammit S, Kounali D, Cannon M, David AS, Gunnell D, Heron J, et al. Psychotic experiences and psychotic disorders at age 18 in relation to psychotic experiences at age 12 in a longitudinal population-based cohort study. *Am J Psychiatry* 2013; **170**(7): 742–50.
- Hanssen M, Bak M, Bijl R, Vollebergh W, van Os J. The incidence and outcome of subclinical psychotic experiences in the general population. *Br J Clin Psychol* 2005; **44**(Pt 2): 181–91.
- Kalman JL, Bresnahan M, Schulze TG, Susser E. Predictors of persisting psychotic like experiences in children and adolescents: a scoping review. *Schizophr Res* 2019; **209**: 32–9.
- Mackie CJ, Castellanos-Ryan N, Conrod PJ. Developmental trajectories of psychotic-like experiences across adolescence: impact of victimization and substance use. *Psychol Med* 2011; **41**(1): 47–58.
- Wigman JT, van Winkel R, Raaijmakers QA, Ormel J, Verhulst FC, Reijneveld SA, et al. Evidence for a persistent, environment-dependent and deteriorating subtype of subclinical psychotic experiences: a 6-year longitudinal general population study. *Psychol Med* 2011; **41**(11): 2317–29.
- Thapar A, Heron J, Jones RB, Owen MJ, Lewis G, Zammit S. Trajectories of change in self-reported psychotic-like experiences in childhood and adolescence. *Schizophr Res* 2012; **140**(1–3): 104–9.
- Mackie CJ, O'Leary-Barrett M, Al-Khudairy N, Castellanos-Ryan N, Struve M, Topper L, et al. Adolescent bullying, cannabis use and emerging psychotic experiences: a longitudinal general population study. *Psychol Med* 2013; **43**(5): 1033–44.
- Bourque J, Afzali MH, O'Leary-Barrett M, Conrod P. Cannabis use and psychotic-like experiences trajectories during early adolescence: the coevolution and potential mediators. *J Child Psychol Psychiatry* 2017; **58**(12): 1360–9.
- 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**(2): 179–95.



- 20 Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009; **42**(2): 377–81.
- 21 Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, et al. The REDCap consortium: building an international community of software platform partners. *J Biomed Inform* 2019; **95**: 103208.
- 22 Fraser A, Macdonald-Wallis C, Tilling K, Boyd A, Golding J, Davey Smith G, et al. Cohort profile: the Avon Longitudinal Study of Parents and Children: ALSPAC mothers cohort. *Int J Epidemiol* 2013; **42**(1): 97–110.
- 23 Boyd A, Golding J, Macleod J, Lawlor DA, Fraser A, Henderson J, et al. Cohort profile: the 'children of the 90s'—the index offspring of the Avon Longitudinal Study of Parents and Children. *Int J Epidemiol* 2013; **42**(1): 111–27.
- 24 Northstone K, Lewcock M, Groom A, Boyd A, Macleod J, Timpson N, et al. The Avon Longitudinal Study of Parents and Children (ALSPAC): an update on the enrolled sample of index children in 2019. *Wellcome Open Res* 2019; **4**: 51.
- 25 Horwood J, Salvi G, Thomas K, Duffy L, Gunnell D, Hollis C, et al. IQ and non-clinical psychotic symptoms in 12-year-olds: results from the ALSPAC birth cohort. *Br J Psychiatry* 2008; **193**(3): 185–91.
- 26 Wing JK, Babor T, Brugha T, Burke J, Cooper JE, Giel R, et al. SCAN. Schedules for clinical assessment in neuropsychiatry. *Arch Gen Psychiatry* 1990; **47**(6): 589–93.
- 27 Jones HJ, Heron J, Hammerton G, Stochl J, Jones PB, Cannon M, et al. Investigating the genetic architecture of general and specific psychopathology in adolescence. *Transl Psychiatry* 2018; **8**(1): 145.
- 28 Pardinás AF, Holmans P, Pocklington AJ, Escott-Price V, Ripke S, Carrera N, et al. Common schizophrenia alleles are enriched in mutation-intolerant genes and in regions under strong background selection. *Nat Genet* 2018; **50**(3): 381–9.
- 29 Major Depressive Disorder Working Group of the Psychiatric GWAS Consortium, Ripke S, Wray NR, Lewis CM, Hamilton SP, Weissman MM, et al. A mega-analysis of genome-wide association studies for major depressive disorder. *Mol Psychiatry* 2013; **18**(4): 497–511.
- 30 Smith DJ, Escott-Price V, Davies G, Bailey ME, Colodro-Conde L, Ward J, et al. Genome-wide analysis of over 106 000 individuals identifies 9 neuroticism-associated loci. *Mol Psychiatry* 2016; **21**(6): 749–57.
- 31 Wechsler D. *Wechsler Intelligence Scale for Children: Manual*. Psychological Corporation, 1949.
- 32 Nowicki S, Iles-Caven Y, Gregory S, Ellis G, Golding J. The impact of prenatal parental locus of control on children's psychological outcomes in infancy and early childhood: a prospective 5 year study. *Front Psychol* 2017; **8**: 546.
- 33 Goodman R. Psychometric properties of the strengths and difficulties questionnaire. *J Am Acad Child Adolesc Psychiatry* 2001; **40**(11): 1337–45.
- 34 Costello EJ, Angold A. Scales to assess child and adolescent depression: checklists, screens, and nets. *J Am Acad Child Adolesc Psychiatry* 1988; **27**(6): 726–37.
- 35 Wolke D, Schreier A, Zanarini MC, Winsper C. Bullied by peers in childhood and borderline personality symptoms at 11 years of age: a prospective study. *J Child Psychol Psychiatry* 2012; **53**(8): 846–55.
- 36 Hofstee WK, de Raad B, Goldberg LR. Integration of the big five and circumplex approaches to trait structure. *J Pers Soc Psychol* 1992; **63**(1): 146–63.
- 37 Croft J, Heron J, Teufel C, Cannon M, Wolke D, Thompson A, et al. Association of trauma type, age of exposure, and frequency in childhood and adolescence with psychotic experiences in early adulthood. *JAMA Psychiatry* 2019; **76**(1): 79–86.
- 38 Mossaheb N, Becker J, Schaefer MR, Klier CM, Schloegelhofer M, Papageorgiou K, et al. The Community Assessment of Psychic Experience (CAPE) questionnaire as a screening-instrument in the detection of individuals at ultra-high risk for psychosis. *Schizophr Res* 2012; **141**(2-3): 210–4.
- 39 Lewis G, Pelosi AJ, Araya R, Dunn G. Measuring psychiatric disorder in the community: a standardized assessment for use by lay interviewers. *Psychol Med* 1992; **22**(2): 465–86.
- 40 Baron-Cohen S, Wheelwright S. The friendship questionnaire: an investigation of adults with Asperger syndrome or high-functioning autism, and normal sex differences. *J Autism Dev Disord* 2003; **33**(5): 509–17.
- 41 Rubin DB. *Multiple Imputation for Nonresponse in Surveys*. John Wiley & Sons, 1987.
- 42 Onitilo AA, Engel JM, Glurich I, Stankowski RV, Williams GM, Doi SA. Diabetes and cancer I: risk, survival, and implications for screening. *Cancer Causes Control* 2012; **23**(6): 967–81.
- 43 Chen M, Chan KL. Effects of parenting programs on child maltreatment prevention: a meta-analysis. *Trauma Violence Abuse* 2016; **17**(1): 88–104.
- 44 Gaffney H, Ttofi MM, Farrington DP. Evaluating the effectiveness of school-bullying prevention programs: an updated meta-analytical review. *Aggress Violent Behav* 2019; **45**: 111–33.
- 45 van den Berg DP, de Bont PA, van der Vleugel BM, de Roos C, de Jongh A, Van Minnen A, et al. Prolonged exposure vs eye movement desensitization and reprocessing vs waiting list for posttraumatic stress disorder in patients with a psychotic disorder: a randomized clinical trial. *JAMA Psychiatry* 2015; **72**(3): 259–67.
- 46 Hardy A. Pathways from trauma to psychotic experiences: a theoretically informed model of posttraumatic stress in psychosis. *Front Psychol* 2017; **8**: 697.
- 47 Linscott RJ, van Os J. 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. *Psychol Med* 2013; **43**(6): 1133–49.
- 48 Fusar-Poli P, Yung AR, McGorry P, van Os J. Lessons learned from the psychosis high-risk state: towards a general staging model of prodromal intervention. *Psychol Med* 2014; **44**(1): 17–24.

