

## Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1. Summary of baseline characteristics in those who did and did not complete the CYBOCS-PDD at 16 weeks by treatment group**

	Fluoxetine Retained N=54	Fluoxetine Lost N=21	Placebo Retained N=55	Placebo Lost N=16
<b>Site</b>				
Royal Children's Hospital (RCH)	14 (26%)	5 (24%)	14 (26%)	3 (19%)
State Child Development Centre (SCDC)	8 (15%)	0 (0%)	8 (15%)	1 (6%)
Westmead	32 (59%)	16 (76%)	33 (60%)	12 (75%)
<b>Age stratification</b>				
13-18 years old	16 (30%)	11 (52%)	19 (35%)	6 (38%)
7.5 – 12 years old	38 (70%)	10 (48%)	36 (66%)	10 (63%)
Age at consent – mean (SD)	10.6 (2.4)	13.1 (3.4)	10.9 (2.7)	11.6 (3.3)
Height (no shoes) – mean (SD)	144.6 (15.8) [42]	155.7 (17.9) [18]	145.7 (15.5) [51]	149.7 (14.9) [16]
Weight (no shoes) – mean (SD)	38.8 (14.8) [54]	51.9 (16.9) [21]	41.8 (15.9) [54]	46.6 (18.7) [16]
<b>Sex</b>				
Male	48 (89%)	21 (100%)	41 (75%)	14 (88%)
Female	6 (11%)	0 (0%)	14 (26%)	2 (13%)
<b>Primary Diagnosis</b>				
Autism	27 (50%)	5 (24%)	25 (46%)	8 (50%)
Asperger's Syndrome	7 (13%)	5 (24%)	4 (7%)	5 (31%)
Autism Spectrum Disorder	20 (37%)	11 (52%)	26 (47%)	3 (19%)
<b>Intellectual disability</b>				
No	36 (67%)	16 (76%)	40 (73%)	10 (63%)
Yes	18 (33%)	5 (24%)	15 (27%)	6 (38%)
<b>Communication Level</b>	N=54	N=21	N=54	N=16
Normal Language for Age	34 (63%)	15 (71%)	36 (67%)	12 (75%)
Impaired Speech and Language	16 (30%)	6 (29%)	15 (28%)	2 (13%)
Has No Speech	4 (7%)	0 (0%)	3 (6%)	2 (13%)
<b>Current Medications (incl. alt. therapies)</b>				
No	30 (56%)	12 (57%)	30 (55%)	12 (75%)
Yes	24 (44%)	9 (43%)	25 (46%)	4 (25%)
<b>On Stimulant Medications at baseline</b>				
No	53 (98%)	20 (95%)	55 (100%)	16 (100%)
Yes	1 (2%)	1 (5%)	0 (0%)	0 (0%)
<b>Family history of ASD</b>	N=54	N=21	N=54	N=16
No	27 (50%)	8 (38%)	31 (57%)	11 (69%)
Yes	20 (37%)	8 (38%)	19 (35%)	3 (19%)
Uncertain	7 (13%)	5 (24%)	4 (7%)	2 (13%)
<b>History of seizures</b>	N=54	N=21	N=54	N=16
No	52 (96%)	21 (100%)	51 (94%)	16 (100%)
Yes	2 (4%)	0 (0%)	3 (6%)	0 (0%)
<b>CYBOS-PDD<sup>a</sup> Behaviour – mean (SD)</b>	12.7 (3.2) [54]	13.0 (3.9) [21]	13.4 (3.1) [55]	12.1 (4.1) [16]
<b>RBS<sup>b</sup> - Total Items – mean (SD)</b>	20.4 (9.4) [54]	21.8 (10.5) [21]	25.3 (9.5) [55]	19.9 (10.8) [16]
<b>RBS<sup>b</sup> - Total Score – mean (SD)</b>	36.1 (22.4) [54]	38.4 (24.4)	48.5 (23.9) [55]	37.1 (24.2) [16]
<b>Spence Children's Anxiety total score – mean (SD)</b>	28.7 (20.9) [54]	38.1 (22.8) [20]	31.6 (19.1) [55]	34.1 (24.0) [16]
<b>ABC<sup>c</sup> I - Irritability – mean (SD)</b>	17.6 (9.1) [54]	21.0 (11.9) [21]	18.2 (12.1) [55]	16.8 (11.1) [16]
<b>ABC<sup>c</sup> II - Lethargy – mean (SD)</b>	12.4 (6.4) [54]	12.9 (11.4) [21]	17.9 (10.2) [55]	12.9 (11.4) [16]
<b>ABC<sup>c</sup> III - Stereotypy – mean (SD)</b>	6.2 (5.0) [54]	5.6 (4.8) [21]	7.1 (5.3) [55]	7.6 (6.7) [16]
<b>ABC<sup>c</sup> IV - Hyperactivity – mean (SD)</b>	21.0 (11.1) [54]	23.6 (11.2) [21]	21.1 (11.6) [55]	22.1 (11.5) [16]
<b>ABC<sup>c</sup> V - Inappropriate speech – mean (SD)</b>	4.3 (3.6) [53]	5.0 (3.8) [21]	5.3 (3.3) [54]	3.2 (3.1) [15]

Results are n (%) unless otherwise stated

a CYBOCS – PDD = Children's Yale-Brown Obsessive Compulsion Scale – Modified for Pervasive Developmental Disorders; b RBS = Repetitive Behaviours Scale; c ABC = Aberrant Behaviours Checklist

**eTable 2. Comparison of outcomes at 16 weeks between the treatment groups using multiple imputation to handle the missing data**

	Fluoxetine		Placebo		Primary analysis <sup>a</sup>			Secondary Analysis <sup>b</sup>		
	N	Mean <sup>c</sup>	N	Mean <sup>c</sup>	MD	95% Confidence Interval	p-value	MD	95% Confidence Interval	p-value
<b>CYBOS-PDD<sup>d</sup></b>	75	8.84	71	10.68	-1.82	(-3.71;0.06)	0.06	-1.62	(-3.57; 0.33)	0.10
<b>RBS<sup>e</sup> - Total Items</b>	75	16.71	71	21.47	-4.78	(-8.60;-0.97)	0.02	-2.93	(-6.81; 0.95)	0.14
<b>RBS<sup>e</sup> - Total Score</b>	75	26.05	71	35.17	-9.23	(-17.08;-1.38)	0.02	-4.48	(-12.11; 3.16)	0.25
<b>Spence Children's Anxiety TOTAL<sup>f</sup></b>	75	21.70	71	24.54	-2.98	(-9.07;3.10)	0.33	-3.00	(-8.42;2.41)	0.27
<b>Spence Children's Anxiety TOTAL – Verbal subgroup<sup>g</sup></b>	71	22.57	66	24.02	-1.62	(-7.92; 4.67)	0.61	-2.10	(-7.62; 3.42)	0.45
<b>ABC<sup>h</sup> I - Irritability</b>	75	12.19	71	13.65	-1.46	(-5.11;2.19)	0.43	-2.23	(-5.88;1.42)	0.23
<b>ABC<sup>h</sup> II - Lethargy</b>	75	9.54	71	14.23	-4.73	(-7.91;-1.54)	0.004	-2.97	(-6.15;0.21)	0.07
<b>ABC<sup>h</sup> III - Stereotypy</b>	75	5.10	71	5.35	-0.26	(-1.92;1.40)	0.76	0.18	(-1.49;1.84)	0.83
<b>ABC<sup>h</sup> IV - Hyperactivity</b>	75	16.29	71	18.06	-1.84	(-6.10;2.43)	0.39	-2.12	(-6.23;1.98)	0.31
<b>ABC<sup>h</sup> V - Inappropriate speech</b>	75	3.82	71	3.87	-0.04	(-1.24;1.17)	0.95	0.28	(-0.89;1.45)	0.64
<b>CGI<sup>i</sup> - Severity of illness</b>	75	3.26	71	3.28	-0.02	(-0.42;0.38)	0.91	0.05	(-0.38;0.47)	0.83
<b>CGI<sup>i</sup> - Global improvement</b>	75	3.18	71	3.39	-0.20	(-0.63;0.24)	0.37	-0.24	(-0.72;0.24)	0.32
<b>CGI<sup>i</sup> - Efficacy index</b>	75	9.71	71	10.58	-0.84	(-2.21;0.53)	0.23	-0.83	(-2.28;0.63)	0.26
<b>Disruptiveness assessment - TOTAL<sup>j</sup></b>	75	3.06	71	3.59	-0.55	(-1.47;0.37)	0.24	-0.19	(-1.11;0.73)	0.68

<sup>a</sup> Results for the primary analysis are adjusted for site, age (8 to <12 years and 12 to 18 years) and intellectual ability (IQ ≥70 and IQ <70) as used in randomization

<sup>b</sup> Secondary analysis: as per the primary analysis but also adjusted for sex, verbal vs non-verbal, baseline measure of the outcome of interest, baseline measures of RBS - Total Items, RBS - Total Score and ABC II - Lethargy.

<sup>c</sup> Mean scores and presented following multiple imputation for the missing data. Given this there is no corresponding standard deviation.

<sup>d</sup> CYBOCS – PDD = Children's Yale-Brown Obsessive Compulsion Scale – Modified for Pervasive Developmental Disorders; range 0-20; higher scores indicating higher severity.

<sup>e</sup> RBS = Repetitive Behaviors Scale; Total Items range 0-43; Total Score range 0-129; higher scores indicate higher severity.

<sup>f</sup> range 0-114; higher score indicating higher severity.

<sup>g</sup> Because of the small sample in the non-verbal subgroup (9 participants at baseline, of which 7 provided data at 16 weeks), the analysis of the Spence Children's Anxiety Scale was conducted only on the verbal subgroup.

<sup>h</sup> ABC = Aberrant Behaviors Checklist; irritability range: 0-45; lethargy range: 0-48; stereotypy range: 0-21; hyperactivity range: 0-48; inappropriate speech range: 0-12; higher scores indicate higher severity

<sup>i</sup> CGI = Clinical Global Impressions Scale; severity of illness range 0-7; global improvement range 0-7; efficacy index range 1-16; higher scores associated with worsening of the condition.

**eTable 3. Comparison of Repetitive Behaviors Scale – Revised subscales and outcomes Spence Children’s Anxiety subscales at 16 weeks using a complete case analysis**

	Fluoxetine		Placebo		Primary analysis <sup>a</sup>			Secondary Analysis <sup>b</sup>		
	baseline mean (SD) <sup>c</sup> [N]	16 week mean (SD) <sup>c</sup> [N]	baseline mean (SD) <sup>c</sup> [N]	16 week mean (SD) <sup>c</sup> [N]	Mean Difference	95% Confidence Interval	P-value	Mean Difference	95% Confidence Interval	P-value
<b>RBS<sup>d</sup> Stereotypic behaviours - Items</b>	3.04 (1.87) [75]	2.74 (1.92) [53]	3.74 (1.98) [70]	3.11 (1.98) [53]	-0.43	(-1.18;0.32)	0.26	-0.13	(-0.85;0.59)	0.72
<b>RBS<sup>d</sup> Stereotypic behaviours - Score</b>	5.20 (4.08) [75]	3.96 (3.36) [53]	6.69 (4.43) [70]	4.66 (3.91) [53]	-0.83	(-2.22;0.55)	0.24	-0.17	(-1.53;1.19)	0.81
<b>RBS<sup>d</sup> Self injurious behaviours - Items</b>	2.47 (2.19) [75]	1.49 (1.90) [53]	2.80 (2.22) [70]	2.34 (2.46) [53]	-0.89	(-1.74;-0.05)	0.04	-0.63	(-1.43;0.18)	0.13
<b>RBS<sup>d</sup> Self injurious behaviours - Score</b>	3.84 (4.26) [75]	2.09 (3.01) [53]	5.03 (4.58) [70]	3.55 (4.59) [53]	-1.54	(-3.04;-0.03)	0.05	-0.24	(-1.56;1.08)	0.72
<b>RBS<sup>d</sup> Compulsive behaviours - Items</b>	3.64 (2.13) [75]	2.58 (2.27) [53]	4.23 (2.31) [70]	3.85 (2.50) [53]	-1.32	(-2.24;-0.40)	0.006	-0.63	(-1.53;0.28)	0.17
<b>RBS<sup>d</sup> Compulsive behaviours - Score</b>	6.23 (4.78) [75]	4.40 (5.02) [53]	7.76 (5.40) [70]	6.11 (5.03) [53]	-1.81	(-3.76;0.14)	0.07	-0.60	(-2.21;1.00)	0.46
<b>RBS<sup>d</sup> Ritualistic behaviours - Items</b>	3.60 (1.99) [75]	2.94 (1.98) [53]	4.14 (1.87) [70]	3.77 (2.13) [53]	-0.88	(-1.68;-0.08)	0.03	-0.22	(-0.96;0.51)	0.54
<b>RBS<sup>d</sup> Ritualistic behaviours - Score</b>	6.81 (5.11) [75]	5.23 (4.70) [53]	8.47 (5.07) [70]	6.79 (4.77) [53]	-1.68	(-3.52;0.15)	0.07	0.25	(-1.34;1.83)	0.76
<b>RBS<sup>d</sup> Sameness behaviours - Items</b>	5.83 (3.00) [75]	5.13 (3.55) [53]	6.96 (3.15) [70]	6.23 (3.59) [53]	-1.17	(-2.56;0.21)	0.1	0.50	(-0.73;1.73)	0.42
<b>RBS<sup>d</sup> Sameness behaviours - Score</b>	10.44 (7.13) [75]	8.42 (7.72) [53]	13.34 (8.43) [70]	10.79 (8.14) [53]	-2.57	(-5.61;0.47)	0.1	1.07	(-1.60;3.74)	0.43
<b>RBS<sup>d</sup> Restricted behaviours - Items</b>	2.32 (1.24) [75]	1.98 (1.26) [53]	2.54 (1.26) [71]	2.28 (1.51) [53]	-0.32	(-0.87;0.22)	0.24	0.02	(-0.49;0.52)	0.95
<b>RBS<sup>d</sup> Restricted behaviours - Score</b>	4.27 (2.88) [75]	3.55 (3.05) [53]	5.20 (3.12) [71]	4.30 (3.65) [53]	-0.83	(-2.14;0.49)	0.25	0.20	(-1.07;1.46)	0.76
<b>Spence Children’s Anxiety Panic Attack</b>	4.58 (4.88) [74]	2.85 (4.11) [53]	4.09 (4.32) [70]	3.42 (3.84) [53]	-0.53	(-2.08;1.03)	0.5	-0.63	(-1.75;0.49)	0.27
<b>Spence Children’s Anxiety Separation Anxiety</b>	5.73 (4.60) [74]	3.87 (4.00) [53]	6.13 (4.77) [70]	4.53 (4.12) [53]	-0.70	(-2.23;0.83)	0.37	-0.33	(-1.54;0.89)	0.60
<b>Spence Children’s Anxiety Physical Injury</b>	4.86 (3.27) [74]	3.02 (2.86) [53]	4.89 (3.65) [70]	4.17 (3.12) [53]	-1.24	(-2.39;-0.09)	0.04	-0.97	(-1.75;-0.18)	0.02
<b>Spence Children’s Anxiety Social anxiety</b>	5.97 (5.22) [74]	4.17 (4.30) [53]	6.63 (4.99) [70]	4.94 (3.92) [53]	-0.65	(-2.16;0.86)	0.39	0.01	(-1.29;1.31)	0.98
<b>Spence Children’s Anxiety Obsessive Compulsive</b>	4.46 (4.09) [74]	3.02 (3.20) [53]	4.61 (4.02) [70]	3.36 (3.18) [53]	-0.37	(-1.60;0.85)	0.55	-0.15	(-1.28;0.99)	0.80
<b>Spence Children’s Anxiety Obsessive Generalised anxiety</b>	5.55 (4.03) [74]	3.68 (3.42) [53]	5.89 (3.79) [70]	4.25 (3.28) [53]	-0.50	(-1.75;0.75)	0.43	-0.30	(-1.37;0.77)	0.58

a Results for the primary analysis are adjusted for site, age (8 to <12 years and 12 to 18 years) and intellectual ability (IQ ≥70 and IQ <70) as used in randomization

b Secondary analysis: as per the primary analysis but also adjusted for sex, verbal vs non-verbal, baseline measure of the outcome of interest, baseline measures of RBS - Total Items, RBS - Total Score and ABC II - Lethargy.

c SD = standard deviation,

d RBS = Repetitive Behaviors Scale;

**eTable 4. Summary of adverse events by treatment group and category**

	Fluoxetine	Placebo
	N	N
<b>TOTAL NUMBER OF AEs<sup>a</sup></b>	86	79
<b>TOTAL NUMBER OF AEs BY CATEGORY</b>		
<b>Appetite Disturbance</b>	3	5
<b>Autonomic Disturbance</b>	5	4
<b>CNS<sup>b</sup> Disturbance</b>	9	11
<b>CNS<sup>b</sup> Disturbance + Respiratory Disorder</b>	0	1
<b>Gastrointestinal Disturbance</b>	10	7
<b>Infection</b>	1	0
<b>Mild Infectious Disease</b>	5	1
<b>Mood Disturbance</b>	23	16
<b>Motor Disturbance</b>	1	3
<b>Respiratory Disorder</b>	3	1
<b>Skin Abnormalities</b>	2	6
<b>Sleep Disturbance</b>	10	14
<b>Sleep Disturbance + Appetite Disturbance</b>	1	0
<b>Sleep Disturbance + Mood Disturbance</b>	2	2
<b>Other</b>	11	8

<sup>a</sup> AE= Adverse Event

<sup>b</sup> CNS = Central Nervous System