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Trajectories in Symptoms of Autism and Cognitive Ability in Autism From Childhood to Adult Life: Findings From a Longitudinal Epidemiological Cohort

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Objective: For the first time, we use a longitudinal population-based autism cohort to chart the trajectories of cognition and autism symptoms from childhood to early adulthood and identify features that predict the level of function and change with development.

Method: Latent growth curve models were fitted to data from the Special Needs and Autism Project cohort at three time points: 12, 16, and 23 years. Outcome measures were IQ and parent-reported Social Responsiveness Scale autism symptoms. Of the 158 participants with an autism spectrum disorder at 12 years, 126 (80%) were reassessed at 23 years. Child, family, and contextual characteristics obtained at 12 years predicted intercept and slope of the trajectories.

Results: Both trajectories showed considerable variability. IQ increased significantly by a mean of 7.48 points from 12 to 23 years, whereas autism symptoms remained unchanged. In multivariate analysis, full-scale IQ was predicted by initial language level and school type (mainstream/specialist). Participants with a history of early language regression showed significantly greater IQ gains. Autism symptoms were predicted by Social Communication Questionnaire scores (lifetime version) and emotional and behavioral problems. Participants attending mainstream schools showed significantly fewer autism disorder symptoms at 23 years than those in specialist settings; this finding was robust to propensity score analysis for confounding.

Conclusion: Our findings suggest continued cognitive increments for many people with autism across the adolescent period, but a lack of improvement in autism symptoms. Our finding of school influences on autism symptoms requires replication in other cohorts and settings before drawing any implications for mechanisms or policy.

Key words: autism disorder, cognition, epidemiology, outcome, SNAP

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Autism spectrum disorder (ASD) is a lifelong disorder characterized by qualitative impairments in social interaction and communication alongside a pattern of restricted or repetitive behaviors and sensory anomalies. There is great diversity in presentation and considerable change over the life span, but most people with autism remain significantly impaired in social and adaptive functioning.[1] A key priority for parents of older children and adolescents with autism is to gain a better understanding of what the future holds for their child in terms of autism spectrum disorder symptoms and cognitive and adaptive functioning to make informed educational, employment, and vocational choices. Early studies of adult outcomes in autism were limited by small sample sizes, which were usually clinically ascertained and hence more likely to have high levels of impairment, and often used descriptive measures of functioning.[2] It is uncertain how relevant these studies are to currently identified people with autism, who encompass a broader group of individuals, some of whom may have received early interventions and targeted educational strategies.

Two approaches have been used in the study of adult autism outcomes. Some investigators have aggregated data from different domains, including autism symptoms, maladaptive behavior, social functioning, employment, and independent living, to broadly classify adult outcomes in autism. A systematic review of studies using this method estimated that 58.2% of adults with autism had poor or fair as opposed to good outcomes.[3] Whereas it is essential to describe global functioning, these broad categories may obscure variation and causal factors in developmental patterns for the different underpinning characteristics and thus

fail to illuminate the mechanisms that underpin outcomes. Alternatively, the developmental patterns of the features thought to underpin the functional outcomes have been studied, including IQ, adaptive function, and autism symptoms.[4,5] IQ and autism symptoms are related to functional adult outcomes,[1] including independent living[5] and employment[6]; therefore, identifying features present in childhood that predict life course is important in personal planning for families as well as for health and social care systems. Previous findings with respect to IQ indicate considerable developmental heterogeneity, and studies vary in finding reduction, no change, or increased IQ from childhood to adulthood,[4] without a clear prevailing pattern. In contrast, longitudinal studies of autism symptoms generally report improvements, although most people remain above diagnostic threshold, where that has been measured.[4]

The literature is characterized by heterogeneity, but comparison of longitudinal adult outcome studies over time has suggested that more recent ones often report better outcomes,[2] likely reflecting sample and intervention differences in earlier reports, and it is therefore especially important to examine outcomes in population-based cohorts identified with the current gold standards for diagnosis, as these will be the most relevant to current populations. With autism, furthermore, most studies are restricted by exploring a limited number of potential predictive factors, with a minority including family and social factors (eg, Woodman *et al.*[7]).

In this study, we use data from the Special Needs and Autism Project (SNAP),[8] a sample drawn from a population-based cohort including people with autism of all ability levels, to explore the trajectories of IQ and autism symptoms from late childhood to early adulthood. We examine which individual, family, and contextual childhood factors implicated in previous literature predict the trajectories of IQ and autism symptoms over time. We use latent growth curve (LGC) modeling to simultaneously estimate the amount of mean change while accounting for individual differences in trajectories and predictors of mean level (intercept) and amount and direction of change (slope).

METHOD

Participants

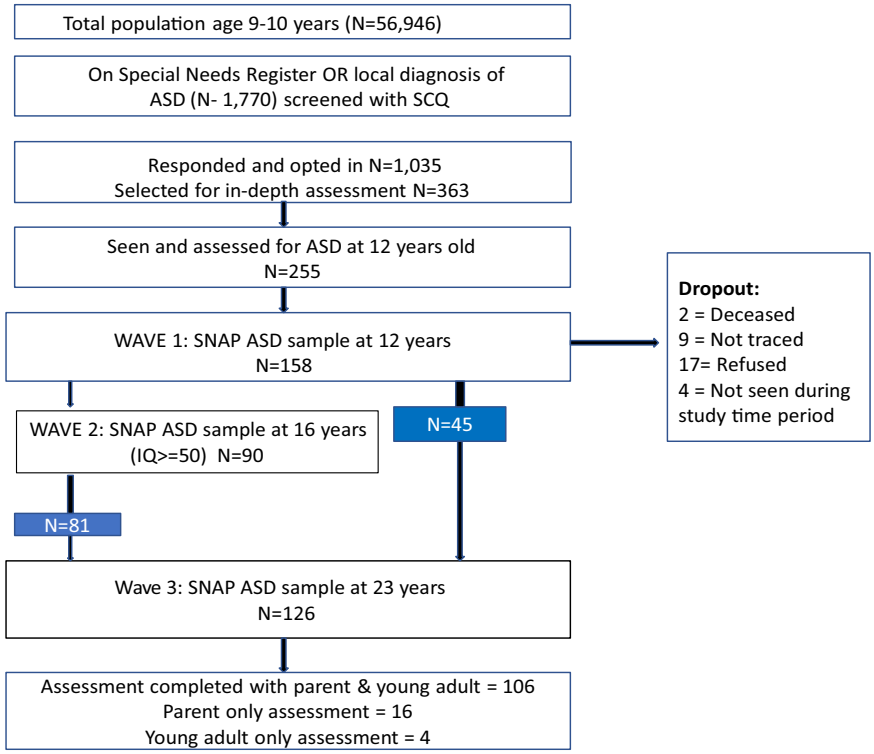
All members of the SNAP cohort who received an *International Statistical Classification of Diseases, 10th Revision* (ICD-10) diagnosis of childhood autism, Asperger syndrome, pervasive developmental disorder not otherwise specified, or atypical autism at the first wave of data collection were eligible for participation. The term autism is used subsequently to refer to this cohort. The SNAP sample was originally drawn from a total population cohort of 56,946 children born between July 1990 and December 1991 in 12 districts in south-east England, as described in detail elsewhere[8] and in Supplement 1, section 1, available online.[9-11] Of these, 158 (132 male participants) met criteria at wave 1, aged 10 to 12 years, for autism (81 childhood autism, 77 other pervasive developmental disorders). A subsample of 100 youths with autism and IQ >50 participated at age 15 to 16 (wave 2). We attempted to contact the families of all 158 participants with autism (full IQ range) at age 23 (wave 3) and successfully completed assessments on 126 (80%; 110 male participants; also 110 with young adults and 16 with parents only), who represent the denominator for all descriptive statistics given below (Figure 1).

Ethical approval was given by the Camberwell and St. Giles National Research Ethics Service Committee number 12/LO/1770, Integrated Research Application Service project number 112286. Written informed consent was obtained from all participating parents and 83 adults with autism who had mental capacity to give consent. Where researchers judged that a participant did not have capacity to consent, a consultee was appointed to determine whether the young adult would wish to participate if he or she had been able to give informed consent.

Measures

Outcome Variables for Trajectories. IQ trajectories were estimated using a combination of standard IQ measures and, for waves 1 and 3, parental reports of adaptive functioning. The latter were included because some participants were unable to access conventional IQ tests and others declined to participate. At wave 1, full-scale IQ on the WISC-III^{UK} and the composite score of the Vineland Adaptive Behavior Scales, First Edition (VABS-I) provided a latent IQ measure. For descriptive purposes and for use in the propensity analysis but not in the growth models, for 29 participants unable to access the WISC (Table 1), recoded full-scale IQ was imputed from the VABS score as an auxiliary variable (Supplement 2, section 2, available online). At wave 3, 108 of the 110 adults participating completed the Wechsler Abbreviated Scale of Intelligence (WASI-II); for 16 whose parents participated but the young adult IQ was missing the WASI, scores were imputed using the general adaptive composite of the parent-reported Adaptive Behavior Assessment System (ABAS-II)[12] as the auxiliary variable. The first 10 participants at wave 3 received the two-subtest WASI-II; others received the four-subtest version. At wave 2, only the four-subtest WASI-I was included. All IQ and adaptive behavior measures are normed to a mean of 100 and SD of 15.

FIGURE 1 Special Needs and Autism Project [SNAP] Cohort Participation Over Waves 1 to 3



Note: *ASD = autism spectrum disorder; SCQ = Social Communication Questionnaire.*

Autism symptoms were measured using the total raw score of the parent-reported Social Responsiveness Scale (SRS)[13] at each wave. The SRS is a validated 65-item rating scale eliciting autistic behavior over the previous 6 months. The SRS-1 child version was used at waves 1 and 2, and the SRS-2 adult version was used at wave 3. The SRS-1 and SRS-2 primarily differ in their norms, but there are minor differences in item content described in Table S1, available online. We used raw rather than standardized scores to examine individual change in actual symptoms. Higher scores indicate more symptoms.

Predictor Variables. These variables were selected from the wave 1 assessment and included child characteristics, parental characteristics, and contextual characteristics.

1. Early autism symptoms were measured using the lifetime Social Communication Questionnaire (SCQ),[9] focusing on symptoms at age 4 to 5 years, acquired at screening. Infant and toddler development was retrospectively measured using 17 items from the Diagnostic Interview for Social Communication Disorders (DISCO),[14] producing scores ranging from 0 to 34, with higher scores indicating abnormality. Developmental language regression (binary, scored 1 if present) was obtained from parental retrospective report on the ADI-R, defined as a loss of five or more words used communicatively for 3 months before loss, with or without loss of skills in other areas.[15] Language ability in verbally fluent children was measured using the Clinical Evaluation of Language Function (CELF).[16] To provide a language estimate on all participants, we included the ADOS module (1–3) used, where the selection is based on the child's expressive language. The total difficulties score of the Strengths and Difficulties Questionnaire (SDQ)[17] measured current co-occurring mental health symptoms. The total difficulties score contains the conduct, emotional, attention-deficit/hyperactivity disorder, and peer problems subscales, representing a broad composite of co-occurring problems.
2. Maternal affective symptoms were measured by self-reports on the General Health Questionnaire (GHQ-30).[18] A binary classification of household parental education was scored 1 when at least one parent was educated beyond high school.[8]
3. Neighborhood deprivation was measured from full post codes using the Carstairs Index, which combines overcrowding, male sex, unemployment, proportion of the population in Registrar General social class 4 and 5, and households without a car; low scores represent low

TABLE 1 Participant Characteristics

	Wave 1 (age 12 years)				Wave 2 (age 16 years)				Wave 3 (age 23 years)			
Variables	***n***	**Mean**	**SD**	**Range**	***n***	**Mean**	**SD**	**Range**	***n***	**Mean**	**SD**	**Range**
Included in IQ analysis	155	—	—	—	90	—	—	—	126	—	—	—
Included in SRS analysis	95	—	—	—	83	—	—	—	122	—	—	—
Age, y	158	11.6	0.96	9.9–14.4	90	15.5	0.46	14.7–16.8	126	23.2	0.79	21.3–25.1
Outcome variables												
Full-scale IQ												
WISC at W1 WASI at W2 WASI-2 at W3	127	78.6	20.7	40–136	90	83.9	17.9	50–119	108	84.8	24.3	40–124
Recorded IQ (rFSIQ)	156	72.2	24.5	19–136	—	—	—	—	—	—	—	—
Adaptive behavior												
VABS at W1 ABAS at W3	141	45.4	16.6	19–93	—	—	—	—	120	66.8	20.8	40–118
Autism severity												
SRS (raw)	95	90.9	20.3	42–137	83	93.4	28.7	21–153	122	96.0	32.7	7–172
Predictor variables												
Child characteristics												
CELF total (raw)	111	121.0	45.8	3–211	—	—	—	—	—	—	—	—
CELF total (standard score)	109	77.2	14.7	63–125	—	—	—	—	—	—	—	—
SCQ total score	158	23.9	6.6	2–37	—	—	—	—	—	—	—	—
SDQ total difficulties	146	21.2	6.0	6–37	—	—	—	—	—	—	—	—
Behaviors in infancy (DISCO)	158	11.9	8.9	0–33	—	—	—	—	—	—	—	—
ADOS module 1/2/3, *n* (%)	154	22/15/117	(14%/10%/76%)	—	—	—	—	—	—	—	—	—
Regression, *n* (% present)	158	35	(22%)	—	—	—	—	—	—	—	—	—
Parental characteristics												
Maternal GHQ	127	5.1	6.5	0–25	—	—	—	—	—	—	—	—
Parental education >high school diploma, *n* (%)	158	104	(61%)	—	—	—	—	—	—	—	—	—
Contextual characteristics												
Carstairs neighborhood deprivation	158	−0.68	2.3	−4.3 to 6.7	—	—	—	—	—	—	—	—
School placement, *n* (% mainstream)	158	79	(50%)	—	90	51	57%	—	—	—	—	—

Note: ABAS = Adaptive Behavior Assessment Schedule; ADOS = Autism Diagnostic Observation Schedule; CELF = Clinical Evaluation of Language Function; DISCO = Diagnostic Interview for Social Communication Disorders; rFSIQ, recoded full-scale IQ; GHQ = General Health Questionnaire; SCQ = Social Communication Questionnaire; SDQ = Strengths and Difficulties Questionnaire; SRS = Social Responsiveness Scale; VABS = Vineland Adaptive Behavior Scale; W1, W2, W3, = wave 1, 2, 3; WASI = Wechsler Adult Scale of Intelligence; WISC = Wechsler Intelligence Scale for Children.

deprivation.[19] Children's school placement was dichotomized as mainstream school, including a special unit in a mainstream school (coded 0), versus a unit or special school for intellectual disabilities, emotional/behavioral problems, or autism.

Additional baseline variables, described in Supplement 1, section 3, available online, were included as potential confounders in a propensity analysis that explored the relationship between wave 1 school placement and autism symptom trajectory.

Statistical Analysis

LGC models, depicted in Figure S1, available online, were used to model separately IQ and autism symptom trajectories. Models were fitted using the sem command in Stata Version 13.1 (StataCorp LP, College Station, Texas). Each of the models was weighted using sampling weights based on the study design calculated as described previously.[8] Full information maximum likelihood estimation was used for all models, with robust standard errors estimated. All participants were included in the model if they had at least one nonmissing observation of the IQ or SRS measure. Only observed (not imputed) values were included. The analysis method assumed missing values were missing at random, a term which, contrary to lay understanding, allows for the selection of participants based on previously measured IQ that was used at wave 2 of the SNAP cohort study design.[20] Typical fit indices were not calculated, as these are not appropriate with sampling weights.

Latent variables were included to model the variation in intercept, representing mean levels of the outcome variable across all three waves, and linear slope of the outcome measure, representing change over time. Pathways between all indicators and the latent intercept were set at 1, and the intercept was centered at age 12. Pathways between observed measures and the latent slope were set corresponding to time passed (wave 1, age 12 = 0; wave 2, age 16 = 4; wave 3, age 23 = 11). The latent slope and intercept were allowed to covary.

As not all participants were able to complete a full-scale IQ at wave 1 or 3, we used the so-called phantom latent variable approach[21] with the VABS/ABAS composite score being used as a surrogate measure for IQ, accounting for the mean VABS-IQ difference (Table S2, available online, shows wave 1 actual and latent scores). In this approach, observed IQ scores are treated as error-free measures of the latent full-scale IQ, while the VABS/ABAS is treated as an error-prone measure. Additionally, we accounted for the impact of floor effects of IQ and adaptive function using regression models of raw scores to predict standardized scores < 40 (detailed in Supplement 1, section 4, available online). The WASI-I IQ at wave 2 was used as the singular observed measure of latent IQ. The latent variables of IQ at all waves were then modeled as indicator variables for the latent intercept and slope.

For the autism symptoms LGC model, parent-reported SRS at each wave were used as indicator variables. To reduce the number of parameters estimated (for model identification), the residual variances of these observed measures were constrained to be equal. Potential predictors of the latent intercept and slope were first tested one at a time. As this work was exploratory, no adjustments were made for multiple testing. The final predictive model was built using backward selection; all variables that showed univariate prediction of either intercept or slope (with $p < .2$) were included in the model. Predictor variables were systematically and sequentially removed in order of decreasing significance with the final retained variables all being significant ($p < .05$). The final model was checked for sensitivity to heavily weighted observations. A nonweighted model was fitted, and predictors were not included in the final model if any major differences in results were due to highly weighted observations.

To investigate the potential confounding on the estimated effect of school type (specialist versus mainstream school), we used propensity score matching on theorized confounders, measured at wave 1 and described in Supplement 1, section 5, available online. Effects of propensity score matching are demonstrated in Tables S3 and S4, available online.

RESULTS

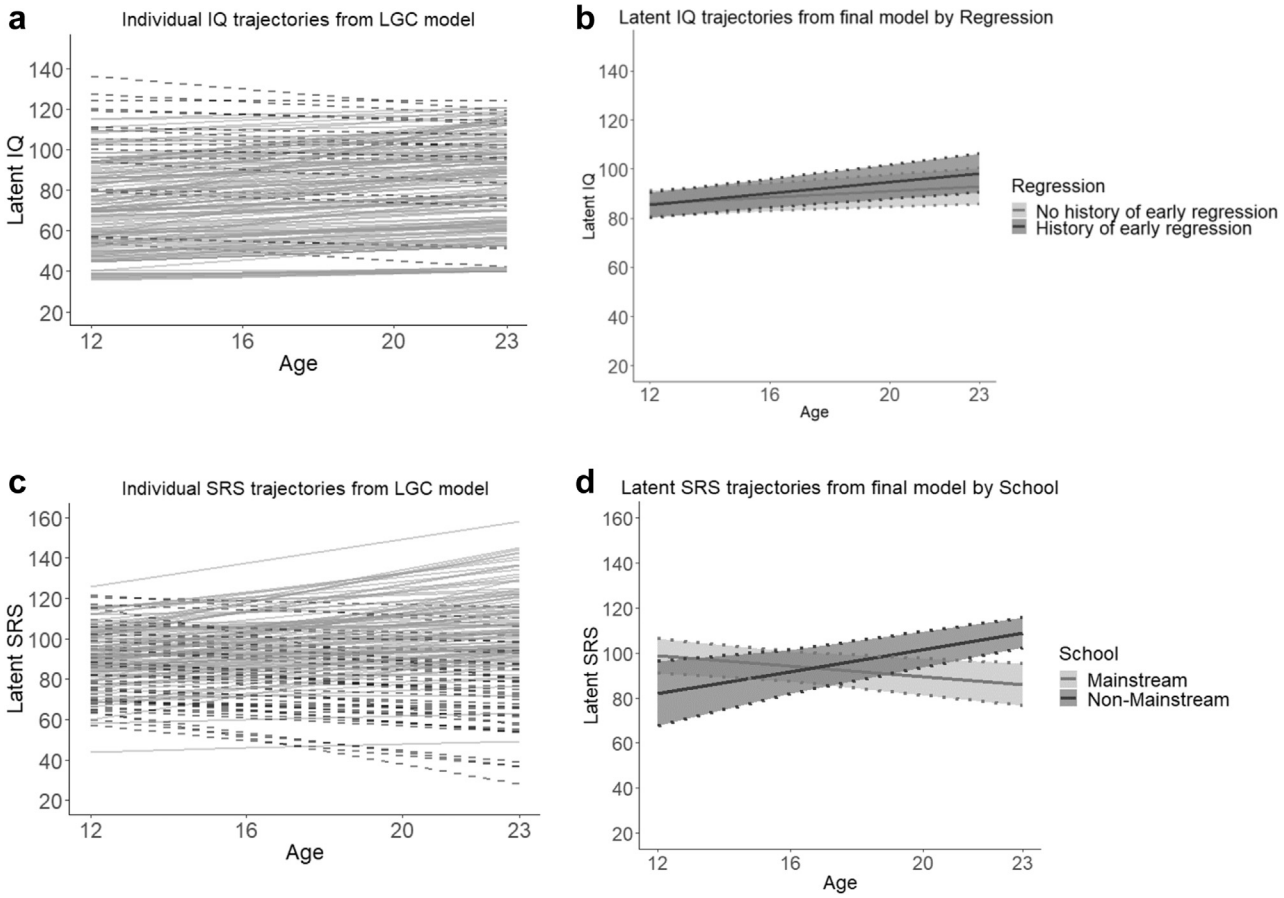
Sample characteristics for observed data used in the IQ model are shown in Table 1 and for the slightly reduced sample in the autism symptom (SRS) model in Table S3, available online. Data from 156 participants (140 male participants) and 138 participants (123 male participants) were included in the IQ and SRS trajectories, respectively.

LGC Model for IQ

The LGC model of IQ (Figure 2a) showed strong evidence of a positive linear slope with an estimated mean increase in latent IQ per year of 0.68 (95% CI [0.45, 0.91]; $p < .001$); total estimated mean increase wave 1 to wave 3 is therefore 7.48 (95% CI [4.95, 10.01]). There was a large amount of variability in initial IQ levels at wave 1, with an estimated mean IQ of 68.95 (95% CI [63.08, 74.82]). Slope and intercept were correlated 0.009 in a model without predictors, indicating that, at age 12, there is little effect of level of IQ on the extent of gain over adolescence.

In univariate analyses (Table 2), using a significance level of $p < .05$, completing ADOS module 1 or 2 (compared with module 3), lower language level on the CELF, more abnormal early childhood development on the DISCO, and attending a specialist school were associated with a lower IQ intercept (wave 1). Only a history of regression predicted a greater increase in IQ (slope) over time but was not associated with IQ intercept. In the final multivariate predictive model, specialist school attendance ($p = .014$), lower CELF ($p < .001$), and ADOS module 1 and 2 (compared with ADOS module 3) strongly predicted

FIGURE 2 Depiction of Developmental Trajectories



Note: *Graphs [a] and [c] show estimated individual trajectories from the latent growth curve [LGC] models without predictors. Black dashed lines denote negative or zero slopes, gray solid lines denote positive slopes. Graphs [b] and [d] show estimates of []SEs trajectories with 95% CIs, calculated using pointwise estimates and SEs at waves 1, 2, and 3 taken from the final predictive structural equation models [such that estimates are adjusted for other predictors in the model].*

lower IQ intercept ($p < .001$). Participants who completed ADOS module 2 versus module 3 had a decrease in slope: latent IQ/y −0.71 (95% CI [−119, −0.23]; $p = .004$). There was weaker (nonsignificant) evidence of a similar decrease in the slope between participants who completed ADOS module 1 and 3 of −1.13 (95% CI [−2.30, −0.05]; $p = .060$). The effect of language regression on slope was significant ($p = .020$), with the regressed group having a greater increase in IQ: nonregressed group increase 0.60 IQ points/y (95% CI [0.23, 0.96]; $p = .001$), regressed group increase 1.18 points/y (95% CI [0.70, 1.65], $p < .001$) (Figure 2b).

LGC Model for Autism Symptoms

SRS raw scores showed a nonsignificant mean increase/year of 0.84 (95% CI [−0.46, 2.14]; $p = .203$) (Figure 2c). There was a large amount of variability in initial autism symptom levels, with estimated mean initial SRS raw score of 86.56 (95% CI [74.99, 98.13]), which equates to a T score of 75 for male participants and 83 for female participants, ≥99th centile. In a model without predictors, intercept and slope were correlated −0.343, indicating participants with higher wave 1 scores showed less increase over time.

The same potential predictors and modeling were used as for IQ with results in Table 3. In univariate analyses, at $p < .05$, only the SCQ score was significant, with higher SCQ scores associated with increased autism symptoms. In terms of slope, univariate analyses revealed that specialist school attendance; lower wave 1 IQ; completing ADOS module 1 (compared with module 3), but not module 2 versus module 3; and greater neighborhood deprivation significantly predicted a greater relative increase in autism symptoms over time.

In the final multivariate model, higher SCQ ($p = .001$) and SDQ total difficulties ($p = .023$) scores predicted greater autism symptom intercept. Carstairs deprivation index was excluded from the model, as its effect on autism

TABLE 2 Latent Growth Curve Model of IQ

	Intercept		Slope	
	Coefficient [95% CI][a]	***p***	**Coefficient [95% CI][a]**	***p***
Univariate models with predictors at wave 1				
SCQ total	−0.01 [−0.24, 0.22]	.914	0.13 [−0.08, 0.0.33]	.244
SDQ total difficulties	−0.01 [−0.24, 0.21]	.925	0.09 [−0.12, 0.30]	.387
Regression (reference category: nonregression)	−6.52 [−15.69, 2.66]	.164	0.56 [0.09, 1.04]	**.019**
DISCO total	−0.31 [−0.50, −0.11]	**.004**	−0.08 [−0.34, 0.17]	.517
ADOS module 1 (reference category: ADOS module 3)	−43.34 [−48.63, −38.04]	< **.001**	−0.88 [−0.34, 1.21]	.138
ADOS module 2 (reference category: ADOS module 3)	−30.75 [−39.38, −22.13]	< **.001**	−0.53 [−1.00, −0.62]	.026
CELF total	0.72 [0.58, 0.87]	< **.001**	−0.09 [−0.40, 0.22]	.589
Maternal GHQ total	−0.13 [−0.37, 0.10]	.277	−0.02 [−0.20, 0.17]	.851
Parental education (reference category: no education or O-levels equivalent)	4.26 [−6.86, 15.37]	.453	−0.19 [−0.61, 0.23]	.367
School (nonmainstream vs mainstream)	−27.00 [−36.16, −17.85]	< **.001**	0.07 [−0.38, 0.51]	.760
Carstairs deprivation	−0.05 [−0.24, 0.15]	.624	0.11 [−0.05, 0.28]	.185
Final predictive multivariable model				
Regression (reference category: nonregression)	1.45 [−4.84, 7.74]	.651	0.58 [0.09, 1.07]	**.020**
ADOS module 1 (reference category: ADOS module 3)	−23.36 [−32.23, −14.49]	< **.001**	−1.13 [−2.30, −0.05]	**.060**
ADOS module 2 (reference category: ADOS module 3)	−20.85 [−31.31, −10.40]	< **.001**	−0.71 [−1.19, −0.23]	**.004**
CELF (centered)	0.79 [0.60, 0.98]	< **.001**	−0.01 [−0.03, 0.01]	.180
School (nonmainstream vs mainstream)	−12.23 [−21.97, −2.50]	**.014**	0.18 [−0.23, 0.59]	.389

Note: Boldface type indicates statistically significant results. ADOS = Autism Diagnostic Observation Schedule; CELF = Clinical Evaluation of Language Function; DISCO = Diagnostic Interview for Social Communication Disorders; GHQ = General Health Questionnaire; SCQ = Social Communication Questionnaire; SDQ = Strengths and Difficulties Questionnaire.

[a]*Coefficients for continuous variables in univariate models are standardized, but p values are taken from unstandardized models.*

symptoms appeared to be overly influenced by a highly weighted outlier, and it was not a predictor in an unweighted model. As depicted in Figure 2d, participants from specialist schools at wave 1 had an estimated 3.63 (95% CI [1.64, 5.61]; $p < .001$) mean increase in latent autism symptoms/year compared with participants from mainstream schools (adjusted for SCQ and SDQ scores). There was weak (nonsignificant) evidence that participants attending specialist schools had lower initial autism symptoms, a mean difference of −16.77 (95% CI [−36.36, 2.81], $p = .093$). The addition of the propensity score for matchable participants ($n = 113$) (Tables S4 and S5, available online) attenuated the mean difference, but school type remained a strong predictor of slope (2.05; 95% CI [1.04, 3.06]; $p < .001$). There was no longer any evidence of a baseline difference in autism symptoms (2.35; 95% CI [−8.35, 13.04], $p = .667$).

DISCUSSION

To our knowledge, this is the first population-based longitudinal study of autism to examine trajectories from childhood to adult life. The proportion followed up at wave 3 (80%) is high, and the use of maximum likelihood as the statistical approach to deal with missing data, along with the implementation of population weights, means that the results reflect the wider population with autism of this age and geographical origin.

There are, however, limitations to the study. The SNAP cohort was created when the participants were 10 to 12 years of age, and the study lacks prospective measures from early childhood. The original sampling strategy focused on participants identified with educational or developmental concerns. It also did not overrecruit girls, and the number of female participants is too small to explore sex differences. At wave 2, only participants with IQ ≥ 50 were included, and data from lower-ability participants were treated as missing at random for these measures. Similar to other longitudinal studies, we used parent-reported measures of autism symptoms, but not independent observations, as these were not available at all three waves.

IQ

We found a substantial mean IQ increase of 7.48 points, 0.5 SD on a standardized score, from wave 1 to 3. As tests are normed for all ages, no change is expected in mean IQ for the general population. The finding should be considered in the context of considerable individual variability, as also reported in other studies.[22-25] Although the Flynn

TABLE 3 Latent Growth Curve Model of Autism Severity

	Intercept		Slope	
	Coefficient [95% CI][a]	***p***	**Coefficient [95% CI][a]**	***p***
Univariate models with predictors at wave 1				
IQ (latent)	0.12 [−0.20, 0.45]	.499	−0.42 [−0.69, −0.14]	**.038**
SCQ total	0.43 [0.14, 0.72]	**.017**	0.17 [−0.26, 0.60]	.422
SDQ	0.27 [−0.16, 0.70]	.147	−0.15 [−0.63, 0.33]	.542
Regression (reference category: nonregression)	11.24 [−4.24, 26.72]	.155	−0.46 [−2.41, 1.48]	.641
DISCO	−0.01 [−0.33, 0.31]	.952	0.38 [0.07, 0.69]	.034
ADOS module 1 (reference category: ADOS module 3)	−4.09 [−26.08, 17.91]	.716	3.21 [1.26, 5.17]	**.001**
ADOS module 2 (reference category: ADOS module 3)	3.00 [−16.53, 22.54]	.763	−0.67 [−2.95, 1.60]	.562
CELF	−0.15 [−0.49, 0.18]	.360	−0.06 [−0.43, 0.31]	.745
Maternal GHQ	0.26 [−0.05, 0.57]	.207	−0.26 [−0.64, 0.12]	.273
Parental education (reference category: no education or O-levels equivalent)	14.93 [−5.20, 35.06]	.146	−1.35 [−3.79, 1.10]	.282
School (nonmainstream vs mainstream)	−7.38 [−28.15, 13.40]	.487	3.39 [1.61, 5.17]	< **.001**
Carstairs deprivation	−0.47 [−0.84, 0.10]	.053	0.55 [0.22, 0.88]	**.011**
Final predictive multivariable model				
SCQ (centered)	1.85 [0.78, 2.93]	**.001**	−0.05 [−0.16, 0.07]	.447
SDQ (centered)	1.38 [0.19, 2.57]	**.023**	−0.11 [−0.23, 0.02]	.094
School (nonmainstream vs mainstream)	−16.77 [−36.36, 2.81]	.093	3.63 [1.64, 5.61]	< **.001**

Note: Boldface indicates statistically significant results. ADOS = Autism Diagnostic Observation Schedule; CELF = Clinical Evaluation of Language Function; DISCO = Diagnostic Interview for Social Communication Disorders; GHQ = General Health Questionnaire; SCQ = Social Communication Questionnaire; SDQ = Strengths and Difficulties Questionnaire; SRS = Social Responsiveness Scale.

[a]*Coefficients for continuous variables in univariate models are standardized, but p values are taken from unstandardized models.*

effect, in which there are secular trends for increased IQ with time, cannot be fully excluded, it is less likely because we used older IQ tests at wave 1 (which would produce relatively higher IQs) and tests at wave 3 that had been more recently normed in relation to testing date (which would produce relatively lower IQs). Furthermore, for many participants, different IQ tests with varying content were used at wave 1 compared with wave 2 and 3, which could artifactually affect full-scale IQ in people with uneven profiles, as often seen in autism. However, the increase is suggestive of continued cognitive development over the adolescent/early adult period that is greater than seen in typically developing individuals. In addition, increases in motivation levels or the capacity to access IQ tests could influence measured IQ; such effects could be more than artifacts and may generalize to functioning in everyday life. Previous longitudinal studies covering a similar age range are sometimes difficult to interpret (because IQ has been reported in categories or a wide variety of measures have been used) and inconsistent in their findings. Some studies report a general increase in IQ,[2,26,27] whereas others report a decrease[28,29] or little apparent change,[22,25,30,31] with one suggesting a difference in trajectories for verbal and performance abilities.[23] Our finding is similar to reports from studies of younger children, where the pattern is more typically of a mean IQ increase, again with considerable variability[30,32] or no change,[33,34] particularly when associated with language acquisition.[34]

We identified several predictors of IQ intercept that withstood multivariate testing. Many are closely linked to cognitive level, such as language abilities and type of school attended. Other longitudinal studies identify childhood IQ as one of the strongest predictors of adult IQ.[22-24,35,36] We did not find an effect of autism symptoms on IQ intercept or slope, but it should be borne in mind that half (20 of 40) of the SCQ items in the lifetime version used in the SNAP cohort refer to behaviors present in the 4- to 5-year age period, some 5 or more years before wave 1 assessments.

Parent-reported history of early language regression significantly increased the growth of IQ from wave 1 to 3. In an earlier report focusing on wave 1, we demonstrated a significant interaction between history of language regression and the association between parent-reported infant developmental problems on the DISCO (as included in the present analyses) and current autism symptoms. In the nonregressive group, early developmental problems were predictive of autism symptoms at wave 1, whereas there was no relationship in the group with a history of language regression, suggesting that regression was a marker for early perturbation in development. The present findings of

continued developmental differences between these groups, albeit in a different sphere of outcome, suggest that people with early regression continue to have a different developmental course even in the second decade of life. There should be reservations about cross-sectional associations between retrospective reports of regression and other characteristics. However, our findings are prospective, the relationship is predictive, and IQ is measured independently of parent report. The ADI language regression cutoff we selected is high and may miss some cases of regression, especially in those with slower development.[37] One possibility is that developmental language regression is a marker of a perturbation in development that is observable only in people with normal or advanced early cognitive milestones.[15,38] In SNAP, parents of the group with regression reported first words occurred at a mean of 15.9 months compared with 26.1 months in the nonregressive group.[38] The follow-up findings are consistent with this idea that this group continues to revert to their original developmental endpoints. Alternatively, regression may simply index a distinct developmental course. Either way, the present findings indicate that a history of regression is an important prognostic factor.

Autism Symptoms

The lack of a significant change in the SRS raw scores indicates that the number of symptoms remains stable over time, although the type may alter. This stability contrasts with our findings in relation to IQ and is also at variance with a number of longitudinal studies reporting a reduction in autism symptoms from childhood through adolescence or adulthood, as measured on the ADI-R[7,29,33,36] or Developmental Behavior Checklist.[39] This difference could be due to instrument effects or sample differences. To our knowledge, no previous studies have explored the longer-term trajectories of the SRS. Using the adult version of the SRS in wave 3 may provide more age-appropriate examples of autism symptoms.

In multivariate analyses, only the baseline SCQ and SDQ total problems scores remained predictive of intercept, with higher scores predicting greater autism symptoms. As the lifetime SCQ is another continuous measure of autism symptoms, albeit reflecting early development as well as contemporaneous state, its predictive relationship is unsurprising. The mechanism for the SDQ prediction is more speculative. Although people with autism are known to have higher rates of mental health problems, the link between scores on the two domains cross-sectionally is inconsistent.[40,41] In SNAP at wave 1, we found no relationship between other psychiatric diagnoses and autism severity as measured by diagnosis (childhood autism versus pervasive developmental disorder) or number of *ICD-10* symptoms.[42] In contrast, several studies have suggested that the SRS is associated with other domains of psychopathology both in youths with autism[43] and their affected[44] and unaffected siblings.[45] Future studies exploring trajectories of autism symptoms would benefit from using measures more clearly independent from other domains of psychopathology.

Our finding that mainstream school placement was associated with a decrease in adult autism symptoms remained significant in both multivariate and propensity analysis aimed at accounting for possible confounding for factors influencing placement. This is consistent with other studies; in a latent profile analysis, the longitudinal Adolescents and Adults With Autism study showed that inclusive secondary education was linked to membership in a group with fewer autism symptoms over time (as well as higher adaptive function and lower maladaptive behavior) and with greater improvement over time.[46] At a much younger age, inclusion in mainstream preschool was linked to better cognitive outcomes in primary school.[47] Neither of these studies was able to control for possible confounders, and all studies, including our own, are limited by their observational design. Hence, our finding is important to replicate in other samples and in quasiexperimental designs. If supported, this finding raises important policy considerations for educational placements and identifying the active ingredients—time spent with neurotypical peers in and outside of school; family and parental expectations; or other aspects of the educational environment, including opportunities after completing statutory education.

A surprising negative finding was the absence of an effect of IQ on either intercept or slope in the final autism symptom model. In univariate analyses, higher IQ was associated with a relative improvement in autism symptoms but failed to survive multivariate analysis. Several studies have previously reported that higher IQ is linked to better adult outcomes specifically in terms of autism symptoms.[28,39,46] Our multivariate analysis included type of school attended, which is strongly associated with IQ, and the current study is likely underpowered to identify independent effects of both characteristics. However, our finding that school experience trumped IQ raises questions about the mechanisms by which IQ exerts an effect on autism symptoms over the course of development. Developmental behavior genetic studies have shown the importance of evocative and active gene–environment correlation, whereby individual differences influence environmental exposures, with knock-on effects on IQ and other characteristics.[48] In the case of autism and IQ, higher ability may extend the range of experiences, including opportunities for

more sophisticated interaction that allows for greater sensitivity to the needs of people with autism, thus having an impact on their symptoms. Our findings suggest that identifying the mediators between IQ and autism outcomes could provide novel insights into interventions, especially ones targeting people with autism in the second and third decades of life.

We found no relationship of language level to either intercept or slope of autism symptoms, despite wide variation in language ability. Several,[28,29,49] but not all,[36] studies have highlighted the importance of early language acquisition. A possible explanation for our negative finding is that we measured language at an older age than other studies and suggests that language ability may exert its effect on outcome much earlier in development.[50]

For both outcomes, we found no evidence of an effect of the family variables, including maternal mental health problems, parental educational level, and neighborhood deprivation. However, factors that are potentially more precisely measured or more proximal, such as quality of parent–child relationships, have shown longitudinal prediction to reduced autism symptoms and maladaptive behaviors, albeit inconsistently,[7] and require further exploration.

In summary, the finding that mean IQ increases from late childhood to adult life points to ongoing development in the second decade of life and the importance of future research to identify experiences and interventions promoting cognitive development in people with autism. In particular, the role of educational and social experiences, for both cognitive and social communicative development, in adolescence and adult life needs further study to improve our understanding of how best to support people with autism across the life span.

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REFERENCES

1. Howlin P, Magiati I. Autism spectrum disorder: outcomes in adulthood. Curr Opin Psychiatry. 2017;30:69-76.
2. Henninger NA, Taylor JL. Outcomes in adults with autism spectrum disorders: a historical perspective. Autism. 2013;17:103-116.
3. Steinhausen HC, Mohr Jensen C, Lauritsen MB. A systematic review and meta-analysis of the long-term overall outcome of autism spectrum disorders in adolescence and adulthood. Acta Psychiatr Scand. 2016;133:445-452.
4. Magiati I, Xiang WT, Howlin P. Cognitive, language, social and behavioural outcomes in adjults with autism spectrum disorders: a systematic review of longitudinal follow-up studies in adulthood. Clin Psychol Rev. 2014;34:73-86.
5. Magiati I, Tay XW, Howlin P. Cognitive, language, social and behavioural outcomes in adults with autism spectrum disorders: a systematic review of longitudinal follow-up studies in adulthood. Clin Psychol Rev. 2014;34:73-86.
6. Taylor JL, Seltzer MM. Employment and post-secondary educational activities for young adults with autism spectrum disorders during the transition to adulthood. J Autism Dev Disord. 2011;41:566-574.
7. Woodman AC, Smith LE, Greenberg JS, Mailick MR. Change in autism symptoms and maladaptive behaviors in adolescence and adulthood: the role of positive family processes. J Autism Dev Disord. 2015;45:111-126.
8. Baird G, Simonoff E, Pickles A, *et al*. Prevalence of disorders of the autism spectrum in a population cohort of children in South East Thames—The Special Needs and Autism Project. Lancet. 2006;368:210-215.
9. Rutter M, Bailey A, Lord C. The Social Communication Questionnaire. Los Angeles: Western Psychological Services; 2003.
10. Lord C, Rutter M, Couteur A. Autism Diagnostic Interview-Revised: a revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. J Autism Dev Disord. 1994;24:659-685.
11. Lord C, Risi S, Lambrecht L, *et al*. The Autism Diagnostic Observation Schedule-Generic: a standard measure of social and communication deficits associated with the spectrum of autism. J Autism Dev Disord. 2000;30:205-223.
12. Harrison P, Oakland T. Adaptive Behavior Assessment System (ABAS) Second Edition. Oxford: Pearson; 2003.

13. Constantino JN, Gruber CP. Social Responsiveness Scale (SRS). Torrance, CA: Western Psychological Services; 2005.
14. Wing L, Leekam SR, Libby SJ, Gould J, Larcombe M. The Diagnostic Interview for Social and Communication Disorders: background, inter-rater reliability and clinical use. J Child Psychol Psychiatry. 2002;43:307-325.
15. Baird G, Charman T, Pickles A, *et al*. Regression, developmental trajectory and associated problems in disorders in the autism spectrum: the SNAP study. J Autism Dev Disord. 2008;38:1827-1836.
16. Semel E, Wiig EH, Secord W. Clinical Evaluation of Language Fundamentals-Revised. London: The Psychological Corporation; 1987.
17. Goodman R, Ford T, Simmons H, Gatward R, Meltzer H. Using the Strengths and Difficulties Questionnaire (SDQ) to screen for child psychiatric disorders in a community sample. Br J Psychiatry. 2000;177:534-539.
18. Goldberg D, Muller P. A User's Guide to the General Health Questionnaire GHQ. Windsor, UK: NFER-Nelson; 1988.
19. Morgan O, Baker A. Measuring deprivation in England and Wales using 2001 Carstairs scores. Health Stat Q. 2006;31:28-33.
20. Little RJA, Rubin DB. Statistical Analysis With Missing Data. New York: John Wiley & Sons; 1987.
21. Hayduk L. LISREL issues, debates and strategies. Baltimore: Johns Hopkins University Press; 1996.
22. Farley MA, McMahon WM, Fombonne E, *et al*. Twenty-year outcome for individuals with autism and average or near-average cognitive abilities. Autism Res. 2009;2:109-118.
23. Howlin P, Goode S, Hutton J, Rutter M. Adult outcome for children with autism. J Child Psychol Psychiatry. 2004;45:212-229.
24. Sigman M, McGovern CW. Improvement in cognitive and language skills from preschool to adolescence in autism. J Autism Dev Disord. 2005;35:15-23.
25. Howlin P, Savage S, Moss P, Tempier A, Rutter M. Cognitive and language skills in adults with autism: a 40-year follow-up. J Child Psychol Psychiatry. 2014;55:49-58.
26. Levy A, Perry A. Outcomes in adolescents and adults with autism: a review of the literature. Res Autism Spectr Disord. 2011;5:1271-1282.
27. Mawhood L, Howlin P, Rutter M. Autism and developmental receptive language disorder—a comparative follow-up in early adult life. I: Cognitive and language outcomes. J Child Psychol Psychiatry. 2000;41:547-559.
28. Billstedt E, Gillberg IC, Gillberg C. Autism in adults: symptom patterns and early childhood predictors. Use of the DISCO in a community sample followed from childhood. J Child Psychol Psychiatry. 2007;48:1102-1110.
29. Gillespie-Lynch K, Sepeta L, Wang Y, *et al*. Early childhood predictors of the social competence of adults with autism. J Autism Dev Disord. 2012;42:161-174.
30. Eaves LC, Ho HH. Young adult outcome of autism spectrum disorders. J Autism Dev Disord. 2008;38:739-747.
31. Whitehouse AJO, Watt HJ, Line EA, Bishop DVM. Adult psychosocial outcomes of children with specific language impairment, pragmatic language impairment and autism. Int J Lang Commun Disord. 2009;44:511-528.
32. Dietz C, Swinkels SH, Buitelaar JK, van Daalen E, van Engeland H. Stability and change of IQ scores in preschool children diagnosed with autistic spectrum disorder. Eur Child Adolesc Psychiatry. 2007;16:405-410.
33. McGovern CW, Sigman M. Continuity and change from early childhood to adolescence in autism. J Child Psychol Psychiatry. 2005;46:401-408.
34. Lord C, Schopler E. Stability of assessment results of autistic and non-autistic language-impaired children from preschool years to early school age. J Child Psychol Psychiatry. 1989;30:575-590.
35. Cederlund M, Hagberg B, Billstedt E, Gillberg IC, Gillberg C. Asperger syndrome and autism: a comparative longitudinal follow-up study more than 5 years after original diagnosis. J Autism Dev Disord. 2008;38:72-85.
36. Howlin P, Moss P, Savage S, Rutter M. Social outcomes in mid- to later adulthood among individuals diagnosed with autism and average nonverbal IQ as children. J Am Acad Child Adolesc Psychiatry. 2013;52:572-581.e571.
37. Ozonoff S, Iosif AM. Changing conceptualizations of regression: what prospective studies reveal about the onset of autism spectrum disorder. Neurosci Biobehav Rev. 2019;100:296-304.
38. Pickles A, Simonoff E, Conti-Ramsden G, *et al*. Loss of language in early development of autism and specific language impairment. J Child Psychol Psychiatry. 2009;50:843-852.
39. Gray K, Keating C, Taffe J, Brereton A, Einfeld S, Tonge B. Trajectory of behavior and emotional problems in autism. Am J Intellect Dev Disabil. 2012;117:121-133.
40. Gadow KD, DeVincent CJ, Pomeroy J, Azizian A. Psychiatric symptoms in preschool children with PDD and clinic and comparison samples. J Autism Dev Disord. 2004;34:379-393.
41. Gjevik E, Eldevik S, Fjaeran-Granum T, Sponheim E. Kiddie-SADS reveals high rates of DSM-IV disorders in children and adolescents with autism spectrum disorders. J Autism Dev Disord. 2011;41:761-769.
42. Simonoff E, Pickles A, Charman T, Chandler S, Loucas T, Baird G. Psychiatric disorders in children with autism spectrum disorders: prevalence, comorbidity and associated factors. J Am Acad Child Adolesc Psychiatry. 2008;47:921-929.
43. Bolte S, Poustka F, Constantino JN, Bolte S, Poustka F, Constantino JN. Assessing autistic traits: cross-cultural validation of the Social Responsiveness Scale (SRS). Autism Res. 2008;1:354-363.
44. Kanne SM, Abbacchi AM, Constantino JN. Multi-informant ratings of psychiatric symptom severity in children with autism spectrum disorders: the importance of environmental context. J Autism Dev Disord. 2009;39:856-864.
45. Hus V, Bishop S, Gotham K, Huerta M, Lord C. Factors influencing scores on the Social Responsiveness Scale. J Child Psychol Psychiatry. 2013;54:216-224.
46. Woodman AC, Smith LE, Greenberg JS, Mailick MR. Contextual factors predict patterns of change in functioning over 10 years among adolescents and adults with autism spectrum disorders. J Autism Dev Disord. 2016;46:176-189.
47. Nahmias AS, Kase C, Mandell DS. Comparing cognitive outcomes among children with autism spectrum disorders receiving community-based early intervention in one of three placements. Autism. 2014;18:311-320.
48. McCartney K, Harris MJ, Bernieri F. Growing up and growing apart: A developmental meta-analysis of twin studies. Psychol Bull. 1990;107:226-237.
49. Gillberg C, Steffenburg S. Outcome and prognostic factors in infantile autism and similar conditions: a population-based study of 46 cases followed through puberty. J Autism Dev Disord. 1987;17:273-287.
50. Pickles A, Anderson DK, Lord C. Heterogeneity and plasticity in the development of language: a 17-year follow-up of children referred early for possible autism. J Child Psychol Psychiatry. 2014;55:1354-1362.