Precursors and Correlates of Transient and Persistent Longitudinal Profiles of Psychotic Experiences from Late Childhood Through Early Adulthood

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Word Count: 3458

Abstract

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

Aims: To investigate how longitudinal profiles of PEs, created from assessments at three different timepoints are influenced by early life and co-occurring factors.

Method: Using data from 8045 individuals from a birth-cohort study, longitudinal profiles of PEs 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 related profiles to concurrent psychopathology and cognition.

Results: Following multiple imputations, the distribution of longitudinal profiles was: "No PEs" 65.7%; "Transient" 24.1%; "Low-frequency persistent" 8.4%; "High-frequency persistent" 1.7%. Individuals with persistent and high-frequency PEs, were more likely than those with transient PEs to have reported traumatic experiences, other psychopathology, a more externalised locus of control, reduced emotional stability and conscientious personality traits in childhood. These characteristics also differed between those who had any PE compared to those without.

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

Introduction

Background

Psychotic experiences (PEs) are not uncommon, with at least 5%-10% of individuals experiencing a PE during their lifetime.(1, 2) 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 PEs during childhood and adolescence.(2, 3)

PEs can be highly distressing and are associated with adverse outcomes such as impaired social and occupational functioning and suicidal thoughts.(4-8) However, in most cases PEs are transient, only ever occurring on a few instances.(1, 9, 10) Studying such transient experiences is likely to be less informative for understanding the aetiology or prediction of later psychiatric disorder in comparison to studying persistent or frequently recurring PEs.(2, 9, 11, 12) Longitudinal studies with repeated measures of PEs allow researchers to study trajectories of PEs over time whilst minimising misclassification error from single time-point assessments.(13) The few studies that have been able to quantify longitudinal profiles of PEs have shown that substance use, other psychopathology, and victimization are more common in those with increasing or persistently high probabilities of having PEs across time.(6, 14-18) However, as the baseline class in these studies combined individuals with either no or low levels of PEs, they do not provide information on factors that differentiate between incidence and persistence of PEs. Additionally, these studies(15-18) have relied on self-reported measures of PEs that over-estimate the presence of PEs compared to semi-structured interview measures,(11, 19) potentially leading to biased (most likely underestimated) estimates of association.

Aim

To address these limitations, we aimed to i) define temporal longitudinal profiles of PEs using semi-structured interviews assessed at 3 time-points over a 12-year period in the population-based Avon Longitudinal Study of Parents and Children (ALSPAC) birth cohort, ii) investigate environmental, cognitive, psychopathlogical and genetic precursors of these longitudinal profiles, and iii) 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 1st April 1991 and 31st December 1992 (N = 14,541; N births alive at 1 year = 13,988). Further recruitment of eligible cases resulted in a sample of 15,454 pregnancies, of which 14,901 were alive at 1 year of age. For information about data available see http://www.bris.ac.uk/ alspac/researchers/data-access/data-dictionary/. 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 using REDCap.(20, 21)

The sample used for this study consisted of 8045 individuals who participated in at least one PLIKS interview (see below) from the assessments at 12 (N=6822), 18 (N=5213) and 24 (N=3862) years of age. Whilst the original cohort was representative of the target population, (22-24), 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 S1).

Outcome Measures

Longitudinal profiles of psychotic experiences: The semi-structured Psychosis-Like Symptom Interview (PLIKSi) was used at ages 12 (mean 12.8, SD=0.23), 18 (mean 17.8, SD=0.46) and 24 (mean 24.1, SD=0.85) years to assess current (past 6-months) PEs.(2, 11, 25) The PLIKSi assesses 12 key PEs 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 PEs followed glossary definitions and rating rules for the Schedules for Clinical Assessment in Neuropsychiatry (SCAN)(26). Interviewers rated PEs as not present, suspected, or definitely present (see Supplement for more detail).

We used an empirical approach rather than a latent model approach to derive our profiles of PEs over time as latent models were unstable and underlying assumptions could not be met. To generate PE 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 PE (0: "No PE", 1: "Low-frequency" - PEs occurring less than weekly, 2: "High-frequency" - PEs 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 PE data across the three time-points and maximised the use of the available information:

i. *No experiences*: Individuals without a PE at any time point

ii. *Transient:* Individuals with a PE rated at only one time-point, regardless of frequency (reference group for primary analyses comparing persistent and transient profiles)

iii. *Low-frequency persistent:* Individuals with a low-frequency PE at two or more time points, or with a low-frequency rating at one time point and a high-frequency rating at another

iv. *High-frequency persistent:* Individuals with a high-frequency PE rated at two or more time points

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

Precursors

Family Psychiatric History: Presence of depression or schizophrenia in the parents and grandparents.

Genetic Data: Polygenic risk scores (at discovery sample p-thresholds of 0.05(27)) for schizophrenia,(28) major depression(29) and neuroticism.(30)

Sociodemographic Characteristics: Data on sex, maternal social class (higher versus lower), and maternal education (≥1 O-level versus lower) were collected from parental questionnaires around the time of birth.

Pregnancy and birth measures: These included binary measures of i) self-reported maternal cigarette smoking during pregnancy, ii) self-reported maternal infection during third trimester of pregnancy, and iii) 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 age 8 using the Wechsler Intelligence Scale for Children (WISC).(31) External locus of control was assessed at age 8 using the 12-item children's Nowicki Strickland Internal–External control scale (CNSIE).(32) Emotional and behavioural difficulties were assessed using the Strengths and Difficulties Questionnaire (SDQ) total score(33) and depression assessed using the Short Moods and Feelings Questionnaire (sMFQ),(34) both administered at age 11. Borderline personality disorder traits covering the nine DSM-IV criteria for disorder were assessed at age 11, and a binary variable was derived using a cut-off of 5 or more criteria to define those at

highest risk of having a disorder.(35) The Big Five personality domains (extraversion, agreeableness, conscientiousness, emotional stability, and intellect/openness) were assessed at age 14 (hence measured after the start of the profiles, but included here as they are trait measures, so likely reflecting pre-PE characteristics) using the International Personality Item Pool.(36) A categorical measure reflecting the number of types (0-4) of childhood trauma exposure (ages 0 to 10) was derived using data from assessments completed by the parents or self-reported by the participants.(37) Self-harm (binary measure of child reporting whether they had "hurt him/herself on purpose") was assessed at age 11. The existence of nightmares or night terrors (binary measure) was assessed during a semi-structured interview at age 12.

Concurrent measures

Additional measures assessed concurrently to the PE measures (i.e. between ages 12 and 24) were examined to relate patterns of these over time to the PE profiles: *Tobacco use* (at least weekly compared to non-weekly smoking at ages 10, 12, 15 and 24); *Cannabis use* (at least weekly compared to non-weekly use at ages 12, 15, 17 and 24); *Negative symptoms* (assessed using the CAPE(38) at ages 16 (past-month), 23 (past-year) & 24 (past-year)); *Past-year self-harm* (at ages 16, 18, 21, 24 and 25); *Depression* and *Generalised Anxiety Disorder* (current, assessed using the CIS-R(39) at ages 18 and 24); *Vocabulary and Digit Symbol scores* (assessed as part of the Wechsler Intelligence Scale(31) at ages 8, 15 (Digit Symbol only) and 24; *Friendship quality* (using the item "I talk with my friends about my problems" from the Cambridge Friendship Questionnaire(40) at ages 8, 14, 17 and 24).

Missing data The number of individuals participating in one, two, or all three of the PLIKS interviews was 2,931, 2,371 and 2,743 respectively. The proportion of people with missing

data on the precursors/concurrent measures ranged from 0% to 44.6% (see Supplementary Table S2 for more detail). We used multiple imputation to minimse the selection bias likely from using a complete-case approach.

Statistical Analysis Statistical analyses were undertaken using R 3.6.0 or STATA 15.1. We performed multiple imputation, using the R package "mice", to 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 PE data, we also used self-reported measures of psychotic-like experiences assessed using the PLIKS questionnaires(16) at ages 11, 13, 14, 16 and 22 to make the missing at random assumption more plausible (see Supplement for more details). The PE profiles were passively imputed with the underlying composite frequency variables actively imputed in each instance.

The associations between the precursors and PE profiles were examined using univariable multinomial logistic regressions separately in each of the imputed data-sets, with Rubin's rules(41) 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 PE 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: no PE (N=5259, 65.4%), transient PE (N=1959; 24.3%), low-frequency persistent PE (N=687; 8.5%), and high-frequency persistent PE (N=140; 1.7%). There was a higher proportion of individuals with transient, low-frequency persistent, and high-frequency persistent PE in the imputed compared to the complete-case data, while the opposite was observed for the no PE profile (Table 1; see also Supplementary Table S3 for more details on the complete-case sample).

Table 1 Here

Precursors of PE profiles

The demographic and childhood psychopathological and cognitive characteristics for the four profiles are summarised in Table 1, while comparisons between the transient and persistent profiles are presented in Figure 1 and Figure 2 as well as Supplement Table S4.

Figure 1 & Figure 2 Here

Compared to those with an outcome of transient PEs, there was evidence that individuals with an outcome of persistent PEs (low- and high-frequency combined) were more likely to be female (OR=1.38; 95%CI 1.12, 1.72) and to have mothers who smoked during pregnancy (OR=1.35; 95%CI 1.06, 1.73). Additionally, they were more likely to have childhood emotional and behavioural problems (OR=1.16; 95%CI 1.05, 1.27), depression (OR=1.13; 95%CI 1.05, 1.26), borderline personality disorder traits (OR=1.10; 95%CI 1.06, 1.13), self-harming behaviours (OR=1.93; 95%CI 1.35, 2.76), nightmares (OR=1.76; 95%CI 1.41, 2.21),

an externalised locus of control (OR=1.08; 95%CI 1.02, 1.14), and to have experienced traumatic events (OR=1.28; 95%CI 1.11, 1.48) compared to individuals with transient PEs. Individuals with persistent PEs also differed on two of the personality traits, scoring lower on conscientousness (OR=0.84; 95%CI 0.75, 0.94) and emotional stability (OR=0.79; 95%CI 0.71, 0.88).

For all of these characteristics, with the exception of female sex 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 (Figure 1 and Figure 2; Supplement Table S4).

There was weaker evidence that lower social class (OR=1.19; 95%CI 0.92, 1.54), maternal education (OR=1.24, 95%CI 0.98, 1.56) and family history of mental health problems (OR=1.22; 95%CI 0.98, 1.51) were more common in those with persistent compared to transient PEs, and little evidence that polygenic risk scores, maternal infection during pregnancy, birth hypoxia, or IQ indices differed between the transient and persistent PE profiles. There was little evidence that predictors of persistence differed across developmental stages (see Supplement Table S9).

Comparison with no PEs

Most of the characteristics that differed between persistent and transient PE profiles also differed between those with and those without PE at any time-point over the 12-year period (Supplement Table S5 and Figures S1 & S2). In other words there were no characteristics that appeared to be related only to the persistence of PEs rather than to both the incidence and subsequent persistence of these experiences. There was stronger evidence however, that poorer performance for both verbal IQ and performance IQ in childhood was associated with the

presence of any PE in adolescence/adulthood, even though there was little evidence that IQ distinguished between tranisent and persistent PE profiles. Risk for transient experiences lay somewhere between that for no PE and persistent PE for all precursors examined apart from birth hypoxia and schizophrenia PRS.

Concurrent correlates of PE profiles

Individuals with high-frequency persistent PEs had more negative symptoms, current self-harm, depressive episodes and generalised anxiety at all ages, and showed a clear separation from the transient PE group, which was itself separate from the no-PE profile (Figure 3 & Supplement Tables S6 and S7). While 27% of individuals with no PEs 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 PE profiles. Additionally, the cumulative risk of deliberate self-harm by age 24 followed a similar pattern, ranging from 31.5% in those with no PEs to 79.3% in the high-frequency persistent group (Supplement Table S8).

Figure 3 Here

A reverse pattern was present in relation to the vocabulary and digit symbol coding tests between ages 8 and 24, with those in the high-frequency persistent profile scoring consistently lower on these measures than the other three profiles, and with these differences seemingly increasing with age. For weekly tobacco and cannabis use, there were no discernible differences until the age of 15, when there was a sharper rise in both in individuals with high-frequency persistent PEs compared to 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 group compared to the other profiles.

Discussion

The aim of our study was to investigate environmental, cognitive and genetic antecedents and co-occuring traits that discriminate between transient and persistent longitudinal profiles of PEs. To achieve that, we utilised longitudinal data from a birth cohort to create temporal profiles of PEs from late childhood through to early adulthood. We found that the main childhood characteristics that distinguished between transient and persistent PE profiles were that the latter were characterised by having (1) greater general psychopathology (borderline personality traits, emotional and behavioural difficulties, depression, self-harm, parasomnic disturbances), (2) fewer emotional stability and conscientiousness personality traits, (3) more traumatic events and (4) a more externalised locus of control. These differences were more pronounced when individuals with transient PEs were compared to those with high-frequency persistent PEs. Whilst female sex and markers of lower socio-economic status were also associated with persistent PEs, these characteristics were more common in individuals with low-frequency compared to those with high-frequency persistent PEs. Finally, there was weak evidence that persistence of PEs was greater in those with a family psychiatric history, but no evidence that this was due to excess schizophrenia polygenic loading in those with persistent PEs.

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

Additionally, individuals with high-frequency persistent PEs scored lower in both cognitive tasks compared to the other groups, and this difference again seemed to increase with age, particularly in comparison to the no PE group (where performance remained relatively stable). However, there was little evidence to support a difference between the transient and persistent PE groups (Supplement Tables S6 and S7).

Implications

All precursors that were associated with persistence in our study were also associated with incidence of PE, whilst for almost all precursors examined, risk for transient experiences lay somewhere between that for no PE and persistent PE. Our findings therefore 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 PEs 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.(42)

Our results, if reflecting causal effects, suggest there might be multiple avenues for prevention of onset and persistence of PE, 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(43, 44)) or addressing post-traumatic symptoms (for example through trauma-focused therapies(45)). 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 group indicates similarity to complex-PTSD, consistent with conceptualisations of psychotic disorders as complex manifestations of post-traumatic psychological mechanisms.(46)

In our study, over 75% of those with high-frequency persistent PEs met ICD-10 criteria for an anxiety disorder or for moderate or severe depression at either age 18 or age 24 compared to 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 PEs had self-harmed by age 24, highlighting that individuals with recurrent or persistent PEs 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 PE 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 PEs has previously been documented.(19, 47) Nevertheless, our findings suggest that the vast majority of those with high-frequency persistent PEs 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.(2, 9, 11, 12)

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 PE profiles, allowing a more comprehensive

examination of characteristics that discriminate between persistent and non-persistent experiences than previous studies to date. Ours is also the first study to use semi-structued interview measures to assess psychotic experiences, thus minimising information bias. Additionally, whilst previous studies, with one exception,(6) examined trajectories over relatively short periods of time (2-6 years), our study is able to provide information on longer-term persistence of PEs over a time-span of more than twelve years, with our findings being similar when examining profiles at different developmental stages (ages 12 to 18, and 18 to 24). 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 whilst including a large number of covariates to make the missing at random assumption more plausible; nevertheless, it remains possible that our results are affected by selecton bias. Second, for variables included in our repeat-measure correlates, we were unable to tease out the direction of effect in relation to the PE 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 PEs once they occur, and which could potentially inform future studies of prediction of psychotic disorder. Third, whilst we examined a broad range of measures encompassing markers of sociodemographic status, genetic risk, psychpathology, cognition, and behaviours in relation to PE profiles, we did not examine all cognitive or psychological contructs, or other biological or neurimaging data .

Finally, we used an empirical approach rather than a latent model approach to derive our profiles of PEs over time as, due to 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 PE 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 PE profiles as distress, as both distress and frequency are likely to index PE severity(48), 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 PEs, suggesting that it is the severity of exposure rather than specific disease-modifying factors that most strongly determines whether PEs are transient or persist over time.

Acknowledgements

The authors are grateful to all the families who took part in the study, the midwives for their help in recruiting them, and the whole ALSPAC team, which includes interviewers, computer and laboratory technicians, clerical workers, research scientists, volunteers, managers, receptionists, and nurses.

Conflicts of Interest

Mary Cannon 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 otherwise declare no conflicts of interest

Funding

The U.K. Medical Research Council (MRC) and Wellcome Trust (WT) (ref. 217065/Z/19/Z) and the University of Bristol provide core support for ALSPAC. A comprehensive list of grants funding is available on the ALSPAC website (http://www.bristol.ac.uk/alspac/external/documents/grant-acknowledgements.pdf); this research was specifically funded by MRC grant MR/M006727/1. SZ, HJ, DK & SS acknowledge support from the NIHR Biomedical Research Centre (BRC) at University Hospitals Bristol NHS Foundation Trust and the University of Bristol; GL from the NIHR BRC at University College London Hospital; PBJ from the NIHR CLAHRC East of England, NIHRPGfARRP-PG-0616-20003(TYPPEX) and the WT Neuroscience in Psychiatry Network (095844/Z/11/Z), MC from a European Research Council Consolidator Award (iHEAR 724809), and GH and LH from WT Fellowships (209138/Z/17/Z and 209158/Z/17/Z). The views expressed in this article are those of the authors and not Necessarily those of the NHS, the National Institute for Health Research, or the Department of Health and Social Care

Author Contribution

All authors contributed to data acquisition, analysis, or interpretation, as well as drafting and critical revision of the manuscript for important intellectual content. All authors approved the final version and agree that any questions related to accuracy or integrity of the work are appropriately investigated and resolved.

Data Availability

Scripts used for the analyses conducted in this study are available on request from the corresponding author, AR. 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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Table 1: Proportion or mean (SD) of demographic, genetic cognitive and psychopathological characteristics stratified by psychotic experience profile in imputed sample (N=8045)

	Psychotic experiences				
Variable	**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, (%)	16.3	22.7	27.8	32.7	28.6
Maternal Pregnancy Infection,(%)	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, (%)	39.5	42	46.4	48.4	46.7
PRS (Schizophrenia), mean (SD)	-0.05 (1)	0.01(1)	0.01(1)	0.02 (1)	0.03 (1)
PRS (Depression), mean (SD)	-0.03 (1)	0.06 (1)	0.1 (1)	0.08 (1)	0.13 (1)
PRS (Neuroticism), mean (SD)	-0.03 (1)	-0.02 (1)	0.04 (1)	0.07 (1)	0.04 (1)
Verbal IQ, mean (SD)	108.4 (19)	106.1(20)	105.1 (20)	103.7(21.5)	104.9(20)
Perform. IQ, mean (SD)	101.5 (17)	99.8(17.3)	98.9 (17.1	99 (17.8)	99 (17.3)
SDQ, mean (SD)	6.1 (4.7)	7.2 (5.1)	7.9 (5.5)	8.8 (5.6)	8 (5.5)
Locus of Control, mean (SD)	5.8 (2.1)	6.2 (2)	6.5 (2.1)	6.7 (2.1)	6.55 (2.1)
MFQ, mean (SD)	2.1 (2.9)	2.7 (3.5)	3.3 (3.9)	3.6(4.1)	3.3 (4)
Extraversion, mean (SD)	35.1 (6.8)	35.3(7)	35.8 (7.1)	34.8 (7.8)	35.6 (7.2)
Agreeableness, mean (SD)	37.8 (5.2)	37.5(5.4)	37.7 (5.5)	38 (6)	37.8 (5.6)
Conscientiousness, mean (SD)	32.2 (5.8)	31.2 (5.9)	30.3 (5.8)	29.4 (6.3)	30.2 (5.9)
Emotional Stability, mean (SD)	32.1 (6.4)	30.4(6.6)	29 (6.7)	27.6(6.9)	28.8 (6.8)

Intellect/Openness, mean (SD)	35.6 (6.0)	35.5(5.8)	35.9 (5.8)	36.1 (6.5)	35.9 (6)
Trauma Types, mean (SD)	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 N (%)	1982 (72.2)	545 (19.9)	188 (6.9)	28 (1)	216 (7.9)
Imputed N (%)	5259 (65.4)	1959 (24.3)	687 (8.5)	140 (1.7)	827 (10.2)

Footnote: Profiles were based on current PEs (past 6-months at ages 18 & 24; average past 8-months at age 12). Transient: Transient or Episodic PEs; Persistent Low: Persistent or recurrent PEs with frequency of less than weekly; Persistent High: Persistent or recurrent PEs with frequency of more than weekly; Persistent (all): Persistent or Recurrent PEs regardless of frequency; PRS: Polygenic Risk Score; ; MFQ: Moods and Feelings Questionnaire, SDQ: Strengths and Difficulties Questionnaire; BPD: Borderline Personality Disorder. ; MFQ: Moods and Feelings Questionnaire, SDQ: Strengths and Difficulties Questionnaire; BPD: Borderline Personality Disorder. Complete-case N: Everyone with PE data at all three time points; Imputed N: Everyone with PE data in at least one time-point.

Figure 1: Univariable Multinomial Logistic Regressions of Persistent versus Transient PEs (Reference): Sociodemographic characteristics, family history and childhood trauma

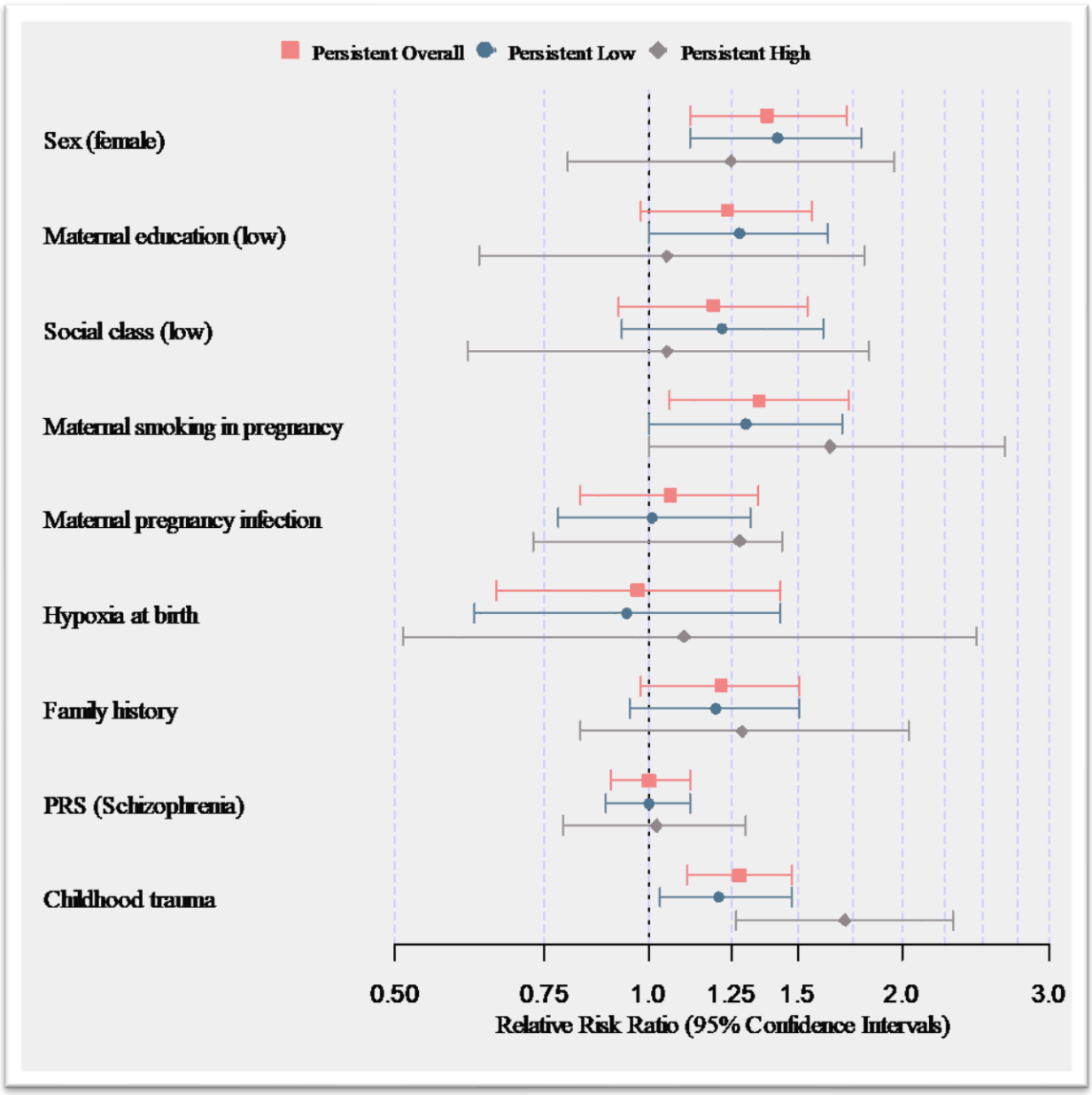


Figure 2: Univariable Multinomial Logistic Regressions of Persistent vs Transient PEs (Reference): Psychopathology and cognition

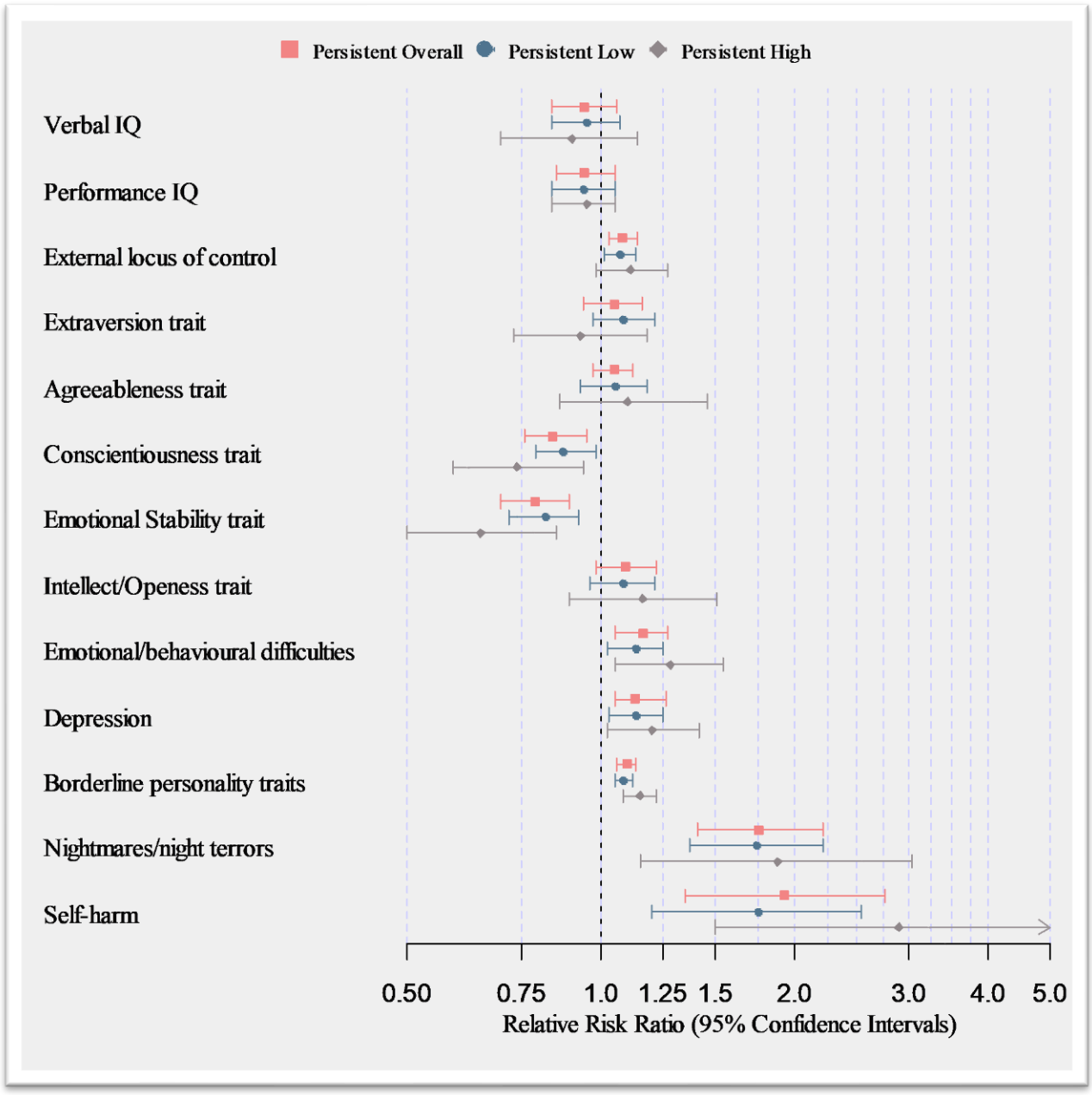
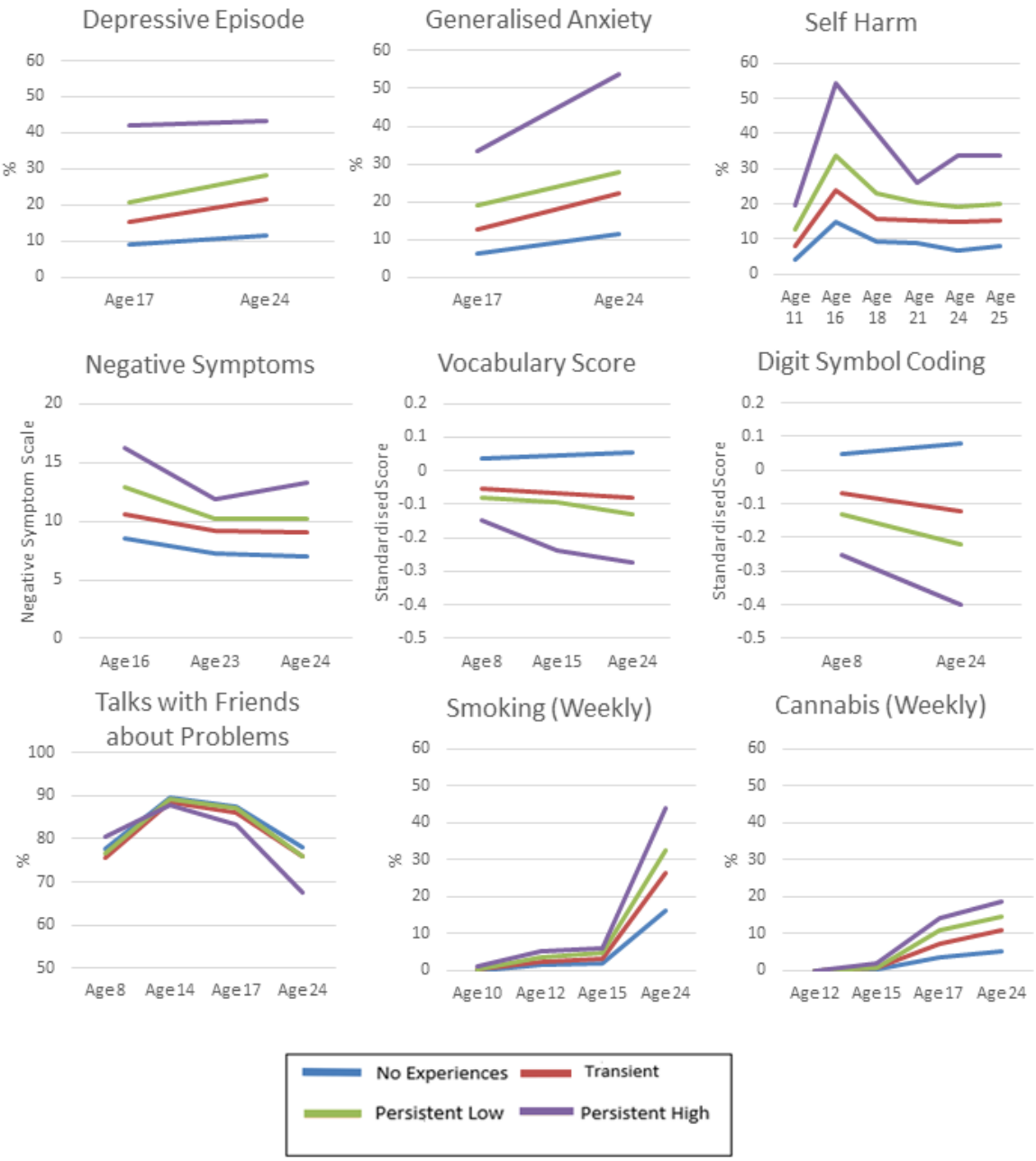


Figure 3: Trajectories of temporal Correlates of Psychotic Experiences



Supplement

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Outcome Measures

Longitudinal profiles of psychotic experiences

The semi-structured Psychosis-Like Symptom Interview (PLIKSi) was used at ages 12 (mean 12.8, SD=0.23), 18 (mean 17.8, SD=0.46) and 24 (mean 24.1, SD=0.85) years to assess current (past 6-months) PEs.The PLIKSi includes 12 core questions eliciting key PEs: hallucinations (visual and auditory), delusions (spied on, persecution, thoughts read, reference, control, grandiosity, other unspecified) and experiences of thought interference (broadcasting, insertion, and withdrawal). Questions about each experience started with a structured stem question asking if the participant had ever had that experience since the age of 12. Interviewers

cross-questioned participants endorsing ‘yes’ or ‘maybe’ responses to establish whether the experience was psychotic or not, and to establish the frequency of these experiences over the previous 6 months. Coding of PEs followed glossary definitions and rating rules for the Schedules for Clinical Assessment in Neuropsychiatry (SCAN)(1). Interviewers rated PEs as not present, suspected, or definitely present. Unclear responses after probing were “rated down”, and items only rated as definite when an example that clearly met SCAN rating rules was provided.

We used an empirical approach rather than a latent model approach to derive our profiles of PEs over time as latent models were not sufficiently stable and assumptions underlying these could not be met. To generate PE longitudinal profiles, a trinary measure at each time-point was constructed that reflected the current (average over past 6-months) frequency of the most frequently reported experience rated as suspected or definitely psychotic (0: “No PE”, 1: “Low-frequency” - PEs occurring less than weekly, 2: “High-frequency” - PEs 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 PE data across the three time-points and maximised the use of the available information:

i. *No experiences*: Individuals without a PE at any time point

ii. *Transient:* Individuals with a PE rated at only one time-point, regardless of frequency (reference group for primary analyses comparing persistent and transient profiles)

iii. *Low-frequency persistent:* Individuals with a low-frequency PE at two or more time points, or with a low-frequency rating at one time point and a high-frequency rating at another

iv. *High-frequency persistent:* Individuals with a high-frequency PE rated at two or more time points

Precursors of longitudinal profiles

Family Psychiatric History: Presence of depression or schizophrenia in the parents and grandparents from parental questionnaires completed during the mother's pregnancy.

Genetic Data: Polygenic risk scores (at discovery sample p-thresholds of 0.05 and using linkage disequilibrium clumping at $r^2 < 0.25$ within 500kb windows(2)) for schizophrenia(3) major depression(4) and neuroticism.(5)

Sociodemographic Characteristics: Data on sex, maternal social class, maternal education, and maternal smoking during pregnancy were collected from parental questionnaires around the time of birth. Maternal social class was indexed by a binary measure comparing classes I-III(N) with classes III(M)-V (1990 Standard Occupational Classifications). Maternal highest education was a binary measure comparing Vocational or CSEs with O-level or higher.

Pregnancy and birth measures: Binary measures of i) self-reported maternal cigarette smoking during pregnancy, ii) self-reported maternal infection during third trimester of pregnancy, and iii) hypoxia at birth (obstetric record of use of bag and mask or intermittent positive pressure ventilation for resuscitation) were included.

Cognitive, psychopathology and trauma measures: All measures were continuous and standardised unless otherwise stated. Verbal IQ and Performance IQ were assessed at age 8 using the Wechsler Intelligence Scale for Children (WISC).(6) External locus of control was assessed at age 8 using the 12-item children's Nowicki Strickland Internal–External control

scale (CNSIE).(7) Emotional and behavioural difficulties were assessed using the Strengths and Difficulties Questionnaire (SDQ) total score(8) and depression assessed using the Short Moods and Feelings Questionnaire (sMFQ),(9) both administered at age 11. Borderline personality disorder traits covering the nine DSM-IV criteria for disorder were assessed at age 11, and a binary variable was derived using a cut-off of 5 or more criteria to define those at highest risk of having a disorder.(10) The Big Five personality domains (extraversion, agreeableness, conscientiousness, emotional stability, and intellect/openness) were assessed at age 14 (hence measured after the start of the profiles, but included here as they are trait measures, so likely reflecting pre-PE characteristics) using the International Personality Item Pool.(11) A categorical measure reflecting the number of types (0-4) of childhood trauma exposure (ages 0 to 10) was derived using data from assessments completed by the parents or self-reported by the participants.(12) Self-harm (binary measure of child reporting whether they had "hurt him/herself on purpose") was assessed at age 11. The existence of nightmares or night terrors (binary measure) was assessed during a semi-structured interview at age 12.

Concurrent measures

Additional measures assessed concurrently to the PE measures (i.e. between ages 12 and 24) were examined to relate patterns of these over time to the PE profiles: *Tobacco use* (at least weekly compared to non-weekly smoking at ages 10, 12, 15 and 24); *Cannabis use* (at least weekly compared to non-weekly use at ages 12, 15, 17 and 24); *Negative symptoms* (assessed using the CAPE(13) at ages 16 (past-month), 23 (past-year) & 24 (past-year)); *Past-year self-harm* (at ages 16, 18, 21, 24 and 25); *Depression* and *Generalised Anxiety Disorder* (current, assessed using the CIS-R(14) at ages 18 and 24); *Vocabulary and Digit Symbol scores* (assessed as part of the Wechsler Intelligence Scale(6) at ages 8, 15 (Digit Symbol only) and

24; *Friendship quality* (using the item "I talk with my friends about my problems" from the Cambridge Friendship Questionnaire(15) at ages 8, 14, 17 and 24).

Persistence Profiles across two different developmental stages

For the purposes of conducting additional analyses to test whether the changes of the PE profiles were time-sensitive, we split the profiles of persistence in two time periods (12-17, 17-24). For each of the two time periods we defined the profiles as:

i. *No experiences*: Individuals without a PE at any time point

ii. *Transient:* Individuals with a PE rated at only one time-point, regardless of frequency (reference group for primary analyses)

iii. *Low-frequency persistent:* Individuals with a low-frequency PE at two points, or with a low-frequency rating at one time point and a high-frequency rating at another

iv. *High-frequency persistent:* Individuals with a high-frequency PE rated at two time points.

For the purposes of the supplementary analysis, iii and iv above were combined into *persistent overall*, as the presence of only two time points for each period would not allow for a definitive rating of "high" or "low" persistence.

Imputation Details

The multiple imputation was performed using the R package mice. The method is based on Fully Conditional Specification, where each incomplete variable is imputed by a separate model. The MICE (Multivariate Imputations by Chained Equations) algorithm can impute mixes of continuous, binary, unordered categorical and ordered categorical data. In addition,

MICE can impute continuous two-level data, and maintain consistency between imputations by means of passive imputation.

105 imputations were performed in total. As a starting point, we selected only individuals who had at least one PLIKS interview measure at one of the three time points (N=8045). For each variable, all other variables of potential interest (described in the "Methods" section as (i) outcomes, (ii) precursors and (iii) concurrent measures) as well as additional cognitive, psychological and socio-demographic auxiliary variables were used as predictors to impute the missing values. For example, data from PLIKS questionnaires at ages 11, 13, 14, 16, and 22 and data on interview-measures of unusual experiences at ages 12, 18 and 24 were additionally used as predictors for the PE data. Continuous predictors were imputed using predictive mean matching, binary predictors were imputed using logistic regression. ordered categorical predictors were imputed using a proportional odds model while unordered categorical predictors were imputed using polytomous logistic regression.

Table S1: Comparison of the Cohort Used (N=8045) with the Full Cohort (N=14,864)in key characteristics (Proportion or mean (CI))**.**

Characteristic	Cohort Used	Full ALSPAC Cohort
Sex (Female), %	52.9%	48.9%
Maternal Education (low), %	22.2%	22.1%
Social Class (low), %	16.3%	17%
Performance IQ (Age 8)	100.5 (100.1, 100.9)	99 (98.6, 99.4)
Verbal IQ (Age 8)	108.1 (107.6, 108.5)	106.7 (106.3,107.1)

Table S2**:** Proportion of missing data in key predictors in the cohort before imputation (N=8045)

Variable	**% Missing**
Sex (female)	0%
Maternal Education (low)	12.4%
Social Class (low)	24.3%
Maternal Smoking	9.6%
Maternal pregnancy infection	44.6%
Hypoxia at birth	44.6%
Family History	11.2%
PRS (schizophrenia)	31.2%
Childhood Trauma	12.1%
Verbal IQ	22.5%
Performance IQ	22.6%
External Locus of Control	33%
Extraversion	29.5%
Agreeableness	29.5%
Conscientiousness	29.5%
Emotional Stability	29.5%
Intellect/Openness	29.5%
Emotional/behavioural problems	24%
Depression	24.6%
Nightmares/terrors	15.4%
Borderline Personality Traits	26.9%
Self-harm	26.8%

Table S3**:** Proportion or mean (SD) of demographic, genetic cognitive and psychopathological characteristics stratified by psychotic experience profile in complete-case sample (N=2743)

	Psychotic experiences			
Variable	**None**	**Transient**	**Persistent Low**	**Persistent High**
Female, (%)	60.6	60.9	71.8	67.8
Low Maternal Education, (%)	12.3	14.6	21.2	15.6
Low Social Class, (%)	26.3	28.7	35.6	39.3
Maternal Smoking, (%)	17.3	20.9	26.8	35.7
Maternal Pregnancy Infection,(%)	22.4	25.4	17.2	27.9
Hypoxia at Birth, (%)	6.8	5.2	7.1	8.2
Family History (%)	39.3	38.11	47.6	50
PRS (Schizophrenia), mean (SD)	-0.1 (1)	-0.01(1)	-0.1(1.1)	0.3 (1.2)
PRS (Depression), mean (SD)	-0.05 (1)	0.1 (1)	-0.1 (1)	0.2 (1)
PRS (Neuroticism), mean (SD)	-0.04 (1)	-0.1 (0.9)	0.01 (0.9)	0.5 (1.1)
Verbal IQ, mean (SD)	112 (16)	110.6(17.3)	109.1 (15)	105 (20.0)
Perform. IQ, mean (SD)	104 (16)	102 (16.4)	100.8 (16.4)	97.7 (20.1)
SDQ, mean (SD)	5.5 (4.3)	6.7 (4.8)	7.9 (5.5)	10.2 (4.5)
Locus of Control, mean (SD)	5.6 (2.1)	6.2 (2)	6.4 (2.1)	6.5 (1.9)
MFQ, mean (SD)	2.0 (2.9)	2.7 (3.3)	3.4 (4)	4.1 (4.9)
Extraversion, mean (SD)	35.1 (7)	34.9 (77.2)	36.2 (7.3)	34.5 (8.8)
Agreeableness, mean (SD)	38.6 (5)	38.5 (5.2)	38.6 (5.2)	39.6 (6.1)
Conscientiousness, mean (SD)	32.6 (5.9)	31.4 (5.9)	30.5 (5.5)	28 (6.8)
Emotional Stability, mean (SD)	32.2 (6.5)	30 (6.5)	29.4 (7)	26 (5.9)
Intellect/Openness, mean (SD)	36.3 (6.0)	36.4(5.7)	37.0 (5.7)	37.6 (7.3)
Trauma Types, mean (SD)	0.6 (0.9)	0.8 (1)	0.9 (1)	1.4 (0.9)
BPD Diagnosis (%)	1	2.2	9.3	15
Nightmares/terrors (%)	26.3	38.2	49.5	50

Footnote: Profiles were based on current PEs (past 6-months at ages 18 & 24; average past 8-months at age 12). Transient: Transient or Episodic PEs; Persistent Low: Persistent or recurrent PEs with frequency of less than weekly; Persistent High: Persistent or recurrent PEs with frequency of more than weekly; PRS: Polygenic Risk Score; ; MFQ: Moods and Feelings Questionnaire, SDQ: Strengths and Difficulties Questionnaire; BPD: Borderline Personality Disorder. ; MFQ: Moods and Feelings Questionnaire, SDQ: Strengths and Difficulties Questionnaire; BPD: Borderline Personality Disorder. Complete-case N: Everyone with PE data at all three time points; Imputed N: Everyone with PE data in at least one time-point.

Table S4: **Univariable Multinomial Logistic Regressions of Persistent vs Transient PEs (Reference)**

Predictor	Persistent Low	Persistent High	Persistent All
	OR (CI)		
Sex (female)	1.42 (1.12, 1.79)	1.25 (0.80, 1.96)	1.38 (1.12, 1.72)
Maternal Education (low)	1.28 (1.00, 1.63)	1.05 (0.62, 1.8)	1.24 (0.98, 1.56)
Social Class (low)	1.22 (0.93, 1.61)	1.05 (0.61, 1.83)	1.19 (0.92, 1.54)
Maternal Smoking	1.30 (1.00, 1.7)	1.64 (1.00, 2.7)	1.35 (1.06, 1.73)
Maternal pregnancy infection	1.01 (0.78, 1.32)	1.28 (0.73, 1.44)	1.06 (0.83, 1.35)
Hypoxia at birth	0.94 (0.62, 1.43)	1.10 (0.49, 2.45)	0.98 (0.66, 1.44)
Family History	1.19 (0.95, 1.49)	1.29 (0.83, 2.04)	1.22 (0.98, 1.51)
PRS (schizophrenia)	1.01(0.9, 1.13)	1.02 (0.79, 1.3)	1.00 (0.90, 1.13)
Childhood Trauma	1.21 (1.04, 1.41)	1.71 (1.27, 2.30)	1.28 (1.11, 1.48)
Verbal IQ	0.95 (0.84, 1.06)	0.89 (0.68, 1.14)	0.94 (0.84, 1.05)
Performance IQ	0.94 (0.84, 1.06)	0.95 (0.74, 1.19)	0.94 (0.85, 1.05)
External Locus of Control	1.07 (1.01, 1.13)	1.11 (0.98, 1.25)	1.08 (1.02, 1.14)
Extraversion	1.08 (0.97, 1.21)	0.93 (0.73, 1.18)	1.05 (0.95, 1.17)
Agreeableness	1.05 (0.93, 1.17)	1.11 (0.86, 1.42)	1.05 (0.95, 1.18)
Conscientiousness	0.86 (0.77, 0.97)	0.74 (0.57 ,0.93)	0.84 (0.75, 0.94)
Emotional Stability	0.81 (0.72, 0.92)	0.65 (0.50, 0.85)	0.79 (0.71, 0.88)
Intellect/Openness	1.08 (0.96, 1.21)	1.13 (0.89, 1.51)	1.09 (0.98, 1.22)
Emotional/behavioural problems	1.13 (1.02, 1.25)	1.28 (1.05, 1.55)	1.16 (1.05, 1.27)
Depression	1.13 (1.03, 1.25)	1.20 (1.02, 1.42)	1.13 (1.05, 1.26)
Nightmares/terrors	1.75 (1.37, 2.23)	1.89 (1.18, 3.04)	1.76 (1.41, 2.21)
Borderline Personality Traits	1.08 (1.05, 1.12)	1.14 (1.08, 1.21)	1.10 (1.06, 1.13)
Self-harm	1.69 (1.12, 2.53)	2.98 (1.50, 5.72)	1.93 (1.35, 2.76)

Table S5: Univariable Logistic Regression Models of any PEs versus no PEs (reference)

Predictor	Odds Ratio	95% Confidence Intervals
Sex (female)	1.05	0.87, 1.25
Maternal Education (low)	1.63	1.39, 1.89
Social Class (low)	1.51	1.27, 1.80
Maternal Smoking	1.67	1.43. 1.93
Maternal pregnancy infection	1.16	1.00, 1.35
Hypoxia at birth	0.97	0.73, 1.28
Family History	1.18	1.04, 1.33
PRS (schizophrenia)	1.07	1.00, 1.14
Childhood Trauma	1.48	1.34, 1.64
Verbal IQ	0.87	0.80, 0.94
Performance IQ	0.89	0.83, 0.96
External Locus of Control	1.13	1.09, 1.16
Extraversion	1.03	0.97, 1.10
Agreeableness	0.96	0.89, 1.03
Conscientiousness	0.78	0.72, 0.85
Emotional Stability	0.71	0.66, 0.77
Intellect/Openness	0.99	0.92, 1.06
Emotional/behavioural problems	1.31	1.22, 1.42
Depression	1.27	1.17, 1.36
Nightmares/terrors	2.02	1.72, 2.36
Borderline Personality Traits	1.17	1.14, 1.21
Self-harm	2.60	1.98, 3.40

Table S6: **Univariable Multinomial Regression models for concurrent characteristics (Transient PEs Reference)**

	No PEs	Persistent Low	Persistent High	FULL MODEL
	OR (95% CI)			Prob>F
Negative Symptoms (Age 16)	0.96 (0.94, 0.97)	1.04 (1.02, 1.06)	1.09 (1.06. 1.13)	$<10^{-5}$
Negative Symptoms (Age 23)	0.95 (0.93, 0.96)	1.02 (1.00, 1.04)	1.06 (1.02, 1.09)	$<10^{-5}$
Negative Symptoms (Age 24)	0.94 (0.92, 0.96)	1.02 (1.01, 1.04)	1.09 (1.05, 1.13)	$<10^{-5}$
Depression (Age 18)	0.54 (0.42, 0.69)	1.43 (1.03, 1.97)	4.14 (2.45, 6.98)	$<10^{-5}$
Depression (Age 24)	0.45 (0.28, 0.73)	1.38 (0.96, 1.99)	2.75 (1.52, 4.97)	$<10^{-5}$
Anxiety (Age 18)	0.47 (0.37, 0.60)	1.65 (1.18, 2.30)	3.47 (1.98, 6.07)	$<10^{-5}$
Anxiety (Age 24)	0.47 (0.31, 0.72)	1.36 (0.96, 1.91)	4.10 (2.37, 7.10)	$<10^{-5}$
Self-Harm (Age 16)	0.57 (046, 0.68)	1.64 (1.23, 2.18)	3.80 (2.30, 6.30)	$<10^{-5}$
Self-Harm (Age 18)	0.54 (0.43, 0.67)	1.59 (1.19, 2.13)	3.66 (2.17, 6.16)	$<10^{-5}$
Self-Harm (Age 21)	0.54 (0.43, 0.68)	1.42 (1.02, 1.95)	1.91 (1.03, 3.58)	$<10^{-5}$
Self-Harm (Age 24)	0.41 (0.25, 0.65)	1.36 (0.91, 2.06)	2.93 (1.60, 5.47)	$<10^{-5}$
Self-Harm (Age 25)	0.48 (0.38, 0.63)	1.36 (0.98, 1.88)	2.79 (1.58, 4.94)	$<10^{-5}$
Vocabulary Score (Age 8)	1.09 (1.01, 1.17)	0.98 (0.87, 1.10)	0.91 (0.71, 1.15)	0.017
Vocabulary Score (Age 15)	1.17 (1.03, 1.21)	0.97 (0.86, 1.09)	0.84 (0.66, 1.07)	0.013
Vocabulary Score (Age 24)	1.14 (1.06, 1.23)	0.95 (0.85, 1.07)	0.85 (0.67, 1.06)	10^{-4}
Digit Symbol Score (Age 8)	1.13 (1.05, 1.22)	0.95 (0.85, 1.05)	0.85 (0.66, 1.08)	10^{-4}
Digit Symbol Score (Age 24)	1.26 (1.12, 1.41)	0.90 (0.79, 1.03)	0.76 (0.59, 0.99)	$<10^{-5}$
Weekly Smoking (Age 12)	0.59 (0.34, 1.02)	1.42 (0.67, 3.00)	2.24 (0.72, 7.10)	0.012
Weekly Smoking (Age 15)	0.55 (0.36, 0.86)	1.48 (0.80, 2.70)	1.93 (0.64, 5.80)	0.0009

Weekly Smoking (Age24)	0.53 (0.45, 0.63)	1.30 (0.99, 1.70)	2.16 (1.30, 3.55)	$<10^{-5}$
Weekly Cannabis (Age 15)	0.44 (0.10, 1.48)	1.46 (0.30, 7.10)	NA	0.27
Weekly Cannabis (Age 17)	0.45 (0.30, 0.60)	1.61 (1.05, 2.46)	2.15 (1.06, 4.37)	$<10^{-5}$
Weekly Cannabis (Age 24)	0.45 (0.33. 0.59)	1.39 (0.99, 1.95)	1.91 (1.04, 3.48)	$<10^{-5}$
Talks with Friends (Age 8)	1.08 (0.92, 1.29)	1.06 (0.81, 1.38)	1.30 (0.73, 2.31)	0.68
Talks with Friends (Age 14)	1.11 (0.87, 1.41)	1.06 (0.73, 1.53)	0.93 (0.45, 1.90)	0.80
Talks with Friends (Age 17)	1.14 (0.92, 1.41)	1.13 (0.79, 1.62)	0.84 (0.42, 1.66)	0.56
Talks with Friends (Age 24)	1.13 (0.95, 1.34)	1.00 (0.75, 1.34)	0.68 (0.40, 1.13)	0.14

Table S7: **Univariable Multinomial Regression models for concurrent characteristics (No PEs Reference)**

	Transient	Persistent Low	Persistent High	FULL MODEL
	OR (95% CI)			Prob>F
Negative Symptoms (Age 16)	1.04 (1.03, 1.06)	1.09 (1.07, 1.11)	1.14 (1.10, 1.18)	$<10^{-5}$
Negative Symptoms (Age 23)	1.05 (1.03,1.06)	1.08 (1.06, 1.10)	1.12 (1.08, 1.15)	$<10^{-5}$
Negative Symptoms (Age 24)	1.06 (1.04, 1.08)	1.09 (1.07, 1.11)	1.16 (1.12, 1.20)	$<10^{-5}$
Depression (Age 18)	1.85 (1.44, 2.36)	2.64 (1.85, 3.79)	7.65 (4.38, 13.30)	$<10^{-5}$
Depression (Age 24)	2.22 (1.36, 3.63)	3.07 (2.05, 4.59)	6.11 (3.20, 11.59)	$<10^{-5}$
Anxiety (Age 18)	2.13 (1.67, 2.72)	3.50 (2.50, 4.95)	7.40 (4.09, 13.40)	$<10^{-5}$
Anxiety (Age 24)	2.11 (1.38, 3.20)	2.87 (1.95, 4.21)	8.66 (4.87, 15.36)	$<10^{-5}$
Self-Harm (Age 16)	1.76 (1.45, 2.13)	2.88 (2.21, 3.77)	6.73 (3.99, 11.36)	$<10^{-5}$
Self-Harm (Age 18)	1.84 (1.48, 2.29)	2.94 (2.20, 3.92)	6.74 (3.98, 11.43)	$<10^{-5}$
Self-Harm (Age 21)	1.82 (1.45, 2.28)	2.57 (1.82, 3.61)	3.50 (1.84, 6,62)	$<10^{-5}$
Self-Harm (Age 24)	2.45 (1.52, 3.92)	3.37 (2.16, 5.2)	7.20 (3.66, 14.16)	$<10^{-5}$
Self-Harm (Age 25)	2.04 (1.58, 2.65)	2.79 (1.95, 3.99)	5.73 (3.12, 10.50)	$<10^{-5}$
Vocabulary Score (Age 8)	0.91 (0.85, 0.98)	0.89 (0.79, 1.00)	0.83 (0.65, 1.05)	0.017
Vocabulary Score (Age 15)	0.89 (0.83, 0.96)	0.87 (0.78, 0.97)	0.76 (0.59, 0.96)	0.013
Vocabulary Score (Age 24)	0.887(0.81, 0.94)	0.83 (0.74, 0.94)	0.74 (0.58, 0.94)	10^{-4}
Digit Symbol Score (Age 8)	0.88 (0.81, 0.95)	0.83 (0.74, 0.93)	0.75 (0.58, 0.95)	10^{-4}
Digit Symbol Score (Age 24)	0.79 (0.70, 0.88)	0.71 (0.61, 0.83)	0.61 (0.46, 0.79)	$<10^{-5}$
Weekly Smoking (Age 12)	1.68 (0.97, 2.90)	2.40 (1.22, 4.77)	3.79 (1.19, 12.03)	0.012
Weekly Smoking (Age 15)	1.79 (1.15, 2.77)	2.65 (1.52, 4.62)	3.46 (1.12, 10.66)	0.0009
Weekly Smoking (Age24)	1.85 (1.57, 2.20)	2.41 (1.86, 3.13)	4.01 (2.43, 6.60)	$<10^{-5}$

Weekly Cannabis (Age 15)	2.27 (0.67, 7,70)	3.34 (0.81, 13.87)	NA	0.27
Weekly Cannabis (Age 17)	2.18 (1.57, 3.03)	3.52 (2.27, 5.46)	4.70 (2.28, 9.70)	$<10^{-5}$
Weekly Cannabis (Age 24)	2.23 (1.67, 2.98)	3.11 (2.16, 4.48)	4.27 (2.36, 7.74)	$<10^{-5}$
Talks with Friends (Age 8)	0.92 (0.78, 1.09)	0.98 (0.76, 1.25)	1.20 (0.67, 2.15)	0.68
Talks with Friends (Age 14)	0.90 (0.71, 1.13)	0.96 (0.66, 1.37)	0.84(0.41, 1.68)	0.79
Talks with Friends (Age 17)	0.88 (0.71, 1.09)	1.00 (0.70, 1.42)	0.74 (0.38, 1.45)	0.56
Talks with Friends (Age 24)	0.88 (0.74, 1.05)	0.88 (0.75, 1.05)	0.60 (0.36, 0.99)	0.14

Table S8**:** Proportion within each PE profile who met criteria for a) a generalised anxiety disorder (GAD) or a moderate or severe depressive (DEP) episode, and b) lifetime deliberate self-harm (DSH) by age 24

PE Profile	**Had GAD or DEP (%)**	**Had DSH (%)**
No Experiences	27.3%	31.6%
Transient	45.2%	48.6%
Low-frequency persistent	53.7%	59.7%
High-frequency persistent	79.6%	80%

Table S9: Split-time Longitudinal Profiles (Transient PEs Reference)

	12-18 Profiles	18-24 Profiles	Overall Profiles
Predictor	Persistent overall	Persistent overall	Persistent overall
	OR(CI)	OR(CI)	OR(CI)
Sex (female)	1.7 (1.2, 2)	1.2 (0.9, 1.7)	1.4 (1.1, 1.7)
Maternal Education (low)	1.2 (0.9, 1.7)	1.2 (0.9, 1.7)	1.2 (1, 1.6)
Social Class (low)	1.1 (0.7, 1.6)	1.2 (0.9. 1.8)	1.2 (0.9, 1.5)
Maternal Smoking	1.1 (0.8, 1.6)	1.2 (0.9 1.7)	1.4 (1.1, 1.7)
Maternal pregnancy infection	0.9 (0.6, 1.4)	1 (0.7, 1.4)	1.1 (0.8, 1.4)
Hypoxia at birth	1.1 (0.5, 2.4)	1 (0.5, 1.9)	1 (0.7, 1.4)
Family History	1.1 (0.8, 1.4)	1.1 (0.8, 1.4)	1.2 (1, 1.5)
PRS (schizophrenia)	1 (0.9, 1.2)	1 (0.8, 1.2)	1. (0.9, 1.1)
Childhood Trauma	1.1 (0.9, 1.4)	1.2 (1, 1.5)	1.3 (1.1, 1.5)
Verbal IQ	1 (0.8, 1.1)	1 (0.8, 1.1)	0.9 (0.8, 1.1)
Performance IQ	0.9 (0.7, 1)	1 (0.9, 1.1)	0.9 (0.9, 1.1)
External Locus of Control	1.1(1, 1.2)	1 (1, 1.1)	1.1 (1, 1.1)
Extraversion	1 (0.9, 1.2)	1.1 (0.9, 1.2)	1.1 (1, 1.2)
Agreeableness	1 (0.9, 1.3)	1 (0.9, 1.2)	1.1 (1, 1.2)
Conscientiousness	0.9 (0.7, 1.1)	0.9 (0.7, 1)	0.8 (0.8, 0.9)
Emotional Stability	0.8 (0.6, 0.9)	0.8 (0.7, 1)	0.8 (0.7, 0.9)
Intellect/Openness	1.1 (0.9, 1.2)	1.1 (0.9, 1.2)	1.1(1, 1.2)
Emotional/behavioural problems	1.1 (1, 1.2)	1.1 (0.9, 1.2)	1.2 (1.1, 1.3)
Depression	1.1 (1, 1.3)	1.1 (1, 1.2)	1.1 (1.1, 1.3)
Nightmares/terrors	2.3 (1.6, 3.2)	1.4 (1.1, 1.9)	1.8 (1.4, 2.2)
Borderline Personality Traits	1.1 (1, 1.2)	1.1 (1, 1.1)	1.1 (1.1, 1.1)
Self-harm	1.8 (1.2, 2.9)	1.5 (1.1, 2.4)	1.9 (1.4, 2.8)

Figure S1: Univariable Multinomial Logistic Regressions of Persistent and Transient PEs vs No PEs (Reference): Sociodemographic characteristics, family history and trauma

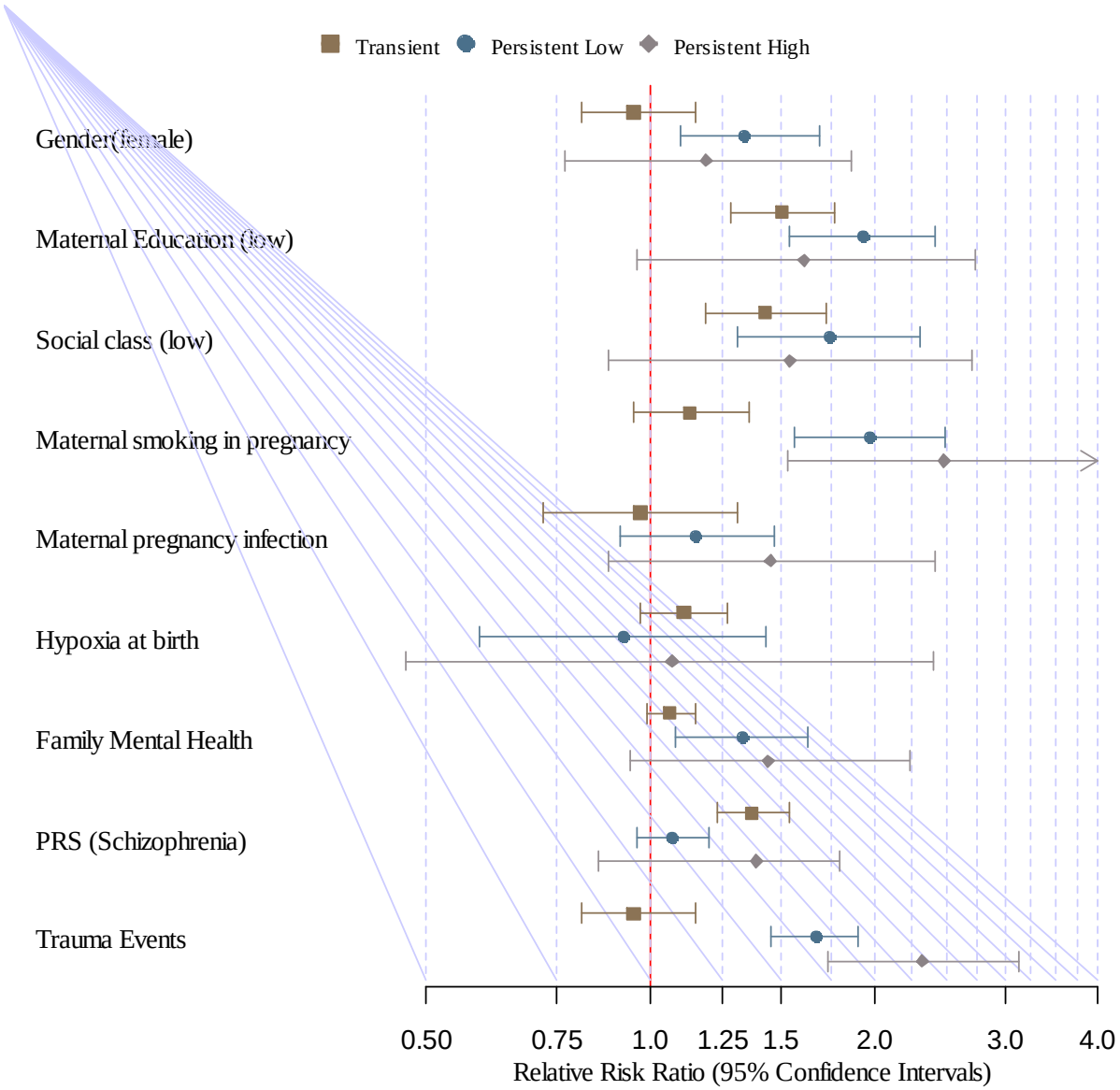
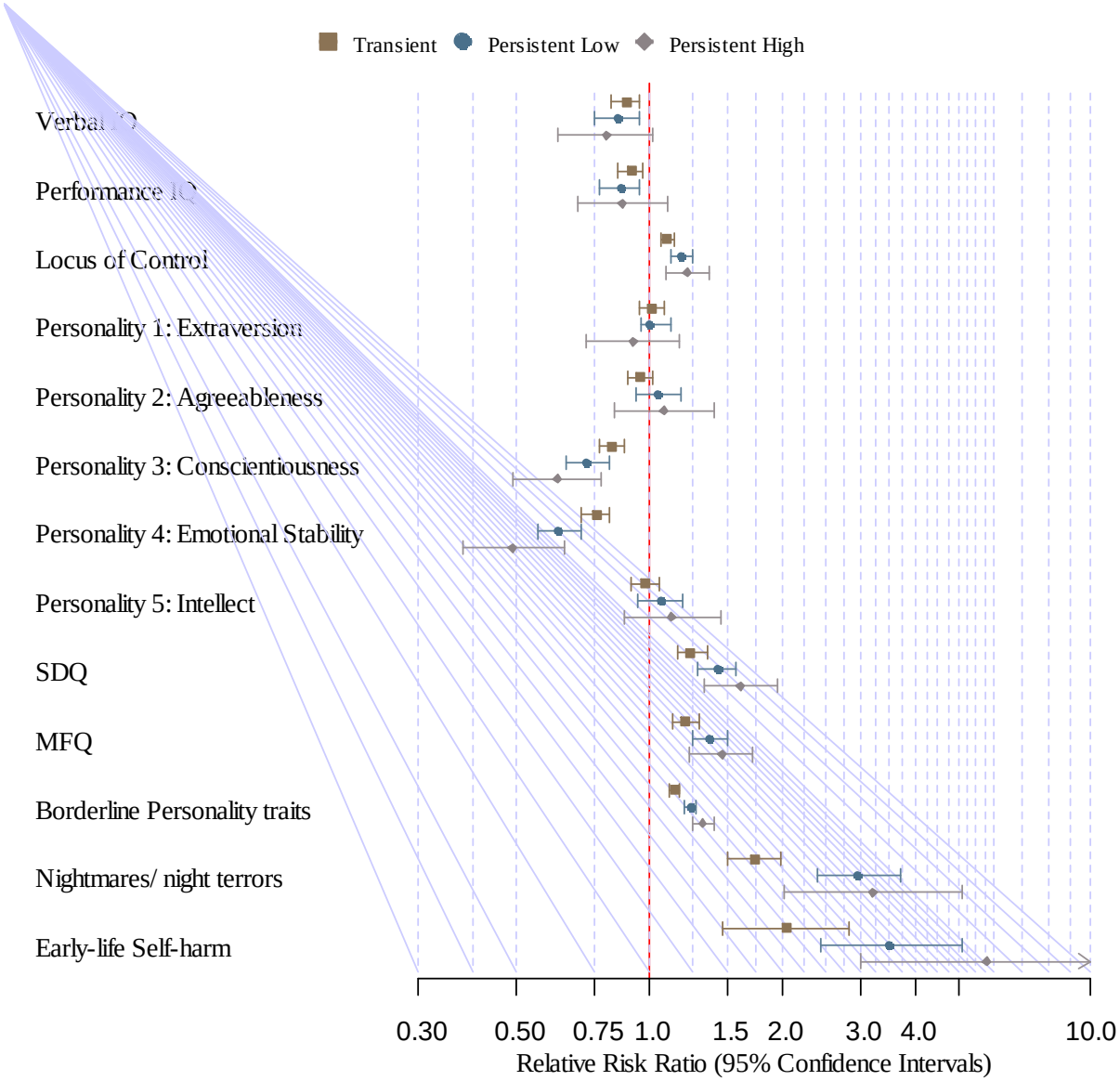


Figure S2: Univariable Multinomial Logistic Regressions of Persistent and Transient PEs vs No PEs (Reference): Cognitive and psychopathological measures



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