



# Psychosis Symptom Trajectories Across Childhood and Adolescence in Three Longitudinal Studies: An Integrative Data Analysis with Mixture Modeling

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## Abstract

Psychotic-like experiences (PLEs) are common throughout childhood, and the presence of these experiences is a significant risk factor for poor mental health later in development. Given the association of PLEs with a broad number of mental health diagnoses, these experiences serve as an important malleable target for early preventive interventions. However, little is known about these experiences across childhood. While these experiences may be common, longitudinal measurement in non-clinical settings is not. Therefore, in order to explore longitudinal trajectories of PLEs in childhood, we harmonized three school-based randomized control trials with longitudinal follow-up to identify heterogeneity in trajectories of these experiences. In an integrative data analysis (IDA) using growth mixture modeling, we identified three latent trajectory classes. One trajectory class was characterized by persistent PLEs, one was characterized by high initial probabilities but improving across the analytic period, and one was characterized by no reports of PLEs. Compared to the class without PLEs, those in the improving class were more likely to be male and have higher levels of aggressive and disruptive behavior at baseline. In addition to the substantive impact this work has on PLE research, we also discuss the methodological innovation as it relates to IDA. This IDA demonstrates the complexity of pooling data across multiple studies to estimate longitudinal mixture models.

**Keywords** Psychotic-like experiences · Integrative data analysis · Mixture modeling

## Introduction

Hallucinations—seeing, hearing, feeling, or smelling things that occur in the absence of an actual stimulus—and delusions—beliefs that are not based in reality and that persist despite contrary evidence—are psychotic symptoms of schizophrenia, a mental illness that is estimated to afflict 0.28% of the world’s population (Charlson et al., 2018). Despite its low prevalence, the complexity and persistence of schizophrenia (Jaaskelainen et al., 2013) increase the risk for a variety of comorbid physical and mental illnesses and for early death (Charlson et al., 2015). Over the long run, outcomes tend to be worse for individuals who do not receive treatment (Penttilä et al., 2014). Thus, programs designed to provide early detection and intervention have been launched in an effort both to improve quality of life and to decrease morbidity and mortality. A recent meta-analysis of early intervention programs as compared to treatment as usual

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found promising outcomes, including reduced symptoms, improved overall functioning, and fewer hospitalizations (Correll et al., 2018).

Typically, schizophrenia is first diagnosed during late adolescence or early adulthood (American Psychiatric Association, 2013). Prior to this time, diagnosis is difficult to make and is rarely given, but the prevalence of psychotic-like experiences (PLEs), including delusions and hallucinations at the subclinical level, is still rare but at least more common than schizophrenia diagnosis (Giocondo et al., 2021; Laurens et al., 2007). In a systematic review of the research literature, Kelleher and colleagues (2012) found that across studies, the median prevalence of psychotic symptoms was 17% among children aged 9 to 12 years and 7.5% among adolescents aged 13 to 18 years (Kelleher et al., 2012). While the prediction of exactly who during childhood or adolescence will develop schizophrenia is difficult (Addington et al., 2019; Lindgren et al., 2014; Therman et al., 2014), PLEs in early life are one of the predictors of interest when determining high clinical risk for psychotic disorders including schizophrenia (Fusar-Poli et al., 2013; Healy et al., 2019; Linscott & van Os, 2013) and a variety of other mental disorders (Kelleher et al., 2012; Kırılı et al., 2019; van Rossum et al., 2011; Varghese et al., 2011) as well as reduced global functioning (Calkins et al., 2014).

While early detection and treatment appear to be a promising avenue for addressing the myriad of difficult outcomes related to schizophrenia, understanding of the developmental epidemiology of symptoms in community-based samples remains a significant gap in the field (Mackie et al., 2011). Thapar et al. (2012) addressed this gap by exploring trajectories of PLEs in the Avon Longitudinal Study of Parents and Children (ALSPAC) sample. Using a mixture modeling approach, these researchers identified four trajectories of PLEs across the period of adolescence. As expected, most of the sample fell into the low PLEs group (87.4%). The second most populous trajectory was an intermittent reporting group (9.9%), followed by a decreasing group (2.3%) and a persistent group (0.5%). While this study represented an important addition to the field, its generalizability is limited in a variety of ways, including a lack of racial and ethnic diversity in the sample. Further, the relations between trajectory membership and subsequent outcomes, most notably a diagnosis of schizophrenia or other types of mental illness, were not examined.

To study the occurrence of PLEs over the course of early development, a specific type of dataset is needed: a diverse, non-clinical sample with longitudinal follow-up with multiple assessment points across trials and a high enough prevalence of PLEs across time to model trajectories. No such dataset exists in the United States. Longitudinal integrative data analysis is ideally suited to fill this gap by harmonizing longitudinal data from multiple sources to capture enough

heterogeneity in symptoms across time. While much of the integrative data analysis literature has focused on measurement issues rather than longitudinal modeling, some have modeled latent growth models. For example, Curran and Hussong (2009) used multilevel piecewise growth models to explore trajectories of internalizing symptomatology across childhood and adulthood in a pooled sample from three studies. This methodology capitalized on the pooled dataset to increase sample heterogeneity, statistical power, and frequency of low-base rate behaviors.

To our knowledge, however, no work has extended integrative data analysis methodology to incorporate mixture modeling. Prior work in the ALSPAC sample suggested that meaningful trajectories exist in PLEs and that key variables are predictive of membership into those trajectories classes (Thapar et al., 2012). This work was done in the Avon Longitudinal Study of Parents and Children cohort. This cohort, which started to explore the role of genetics and environment on health, recruited pregnant women in a specified area of the United Kingdom, making the sample overwhelmingly White. Therefore, our goal is to extend prior work with integrative data analysis (Curran & Hussong, 2009) and trajectories of PLEs (Thapar et al., 2012) to explore the heterogeneity in trajectories of PLEs across childhood and adolescence with more diverse samples. We have found no studies to date exploring subgroup trajectories of PLE in diverse, non-clinical based samples. These datasets also provide an opportunity to explore whether early childhood prevention programming impacts trajectory membership.

### Universal Prevention Programming Reduces PLEs in Non-Clinical Populations

Existing literature provides some support for family-based interventions and skills training (e.g., cognitive behavioral therapy [CBT] approaches) for mitigating risk for PLEs in children and adolescents. For example, a recent meta-analytic review with high-risk child and adolescent samples ( $n = 87$ ) found that although there was limited support for specific interventions preventing transition to psychosis, family interventions, and cognitive remediation may improve pre-psychotic symptoms (Catalan et al., 2021). More specifically, among adolescents and young adults at high-risk for bipolar disorder, Miklowitz and colleagues (2014) found that individuals that received family-focused therapy showed greater decreases in positive symptoms at 6 months relative to those allocated to a family psychoeducation (Miklowitz et al., 2014). Other research has found no differences in cognitive therapy plus monitoring of mental states versus monitoring-only in the transition to psychosis among high-risk adolescents and young adults; however, cognitive therapy plus monitoring reduced severity of psychotic symptoms over 6 months (Morrison

et al., 2012). CBT approaches may also be beneficial by reducing other symptoms of psychopathology, which is important given the high comorbidity among those with PLEs. These interventions were directed to adolescents and young adults but there are also examples of more upstream approaches to prevention of PLEs. These approaches often take a multi-finality approach wherein the prevention program targets a host of mental and behavioral health problems. Given the known multi-finality of PLEs in youth, this type of upstream approach is more appropriate as has been seen in other complex mental health problems like suicide (Wyman, 2014).

In addition to comorbidity, there is some evidence for a causal link between childhood and adolescence externalizing or internalizing psychopathology and PLEs (Lancefield et al., 2016) based on findings from randomized trials. Interventions targeting psychopathology during these developmental periods also have the potential to attenuate PLEs. Unintended positive impacts on outcomes not specifically targeted by the intervention have been identified in recent preventive intervention studies (Dolan et al., 1993). For example, the Multidimensional Treatment Foster Care program was designed to target delinquent and aggressive behavior through a family-based social learning approach among out-of-home care adolescents (Chamberlain, 2003). However, the program also reduced psychosis symptoms in girls over a 24-month period (Poulton et al., 2014).

Another preventive intervention, Fast Track (FT), aimed to prevent the development of serious conduct problems among young at-risk children through parent management training, child social cognitive skills training, peer coaching and mentoring, academic skills tutoring, and a classroom social-emotional learning program (Conduct Problems Prevention Research Group (CPPRG), 2019). Recent findings have shown that FT also reduced psychosis symptoms across childhood, adolescence, and early adulthood, but only while controlling for concurrent cannabis use (Goulter et al., 2019). Taken together, these preliminary findings suggest that preventive interventions targeting disruptive behavior problems may have distal effects on mitigating PLEs in the long term. Integrating data from several preventive intervention studies may facilitate the detection of intervention effects on PLEs that were not the primary targets of the interventions. Fast Track also decreased the probability of suicidal ideation in adolescence and young adulthood (Godwin et al., 2020). FT's improvements to children's interpersonal (e.g., prosocial behavior and authority acceptance), intrapersonal (e.g., emotional recognition and regulation and social problem solving), and academic skills in elementary and middle school partially mediated the intervention effect on adolescent and young adult behaviors suicidal ideation. Interestingly, the Good Behavior Game was also associated with

lower incidence of suicidal ideation and attempts by the time of young adulthood and the effect was partially mediated by more positive childhood peer relations (Newcomer et al., 2016; Wilcox et al., 2008). Thus we wanted to consider the impact FT and GBG could have in terms of PLE and subsequent suicidal thoughts.

### **Integrative Data Analysis (IDA) in Mixture Modeling**

Use of IDA methodology coupled with novel mixture models allows for the harmonization of multiple data sources, which contain discrepant measures of PLEs over time. Although harmonization is relatively common in other domains, integrative data analysis is still a relatively novel concept within mental health intervention research (Brincks et al., 2018; Brown et al., 2018). To date, most IDA studies within mental health research have focused either on cohort studies or data from clinical trials of psychotropic medication (Gibbons et al., 2012a, b; Gibbons, et al., 2012). Our IDA approach will involve extending moderated non-linear factor analysis, developed by Curran and colleagues, which allows for the creation of scale scores based on all available items while accounting for individual differences (Curran & Hussong, 2009). This analytic method explores whether a measure is invariant across a set of covariates with respect to factor means, variances, item intercepts, and factor loadings (Curran et al., 2014). Our methodological innovation extends the Curran et al. approach to include longitudinal mixture models, incorporating recent work focused on analyzing pooled data and use of full information maximum likelihood (Brincks et al., 2018; Brown et al., 2018; Siddique et al., 2015).

### **The Current Study**

This manuscript focuses on the harmonization of PLEs across three randomized control trials of universal school-based prevention programs. The primary objective was to create covariate informed trajectories of psychotic-like experiences to capture heterogeneity in these symptoms across development. This was accomplished by extending prior integrative data analysis work to latent mixture modeling (Bauer & Hussong, 2009; Curran & Hussong, 2009; Curran et al., 2014). The second goal of this manuscript was to determine if receipt of universal school-based prevention program in early childhood significantly impacted PLE trajectories. By integrating three trials targeting early aggressive disruptive behaviors, we can assess the overall impact and possibly identify the proposed mechanisms through which these interventions may have reduced PLEs. Finally, we explore the prevalence of suicidal related behaviors in adulthood across the latent class trajectories. Because psychotic disorders are so disabling, difficult to treat, and

linked with premature mortality, a beneficial impact on PLE from early intervention could have great public health and clinical significance.

## Methods

### Sample

The pooled sample includes three preventive intervention trials with longitudinal follow-up. The JHU Prevention Intervention Research Center Generation 1 (PIRC G1, Kellam et al., 2008; 2014) is a school-based randomized prevention trial, wherein randomization occurred at both the school and classroom level, conducted in first and second grade classrooms in the Baltimore City public school system with long-term prospective follow-up of youth into adulthood. Starting in 1985, two successive first-grade cohorts ( $n_1 = 1196$ ;  $n_2 = 1115$ ; and total  $N = 2311$ ) were recruited from 43 classrooms among 19 elementary schools that were in five areas of eastern Baltimore City.

The Fast Track Project (CPPRG, 2019) was evaluated in a randomized-controlled trial with annual assessments. In January 1991, crime records, poverty statistics, and school dropout rates were used to identify 55 high-risk schools in four geographic sites across the United States (Durham, NC; Nashville, TN; Seattle, WA; and rural central PA) that varied widely in ethnicity and poverty. Within each site, the schools were divided into multiple paired sets matched for demographics, and one school in each pair was randomly assigned to intervention and control conditions. Using a multiple gating screening procedure for each of three annual cohorts (1991–1993), all 9594 kindergarteners in the 55 schools were screened initially for classroom conduct problems by teachers. Within cohort and site, parents of children in the top 40% of teacher-rated conduct problems were asked to complete a 22-item instrument capturing behavior problems at home. Children were selected for inclusion in the study based on a combined teacher and parent screen score.

Linking the Interests of Families and Teachers Study (LIFT; Eddy et al., 2000, 2003) was comprised of the entire population of families of first or fifth-grade youth enrolled in 12 eligible public elementary schools from three adjacent school districts in a moderate size city in the Pacific Northwest. School eligibility was based on location in at-risk neighborhoods characterized by elevated juvenile delinquency rates relative to local norms. The 12 schools were randomly assigned to a control or preventive intervention condition. Either the entire set of first-grade classes (which included some second-grade students) or the entire set of fifth-grade classes (which included some fourth-grade students) within each school were invited to

participate. There were three schools in each of four cells (i.e., first-grade intervention, first-grade control, fifth-grade intervention, and fifth-grade control).

## Measures

### Psychosis Like Experiences (PLEs)

In the FT and LIFT trials, PLEs were assessed using four items of the thought problem subscale of Child Behavior Checklist (CBCL; Achenbach & Ruffle, 2000). The items include the following: 1) hearing things that are not there, 2) seeing things that are not there, 3) strange behaviors, and 4) strange ideas. Parents rated the child's behavior over the past 6 months on a three-point scale of 0 "Not true," 1 "sometimes true," and 2 "Often true". In PIRC G1, PLEs were assessed with 2 items. First, reported on an item similar to the first CBCL item. Children rated how often over the past 12 months they "hear things no one else around you hears" on a five-point scale of 0 "Never" to 4 "Almost always". Similar to the third CBCL item, children also rated how often in the past 6 months they behaved in a way that "others think strange" on a three-point scale of 0 "Not true" to 2 "Often true."

Using a pre-statistical harmonization process, a single binary variable was created indicating whether a student had at least one psychotic-like experience in a given grade. First, each psychosis item was re-coded as a binary item; the three-point items were coded as 0 = not true, 1 = any endorsement of symptoms; the five-point item was recoded as 0 = never or seldom, 1 = any endorsement of symptoms. Finally, in each grade, responses were collapsed across the four binary items (two for PIRC G1) to create a single binary variable capturing any psychotic-like experience which was coded 1 if any of the individual symptoms were endorsed.

### Covariates

Six covariates were included as predictors in the latent class model estimating PLEs. These included intervention status (0 = control, 1 = intervention), race (0 = non-Black, 1 = Black), sex (0 = female, 1 = male), a continuous measure of aggressive-disruptive behavior in first grade, and two binary indicator variables for PIRC G1 and FT studies (with LIFT excluded as the reference study). Aggressive-disruptive behavior was measured by the Authority Acceptance subscale of the Teacher Observation of Classroom Adaptation-Revised (TOCA-R; Werthamer-Larsson et al., 1991). Using an integrative data analytic approach, a moderated non-linear factor analysis (MNLFA) model was constructed to allow for item and factor parameters to be moderated by sex, race, and study membership. Thus, the estimated factor scores of baseline

aggressive–disruptive behavior were scaled commensurately across studies. For more information regarding the MNLFA model and its estimation, please see (Kush et al., 2022).

## Outcomes

A set of suicide-related variables were created from all available data in the pooled sample from eleventh grade to the end of the dataset. Suicidal ideation between grade 11 and age 32 was coded as endorsed if suicidal ideation in past week, past two weeks, past 6 months, and past twelve months was endorsed at any data point over the time period. Similarly, an indicator for suicide attempt between grade 11 and age 32 was created if any attempt (in last year or past 6 months) was reported at any at any data point over the time period.

## Intervention

The PIRC G1 intervention included two components: the Good Behavior Game (GBG; Barrish et al., 1969; Dolan et al., 1993) and Mastery Learning (Bloom, 1971). The GBG is a whole-class strategy that aims to decrease disruptive behaviors by establishing classroom rules, assigning team membership, monitoring behavior while playing GBG, and providing positive reinforcement to individuals and the teams that do not exceed a specified criterion of precisely defined off-task, disruptive, and aggressive behaviors. Participants assigned to the GBG condition received the intervention over the course of the first and second grades (Dolan et al., 1993). The Mastery Learning intervention involved extensive enrichment of the reading curriculum, with a special focus on clear instructional statements, communication of expectations, and a group-based approach to mastery (Bloom, 1971; Dolan et al., 1993). For the purposes of this analysis, those children receiving the GBG and Mastery Learning were categorized as receiving an intervention.

The universal component of the FT intervention was adapted from the Promoting Alternative Thinking Strategies (PATHS) curriculum with the goal of understanding and communicating emotions, increasing positive social behavior, and improving self-control. Indicated intervention components for the high-risk sample during elementary school included children’s social skills groups, peer-pairing with low-risk classmates, parenting groups, guided parent–child interaction sessions, academic tutoring, home visiting, and mentoring. During the adolescent phase of the intervention (grades 6–10), indicated components included parent/youth groups and youth forums focused on adolescent development, life skills, and vocational opportunities and individualized interventions concerning parental monitoring, peer affiliation, academic achievement, and social cognition (CPPRG, 2019).

The LIFT study contained several intervention components. The classroom component improved upon child social and problem-solving skills during 20 h-long social emotional learning (SEL) skills training sessions over the course of the intervention. The playground component was based on a modified version of the GBG that reinforces child positive social behaviors during free (unstructured) play during recess. The family component was a group-based version of parent management training (PMT) emphasizing effective discipline, supervision, and problem-solving skills. Parents met with a PMT coach once a week, for 6 weeks, and received support between sessions. For the purposes of this analysis, intervention status was collapsed to a binary variable indicating whether the participant was in any intervention across all studies.

## Integrative Data Analysis

Data analysis began with pre-statistical harmonization, exploration of the pooled dataset including identifying common domains, response scale types, and the collection of variables across time. These processes are described above in the “Measures” and “Intervention.” Data cleaning and descriptive analysis was done in Stata, version 16 (StataCorp, 2019). To better understand the trajectories of psychotic-like experiences across development, a latent class growth analysis was conducted using Mplus (Muthén & Asparouhov, 2015; Muthén & Muthén, 2000; Muthén et al., 2002; Muthén & Muthén, 1998–2017). This model is conceptually similar to a growth mixture model, except the variances of the latent intercept and latent slope are fixed to zero within class. Within different classes, binary indicators of PLEs are modeled over time with a latent intercept and latent slope forming a growth trajectory (Muthén & Asparouhov, 2015). A priori, we hypothesized the presence of a latent class characterized by zero probability of PLEs. This decision was implemented by fixing the latent intercept at a very small probability ( $\logit = -0$ ) and fixing the latent slope at zero for one latent class. Sensitivity analyses were done to assess this hypothesis as well as the assumption of a linear slope. Both models suggested that the inclusion of a low/no symptom class and linear slopes fit the data best. The initial measurement model is run without the inclusion of covariates and outcomes. Following the decision regarding the measurement model, covariates are included using an IDA approach (Curran & Hussong, 2009). This approach allows us to appropriately account for data from multiple, independent prevention trials, by allowing the latent class means to be moderated by our set of covariates, including intervention status, sex, race, baseline aggressive disruptive behavior, and importantly, study membership. This is accomplished within the latent mixture model environment by including regression statements within the model statement. Finally, in order to explore outcomes of these trajectories, we used modal



class assignment to hard classify individuals into their latent classes and then explored the prevalence of suicide ideation and attempt in each latent class. No significance testing was done with these outcomes. Missing data was handled utilizing full information maximum likelihood (Enders & Bandalos, 2001; Graham, 2009; Schafer & Graham, 2002).

## Results

### Descriptive Statistics

The three studies measured PLEs at different timepoints; PIRC G1 measured PLEs at grades 5, 7, and 8; FT measured PLEs at grades 2, 4, 5, and 7; LIFT measured PLEs at grades 2, 4, 5, 8, and 10. Table 1 summarizes the covariates and frequencies of PLEs across time in the pooled sample. The sample was 55.6% male and 62.6% Black. Intervention status was relatively evenly divided in the pooled sample with approximately 45.8% of individuals belonging to the intervention group.

### Model Building

To determine the optimal number of classes for the latent class growth analysis, we fit 2-class, 3-class, 4-class, and 5-class models, comparing the log-likelihood, sample size-adjusted BIC, entropy, and smallest class sizes (see Supplemental Table 1). Results demonstrated the 3-class model fit the best,

which we now focus on for the remainder of the results. The largest class of the 3-class model included individuals with a very low probability of reporting PLEs at any timepoint (low class;  $n = 1,826$ ; 71.0%). Again, this class was constructed by fixing the probability of reporting PLEs to  $\text{logit} = -30$  across time. The second largest class included individuals with a decreasing probability of reporting PLEs across time (Improving class;  $n = 589$ ; 22.9%). The third and smallest class included individuals with an increasing probability of reporting PLEs across time (Persistent class;  $n = 157$ ; 6.1%). The average latent class probability for each class was 0.84, 0.99, and 0.90, respectively, with an entropy of 0.74. Figure 1 provides a graphical depiction of trajectories of psychotic-like experiences across time.

### Structural Model Results

Examining the regression estimates for the latent class mean on covariates shown in Table 2. There was no evidence that intervention status was related latent class membership. Likewise, there were no statistically significant differences in latent class membership across races. However, males were significantly more likely than females to belong to the improving class than the low class ( $OR = 1.47$ ,  $p = 0.04$ ), while those with higher baseline aggression were also more likely to belong to the improving class than the low class ( $OR = 1.40$ ,  $p < 0.001$ ).

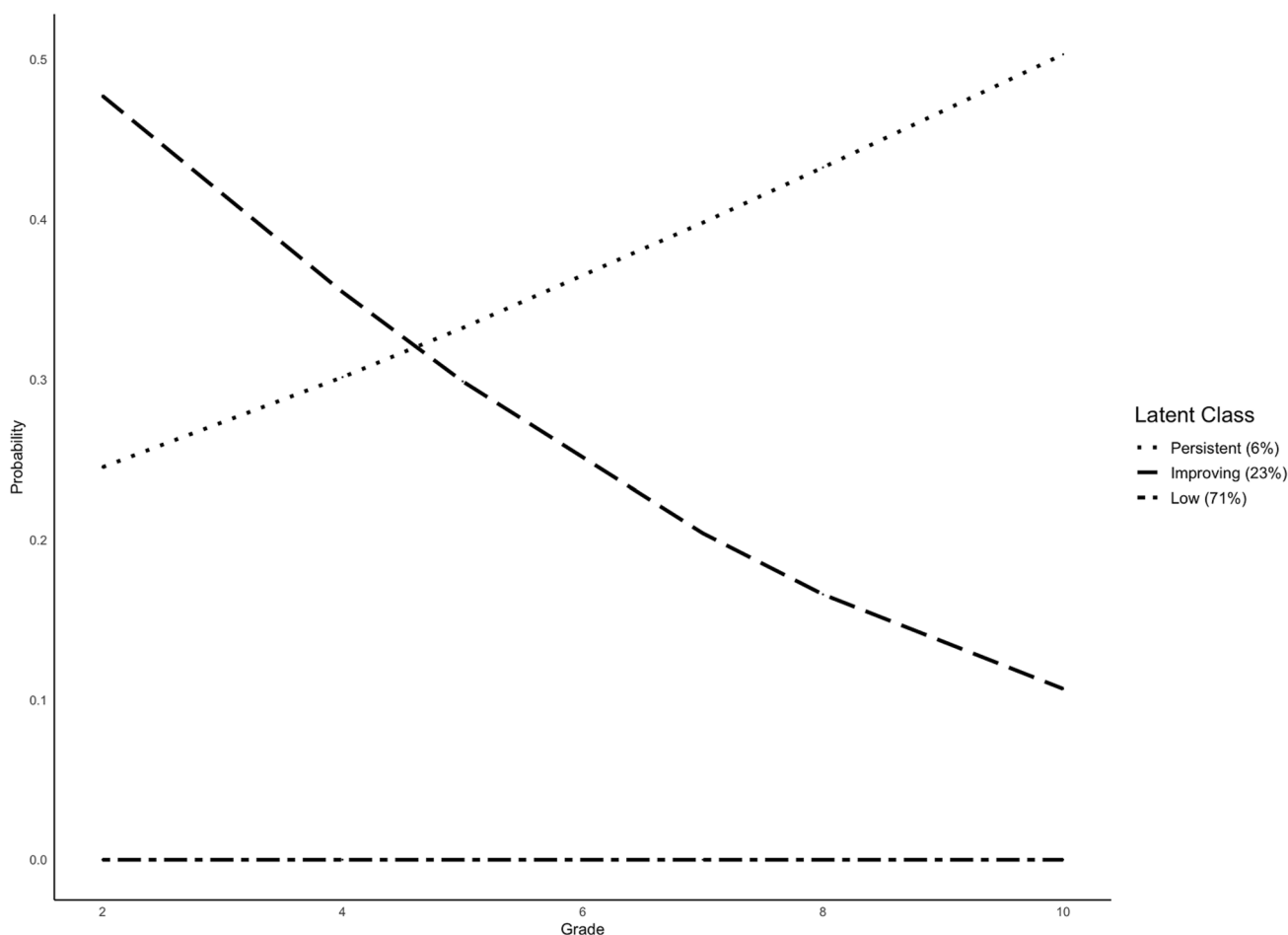
Finally, we examined the proportion of individuals in each class that indicated suicide ideation and/or suicide

**Table 1** Descriptive statistics

	Whole sample <i>N</i> = 2572	Improving class <i>N</i> = 589; 22.9%	Persistent class <i>N</i> = 157; 6.1%	Low class <i>N</i> = 1826; 71.0%
Female	44.4%	28.7%	52.9%	48.8%
Black	62.6%	55.9%	0.6%	70.2%
Study: fast	32.5%	82.7%	0%	19.1%
Study: lift	9.4%	0.3%	100%	4.5%
Study: pirc1	58.1%	17.0%	0%	76.4%
Intervention status	45.8%	49.1%	52.2%	44.1%
Baseline aggression	$M = 1.11$ , $SD = 1.30$	$M = 1.85$ , $SD = 1.05$	$M = 0.34$ , $SD = 1.19$	$M = 0.94$ , $SD = 1.28$
PSE, grade 2	31.6%	57.3%	38.3%	0%
PSE, grade 4	25.6%	46.2%	31.9%	0%
PSE, grade 5	9.6%	38.7%	na	0%
PSE, grade 7	8.1%	30.8%	na	0%
PSE, grade 8	4.5%	18.5%	25.2%	0%
PSE, grade 10	46.5%	0%	73.5%	0%
Later ideation	4.4%	19.7%	7.6%	7.2%
Later attempt	1.4%	7.8%	0%	2.9%

Baseline covariates had no missing data

Whole-sample missing rates for PLEs were as follows: grade 2 = 58.7% missing; grade 4 = 60.1% missing; grade 5 = 12.7% missing; grade 7 = 26.4% missing; grade 8 = 61.6% missing; grade 10 = 91.6% missing. Whole sample missing rates for the two outcomes were as followed: later ideation = 56.5% missing; later attempt = 71.7% missing



**Fig. 1** Trajectories of psychotic-like experiences

attempt from grade eleven on. Regarding ideation, approximately 7.2% ( $n = 131/1825$ ) of those in the low class, 19.7% ( $n = 116/588$ ) of those in the improving class, and 7.6%

( $n = 12/159$ ) of those in the persistent class had at least one report of suicide ideation from grade 11 onward. Similarly, approximately 2.9% ( $n = 53/1,825$ ) of those in the low class, 7.8% ( $n = 46/588$ ) of those in the improving class, and 0% ( $n = 0/159$ ) of those in the persistent class had at least one suicide attempt from grade 11 onward. Thus, those in the improving class had the highest rates of suicide ideation and attempt at later timepoints.

**Table 2** Covariate effects on trajectory membership

	Est	SE	<i>p</i>
<b>Improving class</b>			
PIRC G1	-0.64	1.14	0.577
FT	1.71	1.15	0.135
Intervention	-0.05	0.16	0.746
Male	0.38	0.19	0.041
Black	-0.17	0.23	0.441
Aggression	0.34	0.09	<0.001
<b>Persistent class</b>			
PIRC G1	-5.27	3.84	0.170
FT	-7.87	0.82	<0.001
Intervention	-0.24	0.49	0.617
Male	-0.00	0.66	0.998
Black	-1.99	1.36	0.114
Aggression	0.13	0.24	0.590

Reference is low class, LIFT study, control, female, and White

### Discussion

As has been found in prior samples (e.g., Thapar et al., 2012), we estimated several heterogeneous subgroups based on longitudinal trajectories of PLEs. While prior research suggested that PLEs are normative during childhood and adolescence, persistent experiences of PLEs may serve as an important risk factor for later mental and behavioral health problems and may be an important indicator of the need for preventive intervention. Our findings suggest the presence of three trajectories of PLEs, the most populous of which is characterized by no PLEs across the study period.

The second largest class was characterized by a relatively high intercept with a statistically significant negative slope (the improving class). While members of this class may be considered low risk because PLEs decrease later in development, the higher probability of PLEs early in childhood may serve as a clear indicator of risk. Males and individuals with higher aggressive and disruptive behaviors at baseline were more likely to be in the improving class as compared to the no PLE class. In addition, this trajectory class demonstrated the highest prevalence of suicidal ideation and suicide attempt in late adolescence and young adulthood. Finally, the smallest trajectory class demonstrated low probability at the intercept but a statistically significant positive slope (the persistent class). While the prevalence of suicide ideation and attempt in late adolescence and young adulthood among this subgroup was quite low, it is possible that members of this trajectory are more likely to experience other mental or behavioral disorders.

Prior research has demonstrated a significant association between PLEs during childhood and adolescence and later mental and behavioral health problems. Among the psychiatric conditions, psychotic disorders (both affective and non-affective) are associated with some of the highest rates of death by suicide (Too et al., 2019; Yates et al., 2019), with particularly high rates of suicide among individuals diagnosed with schizophrenia and bipolar disorder. The risk for suicide is especially pronounced shortly after psychotic onset, for both affective and non-affective psychosis, which tends to occur in adolescence or early adulthood (McGinty & Upthegrove, 2020; Sicotte et al., 2021). Our findings suggest that PLEs in middle childhood may be particularly salient for later suicide-related outcomes. This suggests that targeting these experiences during early childhood with prevention programming may have positive impacts later in development. One possible mechanism through which prevention programming could reduce risk for PLEs is through substance use prevention programming (Matheson et al., 2022). Studies have consistently found associations between early cannabis use and risk for PLEs. Similarly, childhood trauma may significantly increase risk, therefore prevention programs in childhood that target increased coping for stressful life events may be useful (Harley et al., 2010).

This study also presents a novel methodology for integrative data analysis with mixture modeling. By pooling data across multiple longitudinal school-based studies, we successfully model PLE trajectories with multilevel mixture modeling. Prior integrative data analysis work has focused primarily on factor analytic methods rather than mixture modeling. A majority of the harmonization efforts for this integrative data analysis occurred during the pre-statistical harmonization phase wherein missing data patterns across study and time were carefully explored so that the measurement model could be built with the least amount of missing

data possible. Future work must further explore the impact of missing data patterns on the extraction of latent classes in longitudinal modeling.

While this study adds to the literature by modeling trajectories of PLEs in a diverse, non-clinical sample and extending integrative data analysis to mixture modeling, there are some limitations. First, to facilitate data harmonization, multiple reporters of PLEs were treated as equal. This may be simplifying differential reporting and should be explored in future research (Hanssen et al., 2003; Schultze-Lutter et al., 2014). Additionally, we were more inclusive in our re-coding of PLEs such that those reporting sometimes experiencing PLE were considered an endorsement of PLEs. We went with this approach given the school-based nature of our sample but acknowledge that this more inclusive characterization is a limitation. The research surrounding trajectories of PLEs in youth is relatively sparse and our findings certainly increase the diversity of the literature in this area. However, our sample is still limited in its diversity. Our sample is majority Black (62.6%), because of this and the relatively small groups of other races and ethnicities, we were unable to make more distinct comparisons between racial and ethnic groups. While efforts are being made to diversify cohort and longitudinal studies moving forward, future research should acknowledge the limitations of extant research in regard to diversity of samples.

Further, the data pooled for these analyses came from randomized controlled trials of school-based prevention programs. There was no impact of the interventions on latent class membership in this study. While it was our intention to explicitly model the impact of each preventive intervention, the relatively small latent classes could not accommodate those analyses. To estimate an individual intervention impact, we need an even larger dataset, particularly when exploring membership in rare latent class trajectories and looking at study arms within a particular study. Future data harmonization efforts should focus on the pooling of studies with consistent measures of PLEs across similar developmental periods. Finally, we were unable to test for statistically significant differences in our outcomes across latent classes. This is a result of the small to zero cell sizes of our rare outcomes across latent classes. Future studies should consider using significance testing to assess these differences but this would likely require significantly bigger sample sizes given the rare exposure trajectories (PLEs) coupled with the rare outcomes (suicide attempt).

Despite these limitations, this study makes an important contribution to the literature. Much of the prior work examining PLEs in childhood and adolescence focuses on clinical samples, whereas our pooled sample was diverse and school-based. While Thapar and colleagues (2012) used a community-based sample and found similar classes of PLE trajectories, our sample is diverse in terms of race and



socioeconomic status whereas their study primarily consists of White participants with high socioeconomic status. Our findings complement this work by estimating trajectories of PLEs from a more ethnically diverse community-based sample followed from childhood into adulthood.

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**the Conduct Problems Prevention Research Group (CPPRG)** The members of the Conduct Problems Prevention Research Group (CPPRG) are, in alphabetical order, Karen L. Bierman (Pennsylvania State University); John D. Coie (Duke University); D. Max Crowley (Pennsylvania State University); Kenneth A. Dodge (Duke University); Mark T. Greenberg (Pennsylvania State University); John E. Lochman (University of Alabama); Robert J. McMahon (Simon Fraser University and the B.C. Children's Hospital Research Institute); and Ellen E. Pinderhughes (Tufts University).

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**Data Availability** Data will be made available through the National Institutes of Mental Health Data archive at the completion of the grant period

## Declarations

**Ethical Approval** All procedures performed in the current study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed Consent** Informed consent was obtained from all individual participants included in the study. The study was approved by the Johns Hopkins Bloomberg School of Public Health IRB.

**Conflict of Interest** Drs. Bierman, Coie, Dodge, Greenberg, Lochman, McMahon, and Pinderhughes are the principal investigators on the Fast Track Project and have a publishing agreement with Guilford Publications, Inc. Royalties from that agreement are donated to a professional organization. They are also authors of the PATHS curriculum and donate all royalties from Channing-Bete, Inc. to a professional organization. Dr. Greenberg is a developer of the PATHS curriculum and

has a separate royalty agreement with PATHS Program LLC. Bierman, Coie, Dodge, Greenberg, Lochman, and McMahon are the developers of the Fast Track curriculum and have a publishing and royalty agreement with Guilford Publications, Inc. McMahon is a coauthor of *Helping the Noncompliant Child* and has a royalty agreement with Guilford Publications, Inc. Dr. Crowley has no conflicts.

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