








## NEW RESEARCH

# Developmental Trajectories of Autistic Social Traits in Youth Born Extremely Preterm

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**Objective:** Autistic social traits (ASTs), evident in the general population, are associated with mental health challenges. ASTs have not been evaluated in youth born extremely preterm (EP), despite their increased prevalence of autism. The current research evaluates AST change from 10 to 17 years in a well-characterized sample of EP youth, including sex differences and associations with health and quality of life.

**Method:** Participants included 527 EP youth ( $n = 275$  female, 67.8% White), assessed at 10 and 17 years, from the Extremely Low Gestational Age Newborn (ELGAN) Study. Adolescents were born at an average of 26 weeks gestation. ASTs were parent-reported via the Social Responsiveness Scale at 10 and 17 years. Adolescents self-reported quality of life, health, and psychopathology at 17 years. AST change scores were calculated to evaluate change over time. AST change scores and increasing, decreasing, and stable trajectories were analyzed in relation to sex and quality-of-life scores.

**Results:** ASTs in EP youth increased an average of 19 raw points from age 10 to 17 years, reflecting a change of 8 standardized points and a change in qualitative description from the “normal” to “mild concern” range. The majority of youth (70%) exhibited an “Increasing” trajectory, reflecting increasing AST as a preterm phenotype. No sex differences emerged in AST change score or trajectory group. Higher AST change scores were associated with worse adolescent-reported health, self-esteem, and externalizing psychopathology.

**Conclusion:** Increasing ASTs were consistent in this sample of EP youth. Increases in ASTs were not associated with child's sex or demographics, suggesting a unique preterm phenotype of social trajectories. These findings have implications for quality of life as adolescents enter young adulthood.

**Key words:** preterm youth; autistic social traits; sex differences; Social Responsiveness Scale

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**A** growing body of literature suggests and supports evidence of chronogeneity in autism spectrum disorder (hereafter referred to as “autism”) or, in other words, heterogeneity over time within and across individuals.<sup>1</sup> Patterns of chronogeneity have been observed for individuals who experience an attenuation of autistic traits<sup>2</sup> or late-emerging autistic traits.<sup>3</sup> These discrepant developmental pathways have resulted in a call to researchers for large, general population studies of autistic traits with the following aims: (1) to improve the quality of the evidence base about autistic trait trajectories, (2) to reduce the omnipresent male bias observed in autism studies,<sup>4,5</sup> and (3) to evaluate the relationship between autistic trait trajectories and quality of life outcomes.<sup>6</sup> The current study sought to address this research gap by evaluating longitudinal developmental trajectories of autistic traits and their relations with demographics, quality of life, and mental health in a novel and understudied sample of youth born extremely preterm.

## Autistic Social Traits Over Time

Autistic social traits (ASTs) have frequently been studied longitudinally in clinical samples of autistic individuals. ASTs have been studied using the Social Responsiveness Scale, 2nd edition (SRS-2)<sup>7</sup> from age 2 to 29 years, with demonstrated trait-like stability from preschool through adulthood.<sup>8</sup> These findings have been replicated in numerous other works suggesting a lack of significant change in ASTs over time in autistic youth (eg, ages 12-23 years).<sup>9</sup> Because autism is a lifelong neurodevelopmental condition, it is generally expected that ASTs remain somewhat stable, or at least in the clinical range, across the lifespan in diagnosed individuals, although the presentation or type of ASTs may change.<sup>9</sup> However, buried within this overarching “trait-like stability” are important sex-related findings, including distinct patterns of ASTs over time, among autistic female individuals, as measured by both parents and teachers, demonstrating an inverted “U” pattern that peaks around age 10 years and decreases by age

20 years.<sup>8</sup> Paired with the viewpoint that autism can be considered a dimensional condition extending across the general population with no natural cut-point,<sup>10,11</sup> it stands to reason that evaluating ASTs in the general population may reveal more nuanced insights into the sex differences of neurodevelopmental trajectories and related behaviors.

ASTs have high clinical relevance, as they are related to mental health concerns including social anxiety,<sup>12</sup> attention difficulties,<sup>13</sup> depression,<sup>14</sup> and other emotional and behavioral concerns.<sup>15</sup> ASTs emerge later in female compared to male individuals, suggesting a sex-based contextual-developmental trajectory with implications for the identification of autism in female individuals and delayed access to supports.<sup>16,17</sup> Previous research has evaluated ASTs in the general population with findings contrary to those observed when investigating clinical groups. Two studies from the Avon Longitudinal Study of Parents and Children<sup>18,19</sup> evaluated ASTs longitudinally in the general population at ages 7, 10, 13, and 16 years. Results from Mandy *et al.* indicated that male individuals had higher ASTs than female individuals between the ages of 7 and 10 years. However, this sex difference was no longer present at 16 years of age because of a rapid increase in ASTs observed in female individuals. Using a growth mixture modeling approach, Pender *et al.*<sup>19</sup> extended these results by identifying 4 distinct patterns of AST trajectories over time, including Persistently Low, Persistently High, Increasing, and Decreasing trajectories. Although the Persistently High and Persistently Low groups were sex balanced, female individuals comprised the majority of the Increasing trajectory, suggesting sharp increases in ASTs for female individuals in the general population between the ages of 10 and 16 years, with concurrent increases in socio-emotional behavioral concerns. In contrast, male individuals comprised the majority of the Decreasing trajectory group, suggesting a decline in ASTs from 10 to 16 years. The authors concluded that for some female individuals, ASTs may emerge later than for male individuals, which drives subsequent emotional and behavioral risk in female individuals.

ASTs have well-documented connections to mental health in autistic individuals<sup>20</sup>; however, little work has evaluated the connection between ASTs and mental health in the general population. Recent investigations in non-autistic adults (aged 18-50 years) evidenced negative associations between broader autism phenotype and mental well-being, wherein higher self-reports of autistic traits was linked to decreased mental well-being after controlling for extraversion, neuroticism, depression, and physical health.<sup>21</sup> Somerville *et al.*<sup>22</sup> replicated these findings, evidencing associations between autistic traits and increased

symptoms of poorer mental health in non-autistic adults; however, this association was null after controlling for camouflaging behaviors (eg, efforts to mask autistic traits).<sup>22</sup> The previous literature provides some evidence that ASTs are connected to global mental health outcomes in adults, which may be mediated by other behavioral factors. Notably, no work has evaluated ASTs in adolescents: specifically, how AST changes over time are related to mental health and quality of life.

These general population longitudinal studies have revealed sex-specific developmental trajectories of ASTs that have impeded identification of female individuals and their quality of life. These studies have focused generally on youth born full-term with limited medical complications or co-occurring conditions, leaving youth born extremely preterm outside the scope of these research inquiries.

### Youth Born Extremely Preterm

Youth born extremely preterm (EP; <27 weeks' gestation) occupy an interesting domain of both theoretical and practical significance, as their neurodevelopment in utero was disrupted. Accordingly, EP youth are at an elevated likelihood of receiving an autism diagnosis ranging from a 10-fold increase (gestational weeks 23-27) to a 2-fold increase (32+ weeks) in likelihood compared to infants born full term.<sup>23</sup> Prevalence rates of autism in EP youth are estimated at 7%,<sup>24-26</sup> which is significantly higher than prevalence estimates observed in full-term youth (~2.7%).<sup>27</sup> Furthermore, the sex ratio for autism prevalence in EP youth (2:1)<sup>25,26</sup> is significantly lower than the sex ratio observed in full-term youth (3.8:1),<sup>27</sup> suggesting a different sex-based developmental trajectory unique to this subgroup of EP youth.

Given the elevated risks of neurodevelopmental disorders and medical complications in EP youth, it is not surprising that EP youth demonstrate higher ASTs compared to full-term youth in both autistic samples<sup>28</sup> and the general population.<sup>29</sup> Using SRS-2-defined cut-offs for social impairment, EP youth who do not meet diagnostic criteria for autism still score in the clinical range at much higher rates than general population norms would indicate at age 10 years, which has been described as a preterm phenotype.<sup>29</sup> Indeed, common pregnancy complications observed in preterm births have been related to child ASTs, not only in youth above the diagnostic threshold for autism but across the general population.<sup>30</sup> Beyond the narrow conceptualization of ASTs, EP youth are at particularly high risk for social difficulties. Results from a systematic review indicated that EP adolescents in 16 of the included 20 studies demonstrated significant difficulties with peer interactions and higher rates of social withdrawal.<sup>31</sup> Taken

together, EP youth present with wide heterogeneity of neurodevelopmental phenotypes and social competence, regardless of autism classification or diagnosis, thus representing a unique subgroup in whom to evaluate the chronicity of ASTs.

### Current Study

In the present study, we evaluated change in ASTs from 10 to 17 years in a longitudinal sample of EP youth born at 23 to 27 weeks' gestation from the Extremely Low Gestational Age Newborn (ELGAN) Study. The specific aims were as follows: (1) to evaluate change in ASTs from 10 to 17 years observed in EP youth, including data-driven trajectory groups; (2) to evaluate sex differences in AST changes in EP youth from 10 to 17 years; and (3) to investigate associations between AST changes and mental health and quality of life at 17 years in EP youth.

We predicted the following: (1) there would be high heterogeneity in change scores, ranging from individuals who would experience attenuations, no changes, and augmentations in ASTs over time; (2) female individuals would show larger AST change scores than male individuals, and increased AST from 10 to 17 years; and (3) larger AST change scores, reflecting an increase in ASTs over time, would be related to poorer mental health and lower quality of life at 17 years of age, as measured by adolescent self-report.

## METHOD

### Data Source

The ELGAN Study is an observational study designed to identify characteristics and developmental trajectories of EP infants. During the years 2002 to 2004, women delivering before 28 weeks gestation at one of 14 participating institutions in 11 cities in 5 US states were invited to enroll in the study. A total of 1,506 infants born to 1249 mothers were enrolled, and 1,198 survived to age 10 years. Among survivors, 1,102 participated in an assessment when they were approximately 24 months of age, 889 were evaluated at 10 years, 700 were evaluated at age 15 years, and 566 (47.2% of surviving members) were evaluated at 17 years. Participants who continued to be seen through 17 years of age were significantly different from those who were lost to follow-up. Participants retained in the longitudinal study were more likely to be female and to have a higher IQ; mothers retained in the study through the 17-year time point were more likely to be White, older, married, and to have higher educational attainment, and were less likely to be enrolled in Medicaid. A detailed demographic comparison of the retained sample compared to attrition

samples is provided in Table S1, available online. Procedures for this study were approved by the institutional review boards of participating institutions.

### Participants

Participants with complete data at age 10 and 17 years were included, which comprised 527 participants (275 female). Adolescents were born at an average of 26 weeks' gestation ( $SD = 1.25$ ), with an average birthweight z score of  $-0.16$  ( $SD = 1.11$ ). Parents identified their child as White (67.8%), Black (23.8%), or another race (8.4%). Mothers were an average of 29.6 years of age ( $SD = 6.6$ ), with 31.0% on Medicaid, 67.7% married, and 40.6% college graduates. Participant demographics are available in Table 1.

### Measures

**Demographics.** A trained research nurse interviewed mothers after birth using a standard demographic interview form. Among mothers, maternal variables included education, marital status, eligibility for government-provided medical care insurance, and racial and ethnic identity. Infant characteristics, including gestational age

**TABLE 1** Demographics of Study Sample (N = 527)

	Mean or count (SD/%)
Sex, female	275 (52.2%)
Gestational age	26.0 (1.25)
Birthweight Z-score	-0.16 (1.11)
Full Scale IQ	101 (17.9)
Maternal age	29.6 (6.59)
Maternal education	
Less than high school	60 (11.6%)
High school graduate/GED	124 (24.0%)
Some college	123 (23.8%)
College graduate	117 (22.6%)
Masters or doctorate education	93 (18.0%)
Medicaid status	
No	360 (69%)
Yes	162 (31%)
Maternal marital status	
Married	357 (67.7%)
Separated or divorced	22 (4.17%)
Not ever married but living together	77 (14.6%)
Not ever married and not living together	70 (13.3%)
Maternal race	
Black	124 (23.8%)
Other	44 (8.4%)
White	354 (67.8%)

**Note:** GED = General Education Development; IQ = intelligence quotient.

and birthweight  $z$  score, were defined according to standard procedures. Gestational age estimates were based on a hierarchy of the quality of available information, ranging from dates of embryo retrieval or fetal ultrasound before the 14th week (62%), fetal ultrasound at 14+ weeks (29%), or other medical records (8%). The birthweight  $z$  score represents the number of standard deviations in the infant's birthweight above or below the median weight of infants at the same gestational age.

### Autistic Social Traits

**Social Responsiveness Scales (SRS and SRS-2).** The SRS<sup>7</sup> and SRS-2<sup>32</sup> are the first and second editions, respectively, of a parent-report measure used to assess autistic social traits. Autism characteristics are rated by parents in 5 domains: social communication, social motivation, social cognition, social awareness, and restricted/repetitive behaviors and interests (called "autistic mannerisms" in the original SRS). In addition to subscale scores, the SRS and SRS-2 generate a total score as a continuous measure of severity from 0 to 195. The SRS-2 school-age form is identical to the original SRS in terms of items and subscales,<sup>33</sup> and both versions have been used previously in longitudinal studies for direct comparisons of this sort.<sup>9</sup> The SRS was administered to the study participant's parent at age 10 years; the SRS-2 was administered to the study participant's parent at age 17 years. SRS raw scores were used so as not to pre-adjust for sex differences<sup>34</sup> and to address any norming differences between the 2 versions.<sup>9</sup> SRS respondents at age 10 years were 90% biological mothers, 6.3% biological fathers, and 2.7% other caregivers. Respondents at age 17 years were 72.5% biological mothers, 7% biological fathers, 2.7% other caregivers, and missing for 17.8% of youth.

### 17-Year Quality of Life Outcomes

**Harter Global Self Worth Scale: Adolescent Self Report.** The Self-Perception Profile for Adolescents<sup>35</sup> is an adolescent self-concept measure that assesses 9 domains of adolescence: scholastic competence, athletic competence, social competence, physical appearance, behavioral conduct, close friendships, romantic appeal, job competence, and the final domain of global self-worth (or self-esteem). The probands completed the Global Self Worth scale at age 17 years. The Global Self Worth scale comprises 5 items scored on a 4-point Likert scale (1-4), where scores of 1 indicate lower feelings of competency and scores of 4 indicate higher feelings of competency.

**PROMIS Measures.** The Patient-Reported Outcomes Measurement Information System (PROMIS) is a National

Institutes of Health initiative to develop measures to assess overall wellbeing and health.<sup>36</sup> Three PROMIS measures were administered to the proband participant at the 17-year visit to capture quality of life: Global Health, Life Satisfaction, and Meaning and Purpose. All PROMIS measures were Pediatric Self Report forms for ages 8 to 17 years. A score of 50 is considered average for the US general population, with a standard deviation of 10.<sup>37</sup> A higher PROMIS  $T$  score represents more of the concept being measured; in other words, higher  $T$  scores in Global Health, Life Satisfaction, and Meaning and Purpose indicate above-average feelings in those domains.

The PROMIS Global Health (v1.2) instrument comprises 10 global health items that represent 5 core domains of physical and mental health (physical function, pain, fatigue, emotional distress, and social health).<sup>38</sup> The PROMIS Pediatric Life Satisfaction scale assesses one's cognitive evaluation of life experiences and whether one likes his/her life with 42 items over a 4-week rating period. Finally, the PROMIS Meaning and Purpose Pediatric Self Report<sup>39</sup> assesses one's sense of purpose and reasons for living using 44 items. Higher scores indicate higher levels of hopefulness, optimism, goal-directedness, and feeling that one's life is worthwhile.

**Youth Self Report (11-18 years).** The Youth Self Report (YSR) 11-18<sup>40</sup> is a standardized, self-report measure of emotional and behavioral problems that is a complement to the parent-reported Child Behavior Checklist. The YSR was administered during the participant's 17-year visit. Using a 3-point scale, youth rate agreement with 119 items (0 = not true, 2 = very/often true). Raw scores are transformed to  $T$  scores (mean = 50, SD = 10) to allow comparisons across ages and sex. The YSR generates several domain  $T$  scores; of interest for the current investigation were the broadband Internalizing and Externalizing Behaviors Scales. Internalizing behaviors comprise anxious, depressed, withdrawn, and somatic behaviors. Externalizing behaviors comprise attention problems, rule breaking, social problems, and aggressive behaviors.

### Data Analytic Plan

Missing data included maternal education (10; 1.9%), Medicaid status (5; 0.95%), maternal race (5; 0.95%), and informant at T2 (94; 17.8%) (Table 1). Only those individuals with complete SRS data were included in the current study. As all missingness values were related to demographic factors, no missingness calculations were required to estimate cells or values in the primary analyses described below. Sensitivity analyses investigating trajectory group differences were conducted only with

complete informant data (82.2% of total sample) (Table S2, available online). The sensitivity analyses conducted only with participants with complete respondent data did not differ from the results presented in the current article.

For the first aim, to evaluate change in SRS scores from 10 to 17 years, paired-samples *t* tests were conducted with the SRS total and domain raw scores at 10 years and SRS-2 Total Raw score at 17 years. AST change scores were also calculated by subtracting the 10-year SRS Total Raw score from the 17-year SRS-2 Total Raw Score to create a difference score. A positive AST change score indicated an increase in SRS scores over time, whereas a negative AST score indicated a decrease in SRS scores over time. To evaluate AST trajectories, participants were grouped based on AST change into the following groups: Decreasing, Stable, and Increasing trajectories. Participants were grouped based on whether their change score fell within  $\pm 0.5SD$  of the sample average SRS change score ( $S = 22.6$  points). In other words, participants with change scores from  $-11.3$  to  $11.3$  were grouped in the “stable” trajectory; those with more than  $11.3$  points increase were grouped in “Increasing”; and those with more than  $11.3$  points decrease were grouped in “Decreasing.” This grouping range of half a standard deviation was chosen to optimize group size for each of the 3 groups and to ensure clinically meaningful relevance for the groups.  $\chi^2$  Tests and *t* tests were used to assess demographic differences among the 3 trajectory groups, and SRS score differences between 10 and 17 years.

For the second aim, to evaluate sex differences in AST changes, an independent sample *t* test was conducted with assigned sex at birth (0 = male, 1 = female) as the predictor and AST change score as the dependent variable. Sex differences in AST trajectory groups (proportion of female individuals in each group) were evaluated using  $\chi^2$  tests.

For the third aim, to evaluate concurrent relations between AST change and mental health and quality of life at 17 years, Pearson correlations were conducted between the calculated AST change score and youth self-reported quality of life measures. Subsequent exploratory analyses were conducted with AST trajectory groups to evaluate whether significant differences emerged in quality of life between trajectory groups. Kruskal–Wallis tests of significance were used to detect significant group differences in the 6 dependent measures of quality of life across the 3 trajectory groups. This statistical approach was used because of the non-normal distribution of the data and the unbalanced cell sizes of trajectory groups.

## RESULTS

### Autistic Social Traits Over Time

Total AST traits increased, on average, by 19 raw points from age 10 years (mean = 38) to age 17 years (mean = 57.17), representing a change of approximately 7 (male) or 8 (female) standardized points and a change in qualitative description from the within-normal ranges at 10 years (*T* scores = 52 [male] or 54 [female]) to mild concern range at 17 years (*T* scores = 59 [male], 62 [female]). The increase in overall ASTs from 10 to 17 years was significant ( $t_{526} = -19.471$ ,  $p < .001$ ). In addition, 4 of the 5 SRS/SRS-2 subscales demonstrated significant increases over time (social communication, social awareness, social motivation, social cognition), whereas the repetitive/restricted behavior index (previously called autistic mannerisms) demonstrated a significant decrease over time. Relative change scores for each SRS subscale were also calculated to determine the amount of change contributing to the total change by each subscale. The relative change scores were calculated by dividing the average change score of each subscale by the number of available items on that subscale (Table 2). Relative change scores were subjected to Wilcoxon paired *t* tests, which revealed significantly different relative contributions: social awareness was significantly higher than the other 4 subscales (relative change = 0.59,  $p$  values  $< .001$ ), and repetitive/restricted behaviors was significantly lower than the other 4 subscales (relative change = 0.12,  $p$  values  $< .001$ ). The second highest relative change score, social motivation (0.39) was significantly higher than social communication (0.33) ( $p = .004$ ), but equivalent to social cognition (0.37) ( $p = .999$ ); social cognition (0.37) and social communication (0.33) were not significantly different ( $p = .135$ ). Mean SRS scores at 10 and 17 years are reported in Table 2, including paired-samples *t* test statistics to indicate whether the change reached statistical significance.

From their AST change score, participants were subsequently grouped into Decreasing, Stable, and Increasing trajectory groups based on their deviation from the average AST change score (mean = 19.17 raw points,  $SD = 22.6$  points). The Increasing trajectory group was the largest ( $n = 368$ ), followed by Stable ( $n = 115$ ), and Decreasing ( $n = 44$ ). Individual SRS changes from 10 to 17 years, color-coded by trajectory group, are depicted in a spaghetti plot in Figure S1, available online. The 3 trajectory groups were compared on demographic factors: the 3 trajectory groups were not significantly different in terms of proportion of female individuals, gestational age, birthweight *z* score, maternal age, or maternal marital status, nor were they different in the proportion of same



**TABLE 2** Autistic Social Trait Mean Change Scores

	Entire sample (N = 527)					Sex differences (n = 275 female, n = 252 male)		
	10 y	17 y	Change score	Relative change (no. of items)	t	Female change score	Male change score	t
Total autistic traits	38.00	57.17	19.17	—	−19.471***	19.73	18.56	0.595
Social awareness	6.18	10.75	4.57	0.59 (8)	−28.101***	4.61	4.54	0.219
Social cognition	7.10	11.49	4.38	0.37 (12)	−19.922***	4.44	4.31	0.295
Social communication	11.67	18.90	7.24	0.33 (22)	−18.349***	7.22	7.26	−0.055
Social motivation	6.77	11.10	4.32	0.39 (11)	−18.894***	4.55	4.10	1.029
Repetitive/restricted behaviors	6.40	4.97	−1.42	0.12 (12)	5.948***	−1.11	−1.76	1.352

**Note:** "Relative Change" score indicates the amount of change in each subscale relative to the number of items per subscale (shown in parentheses). Relative change scores were significantly different from one another in the following pattern: Awareness > Motivation > Communication = Cognition > Repetitive/Restricted Behaviors.

\*\*\* $p < .001$ , \*\* $p < .01$ , \* $p < .05$ .

respondents across timepoints. The 3 trajectory groups were significantly different regarding Full Scale IQ (Increasing > Stable > Decreasing), Medicaid status (Increasing had a larger proportion of individuals not on Medicaid), and maternal race (Increasing had a larger proportion of White mothers; Stable had a larger proportion of Black mothers). Taken together, the Increasing trajectory was more likely to be of higher IQ, privately insured, and White. Demographic characteristics by trajectory group are listed in Table 3.

Trajectory groups significantly differed in their 10-year AST score (Increasing mean mean = 27.8, SD = 22.0; Stable mean = 53.5, SD = 27.4; Decreasing mean = 82.7, SD = 27.0) ( $F_{2,524} = 137.1$ ,  $p < .001$ ). These groups did not significantly differ in the 17-year AST score (Increasing mean = 57.7, SD = 26.1; Stable mean = 55.7, SD = 25.5; Decreasing mean = 57.0, SD = 25.1) ( $F_{2,524} = 0.259$ ,  $p = .772$ ), suggesting evidence of equifinality. The average group trajectories are depicted in Figure 1.

### Sex Differences in AST Change

Results of independent-samples  $t$  tests evaluating sex differences in AST change scores from age 10 to 17 years were not significant for the overall AST change score ( $t_{516.97} = 0.595$ ,  $p = .552$ ) or individual domain change scores ( $p$  values  $> .304$ ). Change scores by sex are available in Table 2.

Sex differences in the likelihood of residing in each trajectory group were also evaluated using  $\chi^2$  analyses. Results indicated that female participants were equally likely to reside in all 3 trajectory groups (Increasing, Stable, Decreasing;  $\chi^2 = 0.183$ ,  $p = .999$ ), indicating no

significant sex differences in likelihood of trajectory group membership (Table 3).

### AST Change and Quality of Life

AST change and quality of life was first assessed continuously by correlating AST change score and quality of life scores across the 6 dependent measures. AST change was not significantly correlated with life satisfaction ( $r = -0.076$ ,  $p = .092$ ) or meaning and purpose ( $r = -0.02$ ,  $p = .640$ ). AST change was significantly and negatively correlated with global self-worth ( $r = -0.165$ ,  $p = .001$ ) and global health ( $r = -0.094$ ,  $p = .037$ ), suggesting that higher parent-reported AST change from 10 to 17 years was associated with lower adolescent-reported self-esteem and overall health at 17 years. AST change was also significantly correlated with self-reported externalizing problems ( $r = 0.119$ ,  $p = .019$ ) but not internalizing problems ( $r = 0.100$ ,  $p = .053$ ), suggesting that greater increases in AST were related to higher self-reports of externalizing, but not internalizing, psychopathology.

AST change and quality of life was also evaluated dichotomously by evaluating trajectory group (Increasing, Stable, Decreasing) differences in quality of life metrics. The 3 groups did not significantly differ on any metric of quality of life ( $p$  values  $> .180$ ). The group means and standard deviations are provided in Table 4.

## DISCUSSION

The current study sought to evaluate change in autistic social traits in EP youth via 3 aims: (1) charting the change

**TABLE 3** Demographic Characteristics by Autistic Social Traits (AST) Trajectory Group

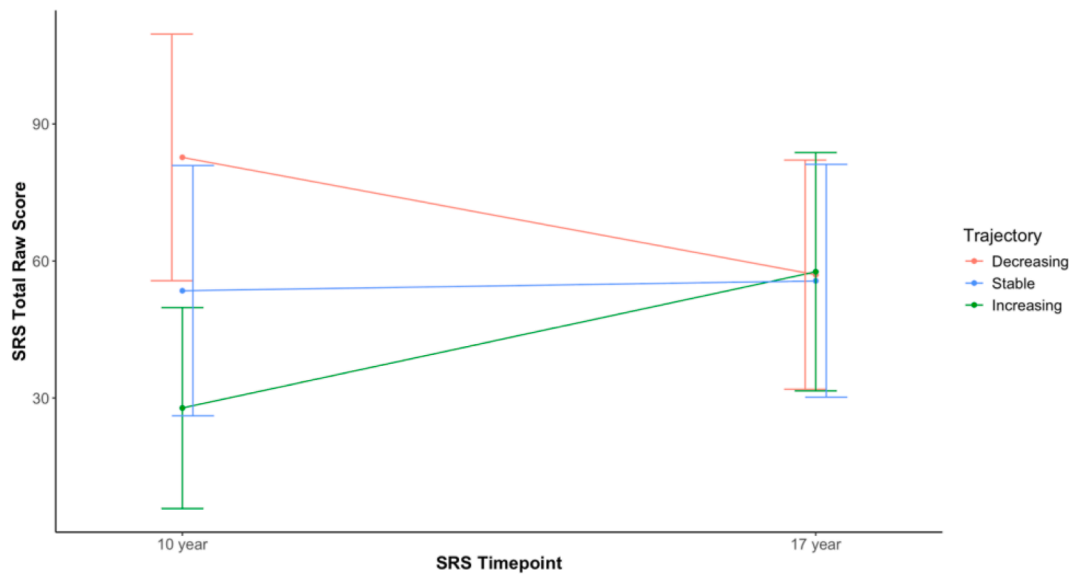
	Decreasing trajectory (n = 44)	Increasing trajectory (n = 368)	Stable trajectory (n = 115)	Total sample (N = 527)	Test of significance (t, $\chi^2$ )
	Mean or count (SD/%)	Mean or count (SD/%)	Mean or count (SD/%)	Mean or count (SD/%)	
Female	23 (52.3%)	194 (52.7%)	58 (50.4%)	275 (52.2%)	0.183
Gestational age	25.7 (1.46)	26.0 (1.22)	26.0 (1.23)	26.0 (1.25)	1.589
Birthweight Z score	−0.23 (1.25)	−0.13 (1.11)	−0.23 (1.07)	−0.16 (1.11)	0.430
Full Scale IQ	92.8 (18.9)	103 (17.6)	96.7 (17.1)	101 (17.9)	8.488***
Maternal age	29.7 (5.86)	29.9 (6.70)	28.9 (6.50)	29.6 (6.59)	0.931
Maternal education					13.173
Less than high school	8 (18.2%)	37 (10.1%)	15 (13.0%)	60 (11.4%)	
High school	10 (22.7%)	81 (22.0%)	33 (28.7%)	124 (23.5%)	
Graduate/GED					
Some college	11 (25.0%)	80 (21.7%)	32 (27.8%)	123 (23.3%)	
College graduate	11 (25.0%)	87 (23.6%)	19 (16.5%)	117 (22.2%)	
Masters or doctorate education	4 (9.09%)	75 (20.4%)	14 (12.2%)	93 (17.6%)	
Missing	0 (0.00%)	8 (2.17%)	2 (1.74%)	10 (1.90%)	
Medicaid status					6.215**
No	28 (63.6%)	263 (71.5%)	69 (60.0%)	360 (68.3%)	
Yes	16 (36.4%)	101 (27.4%)	45 (39.1%)	162 (30.7%)	
Missing	0 (0.00%)	4 (1.09%)	1 (0.87%)	5 (0.95%)	
Maternal marital Status					12.362
Married	27 (61.4%)	261 (70.9%)	69 (60.0%)	357 (67.7%)	
Separated or divorced	3 (6.82%)	13 (3.53%)	6 (5.22%)	22 (4.17%)	
Not ever married but living together	10 (22.7%)	51 (13.9%)	16 (13.9%)	77 (14.6%)	
Not ever married and not living together	4 (9.09%)	42 (11.4%)	24 (20.9%)	70 (13.3%)	
Widowed	0 (0.00%)	1 (0.27%)	0 (0.00%)	1 (0.19%)	
Maternal race					14.804**
Black	12 (27.3%)	71 (19.3%)	41 (35.7%)	124 (23.5%)	
Missing	0 (0.00%)	4 (1.09%)	1 (0.87%)	5 (0.95%)	
Other	4 (9.09%)	29 (7.88%)	11 (9.57%)	44 (8.35%)	
White	28 (63.6%)	264 (71.7%)	62 (53.9%)	354 (67.2%)	
Same SRS informant at 10 and 17 y	33 (75%)	265 (72%)	82 (71%)	380 (72%)	0.703

**Note:** GED = General Education Development; IQ = intelligence quotient; SRS = Social Responsiveness Scale.

\*\*\*p < .001, \*\*p < .01, \*p < .05.

in ASTs from age 10 to 17 years, (2) evaluating sex differences in AST change scores, and (3) mapping AST change onto concurrent quality of life and mental health measures at age 17 years. Our results suggested that EP youth experience significant increases in parent-reported ASTs from age 10 to 17 years, driven primarily by the

social domains (ie, more strongly driven by worsening social awareness, followed by social motivation, social cognition, and social communication) instead of the restricted/repetitive behavior/interest changes, which decreased over time. When grouping AST change by trajectory (Increasing, Stable, Decreasing), significant

**FIGURE 1** Social Responsiveness Scale (SRS) Trajectory Groups (Increasing, Stable, Decreasing) From Age 10 to 17 Years

**Note:** This figure demonstrates the mean trajectory of the 3 groups: Decreasing (red), Stable (blue), and Increasing (green), as defined by grouping participants by change score. Error bars reflect a standard deviation of 11.3 points. Participants were grouped by change score based on whether their 10- to 17-year SRS Raw Score increased by 11.3 or more points (Increasing), remained within  $\pm 11.3$  points of their 10-year data (Stable), or decreased by more than 11.3 points (Decreasing). The value of 11.3 was chosen to reflect half of the average standard deviation of 22.6 points in change score.

demographic differences emerged wherein the Increasing group had significantly higher IQ, was more likely to identify as White, and was more likely to have private insurance. Male and female participants demonstrated equivalent increases in ASTs over time and were equally likely to reside in all trajectory groups. AST change score was associated with worsening self-worth, global health, and externalizing psychopathology at age 17 years. These findings have important ramifications for continued care for EP youth into adolescence and for characterizing a preterm phenotype.

Results of the primary aim evidenced a significant increase in ASTs in EP youth from age 10 to 17 years. The

change in ASTs was large, with changes in median scores of nearly 20 points. When converting to standardized scores, this represents a significant change from the normal range into the mild range. Although previous studies indicated that ASTs typically remain stable with time using the same forms used in the current study,<sup>8,9</sup> our results suggest that EP youth experience significant increases during adolescence, which may signal an increase in psychosocial demands or stressors during this developmental window. The profile of AST increase was consistent and pervasive in our sample, as 368 participants (69.9%) resided in the Increasing group. The increase in ASTs from age 10 to 17 years was driven primarily by increases in the SCI domain

**TABLE 4** Psychopathology and Quality of Life Metrics by Autistic Social Traits (AST) Trajectory Group

	Decreasing trajectory	Increasing trajectory	Stable trajectory	Analytic sample (N)	Kruskal–Wallis test of significance (W, p)
	Mean (SD)	Mean (SD)	Mean (SD)		
YSR Internalizing	48.83 (11.56)	52.23 (11.15)	53.58 (11.21)	391	3.44 (0.179)
YSR Externalizing	43.67 (8.43)	45.71 (8.59)	45.75 (8.48)	391	2.66 (0.265)
PROMIS Global Health	45.94 (7.12)	44.70 (9.43)	44.95 (9.80)	491	1.40 (0.496)
PROMIS Life Satisfaction	48.57 (8.94)	47.17 (9.82)	47.33 (9.97)	493	1.01 (0.602)
PROMIS Meaning and Purpose	46.56 (7.32)	46.51 (9.80)	46.80 (10.29)	388	0.21 (0.901)
Harter Global Self Worth	3.27 (0.64)	3.03 (0.78)	3.17 (0.69)	367	3.43 (0.180)

**Note:** PROMIS = Patient-Reported Outcomes Measurement Information System; YSR = Youth Self Report.



of the SRS, including social awareness, motivation, cognition, and communication, instead of restricted/repetitive behaviors, which evidenced a significant decrease with time. The relative decrease in restricted/repetitive behaviors with age supports similar findings in previous literature.<sup>41</sup> These social domain changes, particularly the highest relative contribution of social awareness, further underscore our hypothesis that EP youth may experience difficulties with the changing social landscape from childhood to adolescence. An additional consideration may be that an increase in ASTs is a characteristic phenotype of EP youth. As described by Korzeniewski *et al.*,<sup>29</sup> the EP youth phenotype includes higher than average AST scores, despite not having a clinical autism diagnosis. Additional literature evaluating adolescent outcomes of EP youth suggested that at 10 years of age, EP youth had less social competence than full-term youth; by 17 years of age, EP youth demonstrated less social integration.<sup>42</sup> Future work should consider an elevated and increasing AST profile as an EP phenotype, and should replicate using different measures, such as self-report inventories.

The increase in ASTs observed in EP youth was observed regardless of the youth's assigned sex at birth: no significant sex differences emerged in overall AST change from age 10 to 17 years when looking at total scores and subscales, nor did the proportion of male to female individuals differ as a function of AST trajectory group. The lack of significant sex differences in EP youth from 10 to 17 years stands apart from previous research indicating a unique pattern of AST change for female individuals in the general population.<sup>18,19</sup> It was anticipated that our current age range, 10 to 17 years, would capture the reported increasing female phenotype of ASTs from age 10 to 16 years as observed in the ALSPAC sample.<sup>18,19</sup> However, we did not observe the reported female increase in ASTs or a significant sex difference at a singular timepoint, as reported in Mandy *et al.*<sup>18</sup> Furthermore, our sex findings in the trajectory groups did not replicate findings by Pender *et al.*,<sup>19</sup> who observed a higher percentage of female individuals occupying an increasing trajectory, compared to a predominance of male individuals in the decreasing trajectory. Our results showed equal likelihood of female individuals in all trajectory groups between age 10 and 17 years. Our sample is unique in that it focuses exclusively on EP youth. Therefore, one possible conclusion is that, for EP youth, sex differences may not play as strong a role in adolescent autistic social traits, which has been evidenced in previous literature.<sup>43</sup> We evaluated the limited time course from only age 10 to 17 years, which was not sensitive enough to detect smaller-scale changes (eg, changes observed from age 10 to 13 years, 13 to 15 years, etc), or

perhaps was not extensive enough to detect longitudinal changes from early childhood, as were analyzed in some previous studies (eg, ages 5-17 years), suggesting an area for future research.

Although sex did not emerge as a significant predictor of trajectory group, other demographic factors were unique to the Increasing group. This group had a higher proportion of White youth, families with private insurance, and youth with a higher IQ relative to the Stable and Decreasing groups. These results contrast with those observed in a systematic review of ASTs over time,<sup>6</sup> wherein higher verbal and nonverbal IQ were associated with decreasing autistic traits. However, our results do align more closely with follow-up work by Pender *et al.*,<sup>19</sup> wherein their persistently high group had the lowest IQ, and the decreasing group was characterized by lower maternal education, socioeconomic status, and likelihood of mothers never marrying and/or teenage pregnancies. The results of Pender *et al.*<sup>19</sup> closely mirror those observed here, wherein the Decreasing group had lower IQ and was most likely to have mothers on Medicaid, a proxy for socioeconomic status in the current study. Our comparisons of the 3 trajectory groups' 10-year data support this interpretation: the decreasing group scored the highest at age 10 years, suggesting somewhat of a ceiling effect in their initial score, with decreases at 17 years due either to statistical regression to the mean or a true improvement in scores. Comparatively, the Increasing group showed a normal score at age 10 years, followed by a sharp rise in ASTs by 17 years into the clinical range. Interestingly, the 3 groups did not differ on their 17-year AST score, evidencing a form of equifinality for EP youth into adolescence, regardless of 10-year starting point.

The highest clinical concern when reviewing these 3 groups is the Increasing trajectory, which was the overwhelming proportion observed in this study. One possibility for this significant shift from a range of no concern to a range of clinical concern could be due to increases in social demands that contribute to rises in ASTs. In some cases, social-communication differences may always have been present, but masked by high achievement or higher verbal abilities, and then when faced with more complex social ecologies, ASTs demonstrated a sharp rise.<sup>16</sup> A second possibility is that these youths in the Increasing trajectory did not demonstrate any social-communication difficulties at age 10 years, but the onset of puberty contributed to the quick emergence of difficult social behaviors, which has some support from a genetic architecture perspective.<sup>44</sup> Future research may benefit from evaluating the role of pubertal timing on AST change to further parse the individual contributors of changing

environmental contexts vs biological processes and their interactions.

As our final aim, we sought to evaluate whether AST change score was related to quality of life at 17 years as reported by the adolescents. Correlations indicated that AST change was negatively associated with self-worth and global health, wherein increases in AST were associated with decreased scores in health variables. Interestingly, changes in AST were not related to overall life satisfaction or purpose/meaning, suggesting that ASTs may have more of an internalizing impact on self-perception than global measures of satisfaction. However, ASTs were not significantly correlated with self-reported internalizing symptoms. Interestingly, AST change was also positively related to externalizing symptoms, inclusive of attention difficulties, rule-breaking behaviors, aggressive behaviors, social problems, and thought problems. Many externalizing behaviors are similar to ASTs (eg, social difficulties, perseverative thoughts, difficulty with transitions, difficulty with sustained or divided attention), and thus may capture more of these facets as opposed to rule-breaking or oppositional components of externalizing behaviors. Taken together, youth with higher AST change reported a worse sense of self-worth, overall health, and externalizing concerns.

The current study has numerous strengths. This is one of the first studies to evaluate EP phenotypes related to AST in a large, longitudinal sample. The use of data spanning age 10 to 17 years presents an unparalleled opportunity to evaluate phenotypic changes over time in this unique sample. Furthermore, the combined use of parent-report and youth self-report is a methodological strength. These strengths are considered in light of limitations. First, the initial ELGAN sample has lost approximately half of its original participants because of follow-up and retention. Although this sample remains one of the largest EP samples to date, the current sample reflects recruitment bias and may not be generalizable to all EP youth. Approximately half the 10-year sample is not represented here, which was largely predicted by socioeconomic factors, suggesting that access to research and research priorities differed among the full EP sample and those who continued through to the 17-year time point. In addition, the sample's average IQ of 101 standard points highlights the strong cognitive skills of the EP group, which does not represent EP youth with more significant cognitive delays. This sample's relatively higher IQ may stand in contrast to that in recent literature in terms of the observed 12-point deficit between preterm and full-term participants, as noted by Twilhaar *et al.* in their meta-analysis.<sup>45</sup> However, the current sample's older cohort age (twice the average of 8.6 years reported by Twilhaar *et al.*<sup>45</sup>), the sample being enriched for families of

higher socioeconomic status, and the Flynn effect together are probable explanations for what appears to be a discrepancy between the current study's reported group IQ of 101 and the reported deficit of 12 points from previous literature.<sup>45</sup> Nevertheless, the generalizability of the hypothesis that social abilities remain stable or deteriorate in EP youth compared to full-term youth should continue to be studied and perhaps replicated in larger samples, when available. The current study did not have a measure of gender identity. The use of assigned sex at birth is well replicated in the literature; however, this reduces an individual's social experience down to their assigned sex, which, if it does not align with their gender identity, does not adequately describe their social experience. Future research may benefit from evaluating the role of gender identity and gender diversity on ASTs over time, as ASTs are reported to be higher in those who identify as gender diverse.<sup>46</sup> Finally, the current research used only 2 time points, which limits the use of longitudinal modeling. Denser sampling could reveal nuanced insights into the timing of AST change.

### CRedit authorship contribution statement

**Tyler C. McFayden:** Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Investigation, Formal analysis. **Clare Harrop:** Writing – review & editing, Supervision, Resources, Conceptualization. **Kyle R. Roell:** Methodology, Investigation, Formal analysis, Data curation. **Robert M. Joseph:** Writing – review & editing, Validation, Supervision. **Jean A. Frazier:** Writing – review & editing, Supervision, Investigation. **Rebecca C. Fry:** Writing – review & editing, Funding acquisition. **T. Michael O'Shea:** Writing – review & editing, Writing – original draft, Supervision, Resources, Investigation, Funding acquisition, Conceptualization.

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Procedures for this study were approved by the institutional review boards of participating institutions. Patients provided consent for data collection and de-identified publication.

Data Sharing: Data for all variables except 15-year outcomes can be obtained from Archived Clinical Research Datasets | National Institute of Neurological

Disorders and Stroke (nih.gov). Data on 15-year outcomes can be obtained from the public use data set available on the NICDH DASH Website.

Kyle R. Roell served as the statistical expert for this research.

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