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Examining the roles of genes, cognition, and health in risk for youth suicidality

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EXAMINING THE ROLES OF GENES, COGNITION, AND HEALTH IN RISK FOR YOUTH SUICIDALITY

by

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EXAMINING THE ROLES OF GENES, COGNITION, AND HEALTH IN RISK FOR YOUTH SUICIDALITY

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ABSTRACT

Suicide is the second leading cause of death in young people, yet it remains difficult to predict. Suicidality in preadolescent children is especially understudied and epidemiological studies suggest that it has been underestimated. This project examined potential health, cognitive, and genetic predictors of suicidal thoughts and/or behaviors in preadolescent youth using data from the ongoing Adolescent Brain and Cognitive Development (ABCD) Study.

Study 1 examined associations between chronic health conditions reported at baseline, when youth were 10 years old on average, and incident suicidality across a two-year follow-up period reported by either parents or youth in ABCD (n=11876, 53% male, 52% white; 10% incident suicidality rate). It was hypothesized that history of chronic health conditions would be associated with higher rates of incident suicidality. After adjusting for covariates including psychopathology, trauma exposure, and family conflict and correcting for multiple comparisons, chronic illness was not significantly associated with incident or lifetime suicidality.

Study 2 examined associations in the same sample between cognitive performance, measured at baseline using the NIMH Toolbox Cognition Battery, and

incident suicidality across follow-up. It was hypothesized that lower cognitive performance at baseline would be associated with higher rates of incident suicidality. Fully adjusted models did not indicate significant associations between cognitive performance and suicidality.

Study 3 examined genetic influences on variance in lifetime suicidality through analysis of ABCD's embedded twin cohort (n=1542; 51% male; 66% white; 21% lifetime suicidality rate). It was hypothesized that additive genetic factors would contribute significantly to suicidality. Results suggested a significant familial influence on youth suicidality; however, analyses were likely underpowered to disentangle the relative contributions of additive genetic and shared environmental factors to variance in youth suicidality.

Studies 1 and 2 suggest that chronic health and cognition, which have been associated with youth suicidality in previous research, may not predict suicidality over and above the effect of risk factors such as psychopathology and family conflict. Study 3 suggests significant familial influences on suicidality. Future studies should continue to disentangle mechanisms of risk and explore unmeasured confounds to improve prediction of preadolescent suicidality.

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LIST OF ABBREVIATIONS

3ST	Three-Step Theory of Suicide
A	Additive Genetic Effects
ABCD	Adolescent Brain and Cognitive Development Study
ADHD	Attention-Deficit/Hyperactivity Disorder
AIC	Akaike Information Criterion
ACS	American Community Survey
C	Shared Environmental Effects
CBCL	Child Behavior Checklist
CI	Confidence Interval
D	Dominance Genetic Effects
DBT	Dialectical Behavior Therapy
DBT-A	Dialectical Behavior Therapy for Adolescents
DBT-C	Dialectical Behavior Therapy for Children
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4th Edition
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5th Edition
DZ	Dizygotic
E	Non-Shared Environmental Effects
EF	Executive Functioning
EMA	Ecological Momentary Assessment
FES	Family Environment Scale
GWAS	Genome-Wide Association Studies

IPTS	Interpersonal Theory of Suicide
IQ	Intelligence Quotient
IRB	Institutional Review Board
K-SADS-PL DSM-5	Schedule for Affective Disorders and Schizophrenia for School-Aged Children Present and Lifetime Version for DSM-5
ML	Maximum Likelihood
MRI	Magnetic Resonance Imaging
MZ	Monozygotic
NDA	National Institute of Mental Health Data Archive
NIH	National Institutes of Health
NIMH	National Institute of Mental Health
NSSI	Non-Suicidal Self-Injury
ODD	Oppositional Defiant Disorder
OR	Odds Ratio
PTSD	Post-Traumatic Stress Disorder
SD	Standard Deviation
SNP	Single-Nucleotide Polymorphism
SPSS	Statistical Package for Social Sciences
STBs	Suicidal Thoughts and/or Behaviors
U.S.	United States
WISC-V	Wechsler Intelligence Scale for Children, 5th Edition

CHAPTER ONE

General Introduction

Suicidality in young people is a major public health problem that requires significant research attention. In 2020, suicide was the second leading cause of death for individuals between the ages of 10 and 14 in the United States (Centers for Disease Control and Prevention & National Center for Injury Control, 2023). Predicting suicide remains challenging despite the development of myriad tools for screening and risk assessment (Cwik et al., 2020). Furthermore, despite its impact on the lives of millions of Americans, suicide remains understudied: suicide research has the lowest "dollar per death" federal funding of the top 27 leading causes of death (Fortgang & Nock, 2021). This problem is particularly evident in the scarce literature on child suicide (Ayer et al., 2020). Although base rates remain low in absolute terms, hundreds of young children die by suicide every year in the United States alone, with suicide rates rising among Black children aged 5-11 in particular (Bridge et al., 2015). Suicide deaths among U.S. youth aged 10-14 years in the United States almost tripled from 0.9 per 100,000 in 2007 to 2.5 per 100,000 in 2017, and youth aged 5-12 years experienced excess suicide deaths during the first year of the COVID-19 pandemic (Bridge et al., 2023; S. C. Curtin & Heron, 2019). Furthermore, thoughts about suicide in young children are not uncommon; in recent United States population-based studies, approximately 8% of preadolescent youth reported experiencing suicidal ideation (Barzilay et al., 2019; Janiri et al., 2020). Because suicidality rates continue to rise into adolescence and emerging adulthood, understanding early trajectories of and risk factors for suicide in preadolescent youth could potentially

help prevent later suicide deaths (Goldston et al., 2015; Steele et al., 2018; Sullivan et al., 2015; Yu & Chen, 2019).

Suicidality is a dimensional phenotype that encompasses a range of thoughts about death and suicide, suicidal intent and planning, suicide attempts, and deaths by suicide. Thoughts about suicide are often differentiated into two categories: passive ideation, i.e., wishing one was dead, and active ideation, i.e., wanting to kill oneself (Liu et al., 2020). Although clinical intuition might suggest that passive ideation confers relatively less risk than active ideation and that risk increases across a spectrum from passive to active ideation, empirical work has challenged this notion by suggesting that passive ideation may not in fact be less risky than active ideation: a recent meta-analysis found that correlates of passive and active suicidal ideation were largely equivalent and that passive suicidal ideation was strongly associated with suicide attempt (Liu et al., 2020). Non-suicidal self-injury (NSSI) is often examined alongside suicidality, and is a behavior that is often correlated with suicidal thoughts and actions; however, it is a separate construct that lies outside the scope of this dissertation, and will not be examined directly in these analyses.

This dissertation will examine suicidality among preadolescent youth. For purposes of clarity, "preadolescent" is used here to describe youth between the ages of approximately 9-12 years old. Some literature uses the term "early adolescence" to refer to this age range (Aguinaldo et al., 2022; Paulich et al., 2021; Thornburg, 1983). Youth of this age may also be categorized colloquially as "tweens" or "pre-teens". Developmental hallmarks and tasks of this period include the development of secondary sex

characteristics and progression towards puberty, a shift towards increased autonomy from parents and caregivers as changes in socialization occur, identity exploration and development, and development of more abstract cognitive skills (Gilmore & Meersand, 2014; Thornburg, 1983). Studying the emergence of suicidality in this age range is critical to promoting a developmental understanding of suicidality trajectories in young people, especially as this may represent the period of time when suicidal thoughts and/or behaviors first emerge in youth. Identifying the earliest markers of risk for suicidality in youth may be the most efficient and effective way to prevent negative outcomes, consistent with principles of developmental psychopathology (Cicchetti & Rogosch, 2002; Oppenheimer et al., 2022).

A specific theoretical framework of childhood suicidality does not exist, and much suicidology research has been conducted using an atheoretical approach. However, "ideation-to-action" theoretical frameworks such as the Interpersonal Theory of Suicide (IPTS) and the Three-Step Theory of Suicide (3ST) suggest that several processes relevant to child development may be implicated in the development of suicidality (Klonsky & May, 2015; Okado et al., 2021; Orden et al., 2010). The IPTS posits that thwarted belongingness, perceived burdensomeness, and acquired capability for suicide—which develops from exposure to painful events and reduced fear of death—all increase suicidality risk (Ayer et al., 2020). Thwarted belongness may be linked to family conflict or childhood abuse; perceived burdensomeness may stem from childhood experiences that convey to children that their care is a source of stress for the family; and acquired capability for suicide, as it relates to reduced fear of death, may be relevant for

youth who engage in more risk-taking behavior due to the still-developing prefrontal cortex or have an incomplete understanding of death due to developmental stage (Stewart et al., 2017). The 3ST suggests that pain and hopelessness lead to suicidal ideation, that lack of social connection strengthens ideation, and that capability of attempting suicide bridges ideation to attempt (Klonsky & May, 2015). The 3ST has been tested in an adolescent sample, with results suggesting that behavioral disinhibition in adolescence potentiates suicide attempt risk and academic performance mitigates the progression from suicidal ideation to attempt (Okado et al., 2021). These findings suggest that a broad array of developmental factors, from behavioral regulation to cognitive development, may be implicated in youth suicidality.

Although understanding the causes of youth suicidality is complex, effective psychological treatments for disorders related to suicidal thoughts and behaviors in youth do exist. Dialectical behavior therapy for adolescents (DBT-A) (Rathus & Miller, 2002) is characterized as a well-established intervention for reducing NSSI and suicidal ideation in youth (Glenn et al., 2019). DBT, an intervention originally developed for adult patients, is effective for reducing suicidality and self-harm (DeCou et al., 2019; Linehan, 1993). That suicidality can be effectively treated in younger populations holds great promise to reduce the global burden of youth death by suicide. However, a large proportion of suicidal and self-harming youth do not receive DBT-A (Lu et al., 2020). Access to evidence-based treatment programs may vary as a function of clinician expertise and clinical decision-making, families' financial resources and time, and/or geographical location. Treatment options for preadolescent children experiencing

suicidality are still further limited. Although an adaptation of DBT-A for preadolescent children (DBT-C), which includes significant caregiver training, has been developed, this treatment is not yet in the mainstream (Perepletchikova et al., 2011; Perepletchikova et al., 2017). Other treatments, including cognitive-behavioral therapy, family therapy, and interpersonal therapy, have shown possible efficacy in reducing suicidal ideation and suicide attempts in youth; however, the evidence base is less strong for these interventions than for DBT-A (Glenn et al., 2019). A through-line of several of these treatments is a focus on cognitions, i.e., thoughts; therefore, understanding the cognitive processes that may be implicated in, or index risk for, youth suicidality could have important implications for choosing the appropriate treatment for a child experiencing suicidality. It could also facilitate an understanding of why certain treatments are more effective than others in reducing youth suicidality. Such an understanding may also enhance the efficacy of broad-based preventative interventions for children at risk for suicidal thoughts and/or behaviors.

Although it is conventionally conceptualized as a symptom of depression, suicidality can present across multiple clinical phenotypes. Global data from the World Mental Health Surveys showed that having a Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) anxiety, mood, impulse-control, or substance use disorder was associated with significantly increased odds of suicidal ideation in both developed (odds ratios [ORs]=1.7-3.5) and developing (ORs=1.8-3.9) countries (Nock et al., 2009). Similarly, a range of psychopathology, including depression, anxiety disorders, oppositional-defiant or conduct disorder, and attention-deficit/hyperactivity disorder

(ADHD), has been associated with youth suicidality (Georgiades et al., 2019). At the dimensional level, symptoms of aggression and psychosis, along with symptoms of depression, also contribute to higher risk of suicidal thoughts and behaviors (Vuijk et al., 2019). Comorbid profiles of psychopathology, such as anxiety + depression or substance use disorders + depression, have also been associated with youth suicidality (Foley et al., 2006). Exposures such as substance use, sexual and physical abuse, and parental depression have also been associated with elevated risk for suicidality in youth (Hammerton et al., 2015; Russell et al., 2019). Given this evidence that suicidality is relevant to multiple dimensions of psychopathology, it follows that suicidality risk may be affected or mediated by genetic, temperamental, emotional, and/or cognitive factors that represent shared underpinnings of these dimensions.

Differences have been observed in the psychopathological profiles of children compared to adolescents presenting for suicidality. In a study of Israeli youth referred to an emergency department due to suicidal ideation or a suicide attempt, ADHD was more prevalent in children under age 12 while mood disorders were more prevalent in adolescents 12-18 years old (Ben-Yehuda et al., 2012). Suicidality is more common among male preadolescent children, whereas being female is a risk factor for suicidality among adolescents and young adults (Ben-Yehuda et al., 2012; Miranda-Mendizabal et al., 2019; Sheftall et al., 2016). Suicidality can and should be considered a transdiagnostic construct, and one that may present differently in children compared to adolescents. It is important to include preadolescent children in studies of suicidality to determine how risk factors may differentially affect youth at different developmental stages. Recent work has

differentiated suicide risk between children (aged 5-11) and early adolescents (aged 12-14), finding that children who died by suicide were more likely to be male, to have experienced relationship problems with family and friends, and to be diagnosed with ADHD than young adolescent suicide decedents, among other differentiators (Sheftall et al., 2016). This is consistent with earlier research suggesting that children younger than 12 years old who experience suicidality are more likely to be male and to be bullied than their adolescent counterparts, as well as more likely to have a family history of depression, to engage in different methods of self-harm, to present with suicidal ideation rather than self-harm acts, and to be discharged after assessment rather than admitted to the hospital (Sarkar et al., 2010). In early childhood, externalizing disorders such as ADHD and oppositional defiant disorder (ODD) have been associated with suicidal cognitions and behaviors (Whalen et al., 2015).

These findings suggest that preadolescent children may have different risk factors for suicidality than their older peers, and should not necessarily be aggregated into a catch-all category of "youth." More work is needed to carefully characterize patterns of risk for suicidality in young children, and to better understand longitudinal trajectories towards risk for suicidal thoughts and behaviors beginning in childhood (Ayer et al., 2020). This is particularly necessary given that suicidal ideation in early childhood is an identified risk factor for continuing suicidal thoughts and behaviors throughout childhood and into adulthood (Herba et al., 2007; Whalen et al., 2015). Early childhood suicidality is associated with school-aged suicidality, and suicidal ideation that occurs before age 11 is associated with increased odds of adult suicide ideation and lifetime suicide attempt,

suggesting that without intervention, suicidality may be a stable construct across the lifespan that carries significant, and perhaps accumulative, longitudinal risk (Herba et al., 2007; Whalen et al., 2015).

Across all age groups, predicting suicide is an imperfect process. Suicidality may be particularly difficult or painful for parents or clinicians to comprehend or discuss with younger children; this underscores the importance of increasing the field's understanding of prevalence, risk factors, and opportunities for prevention and early intervention. Recent research has demonstrated the utility of looking beyond psychopathology for predictors of suicide. In a data-driven approach that analyzed electronic health record data from over 1.7 million patients aged 10-89 to predict suicidal behavior, health events that may be less conventionally connected to suicide—including infections such as hepatitis C and certain wound and injury types—were identified as predictors of suicidality, in addition to well-established risk factors such as depression and substance use (Barak-Corren et al., 2017). Although this work did not specifically disaggregate preadolescent children from adolescent youth (all patients under age 25 were aggregated in a single subgroup), it suggests that to accurately predict suicidality, it may be critical to move beyond conceptualizations of suicidality that center it only within a framework of psychopathology, and instead to extend the field's understanding of pediatric suicidality by treating it as an inclusive construct that is meaningfully related to physical and/or cognitive processes in developing youth.

Some such relationships, i.e., between cognition and suicidality or between chronic health problems and suicidality, have been explored separately in adolescent

samples (Barnes et al., 2010; Bauer et al., 2018; Becker et al., 2016; Bredemeier & Miller, 2015; Ferro et al., 2017; Gifuni et al., 2020; Huber et al., 2020; Moses, 2018; Santos et al., 2014). Recent work has also suggested shared genetic liability between suicidal ideation and emotion identification, a function of social cognition, in an adolescent sample (Brick et al., 2019). However, more work is needed to explicate how genes, health, cognition, and risk for suicidality may interrelate, specifically in younger samples. The purpose of this dissertation is to explore the potential contributions of these domains to risk of preadolescent suicidality.

Understanding associations between three domains of interest—chronic health, cognition, and genetics—on youth suicidality has implications for youth, families, and clinicians. For youth and families, a clearer understanding of the epidemiology of suicide in childhood into early adolescence could provide important psychoeducation, reduce stigma, and clarify options for high-quality treatment. For pediatric providers, including therapists, pediatricians, and others working with youth, understanding how factors such as genetics, chronic health, and cognition could impact risk for suicidality could inform screening protocols. In particular, understanding the association between cognition and suicidality could help enhance existing treatments and develop new effective treatments for youth suicidality. For example, DBT, an established treatment for suicidality, has a strong didactic component and a high cognitive load (Brown, 2018). Elucidating associations between cognition and suicidality could inform how to make such treatments more accessible and impactful.

Measurement of Suicidality

Suicidality is a complex latent construct with multiple potential definitions and sub-constructs. For the purposes of this work, "suicidality" will be defined as encompassing either suicidal thoughts or behaviors. Thoughts may include passive suicidal ideation (i.e., thoughts of death or wishing to die without explicit thoughts of killing oneself) or active suicidal ideation (i.e., thoughts of killing oneself, which may be accompanied by intent or specific planning). Suicidal behaviors may include preparatory actions towards suicide or attempted suicide; suicide attempt may be interrupted by another person or aborted by the individual making the attempt (Posner, n.d.). These constructs are often treated separately in the suicidality literature, and clinical wisdom suggests that they can be understood to represent increasing riskiness, i.e., that active suicidal ideation is more dangerous than passive suicidal ideation (National Action Alliance for Suicide Prevention Research Prioritization Task Force, 2014)). However, empirical work has complicated this understanding, and suggests that passive suicidal ideation is not inherently less risky than active ideation (Baca-Garcia et al., 2011). The relationships between these sub-constructs of suicidality are further complicated when studying youth, as cognitive development necessarily impacts the way an individual can experience, understand, and process suicidal thoughts and behaviors. For example, recent work has suggested that some youth experience suicidal thoughts primarily as imagery, rather than as verbal thoughts (Lawrence et al., 2021).

Understanding the correlates of suicidality is, naturally, an important line of research; however, this work may be limited by imprecise definitions or measurement of suicidality itself. The "how", "when", and "who" of suicidality assessment are all

important questions to consider when studying youth. Youth suicidality can be measured using several different modalities, the most common of which are self-report and clinical interview. These tools ask directly about suicidal experiences. Importantly, research has shown that asking directly about suicidality does not increase risk for suicidality (Dazzi et al., 2014). However, those who are asked directly about suicidality may underreport due to stigma or fear of consequences attached to disclosing suicidal thoughts or behaviors (such as a mandated assessment or a referral to a higher level of care). Alternative methods of suicide risk assessment, such as the Suicide Stroop/Implicit Association Test (Nock et al., 2010; Sohn et al., 2021) more subtly assess an individual's risk for suicidal behaviors, but may not directly capture their conscious experience or awareness of their own suicidality. The timeframe over which suicidality is measured is also important; the usage of ecological momentary assessment (EMA) has revealed that participants report higher rates of suicidality when they are asked frequently to report on present suicidality than when they are asked to report retrospectively through more traditional interview methods (Czyz et al., 2018).

Additionally, best practices in assessment of youth mental health consistently suggest a multi-informant approach to gather data from youth as well as other reporters, such as parents, other caretakers, or teachers. Modest to low agreement across parents and youth is common when assessing suicidality (Jones et al., 2019; Klaus et al., 2009; R. Thompson et al., 2006). This is reflective of broader trends of low to moderate parent-child agreement on emotional and behavioral problems (Orchard et al., 2019; Yeh & Weisz, 2001). Reporting discrepancies across parents and youth may be due to several

factors. Parents may underreport youth suicidality due to lack of awareness of their child's internal symptoms, low mental health literacy, minimization of their child's suffering, or fear of aversive consequences such as their child being psychiatrically hospitalized (Klaus et al., 2009). Parents may not be aware of privately held thoughts or hidden behaviors, even when a youth has multiple previous suicide attempts(Klaus et al., 2009). Conversely, parents may overreport suicidality compared to youth due to misunderstanding of youths' expression of distress; for example, a child saying "I'm going to kill myself" may be either an accurate statement of suicidality or a communication that pulls for parental attention, soothing, and validation.

This suggests that youth may be more accurate reporters on their own suicidal thoughts and behaviors than their parents. Indeed, in both clinical and research settings, it is important to take seriously the reports of youth on their own experiences—particularly internalizing symptoms that may not be readily observed by parents or other adults. However, youth may also underreport suicidality. In a large pediatric sample of youth 11 to 17 years old, 67.5% of adolescents denied thoughts of death reported by their parents (Jones et al., 2019). Young people may choose not to disclose suicidal thoughts due to concerns that these thoughts will not be kept confidential by a mental health professional, concern that they will be judged, or beliefs that these thoughts cannot be treated or helped (McGillivray et al., 2022). Research on clinical decision-making supports the consideration of both adolescent and parent reports of internalizing symptoms, and suggests that there is predictive utility in cases when parents report higher or lower levels of symptoms than youth (Makol et al., 2019). Thus, parent report can provide important

context and additional information when evaluating youth suicidality. Tools such as the K-SADS-PL DSM-5 indicate that clinical judgment is required when interpreting and assessing discrepancies across reporters (Kaufman et al., 2016).

In particular, parent-child agreement on suicidality in younger children is understudied. It is possible that parents of preteens have a different level of insight into their children's suicidal experiences than parents of adolescents or young adults. Younger children may share their experiences with parents more freely than adolescents; on the other hand, parents of younger children may be more likely to dismiss a child's report of suicidal thoughts or behaviors due to beliefs that young children cannot be suicidal. Prior work on the ABCD sample has established that baseline parent-child concordance on suicidality ratings is low, highlighting that parents and youth in this sample may not see eye-to-eye on childhood experiences of suicidality (Deville et al. 2020). This study also found that family history of depression was associated with lower rates of parent-child discordance on suicidal ideation ratings, suggesting that parents who are more familiar with mental health symptoms such as suicidality may have a more accurate perception of their child's own symptoms (DeVille et al., 2020). More work is needed to identify factors associated with parent-child agreement on suicidality ratings, and perhaps to explore what mechanisms could be leveraged through intervention to increase a shared understanding of mental health symptoms between parents and children. This could be especially beneficial as high rates of parent-child discordant reporting on behavioral and emotional problems have been associated with negative outcomes, including future suicidality (Ferdinand et al., 2004).

As discussed further in Chapter 5, parent-youth agreement on suicidality ratings remained low at the two-year follow-up wave of ABCD. This does not necessarily mean that parent reports of suicidality have little value: indeed, it is plausible that youth denial of suicidality may lead to undertreatment if parent report is not considered, and ABCD data demonstrates that many parents do report suicidality when their children deny it (see Table 20). Therefore, although suicidality will be considered endorsed when reported by either parent or child for the purposes of these analyses, it is suggested that future research continue to explore how best to understand and interpret parent-child agreement and disagreement on suicidality ratings.

Sample Description and Characteristics

Data from the ongoing longitudinal Adolescent Brain and Cognitive Development (ABCD) Study will be used for this project. The ABCD Study is the largest study of brain and behavioral development in the United States (Karcher & Barch, 2021). The baseline cohort consists of nearly 12,000 youth aged 9-10 years, and data collection will continue for ten years until participants have entered young adulthood (Karcher & Barch, 2021). The ABCD Study cohort includes an embedded twin study comprising approximately 800 twin pairs recruited at four study sites that are leading twin research centers in the United States; this aspect of the study design strengthens the potential for causal inference from the study data (Iacono et al., 2018). The most recent data release (ABCD Curated Data Release 4.0) contains two-year follow-up data for the full cohort (ABCD Study, 2023). The most recent data release and future data are accessible via application to the National Institute of Mental Health (NIMH) Data Archive (NDA).

ABCD participants were recruited for participation at baseline primarily through elementary schools located within the catchment areas of the 21 nationally distributed ABCD recruitment sites, and the sample was intended to reflect the demographic composition of United States youth (Garavan et al., 2018). Recruitment materials were distributed to all children within the targeted age range (3rd through 5th grades), as well as distributed through classroom mailing lists and school newsletters if schools agreed. Interested families then completed a telephone screening to determine eligibility, and, if deemed eligible, were enrolled and completed the baseline assessment (Garavan et al., 2018). Inclusion criteria for the ABCD Study included age, ability to provide informed consent from parents and assent from children, and attendance at a public or private elementary school within the catchment areas of an ABCD research site (Karcher et al., 2019; Michelini et al., 2019; W. K. Thompson et al., 2019). Exclusion criteria for the ABCD Study included lack of English proficiency in the child, lack of either English or Spanish fluency in parents, the presence of contraindications to MRI scanning (e.g., irremovable ferromagnetic implants or dental appliances, claustrophobia, pregnancy), and the presence of severe sensory, intellectual, medical, or neurological conditions that would impair the validity of data or inhibit the child's ability to participate in the study protocol (e.g., gestational age less than 28 weeks or birthweight less than 1200 grams, a history of traumatic brain injury, or a current diagnosis of schizophrenia, moderate or severe autism spectrum disorder, intellectual disability, or alcohol or substance use disorder) (Karcher et al., 2019; Michelini et al., 2019; W. K. Thompson et al., 2019). The majority of the 21 ABCD research sites are overseen by a central institutional review

board (IRB) at the University of California, San Diego, which reviews and approves the research protocol; certain sites obtain local IRB approval instead (Auchter et al., 2018).

The ABCD protocol includes regular assessment of health, cognition, and suicidality phenotypes. At baseline, information on participants' developmental history, medical history and health services utilization, medication usage, psychopathology, and suicidality is collected from parents and children (Barch et al., 2018). Medical history, psychopathology, and suicidality data are collected at follow-up assessments (Barch et al., 2018). Suicidality is well-characterized in the sample: in an examination of lifetime suicidality via caregiver- and self-report interviews at baseline, 6.4% of the ABCD sample reported passive suicidal ideation, 4.4% reported active nonspecific suicidal ideation, 2.4% reported active ideation with method, intent, or plan, 1.3% reported suicide attempts, and 9.1% reported nonsuicidal self-injury (DeVille et al., 2020). Cognitive phenotypes in the dataset are also well-characterized: at baseline and two-year follow-up, participants complete a comprehensive cognitive battery that includes measures of working memory, inhibition, and shifting from the NIH Toolbox, as well as measures of other cognitive domains (Luciana et al., 2018).

Table 1 provides a description of the demographic characteristics of the ABCD Study sample at baseline. 11,876 youth between the ages of 8 and 11 (mean age 9.92 years; 46.8% female) provided data at the baseline assessment. Approximately one-third of the baseline sample had at least one sibling also participating in the study; this included both intentionally recruited twins for the embedded twin cohort (described in more detail in Chapter Five) and incidentally recruited siblings, twins, and triplets. The

sample was relatively racially and ethnically diverse; 52% of the baseline sample were white; 15.0% were Black; 20.3% were Hispanic; 2.1% were Asian; and 10.5% identified as another race or ethnicity. Approximately 27% of the baseline sample reported an annual household income of less than $50,000, with 38% of the sample reporting a household income greater than $100,000. The majority of youth participating in the study (59.3%) had at least one caregiver who obtained a post-secondary educational degree. Approximately two-thirds of the sample had parents who were married at baseline. 15.4% of the sample reported a family history of attempted or completed suicide.

Youth psychopathology, trauma exposure, substance use, and perception of family conflict were also examined at baseline. The Child Behavior Checklist is a parent-report measure that broadly assesses emotional and behavioral problems across a number of diagnostic categories and symptom dimensions (Achenbach & Rescorla, 2001). The CBCL Total Problems scale provides a summary of internalizing and externalizing domains of psychopathology, wherein higher scores indicate greater difficulty. The mean CBCL Total Problems *T*-score in the baseline sample was 45.85 (SD=11.34). Baseline trauma exposure was assessed using the PTSD module of the computerized K-SADS-PL DSM-5 (Kaufman et al., 2016; Kobak & Kaufman, 2015). 35% of the baseline sample had been exposed to one or more DSM-5 Criterion A trauma. The most commonly reported traumas were learning about the sudden death of a loved one (23.5%), witnessing domestic violence (7.9%), being in a serious car accident (3.6%), or being in another serious accident (4.1%). Substance use history at baseline was assessed via youth interview; less than 1% of the sample reported substance exposure beyond sips of alcohol

or puffs of tobacco or marijuana. Youth report of expressed conflict among family members was assessed using the Conflict subscale of the Family Environment Scale (FES; Moos & Moos, 1994). The Conflict subscale score has a range of 0-9, with higher scores indicating greater family conflict. The mean FES Family Conflict subscale score at baseline was 2.05 (SD=1.95).

Suicidality is assessed in ABCD via parent and youth report using the suicidality module of the computerized Schedule for Affective Disorders and Schizophrenia for School-Aged Children for DSM-5 (K-SADS-PL DSM-5) (Kaufman et al., 2016; Kobak & Kaufman, 2015). This module assesses whether youth have experienced current or past: "passive" suicidal ideation (e.g., wanting to be dead); "active" nonspecific suicidal ideation (e.g., thinking about killing oneself without a plan); "active" suicidal ideation with intent; "active suicidal ideation" with a plan; making preparations for a suicide attempt; making an aborted or interrupted suicide attempt; and making a suicide attempt (Janiri et al., 2020; *NIMH Data Archive - Data Dictionary*, n.d.). Each item is assessed categorically (i.e., as a "yes/no" question). Suicidality phenotypes are further described in Table 2. Suicidal ideation and suicide attempt will be examined as separate outcomes; an overall indicator of suicidality that includes all items (i.e., both suicidal thoughts and suicidal behaviors) will also be constructed and used as an outcome variable. Items assessing NSSI were not included in suicidality analyses.

At baseline, 2.3% of youth (1.4% of parents) reported current suicidal thoughts or behaviors (occurring in the past two weeks), and 7.7% of youth (7.1% of parents) reported suicidal thoughts or behaviors in the more distant past (i.e., a resolved episode

that occurred at least two months prior to the interview). At the one-year follow-up assessment, only youth were queried about suicidality; 1.7% of youth reported current suicidal thoughts or behaviors (occurring in the last two weeks), and 7.2% of youth reported past suicidal thoughts or behaviors. At the two-year follow-up assessment, 1.4% of youth (1.3% of parents) reported current suicidal thoughts or behaviors (occurring in the last two weeks, and 6.3% of youth (7.3% of parents) reported past suicidal thoughts or behaviors (Table 20).

Analytic Aims

This dissertation aims to capitalize on large, nationally representative, longitudinal study beginning in childhood in order to characterize trajectories of risk for suicidality and to better understand the roles that physical health and cognition play in risk for suicidal thoughts and behaviors beginning before adolescence. The following chapters will describe analyses that examine risk trajectories between chronic health problems, cognition, and suicidal thoughts and behaviors, as well as the genetic underpinnings of suicidality in preadolescent youth. Aims include:

1. **Aim 1**. To explore whether certain health problems, including chronic health conditions, relate longitudinally (i.e., over time) to suicidal ideation and/or behaviors in youth.
    a. *Hypothesis 1*: Having a history of chronic health conditions at baseline will be longitudinally associated with increased rates of suicidal thoughts and behaviors in youth.

2. **Aim 2**. To explore whether cognition relates longitudinally (i.e., over time) to suicidal ideation and/or attempt in youth.
    a. *Hypothesis 2*: Lower scores on tasks of executive functioning will be longitudinally associated with increased rates of suicidal thoughts and behaviors in youth.
3. **Aim 2a**. To investigate whether, and to what extent, cognition mediates observed longitudinal associations between health problems and suicidality.
    a. *Hypothesis 2a*: If significant longitudinal associations exist between a history of chronic health problems and suicidality, lower scores on tasks of executive functioning will partially mediate longitudinal associations between chronic health conditions and rates of suicidal thoughts and behaviors in youth.
4. **Aim 3**. To investigate additive genetic contributions to variance in youth suicidality, as well as to investigate additive genetic contributions to the covariance of executive functioning and suicidal thoughts and behaviors in youth, using genetically informative univariate and bivariate twin designs in an embedded twin subsample.
    a. *Hypothesis 3:* In univariate twin analyses, a significant additive genetic effect on youth suicidal thoughts and behaviors will be observed.
    b. *Hypothesis 4:* In bivariate twin analyses, genetic influences on suicidal thoughts and behaviors will be correlated with genetic influences on executive functioning.

CHAPTER TWO

Associations Between Chronic Health and Suicidality in Preadolescent Youth

Introduction

Previous work has suggested that youth with chronic health conditions—including chronic pain, migraines, respiratory diseases such as asthma, and diabetes—may be at elevated risk for suicidality (Iannucci & Nierenberg, 2022). In a sample of youth aged 15 to 30 years, self-reported diagnosis of a chronic condition lasting or expected to last for at least 6 months was associated with suicidal thoughts (OR=1.28), suicidal plans (OR=2.34), and suicide attempts (OR=4.63) (Ferro et al., 2017). Some adverse health events among youth with chronic health conditions, such as serious noncompliance with medical regimens in adolescents with diabetes, may be more accurately conceptualized as suicidal attempts (Goldston et al., 1997). Pain, both acute and chronic, has been associated cross-sectionally and, to some extent, longitudinally with adolescents' suicidal vulnerability (Hinze et al., 2019). Youth who experience the double burden of chronic physical and mental health conditions have been found to be at especially elevated risk for self-harm and suicidality (ORs 2.5-3.5) compared to healthy peers (Barnes et al., 2010).

Youth living with chronic health conditions may face considerable stressors in addition to the typical tasks of development. Chronic illness can impact myriad biological aspects of development, such as timing of puberty or physical growth; psychological aspects of development, such as identity development outside of the "sick role" or independence from a parent or caregiver; and social aspects of development, such as

limited opportunities for peer socialization due to a high burden of medical care or frequent sick days (Suris & Michaud, 2004). These challenges can impact quality of life for youth with chronic conditions (Powers, Patton, & Hommel, 2003). Youth with chronic health conditions are also at heightened risk for anxiety, particularly when the course of illness is unpredictable or uncontrollable, as in pain disorders and epilepsy (Pinquart & Shen, 2011). Parents of youth with chronic health conditions may also be more vulnerable to anxiety, which can also impact youth as well as parent quality of life (Link & Fortier, 2016; Pinquart, 2019). Chronic illness presents a unique set of stressors for the child, caregiver, and family system, and adaptive psychological functioning may be strained by efforts to cope with ongoing medical treatment, physical discomfort or pain, or fear and uncertainty about prognosis.

Indeed, many youth with chronic illness engage in maladaptive behaviors such as treatment non-adherence, which has been conceptualized as an emotionally avoidant response to thoughts and emotions about chronic illness (Lois & Miller, 2018). A youth who is faced with a challenging situation related to their chronic illness—for example, needing to ask about allergens at a restaurant with friends if they have anaphylactic allergies—may experience negative or dysregulated emotions (e.g., embarrassment and frustration) that may lead them to engage in more risky behaviors such as not adhering to their medical regimen (i.e., not checking for allergens in efforts to blend in with peers). This avoidance may lead to short-term relief but long-term negative emotional and/or physical consequences of non-adherence (Lois & Miller, 2018). Although non-adherence is clearly not always analogous with suicidality, suicidal ideation can manifest as

noncompliance behaviors in youth with chronic medical illnesses such as diabetes (Iannucci & Nierenberg, 2022). Non-adherence to medical regimen has been proposed as an analogous treatment target in adaptations of DBT for adolescents with chronic medical illness, as it can be seen as a risky behavior that is emotionally mediated (Lois & Miller, 2018).

Furthermore, survivors of pediatric chronic illness may be vulnerable to later suicidality even after the threat of medical illness has subsided. Pediatric and adult survivors of childhood brain tumors have been found to be at increased risk of suicidal ideation (Brinkman et al., 2013). Examination of psychosocial late effects of pediatric cancer has found increased rates of suicidal ideation among survivors up to 10 years or more after diagnosis (Bitsko et al., 2016; Ernst et al., 2020). Suicidal ideation among adult survivors of pediatric cancer is associated with psychological and social factors such as current loneliness (Ernst et al., 2020). These findings suggest that suicidality-related sequelae of early experiences with chronic illness may take many years to fully emerge.

Hypothesized and studied mechanisms responsible for relationships between chronic health burden and suicidality have included psychopathology, particularly depression (Iannucci & Nierenberg, 2022). Children and adolescents with chronic illnesses, such as chronic fatigue syndrome, fibromyalgia, migraine/tension headache, epilepsy, and cleft lift and palate have a higher burden of depressive symptoms than their healthy peers (Pinquart & Shen, 2011). Additionally, several chronic health conditions, such as recurrent pain and asthma, have documented direct associations with youth

suicidality that are independent of psychopathology, i.e., these health conditions are associated with excess risk of suicidality beyond the risk incurred by mental health conditions such as depression (Bandiera et al., 2013; Barnes et al., 2010; Iannucci & Nierenberg, 2022; Koenig et al., 2015). Potential mechanistic factors, such as impaired coping skills or stress sensitivity, also suggest that examining cognitive processes may help elucidate how a history of chronic health problems may increase risk for suicidality (Iannucci & Nierenberg, 2022). In a sample of 166 pediatric cancer patients aged 6-23, those who experienced suicidality were more likely to have impairments in executive functioning (Sharkey et al., 2022). Existing literature in this area has focused mainly on adolescent samples, or has included younger children without disaggregating child and adolescent subsamples; thus, relationships between chronic health problems and suicidality in younger children remain underexplored.

In any discussion of the psychosocial vulnerabilities associated with pediatric chronic illness, it is important to also acknowledge the considerable resilience displayed by youth living with chronic health conditions. Resilience, which psychologist Ann Masten describes as “ordinary magic,” is the modal outcome for youth who grow up facing various forms of adversity (2001). Chronic illness is no exception to this rule. Many youth with pediatric health conditions not only avoid negative experiences or outcomes but also remain on a typical, positive developmental trajectory (Hilliard et al., 2015). The hypothesis that children living with chronic illness may be at higher risk of experiencing suicidal thoughts and behaviors does not belie the notion that these same youth may display profound psychosocial resilience. Indeed, youth with a history of

suicidal ideation or attempt display profound resilience in their daily lives as they move forward with the tasks of development and of living. Identifying whether chronic illness is a risk factor for suicidality has the potential to inform both prevention of incident suicidality in vulnerable pediatric populations and to promote recovery and prevent recurrence of suicidality in youth who may experience it.

Relationships between chronic health and suicidality have already begun to be explored in the ABCD sample. A recent paper examining associations between asthma and youth-reported suicidality over the first three waves of ABCD found that asthma attacks remained associated with suicide attempt after controlling for several covariates including psychopathology, but asthma history did not remain significantly associated with suicidality when covarying for psychopathology (Hoffman et al., 2022). The authors posited that asthma attack may represent a more specific and severe clinical phenotype than asthma history, which may suggest that the "state" of asthma symptoms and the "trait" of asthma history may be differentially associated with suicidality (Hoffman et al., 2022). The analyses below extend Hoffman et al.'s findings by examining longitudinal associations between asthma history and suicidality, as well as multiple other chronic health conditions, and by additionally co-varying for parental marital status, family conflict, youth trauma exposure, family history of suicide attempt, and youth substance use.

Methods

Sample, Variable Selection and Construction

All available data from ABCD study participants who completed the baseline assessment (n = 11,876) was used in these analyses. Youth were, on average, 9.92 years of age at baseline. 46.8% percent of the sample was female at birth. 52.0% of the sample were white, 15.0% were Black, 20.3% were Hispanic, 2.1% were Asian, and 10.4% identified their race and/or ethnicity as "other." 43.1% of the sample had at least one chronic health condition at baseline. 10.1% of the sample experienced suicidal thoughts and/or behaviors over the follow-up period (between baseline and follow-up year 2); overall, 19.5% of the sample experienced lifetime suicidal thoughts and/or behaviors at any point up until the follow-up year 2 study visit. For additional description of sample characteristics, please refer to Chapter 1 and Tables 1, 5, and 20.

Data on ABCD participants' physical health at baseline was collected from the Parent Medical History Questionnaire, a parent-report questionnaire that assessed medical history and health services utilization for ABCD participants. Parents were asked to report whether a child had ever been to a doctor for any of the following chronic health conditions: asthma, allergies, cancer or leukemia, cerebral palsy, diabetes, epilepsy or seizures, kidney disease, lead poisoning, muscular dystrophy, multiple sclerosis, heart problems, sickle cell anemia, or very bad headaches. These outcomes were considered chronic health conditions for the purposes of this study. The medical history questionnaire also assessed hearing and vision problems, bronchitis, fevers, injuries, other poisonings, and surgeries, which were not considered chronic health conditions for the purposes of this study.

Covariates for all analyses included age, sex at birth, race/ethnicity, household income, highest household education, marital status of guardian, substance use, family history of suicide, youth psychopathology, stressful events, and family conflict. These covariates were chosen based on recently published baseline analyses of suicidal thoughts and behaviors in the ABCD sample as well as the demographic categories that were used as recruitment metrics based on the American Community Survey (ACS) (DeVille et al., 2020; Garavan et al., 2018; Huber et al., 2020; Janiri et al., 2020; The Data Analysis and Informatic Center of the ABCD Study, n.d.).

Follow-up suicidality was assessed by combining parent and child reports of current or past suicidal thoughts and/or behaviors on the computerized K-SADS-PL DSM-5 at one or both follow-up visits for youth with no reported current or past suicidality at baseline (Kaufman et al., 2016; Kobak & Kaufman, 2015) Lifetime suicidality was assessed by combining parent and child reports of current or past suicidal thoughts and/or behaviors at any study timepoint (baseline, one-year follow-up, or two-year follow-up).

Statistical Methods

Generalized linear mixed models were run using the *lme4* package in R (D. Bates et al., 2015; R Core Team, 2023). A multilevel modeling approach was used to account for the hierarchical or "nested" structure of the data (i.e., participants were "nested" within 21 study sites and siblings were "nested" within families). This modeling approach allows for unbiased parameter estimates, allows variance to be correctly partitioned across different levels of the model, and reduces the risk of Type I error by

appropriately accounting for the clustering within families and study sites (McCoach & Black, 2012; Peugh, 2010). Multilevel mixed-effects models used maximum likelihood (ML) estimation to produce estimates of variance-covariance components.

Each of the nine chronic health conditions with incident cases of suicidality reported in the follow-up period (asthma, allergies, diabetes, seizures or epilepsy, kidney disease, lead poisoning, heart problems, sickle cell anemia, or very bad headaches) was first entered into separate models examining longitudinal associations between specific chronic health conditions at baseline and suicidality first reported by parents or youth to occur after baseline (i.e., current or past suicidality first reported at the one-year or two-year follow-up visits). The Bonferroni correction was applied to correct for multiple comparisons across health condition models (Armstrong, 2014). For subsequent models, all chronic health conditions were collapsed into a binary variable indicating the presence or absence of any chronic health condition(s), as well as a continuous variable indicating the number of chronic health conditions in a child's medical history. All models controlled for baseline covariates including age, sex, race/ethnicity, family income, highest household education, parental marital status, general youth psychopathology (assessed using the CBCL Total Problems scale), family history of suicidality, youth substance use, family conflict (assessed using the Family Conflict subscale of the Family Environment Scale), and youth trauma exposure (exposure to DSM-V Criterion A traumas assessed using the K-SADS-PL DSM-5 PTSD module). All continuous variables in models were mean-centered and scaled (divided by their standard deviation) to promote interpretability.

To elucidate whether chronic health history has differential patterns of association with incident suicidality occurring after baseline than with total lifetime suicidality, secondary analyses were also conducted to examine associations between chronic health conditions and lifetime suicidal thoughts and/or behaviors reported at any time during the study. Models were run on 13 specific chronic health conditions, including the 9 conditions listed above and four additional health conditions—cancer or leukemia, cerebral palsy, multiple sclerosis, and muscular dystrophy—with incident cases of suicidality reported over the whole of the study period. The Bonferroni correction was applied to correct for multiple comparisons across health condition models (Armstrong, 2014). These models controlled for the baseline covariates listed above, and all continuous variables were mean-centered and scaled to promote interpretability.

Results

The demographics of youth who experienced no suicidality throughout the study period were compared to those of youth who experienced lifetime suicidality reported at any time over the study period and to those of youth with incident suicidality reported over the follow-up period. Tables 1, 3, and 4 summarize sociodemographic data compared across these three groups. Compared to youth who experienced no suicidality throughout the study period, youth who experienced lifetime suicidality were: more likely to be male; less likely to be white and more likely to be Black or identify their race or ethnicity as "other" (i.e., not white, Black, Hispanic, or Asian); more likely to have an annual household income under $50,000 and less likely to have an annual household income over $100,000; less likely to have married parents and more likely to have

divorced parents or a parent living with an unmarried partner; more likely to have a parent who completed only some college and less likely to have a parent who earned a post-graduate degree; more likely to have a family history of suicide attempt; more likely to have engaged in substance use beyond a sip of alcohol or a puff of tobacco or cannabis; and more likely to have experienced a Criterion A trauma before baseline (assessed using Fisher's exact tests). Youth who experienced lifetime suicidality had significantly higher CBCL Total Problems *T*-scores and Family Conflict subscale scores on the FES than youth who reported no suicidality throughout the study period (assessed using one-way ANOVAs).

Youth for whom suicidality first presented during the follow-up period, compared to youth who experienced no suicidality at any time, were less likely to be white or Asian and more likely to be Black; more likely to have an annual household income under $50,000 and less likely to have an annual household income over $100,000; less likely to have married parents and more likely to have parents who never married; more likely to have parents who completed only some college and less likely to have parents who earned post-graduate degrees; more likely to have a family history of suicide attempt; and more likely to have experienced a Criterion A trauma before baseline (assessed using Fisher's exact tests). Youth with incident suicidality over the follow-up period had significantly higher CBCL Total Problems *T*-scores and Family Conflict subscale scores on the FES than youth who reported no suicidality throughout the study period (assessed using one-way ANOVAs).

Baseline rates of chronic health conditions in the ABCD sample are described in Table 5. The most common chronic health conditions reported in the total sample were allergies (32.1%) and asthma (17.3%); the least commonly reported conditions were cerebral palsy (0.1%), muscular dystrophy (0.1%), and multiple sclerosis (0.1%). 43.1% of the total sample reported at least one chronic health condition at baseline. Rates of baseline chronic health problems were compared between youth who never experienced suicidality and those who experienced incident suicidality after baseline. When examining suicidality as a whole (including either ideation and/or behavior), no significant differences in rates of chronic health problems were found between youth who never experienced suicidality and those who experienced incident suicidality during follow-up. Some chronic health conditions had very low base rates in the overall sample, and there were no youth in the incident suicidality group who had a history of cancer/leukemia, cerebral palsy, muscular dystrophy, or multiple sclerosis (Table 5). Compared to youth who reported no suicidal ideation, youth with incident suicidal ideation after baseline were more likely to have a history of asthma or allergies; were more likely to have a general history of chronic health problems; and had a higher burden of chronic health problems at baseline (Table 6; assessed using Fisher's exact tests and one-way ANOVA). Compared to youth who reported no suicidal behavior, youth with incident suicidal behavior after baseline were more likely to have a history of epilepsy/seizures or very bad headaches (Table 7; assessed using Fisher's exact tests).

Results of longitudinal generalized linear mixed models are described in Table 8. Suicidality was first examined as an omnibus outcome (i.e., any suicidal ideation or

behavior reported over the follow-up period). To examine the potentially distinct pathways to suicidal ideation and suicidal actions/behaviors, suicidal thoughts (including both passive and active suicidal ideation) and behaviors (including preparatory actions or suicide attempts) were also examined as separate outcomes. In fully adjusted models, no specific health conditions, nor a history of chronic health conditions overall, were significantly associated with higher or lower risk of suicidality over the follow-up period. Associations between heart disease and lower odds of incident total suicidality (OR=0.68, 95% CI [0.44, 1.05], p=0.08) and incident suicidal ideation (OR=0.68, 95% CI [0.46, 1.01], p=0.06) trended towards significance before correcting for multiple comparisons. General presence of any chronic health condition(s) (OR=0.73, 95% CI [0.53, 1.01], p=0.06) and total number of chronic health conditions (OR=0.84, 95% CI [0.68, 1.02, p=0.08), as well as asthma (OR=0.66, 95% CI [0.42, 1.04], p=0.08) and allergies (OR=0.71, 95% CI [0.50, 1.01], p=0.06) specifically, were associated with reduced odds of incident suicidal behavior; these associations trended towards significance before correcting for multiple comparisons.

To further characterize overall associations between chronic health conditions and suicidality, lifetime suicidality (i.e., reported at baseline or follow-up) was also examined. Although lifetime suicidality analyses do not allow for causally informative interpretations of longitudinal associations, they still may provide information about how chronic health conditions and suicidality may covary in childhood. Rates of baseline chronic health problems were compared between youth who never experienced suicidality and those who experienced suicidality at any point across the three waves of

study data available. Compared to youth who never experienced any suicidality, youth with lifetime suicidality (either suicidal ideation, behavior, or both) were more likely to have a history of asthma, allergies, or very bad headaches; were more likely to have a general history of chronic health problems; and had a higher burden of chronic health problems at baseline (Table 5; assessed using Fisher's exact tests and one-way ANOVA). Compared to youth who never experienced suicidal ideation, youth with lifetime suicidal ideation were more likely to have a history of allergies, asthma, or very bad headaches; were more likely to have a general history of chronic health problems; and had a higher burden of chronic health problems at baseline (Table 6; assessed using Fisher's exact tests and one-way ANOVA). Compared to youth who never engaged in suicidal behavior, youth with lifetime suicidal behavior were more likely to have a history of very bad headaches; were more likely to have a general history of chronic health problems; and had a higher burden of chronic health problems at baseline (Table 7; assessed using Fisher's exact tests and one-way ANOVA).

Associations between chronic health history and lifetime experiences of suicidality, including suicidality reported at baseline, were additionally examined in lifetime models (Table 9). Across models assessing total lifetime suicidality, lifetime suicidal ideation, and lifetime suicidal behavior, chronic health conditions were not significantly associated with increased or decreased odds of suicidality when examined separately, nor when examined as a composite predictor.

Tables 10 and 11 summarize all covariate coefficients for models examining the association between having a chronic health condition and suicidality outcomes. In

longitudinal models and after correcting for multiple comparisons, CBCL Total Problems, FES Family Conflict scores, and age were significantly associated with increased odds of incident suicidal ideation and/or behavior. Female sex at birth was significantly associated with increased odds of incident suicidal ideation and behavior. In lifetime models, CBCL Total Problems and FES Family Conflict scores were significantly associated with increased odds of lifetime suicidal ideation and/or behavior. Race or ethnicity being identified as "other" (i.e., not white, Black, Hispanic, or Asian) was significantly associated with increased odds of lifetime suicidal ideation.

Discussion

ABCD youth who had experienced lifetime suicidality by age 12 were more likely to be male and/or Black when compared to never-suicidal youth, which is consistent with prior research on childhood suicidality (Sarkar et al., 2010; Sheftall et al., 2016). However, youth who experienced incident suicidality between ages 10 and 12 were more likely to be female than never-suicidal youth. In generalized multilevel mixed-effects models when examined alongside all covariates, female sex was a significant predictor of incident suicidality after baseline. This suggest that the 10-12 age range may represent the inflection point at which sex effects on suicidality are reversed and female sex emerges as a risk factor for suicidality that remains durable throughout adolescence and young adulthood (Miranda-Mendizabal et al., 2019).

Other notable demographic factors associated with the emergence of suicidality between ages 10-12 in fully adjusted generalized multilevel mixed-effects models were age, "other" race/ethnicity (i.e., not white, Black, Hispanic, or Asian), psychopathology

(measured using the CBCL Total Problems subscale), and family conflict (measured using the FES Family Conflict subscale) (see Tables 10-11). This suggests that across preadolescence, suicidality risk may increase with age, rather than abruptly peaking when youth transition into the teenage years. The robust associations between psychopathology, family conflict, and suicidality indicate that both individual-level and familial factors may be opportune targets for treating suicidality in this age group. Family conflict has previously been identified as a risk factor for suicidal ideation in youth (Assari et al., 2021; Machell et al., 2016); the present findings suggest that family conflict contributes to prospective risk for suicidality in preadolescents over and above the stress imparted by chronic illness. As psychopathology and family conflict were found to be predictors of emergent suicidality in this age group, addressing these factors early may help to prevent the development of suicidality in preadolescent youth. Future work could examine whether public health and social service programming that targets family conflict in families of young children (i.e., under age 10) is impactful in reducing the risk that these children go on to develop suicidal ideation and/or engage in suicidal behavior.

The significant association between "other" race/ethnicity and lifetime suicidal ideation warrants further investigation in future research. "Other" race/ethnicity was in ABCD indicates that the participant was *not* identified as white, Black, Hispanic, or Asian; as this subgroup is likely significantly heterogeneous, it deserves more detailed attention in order to better understand how suicidality impacts racial/ethnic minority youth who do not neatly fall into the categories of white, Black, Hispanic, or Asian. Research on racial and ethnic identity in adolescents has found that youth often self-

describe their identity differently than what they endorse on checkbox demographic forms and that existing demographic measurement tools are likely inadequate to fully and accurately measure youth racial/ethnic identity (Woolverton & Marks, 2023). Therefore, it is difficult to disentangle the various possible explanations for why youth in this category had higher odds of suicidal ideation, as it may primarily represent the inadequacy of existing measurement tools to capture youth racial/ethnic identity. However, it is possible that youth in this category experience more frequent discrimination based on their identities, and racial/ethnic discrimination has previously been associated with suicidality in ABCD youth (Argabright et al., 2022). More work is needed to further explore causal and mechanistic pathways in order to inform prevention and intervention efforts. Clinicians working with youth should recognize the role of identity discrimination as a stressor that may increase suicidality risk.

Youth with lifetime suicidality, including both ideation and behavior, were more likely to have a history of chronic health conditions than youth with no suicidality. In particular, suicidal youth were more likely to have a reported history of asthma, allergies, and very bad headaches. It is important to note that these were the three most prevalent chronic health conditions examined in the sample, and base rates of other specific chronic health conditions were quite low; therefore, analyses may have been underpowered to detect a statistically significant difference between suicidality groups across some of the rarer chronic health conditions.

Youth who experienced incident suicidal ideation between ages 10 and 12 had higher rates of chronic health problems in general, and asthma, allergies, and headaches

in particular, than youth who experienced no suicidal ideation across the course of the study. These differences were not observed among youth who experienced incident suicidal behavior between ages 10 and 12. As these analyses allow for temporality, since chronic health burden was measured at baseline and suicidality was measured only if it occurred for the first time after baseline, they may suggest that chronic health problems are a risk factor for suicidal ideation, but not behavior, in youth aged 10-12. However, this pattern of results could again be due to insufficient power to detect effects, as only 191 youth (less than 2% of the sample) reported incident suicidal behavior during the follow-up period.

Overall, when entered into multilevel mixed-effects models and after correcting for a range of demographic, environmental, and psychological covariates and for multiple comparisons, chronic health conditions were not significantly associated with increased odds of suicidality in youth when examined in either longitudinal or lifetime models. These null findings could be due to multiple factors. First, although odds ratios for overall chronic health conditions were generally close to 1.00, odds ratios for specific health conditions ranged from 0.33 to 1.63. While being mindful not to over-interpret non-statistically-significant results, this variability could suggest that certain health conditions—such as heart problems—may be associated with *reduced* odds of suicidality while others—such as seizures or diabetes—may be associated with *increased* odds of suicidality. Heterogeneity of direction of effects across different chronic health conditions may complicate the question of whether chronic health burden increases risk for suicidality. If this is the case, disease-specific mechanisms and their relationship to

suicidality may warrant further exploration in future work to more clearly elucidate how best to support young patients. Another possible explanation for null findings is that although associations between chronic health and suicidality have been observed in previous research, including in the ABCD sample itself (Hoffman et al., 2022), these findings may be the result of incomplete control for confounding. Controlling for important psychosocial factors including psychopathology and family conflict may nullify previously found associations between chronic health and suicidality. For example, Hoffman et al. (2022) found that history of asthma attacks remained associated with suicide attempt, but not suicidal ideation, after controlling for psychopathology, and that history of an asthma diagnosis was only significantly associated with suicidality before controlling for psychopathology.

One limitation of the present analyses is that they may be underpowered to detect statistically significant effects. ABCD participants comprise a community-based sample that is intended to reflect the demographics of United States youth and was not oversampled for either chronic health or suicidality, both of which are relatively rare occurrences among the United States preadolescent cohort. Indeed, some health conditions were so rare in the ABCD sample that they could not be examined as potential predictors of incident suicidality given insufficient case counts. It is therefore possible that studying clinical samples of medically ill youth could reveal more robust associations between chronic health burden and suicidality in preadolescence. Another limitation is that chronic health conditions were assessed via parent-reported health care utilization for each specific health condition; it is possible that the true prevalence of

chronic health conditions was underestimated in the sample if some youth had reduced health care access or if parents had difficulty recalling the specifics of doctor visits for their child's health problems, particularly if health problems occurred early in the child's life. Future research along this line of inquiry could capitalize on electronic health records to evaluate how various types of health care utilization for chronic health problems, including scheduled and emergency visits as well as medication prescription and adherence, might be associated with suicidality in preadolescent youth. Although these analyses did not suggest that chronic health conditions are associated with incident or lifetime suicidality in preadolescent youth, this question merits continued attention in the research literature, particularly in clinical samples.

CHAPTER THREE

Associations Between Cognition and Suicidality in Preadolescent Youth

Introduction

Existing literature has highlighted that youth experiencing suicidality may exhibit unique difficulties in cognitive functioning, including working memory (Bauer et al., 2018), sluggish cognitive tempo (Becker et al., 2016), and difficulty with episodic memory (Huber et al., 2020). In particular, executive functioning (EF)—a higher-order dimension of cognitive processes that contribute to purposive, goal-directed behavior–have been implicated in distress tolerance, a construct that is closely tied to suicidal and self-harm behavior (Best & Miller, 2010; Dour et al., 2011; Stewart et al., 2017; Xie et al., 2018). Executive functions include mental set shifting, updating and monitoring of representations in working memory, and inhibition of prepotent responses (Miyake et al., 2000). These processes are highly relevant to suicidality: for example, the ability to inhibit impulsive behaviors could be protective against suicidal behavior that results from urges to act on impulsive or intrusive thoughts in a moment of crisis; the ability to quickly remember coping strategies could help youth to tolerate distress and regulate emotions; and the ability to think flexibly could help youth to problem-solve in high-stress situations that may trigger strong emotions and suicidal urges. Furthermore, more persistent problem-solving in young children has been linked to decreased rates of active suicidal ideation in adolescence, suggesting that problem-solving may represent a protective factor or a target for prevention efforts (Sarkisian et al., 2021).

Relative impairments in EF in youth—specifically on tasks of working memory, inhibition, and shifting/flexibility—have been observed transdiagnostically across multiple forms of psychopathology that are relevant to suicidality, including mood disorders, attention-deficit/hyperactivity disorder (ADHD), and psychosis (Doyle et al., 2018). ADHD in childhood, which can be considered a disorder of EF and attentional regulation, is related to increased risk for suicidality in adolescence (Barkley, 1997; Chronis-Tuscano et al., 2010; Groves et al., 2022). Among a community sample of youth aged 7-12 years with ADHD, working memory, an EF-related construct, was found to mediate increased negative affect and suicidal ideation (Bauer et al., 2018). As EF is a developmentally acquired skillset associated with prefrontal cortical development, children and adolescents are not expected to have fully developed EF (Best & Miller, 2010). However, failure to acquire EF skills on an expected developmental trajectory may suggest vulnerability to impulsive behaviors, risk-taking, or cognitive distortions that increase risk for suicidality.

In adult samples, there is some evidence for associations between EF difficulties and suicidality, including suicidal ideation and attempt (Marzuk et al., 2005; Saffer & Klonsky, 2017). Individuals experiencing suicidality may be clinically described as cognitively "rigid," exhibit dichotomous (e.g., all-or-nothing, black-and-white) thinking patterns, and demonstrate impaired problem-solving abilities; these cognitive characteristics can be related to EF. Cognitive inflexibility, exemplified by difficulty with set-shifting on the Wisconsin Card Sorting Test, has been distally linked to greater vulnerability to suicidal ideation in young adults; this relationship is mediated by

maladaptive cognitive patterns such as rumination, which can lead to hopelessness (Miranda et al., 2012, 2013). This suggests that impairments in executive functions, such as set-shifting, may lead to a cascade of other maladaptive cognitive processes that generate more negative thoughts and increase vulnerability to suicidal ideation.

Aspects of cognition beyond EF have also been examined in relation to suicidality. In adults, a negative relationship between IQ and suicidality has been observed, suggesting that higher IQ is protective against risk for suicidality (Batty et al., 2018). However, the same may not be true for children: in a community sample of youth aged 11-21, suicidality was associated with greater functional impairment but better cognitive performance, suggesting that greater cognitive ability may not be protective against suicidality for youth (Barzilay et al., 2019). In some cases, cognitive ability may interact with other factors to moderate risk for suicidality. For example, a study of high-ability autistic individuals found that autistic children with exceptional cognitive ability and/or higher polygenic scores for cognitive performance experienced increased rates of suicidal thoughts (Casten et al., 2023). In the Avon Longitudinal Study Parents and Children, higher IQ in boys, but not girls, at age 8 was associated with increased risk of suicidal ideation assessed in adolescence (Chang et al., 2014). Mixed findings on the associations between general cognitive ability and suicidality suggest that more research is needed to understand how these relationships may differ across different groups and stages of development.

Overall, research evidence on the cognitive correlates of suicidality is somewhat mixed, and recent systematic qualitative reviews have been inconclusive as to whether

and how deficits in EF and cognitive control contribute to suicidality (Bredemeier & Miller, 2015; Ellis & Rutherford, 2008; Gifuni et al., 2020). Notably, a recent cross-sectional analysis of ABCD baseline data found that in this cohort, youth with a history of suicidality (reported by their parent or by both the youth and parent) had lower episodic memory performance, suggesting that cognitive domains beyond EF may be implicated in preadolescent suicidality (Huber et al., 2020). More longitudinal studies, and more studies in pediatric and especially preadolescent samples, are needed to further elucidate the role of EF and other cognitive processes in youth suicidality (Bredemeier & Miller, 2015; Gifuni et al., 2020). The following analyses aimed to examine associations between cognitive performance, including on measures of EF as well as other aspects of cognition, and suicidality in preadolescent youth.

Methods

Sample Characteristics

As with Chapter 2, all available data from ABCD study participants who completed the baseline assessment (n = 11,876) was used in these analyses. For additional description of sample characteristics, please refer to Chapters 1-2 and Tables 1 and 20.

Measurement of Cognition

The ABCD cognitive battery was selected to be neuroscientifically informed, appropriate for a developing population, and psychometrically valid and reliable (Luciana et al., 2018). Tasks were also selected to be appropriate for longitudinal assessment with minimal practice effects: for this reason, most measures in the cognitive battery (with the

exception of the NIH Toolbox Dimensional Change Card Sort Test) do not require rule-based learning (Luciana et al., 2018). Tasks with minimal floor and ceiling effects were selected in order to be sensitive to effects of cognitive development in the sample (Luciana et al., 2018). ABCD participants complete the NIH Toolbox Cognition Battery at baseline and two-year follow-up. The Cognition Battery is a set of brief cognitive measures that are designed to measure cognitive domains including executive function, attention, episodic memory, language, processing speed, and working memory across the lifespan (Denboer et al., 2014; Luciana et al., 2018; Mungas et al., 2013). In the ABCD protocol, the Cognition Battery is administered on an iPad and administration takes approximately 35 minutes (Luciana et al., 2018). Two tasks within the Cognition Battery—the Toolbox Flanker Inhibitory Control and Attention Test and the Toolbox Dimensional Change Card Sort Test—specifically assesses executive function, and a third task—the Toolbox List Sorting Working Memory Test – assesses working memory, which is an EF-related construct (McCabe et al., 2010). The remaining Cognition Battery tasks assess language (the Toolbox Picture Vocabulary Test and the Toolbox Oral Reading Recognition Test), memory (the Toolbox Picture Sequence Memory Test), and processing speed (the Toolbox Pattern Comparison Processing Speed Test). Summary scores are available for all seven measures in the Cognition Battery. Three composite scores with robust psychometric properties—a Total Score composite, a Crystallized Intelligence composite, and a Fluid Intelligence composite—can be calculated from the Cognition Battery (Akshoomoff et al., 2013). The present analyses used uncorrected standard Cognition Battery scores to promote consistency with published literature on baseline

cognition in the ABCD sample and because demographic variables, including age, were included as covariates in all analyses (Anokhin et al., 2022; Dick et al., 2019; Huber et al., 2020; W. K. Thompson et al., 2019).

Table 12 contains descriptive statistics for ABCD baseline cognitive measures. Mean uncorrected standard scores on NIH Toolbox Cognitive Battery tasks ranged from 84.46 (Picture Vocabulary Test) to 102.81 (Picture Sequence Memory Test). The mean Fluid Intelligence composite uncorrected standard score was 91.55; the mean Crystallized Intelligence composite uncorrected standard score was 86.36; and the mean Total Composite uncorrected standard score was 86.22. The mean scaled score on the WISC-V Matrix Reasoning subtest was 9.86.

Statistical Methods

Generalized linear mixed models were run using the *lme4* package in R (D. Bates et al., 2015; R Core Team, 2023). A multilevel modeling approach was used to account for the hierarchical or "nested" structure of the data. Multilevel mixed-effects models used maximum likelihood (ML) to produce estimates of variance-covariance components. Baseline uncorrected standard scores from the seven tasks in the NIH Toolbox Cognition Battery were first examined as separate predictors of incident total suicidality, suicidal ideation, and suicidal behavior that first occurred between ages 10-12. Each of the seven Cognition Battery tasks was also examined in association with lifetime total suicidality, suicidal ideation, and suicidal behavior. Scaled scores from the Matrix Reasoning subtest from the Wechsler Intelligence Scale for Children-V (WISC-5) were included as a covariate in analyses examining each NIH Toolbox Cognition Battery

task separately to serve as a proxy control for general intellectual ability (Luciana et al., 2018; Wechsler, 2014). Matrix Reasoning was also examined separately as a predictor of all suicidality outcomes. All analyses additionally controlled for baseline covariates described in Paper 1, including age, sex, race/ethnicity, family income, highest household education, parental marital status, general youth psychopathology (assessed using the CBCL Total Problems scale), family history of suicidality, youth substance use, family conflict (assessed using the Family Conflict subscale of the Family Environment Scale), and youth trauma exposure (exposure to DSM-V Criterion A traumas assessed using the K-SADS-PL DSM-5 PTSD module). All continuous variables in models were mean-centered and scaled to promote interpretability.

Broader domains of cognition were also examined as potential predictors of suicidality. The Crystallized Intelligence, Fluid Intelligence, and Total composite scores from the NIH Toolbox Cognition Battery were entered into separate generalized linear mixed models to explore the potential associations between these general domains of cognition and suicidality. In order to examine associations between latent cognitive factors and suicidality, exploratory factor analysis was conducted to examine the factor structure of the NIH Toolbox Cognition Battery data in the baseline ABCD sample. Although previous work has explored the factor structure of this data in ABCD, it has done so only in a subsample of 4,521 children, whereas the present analysis was conducted on the full baseline sample of 11,876 youth (W. K. Thompson et al., 2019). Exploratory factor analysis of the seven NIH Toolbox Cognition Battery tasks was conducted in SPSS and R using a *varimax* rotation and maximum likelihood estimation,

and resultant factors were also examined as potential predictors of longitudinal and lifetime suicidality outcomes (IBM Corp, 2020; R Core Team, 2023). As above, these analyses additionally controlled for age, sex, race/ethnicity, family income, highest household education, parental marital status, general youth psychopathology, family history of suicidality, youth substance use, family conflict, and youth trauma exposure. All continuous variables in models were mean-centered and scaled to promote interpretability.

Results

Descriptive statistics of uncorrected cognitive scores for the total sample as well as three subgroups (youth who never experienced suicidality, those who experienced lifetime suicidality, and those who experienced incident suicidality over the follow-up period) can be found in Tables 12, 13, and 14. Compared to youth who experienced no suicidal thoughts and/or behaviors (STBs), youth with lifetime STBs had lower scores on the Dimensional Change Card Sort, List Sort Working Memory, Picture Vocabulary, Oral Reading Recognition, Pattern Comparison Processing Speed, and Picture Sequence Memory Tests, as well as on all composite scores. Compared to youth who experienced no STBs, youth with incident STBs over the follow-up period had lower scores on the Dimensional Change Card Sort and List Sort Working Memory Tests (assessed using one-way ANOVAs). Compared to youth who experienced no suicidal ideation, youth with lifetime suicidal ideation had lower scores on the Dimensional Change Card Sort, List Sort Working Memory, Pattern Comparison Processing Speed, and Picture Sequence Memory Tests as well as the Fluid Intelligence and Total composites (assessed using one-

way ANOVAs). Compared to youth who experienced no suicidal ideation, youth with incident suicidal ideation over the follow-up period had lower scores on the Dimensional Change Card Sort and List Sort Working Memory Tests (assessed using one-way ANOVAs). Compared to youth who experienced no suicidal behavior, youth with lifetime suicidal behavior had lower scores on the Dimensional Change Card Sort, List Sort Working Memory, Picture Vocabulary, Oral Reading Recognition, and Picture Sequence Memory Tests, as well as all composite scores and the WISC-V Matrix Reasoning subtest (assessed using one-way ANOVAs). Compared to youth who experienced no suicidal behavior, youth with incident suicidal behavior over the follow-up period had lower scores on the Picture Vocabulary Test, Oral Reading Recognition Test, and the WISC-V Matrix Reasoning subtest (assessed using one-way ANOVAs).

Results of longitudinal generalized linear mixed models are reported in Table 16. Suicidality was first examined as an omnibus outcome (i.e., any suicidal ideation or behavior reported over the follow-up period), and was also separated into suicidal ideation (including both passive and active ideation) and behavior (including preparatory actions or suicide attempts) outcomes. In fully adjusted multilevel mixed-effects models, only the WISC-V Matrix Reasoning subtest was significantly associated with overall incident suicidality (OR=1.03, 95% CI [1.00, 1.06], p=0.02) as well as with incident suicidal ideation (OR=1.03, 95% CI [1.01, 1.06], p=0.009). No cognitive measures were longitudinally associated with a specific outcome of suicidal behavior. Results of lifetime models are reported in in Table 17. In fully adjusted multilevel mixed-effects models, only the WISC-V Matrix Reasoning subtest was significantly associated with overall

lifetime suicidality (OR=1.02, 95% CI [1.00, 1.04], p=0.04) as well as with lifetime suicidal ideation (OR=1.02, 95% CI [1.00, 1.04], p=0.009). These results did not survive correction for multiple comparison using the Bonferroni method.

Using exploratory factor analysis, a three-factor model was found to best fit the data. Factor loadings were calculated using maximum likelihood estimation and *varimax* rotation (Table 15). Factor 1, which had the highest loadings across the Flanker Inhibitory Control and Attention Test, the Dimensional Change Card Sort test, and the Pattern Comparison Processing Speed Test, was designated to represent "Executive Functioning". Factor 2, which had the highest loadings across the Picture Vocabulary Test and Oral Reading Recognition Test, was designated to represent "Verbal Comprehension". Factor 3, which had the highest loadings across the List Sort Working Memory Test and the Picture Sequence Memory Test, was designated to represent "Memory and Learning". This pattern of factor loadings are similar, but not identical, to results from a published factor analysis on a subset of ABCD baseline cognitive data, which used Bayesian probabilistic principal components analysis that incorporated nesting of subjects within families and data collection sites; results from this analysis indicated a three-factor structure consisting of a "General Ability" factor with strongest loadings on Oral Reading, Picture Vocabulary, and List Sort Working Memory tasks, an "Executive Function" factor with strongest loadings on Flanker, Dimensional Change Card Sort, and Pattern Comparison Processing Speed tasks, and a "Memory" component with strongest loadings on the Picture Sequence Memory and List Sort Working Memory tasks (Thompson et al., 2019). In the current analyses, factor loadings were then used as

predictor variables in fully adjusted multilevel mixed-effects models examining associations with incident and lifetime suicidality outcomes. None of the three factors were significantly associated with incident or lifetime suicidal thoughts or behaviors (Tables 16-17).

Tables 18 and 19 summarize all covariate coefficients for models examining the association between cognition and suicidality outcomes. In longitudinal models and after correcting for multiple comparisons, CBCL Total Problems score was significantly associated with increased odds of incident suicidal ideation and/or behavior. FES Family Conflict score was significantly associated with increased odds of incident suicidal ideation and total suicidality. Female sex at birth was significantly associated with increased odds of incident suicidal ideation and behavior. Family history of suicide was significantly associated with increased odds of suicidal behavior. In lifetime models, CBCL Total Problems and FES Family Conflict scores were significantly associated with increased odds of lifetime suicidal ideation and/or behavior. Race or ethnicity being identified as "other" (i.e., not white, Black, Hispanic, or Asian) was significantly associated with increased odds of lifetime suicidal ideation and total suicidality.

Discussion

Significant differences in cognitive performance were found between ABCD youth who experienced suicidality and those who did not, suggesting that slightly reduced cognitive performance in preadolescent youth may be a marker of suicidality risk. Differences were observed across mean scores on multiple domains of cognition when comparing youth with and without lifetime suicidal ideation and/or behaviors.

When compared to youth with no suicidal ideation, those who developed suicidal ideation between ages 10-12 had slightly lower mean scores on EF-related tasks (the Dimensional Change Card Sort and List Sort Working Memory Tests). When compared to youth with no suicidal behaviors, those who developed suicidal ideation between ages 10-12 had slightly lower mean scores on two tasks of verbal comprehension (the Picture Vocabulary and Oral Reading Recognition Tests). It is important to note that these differences in cognitive performances were statistically significant but clinically negligible (i.e., mean uncorrected standard scores within one point). Although these results do not suggest gross impairment in cognition among youth who experience suicidality, they do suggest subtle but notable patterns of relatively lower cognitive performance that are different for suicidal ideation vs. behavior. Slightly lower scores on the Dimensional Change Card Sort and List Sort Working Memory Tests among youth with suicidal ideation could indicate difficulties with thinking flexibly, disregarding distracting negative thoughts, or accessing coping-relevant information that may lead to less problem-solving and more catastrophic thinking in youth (Bauer et al., 2018; Joormann & Gotlib, 2008). Slightly lower scores on the Picture Vocabulary and Oral Reading Recognition Tests among youth with suicidal behavior could indicate difficulties with verbally articulating distress or insufficient vocabulary to describe symptoms and emotions. Although these differences are subtle, they suggest specific relative weaknesses in cognition related to suicidal ideation versus suicidal behavior, which highlights the importance of considering distinct pathways of risk to these forms of suicidality.

In fully adjusted multilevel mixed-effects models, no NIH Toolbox cognitive measures or composite scores were significantly associated with suicidality. These null findings differ from Huber et al. (2020)'s finding that in baseline ABCD data, youth with a history of suicidal ideation at baseline had lower performance on the Picture Sequence Memory Test, an episodic memory task. This difference could be due to several factors. First and most notably, the present analyses examined follow-up suicidality first reported after baseline (approximately between ages 10-12) as well as lifetime suicidality reported at any point up to approximately age 12, whereas Huber et al. (2020) examined suicidality at baseline (ages 9-10). Also, Huber et al. (2020) examined nonspecific active suicidal ideation (i.e., thinking of killing oneself without considering a specific method, intent, or plan), whereas the present analyses combined passive, nonspecific active, and specific active suicidal ideation into a single outcome variable. This was done in light of empirical findings that passive and active suicidal ideation are strikingly similar (Liu, 2020); however, a limitation of collapsing suicidal ideation into a single outcome variable could be loss of nuance in specific findings relating to passive versus active suicidal ideation.

Additionally, the present analyses adjusted for some covariates that Huber et al.'s analyses did not, namely family conflict, youth substance use, and youth trauma exposure, as well as total psychopathology rather than internalizing psychopathology (2020).Total psychopathology (which assesses a broader range of emotional behavioral problems beyond internalizing problems) and family conflict were significantly associated with all suicidality outcomes in longitudinal and lifetime cognition models.

Future work should continue to examine whether cognition has an association with suicidality above and beyond individual psychopathology and family conflict in youth.

Although the factor structure of cognition in the full baseline sample was similar to previous findings in a subsample of ABCD youth, none of the three factors derived from exploratory factor analysis were significantly associated with suicidality (W. K. Thompson et al., 2019). It is important to note that while previous exploratory factor analysis used Bayesian probabilistic principal components analysis to account for the nested structure of the data, the present analyses used maximum likelihood estimation and did not account for the nested structure of the data in the exploratory factor analysis stage. This may change or limit the interpretation of the present factor analysis findings. Despite this, the nested structure of the data was taken into consideration in the regression modeling stage by using multilevel mixed-effects models into which factor scores were entered as predictors of suicidality.

Intriguingly, when WISC-V Matrix Reasoning was examined as a stand-alone predictor of suicidality in models adjusted for demographic, psychological, and environmental covariates, there was a trend towards significance. Matrix Reasoning is included in the ABCD cognitive battery as a well-validated measure of fluid, nonverbal reasoning that is correlated with general intellectual ability (Luciana et al., 2018; Wechsler, 2014). However, this trend towards significance was not apparent in analyses utilizing the NIH Toolbox Fluid Intelligence composite, which is an average of five Toolbox tasks (Dimensional Change Card Sort, Flanker Inhibitory Control and Attention, Picture Sequence Memory, List Sorting Working Memory, and Pattern Comparison

Processing Speed Tests) (Akshoomoff et al., 2013). Although the Fluid Intelligence composite is well-validated, it is possible that it taps different aspects of cognition than the WISC-V Matrix Reasoning subtest. Further, more detailed exploration of fluid reasoning as a potential predictor of suicidality is warranted in future analyses.

Another possible limitation of this work is that ABCD is a general community sample, and therefore may be underpowered to examine associations between cognition and suicidality due to low base rates of suicidality. Relationships between cognition and suicidality may be different in clinically-referred youth with conditions such as autism, depression, or psychosis (Casten et al., 2023; Vuijk et al., 2019). Future work could extend these analyses by examining associations between cognition and suicidality among clinically-referred youth.

CHAPTER FOUR

Genetic Contributions to Variance in Youth Suicidality in a Preadolescent Twin Sample

Introduction

Efforts to understand genetic influences on behavior have concentrated on two methods of analysis: twin, family, and adoption studies, which allow for the estimation of heritability of phenotypes, and genomic methods, which seek to identify particular genetic variations associated with traits or diseases. Both methods have been employed to examine genetic underpinnings of suicidality, although most of this research has focused on adult samples. Classical twin study design enables the decomposition of variance in an observed phenotype into additive genetic effects (A), dominance genetic effects (D), shared environmental effects (C), and/or non-shared environmental effects (E) by comparing monozygotic (MZ) or "identical" twins, who share 100% of their genetic material, to dizygotic (DZ) or "fraternal" twins, who share 50% of their genetic material. When monozygotic twins reared together are more similar than dizygotic twins reared together on a given phenotype, this is due to genetic contributions to the phenotype. The proportion of total phenotypic variation attributable to additive genetic factors is referred to as the heritability of the phenotype (Boomsma et al., 2002). Evidence from adolescent and adult twin studies suggest that suicidality is moderately heritable, with heritability estimates ranging from approximately 0.36 to 0.59 for suicidal ideation and from 0.17 to 0.55 for suicide attempt (Fu et al., 2002; Glowinski et al., 2001; Maciejewski et al., 2014). In a twin study that examined self-harm and suicidal thoughts together, heritability

estimates of this combined phenotype were higher for women (0.74) than for men (0.45) (Althoff et al., 2012). However, the heritability of suicidality in preadolescent youth has been understudied to date.

Genetic influences on suicidality have also been demonstrated across a small number of genome-wide association studies (GWAS) that directly examine genomic data, which that have focused primarily on suicide attempt (Erlangsen et al., 2020; Kimbrel et al., 2018; Levey et al., 2019; Sokolowski et al., 2018; Stein et al., 2017). However, reproducibility has been a challenge in this work, and GWAS efforts have not resulted in consensus regarding the top genes implicated in suicidal phenotypes (Niculescu & Le-Niculescu, 2020; Sokolowski et al., 2014). Prior work, including within ABCD itself, has connected polygenic risk scores for various forms of psychopathology, including depression, ADHD, schizophrenia, and PTSD, to suicidality phenotypes in youth (Daskalakis et al., 2021; Joo et al., 2022; Martinez-Levy et al., 2021). Additional work is needed to directly examine genetic risk for suicidality in youth.

It is plausible that genetic contributions to suicidality may differ in children versus adults. Genetic influences on depression are thought to change across the lifespan, with findings suggesting both that early-onset depression may be more strongly genetically mediated than adult-onset depression and that the heritability of depression may increase across childhood, adolescence, and young adulthood (Bergen et al., 2007; Nguyen et al., 2022; Rice et al., 2002a, 2002b). Depression with suicidal thoughts has also been found to be slightly more heritable than depression without suicidal thoughts

(Nguyen et al., 2022). Given phenotypic links between depression and suicidality, it follows that the heritability of suicidality may differ across age groups.

The genetic underpinnings of aspects of cognition may also be related to suicidality. In a sample of autistic youth aged 8 to 15, higher polygenic scores for cognitive performance were associated with increased suicidal thoughts (Casten et al., 2023). However, the directionality of associations between cognition-relevant genetic factors and suicidality is variable across studies and cohorts; in a sample of probands with alcohol dependence and their families, *lower* polygenic scores for cognitive performance were associated with increased risk for suicide attempt (Johnson et al., 2021). Recent work has also found evidence for overlapping genetic effects between suicidal ideation and emotion identification in adolescents, suggesting that the use of genetically-informed models may help to identify shared genetic underpinnings of cognitive processes and suicidality in youth (Brick et al., 2019). Further research is needed to characterize whether and how cognitive processes may play a mechanistic role in genetic liability for suicidality risk in children and during adolescent development. To date, no known studies have directly examined potential genetic contributions to the covariance of cognition and suicidality.

The following analyses leveraged the ABCD Study's embedded twin cohort, the ABCD Twin Hub, in order to estimate genetic, shared environmental, and non-shared environmental contributions to lifetime suicidality, and to the covariance of suicidality and cognition, in preadolescent youth. Understanding genetic underpinnings of suicidality in youth could inform future prevention and early intervention efforts in that

youth at high genetic risk for suicidality could potentially be identified and supported before they begin to experience suicidal thoughts and/or behaviors.

Methods

Data from ABCD's embedded twin cohort were analyzed using genetically informative twin modeling approaches to assess genetic, shared environmental, and individual-specific environmental sources of variation affecting suicidality, as well as genetic and environmental contributions to the covariance of cognition and suicidality (Iacono et al., 2018). ABCD's embedded twin cohort is comprised of approximately 200 twin pairs recruited at baseline through each of four ABCD research sites known for their expertise in twin modeling (the University of Colorado Boulder, the University of Minnesota, Virginia Commonwealth University, and Washington University in St. Louis) using registries of twin births in each state from 2006-2008 (Iacono et al., 2018). The resulting twin dataset, known as the ABCD Twin Hub, was included in ABCD's research design in order to strengthen the quality of causal inference in ABCD analyses (Iacono et al., 2018). Only monozygotic and like-sex dizygotic twin pairs were recruited through the ABCD Twin Hub, given that estimates of the magnitude of genetic effects can be inflated with the inclusion of unlike-sex dizygotic twin pairs (Iacono et al., 2018).

For the purposes of these analyses, twins that had genetically determined zygosity data available and who were intentionally recruited as twin pairs were selected (Iacono et al., 2018; Maes et al., 2023). A small number of twins and triplets were incidentally recruited through the broader ABCD recruitment channels, but were not included in twin analyses here. Twin data have previously been compared to singleton data at the

Washington University study site, and findings suggested that the sociodemographic characteristics of mothers of twins and mothers of singletons at birth were comparable (Iacono et al., 2018). Correction for non-independence of twin pairs and other siblings through multilevel modeling approaches enabled the inclusion of this twin subsample, along with incidentally recruited siblings, twins, and triplets, in analyses using the overall dataset described in Chapters 2 and 3.

A total of 672 monozygotic twins (336 pairs) and 870 like-sex dizygotic twins (435 pairs) were included in these analyses, for a total of 771 twin pairs (*n*=1542 individuals). 50.6% of twins were male. The twin sample was somewhat less racially/ethnically diverse than the overall ABCD sample; 66.2% of twins were white, 14.3% were Black, 9.9% were Hispanic, 0.2% were Asian, and 9.4% described their race and/or ethnicity as "other." To promote interpretability as these analyses were not longitudinal, lifetime suicidality outcomes (i.e., suicidal ideation and/or behavior reported at any time throughout the study period) were examined. Lifetime rates of suicidality were comparable to those in the broader ABCD sample: 20.5% of twins experienced overall lifetime suicidality; 18.7% experienced lifetime suicidal ideation; and 3.2% experienced lifetime suicidal behavior. See Table 21 for full sociodemographic characteristics of the twin sample.

As a preliminary step, tetrachoric correlations of suicidal phenotypes between MZ and DZ twins were examined to determine whether ACE or ADE models would be fit to the data. Dominance genetic effects (D) are modeled when between-twin phenotypic correlations among MZ twins are more than double the size of DZ twin correlations,

whereas shared environmental effects (C) are modeled when MZ twin correlations are less than double the size of DZ twin correlations. Table 22 contains tetrachoric correlations across MZ and DZ twin pairs for lifetime suicidality phenotypes. Since all MZ twin correlations were less than twice the value of DZ twin correlations, ACE models, rather than ADE models, were run.

Biometric twin modeling was conducted using the *OpenMx* and *umx* packages in R (T. C. Bates et al., 2019; Boker et al., 2023; Neale et al., 2016; R Core Team, 2023). Univariate ACE models were run to decompose the additive genetic (A), shared environmental (C), and unique environmental contributions (E) to variance in youth suicidality phenotypes. As MZ twins are assumed to share 100% of their genes, the correlation of their additive genetic factors was set as 1.0; as DZ twins are assumed to share 50% of their genes, the correlation of their additive genetic factors was set as 0.5 (Iacono et al., 2018). Model reduction was then performed to run sub-models (i.e., AE, CE, and E models). The Akaike information criterion (AIC) of each model was examined in order to determine the best-fitting and most parsimonious model, and the model with the lowest AIC weight, or conditional probability, was selected (Wagenmakers & Farrell, 2004). Model output was squared in order to interpret variance component estimates.

In order to determine whether to proceed with bivariate models comparing cognition and suicidality, point-biserial correlations between lifetime suicidality phenotypes and three summary cognitive outcomes from the NIH Toolbox Cognitive Battery—uncorrected standard scores for the Fluid Intelligence composite, Crystallized Intelligence composite, and total composite scores—were examined. The point-biserial

correlation is equivalent to Pearson's product-moment correlation when one variable is dichotomous and the other is continuous (Kornbrot, 2014). After correcting for multiple comparisons across MZ and DZ twins, suicidality phenotypes, and cognitive phenotypes (F. Curtin & Schulz, 1998), only one correlation coefficient – between suicidal behavior and crystallized intelligence among MZ twins – remained significantly different from zero, and the coefficient indicated a very weak negative correlation (Table 24). Therefore, bivariate ACE models were not run to assess genetic influences on the covariance between cognition and suicidality; however, future directions are discussed below.

Results

Table 22 summarizes the prevalence and concordance of lifetime suicidality phenotypes between and across MZ and DZ twin pairs with complete suicidality data. Rates of each suicidality phenotype (suicidal ideation, suicidal behavior, and a composite phenotype including both) were similar across MZ and DZ twins. Concordance rates of suicidality phenotypes were higher among MZ twins (76 – 95%) than among DZ twins (73 – 93%). Among MZ twins with complete suicidality data, 21% experienced suicidal ideation, 3% experienced suicidal behavior, and 22% experienced any form of suicidality. Among DZ twins with complete suicidality data, 23% experienced suicidal ideation, 4% experienced suicidal behavior, and 22% experienced any form of suicidality. Tetrachoric correlations for lifetime suicidality phenotypes among MZ twins ranged from 0.51-0.63; tetrachoric correlations among DZ twins ranged from 0.39-0.50.

Table 23 summarizes univariate ACE and nested model results for lifetime suicidality phenotypes. For the total STB phenotype, a CE model was found to best fit the

data, with shared environmental effects explaining 45% of variance and non-shared environmental effects explaining 55% of variance. For the suicidal ideation phenotype, a CE model was also found to best fit the data, with shared environmental effects explaining 44% of variance and non-shared environmental effects explaining 56% of variance. For the suicidal behavior phenotype, an AE model was found to best fit the data, with additive genetic effects explaining 55% of variance and non-shared environmental effects explaining 44% of variance. These best-fitting models were not significantly different from full ACE models, in which A and C were not significant.

Discussion

Overall results of ACE models for suicidality phenotypes indicate a familial influence on preadolescent suicidal ideation and behavior. Although A and C were not significant in full ACE models, they were significant in reduced AE and CE models across all three phenotypes (suicidal ideation, suicidal behavior, and a combined ideation/behavior phenotype). This indicates that familiality, whether due to shared genetics or shared environment, plays a significant role in the variance of childhood suicidality.

The heritability of suicidal behavior derived from the best-fitting model in the ABCD Twin Hub cohort was estimated at 55%, a finding that is generally consistent with previous adolescent and young adult twin studies (Glowinski et al., 2001; Lim et al., 2022). However, when nested models were examined and compared, results of best-fitting models suggested that shared and non-shared environmental factors contribute to variance in suicidal ideation, but that additive genetic effects do not. This suggests that

the heritability of suicidal behavior may be measurable by age 12, but that suicidal ideation may be primarily influenced by environmental factors until later in adolescence or young adulthood. This is somewhat consistent with a previous study of adolescent and young adult twins that found that environmental factors predominantly explained ideation in adolescence, whereas both genetic and shared environmental factors explained ideation in young adulthood (Linker et al., 2012). Prior twin studies have suggested that in adulthood, the heritability of suicidal ideation is moderate (36-55%; Fu et al., 2002; Maciejewski et al., 2014). Future work should continue to assess whether the heritability of suicidal behavior and/or ideation changes over time for youth throughout preadolescence to adolescence and into young adulthood; this could be done by continuing to examine the heritability of suicidality in the ABCD Twin Hub cohort, as data collection is scheduled to continue until participants are 19-20 years old. Future work may also utilize molecular genetic data to more closely examine potential genetic contributions to suicidal ideation in youth; a recent study estimated single-nucleotide polymorphism (SNP)-based heritability of suicidal ideation in youth as marginally significant at 11% (Brick et al., 2019). SNP and GWAS data could be leveraged to inform future research on the genetics of preadolescent suicidality.

Importantly, genetic influences on suicidal behavior and ideation should continue to be examined separately, as it is reasonable that genetics and environment may play differential roles in suicidal actions, such as preparatory behaviors or attempts, than in suicidal thinking. For example, environmental stressors may trigger suicidal ideation without directly leading to suicidal behavior. Suicidal ideation is more common than

suicidal behavior, and also more difficult to accurately observe and measure; seeking greater accuracy and precision in the definition and measurement of suicidal ideation will also improve the accuracy of research that treats suicidal ideation as an outcome. Combining suicidal ideation and behavior into a single phenotype could result in inaccurate estimation of genetic contributions to distinct cognitive vs. behavioral processes.

These results suggest that suicidal ideation in young children is substantially shaped by shared environmental effects. Shared environmental effects at this age likely consist substantially of family factors, although influences from school, neighborhood, and peer group may also be shared among twins. This is consistent with findings from Chapters 2 and 3, as well as previous work, that family conflict is significantly associated with preadolescent suicidality (Assari et al., 2021; Janiri et al., 2020). Family-level factors, such as greater parental supervision (which was measured at the individual level but is likely similar across siblings within the same family) and lower number of household cohabitants, have also been found to protect against preadolescent suicidality (Janiri et al., 2020).

A clearer understanding of how genetic and environmental factors, including the family environment and broader social environment, impact suicidality could provide more robust data to support clinical theories such as the biosocial developmental model of borderline personality disorder (Crowell et al., 2009). Developed by Marsha Linehan, the creator of DBT, the biosocial model posits that both biological and environmental factors contribute in a transactional manner to vulnerability for chronic emotion

dysregulation and a borderline personality disorder diagnosis, two phenotypes to which suicidality is central. Recent work on the epigenetics of suicidality has highlighted that early life experiences, such as childhood trauma, may play an important role in epigenetic changes related to suicidality (Cheung et al., 2020; Musci et al., 2019). Clarifying the role that genes may have in the earliest expression of suicidality phenotypes –here measured before youth have reached adolescence—could both lend empirical support to developmental psychopathology models and underscore opportunities for prevention. Although research to reliably identify polygenic influences on suicidality remains ongoing, future findings could lead to risk identification methods that focus prevention or early intervention efforts on youth with high genetic risk.

Although findings were mixed regarding the role that cognition may play in suicidality, future work is warranted to continue to explore associations between genes, cognition, and suicidality. Future directions may include clarifying the directionality of cognition-suicidality associations across specific clinical populations, as cognition may serve to either increase or decrease suicidality risk depending on the population. A nuanced understanding of how cognitive factors may intersect with suicidality risk across different psychiatric or neurodevelopmental disorders, especially in youth at elevated genetic risk, could inform future personalized treatment approaches, especially in evidence-based modalities that heavily employ cognitive skills and strategies such as variants of cognitive-behavioral therapy.

Limitations of this study include the nature of the ABCD Twin Hub as a community twin sample that was not oversampled for suicidality or other clinical

presentations; therefore, analyses could be underpowered to detect effects. Specifically, these analyses were likely not adequately powered to parse whether additive genetic effects or shared environmental effects are more important to preadolescent suicidality. This could be addressed in future twin studies with larger preadolescent samples or in future ABCD research by leveraging longitudinal bivariate or multivariate designs to clarify the relative influences of genetic and environmental familial influences on suicidality. Other limitations include the likelihood of measurement error in suicidality phenotypes due to retrospective reporting on suicidality as well as low rates of agreement between parent and youth reports on suicidality. These limitations will be discussed further in Chapter 5.

CHAPTER FIVE

General Discussion

The goal of this dissertation was to improve our understanding of preadolescent suicidality in a nationally representative sample of community youth. Suicidality, a term here used to indicate suicidal thoughts and/or behaviors, is a serious outcome in its own right; it indicates significant distress and suffering, and can be traumatic for youth to experience and for their loved ones or peers to witness. It also indexes significant risk for death by suicide, a preventable outcome that is a leading cause of death for youth. The goals of this work were to examine non-psychological risk factors for suicidality—chronic health, cognition, and genetics—that have been implicated in older adolescents and adults to determine whether they are associated with suicidality in preadolescent youth.

Overall, although chronic health and cognition appeared to be related to suicidality in preliminary analyses, after controlling for a range of covariates relevant to suicidality, chronic health and cognition do not emerge as significant predictors of preadolescent suicidality. Instead, previously identified factors including age, race, broadband psychopathology, and family conflict were robustly and reliably associated with suicidality phenotypes. This highlights the importance of controlling for potential confounding variables, especially when studying a complex and multifactorial outcome. Results also suggest the value of future work to disentangle the potentially heterogeneous effects of various domains of chronic health and cognition on preadolescent suicidality. Results from Chapter 4 suggest that suicidal ideation and behavior in this age range are

moderately but differentially heritable, highlighting the value of examining these phenotypes separately as well as the important role of biological factors in a comprehensive understanding of youth suicidality risk.

This dissertation focused on preadolescent youth to gain a clearer understanding of suicide etiology. The majority of suicidology literature studies adults or adolescents, who may have a longstanding history of suicidal thoughts and/or behaviors by the time suicidality is first brought to clinical attention. Developmental psychopathology offers a framework from which to understand etiology prospectively by charting courses of "normal" and "abnormal" development (Cicchetti & Rogosch, 2002). Following youth over a significant period of development, as is the goal of the ABCD Study, enables researchers to identify the emergence of clinically significant deviations from expected developmental trajectories; in other words, to track when, how, and why development may veer off-course. Thus, one goal of this work was to examine whether following youth prospectively starting at age 9-10 years could provide insight into the development of suicidality.

It is important to note that ABCD's longitudinal design will result in another 8 years of data collection beyond what was analyzed in this dissertation. This wealth of data will enable future researchers to continue to explore trajectories of suicidality. However, the relatively high rate of past suicidality (~12.8% combined parent-youth report) endorsed at baseline suggests that future studies on the emergence of suicidality should begin at a younger age. This base rate suggests that suicidality begins for a significant portion of youth before age 10, and that prospective longitudinal research is

needed to follow younger children over time to better understand risk and protective factors for the development of suicidality in childhood. As is shown in retrospective studies of adolescents, which previously suggested that rates of STBs were less than 1% prior to age 12 (Nock et al., 2013), retrospective self-report likely significantly overestimates suicidality age at onset and underestimates the true prevalence of suicidality among preadolescent children.

One major limitation of this work is the inherent difficulty in assessing suicidality, particularly in preadolescent youth. Suicidal thoughts and behaviors are complex constructs that prove difficult for even seasoned clinicians to accurately assess (Airey & Iqbal, 2022), and may also be difficult for youth and parents to consistently report. Suicide is a concept that has historically carried stigma; although younger generations display lower levels of stigma towards some aspects of mental health (Pescosolido et al., 2021), many youth continue to not disclose the extent of their psychological distress. Given the size and scope of the ABCD Study, which was designed as a broadband longitudinal project to assess development holistically across adolescence and not as a specialized suicidology study, the methods of suicidality assessment are relatively blunt and imprecise. The K-SADS-PL DSM-5 has considerable strengths as a tool to assess psychopathology in youth, including a semistructured format and adherence to DSM-5 diagnostic criteria; however, the suicidality items are relatively brief and may not adequately capture the full extent of possible suicidal experiences, such as the presence of mental imagery rather than verbal ideation (Lawrence et al., 2021, 2022). The K-SADS-PL DSM-5 also relies on recall of lifetime past suicidal events, which research suggests

may lead to underreporting when compared to methods such as EMA that assess suicidality in real time (Czyz et al., 2018). Rates of reported past suicidality drop slightly over the course of follow-up in the ABCD sample (see Table 20), suggesting that underreporting of suicidality may have increased from baseline to follow-up waves. It is possible that youth or parents experienced the reporting of suicidality at baseline to be an aversive experience, thus suppressing future endorsement of suicidality.

Another, related limitation concerns low parent-child agreement on suicidality items in the ABCD Study. Although low base rates of agreement are a hallmark of multi-informant approaches to measuring youth suicidality (Jones et al., 2019; Klaus et al., 2009; R. Thompson et al., 2006), how best to interpret discrepancies in suicidality reporting remains unclear. The combined use of both parent and youth ratings in this dissertation may have led to an overestimation of the true prevalence of suicidality in the sample by including false positives. However, given that neither parent or youth report of suicidality can be easily discarded, especially in an age range wherein suicidality is understudied, and the likelihood that requiring parent-child agreement on suicidality would result in significant underestimation, this was deemed to be a reasonable option among imperfect choices. As seen in Table 20, Cohen's kappa statistics across suicidality phenotypes at baseline and year 2 follow-up—the timepoints when both parent and youth data were collected—indicated generally low agreement rates and substantial variability across parent and child reports (McHugh, 2012). Kappa statistics for lifetime suicidality ratings were slightly higher than kappa ratings assessing present and past suicidality at a particular study point, suggesting that parents and youth may agree to a slightly greater

extent on the global presence or absence of suicidality in the youth than on precisely when suicidal thoughts and/or behavior occurred. However, the highest interrater reliability score was just 0.32 (for lifetime suicidality), indicating only fair agreement (McHugh, 2012). Furthermore, although follow-up and lifetime suicidality were broadly self-reported at slightly higher rates than parent reports indicated, there were also cases in which parents reported higher rates of a particular suicidal phenotype than were self-reported by youth; for example, at the two-year follow-up visit, 7.3% of parents but only 6.3% of youth reported a history of active suicidal ideation. Future research is needed to clarify how best to measure and assess suicidality in preadolescent youth; statistical methods to optimize across multiple informant ratings may prove fruitful in future research as well as to inform clinical decision-making when multiple informants provide data (Makol et al., 2020).

Although ABCD's design as a community, rather than clinical, sample promotes generalizability to the American adolescent population across an impressive range of outcomes, there are also limitations to using this dataset to examine clinical presentations that are relatively rare in young children, such as chronic health problems and suicidality. Low base rates of the former may particularly explain the lack of significant findings in Chapters 2, as analyses may have been underpowered to detect effects. Future work in clinical settings—i.e., with clinically-referred youth with psychopathology or in hospital settings where youth may present with chronic illness—could continue to explore these questions in more targeted samples.

Understanding how and when suicidality starts in youth is critical to understanding how to end it (Oppenheimer et al., 2022). Baseline rates of suicidality at 9-to-10 years old in ABCD indicate that a considerable proportion of youth at this age have already experienced suicidality. Comparisons across youth with no suicidality throughout the study period to date, those with lifetime suicidality throughout the study period to date, and those with incident suicidality identified after baseline suggest that even starting to study suicidality phenotypes at age 9-10 is too late to capture true etiological phenomena for many youth. This is also reflected by the more striking and meaningful differences between the comparison groups of "never" and "ever" suicidality compared to never and incident suicidality across cognition and chronic health factors. Youth suicidology may benefit from adopting principles of treatment programs for psychosis, which aim to reduce the duration of untreated psychosis in youth and even intervene early to prevent those at clinical high risk from experiencing a psychotic episode (Albert & Weibell, 2019). Continued efforts to disentangle biological (e.g., genetic) and environmental (e.g., social and familial) risk factors that place youth at clinical high risk for suicidality will enable clinicians and caregivers to intervene early and reduce rates of untreated youth suicidality. Future work to elucidate the pathways leading to early suicidality in young people can also inform clinical targets for intervention or broadband prevention efforts.

Table 1. *Sociodemographic Characteristics of Sample*

	Total Sample (*n*=11,876)	No STBs (*n*=7341)	Ever STBs^ (*n*=2707)	Follow-Up STBs^^ (*n*=1034)
Age at baseline, mean (SD)	9.92 (0.62)	9.91 (0.63)	9.92 (0.63)	9.96 (0.62)
Sex at birth (female), *n* (%)	5680 (46.8%)	3555 (48.4%)	1195 (44.1%)***	527 (51.0%)
White race, *n* (%)	6180 (52.0%)	4068 (55.4%)	1398 (51.6%)***	534 (51.6%)*
Black race, *n* (%)	1784 (15.0%)	949 (12.9%)	392 (14.5%)*	165 (16.0%)**
Asian race, *n* (%)	252 (2.1%)	151 (2.2%)	52 (1.9%)	11 (1.1%)*
Other race/ethnicity, *n* (%)	1049 (10.4%)	715 (9.7%)	334 (12.3%)***	117 (11.3%)
Hispanic ethnicity, *n* (%)	2411 (20.3%)	1450 (19.8%)	531 (19.6%)	207 (20.0%)
Household income < $50K, *n* (%)	3223 (27.1%)	1777 (24.2%)	785 (29.0%)***	297 (28.7%)**
Household income $50K-$100K, *n* (%)	3071 (25.9%}	1971 (26.8%)	741 (27.4%)	279 (27.0%)
Household income >$100K, *n* (%)	4564 (38.4%)	3033 (40.3%)	955 (35.3%)***	373 (36.1%)**
Parent married, *n* (%)	7990 (67.3%)	5213 (71.0%)	1732 (64.0%)***	690 (66.7%)**
Parent divorced, *n* (%)	1081 (9.1%)	629 (8.6%)	284 (10.5%)**	90 (8.7%)
Parent separated, *n* (%)	464 (3.9%)	264 (3.6%)	100 (3.7%)	39 (3.8%)
Parent never married, *n* (%)	1460 (12.3%)	763 (10.4%)	363 (13.4%)***	132 (12.8%)*
Parent living with partner, *n* (%)	688 (5.8%)	371 (5.1%)	182 (6.7%)**	63 (6.1%)
Parent widowed, *n* (%)	79 (0.8%)	51 (0.7%)	28 (1.0%)	13 (1.3%)
Parent < high school diploma, *n* (%)	578 (4.9%)	307 (4.2%)	111 (4.1%)	43 (4.2%)
Parent high school diploma/GED, *n* (%)	1110 (9.3%)	604 (8.3%)	237 (8.8%)	91 (8.9%)
Parent completed some college, *n* (%)	3058 (25.7%)	1745 (23.9%)	771 (28.7)***	283 (27.6%)*
Parent earned bachelor's degree, *n* (%)	3010 (25.3%)	1944 (26.6%)	689 (25.7%)	272 (26.5%)
Parent earned post-graduate degree, *n* (%)	4041 (34.0%)	2695 (36.9%)	878 (32.7%)***	337 (32.8%)*
Family history of suicide/attempt, *n* (%)	1826 (15.4%)	1036 (14.1%)	542 (20.0%)***	181 (17.5%)**
CBCL Total Problems *T*-score, mean (SD)	45.85 (11.34)	43.97 (10.39)	51.45 (11.71)***	48.50 (11.07)***
Substance exposure (> puff/sip), *n* (%)	92 (0.8%)	38 (0.5%)	38 (1.4%)***	6 (0.6%)
FES Family Conflict score, mean (SD)	2.05 (1.95)	1.85 (1.86)	2.60 (2.14)***	2.38 (2.06)***
Exposure to 1+ Criterion A trauma, *n* (%)	4153 (35.0%)	2410 (33.4%)	1160 (43.4%)***	415 (40.6%)***

^=STBs reported by youth and/or parent at any point over the study period (baseline, follow-up year 1, or follow-up year 2).

^^=STBs first reported by youth and/or parent after baseline (follow-up year 1 or follow-up year 2).

*Significantly different from reference group (no STBs) at $p<.05$ (Fisher's exact test, 2 sided).

**Significantly different from reference group at $p<.01$ (Fisher's exact test, 2 sided).

***Significantly different from reference group at $p<.001$ (Fisher's exact test, 2 sided or one-way ANOVA).

STBs=suicidal ideation and/or behavior, SD=standard deviation.

Table 2. *Suicidality Phenotypes*

Phenotype	**Definition**	**ABCD NDA Variables**	**Description***
Passive Suicidal Ideation	Thoughts about death without specific thoughts about killing oneself	*Current*: ksads_23_946 *Past:* ksads_23_957	Child wished they were dead or felt they would be better off dead.
Active Suicidal Ideation	Thoughts about killing oneself (may include intent or planning)	*Current:* ksads_23_947, ksads_23_948, ksads_23_949, ksads_23_950 *Past:* ksads_23_958, ksads_23_959, ksads_23_960, ksads_23_961	Child thought about killing themselves; thoughts may have included suicidal intent and/or details about method and planning.
Any Suicidal Ideation	Passive and/or active suicidal ideation	See above	Child experienced passive and/or active suicidal ideation.
Suicidal Behavior	Preparatory actions taken towards imminent suicidal behavior or a suicide attempt	*Current*: ksads_23_951, ksads_23_952, ksads_23_953, ksads_23_954 *Past*: ksads_23_962, ksads_23_963, ksads_23_964, ksads_23_965	Child took preparatory actions towards imminent suicidal behavior, or engaged in a suicide attempt (which may have been interrupted or aborted).
Any Suicidal Thoughts or Behaviors (STBs)	Passive suicidal ideation, active suicidal ideation, and/or suicidal behavior	See above	Child experienced suicidal ideation and/or behavior.

(Kaufman et al., 2016; *NIMH Data Archive - Data Dictionary*, n.d.)

Table 3. *Sociodemographic Characteristics Compared Across Suicidal Ideation Groups*

	No Suicidal Ideation (*n*=7349)	Ever Suicidal Ideation^ (*n*=2435)	Follow-Up Suicidal Ideation^^ (*n*=1217)
Age at baseline, mean (SD)	9.91 (0.63)	9.93 (0.66)	9.95 (0.62)*
Sex at birth (female), *n* (%)	3557 (48.4%)	1094 (44.9%)	616 (50.6%)
White race, *n* (%)	4070 (55.4%)	1275 (52.4%)*	641 (52.7%)
Black race, *n* (%)	953 (13.0%)	334 (13.7%)	174 (14.2%)
Asian race, *n* (%)	159 (2.2%)	47 (1.9%)	15 (1.2%)*
Other race/ethnicity, *n* (%)	715 (9.7%)	307 (12.6%)***	147 (12.1%)*
Hispanic ethnicity, *n* (%)	1452 (19.8%)	472 (19.4%)	241 (19.8%)
Household income < $50K *n* (%)	1782 (24.2%)	688 (28.3%)***	348 (28.6%)**
Household income $50K-$100K, *n* (%)	1971 (26.8%)	677 (27.8%)	336 (27.6%)
Household income >$100K, *n* (%)	3035 (41.3%)	873 (35.9%)***	434 (35.7%)***
Parent married, *n* (%)	5216 (71.0%)	1578 (64.8%)***	797 (65.5%)***
Parent divorced, *n* (%)	630 (8.6%)	257 (10.6%)**	124 (10.2%)
Parent separated, *n* (%)	264 (3.6%)	87 (3.6%)	43 (3.5%)
Parent never married, *n* (%)	766 (10.4%)	314 (12.9%)***	153 (12.56%)*
Parent living with partner, *n* (%)	373 (5.1%)	161 (6.6%)**	78 (6.4%)
Parent widowed, *n* (%)	51 (0.7%)	25 (1.0%)	13 (1.1%)
Parent < high school diploma, *n* (%)	308 (4.2%)	91 (3.8%)	49 (4.1%)
Parent high school diploma/GED, *n* (%)	606 (8.3%)	202 (8.4%)	98 (8.1%)
Parent completed some college, *n* (%)	1747 (23.9%)	682 (28.2%)***	347 (28.7%)***
Parent earned bachelor's degree, *n* (%)	1944 (26.6%)	634 (26.3%)	314 (26.0%)
Parent earned post-graduate degree, *n* (%)	2698 (36.9%)	806 (33.4%)**	400 (33.1%)*
Family history of suicide/attempt, *n* (%)	1037 (14.1%)	497 (20.4%)***	225 (18.5%)***
CBCL Total Problems *T*-score, mean (SD)	43.97 (10.40)	51.50 (11.74)***	49.72 (11.46)***
Substance exposure (> puff/sip), *n* (%)	38 (0.5%)	32 (1.3%)***	9 (0.7%)
FES Family Conflict score, mean (SD)	1.84 (1.86)	2.58 (2.13)***	2.46 (2.10)***
Exposure to 1+ Criterion A trauma, *n* (%)	2413 (33.4%)	1049 (43.7%)***	508 (42.3%)***

^=Suicidal ideation reported by youth and/or parent at any point over the study period (baseline, follow-up year 1, or follow-up year 2).

^^=Suicidal ideation first reported by youth and/or parent after baseline (follow-up year 1 or follow-up year 2).

*Significantly different from reference group (no suicidal ideation) at $p<.05$ (Fisher's exact test, 2 sided).

**Significantly different from reference group at $p<.01$ (Fisher's exact test, 2 sided).

***Significantly different from reference group at $p<.001$ (Fisher's exact test, 2 sided or one-way ANOVA).

SD=standard deviation.

Table 4. *Sociodemographic Characteristics Compared Across Suicidal Behavior Groups*

	No Suicidal Behavior (*n*=9217)	Ever Suicidal Behavior^ (*n*=460)	Follow-Up Suicidal Behavior^^ (*n*=191)
Age at baseline, mean (SD)	9.91 (0.62)	9.98 (0.63)*	10.00 (0.66)*
Sex at birth (female), *n* (%)	4390 (47.6%)	213 (46.3%)	104 (54.5%)
White race, *n* (%)	5091 (55.2%)	196 (42.6%)***	96 (50.3%)
Black race, *n* (%)	1195 (13.0%)	80 (17.4%)**	26 (13.6%)
Asian race, *n* (%)	198 (2.1%)	5 (1.1%)	1 (0.5%)
Other race/ethnicity, *n* (%)	951 (10.3%)	56 (12.2%)	27 (14.1%)
Hispanic ethnicity, *n* (%)	1782 (19.3%)	123 (26.7%)***	41 (21.5%)
Household income < $50K, *n* (%)	2253 (24.4%)	186 (40.4%)***	59 (30.9%)
Household income $50K-$100K, *n* (%)	2499 (27.1%)	119 (25.9%)	60 (31.4%)
Household income >$100K, *n* (%)	3765 (40.8%)	111 (24.1%)***	57 (29.8%)**
Parent married, *n* (%)	6488 (70.4%)	252 (54.8%)***	113 (59.2%)***
Parent divorced, *n* (%)	810 (8.8%)	55 (12.0%)*	22 (11.5%)
Parent separated, *n* (%)	326 (3.5%)	21 (4.6%)	5 (2.6%)
Parent never married, *n* (%)	992 (10.8%)	78 (17.0%)***	30 (15.7%)*
Parent living with partner, *n* (%)	478 (5.2%)	42 (9.1%)***	16 (8.4%)
Parent widowed, *n* (%)	70 (0.8%)	4 (0.9%)	2 (1.0%)
Parent < high school diploma, *n* (%)	369 (4.0%)	29 (6.4%)*	6 (3.2%)
Parent high school diploma/GED, *n* (%)	742 (8.1%)	54 (11.9%)**	18 (9.6%)
Parent completed some college, *n* (%)	2234 (24.4%)	157 (34.6%)***	63 (33.5%)**
Parent earned bachelor's degree, *n* (%)	2438 (26.6%)	110 (24.2%)	51 (27.1%)
Parent earned post-graduate degree, *n* (%)	3377 (36.9%)	104 (22.9%)***	50 (26.6%)**
Family history of suicide/attempt, *n* (%)	1398 (15.2%)	118 (25.7%)***	41 (21.5%)*
CBCL Total Problems *T*-score, mean (SD)	45.24 (10.88)	55.94 (12.07)***	55.13 (12.24)***
Substance exposure (> puff/sip), *n* (%)	57 (0.6%)	11 (2.4%)***	0 (0.0%)
FES Family Conflict score, mean (SD)	1.96 (1.92)	2.99 (2.28)***	2.68 (2.14)***
Exposure to 1+ Criterion A trauma, *n* (%)	3183 (35.1%)	222 (49.1%)***	98 (52.4%)***

^=Suicidal behavior reported by youth and/or parent at any point over the study period (baseline, follow-up year 1, or follow-up year 2).

^^=Suicidal behavior first reported by youth and/or parent after baseline (follow-up year 1 or follow-up year 2).

*Significantly different from reference group (no suicidal behavior) at $p<.05$ (Fisher's exact test, 2 sided).

**Significantly different from reference group at $p<.01$ (Fisher's exact test, 2 sided).

***Significantly different from reference group at $p<.001$ (Fisher's exact test, 2 sided or one-way ANOVA).

SD=standard deviation.

Table 5: *Rates of Chronic Health Conditions*

	Total Sample (*n*=11,876)	No STBs (*n*=7341)	Ever STBs^ (*n*=2707)	Follow-Up STBs^^ (*n*=1034)
Asthma, *n* (%)	2054 (17.3%)	1224 (16.7%)	533 (19.7%)***	193 (18.7%)
Allergies, *n* (%)	3818 (32.1%)	2286 (31.1%)	958 (35.4%)***	353 (34.1%)
Cancer/leukemia, *n* (%)	24 (0.2%)	14 (0.2%)	5 (0.2%)	0 (0.0%)
Cerebral palsy, *n* (%)	17 (0.1%)	12 (0.2%)	2 (0.1%)	0 (0.0%)
Diabetes, *n* (%)	47 (0.4%)	27 (0.4%)	13 (0.5%)	4 (0.4%)
Epilepsy or seizures, *n* (%)	223 (1.9%)	145 (2.0%)	53 (2.0%)	25 (2.4%)
Kidney disease, *n* (%)	60 (0.5%)	41 (0.6%)	10 (0.4%)	2 (0.2%)
Lead poisoning, *n* (%)	53 (0.4%)	27 (0.4%)	17 (0.6%)	6 (0.6%)
Muscular dystrophy, *n* (%)	16 (0.1%)	11 (0.1%)	2 (0.1%)	0 (0.0%)
Multiple sclerosis, *n* (%)	13 (0.1%)	9 (0.1%)	2 (0.1%)	0 (0.0%)
Heart problems, *n* (%)	384 (3.2%)	252 (3.4%)	88 (3.3%)	26 (2.5%)
Sickle cell anemia, *n* (%)	39 (0.3%)	19 (0.3%)	7 (0.3%)	4 (0.4%)
Very bad headaches, *n* (%)	559 (4.7%)	320 (4.4%)	150 (5.5%)*	47 (4.5%)
1+ chronic health problem, *n* (%)	5120 (43.1%)	3087 (42.1%)	1264 (46.7%)***	466 (45.1%)
No. of chronic health problems, mean (SD)	0.62 (0.90)	0.60 (0.90)	0.68 (0.90)***	0.64 (0.82)

^=STBs reported by youth and/or parent at any point over the study period (baseline, follow-up year 1, or follow-up year 2).

^^=STBs first reported by youth and/or parent after baseline (follow-up year 1 or follow-up year 2).

*Significantly different from reference group (no STBs) at $p<.05$ (Fisher's exact test, 2 sided).

***Significantly different from reference group at $p<.001$ (Fisher's exact test, 2 sided or one-way ANOVA).

STBs=suicidal ideation and/or behavior.

Table 6: *Rates of Suicidal Ideation Across Chronic Health Conditions*

	No Suicidal Ideation (*n*=7349)	Ever Suicidal Ideation^ (*n*=2345)	Follow-Up Suicidal Ideation^^ (*n*=1217)
Asthma, *n* (%)	1226 (16.7%)	489 (20.1%)***	236 (16.7%)*
Allergies, *n* (%)	2288 (31.1%)	864 (35.5%)***	428 (35.2%)**
Cancer/leukemia, *n* (%)	14 (0.2%)	5 (0.2%)	0 (0.0%)
Cerebral palsy, *n* (%)	12 (0.2%)	2 (0.1%)	0 (0.0%)
Diabetes, *n* (%)	27 (0.4%)	13 (0.5%)	6 (0.5%)
Epilepsy or seizures, *n* (%)	146 (2.0%)	49 (2.0%)	32 (2.6%)
Kidney disease, *n* (%)	41 (0.6%)	10 (0.4%)	4 (0.3%)
Lead poisoning, *n* (%)	27 (0.4%)	15 (0.6%)	8 (0.6%)
Muscular dystrophy, *n* (%)	11 (0.1%)	2 (0.1%)	0 (0.0%)
Multiple sclerosis, *n* (%)	9 (0.1%)	2 (0.1%)	0 (0.0%)
Heart problems, *n* (%)	253 (3.4%)	80 (3.3%)	32 (2.6%)
Sickle cell anemia, *n* (%)	19 (0.3%)	7 (0.3%)	5 (0.4%)
Very bad headaches, *n* (%)	320 (4.4%)	135 (5.5%)*	64 (5.3%)
1+ chronic health problem, *n* (%)	3091 (42.1%)	1146 (47.1%)***	574 (47.2%)***
No. of chronic health problems, mean (SD)	0.60 (0.90)	0.69 (0.91)***	0.67 (0.89)**

^=Suicidal ideation reported by youth and/or parent at any point over the study period (baseline, follow-up year 1, or follow-up year 2).

^^=Suicidal ideation first reported by youth and/or parent after baseline (follow-up year 1 or follow-up year 2).

*Significantly different from reference group (no suicidal ideation) at $p<.05$ (Fisher's exact test, 2 sided).

**Significantly different from reference group at $p<.01$ (Fisher's exact test, 2 sided or one-way ANOVA).

***Significantly different from reference group at $p<.001$ (Fisher's exact test, 2 sided or one-way ANOVA).

Table 7: *Rates of Suicidal Behavior Across Chronic Health Conditions*

	No Suicidal Behavior (*n*=9217)	Ever Suicidal Behavior^ (*n*=460)	Follow-Up Suicidal Behavior^^ (*n*=191)
Asthma, *n* (%)	1587 (17.2%)	95 (20.7%)	28 (14.7%)
Allergies, *n* (%)	2956 (32.1%)	166 (36.1%)	58 (30.4%)
Cancer/leukemia, *n* (%)	18 (0.2%)	1 (0.2%)	0 (0.0%)
Cerebral palsy, *n* (%)	14 (0.2%)	0 (0.0%)	0 (0.0%)
Diabetes, *n* (%)	37 (0.4%)	3 (0.7%)	2 (1.0%)
Epilepsy or seizures, *n* (%)	179 (1.9%)	13 (2.8%)	9 (4.7%)*
Kidney disease, *n* (%)	48 (0.5%)	3 (0.7%)	2 (1.0%)
Lead poisoning, *n* (%)	39 (0.4%)	2 (0.4%)	0 (0.0%)
Muscular dystrophy, *n* (%)	13 (0.1%)	0 (0.0%)	0 (0.0%)
Multiple sclerosis, *n* (%)	11 (0.1%)	0 (0.0%)	0 (0.0%)
Heart problems, *n* (%)	315 (3.4%)	18 (3.9%)	3 (1.6%)
Sickle cell anemia, *n* (%)	22 (0.2%)	2 (0.4%)	1 (0.5%)
Very bad headaches, *n* (%)	412 (4.5%)	39 (8.5%)***	19 (9.9%)**
1+ chronic health condition, *n* (%)	3958 (42.9%)	232 (50.4%)**	84 (44.0%)
No. of chronic health conditions, mean (SD)	0.61 (0.90)	0.74 (0.87)**	0.64 (0.84)

^=Suicidal behavior reported by youth and/or parent at any point over the study period (baseline, follow-up year 1, or follow-up year 2).

^^=Suicidal behavior first reported by youth and/or parent after baseline (follow-up year 1 or follow-up year 2).

*Significantly different from reference group (no suicidal behavior) at $p<.05$ (Fisher's exact test, 2 sided).

**Significantly different from reference group at $p<.01$ (Fisher's exact test, 2 sided or one-way ANOVA).

***Significantly different from reference group at $p<.001$ (Fisher's exact test, 2 sided).

Table 8: *Longitudinal Associations Between Chronic Health Conditions at Baseline and STBS Across Follow-Up Period* (OR [95% CI], *p*-value)

	Model 1: Any STBs	Model 2: Suicidal Ideation	Model 3: Suicidal Behavior
Asthma	1.03 [0.85, 1.24], *p*=0.76	1.07 [0.90, 1.27], *p*=0.46	0.66 [0.42, 1.04], *p*=0.08
Allergies	1.07 [0.92, 1.25], *p*=0.36	1.09 [0.95, 1.26], *p*=0.23	0.71 [0.50, 1.01], *p*=0.06
Diabetes	1.19 [0.40, 3.55], *p*=0.76	1.27 [0.47, 3.44], *p*=0.65	1.56 [0.20, 12.03], *p*=0.67
Seizures or epilepsy	1.04 [0.63, 1.69], *p*=0.89	1.13 [0.73, 1.76], *p*=0.59	1.14 [0.41, 3.19], *p*=0.80
Kidney disease	0.33 [0.08, 1.40], *p*=0.13	0.54 [0.19, 1.55], *p*=0.25	2.00 [0.45, 8.81], *p*=0.36
Lead poisoning	1.15 [0.37, 3.56], *p*=0.81	1.58 [0.60, 4.17], *p*=0.36	N/A[2]
Heart problems	0.68 [0.44, 1.05], *p*=0.08	0.68 [0.46, 1.01], *p*=0.06	0.40 [0.12, 1.27], *p*=0.12
Sickle cell anemia	0.97 [0.20, 4.57], *p*=0.96	0.88 [0.19, 4.21], *p*=0.88	N/A[2]
Very bad headaches	0.81 [0.57, 1.14], *p*=0.22	0.88 [0.64, 1.19], *p*=0.40	1.53 [0.89, 2.64], *p*=0.12
Any chronic health condition	1.03 [0.89, 1.18], *p*=0.74	1.09 [0.95, 1.25], *p*=0.22	0.73 [0.53, 1.01], *p*=0.06
No. of chronic health conditions	0.99 [0.91, 1.07], *p*=0.75	1.01 [0.94, 1.09], *p*=0.82	0.84 [0.68, 1.02], *p*=0.08

All models controlled for the following baseline covariates: age, sex at birth, race/ethnicity, household income, parental marital status, highest household educational attainment, family history of attempted or completed suicide, CBCL Total Problems Score, youth substance exposure, FES Conflict Score, and youth trauma exposure.

[2] Odds ratios not reported due to insufficient case counts.

STBs=suicidal ideation and/or behavior; OR=odds ratio.

* Remained significant after applying Bonferroni correction.

Bonferroni correction threshold (11 tests): $p<0.005$.

Table 9: *Associations Between History of Chronic Health Conditions and Lifetime STBs* (OR [95% CI], *p*-value)

	Model 1: STBs	Model 2: Suicidal Thoughts	Model 3: Suicidal Behaviors
Asthma	1.04 [0.91, 1.19], *p*=0.53	1.07 [0.93, 1.22], *p*=0.36	0.99 [0.76, 1.29], *p*=0.94
Allergies	1.04 [0.94, 1.17], *p*=0.44	1.04 [0.93, 1.17], *p*=0.45	0.90 [0.72, 1.13], *p*=0.39
Cancer or leukemia	1.02 [0.31, 3.37], *p*=0.98	1.13 [0.34, 3.73], *p*=0.84	N/A[2]
Cerebral palsy	0.65 [0.13, 3.11], *p*=0.59	0.72 [0.15, 3.46], *p*=0.68	N/A[2]
Diabetes	1.47 [0.69, 3.13], *p*=0.32	1.63 [0.77, 3.45], *p*=0.20	1.31 [0.30, 5.81], *p*=0.72
Seizures or epilepsy	0.86 [0.60, 1.24], *p*=0.43	0.87 [0.60, 1.27], *p*=0.47	0.89 [0.42, 1.88], *p*=0.75
Kidney disease	0.64 [0.30, 1.35], *p*=0.24	0.70 [0.33, 1.48], *p*=0.35	1.16 [0.33, 4.07], *p*=0.82
Lead poisoning	1.59 [0.74, 3.43], *p*=0.24	1.56 [0.70, 3.47] *p*=0.28	0.45 [0.06, 3.57], *p*=0.45
Muscular dystrophy	0.79 [0.16, 3.98], *p*=0.78	0.89 [0.18, 4.46], *p*=0.89	N/A[2]
Multiple sclerosis	0.95 [0.18, 4.88], *p*=0.95	1.06 [0.21, 5.44], *p*=0.95	N/A[2]
Heart problems	0.81 [0.61, 1.07], *p*=0.13	0.80 [0.60, 1.07], *p*=0.14	0.99 [0.58, 1.69], *p*=0.96
Sickle cell anemia	0.87 [0.26, 2.93], *p*=0.83	0.99 [0.30, 3.34], *p*=0.99	N/A[2]
Very bad headaches	0.86 [0.68, 1.09], *p*=0.22	0.86 [0.68, 1.10], *p*=0.23	1.13 [0.75, 1.70], *p*=0.55
Any chronic health condition	1.01 [0.91, 1.12], *p*=0.92	1.02 [0.91, 1.13], *p*=0.78	0.97 [0.78, 1.21], *p*=0.80
No. of chronic health conditions	1.00 [0.94, 1.06], *p*=0.95	1.00 [0.95, 1.06], *p*=0.90	0.97 [0.86, 1.09], *p*=0.59

[1] Models controlled for the following baseline covariates: age, sex at birth, race/ethnicity, household income, parental marital status, highest household educational attainment, family history of attempted or completed suicide, CBCL Total Problems Score, youth substance exposure, FES Conflict Score, and youth trauma exposure.

[2] Odds ratios not reported due to insufficient case counts.

STBs=suicidal ideation and/or behavior; OR=odds ratio; CI=confidence interval.

* Remained significant after applying Bonferroni correction.

Bonferroni correction threshold (15 tests): $p<0.003$.

Table 10. *Summary of All Covariate Coefficients for Models Examining Association Between Overall Chronic Health Burden (1+ Condition) and Incident STBs* (OR [95% CI], *p*-value)

	Model 1: Any STBs	Model 2: Suicidal Ideation	Model 3: Suicidal Behavior
Any chronic health condition	1.03 [0.89, 1.18], p=0.74	1.09 [0.95, 1.25], p=0.22	0.73 [0.53, 1.01], p=0.06
Age at baseline	1.19 [1.06, 1.33], p=0.003*	1.19 [1.07, 1.32], p=0.002*	1.34 [1.04, 1.73], p=0.03*
Sex at birth (female)	1.22 [1.06, 1.41], p=0.006	1.23 [1.08, 1.41], p=0.002*	1.80 [1.31, 2.48], p<0.001*
Black race	1.26 [0.98, 1.63], p=0.08	1.03 [0.80, 1.32], p=0.81	0.86 [0.48, 1.55], p=0.63
Hispanic ethnicity	1.12 [0.91, 1.38], p=0.30	1.06 [0.87, 1.30], p=0.54	0.98 [0.62, 1.56], p=0.93
Asian race	0.72 [0.37, 1.40], p=0.34	0.90 [0.51, 1.61], p=0.74	0.51 [0.07, 3.75], p=0.51
Other race/ethnicity	1.23 [0.97, 1.56], p=0.09	1.25 [1.00, 1.56], p=0.045	1.27 [0.75, 1.89], p=0.47
Household income $50-$100K	0.92 [0.73, 1.15], p=0.46	0.97 [0.79, 1.20], p=0.79	1.19 [0.75, 1.89], p=0.47
Household income >$100K	0.89 [0.69, 1.14], p=0.36	0.92 [0.73, 1.16], p=0.48	0.99 [0.58, 1.71], p=0.98
Parent high school diploma	1.09 [0.69, 1.71, p=0.71	1.02 [0.66, 1.58], p=0.92	1.36 [0.42, 4.43], p=0.61
Parent completed some college	1.09 [0.72, 1.64], p=0.70	1.13 [0.76, 1.67], p=0.56	1.76 [0.60, 5.16], p=0.30
Parent earned bachelor's degree	1.15 [0.74, 1.77], p=0.54	1.13 [0.74, 1.71], p=0.58	1.79 [0.58, 5.47], p=0.31
Parent earned post-graduate degree	1.16 [0.75, 1.81], p=0.50	1.18 [0.77, 1.80], p=0.44	1.48 [0.47, 4.62], p=0.50
Parent divorced	1.18 [0.57, 2.47], p=0.65	1.01 [0.48, 2.10], p=0.99	0.51 [0.07, 3.95], p=0.52
Parent separated	0.94 [0.72, 1.22], p=0.63	1.06 [0.84, 1.35], p=0.61	1.28 [0.76, 2.16], p=0.36
Parent never married	0.95 [0.64, 1.41], p=0.80	0.95 [0.65, 1.39], p=0.78	0.65 [0.23, 1.87], p=0.42
Parent living with partner	0.95 [0.72, 1.27], p=0.74	1.02 [0.78, 1.34], p=0.88	1.38 [0.78, 2.44], p=0.27
Parent widowed	1.11 [0.80, 1.54, p=0.54	1.19 [0.88, 1.61], p=0.26	1.38 [0.71, 2.66], p=0.34
CBCL Total Problems T-score	1.04 [1.03, 1.05], p<0.001*	1.05 [1.04, 1.06], p<0.001*	1.08 [1.06, 1.10], p<0.001*
Family history of suicide	1.11 [0.91, 1.34], p=0.30	1.08 [0.90, 1.29], p=0.40	1.02 [0.69, 1.51], p=0.92
Substance exposure	0.51 [0.17, 1.51], p=0.23	0.69 [0.29, 1.65], p=0.41	0.00 [0.00, ∞]. p=0.99
FES Family Conflict score	1.10 [1.06, 1.14], p<0.001*	1.11 [1.07, 1.14], p<0.001*	1.12 [1.04, 1.20], p=0.003*
Exposure to 1+ Criterion A Trauma	1.13 [0.97, 1.31], p=0.12	1.15 [1.00, 1.32], p=0.06	1.41 [1.01, 1.95], p=0.04

* Remained significant after applying Bonferroni correction.

Bonferroni correction threshold (11 tests): p<0.005.

Table 11. *Summary of All Covariate Coefficients for Models Examining Association Between Overall Chronic Health Burden (1+ Condition) and Lifetime STBs* (OR [95% CI], *p*-value)

	Model 1: Any STBs	Model 2: Suicidal Ideation	Model 3: Suicidal Behavior
Any chronic health condition	1.01 [0.91, 1.12], *p*=0.92	1.02 [0.91, 1.13], *p*=0.78	0.97 [0.78, 1.21], *p*=0.80
Age at baseline	1.09 [1.00, 1.18], *p*=0.04	1.10 [1.01, 1.20], *p*=0.03	1.30 [1.09, 1.54], *p*=0.003
Sex at birth (female)	0.99 [0.89, 1.09], *p*=0.78	1.02 [0.92, 1.14], *p*=0.71	1.26 [1.02, 1.56], *p*=0.04
Black race	1.22 [1.01, 1.48], *p*=0.04	1.12 [0.91, 1.36], *p*=0.28	1.39 [0.97, 2.00], *p*=0.08
Hispanic ethnicity	1.08 [0.92, 1.27], *p*=0.34	1.09 [0.93, 1.29], *p*=0.29	1.48 [1.10, 2.00], *p*=0.009
Asian race	1.49 [1.02, 2.18], *p*=0.04	1.50 [1.01, 2.22], *p*=0.04	1.08 [0.38, 3.07], *p*=0.88
Other race/ethnicity	1.30 [1.09, 1.54], *p*=0.003	1.32 [1.11, 1.57], *p*=0.002*	1.25 [0.88, 1.78], *p*=0.21
Household income $50-$100K	1.05 [0.89, 1.23], *p*=0.55	1.06 [0.90, 1.26], *p*=0.47	0.84 [0.62, 1.14], *p*=0.27
Household income >$100K	1.03 [0.86, 1.23], *p*=0.76	1.03 [0.85, 1.24], *p*=0.75	0.73 [0.51, 1.05], *p*=0.09
Parent high school diploma	1.14 [0.82, 1.60], *p*=0.44	1.15 [0.81, 1.64], *p*=0.43	0.93 [0.51, 1.67], *p*=0.80
Parent completed some college	1.11 [0.82, 1.51], *p*=0.50	1.15 [0.83, 1.69], *p*=0.39	1.01 [0.59, 1.73], *p*=0.96
Parent earned bachelor's degree	1.12 [0.81, 1.56], *p*=0.48	1.20 [0.85, 1.69], *p*=0.29	1.02 [0.57, 1.81], *p*=0.95
Parent earned post-graduate degree	1.18 [0.85, 1.65], *p*=0.31	1.27 [0.90, 1.79], *p*=0.18	0.88 [0.48, 1.59], *p*=0.67
Parent divorced	1.01 [0.57, 1.78], *p*=0.98	1.01 [0.56, 1.81], *p*=0.97	0.48 [0.14, 1.69], *p*=0.25
Parent separated	1.11 [0.92, 1.34], *p*=0.27	1.10 [0.91, 1.33], *p*=0.34	1.21 [0.85, 1.73], *p*=0.29
Parent never married	0.97 [0.73, 1.30], *p*=0.85	0.98 [0.72, 1.32], *p*=0.88	1.00 [0.58, 1.73], *p*=0.99
Parent living with partner	1.09 [0.89, 1.34], *p*=0.40	1.09 [0.88, 1.34], *p*=0.44	0.92 [0.63, 1.35], *p*=0.68
Parent widowed	1.29 [1.02, 1.63], *p*=0.03	1.29 [1.01, 1.64], *p*=0.04	1.36 [0.89, 2.09], *p*=0.15
CBCL Total Problems T-score	1.06 [1.06, 1.07], *p*<0.001*	1.06 [1.06, 1.07], *p*<0.001*	1.08 [1.07, 1.09], *p*<0.001*
Family history of suicide	1.17 [1.02, 1.34], *p*=0.03	1.19 [1.03, 1.37], *p*=0.02	1.29 [1.00, 1.66], *p*=0.05
Substance exposure	1.20 [0.69, 2.09], *p*=0.53	1.17 [0.66, 2.09], *p*=0.59	1.63 [0.73, 3.64], *p*=0.23
FES Family Conflict score	1.15 [1.12, 1.18], *p*<0.001*	1.14 [1.12, 1.18], *p*<0.001*	1.17 [1.11, 1.23], *p*<0.001*
Exposure to 1+ Criterion A Trauma	1.13 [1.01, 1.26], *p*=0.03	1.15 [1.02, 1.28], *p*=0.02	1.09 [0.87, 1.36], *p*=0.47

* Remained significant after applying Bonferroni correction.

Bonferroni correction threshold (15 tests): $p<0.003$.

Table 12. *Descriptive Statistics of Cognitive Scores in Total Sample and Across STB Groups*

	Total Sample (*n*=11,876)	No STBs (*n*=7341)	Ever STBs^ (*n*=2707)	Follow-Up STBs^^ (*n*=1034)
NIH Toolbox Cognitive Battery (Uncorrected Standard Scores)		Mean (SD)		
Flanker Inhibitory Control and Attention Test	94.00 (9.14)	94.27 (8.88)	94.08 (9.21)	94.15 (8.98)
Dimensional Change Card Sort Test	92.52 (9.51)	92.95 (9.22)	91.99 (9.90)***	92.24 (9.58)*
List Sort Working Memory Test	96.65 (12.08)	97.31 (11.83)	96.57 (11.96)**	96.33 (11.69)*
Picture Vocabulary Test	84.46 (8.12)	84.90 (7.97)	84.44 (8.16)*	84.56 (7.89)
Oral Reading Recognition Test	90.86 (6.91)	91.21 (6.86)	90.74 (6.92)**	90.90 (6.74)
Pattern Comparison Processing Speed Test	88.06 (14.58)	88.42 (14.35)	87.55 (14.91)**	88.01 (15.19)
Picture Sequence Memory Test	102.81 (12.07)	103.38 (12.03)	102.23 (12.05)***	103.21 (11.83)
Fluid Intelligence Composite	91.55 (10.66)	92.17 (10.39)	91.11 (10.70)***	91.56 (10.54)
Crystallized Intelligence Composite	86.36 (7.07)	86.78 (6.95)	86.30 (7.08)**	86.45 (6.98)
Total Composite	86.22 (9.14)	86.84 (8.91)	85.95 (9.09)***	86.32 (8.89)
WISC-V (Scaled Score)				
Matrix Reasoning	9.86 (2.99)	9.99 (2.97)	9.89 (3.00)	10.02 (3.01)

^=STBs reported by youth and/or parent at any point over the study period (baseline, follow-up year 1, or follow-up year 2).

^^=STBs first reported by youth and/or parent after baseline (follow-up year 1 or follow-up year 2).

*Mean difference compared to reference group (no STBs) significant at $p<.05$ (one-way ANOVA).

**Mean difference compared to reference group significant at $p<.01$ (one-way ANOVA).

***Mean difference compared to reference group significant at $p<.001$ (one-way ANOVA).

STBs=suicidal ideation and/or behavior, SD=standard deviation.

Table 13. *Descriptive Statistics of Cognitive Scores Across Suicidal Ideation Groups*

	No Suicidal Ideation (*n*=7349)	Ever Suicidal Ideation^ (*n*=2435)	Follow-Up Suicidal Ideation^^ (*n*=1217)
NIH Toolbox Cognitive Battery (Uncorrected Standard Scores)		Mean (SD)	
Flanker Inhibitory Control and Attention Test	94.27 (8.88)	94.22 (9.10)	94.17 (9.04)
Dimensional Change Card Sort Test	92.95 (9.22)	92.12 (9.77)***	92.36 (9.54)*
List Sort Working Memory Test	97.31 (11.83)	96.68 (11.84)*	96.47 (11.80)*
Picture Vocabulary Test	84.90 (7.97)	84.59 (8.17)	84.61 (8.19)
Oral Reading Recognition Test	91.21 (6.86)	90.90 (6.83)	90.95 (6.82)
Pattern Comparison Processing Speed Test	88.42 (14.35)	87.52 (14.87)**	88.09 (15.15)
Picture Sequence Memory Test	103.37 (12.03)	102.39 (12.09)***	103.19 (11.75)
Fluid Intelligence Composite	92.17 (10.39)	91.23 (10.63)***	91.62 (10.62)
Crystallized Intelligence Composite	86.78 (6.95)	86.47 (7.09)	86.51 (7.18)
Total Composite	86.85 (8.91)	86.11 (9.04)***	86.39 (9.02)
WISC-V (Scaled Score)			
Matrix Reasoning	9.99 (2.97)	9.96 (2.97)	10.06 (2.98)

^=Suicidal ideation reported by youth and/or parent at any point over the study period (baseline, follow-up year 1, or follow-up year 2).

^^=Suicidal ideation first reported by youth and/or parent after baseline (follow-up year 1 or follow-up year 2).

*Mean difference compared to reference group (no suicidal ideation) significant at $p<.05$ (one-way ANOVA).

**Mean difference compared to reference group significant at $p<.01$ (one-way ANOVA).

***Mean difference compared to reference group significant at $p<.001$ (one-way ANOVA).

SD=standard deviation.

Table 14. *Descriptive Statistics of Cognitive Scores Across Suicidal Behavior Groups*

	No Suicidal Behavior (*n*=9217)	Ever Suicidal Behavior^ (*n*=460)	Follow-Up Suicidal Behavior^^ (*n*=191)
NIH Toolbox Cognitive Battery (Uncorrected Standard Scores)		Mean (SD)	
Flanker Inhibitory Control and Attention Test	94.30 (8.87)	93.56 (10.01)	93.52 (9.81)
Dimensional Change Card Sort Test	92.84 (9.28)	91.25 (10.50)***	91.66 (9.58)
List Sort Working Memory Test	97.28 (11.82)	95.05 (12.08)***	95.79 (12.30)
Picture Vocabulary Test	84.94 (7.95)	82.76 (9.22)***	83.74 (9.30)*
Oral Reading Recognition Test	91.19 (6.85)	90.31 (6.83)**	91.10 (6.46)*
Pattern Comparison Processing Speed Test	88.28 (14.46)	87.33 (14.92)	87.56 (15.18)
Picture Sequence Memory Test	103.24 (12.02)	100.81 (12.26)***	101.97 (11.73)
Fluid Intelligence Composite	92.06 (10.40)	89.97 (11.12)***	90.75 (11.00)
Crystallized Intelligence Composite	86.80 (6.95)	85.15 (7.50)***	86.08 (7.51)
Total Composite	86.79 (8.89)	84.69 (9.54)***	85.76 (9.19)
WISC-V (Scaled Score)			
Matrix Reasoning	10.02 (2.96)	9.34 (2.85)***	9.48 (2.66)*

^=Suicidal behavior reported by youth and/or parent at any point over the study period (baseline, follow-up year 1, or follow-up year 2).

^^=Suicidal behavior first reported by youth and/or parent after baseline (follow-up year 1 or follow-up year 2).

*Mean difference compared to reference group (no suicidal behavior) significant at $p<.05$ (one-way ANOVA).

**Mean difference compared to reference group significant at $p<.01$ (one-way ANOVA).

***Mean difference compared to reference group significant at $p<.001$ (one-way ANOVA).

SD=standard deviation.

Table 15: *Varimax Factor Loadings for Three-Factor Cognitive Structure*

	Factor 1: Executive Functioning	Factor 2: Verbal Comprehension	Factor 3: Memory and Learning
Flanker Inhibitory Control and Attention Test	**0.564**	0.177	0.192
Dimensional Change Card Sort Test	**0.646**	0.177	0.237
List Sort Working Memory Test	0.189	0.302	**0.677**
Picture Vocabulary Test	0.193	**0.553**	0.317
Oral Reading Recognition Test	0.174	**0.778**	0.210
Pattern Comparison Processing Speed Test	**0.593**	0.088	0.106
Picture Sequence Memory Test	0.231	0.159	**0.378**

Table 16: *Longitudinal Associations Between Cognitive Scores at Baseline and STBs Across Follow-Up Period* (OR, 95% CI, *p*-value)

	Model 1: Any STBs	Model 2: Suicidal Ideation	Model 3: Suicidal Behavior
Flanker Inhibitory Control & Attention Test	1.00 [0.99, 1.01], *p*=0.85	1.00 [0.99, 1.01], *p*=0.74	0.99 [0.97, 1.01], *p*=0.34
Dimensional Change Card Sort Test	1.00 [0.99, 1.01], *p*=0.50	1.00 [0.99, 1.01], *p*=0.83	1.00 [0.98, 1.01], *p*=0.64
List Sort Working Memory Test	1.00 [0.99, 1.00], *p*=0.30	1.00 [0.99, 1.00], *p*=0.48	1.00 [0.98, 1.01], *p*=0.94
Picture Vocabulary Test	1.00 [0.99, 1.01], *p*=0.79	1.00 [0.99, 1.01], *p*=0.42	0.98 [0.96, 1.01], *p*=0.22
Oral Reading Recognition Test	1.00 [0.99, 1.01], *p*=0.96	1.00 [0.99, 1.01], *p*=0.91	1.01 [0.99, 1.04], *p*=0.41
Pattern Comparison Processing Speed Test	1.00 [0.99, 1.01], *p*=0.98	1.00 [1.00, 1.01], *p*=0.76	1.00 [0.99, 1.01], *p*=0.64
Picture Sequencing Memory Test	1.00 [0.99, 1.01], *p*=0.88	1.00 [0.99, 1.01], *p*=0.98	1.00 [0.98, 1.01], *p*=0.57
WISC-V Matrix Reasoning	1.03 [1.00, 1.06], *p*=0.02	1.03 [1.01, 1.06], *p*=0.009	0.97 [0.91, 1.02], *p*=0.24
Factor 1: Executive Functioning	1.02 [0.94, 1.10], *p*=0.70	1.02 [0.94, 1.10], *p*=0.68	0.99 [0.83, 1.19], *p*=0.95
Factor 2: Verbal Comprehension	1.01 [0.93, 1.09], *p*=0.85	1.02 [0.95, 1.09], *p*=0.62	0.98 [0.83, 1.15], *p*=0.77
Factor 3: Memory and Learning	1.01 [0.93, 1.08], *p*=0.86	1.00 [0.93, 1.07], *p*=0.95	0.94 [0.79, 1.11], *p*=0.44
Crystallized Intelligence Composite	1.00 [0.99, 1.02], *p*=0.45	1.00 [0.99, 1.02], *p*=0.48	0.99 [0.97, 1.02], *p*=0.51
Fluid Intelligence Composite	1.00 [0.99, 1.01], *p*=0.80	1.00 [0.99, 1.01], *p*=0.63	0.99 [0.98, 1.01], *p*=0.49
Total Composite	1.00 [0.99, 1.01], *p*=0.54	1.00 [0.99, 1.01], *p*=0.43	0.99 [0.97, 1.02], *p*=0.53

All models controlled for the following baseline covariates: age, sex at birth, race/ethnicity, household income, parental marital status, highest household educational attainment, family history of attempted or completed suicide, CBCL Total Problems Score, youth substance exposure, FES Conflict Score, and youth trauma exposure. Models for individual NIH Toolbox Cognition Battery measures additionally controlled for WISC-V Matrix Reasoning scaled score.

STBs=suicidal ideation and/or behavior; OR=odds ratio; CI=confidence interval.

* Remained significant after applying Bonferroni correction.

Bonferroni correction threshold (14 tests): $p<0.004$.

Table 17: *Associations Between Cognitive Scores at Baseline and Lifetime STBs* (OR [95% CI], *p*-value)

	Model 1: Any STBs	Model 2: Suicidal Ideation	Model 3: Suicidal Behavior
Flanker Inhibitory Control & Attention Test	1.00 [1.00, 1.01], *p*=0.46	1.00 [1.00, 1.01], *p*=0.35	1.00 [0.99, 1.01], *p*=0.75
Dimensional Change Card Sort Test	1.00 [0.99, 1.00], *p*=0.57	1.00 [0.99, 1.00], *p*=0.56	1.00 [0.99, 1.01], *p*=0.75
List Sort Working Memory Test	1.00 [1.00, 1.01], *p*=0.40	1.00 [1.00, 1.01], *p*=0.68	1.00 [0.99, 1.01], *p*=0.50
Picture Vocabulary Test	1.00 [0.99, 1.00], *p*=0.29	1.00 [0.99, 1.00], *p*=0.35	0.98 [0.96, 1.00], *p*=0.03
Oral Reading Recognition Test	1.00 [0.99, 1.01], *p*=0.81	1.00 [0.99, 1.01], *p*=0.69	1.01 [1.00, 1.03], *p*=0.15
Pattern Comparison Processing Speed Test	1.00 [1.00, 1.00], *p*=0.86	1.00 [1.00, 1.00], *p*=0.74	1.00 [0.99, 1.01], *p*=0.61
Picture Sequencing Memory Test	1.00 [0.99, 1.00], *p*=0.09	1.00 [0.99, 1.00], *p*=0.14	0.99 [0.98, 1.00], *p*=0.30
WISC-V Matrix Reasoning	1.02 [1.00, 1.04], *p*=0.04	1.02 [1.00, 1.04], *p*=0.02	0.99 [0.95, 1.03], *p*=0.49
Factor 1: Executive Functioning	1.03 [0.97, 1.09], *p*=0.35	1.03 [0.97, 1.10], *p*=0.28	1.00 [0.88, 1.13], *p*=0.96
Factor 2: Verbal Comprehension	1.01 [0.96, 1.07], *p*=0.59	1.01 [0.95, 1.07], *p*=0.75	1.04 [0.93, 1.16], *p*=0.52
Factor 3: Memory and Learning	0.97 [0.92, 1.02], *p*=0.28	0.97 [0.92, 1.03], *p*=0.32	0.95 [0.85, 1.06], *p*=0.36
Crystallized Intelligence Composite	1.00 [0.99, 1.01], *p*=0.59	1.00 [0.99, 1.01], *p*=0.42	0.99 [0.98, 1.01], *p*=0.48
Fluid Intelligence Composite	1.00 [1.00, 1.01], *p*=0.79	1.00 [0.99, 1.01], *p*=0.92	1.00 [0.99, 1.01], *p*>0.99
Total Composite	1.00 [1.00, 1.01], *p*=0.59	1.00 [0.99, 1.01], *p*=0.62	1.00 [0.99, 1.01], *p*=0.95

All models controlled for the following baseline covariates: age, sex at birth, race/ethnicity, household income, parental marital status, highest household educational attainment, family history of attempted or completed suicide, CBCL Total Problems Score, youth substance exposure, FES Conflict Score, and youth trauma exposure.

STBs=suicidal ideation and/or behavior; OR=odds ratio; CI=confidence interval.

* Remained significant after applying Bonferroni correction.

Bonferroni correction threshold (14 tests): *p*<0.004.

Table 18. *Summary of All Covariate Coefficients for Models Examining Association Between Total Composite Cognitive Score and Incident STBs* (OR [95% CI], *p*-value)

	Model 1: Any STBs	Model 2: Suicidal Ideation	Model 3: Suicidal Behavior
Total composite cognitive score	1.00 [0.99, 1.01], *p*=0.54	1.00 [0.99, 1.01], *p*=0.43	0.99 [0.97, 1.02], *p*=0.59
Age at baseline	1.16 [1.03, 1.32], *p*=0.01	1.16 [1.04, 1.31], *p*=0.01	1.41 [1.08, 1.85], *p*=0.01
Sex at birth (female)	1.22 [1.05, 1.41], *p*=0.008	1.23 [1.08, 1.41], *p*=0.002*	1.83 [1.33, 2.53], *p*<0.001*
Black race	1.22 [0.94, 1.59], *p*=0.14	1.04 [0.81, 1.34], *p*=0.77	0.78 [0.43, 1.43], *p*=0.43
Hispanic ethnicity	1.09 [0.88, 1.35], *p*=0.42	1.04 [0.86, 1.28], *p*=0.67	0.97 [0.61, 1.55], *p*=0.91
Asian race	0.72 [0.37, 1.41], *p*=0.34	0.91 [0.51, 1.63], *p*=0.75	0.50 [0.07, 3.68], *p*=0.49
Other race/ethnicity	1.23 [0.97, 1.57], *p*=0.08	1.25 [1.00, 1.56], *p*=0.046	1.22 [0.75,199], *p*=.042
Household income $50-$100K	0.89 [0.71, 1.12], *p*=0.32	0.95 [0.77, 1.17], *p*=0.61	1.16 [0.72, 1.85], *p*=0.54
Household income >$100K	0.86 [0.67, 1.11], *p*=0.25	0.89 [0.70, 1.13], *p*=0.33	1.00 [0.58, 1.72], *p*=0.99
Parent high school diploma	1.06 [0.67, 1.69], *p*=0.79	1.00 [0.64, 1.56], *p*>0.99	1.70 [0.46, 6.28], *p*=0.43
Parent completed some college	1.07 [0.70, 1.63], *p*=0.77	1.11 [0.74, 1.67], *p*=0.60	2.20 [0.66, 7.41], *p*=0.20
Parent earned bachelor's degree	1.13 [0.72, 1.77], *p*=0.61	1.11 [0.72, 1.71], *p*=0.64	2.24 [0.64, 7.86], *p*=0.21
Parent earned post-graduate degree	1.13 [0.71, 1.79], *p*=0.60	1.16 [0.75, 1.79], *p*=0.51	1.80 [0.50, 6.47], *pt*=0.37
Parent divorced	1.21 [0.58, 2.52], *p*=0.62	1.02 [0.49, 2.14], *p*=0.96	0.51 [0.07, 3.97], *p*=0.52
Parent separated	0.93 [0.71, 1.21], *p*=0.59	1.07 [0.84, 1.36], *p*=0.59	1.21 [0.71, 2.08], *p*=0.48
Parent never married	0.96 [0.65, 1.43], *p*=0.85	0.93 [0.64, 1.37], *p*=0.73	0.67 [0.23, 1.93], *p*=0.46
Parent living with partner	0.93 [0.69, 1.24], *p*=0.61	0.99 [0.76, 1.31], *p*=0.97	1.35 [0.76, 2.41], *p*=0.31
Parent widowed	1.12 [0.81, 1.56], *p*=0.49	1.23 [0.90, 1.66], *p*=0.19	1.38 [0.71, 2.67], *p*=0.34
CBCL Total Problems T-score	1.04 [1.03, 1.05], *p*<0.001*	1.05 [1.04, 1.06], *p*<0.001*	1.08 [1.06, 1.09], *p*<0.001*
Family history of suicide	1.08 [0.89, 1.32], *p*=0.42	1.07 [0.89, 1.29], *p*=0.45	1.03 [0.69, 1.53], *p*<0.001*
Substance exposure	0.55 [0.19, 1.63], *p*=0.28	0.73 [0.30, 1.76], *p*=0.49	0,00 [0,00, ∞], *p*=0.99
FES Family Conflict score	1.09 [1.05, 1.13], *p*<0.001*	1.10 [1.06, 1.14], *p*<0.001*	1.11 [1.03, 1.20], *p*=0.005
Exposure to 1+ Criterion A Trauma	1.12 [0.96, 1.30], *p*=0.15	1.15 [1.00, 1.33], *p*=0.047	1.36 [0.98, 1.89], *p*=0.07

* Remained significant after applying Bonferroni correction.

Bonferroni correction threshold (14 tests): *p*<0.004.

Table 19. *Summary of All Covariate Coefficients for Models Examining Association Between Total Composite Cognitive Score and Lifetime STBs* (OR [95% CI], *p*-value)

	Model 1: Any STBs	Model 2: Suicidal Ideation	Model 3: Suicidal Behavior
Total composite cognitive score	1.00 [1.00, 1.01], *p*=0.59	1.00 [0.99, 1.01], *p*=0.62	1.00 [0.99, 1.01], *p*=0.95
Age at baseline	1.07 [0.98, 1.17], *p*=0.12	1.08 [0.99, 1.01], *p*=0.08	1.31 [1.09, 1.57], *p*=0.004
Sex at birth (female)	0.99 [0.89, 1.10], *p*=0.84	1.02 [0.99, 1.19], *p*=0.67	1.26 [1.01, 1.57], *p*=0.04
Black race	1.21 [0.99, 1.47], *p*=0.06	1.12 [0.91, 1.37], *p*=0.29	1.40 [0.96, 2.04], *p*=0.08
Hispanic ethnicity	1.06 [0.90, 1.25], *p*=0.46	1.08 [0.91, 1.27], *p*=0.39	1.45 [1.07, 1.97], *p*=0.02
Asian race	1.51 [1.03, 2.21], *p*=0.04	1.51 [1.02, 2.24], *p*=0.04	1.11 [0.39, 3.15], *p*=0.85
Other race/ethnicity	1.31 [1.10, 1.55], *p*=0.002*	1.33 [1.12, 1.59], *p*=0.001*	1.29 [0.91, 1.84], *p*=0.16
Household income $50-$100K	1.04 [0.88, 1.22], *p*=0.64	1.05 [0.88, 1.24], *p*=0.59	0.86 [0.63, 1.17], *p*=0.33
Household income >$100K	1.01 [0.84, 1.21], *p*=0.94	1.00 [0.83, 1.21], *p*=0.97	0.75 [0.51, 1.08], *p*=0.13
Parent high school diploma	1.08 [0.76, 1.52], *p*=0.67	1.08 [0.76, 1.56], *p*=0.66	0.92 [0.50, 1.69], *p*=0.78
Parent completed some college	1.06 [0.77, 1.45], *p*=0.72	1.10 [0.79, 1.53], *p*=0.57	1.01 [0.58, 1.77], *p*=0.96
Parent earned bachelor's degree	1.07 [0.77, 1.45], *p*=0.71	1.14 [0.81, 1.62], *p*=0.45	1.00 [0.55, 1.82], *p*>0.99
Parent earned post-graduate degree	1.12 [0.80, 1.57], *p*=0.52	1.21 [0.85, 1.73], *p*=0.29	0.83 [0.44, 1.54], *p*=0.55
Parent divorced	1.02 [0.80, 1.57], *p*=0.95	1.02 [0.57, 1.84], *p*=0.94	0.49 [0.14, 1.72], *p*=0.26
Parent separated	1.09 [0.91, 1.32], *p*=0.35	1.09 [0.90, 1.32], *p*=0.38	1.18 [0.82, 1.70], *p*=0.37
Parent never married	0.96 [0.72, 1.29], *p*=0.79	0.96 [0.71, 1.30], *p*=0.79	0.99 [0.56, 1.73], *p*=0.96
Parent living with partner	1.06 [0.86, 1.31], *p*=0.56	1.06 [0.86, 1.32], *p*=0.58	0.90 [0.61, 1.33], *p*=0.60
Parent widowed	1.30 [1.03, 1.65], *p*=0.03	1.30 [1.02, 1.66], *p*=0.03	1.39 [0.91, 2.13], *p*=0.13
CBCL Total Problems T-score	1.06 [1.06, 1.07], *p*<0.001*	1.06 [1.06, 1.07], *p*<0.001*	1.08 [1.07, 1.09], *p*<0.001*
Family history of suicide	1.17 [1.02, 1.35], *p*=0.02	1.19 [1.04, 1.38], *p*=0.01	1.30 [1.00, 1.68], *p*=0.05
Substance exposure	1.27 [0.72, 2.24], *p*=0.41	1.24 [0.69, 2.23], *p*=0.48	1.71 [0.76, 3.86], *p*=0.20
FES Family Conflict score	1.15 [1.12, 1.27], *p*<0.001*	1.14 [1.11, 1.17], *p*<0.001*	1.17 [1.11, 1.23], *p*<0.001*
Exposure to 1+ Criterion A Trauma	1.13 [1.02, 1.27], *p*=0.02	1.16 [1.03, 1.30], *p*=0.01	1.07 [0.85, 1.35], *p*=0.55

* Remained significant after applying Bonferroni correction.

Bonferroni correction threshold (14 tests): $p<0.004$.

Table 20: *Agreement Across Self-Reported and Parent-Reported STBs* (*N*=11,876), *n* (%)

	Youth Endorsed	Parent Endorsed	Either Youth or Parent Endorsed	Youth Endorsed, Parent Denied	Parent Endorsed, Youth Denied	Cohen's Kappa
BL: Passive SI, current	142 (1.2%)	63 (0.5%)	196 (1.7%)	133 (67.9%)	56 (28.6%)	0.06
BL: Passive SI, past	703 (5.9%)	759 (6.4%)	1292 (10.9%)	538 (41.6%)	590 (45.7%)	0.17
BL: Active SI, current	191 (1.6%)	132 (1.1%)	308 (2.6%)	176 (57.1%)	118 (38.3%)	0.08
BL: Active SI, past	433 (3.6%)	370 (3.1%)	722 (6.1%)	354 (49.0%)	292 (40.4%)	0.16
BL: Any SI, current	262 (2.2%)	161 (1.4%)	398 (3.4%)	237 (59.5%)	139 (34.9%)	0.09
BL: Any SI, past	903 (7.6%)	845 (7.1%)	1514 (12.7%)	674 (44.5%)	614 (40.6%)	0.20
BL: Suicidal behavior, current	65 (0.5%)	20 (0.2%)	82 (0.6%)	62 (75.6%)	18 (22.0%)	0.05
BL: Suicidal behavior, past	149 (1.3%)	92 (0.8%)	223 (1.9%)	132 (56.7%)	74 (31.8%)	0.13
BL: Any STBs, current	276 (2.3%)	169 (1.4%)	417 (3.5%)	248 (59.5%)	144 (34.5%)	0.10
BL: Any STBs, past	918 (7.7%)	848 (7.1%)	1524 (12.8%)	681 (44.7%)	609 (40.0%)	0.21
1Y: Passive SI, current	111 (0.9%)	--	--	--	--	--
1Y: Passive SI, past	683 (5.8%)	--	--	--	--	--
1Y: Active SI, current	144 (1.2%)	--	--	--	--	--
1Y: Active SI, past	429 (3.6%)	--	--	--	--	--
1Y: Any SI, current	194 (1.6%)	--	--	--	--	--
1Y: Any SI, past	845 (7.1%)	--	--	--	--	--
1Y: Suicidal behavior, current	39 (0.3%)	--	--	--	--	--
1Y: Suicidal behavior, past	159 (1.3%)	--	--	--	--	--
1Y: Any STBs, current	199 (1.7%)	--	--	--	--	--
1Y: Any STBs, past	856 (7.2%)	--	--			--
2Y: Passive SI, current	95 (0.8%)	64 (0.5%)	145 (1.2%)	82 (56.6%)	52 (35.9%)	0.14
2Y: Passive SI, past	625 (5.3%)	704 (5.9%)	1121 (9.4%)	422 (37.6%)	508 (45.3%)	0.24
2Y: Active SI, current	133 (1.1%)	129 (1.1%)	233 (2.0%)	107 (45.9%)	104 (44.6%)	0.16
2Y: Active SI, past	382 (3.2%)	515 (4.3%)	770 (6.5%)	259 (33.6%)	394 (51.2%)	0.23
2Y: Any SI, current	162 (1.4%)	158 (1.3%)	284 (2.4%)	130 (45.8%)	128 (45.1%)	0.16
2Y: Any SI, past	740 (6.2%)	830 (7.2%)	1324 (11.1%)	471 (35.6%)	599 (45.2%)	0.27
2Y: Suicidal behavior, current	40 (0.3%)	23 (0.2%)	59 (0.5%)	38 (64.4%}	19 (32.2%)	0.06
2Y: Suicidal behavior, past	167 (1.4%)	134 (1.1%)	263 (2.2%)	132 (50.2%)	100 (38.0%)	0.20
2Y: Any STBs, current	164 (1.4%)	160 (1.3%)	287 (2.4%)	132 (46.0%)	129 (44.9%)	0.15
2Y: Any STBs, past	751 (6.3%)	864 (7.3%)	1330 (11.2%)	473 (35.6%)	594 (44.7%)	0.27
Ever: Passive SI	1358 (11.4%)	1210 (10.2%)	1906 (16.0%)	788 (41.3%)	693 (36.4%)	0.28

Ever: Active SI	1024 (8.6%)	839 (7.1%)	1409 (11.9%)	631 (44.8%)	504 (35.8%)	0.26
Ever: Any SI	1729 (14.6%)	1421 (12.0%)	2292 (19.3%)	969 (42.3%)	746 (32.5%)	0.30
Ever: Suicidal behavior	420 (3.5%)	213 (1.8%)	493 (4.2%)	300 (60.9%)	127 (25.8%)	0.22
Ever: Any STBs	1781 (15.0%)	1430 (12.0%)	2318 (19.5%)	985 (42.5%)	722 (31.1%)	0.32
Follow-Up*: Passive SI	850 (7.2%)	431 (3.6%)	875 (7.4%)	527 (60.2%)	221 (25.3%)	0.21
Follow-Up*: Active SI	625 (5.3%)	404 (3.4%)	750 (6.3%)	418 (55.7%)	221 (29.5%)	0.22
Follow-Up*: Any SI	1117 (9.4%)	645 (5.4%)	1165 (9.8%)	655 (56.2%)	287 (24.6%)	0.27
Follow-Up*: Suicidal behavior	220 (1.9%)	107 (1.1%)	256 (2.2%)	164 (64.1%)	63 (24.6%)	0.19
Follow-Up*: Any STBs	1146 (9.6%)	673 (5.7%)	1202 (10.1%)	668 (55.6%)	295 (24.5%)	0.28

BL=Baseline; 1Y=1-year follow-up; 2Y=2-year follow-up; SI=suicidal ideation; STB=suicidal thoughts or behaviors.

*Suicidality first reported by relevant party after baseline.

Table 21. *Sociodemographic Characteristics of Twin Sample*

	Twin Sample (*n*=1542)
Age at baseline, mean (SD)	10.14 (0.55)
Sex at birth (female), *n* (%)	762 (49.4%)
White race, *n* (%)	1021 (66.2%)
Black race, *n* (%)	220 (14.3%)
Asian race, *n* (%)	3 (0.2%)
Other race/ethnicity, *n* (%)	145 (9.4%)
Hispanic ethnicity, *n* (%)	152 (9.9%)
Household income < $50K, *n* (%)	248 (16.1%)
Household income $50K-$100K, *n* (%)	433 (28.1%)
Household income >$100K, *n* (%)	777 (50.4%)
Parent married, *n* (%)	1144 (74.2%)
Parent divorced, *n* (%)	152 (9.9%)
Parent separated, *n* (%)	44 (2.9%)
Parent never married, *n* (%)	126 (8.2%)
Parent living with partner, *n* (%)	50 (3.2%)
Parent widowed, *n* (%)	16 (1.0%)
Parent < high school diploma, *n* (%)	25 (1.6%)
Parent high school diploma/GED, *n* (%)	75 (4.9%)
Parent completed some college, *n* (%)	398 (25.8%)
Parent earned bachelor's degree, *n* (%)	510 (33.1%)
Parent earned post-graduate degree, *n* (%)	532 (34.5%)
Family history of suicide/attempt, *n* (%)	224 (14.5%)
CBCL Total Problems *T*-score, mean (SD)	42.98 (10.67)
Substance exposure (> puff/sip), *n* (%)	12 (0.8%)
FES Family Conflict score, mean (SD)	2.09 (1.93)
Exposure to 1+ Criterion A trauma, *n* (%)	521 (33.8%)
Lifetime Total Suicidality, *n* (%)	316 (20.5%)
Lifetime Suicidal Ideation, *n* (%)	289 (18.7%)
Lifetime Suicidal Behaviors, *n* (%)	49 (3.2%)

Table 22: *Prevalence and Concordance Between Twins for STBs*

Phenotype	Complete Pairs	Cases (*n*, %)*	Discordant Pairs	Concordant Pairs	Tetrachoric Correlations [95% CI]
Ever STBs					
MZ	282	125 (22.16%)	67	215	0.51 [0.33, 0.66]
DZ	365	170 (23.29%)	100	265	0.40 [0.23, 0.55]
Ever Suicidal Ideation					
MZ	276	116 (21.01%)	64	212	0.51 [0.32, 0.66]
DZ	357	155 (21.71%)	95	262	0.39 [0.20, 0.54]
Ever Suicidal Behavior					
MZ	275	19 (3.45%)	15	260	0.63 [0.24, 0.86]
DZ	353	27 (3.82%)	23	330	0.50 [0.08, 0.77]

CI=confidence interval; STBs=suicidal thoughts and/or behaviors; MZ=monozygotic twin pairs; DZ=dizygotic twin pairs.

*Cases calculated from pairs with complete data for relevant suicidality phenotype.

Table 23. *Variance Component Analysis of Suicidality Phenotypes*

Phenotype/Model	A (95% CI)	C (95% CI)	E (95% CI)	AIC	Model Significance (*p*)
Lifetime STBs					
ACE	0.25 (-0.25, 0.73)	0.27 (-0.12, 0.64)	0.48 (0.32, 0.67)	1436.40	--
CE	--	0.45 (0.32, 0.45)	0.55 (0.43, 0.68)	1435.40	0.317
AE	0.56 (0.41, 0.70)	--	0.43 (0.30, 0.59)	1436.26	0.172
E	--	--	1.00 (1.00, 1.00)	1474.98	<0.001
Lifetime Suicidal Ideation					
ACE	0.26 (-0.26, 0.76)	0.25 (-0.16, 0.63)	0.49 (0.33, 0.69)	1364.37	--
CE	--	0.44 (0.30, 0.56)	0.56 (0.44, 0.70)	1363.38	0.315
AE	0.55 (0.39, 0.69)	--	0.45 (0.31, 0.61)	1363.78	0.235
E	--	--	1.00 (1.00, 1.00)	1397.59	<0.001
Lifetime Suicidal Behavior					
ACE	0.29 (-0.87, 1.38)	0.24 (-0.71, 1.03)	0.49 (0.19, 0.95)	423.03	--
CE	--	0.43 (0.11, 0.67)	0.57 (0.33, 0.88)	421.28	0.613
AE	0.55 (0.16, 0.82)	--	0.44 (0.18, 0.84)	421.25	0.633
E	--	--	1.00 (1.00, 1.00)	426.48	0.024

All models adjusted for age and sex.

CI=confidence interval.

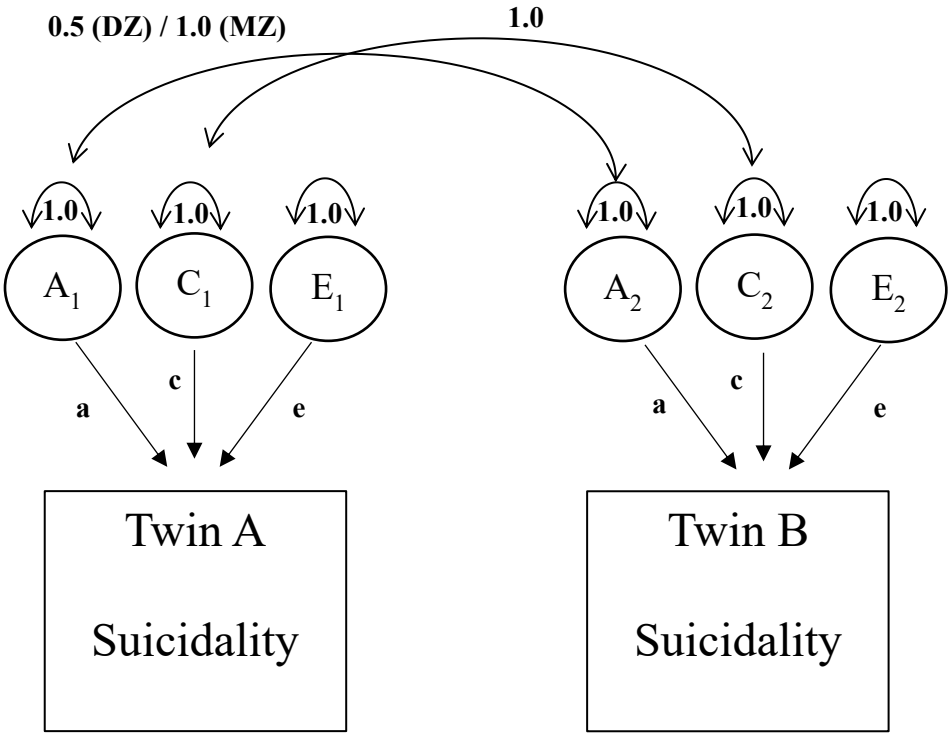
Table 24. *Point-Biserial Correlations between Suicidality and Cognition*

Correlation [95% CI], *p*-value			
	Cognition: Total Composite	Cognition: Fluid Intelligence	Cognition: Crystallized Intelligence
Suicidality: Total STBs			
MZ	-0.04 [-0.10, 0.01], *p*=0.11	-0.03 [-0.08, 0.02], *p*=0.28	-0.04 [-0.10, 0.01], *p*=0.08
DZ	-0.03 [-0.11, 0.04], *p*=0.34	-0.02 [-0.09, 0.05], *p*=0.58	-0.05 [-0.12, 0.02], *p*=0.20
Suicidal Ideation			
MZ	-0.04 [-0.09, 0.02], *p*=0.16	-0.03 [-0.08, 0.02], *p*=0.27	-0.03 [-0.09, 0.02], *p*=0.21
DZ	-0.03 [-0.10, 0.04], *p*=0.44	-0.02 [-0.09, 0.05], *p*=0.54	-0.03 [-0.10, 0.04], *p*=0.41
Suicidal Behaviors			
MZ	-0.06 [-0.12, -0.01], *p*=0.02	-0.03 [-0.09, 0.02], *p*=0.21	-0.09 [-0.14, -0.03], *p*=0.002
DZ	-0.02 [-0.09, 0.05], *p*=0.56	0.01 [-0.07, 0.08], *p*=0.87	-0.05 [-0.13, 0.02], *p*=0.13

CI=confidence interval; STBs=suicidal thoughts and/or behaviors.

Bonferroni correction threshold (18 tests): $p<0.003$.

Figure 1. *Univariate ACE Model of Suicidality*



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