

2 **Recognising autism: a latent transition analysis of parental reports**
3 **of child autistic spectrum disorder 'red flag' traits before and after age**
4 **3**5 Amanda Spikol¹ · Donal McAteer¹ · Jamie Murphy¹ 6 Received: 8 January 2018 / Accepted: 21 January 2019
7 © The Author(s) 20198 **Abstract**9 **Purpose** It has been proposed that parents should be educated about child autistic spectrum disorder (ASD) 'red flag' traits
10 to help professionals identify and address concerning behaviours as early as possible. This study aimed to empirically demon-
11 strate that established/recognised 'red flag' traits in the first 3 years of life would reliably predict ASD risk severity in later
12 childhood, associated with established ASD risk correlates and mirroring functioning diagnostic categories.13 **Methods** Using retrospective parental report data from the Mental Health of Children and Young People in Great Britain
14 survey ($N=7977$), latent class analysis (LCA) and a quasi -latent transition analysis were used to (1) identify profiles of
15 variation in parent reports of child 'red flag' traits before and after age 3 and (2) model transitions in risk from 3 years and
16 below to ≥ 3 years, respectively, per the 'optimal outcome' model.17 **Results** Three distinct classes, each characterised by variation in parent 'red flag' trait reporting were identified for the ' \leq
18 3 years of age' and the ' ≥ 3 years of age' data. Both LCA class profiles comprised groups of children characterised by low,
19 medium and high ASD risk. Dose-response effects for a number of recognised ASD correlates across the low, moderate
20 and high risk ' ≥ 3 years of age' classes seemed to validate older classes in terms of ASD relevance. Over 54% of children
21 characterised by the highest levels of ASD 'red flag' trait probability at 3 years and below (2% of sample), also populated
22 the high-risk class evidenced in the ' ≥ 3 years of age' LCA.23 **Conclusions** Retrospective parental reports of child ASD 'red flag' traits ≤ 3 years of age were reliable indicators of ASD
24 risk in later childhood.25 **Keywords** Autism spectrum disorders · Red flag traits · Epidemiology · Latent class analysis26 **Introduction**27 Autism spectrum disorder (ASD) is a lifelong neurodevelop-
28 mental disorder characterized by difficulties in social inter-
29 action, communication, and repetitive behaviours [1]. It is
30 commonly described as a childhood disorder, as symptoms
31 often first become apparent during early development. Its
32 symptoms are diverse and behaviours associated with ASD
33 vary in expression among those with the disorder, which can
34 often make diagnosis difficult [2]. Recently, diagnostic cat-
35 egories for variants of autism, e.g. pervasive developmentaldisorder not otherwise specified (PDD-NOS) and Asperger's
36 syndrome (AS), have been reclassified as ASD in the DSM-5
37 [1], (see [3–5] for re-diagnosis review). ASD has been rec-
38 ognised as a more meaningful and sufficiently inclusive con-
39 struct to describe the variations in behaviour, functioning,
40 and presentation that commonly characterise the phenotype
41 [6–8]. However, there is evidence that individuals with these
42 variant diagnoses differ significantly from more severe ASD
43 in intelligence [9–11], verbal ability [12], and overall cogni-
44 tive profile [13, 14], including discreet differences in brain
45 morphology [15]. The diagnostic definitions used in assess-
46 ment have changed despite evidence of differences in symp-
47 tomology between PDD-NOS/AS and ASD [16] with these
48 differences in behavioural trait severity evident in early life
49 and showing trait stability [17].
50During the first years of a child's life, parents and care-
51 takers are most likely to be the first to observe, evaluate and
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53 interpret a child's behaviour. They are also often the first to
 54 seek professional advice when a child's behaviour seems
 55 'odd' or 'unusual' [18, 19]. While developmental variation
 56 in the population is to be expected, a cluster of behaviours or
 57 missed milestones ('red flags') can signal the presence of a
 58 potential underlying problem and may be indicative of disor-
 59 dered behaviour [20]. Parental 'prediction' of ASD diagno-
 60 sis via problematic behaviours has been shown to be reliable,
 61 both in prospective and longitudinal studies [21, 22] and in
 62 studies utilising retrospective population data [23, 24].

63 It has been proposed, therefore, that assessment should
 64 take place as soon as developmental issues become apparent
 65 [25, 26]. The average ASD diagnosis age in the US is 4 years
 66 [27] though diagnosis can be made as early as 2 years [28]
 67 with predictive diagnostic tools existing for those as young
 68 as 12 months [29]. Early intervention strategies have been
 69 shown to be advantageous in capitalising on toddlers' devel-
 70 opmental plasticity [30] and have shown significant benefits
 71 in adaptive behaviour, language, and overall functioning
 72 [31–33].

73 While critics of early diagnosis cite 'normal' slow devel-
 74 opment and ASD false-positive diagnoses [34] the benefits
 75 of early diagnosis and intervention have been strongly advo-
 76 cated. Initial diagnoses are routinely revisited and show early
 77 behavioural symptoms to be consistent with ASD outcomes
 78 [35–37]. Early intervention has been shown to be beneficial
 79 for the development of cognitive, social, and communica-
 80 tion skills [38] and because further refinement of these skills
 81 comes with growth and experience, an early ASD diagno-
 82 sis does not always predict diagnostic outcomes or level
 83 of deficit in later childhood [36]. A favourable or 'optimal
 84 outcome' (OO) of improvement in functioning to the point
 85 the child loses the ASD diagnosis is not a recent concept
 86 [39]. Recent research has highlighted that OO children still
 87 show deficits in social relationships and some developmental
 88 issues that affect social functioning [40, 41] but can function
 89 normally with typically developing children. Higher initial
 90 functioning in combination with early intervention seems
 91 to be the strongest predictor of OO [42–44] and while trait
 92 expression and behaviour improve out of the clinical range,
 93 physical brain activity is closer to an ASD population [45].

94 The current study, therefore, utilised retrospective data
 95 with the aim to explore the variation in parent reports of
 96 child 'red flag' traits, before and after age 3, in the general
 97 population, to test (1) whether a spectrum of presentation
 98 in behavioural ('red flag') traits could be identified in both
 99 early and later childhood while displaying the variance of
 100 previous autism diagnostic categories, (2) whether sever-
 101 ity in 'red flag' traits ≥ 3 years would be associated with
 102 established ASD risk correlates and (3) whether severity
 103 in 'red flag' traits ≤ 3 years of age would meaningfully cor-
 104 relate with severity in later childhood or an 'optimal out-
 105 come'. It was predicted that distinct profiles of 'red flag'

106 traits would emerge for both time periods and that these
 107 profiles would reflect variation in ASD risk mirroring the
 108 PDD-NOS/AS/HFA variant diagnoses. It was also predicted
 109 that parental reporting of 'red flag' traits would be a reliable
 110 indicator of ASD risk and that this would be demonstrated
 111 via dose–response associations with established ASD risk
 112 correlates. Finally, given that extant evidence supports the
 113 'parental concern' model, with concerns raised in specific
 114 developmental domains between the ages of 1 and 3 years
 115 correlating with ASD diagnosis and later diagnostic out-
 116 comes [46–50] it was hypothesised that the most severe
 117 'red flag' trait profiles, retrospectively reported by parents,
 118 at ≤ 3 years of age, would be associated with the severity of
 119 'red flag' trait reporting in later childhood in keeping with
 120 previous 'optimal outcome' findings.

121 Method

122 Sample

123 Data for this study were sourced from the national survey,
 124 Mental Health of Children and Young People in Great Brit-
 125 ain (GB), 2004 [51], collected by the Office of National
 126 Statistics (ONS; all analyses were performed in accordance
 127 with ONS ethical and data handling regulations); the survey
 128 was a thorough census of medical, emotional, and social
 129 health of young people in GB. A sample was obtained from
 130 the Department for Work and Pensions' Child Benefit Centre
 131 (CBC) based on Child Benefit records and from this, a sam-
 132 ple of postal areas in England, Scotland, and Wales, and ulti-
 133 mately a random sample of addresses was selected, exclud-
 134 ing any household where the CBC had an 'action' open such
 135 as child death or CBC involvement, describing these cases as
 136 'sensitive'. This census was multiphasic, conducted in 1999
 137 and 2004. As the chosen measure did not appear in the 1999
 138 phase, this study utilises only the 2004 data.

139 The resultant sample of 12,294 households was contacted
 140 via post by the CBC with survey details/opt-out instructions
 141 with 1085 (9%) opting out, 631 (5%) having moved, 82 (1%)
 142 being found ineligible, and 1798 (15%) not approached for
 143 an interview. Of the 10,496 approached for an interview,
 144 2183 (21%) refused and 313 (3%) could not be contacted,
 145 leaving a sample of 7977 households where an ONS rep-
 146 resentative conducted interviews with a parent. The final
 147 interview sample ($N = 7977$) was 52% male (4111) with a
 148 mean age of 10.54 (SD 3.40) and range of 4–17.

149 Measures

150 A general development questionnaire was created by
 151 the ONS for this survey, containing a parent/caregiver
 152 directed autism sub-questionnaire of 43 items. Led by five

153	binary-answer anchor questions pertaining to the parent/car-	in social and behavioural sciences see Nylund [54]. LTA was	200
154	giver's child before the age of 3, each concerned an area of	conducted in the following steps.	201
155	potential autistic behaviour:		
156	1. Was there anything that seriously worried you or anyone	Step 1: determine the best measurement model	202
157	else about the way his/her speech developed?		
158	2. Was there anything that seriously worried you or anyone	To determine the best measurement model, a series of	203
159	else about how s/he got on with other people?	LCAs were specified and tested separately at the two time	204
160	3. Was there anything that seriously worried you or anyone	points using available binary red flag ASD trait variables as	205
161	else about the way his/her pretend or make-believe play	observed indicators. The first LCA was used to determine the	206
162	developed?	number and qualities of sub-types of autistic trait variation	207
163	4. Was there anything that seriously worried you or anyone	(red flags) based on endorsement of each of the five behav-	208
164	else about any odd rituals or unusual habits that were	ioural anchor questions (≤ 3 years of age) from the general	209
165	very hard to interrupt?	development questionnaire devised by the ONS. These five	210
166	5. Was there anything that seriously worried you or anyone	items were binary and treated as categorical. Three latent	211
167	else about his/her ability to learn and do new things—	class models were tested (a 2-through a four-class latent	212
168	such as puzzles or helping get dressed?	class model). The second LCA was used to determine the	213
169	Following was a binary-answer gatekeeper question	number and qualities of sub-types of autistic trait variation	214
170	'Have the things that seriously worried you or someone else	based on endorsement of each of the ten behavioural ques-	215
171	now cleared up completely?' A positive answer ended the	tions from the body of the questionnaire relating to red flag	216
172	autism section while a negative answer led to the remain-	traits ≥ 3 years of age. These items were treated as categori-	217
173	ing autism questions. Ten questions were selected from the	cal. Three latent class models were tested (a 2 through to a	218
174	body of this questionnaire; two questions to approximate	four-class latent class model).	219
175	each of the five behaviours detailed in the anchor questions	Models were compared using a range of common fit sta-	220
176	(see "Appendix 1") acting as broad early 'red flag' behav-	tistics. The Akaike information criterion (AIC) [55], the	221
177	ioural markers [37].	Bayesian information criterion (BIC) [56], and the sample	222
178	Additional data	size-adjusted Bayesian Information Criterion (ssaBIC) [57]	223
179	The Mental Health of Children and Young People in Great	were used to compare model fit, with lower values indica-	224
180	Britain, 2004 [51] survey also involved a full health ques-	tive of better fit. The Lo–Mendel–Rubin likelihood ratio test	225
181	tionnaire, including ICD-10 criteria of mental and physical	(LMR-LRT) is used to compare a solution with k number of	226
182	health issues. Four known comorbid conditions for autism	classes with a solution with $k - 1$ classes [58]. A non-signif-	227
183	were chosen as covariates for analysis; epilepsy, learning dif-	icant p value indicates that the model with $k - 1$ classes pro-	228
184	iculties, poor coordination, and any anxiety disorder. These	vides a better fit [58]. Model fit was also assessed using the	229
185	were scored as binary variables indicating either presence or	entropy criterion [59]. This statistic determines how accu-	230
186	absence of each condition. In addition, an ICD-10 diagnosis	rately individuals were assigned to their classes based on the	231
187	of autism spectrum disorder was also used as a validator in	posterior probabilities [59]. Entropy values range from 0 to	232
188	support of the latent factor typified by 'red flag' behaviours	1, with higher values reflecting more accurate classification	233
189	being autistic behavioural traits.	[59]. To ensure that the models converged on global rather	234
190	Analytic strategy	than local solutions, 100 random sets of starting values and	235
191	LTA is a longitudinal modelling technique used to examine	50 final stage optimizations were used.	236
192	whether individuals transition between latent classes over	It remains debated whether the LMR-LRT or BIC is more	237
193	time. LTA consists of two components; a measurement	useful when it comes to determining the optimal number	238
194	model and an autoregressive model [52, 53]. In LTA, the	of classes in an LCA [54]. A number of simulation studies	239
195	measurement model (i.e. LCA) describes the structure of	suggest that the BIC is highly effective at identifying the	240
196	the latent classes at the various time points. The autoregres-	correct underlying class structure, while the LMR-LRT can	241
197	sive model (i.e. Markov model) examines individual-level	occasionally extract too many classes when the sample size	242
198	transitions between these classes over time [52, 53]. For a	is large ($N > 1000$) [54, 60]. Given that the sample size was	243
199	much more detailed description of LTA and its applications	relatively large in the present study, the BIC was considered	244
		a more reliable indicator of the optimal class solution.	245

246 Step 2: validate classes using ASD diagnosis and clinical 247 correlates

248 Multinomial logistic regression was used to test whether the
249 red flag trait classes/typologies at time one were meaningful
250 in relation to ASD. Associations between class membership
251 and an ASD diagnosis variable and four common clinical
252 correlates of ASD was conducted.

253 Step 3: specify latent transition model

254 In this step, the LTA model is specified, producing a matrix
255 of latent transition probabilities. This model affords the
256 opportunity to classify individuals as ‘movers’ (i.e. those
257 who transition from one class to a different class over time)
258 or ‘stayers’ (i.e. those who remain in the same class across
259 time) [52, 53]. Mover–stayer models more accurately
260 describe transitions between classes, as transition probabili-
261 ties are estimated for ‘movers’ only [52, 53].

262 All analyses included the first-stage sampling were made
263 weighted variables to account for non-equal probabilities of
264 selection. This standardising technique adds an additional
265 ‘weight’ to under-represented sub-populations that may not
266 be accurately represented due to missing data and was used
267 rather than excluding cases listwise. Analyses were con-
268 ducted using Mplus 4 [61].

269 Results

270 Table 1 (section a) shows the fit indices for the first latent
271 class analysis (≤ 3 years of age). The three-class solution
272 was the model of best fit; the likelihood ratio Chi square
273 was non-significant, the AIC was lower for the three-class
274 solution than for the two-class solution, and the Lo–Men-
275 dell–Rubin’s LRT showed that the four-class solution was
276 not significantly better than the three-class solution. The

entropy value (0.83) also showed a meaningful classifica-
277 tion of cases. 278

279 The three-class model, shown in Fig. 1, revealed a
280 ‘High endorsement class’ comprised of 1.9% of the popu-
281 lation where the probability of ‘red flag’ trait endorse-
282 ment was $> 70\%$ for all five traits. A larger ‘Moderate
283 endorsement class’ also emerged, representing 10.8% of
284 the population and was characterised by moderate endorse-
285 ment probabilities of language, social, and developmen-
286 tal problem behaviours. A large ‘Low endorsement class’
287 (baseline class) comprised of 87.3% of the population was
288 characterised by extremely low endorsement probabilities
289 ($< 10\%$) across all ‘red flag’ traits.

290 A second LCA was carried out to identify distinct
291 groups characterised by red flag traits after the age of 3
292 using 10 questions from the body of the questionnaire
293 (see “Appendix 1”); two exemplifying each of the five
294 behaviours described by the anchor questions. Another
295 three-class solution emerged. Table 1 (section B) shows
296 the fit indices for the second latent class analysis. The
297 three-class solution was the model of best fit; the AIC
298 was lower for the three-class solution than for the two-
299 class and the Lo–Mendell–Rubin’s LRT showed that the
300 four-class solution was not significantly better than the
301 three-class solution. The entropy value (0.72) showed a
302 meaningful classification of cases. Probability estimates
303 for class membership in both LCAs were robust.

304 The three-class model for the ‘ ≥ 3 years of age’ data,
305 shown in Fig. 2, revealed a small moderate presenta-
306 tion class; 16.7% of the sample characterised by varied
307 endorsement of the five ‘red flag’ behaviour categories.
308 A larger high presentation class emerged, where 31.5% of
309 the sample were characterised by high endorsement prob-
310 abilities of most items. A larger low presentation class was
311 also evident, 51.8% of the sample which was characterised
312 mainly by moderate endorsement probabilities relating to

Table 1 Fit indices for the latent class analyses

	$LR\chi^2$ (<i>df</i>) <i>p</i>	AIC	BIC	SSABIC	LRT (<i>p</i>)	Entropy
A (≤ 3 years)						
2 class	229.81 (20) < 0.01	16,831.08	16,907.72	16,872.77	2557.63 (< 0.01)	0.91
3 class	50.10 (14) < 0.01	16,661.71	16,780.16	16,726.14	178.06 (< 0.01)	0.83
4 class	16.41 (8) 0.03	16,639.72	16,799.98	16,726.89	33.36 (0.02)	0.85
5 class	1.32 (2) 0.51	16,636.51	16,838.58	16,746.42	14.93 (0.01)	0.85
B (≥ 3 years)						
2 class	888.92 (981) 0.98	8950.98	9047.81	8981.12	510.67 (< 0.01)	0.67
3 class	800.25 (970) 1.0	8880.38	9027.92	8926.31	91.34 (0.08)	0.72
4 class	744.87 (959) 1.0	8849.06	9047.32	8910.78	52.59 (0.33)	0.67
5 class	716.87 (951) 1.0	8839.72	9088.69	8917.22	30.91 (0.51)	0.73

$LR\chi^2$ likelihood ratio Chi square, AIC Akaike information criterion, BIC Bayesian information criterion, SSABIC sample size adjusted BIC, LRT Lo–Mendell–Rubin’s adjusted likelihood ratio test

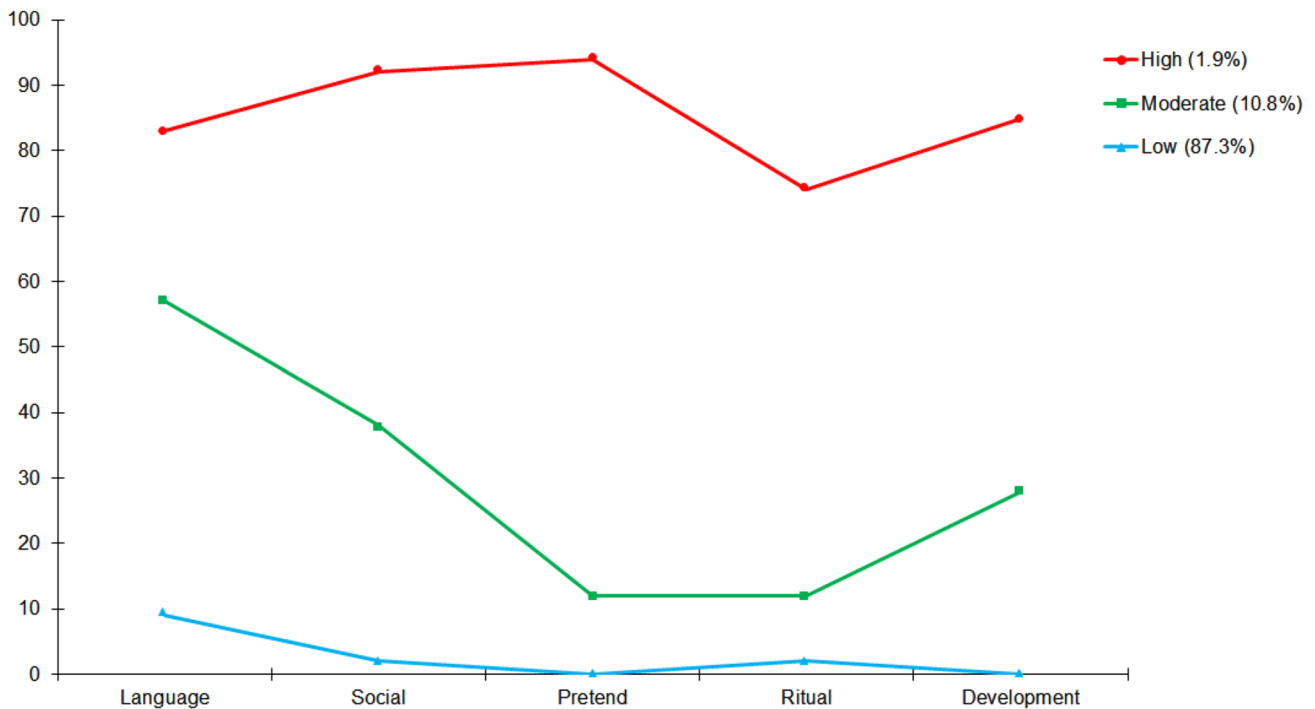


Fig. 1 Endorsement probability plot for autism anchor questions

Table 2 ASD risk for high, moderate, and low presentations at ≤ 3 years of age

	Odds ratio (95% confidence intervals)	
	High	Moderate
Epilepsy (absence)	36.72*** (8.96–150.58)	4.94*** (2.02–12.08)
Learning D (absence)	70.36*** (33.63–147.22)	8.23*** (5.87–11.52)
Coordination (absence)	26.55*** (11.36–62.08)	14.37*** (7.41–27.87)
Anxiety (absence)	3.47** (1.36–8.88)	3.40*** (2.11–5.48)
ASD diagnosis (absence)	954*** (57.61–15,830.94)	20.73* (1.12–382.38)

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

313 pretend/play and ritual/habit traits, with a higher endorse-
 314 ment of language issues.

315 A multinomial logistic regression was conducted to test
 316 whether severity in ‘red flag’ traits ≤ 3 years would be asso-
 317 ciated with established ASD risk correlates (see Table 2).
 318 The ASD risk variables showed significant odds ratios
 319 across the high and moderate classes when compared to the
 320 low class. Moderate presentation was described by highly
 321 significant odds ratios of epilepsy, learning difficulties, poor
 322 coordination, and anxiety and by significant odds ratios of
 323 ASD diagnosis. High presentation showed very highly sig-
 324 nificant odds ratios of epilepsy, learning difficulties, poor
 325 coordination, and ASD diagnosis and highly significant odds
 326 ratios of anxiety.

327 A latent transition analysis (LTA) was used to identify
 328 transitions in class membership from early to later childhood
 329 (see Tables 3, 4).

Members of the ‘≤ age 3’ high class were more likely
 to remain in the high class ≥ age 3 (82.3%) than transition
 to the moderate (15.1%) or low (2.6%) classes. The mod-
 erate class showed a mixed effect, with 22.6% remaining
 moderate, 33.1% transitioning ‘up’ to high and 44.2% tran-
 sitioning ‘down’ to low. The low class were more likely
 to remain low (74.2%) than to transition into either the
 moderate (14.5%) or high (11.3%) classes. When examined
 in the context of a move-or-stay model (see Table 5), the
 majority of the overall sample (89.9%) fell into the stayer
 category; beginning and remaining low. Movers showed a
 ‘downward’ transitional trend, with 72.7% of this sample
 category transitioning from high to moderate or moderate
 to low.

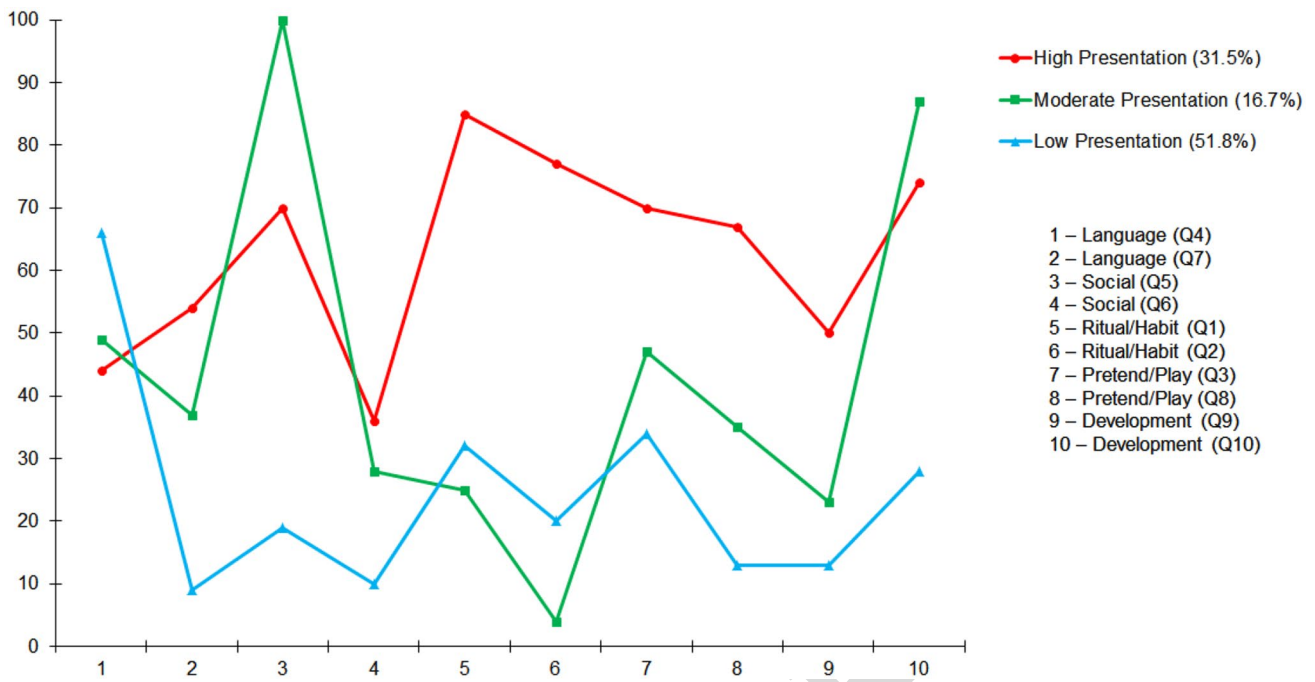


Fig. 2 Endorsement probability plot for > 3 years of age ASD items

Table 3 Average latent class probabilities for most likely latent class membership

	High (%)	Moderate (%)	Low (%)
A (≤ 3 years)			
High	88.4	11.6	0
Moderate	3.6	81.7	14.7
Low	0	5.3	94.7
B (≥ 3 years)			
High	87.1	5.9	7
Moderate	11.7	80.8	7.5
Low	4.6	5.3	90.1

Table 4 Latent transition probabilities from ≤ 3 years of age to > 3 years of age

≤ 3 years of age	> 3 years of age		
	High	Moderate	Low
High	0.823	0.151	0.026
Moderate	0.331	0.226	0.442
Low	0.113	0.145	0.742

344 **Discussion**

345 The first analysis revealed three profiles characterised by
 346 behaviours that would strongly reflect ‘red flag’ risk at an

age where initial assessment is common. The scale ques- 347
 tions narrowed in focus, helping to present a better pic- 348
 ture of these behaviours, for example, going from ‘speech 349
 development’ to correct application of speech to the situ- 350
 ation and appropriate phrase use. The differences in func- 351
 tioning between the classes may have demonstrated varied 352
 expression of ASD in accordance with older diagnostic 353
 categories, however, it is important to note that they were 354
 only approximations of ASD ‘red flags’. Variation in the 355
 latent class profiles after the age of 3, however, showed 356
 levels of expression in specific traits that were consistent 357
 with variation in ASD presentation [62]. The Low Presen- 358
 tation profile, largest at 51.8% of the subsample, was 359
 described by in/formal language use problems and some 360
 repetitive play and obsession behaviours but low instances 361
 of the other traits. These issues were enough for parents to 362
 report when asked, but may not have constituted an actual 363
 clinical threshold for ASD, as such traits vary naturally in 364
 the population [8]. The line between ‘personality quirk’ 365
 and ‘symptom’ is often quite thin [63], especially for the 366
 atypical functioning of individuals formerly categorised 367
 under PDD-NOS [16]. The Low Presentation profile rep- 368
 resents a group that varies from a baseline population (‘no 369
 ongoing concerns’ or minimal trait expression) to just over 370
 the cusp of an older clinical designation. The moderate 371
 presentation profile, smallest at 16.7%, was typified by 372
 all-cause developmental problems, repetitive play, and in/ 373
 formal language use problems in keeping with the presen- 374
 tation of AS. This profile also showed a 100% endorsement 375

Table 5 Count and relative percent of mover–stayer patterns

		≤ 3 years of age	> 3 years of age	<i>n</i>	% within movers/ stayers (%)	% of total sample (%)
Movers	High	Moderate		23	3.9	< 1
	High	Low		1	< 1	< 1
	Moderate	High		95	15.9	1.2
	Moderate	Low		411	68.8	5.2
	Low	High		30	5	< 1
	Low	Moderate		37	6.2	< 1
Stayers	High	High		133	1.8	1.7
	Moderate	Moderate		65	< 1	< 1
	Low	Low		7054	97.3	89.9

of eye contact issues, one of the hallmarks of ASD [64, 65], though it was low in other domains. The high presentation profile, 31.5% of the subsample, showed overall higher endorsements of more behaviours at levels which could be interpreted as past the clinical threshold for disorder and fitting the perception of ‘classical’ autism.

The LTA exposed a rough estimation of ‘red flag’ behaviour before the age of 3 and the second analysis focused on a more nuanced picture of these behaviours after the age of 3. A quasi-latent transitional analysis between those two ‘time points’ described transition between the latent classes, representing changes in symptom severity and occurrence over time. Those with membership in the ‘≤ age 3’ high class had the highest probability of remaining high ≥ age 3 while the greatest percentage of the sample population were those classified as low ≤ age 3 who remained so after. Those classified as moderate showed the greatest variance of transition ≥ age 3 as would be expected from this class, having the lowest overall classification probabilities in both LCAs. These results showed a clear relationship between initial ‘red flag’ behaviour severity (ASD risk) and behaviour persistence. Wolff et al. [66] observed this effect in the persistence of repetitive behaviour in toddlers over time, with the most severe behaviour persisting in an ASD sample. It is important to note, however that possible interventions, family/school socialisation, and general development [36] may have accounted for the downward trend in symptom severity over time but detailed intervention/treatment data was not available (see limitations below).

In seeking external validation for the hypothesis of the latent factor being ASD risk, the resultant high and moderate profiles were examined against the low category as a baseline in terms of four known ASD comorbidities (learning difficulties, poor coordination, any anxiety disorder, and epilepsy) and instances of ICD-10 ASD diagnosis in the sample. Odds ratios were highly significant as empirical predictors of ASD risk and confirmation that it was the latent factor. ASD diagnosis odds were 954 times higher

than baseline for the high class and 20.73 times higher for the moderate class, indicating that ‘red flag’ behaviour traits are a predictor of ASD risk. Higher odds ratios were found in the High class than the moderate class for all items, further confirming a difference in severity in accordance with the hypothesis of multiple levels of severity and functioning aligning with older variant diagnoses. Epilepsy rates are important to note here as the relationship between ASD and epilepsy is well established with research indicating a potential genetic relationship [67–70].

These results support the hypothesis of parental perception of ‘red flag’ behaviours before the age of 3 being predictive of ASD risk and severity. Analysis revealed distinct behavioural profiles with variance in expression of ASD conducive with variant diagnostic categories, validated by the presence of known comorbidities and gender rates. The data from this survey are from 2004 and the sample’s mean age was 10.51 (SD 3.39), indicating that most children from the sample were below the age of 3 in the mid to late 1990s. Research into ASD as a developmental disorder increased during the 1970s–1980s, challenging the notion of autism resulting from ‘refrigerator mothers’ [71]. The 1990s saw a wider awareness of variation in ASD and the concept of a spectrum of behaviours/diagnoses but the true tipping point of media awareness (and perhaps over-awareness) would not come until the early 2000’s [72]. The survey asked about ‘red flag’ behaviours worrying parents at that time, meaning before widespread ASD awareness and media coverage of the ‘autism epidemic’, removing an element of potential contamination in parental perception.

There is a solid foundation of research supporting the stability of ASD behaviours in early diagnosis ≤ age 3 to later reassessment ≥ age 4 in both general population [73, 74] and high risk samples [75, 76]. That stability does not contradict the OO model of improvement through early intervention programs and socialisation based on severity of initial symptomology. The trend for functioning-based improvement [40, 42] was replicated in this study as severe

452 individuals tending to stay severe and moderate-to-low
453 severity individuals tended to improve.

454 The evidence presented should be evaluated with the
455 study's limitations in mind.

456 The ASD section of the general development question-
457 naire designed by the ONS was in nonclinical language, was
458 not a measure intended for clinical diagnosis, and was not a
459 pre-existing, tested psychometric. The latent classes in the
460 first LCA had a large catchment due to the general 'red flag'
461 ASD terminology used; intended for parents rather than cli-
462 nicians. The wording, "Was there anything that seriously
463 worried you or anyone else about the way his/her speech
464 developed?" failed to differentiate between language use and
465 speech disorder. "Odd rituals or unusual habits that were
466 very hard to interrupt" could have described the repetitive
467 behaviours of ASD but could also have described the ritual-
468 istic learning behaviour common in toddlers [77, 78]. Issues
469 of 'learning development' could have referred to any devel-
470 opmental delay or learning disability; even the traditional
471 'late bloomer' who goes on to develop with no impairment
472 [79, 80]. While this may have seemed like a limitation to the
473 validity of the study, the non-clinical language was actually
474 considered a strength of the analysis, in that it described
475 issues in a way that might be considered consistent with
476 parental disclosures of concern to GPs/paediatricians. No
477 health professionals were involved in the interviews and
478 questionnaire responses were only parental perception/inter-
479 pretation of the child's behaviour. No data were collected
480 concerning any treatment the children may have received
481 for their issues after the age of 3, any effects that treatment
482 may have had, or the presence of other developmental dis-
483 orders. In addition, this parental-report data was susceptible
484 to hindsight bias as no prospective screening was performed
485 to isolate an ASD risk sample. Hindsight bias appears in
486 diagnosis amongst clinicians trained to use diagnostic crite-
487 ria and conduct assessments [81, 82] so its effect cannot be
488 understated in non-clinical individuals. As there was little
489 diagnostic outcome information available for the sample,
490 the model of change in ASD behaviours over time could
491 only be described as a trend model; further studies would
492 benefit from a longer longitudinal design. In addition, the
493 LTA performed was only a quasi-LTA, as the data used for
494 each time period differed, and the items in the second model
495 attempted only to approximate those in the first.

496 Parents' perception of early 'red flag' behaviours cer-
497 tainly seem to act as valid predictors of future ASD risk
498 while reinforcing the variation in expression of ASD that
499 had been previously described by variant diagnosis. While
500 many missed milestones or developmental delays can often
501 clear up in time, some behavioural symptomology may per-
502 sist and signify developmental disorder. Meaningful transi-
503 tion from disorder to a typical development population is
504 the hoped-for OO model depending on the initial level of

505 functioning. Further studies of large general population data
506 with a longitudinal design, featuring clinical measures and
507 clinician involvement could help create a clearer picture of
508 ASD variation and transition in the population. Such paren-
509 tal report data would be valuable assets in the development
510 and testing of future diagnostic tools.

511 Compliance with ethical standards

512 **Conflict of interest** On behalf of all authors, the corresponding author
513 states that there is no conflict of interest.

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520 Appendix 1

521 Q1. (Pretend/Play) "Some children spend a lot of their play
522 time repeating the same action over and over again, for
523 example spinning the wheels on a toy car, turning taps or
524 light switches on and off, or opening and shutting doors. Has
525 this ever been true of CHILD?"

526 Q2. (Pretend/Play) "Children are sometimes very inter-
527 ested in unusual aspects of toys or other things. For example,
528 rather than playing with a toy, they may spend their time
529 sniffing it, or running their fingers over its surface, or listen-
530 ing to any noise or vibration that it makes. Has this ever been
531 true of CHILD?"

532 Q3. (Ritual/Habit) "Some ^Children/teenagers enjoy
533 putting a lot of time into collecting things, or get a lot of
534 pleasure out of focusing on just one topic, such as sport,
535 cars or a particular pop group. In everyday language, we
536 often say that these ^Children/teenagers are 'obsessed' by
537 their interest, but this is not an unpleasant obsession—this
538 is something they like and usually enjoy talking about. Has
539 CHILD had any long-lasting obsessions of this sort?"

540 Q4. (Language) "Some ^Children/teenagers have trouble
541 adjusting their language to suit different social occasions.
542 For example, they may speak too casually to a teacher or
543 too formally to other children. Does CHILD change the way
544 ^s/he speaks according to whether it is a formal or informal
545 situation?"

546 Q5. (Social) "When we're talking with someone face-to-
547 face, eye contact is very important. It generally makes us
548 feel uneasy, or as if there's something wrong, if the other
549 person makes too little eye contact, or too much, or makes
550 it at the wrong time. Has CHILD ever been through a phase
551 of making too little or too much eye contact, or making it in
552 the wrong sort of way?"

553 Q6. (Social) “^Children/Teenagers respond in differ- 605
 554 ent ways to other people’s emotions. For example, if their 606
 555 mother is upset because she has cut her finger badly with a 607
 556 knife, children can be sympathetic, or not pay much atten- 608
 557 tion, or respond in unusual ways such as laughing. What 609
 558 would CHILD typically do in this sort of situation?” 610

559 Q7. (Language) “Another way in which children repeat 611
 560 themselves is by using the same catch-phrase or cliché over 612
 561 and over again. For example, almost every sentence may 613
 562 begin ‘If you want my opinion...’ or ‘Logically speaking...’ 614
 563 Occasionally the phrase is appropriate, but it is used far 615
 564 more than is really needed. Has CHILD ever filled ^his/ 616
 565 her speech with a lot of these fairly empty catch-phrases or 617
 566 clichés?” 618

567 Q8. (Ritual/Habit) “Some children enjoy routines and 619
 568 want things to be the same every day. For example, they may 620
 569 want to eat the same food off the same plate while sitting 621
 570 in the same chair every single day. Or there may be very fixed 622
 571 routines for dressing or undressing. Has CHILD ever had 623
 572 strong or unusual routines that ^s/he has insisted on because 624
 573 ^s/he enjoyed doing it that way?” 625

574 Q9. (Development) “Some preschool children go through 626
 575 a phase of flapping or waving their hands or arms up and 627
 576 down if they are excited or upset. Some continue doing this 628
 577 for years. Since CHILD has been going to school, has ^s/he 629
 578 tended to flap ^his/her arms when excited or upset?” 630

579 Q10. (Development) “You have answered a lot of ques- 631
 580 tions about CHILD’s pattern of development - focusing par- 632
 581 ticularly on language, play, routines and ^his/her ability to 633
 582 get along with other people. Are you concerned at present 634
 583 about any of these aspects of CHILD’s development?” 635

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