

## What we have learned about adolescent mental health and where we are going after a decade with the Adolescent Brain Cognitive Development Study

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### ABSTRACT

This review synthesizes ten years of research utilizing data from the Adolescent Brain Cognitive Development (ABCD) Study, emphasizing how the study's comprehensive, longitudinal design supports a multivariate understanding of adolescent mental health. We focus on studies that have examined the collective or interacting relations of multiple factors to mental health in adolescents, as this unique dataset allows for examining more complex configurations of risk factors. We highlight key findings from ABCD data that have deepened our understanding of the risk factors shaping mental health outcomes in adolescence. Findings underscore the complex interplay of biological, psychological, and/or contextual factors on adolescent mental health. We conclude with a forward-looking discussion of emerging research priorities and opportunities to further leverage the ABCD dataset to inform developmental theory, prevention, and intervention efforts.

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Approximately half the world's population will experience at least one mental health disorder during their lifespan (McGrath et al., 2023). The majority of such disorders onset during the second decade of life. Adolescents who experience mental health disorders are at greater risk of negative outcomes in adulthood including chronic mental and physical health challenges, social functioning issues, lower educational attainment, and involvement with the legal system (Johnson et al., 2018; Clayborne et al., 2019; Copeland et al., 2021). Among people aged 10–24, mental health disorders are the leading cause of disability across the world (Gore et al., 2011). As such, identifying the key factors, and the likely complex interactions among multiple factors, predicting risk and resilience for mental health challenges in adolescence is a pressing need. The Adolescent Brain Cognitive Development Study (ABCD) is uniquely positioned to help address this goal.

A central objective of the ABCD Study is to characterize youth mental health trajectories using a longitudinal, multi-method, and multi-informant framework (Barch et al., 2021, 2018). Mental health data are collected annually from both caregivers and youth via the self-administered computerized Kiddie Schedule for Affective Disorders and Schizophrenia for DSM-5 (KSADS-COMP) and by dimensional self-, parent-, and teacher-report measures from the Achenbach suite of measures (Fig. 1). At the time of writing this review, data from when youth were 9–10 years old to 16–17 years old have been released. The prevalence and developmental course of mental health conditions observed in the ABCD cohort align closely with findings from prior large-scale epidemiological studies (Merikangas et al., 2010; Olfson et al., 2023; Levin and Liu, 2024; Ivankovic et al., 2025). By age 16, over one-third of youth self-reported symptoms consistent with a lifetime mental health diagnosis, while caregiver reports estimate a higher prevalence of 46 %. The most frequently endorsed symptoms included sleep disturbances and suicidality, with attention-deficit/ hyperactivity disorder (ADHD), mood disorders, and anxiety disorders being the most commonly reported diagnostic categories. Notably, youth-reported symptoms increased with age, diverging from caregiver reports—a pattern consistent with developmental trends observed in other epidemiological samples (Costello et al., 2011). Beyond prevalence estimates, the comprehensive protocol of the ABCD Study enables the identification of complex factors contributing to the onset and persistence of

mental health problems, offering important insights during the first decade of the study.

Along with data that inform this rich characterization of the emergence and trajectory of mental health challenges in youth, the ABCD Study also collects data on a wide variety of potential risk factors that may help us understand why and how youth develop mental health problems (Barch et al., 2021, 2018). At the time of writing this review over 913 publications have used mental health data from the ABCD Study (the last search was conducted on January 16, 2026). This review aims to highlight key advances in understanding how multiple domains of factors work in concert to influence adolescent mental health. Specifically, we organize our review around key themes in adolescent mental health research, highlighting the ways in which ABCD-based science advances understanding of those themes. We start by noting themes that designate certain variables as risk factors, broadly defined (e.g., predictors, mediators, moderators). We note that a wide range of statistical methods are used to examine risk factors for mental health experiences, and that careful application of inferential principles is essential for interpreting the current evidence and guiding future scientific progress (see Table 1). We then highlight a theme focused on parsing the heterogeneity of risk factors and mental health experiences themselves. Finally, we outline practical steps for advancing science in the years ahead. We provide a selective review, based on existing publications using the ABCD data, of findings related to mental health outcomes that highlight consideration of multiple factors (*NB*: other pieces in this special issue go into detail about the relationship between single variables and mental health outcomes, as well as focus specifically on substance use and misuse outcomes).

## 1. Emerging themes from ABCD research on multivariate factors in adolescent mental health

### 1.1. Brain development differences were known risk factors for mental health outcomes, and ABCD research reveals they also function as important moderators

Recent research using ABCD data has revealed that the relationship between brain function and mental health outcomes in adolescents is far

|                                                                                                                            | Baseline | 1yr follow-up | 2yr follow-up | 3yr follow-up | 4yr follow-up | 5yr follow-up | 6yr follow-up | 7yr follow-up | 8yr follow-up | 9yr follow-up |
|----------------------------------------------------------------------------------------------------------------------------|----------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|
|                                                                                                                            | Age 9-10 | Age 10-11     | Age 11-12     | Age 12-13     | Age 13-14     | Age 14-15     | Age 15-16     | Age 16-17     | Age 17-18     | Age 18-19     |
| <b>Youth Measures</b>                                                                                                      |          |               |               |               |               |               |               |               |               |               |
| KSADS-Y                                                                                                                    |          |               |               |               |               |               |               |               |               |               |
| Brief Problem Monitor-Youth (BPM-Y)                                                                                        |          |               |               |               |               |               |               |               |               |               |
| Youth Self Report (YSR)                                                                                                    |          |               |               |               |               |               |               |               |               |               |
| Prodromal Questionnaire-Brief Child Version                                                                                |          |               |               |               |               |               |               |               |               |               |
| Mania 7 Up Inventory                                                                                                       |          |               |               |               |               |               |               |               |               |               |
| NIH Toolbox Positive Affect Items                                                                                          |          |               |               |               |               |               |               |               |               |               |
| Life Events                                                                                                                |          |               |               |               |               |               |               |               |               |               |
| Peer Experiences Questionnaire                                                                                             |          |               |               |               |               |               |               |               |               |               |
| Urgency, Premeditation, Perseverance, Sensation Seeking, Positive Urgency, Impulsive Behavior Scale (UPPS-P)-short version |          |               |               |               |               |               |               |               |               |               |
| Behavioral Inhibition/Behavioral Activation Scale (BIS/BAS)                                                                |          |               |               |               |               |               |               |               |               |               |
| Cyber-bullying                                                                                                             |          |               |               |               |               |               |               |               |               |               |
| Resilience (friendship, religion)                                                                                          |          |               |               |               |               |               |               |               |               |               |
| Emotion Regulation Questionnaire (ERQ)                                                                                     |          |               |               |               |               |               |               |               |               |               |
| <b>Caregiver Measures</b>                                                                                                  |          |               |               |               |               |               |               |               |               |               |
| KSADS-Parent                                                                                                               |          |               |               |               |               |               |               |               |               |               |
| Adult Behavior Checklist (ABCL) on Other Parent                                                                            |          |               |               |               |               |               |               |               |               |               |
| Adult Self Report (ASR)                                                                                                    |          |               |               |               |               |               |               |               |               |               |
| Child Behavior Checklist (CBCL)                                                                                            |          |               |               |               |               |               |               |               |               |               |
| Early Adolescent Temperament Q (EATQ)                                                                                      |          |               |               |               |               |               |               |               |               |               |
| Family History                                                                                                             |          |               |               |               |               |               |               |               |               |               |
| General Behavior Inventory-10M                                                                                             |          |               |               |               |               |               |               |               |               |               |
| Life Events (of youth)                                                                                                     |          |               |               |               |               |               |               |               |               |               |
| Short Social Responsiveness Scale                                                                                          |          |               |               |               |               |               |               |               |               |               |
| Difficulties in Emotion Regulation Scale (of Youth)                                                                        |          |               |               |               |               |               |               |               |               |               |
| Perceived Stress Scale (of Parent)                                                                                         |          |               |               |               |               |               |               |               |               |               |
| Brief Problem Monitor-Teacher form                                                                                         |          |               |               |               |               |               |               |               |               |               |

Fig. 1. Overview of Mental Health Measures in ABCD.

**Table 1**  
Association types across statistical models.

| Data type       | Description                                                                                   | Commonly Used Method                                                                                                                                                                            | Inferential Category                                                                                                                                                                |
|-----------------|-----------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Cross-sectional | Assess relationships between variables measured at the same time (concurrent association)     | <ul style="list-style-type: none"> <li>Correlation</li> <li>Linear regression</li> <li>Atemporal mediation</li> <li>Structural equation</li> </ul>                                              | <ul style="list-style-type: none"> <li>Correlational</li> <li>Correlational / Pseudocausal</li> <li>Correlational / Pseudocausal</li> </ul>                                         |
|                 | Identify subgroups within a population                                                        | <ul style="list-style-type: none"> <li>Exploratory factor analysis</li> <li>Latent profile analysis</li> <li>Unsupervised machine learning</li> <li>Deep clustering</li> </ul>                  | <ul style="list-style-type: none"> <li>Descriptive / Correlational</li> <li>Descriptive / Correlational</li> <li>Descriptive / Correlational</li> </ul>                             |
| Longitudinal    | Assess relationships between variables measured across time points (longitudinal association) | <ul style="list-style-type: none"> <li>Linear mixed model</li> <li>Longitudinal mediation</li> <li>Structural equation analysis (e.g., cross-lagged panel models; trajectory models)</li> </ul> | <ul style="list-style-type: none"> <li>Correlational / Formal Prediction</li> <li>Correlational / Pseudocausal</li> <li>Correlational / Pseudocausal / Formal Prediction</li> </ul> |

more nuanced than previously understood, with neural context serving as a critical moderator of these associations (Conley et al., 2023). We highlight several examples here.

For instance, while stronger executive functioning is generally protective against mental health problems (Yang et al., 2022a), this benefit appears dependent on neural context. In the ABCD Study sample, researchers found that high inhibitory control predicted fewer internalizing symptoms only among youth with higher resting-state functional connectivity between the frontoparietal network (a network implicated in cognitive control and executive function) and the amygdala (Gunther et al., 2023). In contrast, inhibitory control was not protective – and may even be maladaptive – in youth with lower connectivity, relating to risk for “over-controlled” behavior and anxiety (Gilbert et al., 2022). This work challenges the conceptualization that improved top-down cognitive control is inherently adaptive (Luna et al., 2015) - a nuance that is clarified through multivariate analyses of large, population-based data from the ABCD Study.

Several analyses of ABCD Study data have also demonstrated alterations in brain systems that moderate the relationship between family history and symptom expression. Family history is known to be a robust predictor of a multitude of psychiatric disorders, including major depression, and is thought to confer risk via alterations in brain systems associated with emotional processing and stress reactivity. Indeed, functional alterations of the default mode network (DMN) have been postulated to play a role, due to the network’s central role in self-referential thought, rumination, and emotional processing (Sheline et al., 2009; Hamilton et al., 2015), though the directionality of this relationship is unclear (Posner et al., 2016; Sacchet et al., 2016). Using data from the ABCD Study, researchers demonstrated that negative within-network DMN functional connectivity was linked to depression history, but that this effect was specific to adolescents with a family history of mood disorder (Cai et al., 2021). Not only does this work help to reconcile mixed results on DMN connectivity by showing that the context of familial predisposition matters, but when taken together with the aforementioned studies, it highlights a recurring theme: interactive effects - whether between cognitive control and brain networks, or between brain function and familial risk - play a significant role in predicting mental health outcomes in youth. These findings underscore the importance of adopting sophisticated analytical approaches that

account for individual differences in neural architecture when studying mental health in development, as they reveal that seemingly beneficial cognitive abilities and risk factors operate within complex, interdependent systems rather than as isolated influences on adolescent mental health.

### 1.2. Adversity was a known risk factor for mental health outcomes, and ABCD research shows the need to examine multi-contextual influences

Environmental context can likewise moderate the link between neurocognitive development and mental health outcomes. Johnson and colleagues (2022) examined youth who had experienced parental arrest - an adverse environmental influence that has been linked to increased risk for mental health problems. They found that stronger executive function was associated with both fewer internalizing and externalizing symptoms among White children regardless of adversity exposure. However, stronger executive function did not provide the same buffer among Black children. In fact, lower executive function exacerbated internalizing symptoms, but stronger executive function was not significantly protective. Executive function also did not relate to externalizing symptoms in the subgroup of Black youth. These results, viewed through a lens of social and cultural context, suggest that the protective buffer effect of cognitive skills can be constrained by systemic or environmental factors. In adverse or inequitable contexts, youth with stronger cognitive control may still face extreme stress or limited support, blunting the expected positive impact on mental health. This aligns with broader theories of differential efficacy of executive function and self-regulation across environments (Blair and Ku, 2022), and highlights the importance of interventions that account for contextual factors in order to truly mitigate risk for adverse health outcomes.

Building on this evidence that environmental adversity can diminish the protective effects of other factors, recent research has begun to examine how multiple environmental stressors simultaneously influence brain development and mental health outcomes. Maxwell and colleagues (2023) set out to model the relationships between proximal and broader environmental systems (i.e., socioemotional support, neighborhood poverty, neighborhood threat, environmental toxins), brain structure and microstructure, and internalizing/externalizing symptoms. Neighborhood poverty was positively associated with externalizing symptoms, a relationship that was mediated by child and parent feelings of safety as well as intracranial volume. Greater parental support reduced this effect in children experiencing less neighborhood poverty, but did not have a significant effect in children with higher neighborhood poverty. This may indicate that protective factors such as parental support have less of a positive impact when children are faced with other environmental stressors.

### 1.3. Prenatal substance exposure was known as a risk factor for mental health outcomes, and ABCD research shows it clusters with environmental factors to affect outcomes

Prenatal substance exposure is known to impact adolescent mental health (Williams and Ross, 2007; Guille and Aujla, 2019; Ruiz et al.). Research on prenatal substance exposure consistently demonstrates that in-utero exposure to substances such as alcohol, tobacco, and illicit drugs is associated with long-term risks for emotional dysregulation, behavioral problems, and cognitive impairments that often persist into adolescence. Studies using the ABCD data solidify the robustness of the association between prenatal substance use and mental health outcomes (Orendain et al., 2023; Roffman et al., 2021), especially cannabis (Paul et al., 2021; Cioffredi et al., 2022), even after accounting for potential confounding variables. Further, given the multiple environmental factors measured in the ABCD Study, new evidence has emerged showing how prenatal exposures cluster with other environmental factors and set up postnatal vulnerabilities.

For example, Lees and colleagues (2020) and Long and Lebel (2022)

evaluated outcomes of children exposed to low to moderate levels of prenatal alcohol use (Long and Lebel, 2022). Results replicate previous literature suggesting a potentially dose-dependent association with child behavior outcomes (Sood et al., 2001), and extend the evidence that this prenatal exposure has an independent effect that may be compounded by other environmental factors (e.g., socioeconomic differences, early life stress). Lepow and colleagues (2024) completed an analysis using four groups of the possible combinations of prenatal drug exposure and childhood trauma. Their study found that prenatal drug exposure acted as a vulnerability for later childhood trauma to be associated with adolescent psychological problems through altered neurodevelopment. These studies show that accounting for numerous environmental and social factors in the same analysis has the benefit of better isolating the exposure of interest, and potentially identifying opportunities for intervention to support healthy development. Together, these findings emphasize that the impact of prenatal substance exposure on adolescent mental health is not solely about whether exposure occurred, but critically depends on the type and amount of exposure—as well as the broader environmental context in which development unfolds.

#### *1.4. Brain and environmental factors were known risks for mental health outcomes, and ABCD research shows their nonlinear, multivariate interactions shape adolescent outcomes*

In addition to complex interactions, multivariate analyses of ABCD Study data have also provided valuable insights into nonlinear associations between biological factors, environment, and mental health. One example comes from a recent investigation regarding cognitive predictors of mental health symptom trajectories. Researchers identified an inverted U-shaped relationship between executive function at baseline and subsequent changes in symptoms across a three-year period (Li et al., 2025). Specifically, among children who went on to develop significant internalizing or externalizing problems at age 12, both low and high initial executive function predicted worse symptom trajectories compared to moderate executive function. Notably, this association was mediated by developmental changes in the lateral occipital cortex and inferior frontal gyrus - regions involved in visual processing and executive control. These findings illustrate how multivariate approaches in the ABCD Study have advanced our understanding of adolescent neurocognition and mental health.

As another example, recent work has shown that more complex behaviors are best captured by nonlinear interactions between brain and environment factors. A family of nonlinear approaches called “manifold learning,” which seeks to faithfully represent the nonlinearities inherent in neural data, has been adapted to examine nonlinear associations between brain and environment. Busch and colleagues (2025) combined measures of brain activity and family/neighborhood adversity into a single exogenous-PHATE (E-PHATE) manifold. This allowed researchers to test how family and neighborhood features interact with brain function and predict mental health experiences. E-PHATE embeddings yielded higher accuracy than other approaches, including spatial averaging, dimensionality reduction with linear or other nonlinear methods, or retaining high-dimensional measures (voxel), used in the same brain areas and networks. Moreover, E-PHATE embeddings yielded selective longitudinal insight into adolescent mental health experiences: future externalizing symptoms were moderately predicted from embeddings of ventral attention network activation, and future internalizing symptoms were moderately predicted from embeddings of both frontoparietal and ventral attention network activation. These methodological advances demonstrate the critical importance of accounting for the inherent complexity and nonlinearity of brain-environment-behavior relationships when seeking to understand and predict adolescent mental health.

#### *1.5. Screen time and social media use were considered harmful risk factors for mental health, and ABCD research adds to findings that reveal a more nuanced impact*

The public and scientists debate the extent to which screen time and social media use is a “good thing” or the root cause of the current mental health crisis among teens (Reid and Weigle, 2014; Sewall and Parry, 2024; Odgers, 2024; Haidt, 2024). Recent work from the ABCD Study shows that the association between these experiences really depends on what is being used, how frequently, and by whom (Zhao et al., 2025).

Nagata and colleagues (2024) identified that greater overall screen time was positively associated with adverse mental health symptoms, and that the specific digital behaviors showing the highest associations were video chatting, watching videos, gaming, and texting. The association between screen time and depressive symptoms was stronger among White adolescents compared to their Black or Asian counterparts, and the associations between screen time and ADHD or oppositional defiant symptoms were stronger among White than Black adolescents. Further, Pagliaccio and colleagues (2024) compared social media use with mental health using a digital exposomic approach, revealing that multiple digital exposures beyond general screen time, especially social media, negatively related to youth mental health problems and risk for suicide attempts. Addictive patterns of screen usage were associated with worse mental health outcomes in youth, suggesting that the type of digital behavior may have a larger effect on adolescent mental health than the amount of screen time alone (Xu et al., 2025).

However, in another study, the association between screen time and internalizing (e.g., depression) was small, questioning whether the evidence was strong enough to make a clear recommendation (Paulich et al., 2021). The negative associations between screen time and mental health outcomes appeared stronger for male adolescents, yet youth who reported higher screen time also reported having more close friends. Dall’Aglio and colleagues (2025) studied the potential effects of adhering to more or less stringent screen time guidelines (compared to standard 2 h/day recommended by the American Academy of Pediatrics and World Health Organization) on internalizing and externalizing symptoms in the full ABCD sample and an at-risk subsample, and demonstrated that adhering to more stringent guidelines was associated with decreased internalizing symptoms, but that the effect was greater in the at-risk youth, suggesting that the magnitude of association between screen time and symptoms may depend on other risk factors (e.g., genetics, other environmental factors).

Zhang and colleagues (2023a) studied the impact of genetics in the association between screen time and poor mental health. Results indicated that genetic variance may account for a substantial proportion of the positive association between screen time and mental health. In consideration with genetic differences, brain differences may also mediate the association between youth screen time and mental health outcomes. For example, Yang and colleagues (2022b) leveraged longitudinal data from ABCD to examine multivariate associations among polygenic risk, ADHD, screen time, and white matter microstructure. The association between polygenic risk for ADHD and screen time was mediated by white matter differences and ADHD symptoms such that a stronger genetic risk for ADHD was associated with alterations in white matter tracts and increased trait ADHD symptoms that related directionally (white matter) or bidirectionally (ADHD symptoms) to increased screen time. Conversely, another study that investigated the association among sleep patterns, screen time, and mental health problems using structural MRI data found that patterns of structural brain data at baseline were correlated with higher externalizing scores a year later, which predicted future increases in screen time two years later. These findings suggest externalizing behaviors as the partial mediator of this relationship rather than structural brain differences (Zhao et al., 2024) (see also (Li et al., 2024)). Further work is needed to identify the temporal order of effects, but it is clear that biological factors may amplify risk for poor mental health outcomes as they relate to

screen time.

Research from ABCD underscores the intricate and multifaceted relationships between behavioral health guidelines and adolescent mental health. Nagata and colleagues (2025) prospectively examined the association between daily screen time and mania symptoms and found potential mechanistic associations such that problematic social media use, problematic video game use, and sleep duration all mediated the positive association between screen time and mania symptoms (see also (Guerrero et al., 2019; Zink et al., 2024)). Sampasa-Kanyinga and colleagues (2021) studied the compounding effects of following screen time, sleep, and physical activity guidelines on mental health symptoms and demonstrated a dose-dependent effect such that those who followed two or all three recommendations had increased positive mental health outcomes compared to those following one or none. Fung and colleagues (2023) examined these effects as well, determining that those who adhered to both the screen time and sleep guidelines, but not physical activity guidelines, showed stronger cognition, greater cortical volume, lower body mass index, and fewer psychosocial problems than those that met none of the recommendations, emphasizing complex interactions of sleep, screen time, and adolescent development, and the importance of adhering to multiple behavior guidelines simultaneously. Lin and colleagues (2020) used network analysis to examine the complex associations between different mood symptoms and types of screen time, controlling for temperamental characteristics (e.g., behavioral approach and behavioral inhibition) and parental monitoring. Engagement in age-inappropriate screen content was associated with variable mood symptoms but there were some sex-related differences as well as distinct patterns between types of content (e.g., watching R-rated movies vs. playing mature video games) and both type and network connectivity of mood symptoms, highlighting the complexity introduced by considering variability in types of symptoms and media experiences. Given the complexity of the associations among screen time, social media use, and adolescent mental health, it seems difficult to prescribe a single recommendation for how these tools should be used. Instead, a more personalized approach considering key risk and resilience factors should be considered.

#### 1.6. Sleep problems were known risk factors for mental health problems, and ABCD research clarifies their predictive, genetic, and neurobiological pathways

Interest in the associations between sleep problems and mental health in adolescence has burgeoned over the past decade, with research demonstrating robust univariate associations between sleep problems and mental health problems (Gregory and Sadeh, 2016). Certain patterns of sleep and sleep-related problems (e.g., sleep onset delay; poor sleep efficiency; nightmares) have been tied to nearly every major mental health problem in youth, from depression to psychosis to impulse control problems. Leveraging the ABCD data, researchers are now applying sophisticated multivariate approaches (e.g., machine learning variants, canonical correlation analyses) to show that sleep problems are strong concurrent and longitudinal predictors of mental health problems in adolescents, even more so than indices of adverse childhood experiences and brain structure and function (McCurry et al., 2024; Santos et al., 2025; Zhang et al., 2024a; Hill et al., 2025; Ho et al., 2022; Kiss et al., 2025). Xiang and colleagues (2022) used four different supervised machine learning models to compare four trajectories two-years post-baseline of depressive symptoms (i.e., persistently low, decreasing, increasing, and persistently high) with 188 variables spanning family and neighborhood environmental systems, physical health, and mental health to identify predictive features of different types of depressive symptoms. They identified several predictive features, with sleep disturbance appearing in the top three features as having the highest predictive value. However, some longitudinal, bidirectional work has suggested that mental health problems predict subsequent sleep problems, but not the reverse (Cheng et al., 2021; Shen et al., 2020).

Therefore, investigations into temporal order and mechanisms are a main goal of current research on the association between sleep problems and adolescent mental health.

The mechanisms of the sleep-mental health problems association have been a key focus of researchers using the rich ABCD dataset. For example, a cross-sectional investigation found that sleep disturbance significantly interacted with ADHD polygenic risk scores to enhance ADHD symptom expression (Feng et al., 2025). Moreover, longitudinal research found that ADHD and insomnia have shared genetic risk that drives smaller cortical surface areas (in frontal, temporal, and parietal regions) and increased externalizing, ADHD, and insomnia symptoms at 1-year follow-up (Hernandez et al., 2023). Others have found that altered genetic expression in certain brain structures may contribute to ADHD symptoms, which then give rise to sleep problems (Shen et al., 2020). Additional longitudinal research is warranted to clarify the directionality of the genetic associations between sleep and mental health problems in youth and the pathways by which sleep disturbances might augment genetic impacts on behavior.

Sleep may also be associated with mental health problems by facilitating the intergenerational transmission of mental health problems from parent to offspring. For example, Roberts and colleagues (2025) found significant indirect effects of parental mental health problems on offspring depression through offspring sleep problems (insomnia, hypersomnia) for several forms of parental mental health problems (except mania) in combined models. Further, Cheng and colleagues (2021) found that parental mental health problems were inversely associated with offspring sleep duration, which was, in turn, inversely associated with depressive symptoms in youth. These intriguing results provide initial evidence that sleep problems may facilitate the intergenerational transmission of mental health problems.

Finally, other research has suggested that alterations in brain structure and connectivity may be a mediating mechanism of the association between sleep and mental health problems in youth. Among ABCD youth, sleep disturbance has been generally associated with lower cortical area and brain volumes, which have, in turn, been associated with increased behavioral problems (Isaiah et al., 2021) and psychotic-like experiences (subclinical hallucinatory experiences or unusual perceptions, thoughts, or beliefs) (Lunsford-Avery et al., 2021). Regarding brain connectivity, Yang and colleagues (2022c) found that insufficient sleep duration was associated with altered cortico-basal ganglia resting-state functional connectivity, which cross-sectionally mediated the association between insufficient sleep, depression and thought problems, and longitudinally mediated the association between sleep and thought problems. Moreover, Yang and colleagues (2022d) found that sleep disturbance and dimensional mental health problems were associated with between- and within- network connectivity of the default-mode and dorsal-attention networks, and that the sleep-mental health problems association was, in turn, longitudinally mediated by these connectivities, suggesting a shared neural mechanism of sleep and mental health problems in ABCD youth. Collectively, these findings highlight that brain structure and connectivity are potential neurobiological avenues through which sleep disturbances contribute to youth mental health problems.

Overall, these findings underscore the role sleep plays in shaping adolescent mental health—connecting with genetics, family systems, and neurodevelopment. As research continues to refine the temporal and mechanistic links, sleep may emerge not just as a symptom or consequence, but as a central lever for early intervention and prevention in adolescent mental health.

#### 1.7. We knew physical activity was a protective factor for adolescents' mental health, and ABCD research reveals differential benefits across sport types and social contexts

As adolescents navigate the challenges of identity formation, academic pressure, and social dynamics, participation in organized sports

can provide structure, community, and a sense of purpose. Regular physical activity through sports is linked to reduced symptoms of anxiety and depression (Panza et al., 2020), higher self-esteem (Bowker, 2006), and enhanced cognitive function (Hernández-Mendo et al., 2019). Research from the ABCD Study provides more specification about which types of sports, for whom, and why sports impact mental health symptoms. Moeijes and colleagues (2019) found that participation in non-contact sports was linked to fewer externalizing behaviors, whereas participation in contact sports was related to greater aggression and other externalizing problems, consistent with earlier studies. Involvement in team sports over individual sports related to fewer adverse mental health outcomes (e.g., lower rates of anxiety and depression symptoms), confirming prior research (Hoffmann et al., 2022). Social physical activities (i.e., team sports) appear to be related to reduced adverse mental health outcomes, in part, because of potentially building social connections among teens (Conley et al., 2020). Taken together, these findings highlight the importance of considering the type and context of sports participation in adolescence.

Some researchers have explored the link between genetics and physical activity on mental health for adolescents. One study found that adolescents with elevated genetic risk for mental health problems (by virtue of high polygenic risk scores) took fewer steps per day than their lower-risk peers (Yu et al., 2025), highlighting a potential feedback loop in which genetic vulnerability may contribute to less physical activity, thereby accelerating the onset of psychiatric symptoms during this period of development. Other ABCD research has interrogated how sports participation interacts with genetic risk for mental health problems to shape mental health outcomes in youth. Building on prior work (Kunitoki et al., 2023), Misztal and colleagues (2023) found that sports participation differentially interacted with polygenic risk scores to attenuate or amplify mental health problems among ABCD youth. For example, among youth with elevated genetic risk for obsessive-compulsive disorder, more frequent sport participation buffered against problematic behaviors, such as poor impulse control. These results support the idea that physical activity, such as sports participation, can attenuate the impact of genetic risk on mental health problems in youth.

#### *1.8. Cognitive factors were known to shape mental health outcomes, and ABCD research clarifies when they are a precursor, a product, or both*

Understanding the interplay between cognitive factors and mental health requires disentangling their dual roles as both precursors and products of mental health symptoms. Impairments in executive function, attention, or decision-making may predispose individuals to mental health challenges, yet these same deficits often emerge as consequences of prolonged distress or mental health problems (Sheffield et al., 2018). Clarifying the directional relationships is critical for identifying intervention points and refining models of risk and resilience.

Analyses using the ABCD Study data have started to provide insight into differential influences of pre-existing cognitive risk factors for mental health problems versus trait- and state-specific effects. For example, when researchers examined cognitive performance among youth with current depression, remitted depression, high familial risk, or low familial risk, they found that impairments in language and reasoning ability were specific markers of current or past depression, but not pre-existing vulnerability (Ang et al., 2020; Trivedi, 2006). These findings suggest that perhaps some of the cognitive differences commonly observed in youth with depression reflect consequences of the condition rather than a premorbid risk factor. However, the longitudinal design of the ABCD is a key strength of this study, as it enables us to more effectively disentangle temporal dynamics—clarifying whether cognitive outcomes serve as antecedents, consequences, or both in the development of mental health difficulties.

In a longitudinal analysis, researchers found that effortful control (a temperament trait related to executive function), moderated familial

risk for ADHD such that youth who exhibited high levels of effortful control were significantly less likely to develop ADHD symptoms 1-year later compared to youth with low effortful control, despite similar levels of familial risk (Peisch et al., 2024). Similarly, in a study examining the interplay between genetic predisposition and mental health problems, researchers found that a polygenic risk score for ADHD was associated with higher ADHD-related traits in youth, but that this link was partially mediated by neurocognitive performance. Specifically, youth with higher genetic risk tended to have lower scores on working memory tasks and more variable reaction times, which in turn predicted higher ADHD symptoms (Moses et al., 2022). Such findings suggest that one pathway by which genetic liability manifests as ADHD behaviors is through its effect on cognitive processes—in this case, attentional control and working memory capability. Even genetic predisposition for other forms of mental health problems, such as psychotic-like experiences, appear to be at least partly expressed via impairments in attention (Chang et al., 2024), suggesting that multiple forms of mental health problems may manifest via neurocognitive pathways.

Studies that capitalize on the longitudinal design of the ABCD Study to examine temporal variations across development are already lending insight into the mechanisms that may drive symptom trajectories and influence remission vs. relapse. For example, Pang and colleagues (2025) found that trajectories of ADHD symptoms during adolescence are dynamically coupled with the development of inhibitory control. As inhibitory control improved over a span of two years, ADHD symptoms tended to decline, whereas persistently low inhibitory control correlated with steady or worsening symptoms. Another study of ABCD data implemented a machine learning approach to predict the new onset of externalizing psychiatric disorders two years post-baseline (e.g., ADHD, oppositional defiant disorder, conduct disorder) from a variety of multimodal predictors, including several measures of cognitive function and neuroimaging metrics (De Lacy and Ramshaw, 2023). They reported strong performance of the multivariate models (AUROC: ~91–99 %), surpassing comparative models that only included neuroimaging measures for prediction. These results echo growing consensus that brain metrics alone explain only a modest portion of mental health variance (Marek et al., 2022; Tandberg et al., 2024; Poldrack et al., 2017). Rather, integrated multivariate models incorporating cognitive, behavioral, and genetic data provide the strongest predictive power.

Nearly a decade of research resulting from the ABCD Study highlights how longitudinal, multimodal data from the ABCD Study are reshaping our understanding of cognitive mechanisms in mental health. Analyses reveal when and how cognitive factors contribute to mental health problems in adolescents.

#### *1.9. We knew mental health problems and their risk factors were heterogeneous, and ABCD research enables data-driven subtyping to clarify that complexity*

Psychiatric nosology has long struggled with both over- and under-specificity: symptoms and biological features frequently overlap across diagnoses, and substantial heterogeneity exists within each condition. Two separate but related issues arise in the discussion of psychiatric nosology: (1) how to cluster symptoms and experiences together into meaningful categories and (2) what biological features or “risk factors” meaningfully underlie expressions of mental health problems. With access to large, multimodal datasets such as ABCD, researchers can now embrace data-driven approaches that characterize heterogeneity both within and across categories of mental health problems (e.g., Wu et al., 2022; Qiu and Liu, 2023; Russell et al., 2025; Vedeckina and Holmes, 2024; Visoki et al., 2024; Aguinaldo et al., 2022).

One example of how researchers are using the ABCD dataset to classify heterogeneity of symptoms/experiences is within the domain of early life stress and adversity. Much attention has been paid to considering frameworks that account for adversity across multiple contexts. One type of framework takes a cumulative approach where the total

number of adverse experiences youth have had across any social context are tallied across a predefined set of potential exposures to generate a cumulative risk measure that is then related to developmental outcomes (Evans et al., 2013; Felitti et al., 1998; Finkelhor et al., 2007; Steine et al., 2017). Another type of framework focuses on identifying dimensions of adversity thought to influence distinct components of cognitive, emotional, and brain development (e.g., threat-deprivation; harshness-unpredictability (McLaughlin et al., 2019; Ellis et al., 2022)). There has been some disagreement about the empirical support for these frameworks. As such, researchers using the ABCD data are looking for ways to take data-driven approaches to understanding the association between types of adversity and mental health outcomes.

For example, Chow and colleagues (2025) used exploratory factor analysis to identify the naturally occurring factor structure across several indicators of adversity. Researchers found four latent dimensions: parental threat, deprivation, victimization, and traumatic events. Advancing beyond the threat-deprivation dimensions, the victimization dimension, over and above the other identified dimensions, was associated with internalizing and externalizing symptoms. In another study using an exploratory factor analysis approach with a wide range of adverse experiences, Orendain and colleagues (2023) identified six dimensions: 1) physical and sexual violence; 2) parental psychopathology; 3) neighborhood threat; 4) prenatal substance exposure; 5) scarcity; and 6) household dysfunction (see also (Briente et al., 2023)). Youth with higher scores on physical and sexual violence, parental psychopathology, and scarcity had more internalizing problems. Youth with higher scores on neighborhood threat, prenatal substance exposure, and household dysfunction had higher externalizing problems. While these approaches use variable-centered clustering (i.e., how variables load onto similar factors), other researchers are taking the clustering approach from a person-centered perspective to parse the heterogeneity in youth's experiences and identify subgroups of youth with similar experiences. As an example, Conley and colleagues (2022) examined the heterogeneity in perceived threat across family, school, and neighborhood systems and found four distinct profiles that characterized low threat across all systems, elevated threat across all systems, elevated family threat, and elevated neighborhood threat. Youth in the profile with elevated threat across all systems had poorer mental health outcomes two years later, but youth in the family threat profile uniquely showed more disruptive behavior symptoms and youth in the elevated neighborhood threat profile displayed increased sleep problems. More recently, a new Bayesian latent profile method was applied to identify subgroups across family, school, neighborhood, and policy systems (Ramduny et al., 2025). Nine distinct profiles emerged with variation in experiences across systems; however, profiles displaying adversity across systems or high family conflict/low school involvement directly related to higher levels of externalizing, whereas a profile related to family economic and neighborhood adversity indirectly related to externalizing through the presence of lower subcortical volume. Together, these studies highlight how both variable-centered and person-centered approaches reveal distinct yet complementary insights into the multidimensional nature of adversity and its diverse pathways to youth mental health outcomes.

Another example of how researchers are using the ABCD dataset to classify heterogeneity is to use biological data to identify commonalities and uniqueness in symptom expressions. This approach aligns closely with the Research Domain Criteria (RDoC) framework, which emphasizes understanding mental health through underlying biological, cognitive, and behavioral processes rather than relying solely on traditional diagnostic symptoms and categories. Biomarkers can be especially important because they can help disentangle overlapping symptom profiles, improve early identification of risk, and guide the development of more precise interventions.

As one example, several research groups have leveraged ABCD Study data to evaluate underlying differences in brain and cognition that go beyond the traditional inattentive vs. hyperactive subtyping of ADHD.

Unsupervised machine learning applied to cognitive task performance measures of attention and working memory was used to identify several subgroups of youth with ADHD symptoms that were distinguished by their cognitive profiles (Yamashita et al., 2024). These subgroups also differed in brain structure, suggesting that more biologically informed sub-classification of psychiatric disorders could explain why one-size-fits-all treatment approaches often fall short. Indeed, other clustering approaches have shown promise for identifying subgroups that may be particularly responsive to specific treatments. Using multimodal MRI data from the ABCD Study, Feng and colleagues (2024) were able to characterize functional connectivity-based subgroups of youth with ADHD - one of which exhibited a better recovery rate in psychosomatic symptoms when treated with methylphenidate. Imaging-driven biotypes derived from large, population-based datasets such as ABCD may not only help to reconcile decades of incongruent findings with respect to underlying neurobiology and mechanisms of risk, but also provide insight into personalized treatment approaches to improve medication efficacy - a crucial step for improving health outcomes. Certain risk processes, such as impaired cognitive control or alterations in brain connectivity, may only operate in subsets of youth or during particular developmental windows, which would necessitate tailored intervention strategies.

Similarly, machine-learning clustering of multimodal neuroimaging data in children with mood and anxiety disorders has been used to uncover three distinct neurodevelopmental subtypes of youth with varying brain maturation profiles (Ge et al., 2023). One subtype exhibited an "accelerated" maturation pattern in the cortex (advanced cortical thinning and myelination), but lagging subcortical development relative to the others. Interestingly, this group had above-average cognitive functioning compared to typically developing peers. In contrast, a second subtype showed a "delayed" cortical development profile (thicker cortex, less myelination), while the third subtype displayed atypical maturation patterns (lower cortical thickness and surface area but higher myelination density). Despite distinct brain profiles, all three groups had elevated exposure to adverse social contexts - reinforcing the value of multivariate subtyping to clarify pathways of equifinality.

## 2. Looking forward

The work reviewed here represents the power and utility of a large, multifactorial, and longitudinal study that allows for the examination of many different forms of risk factors, and affords the ability to identify complex and likely dynamic interactions among such processes. This multivariate perspective is likely to be much closer to the "ground truth" of the varying pathways to mental health challenges, and as noted above, provides the opportunity to identify more person-centered and individualized opportunities for prevention and intervention. However, at the same time, such complexity comes with its own challenges that we need to address, some of which can be addressed with further ABCD Study analyses, and some of which require us to look beyond the ABCD Study.

### 2.1. Replicating findings that are complex and data-driven

As illustrated above, researchers have been making creative and imaginative use of the ABCD data to apply a range of sophisticated data-driven tools to explore the structure of mental health experiences and the mutually interacting risks and consequences of mental health challenges. This has led to a number of findings about new ways to think about the organization of mental health challenges, when and how risk factors interact, and the mechanistic pathways by which genetics and the environment might confer risk for mental health problems. However, these potentially important new insights require replication in order to understand their robustness and their utility for driving prevention and intervention efforts. This is particularly true when the insights come from highly exploratory and data-driven methods, even

when those studies used the best practices for this type of analysis. Using the ABCD data, researchers can pursue opportunities for replication through hold-out samples or split-half approaches. However, these methods remain limited because they still draw on the same underlying dataset and therefore reflect the same sampling frame, measurement choices, and inherent study-specific biases. This leaves us in a conundrum, as no other study is like ABCD in which these findings can be replicated directly. However, some other studies have the same or similar measures as the ABCD, and could be used for a conceptual replication of some of the findings. This includes important studies such as IMAGEN (Schumann et al., 2010), the National Consortium on Alcohol and Neurodevelopment in Adolescence (NCANDA) (Brown et al., 2015), the Penn Neurodevelopmental Cohort (Satterthwaite et al., 2014), the Tokyo Teen Study (Okada et al., 2019), and the Generation R study (Jaddoe et al., 2006), as well as some emerging data sets, such as the Chinese Color Nest Project (Liu et al., 2021) and the Brazilian High-Risk Cohort (Salum et al., 2015). While none of these studies is identical to ABCD in the sense of having all of the same types of measures and longitudinal structure, they represent important potential opportunities for conceptual replication that can demonstrate that a finding is broadly generalizable, robust, and does not depend on a particular assessment method or population. Thus, a key future direction is to start to identify harmonization and replication pathways in these other studies so that we can determine which novel findings are robust to replication and should be moved forward towards clinical application. In particular, it could be that our best chance for replication comes in combining data from multiple other studies that have complementary types of data and designs. However, determining where there is overlap in constructs and measures will be a massive effort, and something that might benefit from a collective effort of a larger group of investigators who can work together, ideally making the outcome of their efforts publicly available.

## 2.2. Identify generality versus specificity of outcomes

Another key future direction is to determine which risk factors, or which interactions among risk factors, reflect broad vulnerabilities that might put youth at risk for many different forms of mental health problems, and which are more specific to only certain forms of mental health problems. In this context, it is useful to think about constructs such as the “p-factor” (Smith et al., 2020; Clark et al., 2021; Caspi et al., 2014) which has been identified as a potential general factor of psychopathology, analogous to the “g-factor”, which is thought to be a general intelligence factor. There is still much debate as to whether the p-factor is simply a statistical entity versus whether it reflects a latent construct with a specific content (e.g., emotion dysregulation, executive function) (Xiao et al., 2024; Patel et al., 2022; Cardenas-Iniguez et al., 2022). Nonetheless, it could be fruitful to determine which sets of risk factors, or interactions among risk factors, contribute to something like a p-factor, versus which ones inform unique presentations or forms of mental health challenges.

## 2.3. Focus on resilience factors, and not just the absence of risk factors – are there truly protective factors? What are they? Are they modifiable?

The majority of the work being published from the ABCD Study has focused on identifying factors that are risks for the development of mental health challenges, and relatively little work has focused on identifying resilience factors. There are of course exceptions to this, and the review above identified some of these. For example, we reviewed work looking at the contexts in which executive function is a protective factor against internalizing symptoms, and when it is not. We also reviewed when participation in sports is a protective factor, and when it is not. However, a challenge in the domain of understanding resilience is to identify factors that are not just the absence of risk factors or the opposite end of a continuum that goes from risk to “resilience.” One

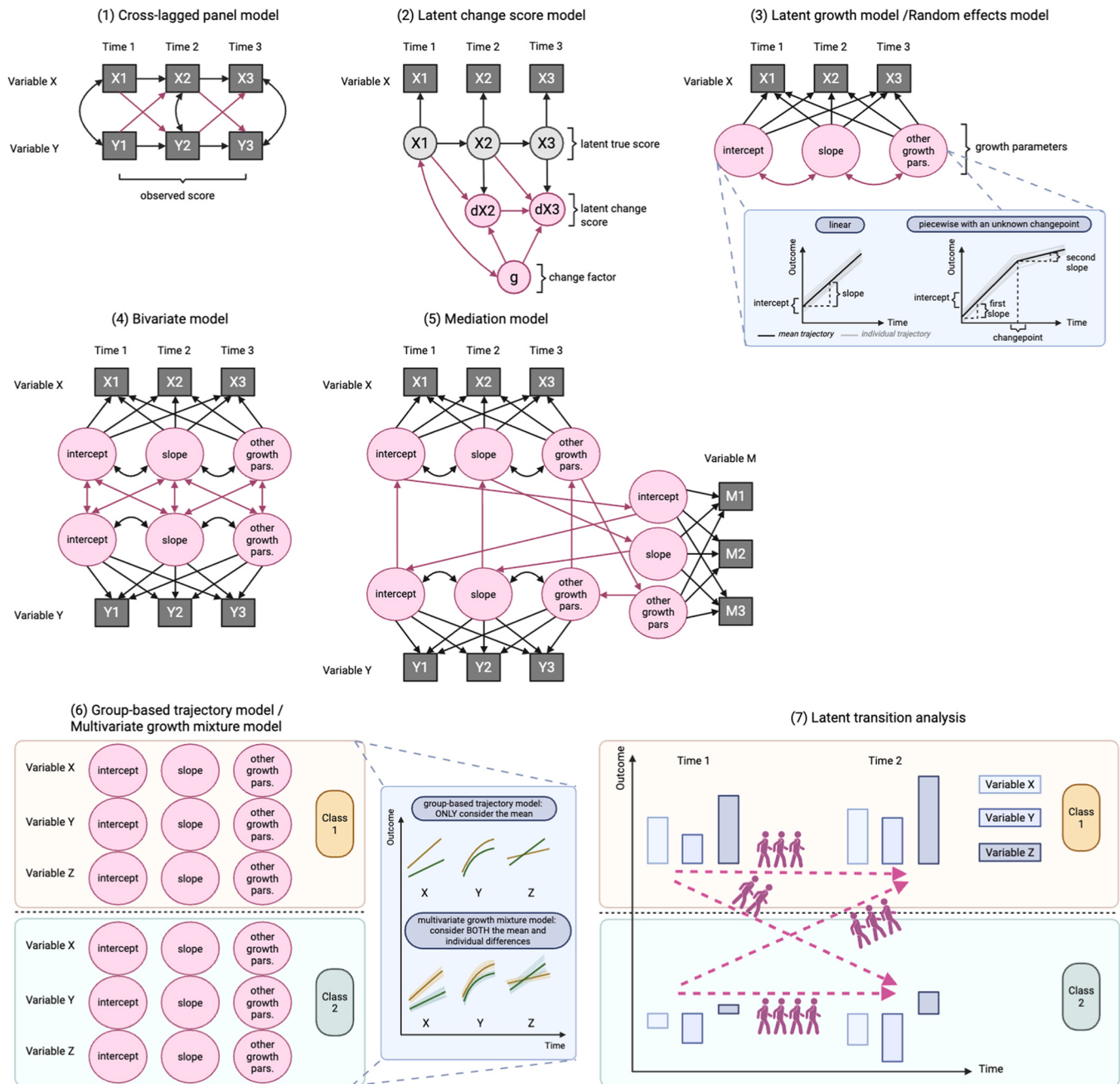
might argue that good executive function is such a resilience factor, but it is often difficult to know whether the positive associations of strong cognition with more positive outcomes are really resilience, or simply the absence of a known risk factor for mental health challenges – namely impaired cognition.

Analytic designs that look at interactions between factors help to address this question, as it is clearer that something is a resilience or protective factor when it is only (or more) beneficial in the face of some other driver that would otherwise contribute to mental health problems. For example, one might argue that strong versus weak sibling relationships are not a dimension that has much of a “univariate” impact on risk for mental health problems. However, if we were to see that the impact of parental psychopathology or parent-child conflict on risk for mental health problems was attenuated among youth with strong sibling relationships, we might consider this to be a resilience factor. Another example is neighborhood cohesion (strong sense of community or friendships among families in a neighborhood). By itself, the presence or absence of such cohesion is likely not related to risk for mental health challenges in youth. However, it might serve as an important protective or resilience factor for youth who have high levels of family conflict, or who have lost a parent, or who have some other challenge that might otherwise put them at risk. The ABCD Study has tried to include assessment of a number of constructs that might serve as such resilience or protective factors, including measures in the friends, family, and community domain. But there may be many others that we have not yet conceptualized as potential resilience or protective factors, but which might emerge through analytic designs that focus on interactions and multivariate approaches in contrast to main effect and univariate analyses. For example, it is possible that various forms of neural or psychological adaptation to adversity can serve as resilience factors that help protect individuals from developing future mental or physical health challenges (Suarez et al., 2025). Identifying such resilience or protective factors will also advance a more personalized understanding of developmental pathways, recognizing that earlier experiences help establish the foundational platform from which youth assume adult roles, confront new challenges, and consolidate habitual behaviors that either promote healthy functioning or perpetuate chronic difficulties. The insights generated from ABCD could inform the design of prospective studies that evaluate modifiable factors or mechanisms that may promote resilience, adaptive functioning, and thriving.

## 2.4. Using advanced statistical methods to capture the complexity of biopsychosocial development across time

To identify and test complex models of the development of mental health problems across time will require longitudinal biopsychosocial designs that allow for estimation of development across stages, time, and/or periods (Hawes et al., 2025). With more waves of data being released, ABCD Study researchers can employ various forms of structural equation modeling (e.g., cross-lagged panel model, latent change score modeling, latent growth curve model) or mixed effects modeling to examine changes in the environment, brain, and mental health experiences across time (Fig. 2). These modeling approaches address changes in different ways.

Specifically, the cross-lagged panel model focuses on how earlier values of a variable predict later values of itself, as well as how one variable predicts another across adjacent waves (e.g., T1→T2, T2→T3). In contrast, the latent change score model directly assesses the amount of change from one time point to the next as a latent construct. Latent growth curve models and mixed-effects models instead describe long-term developmental trajectories by estimating overall change patterns, such as intercepts and slopes, which account for both inter-individual variability and intra-individual heterogeneity. However, the mixed effects model offers greater flexibility to accommodate intrinsically nonlinear functions, such as exponential, logistic, or piecewise functions with unknown change points (Zhang et al., 2023b). It also would be



**Fig. 2.** Conceptual Diagrams of Different Types of Longitudinal Models. *Note:* Squares denote observed variables, and circles denote latent variables. Pink shading highlights the primary parameters or relationships estimated in each model. (1) The cross-lagged panel model includes cross-lagged effects between variables X and Y, autoregressive effects for each variable, and within-time associations. (2) The latent change score model specifies latent change score between adjacent time points, which is impacted by both a change factor and the initial latent true score. (3) The latent growth model and random effects model estimate growth parameters (e.g., intercepts and slopes) that reflect both inter-individual variability (i.e., mean) and intra-individual heterogeneity (e.g., individual deviation from the mean). The illustration includes a linear function, which can be estimated by either model, and a linear-linear piecewise function with an unknown changepoint, which is directly estimable only under random effects models. (4) A bivariate model estimating bidirectional associations between the growth parameters of variables X and Y. (5) A mediation growth model specifying mediation among the growth parameters of variables X, M, and Y. (6) The group-based trajectory model and the multivariate growth mixture model, both of which estimate growth parameters across latent classes; the former estimates class-specific means only, whereas the latter estimates both means and variances. (7) The latent transition analysis, which quantifies the proportion of individuals who remain in the same latent classes or transition to different classes over time.

useful for researchers to increasingly model the co-occurring relationships among variables (including neuroimaging data). While cross-lagged panel models typically focus on examining two or more variables, methodologists have developed additional approaches to assess these longitudinal relationships within both structural equation modeling and mixed effects modeling frameworks, including bivariate models (Peralta et al., 2022) and mediation models (Liu and Perera,

2022; Zhang et al., 2024b).

It is important to consider that study samples are not always homogeneous entities. Based on the existing research, we know environments and neurobiological capacity can vary across youth. Models have been offered for how environments shape some youth's behavior, and neurobiological research suggests that brain structure and function may fit well within these models (Baskin-Sommers et al., 2024; Hyde et al.,

2020). However, these models are only supported in the broadest sense with little research testing multiple components of the model in the same study (e.g., few studies have included multiple aspects of the environment, brain, and other factors in a single study). The complexity of mental health problems requires that we test multi-level models (Bronfenbrenner and Ceci, 1994; Bronfenbrenner and Morris, 2007; Sameroff, 2010, 2000). We need more work examining the brain and cognition as embedded within ongoing transactions that occur within hierarchical and clustered settings of risk and protective factors (Busch et al., 2025; Baskin-Sommers et al., 2024; Viding et al., 2024). Further, we need to examine how these relationships might shift over time. Three methods often are used to examine changes across different subgroups or latent classes: group-based multi-trajectory modeling, growth mixture models, and latent transition analysis.

Group-based multi-trajectory modeling is a form of latent class growth analysis that identifies subgroups of individuals who show similar patterns of change over time on multiple variables simultaneously (Nagin et al., 2018). This approach is an extension of the dual-trajectory approach, which estimates the association between two variables by measuring the probability of a trajectory for the first variable given membership in a specific trajectory for the second variable. The group-based multi-trajectory approach, though, examines the association by defining trajectory groups based on patterns of change for multiple variables simultaneously. For example, this modeling technique would allow for estimation of co-occurring change in neurocognitive performance, executive control network functioning, and parenting factors that span risk and protective factors.

Similarly, growth mixture models assess trajectories for different classes. However, growth mixture models also account for individual differences within a class, while group-based multi-trajectory models assume that all individuals within a class follow the same trajectory (Nguena Nguetack et al., 2020). In growth mixture models, to model the simultaneous relationships among variables, researchers can incorporate both time-invariant covariates (Liu and Perera, 2023a) and time-varying covariates (Liu and Perera, 2023b). The covariates can be predictive of both the trajectory and the class membership.

Alternatively, researchers can employ latent profile analyses to identify subgroups of individuals and then latent transition analysis to quantify if people remain in the same profile across time or switch to a new profile across time (Conley et al., 2024). Examining co-occurring trajectories or latent profile transitions would provide strong evidence that factors theoretically integral to mental health problems empirically align.

## 2.5. Identifying when and how mental health experiences change across development

The longitudinal nature of the ABCD Study also allows us to ask questions about potential sensitive periods, both for the impact of risk factors, but also for the potential benefits of protective factors. Additional releases of data from ABCD, that extend into later adolescence, will allow researchers to ask questions about whether various forms of life events have greater or lesser impacts at different developmental states, versus more cumulative effects that are insensitive to timing. We may also be able to see shifts in the relative importance of different risk or protective factors across different developmental stages, such as the relative importance of familial versus peer relations across development, or the differential salience of challenges in the educational versus occupational versus interpersonal domains and how that may vary based on life stage.

As youth develop, it is important not only to explore how risk and protective factors change across time, but also to identify critical transition points. The concept of tipping points, which originated in physics and has been used in disciplines such as environmental science and sociology (Lenton, 2013), may be useful in the study of mental health problems. We know that emotion and behavior problems can fluctuate

across situations and across time for a given individual. A big question remains, though, about what small perturbation in the social environment might trigger a larger response that shifts both the internal state (brain) and external world (social environment)? For example, a move to a new neighborhood or the introduction of a new positive adult figure in a young person's life can alter emotion and behavioral experiences. Do those small perturbations lead to shifts in neurobiological and/or behavioral changes? That is, just as we know that risk can compound on itself, creating fewer new options, are there times and experiences that can shift the whole system/ trajectory of youth development to a new state? And what experiences might just reflect stochastic effects?

At another level, in biology and sociology, tipping points associated with changes in the ecological system, such as transitions in neighborhood racial composition or violent infighting, can provide feedback that can impact individual and collective behaviors. An open question is then how and when do socio-structural shifts impact the development and change in individual behavior? Alternatively, when are points where shifting to new trajectories is particularly difficult? We know very little about how behavior becomes canalized (for better or worse) and how, when, and what type of tipping points can shift individual development into new options and systems of behavior (Baskin-Sommers et al., 2024). Leveraging longitudinal data and applying segmented or 'piecewise' regression or inflection point analyses can be useful in advancing our understanding of how mental health problems grow and change within youth. Current methods can detect multiple random changepoints in multi-phase piecewise growth mixture models (Lock et al., 2018). Further research is needed to explore how time-invariant and time-varying covariates impact these changepoints. It could also be beneficial to consider transitions between different latent classes and analyze which variables impact these transitions, considering another variable as either categorical or longitudinal. Moving forward it will be key to understand how complex transitions and how intervention can help promote these shifts, a core set of questions that the ABCD Study is poised to help answer.

## 3. Closing words

As illustrated by this selective review, the first 10 years of mental health-related analyses in the ABCD Study have generated rich and distinctive findings about the risk factors and consequences of mental health challenges among adolescent youth in the United States. In some cases, these findings have confirmed what we have known, or at least suspected, about the factors related to mental health problems in adolescence; namely that they are complex and multi-factorial, with a range of genetic, familial, and broader environmental factors working synergistically to promote risk or to facilitate resilience. In other cases, these findings offer novel insights, highlighting for example the critical interplay of physical and mental health, the complexity of the relationships between emerging technologies and mental health in adolescence, and the challenges of identifying non-linear and often bidirectional relationships among putative risk factors and mental health outcomes. While the findings accumulated to date are impressive, we believe that the true value of the ABCD data will be fully realized in the coming decade. With the release of additional waves of data that will capture later adolescent ages, we may be able to unlock new questions or conduct analyses that seek to tackle the critical challenge of establishing pseudocausal relationships and to uncover new opportunities for early intervention and prevention.

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