

Supplementary material for:

“Identifying predictive features of autism spectrum disorders in a clinical sample of adolescents and adults using machine learning”

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Supplement 1 (Psychopathological Description):

Table S1. Psychopathological Description of Participants.

Psychopathological description	ASD (n=385)	non-ASD (n=288)
Other psychiatric disorders than ASD	n=160 (42%)	n=189 (66%)
ICD-10: F10-F19	n=8 (2%)	n=6 (2%)
Mental and behavioral disorders due to psychoactive substance use		
ICD-10: F20-F29	n=2 (0.6%)	n=3 (1%)
Schizophrenia, schizotypal and delusional disorders		
ICD-10: F30-F39	n=88 (23%)	n=53 (18%)
Affective disorders		
ICD-10: F40-F48	n=56 (15%)	n=61 (21%)
Neurotic, stress-related and somatoform disorders		
ICD-10: F50-F59	n=2 (0.6%)	n=0 (0%)
Behavioral syndromes associated with physiological disturbances and physical factors		
ICD-10: F60-F69	n=15 (4%)	n=45 (16%)
Disorders of adult personality and behavior		
ICD-10: F80-F89 <i>except</i> F84	n=15 (4%)	n=17 (6%)
Disorders of psychological development other than pervasive developmental disorders		
ICD-10: F90-F98	n=44 (11%)	n=66 (23%)
Behavioral and emotional disorders with onset usually occurring in childhood and adolescence		
No other psychiatric disorder	n=225 (58%)	n=99 (34%)

Abbreviations: ASD, autism spectrum disorder; ICD-10, International Statistical Classification of Diseases and Related Health Problems 10th Revision.

Supplement 2 (ADOS code distribution):

Table S2. Distribution of ADOS Module 4 codes in the ASD and non-ASD group. Code of 0 = no abnormality related to autism; Code of 1 = some abnormality; Code of 2 = definite evidence of abnormality; Code of 3 = profound severity; Code of 7 = abnormal behavior of a type that is not encompassed by the other ratings; Code of 8 = behavior not exhibited during the observation and/or the rating is inapplicable; Code of 9 = missing values (i.e. answers omitted or left blank).

		ADOS Code						
ADOS Item	Group	0 n (%)	1 n (%)	2 n (%)	3 n (%)	7 n (%)	8 n (%)	9 n (%)
ADOS Domain: Language/Communication								
A1	Non-ASD	278 (96.5)	7 (2.4)	2 (0.7)	0	-	-	1 (0.3)
	ASD	356 (92.5)	15 (3.9)	6 (1.6)	2 (0.5)	-	-	6 (1.6)
A2	Non-ASD	192 (66.7)	82 (28.5)	7 (2.4)	0	4 (1.4)	0	3 (1.0)
	ASD	119 (30.9)	206 (53.3)	50 (13.0)	0	1 (0.3)	1 (0.3)	8 (2.1)
A3	Non-ASD	287 (99.7)	0	0	0	-	-	1 (0.3)
	ASD	373 (96.9)	7 (1.8)	0	0	-	-	5 (1.3)
A4	Non-ASD	255 (88.5)	33 (11.5)	0	0	-	-	0
	ASD	261 (67.8)	113 (29.4)	11 (2.9)	0	-	-	0
A5	Non-ASD	233 (80.9)	39 (13.5)	15 (5.2)	-	-	-	1 (0.3)
	ASD	224 (58.2)	111 (28.8)	44 (11.4)	-	-	-	6 (1.6)
A6	Non-ASD	117 (40.6)	79 (27.4)	65 (22.6)	14 (4.9)	-	-	13 (4.5)
	ASD	69 (17.9)	108 (28.1)	137 (35.6)	55 (14.3)	-	-	16 (4.2)
A7	Non-ASD	205 (71.2)	63 (21.9)	12 (4.2)	3 (1.0)	-	-	5 (1.7)
	ASD	145 (37.7)	158 (41.0)	63 (16.4)	7 (1.8)	-	-	12 (3.1)
A8	Non-ASD	198 (68.8)	71 (24.7)	16 (5.6)	2 (0.7)	-	-	1 (0.3)
	ASD	109 (28.3)	188 (48.8)	81 (21.0)	7 (1.8)	-	-	0
A9	Non-ASD	211 (73.3)	51 (18.8)	13 (4.5)	7 (2.4)	-	1 (0.3)	2 (0.7)
	ASD	110 (28.6)	159 (41.3)	69 (17.9)	41 (10.6)	-	1 (0.3)	5 (1.3)

A10	Non- ASD	148 (51.4)	79 (27.4)	2 (0.7)	52 (18.1)	-	1 (0.3)	6 (2.1)
	ASD	68 (17.7)	130 (33.8)	34 (8.8)	139 (36.1)	-	3 (0.8)	11 (2.9)
ADOS Domain: Reciprocal Social Interaction								
B1	Non- ASD	243 (84.4)	-	43 (14.9)	-	-	-	2 (0.7)
	ASD	157 (40.8)	-	226 (58.7)	-	-	-	2 (0.5)
B2	Non- ASD	180 (62.5)	92 (31.9)	15 (5.2)	-	-	-	1 (0.3)
	ASD	58 (15.1)	248 (64.4)	76 (19.7)	-	-	-	3 (0.8)
B3	Non- ASD	186 (64.6)	39 (13.5)	1 (0.3)	-	1 (0.3)	57 (19.8)	4 (1.4)
	ASD	50 (13.0)	63 (16.4)	1 (0.3)	-	1 (0.3)	265 (68.8)	5 (1.3)
B4	Non- ASD	197 (68.4)	50 (17.4)	20 (6.9)	-	-	2 (0.7)	19 (6.6)
	ASD	147 (38.2)	114 (29.6)	74 (19.2)	-	-	2 (0.5)	48 (12.5)
B5	Non- ASD	131 (45.5)	121 (42.0)	27 (9.4)	5 (1.7)	-	-	4 (1.4)
	ASD	65 (16.9)	217 (56.4)	75 (19.5)	22 (5.7)	-	-	6 (1.6)
B6	Non- ASD	151 (52.4)	106 (36.8)	25 (8.7)	4 (1.4)	-	-	2 (0.7)
	ASD	67 (17.4)	185 (48.1)	100 (26.0)	32 (8.3)	-	-	1 (0.3)
B7	Non- ASD	171 (59.4)	79 (27.4)	27 (9.4)	7 (2.4)	-	-	4 (1.4)
	ASD	82 (21.3)	151 (39.2)	121 (31.4)	24 (6.2)	-	-	7 (1.8)
B8	Non- ASD	195 (67.7)	71 (24.7)	14 (4.9)	-	-	-	8 (2.8)
	ASD	202 (52.5)	122 (31.7)	56 (14.5)	-	-	-	5 (1.3)
B9	Non- ASD	212 (73.6)	57 (19.8)	4 (1.4)	15 (5.2)	-	-	0
	ASD	113 (29.4)	208 (54.0)	33 (8.6)	31 (8.1)	-	-	0
B10	Non- ASD	206 (71.5)	79 (27.4)	2 (0.7)	1 (0.3)	-	-	0
	ASD	88 (22.9)	1 (69.1)	28 (7.3)	3 (0.8)	-	-	0
B11	Non- ASD	168 (58.3)	98 (34.0)	16 (5.6)	4 (1.4)	-	-	2 (0.7)
	ASD	55 (14.3)	223 (57.9)	101 (26.2)	6 (1.6)	-	-	0

B12	Non- ASD	231 (80.2)	45 (15.6)	5 (1.7)	2 (0.7)	-	-	5 (1.7)
	ASD	187 (48.6)	156 (40.5)	28 (7.3)	5 (1.3)	-	-	9 (2.3)
ADOS Domain: Imagination/Creativity								
C1	Non- ASD	142 (49.3)	87 (30.2)	21 (7.3)	5 (1.7)	-	-	33 (11.5)
	ASD	109 (28.3)	150 (39.0)	67 (17.4)	25 (6.5)	-	-	41 (8.8)
ADOS Domain: Stereotyped Behaviors and Restricted Interests								
D1	Non- ASD	280 (97.2)	3 (1.0)	0	-	-	-	5 (1.7)
	ASD	360 (97.2)	16 (4.2)	3 (0.8)	-	-	-	6 (1.6)
D2	Non- ASD	276 (95.8)	2 (0.7)	3 (1.0)	-	-	-	7 (2.4)
	ASD	350 (90.9)	27 (7.0)	3 (0.8)	-	-	-	5 (1.3)
D3	Non- ASD	282 (97.9)	0	0	-	-	-	6 (2.1)
	ASD	376 (97.7)	2 (0.5)	0	-	-	-	7 (1.8)
D4	Non- ASD	253 (87.8)	26 (9.0)	2 (0.7)	0	-	-	7 (2.4)
	ASD	305 (79.2)	61 (15.8)	13 (3.4)	0	-	-	6 (1.6)
D5	Non- ASD	269 (93.4)	12 (4.2)	1 (0.3)	-	-	-	6 (2.1)
	ASD	330 (85.7)	42 (10.9)	3 (0.8)	-	-	-	10 (2.6)
ADOS Domain: Other abnormal behaviors								
E1	Non- ASD	258 (89.6)	12 (4.2)	1 (0.3)	-	1 (0.3)	-	16 (5.6)
	ASD	354 (91.9)	14 (3.6)	0	-	4 (1.0)	-	13 (3.4)
E2	Non- ASD	260 (90.3)	11 (3.8)	1 (0.3)	-	-	-	16 (5.6)
	ASD	358 (93.0)	11 (2.9)	0	-	-	-	16 (4.2)
E3	Non- ASD	213 (74.0)	50 (17.4)	9 (3.1)	-	-	-	16 (5.6)
	ASD	287 (74.5)	74 (19.2)	8 (2.1)	-	-	-	16 (4.2)

Abbreviations: ASD, autism spectrum disorder; ADOS, Autism Diagnostic Observation Scale.

Supplement 3 (random forest models):

For random forest models, we used ‘rf’ R package in caret. We used 500 fully grown random forests with the parameter “minimum node size” fixed at 1 (default for classification) to fine-tune the number of randomly selected predictors per split (‘mtry’) using cross-validation. All other hyperparameters were set to default values.

Table S3. Performance of the machine learning models on the training and test set using random forest.

	Random Forest Models			
	5-feature model*	11-feature model (ADOS algorithm)	12-feature model (Kosmicki et al. [41])	All-feature model (all ADOS items)
Training Set AUC (Sensitivity, Specificity)	.85 (.72, .81)	.88 (.76, .86)	.87 (.77., .86)	.88 (.77., .86)
Test Set AUC (Sensitivity, Specificity)	.80 (.76, .75)	.84 (.79, .79)	.83 (.79, .78)	.84 (.74, .85)

*5-feature model for "all ages": items A9, B1, B2, B10, B11.

Abbreviation: AUC, Area under the ROC curve; RF, random forest.

Supplement 4 (age distribution of the whole sample and the age subgroups):

Figure S1. Age frequency distribution in the whole sample (“all ages”).

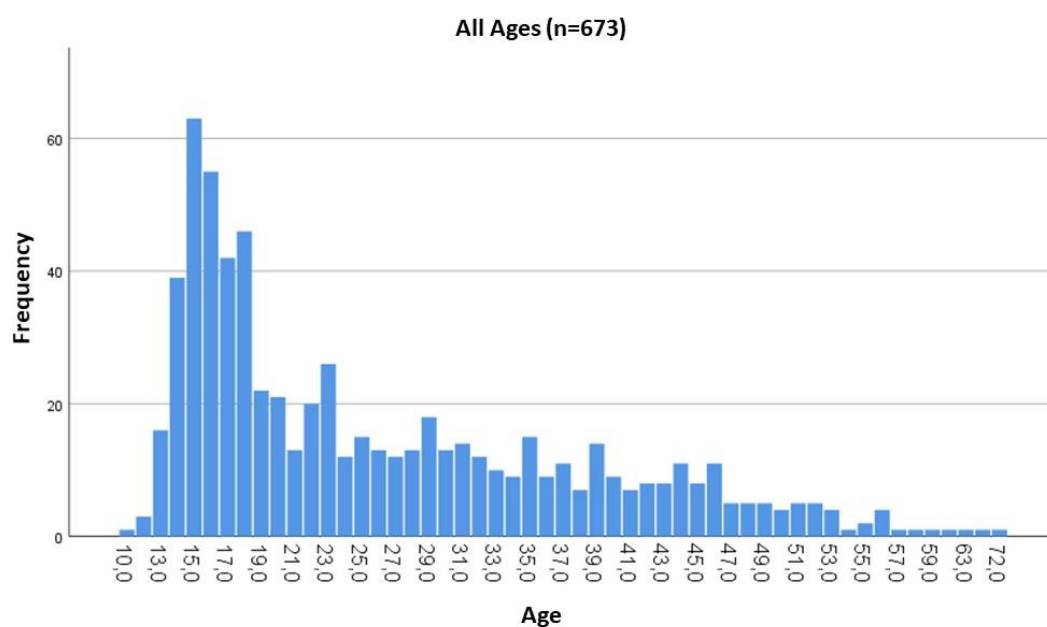


Table S4. Sample Description of the age subgroups (“adolescents”, “adults”).

Characteristic	Adolescents ≤ 21 years (n=321)	Adults > 21 years (n=352)
ASD: % ASD diagnosis [n]	56,7% ASD [n=182]	57,7% ASD [n=203]
Mean Age (SD)	16.42 years (2.14)	34.97 years (9.90)
Median Age	16 years	33 years
Gender: % male [n]	81.3% male [n=261]	66.8% male [n=235]

Abbreviation: ASD, autism spectrum disorder; SD, standard deviation.

Figure S2. Age frequency distribution in the “adolescents” subgroup.

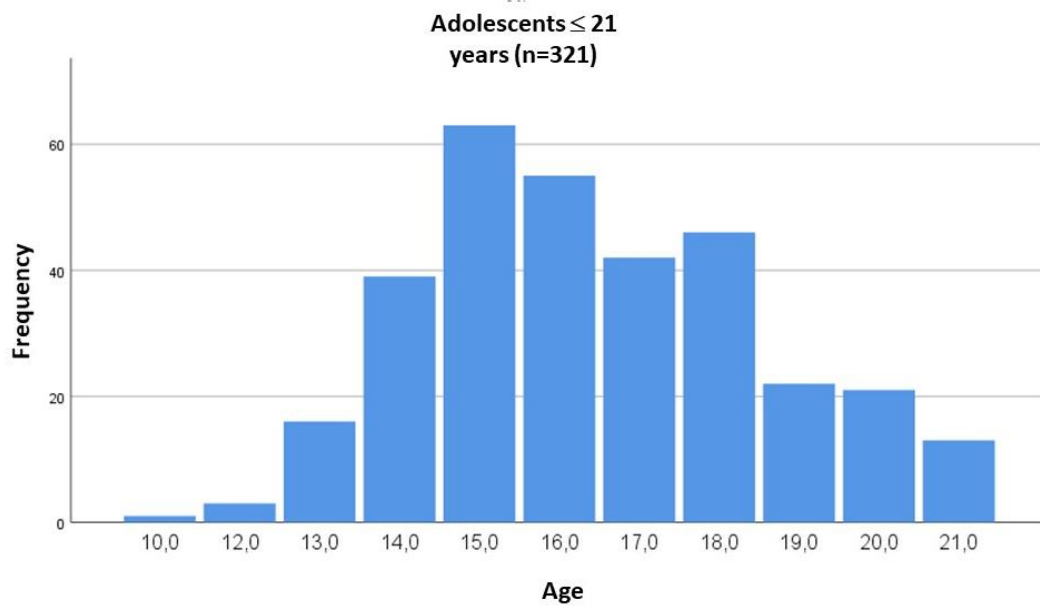
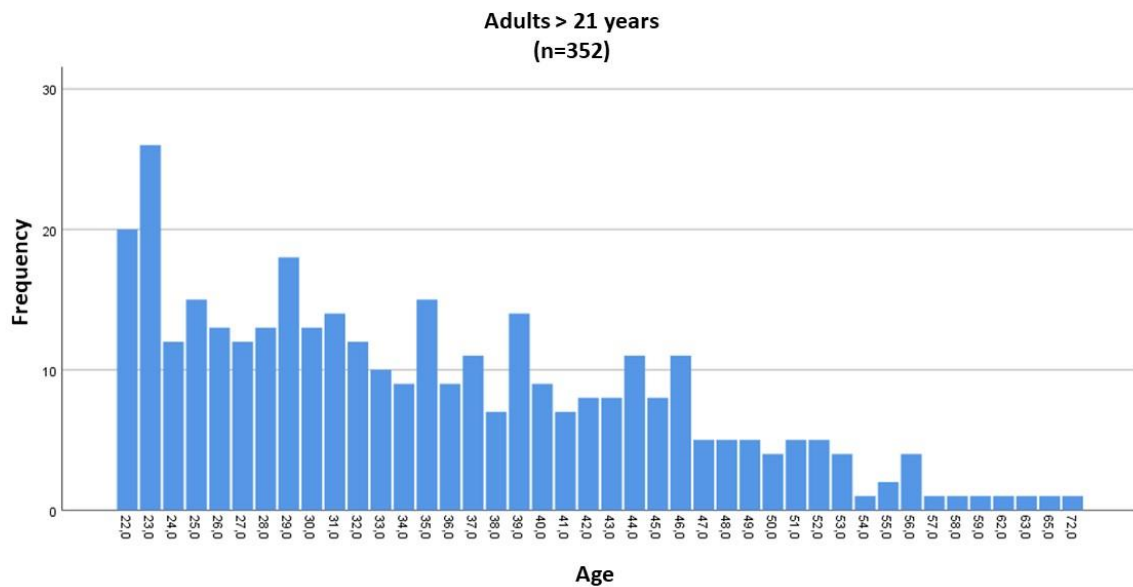
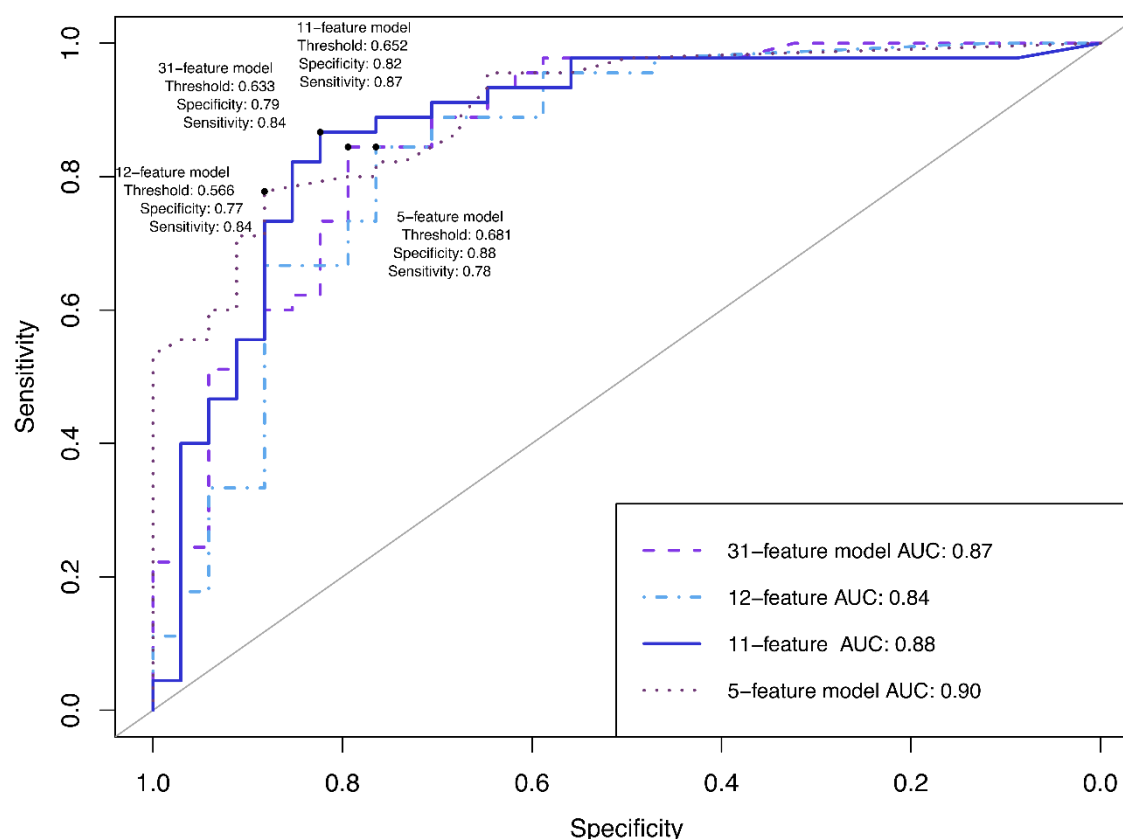


Figure S3. Age frequency distribution in the “adults” subgroup.



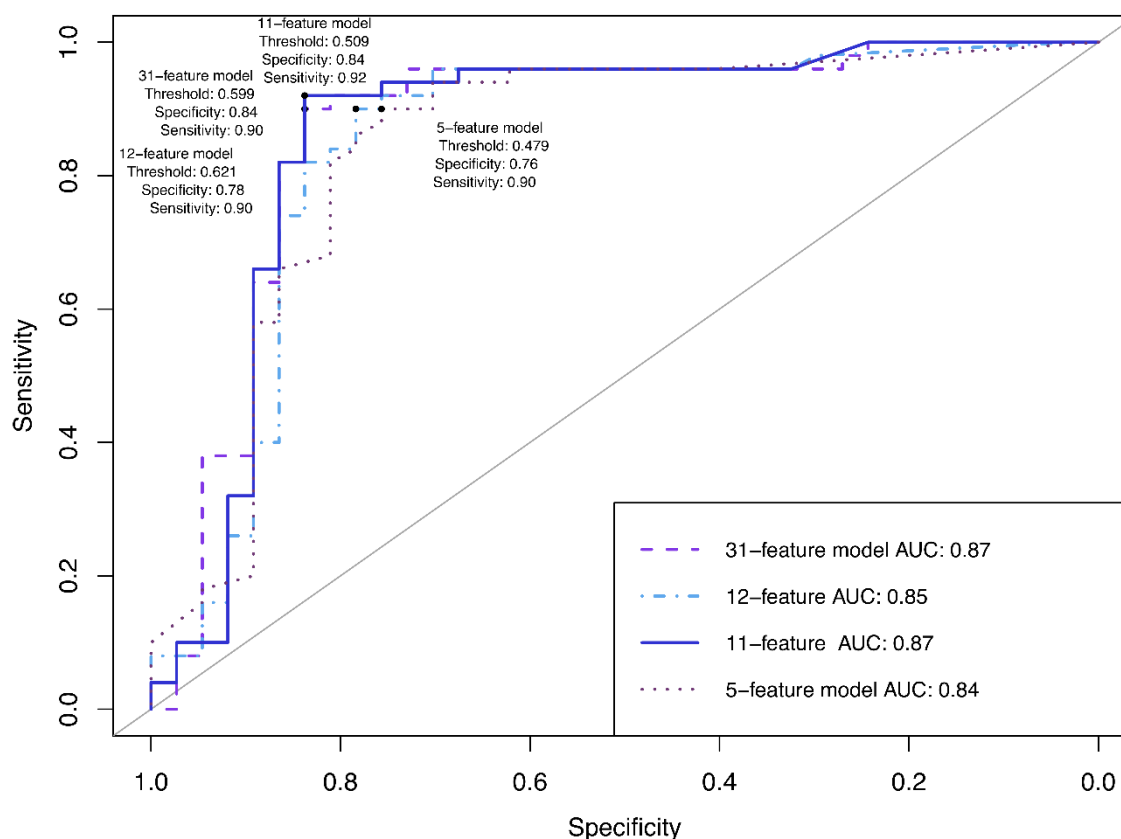
Supplement 5 (ROC curves of the age subgroups (“adolescents” and “adults”)):

Figure S4. Receiver operating characteristic (ROC) curves for the “adolescents” subgroup evaluating the predictive power in the test set. Optimal ROC threshold with the highest sum of sensitivity + specificity is plotted.



“Adolescents” subgroup: No significant differences were found when comparing the AUCs of the reduced 5-feature model with the 11-feature model suggested by the ADOS algorithm (DeLong’s test: $Z = 0.85$, $p = .40$; bootstrapping: $D = 0.85$, $p = .39$, number of bootstrapped resampled = 10 000), the 12-feature model proposed by Kosmicki et al. [41] (DeLong’s test: $Z = 1.49$, $p = .14$; bootstrapping: $D = 1.48$, $p = .14$, number of bootstrapped resampled = 10 000) and the all-feature model (DeLong’s test: $Z = 0.94$, $p = .35$; bootstrapping: $D = 0.93$, $p = .35$, number of bootstrapped resamples = 10 000).

Figure S5. Receiver operating characteristic (ROC) curves for the “adults” subgroup evaluating the predictive power in the test set. Optimal ROC threshold with the highest sum of sensitivity + specificity is plotted.



“Adults” Subgroup: No significant differences were found when comparing the AUCs of the reduced 5-feature model with the 11-feature model suggested by the ADOS algorithm (DeLong’s test: $Z = -1.60$, $p = .11$; bootstrapping: $D = -1.54$, $p = .12$, number of bootstrapped resampled = 10 000), the 12-feature model proposed by Kosmicki et al. [41] (DeLong’s test: $Z = -0.30$, $p = .76$; bootstrapping: $D = -0.30$, $p = .76$, number of bootstrapped resampled = 10 000) and the all-feature model (DeLong’s test: $Z = -1.76$, $p = .08$; bootstrapping: $D = -1.71$, $p = .09$, number of bootstrapped resamples = 10 000).