



## Suicide attempt endophenotypes: Latent profiles of child and adolescent aggression and impulsivity differentially predict suicide attempt in females

Rashelle J. Musci<sup>a,\*</sup>, Elizabeth D. Ballard<sup>b,c</sup>, Emma K. Stapp<sup>a,d</sup>, Leslie Adams<sup>a</sup>, Holly C Wilcox<sup>a,c</sup>, Nicholas Ialongo<sup>a</sup>

<sup>a</sup> Department of Mental Health, Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD, USA

<sup>b</sup> Experimental and Pathophysiology Branch, National Institute of Mental Health, Bethesda, MD, USA

<sup>c</sup> Division of Child and Adolescent Psychiatry, Johns Hopkins University School of Medicine, Baltimore, MD, USA

<sup>d</sup> Genetic Epidemiology Research Branch, National Institute of Mental Health, Bethesda, MD, USA

### ABSTRACT

Suicide is a leading cause of death in young adulthood. Identifying early prevention targets to reduce later suicide is a public health priority. Impulsivity and aggression in early childhood may represent actionable early prevention candidate endophenotypes for later suicidal behavior. Our objective is to understand the association of aggression and impulsivity trajectories with mental health outcomes to inform future prevention efforts. Participants were part of a preventative intervention trial ( $n = 597$ ) and predominantly Black. They were assessed for aggressive and impulsive behaviors yearly in 1st–3rd and 6th–12th grades, and provided mental health data via self-report beginning in 6th grade. Longitudinal latent profiles of aggressive and impulsive behaviors were derived for males and females and used to determine whether profiles was associated with lifetime suicide attempt and meeting diagnostic criteria for major depressive disorder. Two impulsivity and aggression classes were found for males, characterized by low behaviors or moderate to high behaviors across development. Three classes were found for females, one of which was characterized by an undulating pattern of behaviors. For females, the class of severe behaviors was associated with significant risk of suicide attempt (Wald = 6.01,  $p = 0.05$ ). No relationship was found for males or for MDD diagnosis. An endophenotype model of impulsivity and aggression in predicting later suicide attempt was supported in females, but not males. Results underscore the importance of evaluating sex differences in suicide research and the potential identification of females at risk for later suicidal behavior in school settings.

### 1. Implications & contributions

Given that suicide is the second leading cause of death among adolescents, identifying mechanisms for suicide risk and avenues for early prevention programs remains a priority among adolescent health researchers and practitioners. Our results suggest that early childhood prevention programs targeting aggressive and impulsive behavior could significantly reduce suicidal behaviors.

**Suicide Attempt Endophenotypes: Latent profiles of child and adolescent aggression and impulsivity differentially predict suicide attempt in females.**

Suicide ranks as the second leading cause of death among children and adolescents ages 10–24 years in the United States (Heron, 2019), surpassed only by unintentional injury. The age adjusted suicide rate in the US has increased from 1999 through 2018, but rates were significantly lower in 2019 (13.0 per 100,000) (Hedegaard, 2021). Overall, there have been concerning increases in the suicide rate for adolescent girls (Hedegaard et al., 2020) and a narrowing of the gender gap in

suicide between girls and boys, highlighting the importance of understanding sex-driven differences in suicide risk (Ruch et al., 1975). Additionally, while developmental influences on suicidal behavior have been studied (Turecki et al., 2012), the majority of suicide research occurs *after* the initiation of the first suicidal attempt or thought. Identifying the antecedents of suicidal behavior in childhood can be a powerful tool for the prediction of suicidal behavior and is a goal of the 2012 United States National Strategy for Suicide Prevention (U.S., 2012).

One malleable suicide risk factor that occurs early in development is impulsive and aggressive behavior (Wilcox et al., 2008; Gvion and Apter, 2011). Prospective studies of brain development show that developmental and maturational factors influence the variability of impulsive and aggressive behavior over the course of early development (Romer, 2010). Retrospective studies have linked aggressive and impulsive behavior to suicide attempts and death, as well as violent methods and younger age of attempt (Dumais et al., 2005). Furthermore, the familial transmission of risk for suicide attempt has been linked to

\* Corresponding author.

E-mail address: [rmusc1@jhu.edu](mailto:rmusc1@jhu.edu) (R.J. Musci).

<https://doi.org/10.1016/j.pmedr.2022.101829>

Received 30 November 2021; Received in revised form 6 April 2022; Accepted 10 May 2022

Available online 14 May 2022

2211-3355/© 2022 Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

the familial aggregation of impulsive aggression (Brent et al., 2015). As impulsive and aggressive behaviors are associated with suicide attempts, have been linked to the familial aggregation of suicidal behavior, and are moderately heritable in their own right (Waltes et al., 2016), they may represent ideal candidate endophenotypes for suicide risk (Mann et al., 2009). However, in order to translate these clinical findings into scalable suicide prevention efforts, it is important to determine prospectively the influence of impulsive and aggressive behavior on suicide risk in community samples. In particular, as universal prospective identification of at-risk youth is likely to occur outside of mental health clinics (Horowitz et al., 2009), it is important to determine if at-risk youth can be prospectively identified in community settings such as schools. Furthermore, due to the overlap between impulsivity, aggression, and depressive symptoms (Brent et al., 2015), it is essential to determine if these trajectories are unique to suicide attempts or represent an underlying depressive process.

The aim of this study was to estimate the longitudinal association between aggression and impulsivity in childhood and adolescence in the prediction of suicide attempt and major depressive disorder (MDD) diagnosis by young adulthood. The use of a community-based cohort of students followed from 1st grade through high school and ratings of aggression and impulsivity by teachers decreases the likelihood of sampling and reporting biases inherent in clinical samples and self-report. Additionally, the use of teacher ratings highlights potential avenues for early identification of high-risk individuals through school systems. Also, due to sex differences in suicide ideation, attempts, and deaths (King et al., 2014), latent trajectories of impulsivity and aggression were derived separately for males and females. Of note, this sample was predominately Black, which is of particular relevance due to recent increases in suicide rates in Black children and adolescents (Caucas CB, 2019). Through such an analysis, a potential aggressive/impulsivity suicide attempt endophenotype could be defined for use in future investigations of individuals at high risk for suicide and preventive intervention.

## 2. Method

### 2.1. Participants and procedures

Data were drawn from a longitudinal study conducted by the Johns Hopkins Prevention Intervention Research Center. The original study sample included 798 children who entered first grade (approximately 6 years old) over the 1993–94 school year in nine Baltimore City public elementary schools in 1993, plus their caregivers. Six-hundred and seventy-eight of the larger sample of 798 were available for teacher ratings of their aggressive and impulsive behaviors in the fall of the 1993–94 school year. Children were recruited into a universal, preventive intervention trial targeting early learning and aggressive/disruptive behavior (Ialongo et al., 1999). One of the 2 intervention conditions was classroom-based and included a combination of the Good Behavior Game and Mastery Learning and the second consisted of a family-school partnership intervention. Interventions were provided over the first-grade year, following a pretest assessment in the early fall (Ialongo et al., 1999). Written informed consent was obtained from each participant's legal guardian and assent was obtained from the participant annually through age 17. At age 18 and beyond, written consent from the participant was obtained for all subsequent assessments. The initial trial and subsequent follow-up studies were approved by the Johns Hopkins Bloomberg School of Public Health Institutional Review Board.

### 2.2. Measures

**Demographic Information.** Race, sex, and free or reduced lunch status, a proxy for socioeconomic status (SES) (Ensminger et al., 2000), were collected from school records. Family adversity was reported by parents

in the fall of first grade using nine items: parent death, prolonged parental separation, marriage difficulties, divorce, financial difficulties, substance misuse, legal problems, and mental/physical health problems. Items were scored from 0 (not at all) to 3 (a lot), and then recoded into a binary variable (0 vs. 1–3). The 9 items were summed into a family adversity score (range 0–9).

**Aggression and Impulsivity.** The Teacher Observation of Classroom Adaptation-Revised (TOCA-R) was used to assess the participants' aggressive behaviors and impulsivity in the spring of grades 1 through 3 (Werthamer-Larsson et al., 1991). Teachers completed the Teacher Report of Classroom Behavior Checklist (TRCBC), an adolescent adaptation of the TOCA-R, in the spring of grades 6 through 12. Both measures included items such as "harms or hurts others physically" and "starts fights with classmates" to assess aggression, whereas impulsivity was measured using items such as "waits for turn" and "blurts out answer". Teachers rated the student's behavior on a six-point Likert scale from "almost never" to "always". Coefficient alphas for the TOCA-R subscales were 0.92 (aggression) and 0.78 (impulsivity). Similarly, TRCBC subscales in middle school were 0.91 (aggressive behavior) and 0.79 (impulsivity). See Petras et al. (Petras et al., 2011) for additional information on reliability and validity.

**Distal outcomes.** Suicide attempt was measured annually beginning in 6th grade by a single question ("In the past year have you tried to kill yourself or made a suicide attempt?"). A lifetime suicide attempt variable was created and indicated a participant endorsed the suicide attempt item at any time during the study period (6th grade through age 25). Additionally, meeting diagnostic criteria for major depressive disorder (MDD) was explored as a distal outcome, using items from the Computerized Diagnostic Schedule for Children-IV (C DISC-IV) (Shaffer et al., 2000). For this outcome, individuals meeting diagnostic criteria for MDD at any time between the ages of 19 and 25 were included.

**Analytic Strategy.** In order to explore trajectories of aggression and impulsivity, a longitudinal latent profile analysis was conducted across childhood and adolescence. This method of analysis allows for the joint modeling of change over time. That is, profiles/classes are derived based upon different patterns of indicator responses over time, or trajectories (Masyn and Little, 2013). For this study, the indicators were teacher-reported impulsive and aggressive behaviors scores. Models were run separately for males and females based on previous work indicating significant sex differences in aggressive and impulsive behaviors (Petras et al., 2011). Covariates and distal outcomes were included to help understand the prognostic ability of these classes or trajectories.

Analysis began with class enumeration whereby models were fit with an increasing number of classes. Each model was then compared using standard fit statistics such as the Bayesian information criterion (BIC) and the Lo-Mendell-Rubin Likelihood Ratio Test (LMR). The impact of covariates and distal outcomes were explored utilizing the manual three-step approach, which allows for the final model to account for measurement error (Nylund-Gibson et al., 2019). Free or reduced lunch status, intervention status, family adversity, and race (obtained from school records) were included as covariates. Two outcomes were tested for their relationship with the aggressive and impulsive class membership: lifetime suicide attempt and meeting diagnostic criteria for MDD in early adulthood. Current research standards indicate data can be treated as missing at random (MAR) when the missing data are unrelated to the outcome of interest. While there is no way to confirm that this data is, in fact, MAR, we do believe that our data is MAR. When comparing the participants included in our analyses to those not included, they did not differ in terms of basic demographics including intervention status (chi (Hedegaard, 2021) = 3.19,  $p = 0.07$ ), sex (chi (Hedegaard, 2021) = 2.96,  $p = 0.09$ ), adversity ( $t = 2.01$ ,  $p = 0.05$ ). Race did significantly differ, with Black participants being more likely to be not missing (chi (Hedegaard, 2021) = 8.45,  $p < 0.05$ ). In order to handle missing data, analysis was completed in Mplus, version 8 (Muthen and Muthen, 2017), using full information maximum likelihood estimation.

### 3. Results

#### 3.1. Sample characteristics

Of the original sample of 678 participants who were available for assessment in the fall of 1st grade during the 1993–94 school year, 564 were included in the analytic sample. 85.6% were Black and 14.4% were White; 53.7% were male. Approximately 67.7% of the sample received free or reduced lunch (SES; <sup>18</sup>). Within the full sample, 19.9% reported a lifetime suicide attempt, by age 25 while 7.4% met diagnostic criteria for at least one last year episode of MDD in young adulthood. The prevalences of both were higher among females as compared to males (see Table 1). Mean aggression and impulsivity scores at each time-point are reported in Table 1.

#### 4. Class enumeration

Fit statistics for class enumeration in males and females separately are in Table 2. Fit statistics were conflicting for the females, with the LMR value pointing toward a two class model, and the BIC suggested a three class model. When conflicting fit statistics are present in the class enumeration process, we look toward substantive meaning of the latent classes. The third class in the three class model represents a substantively meaningful trajectory, which supported our decision to proceed with a three class model for females. Fit statistics for the male model were less conflicting, with both the LMR and BIC pointing towards a two class model.

#### 5. Aggressive-impulsive trajectories in males

The majority (65%) of males were in a class characterized by low and

Table 1

LPA Indicators	Analytic Sample (mean, SD)	Males (mean, SD)	Females (mean, SD)
Aggression 1st	1.68 (0.87)	1.85 (0.98)	1.49 (0.69)
Aggression 2nd	1.85 (0.99)	2.07 (1.11)	1.61 (0.77)
Aggression 3rd	1.90 (0.94)	2.13 (1.03)	1.66 (0.76)
Aggression 6th	1.83 (0.81)	2.02 (0.90)	1.61 (0.62)
Aggression 7th	1.73 (0.70)	1.90 (0.77)	1.52 (0.54)
Aggression 8th	1.74 (0.69)	1.94 (0.75)	1.50 (0.50)
Aggression 9th	1.67 (0.72)	1.81 (0.78)	1.50 (0.58)
Aggression 10th	1.57 (0.59)	1.68 (0.65)	1.43 (0.47)
Aggression 11th	1.49 (0.53)	1.63 (0.62)	1.34 (0.38)
Aggression 12th	1.44 (0.49)	1.55 (0.57)	1.32 (0.35)
Impulsivity 1st	2.21 (1.18)	2.37 (1.23)	2.03 (1.09)
Impulsivity 2nd	2.32 (1.27)	2.62 (1.36)	1.98 (1.07)
Impulsivity 3rd	2.35 (1.21)	2.57 (1.29)	2.12 (1.08)
Impulsivity 6th	2.38 (1.08)	2.63 (1.10)	2.07 (0.97)
Impulsivity 7th	2.22 (1.03)	2.47 (1.08)	1.92 (0.87)
Impulsivity 8th	2.28 (1.03)	2.59 (1.05)	1.92 (0.88)
Impulsivity 9th	2.17 (1.00)	2.34 (1.05)	1.96 (0.89)
Impulsivity 10th	2.02 (0.97)	2.14 (1.05)	1.88 (0.85)
Impulsivity 11th	1.86 (0.83)	2.01 (0.90)	1.70 (0.72)
Impulsivity 12th	1.76 (0.81)	1.90 (0.90)	1.62 (0.67)
<b>Demographics</b>	<b>Analytic Sample</b>	<b>Males</b>	<b>Females</b>
Race (Black)	85.6% (483)	84.8% (257)	86.6% (226)
Free/reduced lunch	67.7% (382)	69.0% (209)	66.3% (173)
Early Family Adversity	1.60 (1.40)	1.48 (1.34)	1.74 (1.43)
Intervention Status	67.9% (383)	67.8% (209)	66.7% (174)
<b>Outcomes</b>	<b>Analytic Sample</b>	<b>Males</b>	<b>Females</b>
Lifetime suicide attempt, 6th grade through age 25 years	19.9% (112)	16.5% (50)	24.1% (62)
Major Depressive Disorder diagnosis	7.4% (42)	5.9% (18)	9.2% (24)

Note: SD, Standard Deviation; N = 564. Numbers 1st through 12th refer to academic years in the US school system following kindergarten.

Table 2

Mode Fit Statistics for Full Sample Estimating 1 through 5 Aggression and Impulsivity profiles.

MALES Fit measure	Number of Classes				
	1	2	3	4	5
Loglikelihood	-7828.19	-7068.84	-6891.58	-6749.94	-6645.29
# parameters	40	61	82	103	124
BIC	15897.52	14505.40	14277.47	14120.80	14038.08
Entropy	na	0.88	0.83	0.85	0.87
LMR	na	1506.81	351.74	281.05	207.66
LMR p-value	na	<0.001	0.41	0.24	0.53
Smallest class	na	39% (161)	18% (75)	14% (57)	7% (30)
FEMALES Fit measure	Number of Classes				
	1	2	3	4	5
Loglikelihood	-5384.20	-4872.39	-4612.06	-4502.79	-4411.81
# parameters	40	61	82	103	124
BIC	11001.45	10100.17	9701.85	9605.66	9546.05
Entropy	na	0.85	0.86	0.83	0.85
LMR	na	1015.33	516.44	216.77	180.48
LMR p-value	na	0.06	0.25	0.60	0.68
Smallest class	na	31% (107)	6% (21)	6% (19)	5% (18)

stable levels of aggressive behaviors and somewhat higher levels of impulsivity; we refer to this class as the low problem behaviors class (Fig. 1). The peak of aggressive behaviors in this class appeared in third grade whereas the peak of impulsive behaviors appeared in eighth grade. The second class (35%) was characterized by higher overall aggressive and impulsive behaviors, both peaking in second grade and decreasing through adolescence; we refer to this as the higher problem behaviors class.

Baseline free or reduced lunch status was a significant predictor of membership in the higher problem behaviors class (est. = 1.27, S.E. = 0.35,  $p < 0.001$ , OR = 3.56). Race and family adversity did not significantly predict membership in aggressive-impulsive behavior classes. Prevalence of lifetime suicide attempt did not differ significantly across classes (Wald = 1.104,  $p = 0.31$ ) with 21.5% of males in the higher problem behaviors class reporting a lifetime suicide attempt as compared to 13.9% in the low problem behaviors class (Table 3). Males with a MDD diagnosis were significantly more likely to report a suicide attempt (est. = 0.281, S.E. = 0.12,  $p = 0.02$ , OR = 1.32). A separate model with MDD as an outcome was also explored; however, prevalence of meeting diagnostic criteria for MDD also did not significantly differ across aggression and impulsivity behavior classes (Wald = 0.81,  $p = 0.37$ ).

#### 6. Aggressive-impulsive trajectories in females

As shown in Fig. 2, the majority of females (56%) were in the low behaviors class, with low and stable levels of teacher-reported aggressive and impulsive behaviors; we refer to this as the low problem behaviors class. A second class, with 38% of females, was characterized by moderate and stable levels of aggression and somewhat higher but stable levels of impulsive behaviors; we refer to this as the moderate problem behaviors class. Finally, a small but substantively important class (6%) was characterized by higher and undulating levels of aggressive and impulsive behaviors, peaking in sixth and ninth grades; we refer to this as the undulating problem behaviors class.

Among females, there were no statistically significant predictors of class membership, in contrast to the models for males (data not shown). Importantly, aggression and impulsivity behavior class membership was significantly related to lifetime suicide attempt (Wald = 6.01,  $p = 0.05$ ) with 48.5% of the undulating problem behaviors class reporting a lifetime suicide attempt as compared to 28.5% in the moderate problem behaviors class, and 18.9% in the low problem behaviors class (Table 3).

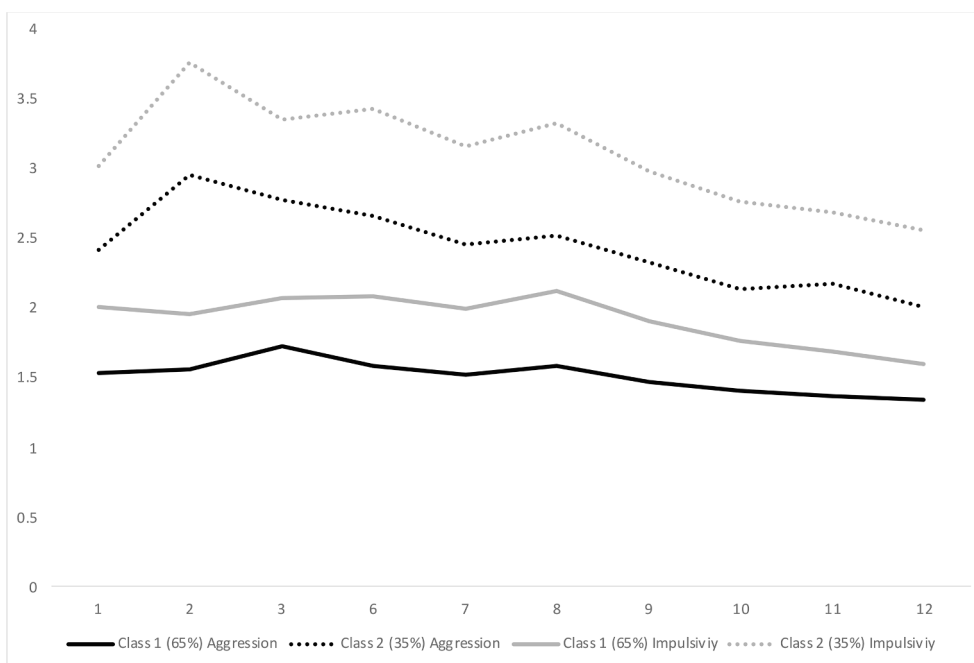


Fig. 1. Two trajectories of aggressive and impulsive behavior found in males. Black colored lines represent the aggressive trajectories in each class while grey colored lines represent the impulsive trajectories in each class.

**Table 3**  
Distal Outcomes across Latent Classes of Aggression and Impulsivity in Adjusted Analyses: Overall Model Statistics and Pairwise Comparisons.

Aggression and Impulsivity Behavior classes	Suicide Attempt Proportion with SA	Major Depressive Disorder Proportion with MDD	
		Model Significance Tests Overall (Wald) and Pairwise (z)	Model Significance Tests Overall (Wald) and Pairwise (z)
<b>Males</b>			
Low problem behaviors	0.139	Wald = 1.10, p = 0.31	Wald = 0.81, p = 0.37
Higher problem behaviors	0.215	–	–
<b>Females</b>			
Low problem behaviors	0.189	Wald = 6.01, p = 0.05	Wald = 4.23, p = 0.12
Moderate problem behaviors	0.285	z = -0.10, p = 0.12 <sup>a</sup>	z = -0.06, p = 0.17 <sup>a</sup>
Undulating problem behaviors	0.485	z = -0.31, p = 0.05 <sup>a</sup>	z = -0.21, p = 0.23 <sup>a</sup>

Notes: MDD, Major Depressive Disorder in young adulthood (between ages 19 and 25 years); SA, suicide attempt between 6th grade through age 25 years. <sup>a</sup>Low problem behaviors class serving as the reference class.

Along with the standard covariates, a MDD diagnosis was also explored as a predictor of suicide attempt (est. = 0.20, S.E. = 0.10, p = 0.06, OR = 1.2), which showed that females with a MDD diagnosis were marginally more likely to also have a suicide attempt. Similar, albeit non-significant, results were found with meeting diagnostic criteria for MDD (Wald = 4.23, p = 0.12) with 25.8% in the undulating problem behaviors class, 11.6% in the moderate problem behaviors class, and 5.9% in the low problem behaviors class meeting criteria.

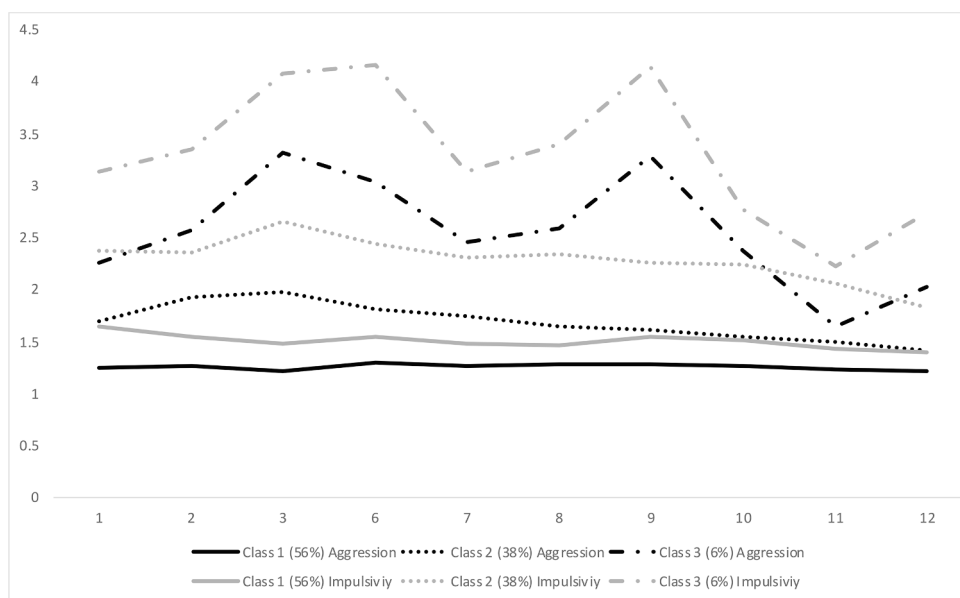
7. Discussion

In a longitudinal, community sample of youth followed from childhood through adolescence and into young adulthood, latent profiles of teacher-reported impulsivity and aggression were significantly associated with lifetime suicide attempt by young adulthood in females but not males. Specifically, nearly half of the females with the highest impulsivity and aggression levels, peaking in sixth and ninth grade, reported suicide attempt between 6th grade and age 25. Impulsive-aggressive trajectories did not predict MDD diagnosis in young adulthood in either sex, although MDD diagnosis was significantly associated with suicide attempt in males and marginally so among females. Results underscore the importance of stratification by sex in analyses examining suicide attempts, as well as potential avenues for early recognition and intervention with aggressive and impulsive behaviors among females following elementary school.

Of particular note, this analysis was conducted in a community sample of children and adolescents who were over 80% Black. Historically, rates of Black suicide were lower than that of white individuals in the United States, but recent data suggests that this gap is closing (Caucas CB, 2019). In particular, recent increases in suicide rates in Black youth may be related to a specific increase in suicide in earlier stages of childhood (aged 12 and under) in Black communities. Importantly, Black child suicide decedents were more likely to be diagnosed with attention deficit disorders and less likely to be diagnosed with depression than Black adolescent suicide decedents, suggesting possible underlying influences of impulsivity in these deaths as well as highlighting a potential precursor of severe clinical course (Sheftall et al., 2016; Nurnberger et al., 2011; Duffy et al., 2019).

Similar to national data estimates (Ivey-Stephenson et al., 2020), our study found higher prevalence of lifetime suicide attempt among females than males. Reasons for this finding are multifaceted, but it is consistent with a recent study by Lindsey and colleagues (2019) which highlights the growing trend of increased suicide attempts among Black adolescent girls despite downward trends from female adolescents in other racial and ethnic groups (Lindsey et al., 2019). Our findings may be related to the documented disparities in treatment for aggression and impulsivity among Black adolescents, which may lead to more





**Fig. 2.** Three trajectories of aggressive and impulsive behavior found in females. Black colored lines represent the aggressive trajectories in each class while grey colored lines represent the impulsive trajectories in each class.

psychological distress over time (Oliver et al., 2016). Our findings also highlight the need for additional research on externalizing and internalizing behavior by sex, racial and ethnic background as well as a potential avenue for prevention by training teachers to recognize early aggressive and impulsive behavior among girls.

It is also important to note that the sample consisted of school children from a specifically defined geographic area of Baltimore, so that patterns of aggression and impulsivity could be detected within this particular community by teachers working within the school system. It may be that, compared to school-based reporting from teachers, Black females may contradict clinical presentations of DSM criteria for problematic externalized behavior in the healthcare setting, leading to fewer diagnoses, treatment options, and subsequent suicidal behavior compared to their male counterparts. Additionally, in contrast with Black boys, this suicide attempt endophenotype may represent a 'cry for help' or a more severe form of distress among females that requires early intervention to prevent further psychological distress associated with suicidal behavior. Taken together, our findings support further investigation of combined sex and racial/ethnic group differences in suicidal behavior within the Black population. Such studies could transition to examine gender norms related to aggression and impulsivity to disentangle differential clinical and community responses between Black boys and girls (Bath and Njoroge, 2021). To date, few studies examine the role of suicide endophenotypes from an intersectional lens, which suggests a critical path forward in future suicide prevention research (Standley, 2022).

The results of this study suggest that aggressive and impulsive behaviors during childhood and adolescence may offer a unique avenue for intervention, particularly for females. Although suicide prevention programs during high school exist, more work should be focused on adapting and developing evidenced based suicide prevention programs during middle school in addition to the scaling up of programs targeting aggressive, disruptive behaviors in elementary school (Musci et al., 2016). Critically, our findings did not support a relationship between impulsivity/aggression trajectories and MDD diagnosis. Suicide prevention efforts in schools often focus on identification of depressive symptoms (Horowitz et al., 2009), which may not be sufficient for adequate detection.

It is important to note the current study's limitations. This sample was collected as part of a large, randomized control trial testing the

efficacy of two school-based interventions targeting disruptive behavior in first grade classrooms. While we did adjust for intervention status in analyses, we did not fully explore the impact of the intervention as it was outside the scope of the current paper and such analyses would likely be underpowered. Research has, however, demonstrated a significant impact of the classroom based prevention program on suicide ideation in an earlier, larger cohort. (Gvion and Apter, 2011) Future work with larger datasets will explore the relationship between the intervention, aggressive/disruptive behavior, and risk for suicide attempt. Finally, no significant association was found between aggressive/impulsive behaviors and suicide attempt in males. There is a possibility that this lack of association is due to power as suicide attempt was not as prevalent in males as it was in females. Low base rates of suicide attempt in community-based samples likely require larger sample sizes in order to explore these complex relationships.

There are a number of strengths to the current study. First, many studies exploring suicidality among adolescents and emerging adults are clinical in nature. The current study used a community-based sample and therefore the results can be generalized outside of those receiving clinical treatment (Merikangas et al., 2011). Additionally, the longitudinal nature of the analysis and collection of data on suicide attempt each year starting in 6th grade allows us to identify change in aggressive and impulsive behaviors across time and how they relate to suicide attempt and young adult diagnosis of depression. Finally, although suicide attempt was a self-report measure, aggressive and impulsive behaviors were reported by teachers during middle school and high school, which strengthens the results with the multiple sources of reporting.

The results of this study suggest that aggressive and impulsive endophenotypes for suicide attempt appear to be present for females who are part of an urban, predominately Black population. This offers a possible avenue for intervention, as school-based identification of and support services for aggressive and impulsive behaviors during adolescence may result in decreased risk for suicide attempt in females<sup>nn</sup>. Future work should focus on elucidating possible endophenotypes for suicide attempts in males. With suicide as the second leading cause of death among adolescents and young adults, identifying mechanisms for suicide risk as well as possible avenues for prevention and intervention programs should remain a priority among researchers and clinicians.

## Ethical approval

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

## Informed consent

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

## 10. Funding statement

This study was supported by NIH MH122214 to RJM and HCW, HD093643 to RJM, and NIH MH57005 and DA11796 to NSI.

## 11. Disclaimer

The views expressed in this article do not necessarily represent the views of the National Institutes of Health, the Department of Health and Human Services, or the United States Government.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## References

- Heron, M., 2019. Deaths: Leading Causes for 2017. *Natl. Vital. Stat. Rep.* 68 (6), 1–77.
- Hedegaard HC, SC, Warner M. 2021. Suicide Mortality in the United States, 1999–2019. National Center for Health Statistics.
- Hedegaard, H., Curtin, S.C., Warner, M., 2020. Increase in Suicide Mortality in the United States, 1999–2018. *NCHS Data Brief.* 362, 1–8.
- Ruch DA, Sheftall AH, Schlagbaum P, Rausch J, Campo JV, Bridge JA. 2019. Trends in Suicide Among Youth Aged 10 to 19 Years in the United States, 1975 to 2016. *JAMA Netw Open.* 2(5):e193886.
- Turecki, G., Ernst, C., Jollant, F., Labonte, B., Mechawar, N., 2012. The neurodevelopmental origins of suicidal behavior. *Trends Neurosci.* 35 (1), 14–23. Epub 2011 Dec 2015.
- U.S. Department of Health and Human Services (HHS) 2012 National Strategy for Suicide Prevention: Goals and Objectives for Action. 2012. Office of the Surgeon General and National Action Alliance for Suicide Prevention. In. Washington, DC: HHS.
- Wilcox, H.C., Kellam, S.G., Brown, C.H., Poduska, J.M., Ialongo, N.S., Wang, W., Anthony, J.C., 2008. The impact of two universal randomized first- and second-grade classroom interventions on young adult suicide ideation and attempts. *Drug Alcohol Depend.* 95, S60–S73.
- Gvion, Y., Apter, A., 2011. Aggression, impulsivity, and suicide behavior: a review of the literature. *Arch Suicide Res.* 15 (2), 93–112.
- Romer, D., 2010. Adolescent risk taking, impulsivity, and brain development: implications for prevention. *Dev. Psychobiol.* 52 (3), 263–276.
- Dumais, A., Lesage, A.D., Lalovic, A., Séguin, M., Tousignant, M., Chawky, N., Turecki, G., 2005. Is violent method of suicide a behavioral marker of lifetime aggression? *Am. J. Psychiatry.* 162 (7), 1375–1378.
- Brent, D.A., Melhem, N.M., Oquendo, M., Burke, A., Birmaher, B., Stanley, B., Biernesser, C., Keilp, J., Kolko, D., Ellis, S., Porta, G., Zelazny, J., Iyengar, S., Mann, J.J., 2015. Familial pathways to early-onset suicide attempt: a 5.6-year prospective study. *JAMA Psychiatry.* 72 (2), 160.
- Waltes, R., Chiocchetti, A.G., Freitag, C.M., 2016. The neurobiological basis of human aggression: A review on genetic and epigenetic mechanisms. *Am. J. Med. Genet. Part B, Neuropsych. Genet. Off. Publicat. Int. Soc. Psychiat. Genet.* 171 (5), 650–675.
- Mann, J.J., Arango, V.A., Avenevoli, S., Brent, D.A., Champagne, F.A., Clayton, P., Currier, D., Dougherty, D.M., Haghghi, F., Hodge, S.E., Kleinman, J., Lehner, T., McMahon, F., Mościcki, E.K., Oquendo, M.A., Pandey, G.N., Pearson, J., Stanley, B., Terwilliger, J., Wenzel, A., 2009. Candidate endophenotypes for genetic studies of suicidal behavior. *Biol. Psychiatry* 65 (7), 556–563.
- Horowitz, L.M., Ballard, E.D., Pao, M., 2009. Suicide screening in schools, primary care and emergency departments. *Curr. Opin. Pediatr.* 21 (5), 620–627.
- King, C.A., Jiang, Q., Czyz, E.K., Kerr, D.C., 2014. Suicidal ideation of psychiatrically hospitalized adolescents has one-year predictive validity for suicide attempts in girls only. *J. Abnorm. Child. Psychol.* 42 (3), 467–477.
- Caucas CB. 2019. Ring the Alarm: The Crisis of Black Youth Suicide in America, A Report to Congress from The Congressional Black Caucus Emergency TaskForce on Black Youth Suicide and Mental Health.
- Ialongo, N.S., Werthamer, L., Kellam, S.G., Brown, C.H., Wang, S., Lin, Y., 1999. Proximal impact of two first-grade preventive interventions on the early risk behaviors for later substance abuse, depression, and antisocial behavior. *Am. J. Commun. Psychol.* 27 (5), 599–641.
- Ensminger, M.E., Forrest, C.B., Riley, A.W., Kang, M., Green, B.F., Starfield, B., Ryan, S.A., 2000. The validity of measures of socioeconomic status of adolescents. *J. Adolescent Res.* 15 (3), 392–419.
- Werthamer-Larsson, L., Kellam, S., Wheeler, L., 1991. Effect of first-grade classroom environment on shy behavior, aggressive behavior, and concentration problems. *Am. J. Commu. Psychol.* 19 (4), 585–602.
- Petrus, H., Masyn, K., Ialongo, N., 2011. The developmental impact of two first grade preventive interventions on aggressive/disruptive behavior in childhood and adolescence: an application of latent transition growth mixture modeling. *Prevent. Sci. Off. J. Soc. Prevent. Res.* 12 (3), 300–313.
- Shaffer, D., Fisher, P., Lucas, C.P., Dulcan, M.K., Schwab-Stone, M.E., 2000. NIMH Diagnostic Interview Schedule for Children Version IV (NIMH DISC-IV): description, differences from previous versions, and reliability of some common diagnoses. *J. Am. Acad. Child Adolesc. Psychiatry* 39 (1), 28–38.
- Masyn, K.E., 2013. Latent Class Analysis and Finite Mixture Modeling. In: Little, T.D. (Ed.), *The Oxford Handbook of Quantitative Methods: Statistical Analysis.* Oxford University Press, Oxford, pp. 551–611.
- Nylund-Gibson, K., Grimm, R.P., Masyn, K.E., 2019. Prediction from Latent Classes: A Demonstration of Different Approaches to Include Distal Outcomes in Mixture Models. *Struct. Eq. Model.-a Multidiscipl. J.* 26 (6), 967–985.
- Muthen, L., Muthen, B.O., 2017. *Mplus User's Guide, Eighth Edition.* Muthen & Muthen, Los Angeles, CA.
- Sheftall, A.H., Asti, L., Horowitz, L.M., Felts, A., Fontanella, C.A., Campo, J.V., Bridge, J.A., 2016. Suicide in Elementary School-Aged Children and Early Adolescents. *Pediatrics* 138 (4).
- Nurnberger Jr., J.I., McInnis, M., Reich, W., et al., 2011. A high-risk study of bipolar disorder. Childhood clinical phenotypes as precursors of major mood disorders. *Arch. Gen. Psychiatry* 68 (10), 1012–1020.
- Duffy, A., Goodday, S., Keown-Stoneman, C., Grof, P., 2019. The Emergent Course of Bipolar Disorder: Observations Over Two Decades From the Canadian High-Risk Offspring Cohort. *Am. J. Psychiatry* 176 (9), 720–729.
- Ivey-Stephenson, A.Z., Demissie, Z., Crosby, A.E., et al., 2020. Suicidal Ideation and Behaviors Among High School Students - Youth Risk Behavior Survey, United States, 2019. *MMWR Suppl.* 69 (1), 47–55.
- Lindsey MA, Sheftall AH, Xiao Y, Joe S. Trends of Suicidal Behaviors Among High School Students in the United States: 1991-2017. *Pediatrics.* 2019;144(5).
- Oliver DG, Caldwell CH, Faison N, Sweetman JA, Abelson JM, Jackson JS. Prevalence of DSM-IV intermittent explosive disorder in Black adolescents: Findings from the National Survey of American Life, Adolescent Supplement. *Am. J. Orthopsych.* 2016; 86(5):552-563.
- Bath, E., Njoroge, W.F.M., 2021. Coloring Outside the Lines: Making Black and Brown Lives Matter in the Prevention of Youth Suicide. *J. Am. Acad. Child Adolesc. Psychiatry* 60 (1), 17–21.
- Standley, C.J., 2022. Expanding our paradigms: Intersectional and socioecological approaches to suicide prevention. *Death Stud.* 46 (1), 224–232.
- Musci, R.J., Hart, S.R., Ballard, E.D., Newcomer, A., Van Eck, K., Ialongo, N., Wilcox, H., 2016. Trajectories of Suicidal Ideation from Sixth through Tenth Grades in Predicting Suicide Attempts in Young Adulthood in an Urban African American Cohort. *Suicid. Life-Threaten. Behav.* 46 (3), 255–265.
- Merikangas, K.R., He, J.-P., Burstein, M., Swendsen, J., Avenevoli, S., Case, B., Georgiades, K., Heaton, L., Swanson, S., Olfson, M., 2011. Service utilization for lifetime mental disorders in U.S. adolescents: results of the National Comorbidity Survey-Adolescent Supplement (NCS-A). *J. Am. Acad. Child Adolesc. Psychiatry* 50 (1), 32–45.