

Table F-3. Key findings in studies of nutritional interventions

Author, Year Study Design	Mean age, years \pm SD	Outcome measure/Baseline scores, mean \pm SD	Outcome measure/Post- treatment scores, mean \pm SD
Groups (dose), N enrollment / N final	Mean IQ \pmSD		
Treatment duration/Follow-up timepoint post-treatment			
Risk of Bias			
Sun et al., 2016 ³⁸ RCT G1: TEACCH+folic acid, 44/44 G2: TEACCH alone, 22/22 3 months/EOT Moderate ROB (Note: Discussed in section on combined treatments in main report)	Age (months) G1: 57.23 \pm 15.06 G2: 51.75 \pm 12.72 IQ NR	ABC - Total Score G1: 54.55 \pm 26.58 G2: 67.59 \pm 27.6 CARS – Total Score G1: 33.86 \pm 7.08 G2: 33.41 \pm 6.04 ATEC – Total Score G1: 48.68 \pm 21.43 G2: 57.36 \pm 20.38 PEP – Cognitive Verbal/Preverbal G1: 12 \pm 3 G2: 12.95 \pm 2.38 PEP – Expressive Language G1: 11.41 \pm 3.41 G2: 11.91 \pm 2.86 PEP – Receptive Language G1: 12.36 \pm 2.42 G2: 13.32 \pm 1.96 PEP – Fine Motor G1: 11.8 \pm 1.79 G2: 11.91 \pm 2 PEP – Gross Motor G1: 12.07 \pm 1.78 G2: 12.36 \pm 1.92 PEP – Visual Motor Imitation G1: 11.55 \pm 2.17 G2: 12 \pm 2.16 PEP – Affective Expression G1: 11.8 \pm 2.06 G2: 10.95 \pm 2.3 PEP – Social Reciprocity G1: 10.36 \pm 2.08 G2: 10.5 \pm 1.87	ABC - Total Score G1: 39.4 \pm 26.73 G2: 46.18 \pm 22.71 G1 vs G2, p=ns CARS – Total Score G1: 29.34 \pm 5.52 G2: 30.82 \pm 5.06 G1 vs G2, p=ns ATEC – Total Score G1: 36.3 \pm 17.49 G2: 46.36 \pm 18.56 G1 vs G2, p=0.052 PEP – Cognitive Verbal/Preverbal G1: 14.2 \pm 1.97 G2: 13.91 \pm 2.79 G1 vs G2, p=ns PEP – Expressive Language G1: 13.07 \pm 3.19 G2: 13.14 \pm 2.87 G1 vs G2, p=ns PEP – Receptive Language G1: 13.75 \pm 1.4 G2: 13.73 \pm 1.75 G1 vs G2, p=ns PEP – Fine Motor G1: 12.48 \pm 1.68 G2: 13 \pm 1.75 G1 vs G2, p=ns PEP – Gross Motor G1: 12.77 \pm 0.99 G2: 13.09 \pm 1.31 G1 vs G2, p=ns PEP – Visual Motor Imitation G1: 12.27 \pm 1.48 G2: 13.64 \pm 1.97 G1 vs G2, p=ns PEP – Affective

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Risk of Bias			
		PEP – Characteristic Motor Behaviors G1: 11.98 \pm 2.39 G2: 11.95 \pm 2.3 PEP – Characteristic Verbal Behaviors G1: 8 \pm 3.58 G2: 9.05 \pm 2.9 PEP – Communication G1: 35.77 \pm 8.21 G2: 38.18 \pm 6.71 PEP – Motor G1: 35.41 \pm 5.18 G2: 36.27 \pm 5.54 PEP – Maladaptive Behavior G1: 42.14 \pm 7.84 G2: 42.45 \pm 7.31 PEP – Problem Behaviors G1: 8.25 \pm 2.36 G2: 8.27 \pm 2.39 PEP – Personal Self-Care G1: 11.7 \pm 2.41 G2: 12.09 \pm 2.24 PEP – Adaptive Behaviors G1: 11.14 \pm 2.36 G2: 11.36 \pm 2.63	Expression G1: 11.98 \pm 2.25 G2: 12.45 \pm 1.26 G1 vs G2, p=ns PEP – Social Reciprocity G1: 11.3 \pm 2.09 G2: 11.64 \pm 1.65 G1 vs G2, p=ns PEP – Characteristic Motor Behaviors G1: 11.66 \pm 2.58 G2: 12.59 \pm 2.26 G1 vs G2, p=ns PEP – Characteristic Verbal Behaviors G1: 9.64 \pm 3.72 G2: 10.5 \pm 2.65 G1 vs G2, p=ns PEP – Communication G1: 41.02 \pm 5.91 G2: 40.77 \pm 7.04 G1 vs G2, p=ns PEP – Motor G1: 37.52 \pm 3.79 G2: 38.73 \pm 4.69 G1 vs G2, p=ns PEP – Maladaptive Behavior G1: 44.57 \pm 9.59 G2: 47.18 \pm 6.53 G1 vs G2, p=ns PEP – Problem Behaviors G1: 9.05 \pm 2.9 G2: 9 \pm 2.65 G1 vs G2, p=ns PEP – Personal Self-Care G1: 12.34 \pm 1.7 G2: 12.41 \pm 2.48 G1 vs G2, p=ns

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Treatment duration/Follow-up timepoint post-treatment			
Risk of Bias			
			PEP – Adaptive Behaviors G1: 12.32 ± 2.59 G2: 11.77 ± 2.51 G1 vs G2, p=ns
Mankad et al., 2015 ³⁹ RCT G1: Omega-3 fatty acid (3.5 mL/day), 19/18 G2: Placebo, 19/19 6 months/EOT Moderate RoB	Age G1: 3.5 ± 1.1 G2: 3.8 ± 1.0 IQ NR	Baseline scores NR	Change from Baseline PDDBI – Autism Composite G1: -4.5 G2: -6.4 G1 vs G2: p=ns BASC – Externalizing G1: 3.2 G2: -3.0 G1 vs G2: p=0.02 CGI G1: NR G2: NR G1 vs G2:p=ns VABS G1: 2.8 G2: -0.2 G1 vs G2: p=ns Preschool Language Scale (PLS4) G1: 0.7 G2: -0.6 G1 vs G2: p=ns
Saad et al., 2015 ⁴⁰ RCT G1: Digestive enzymes (15 mL/day), 51/47 G2: Placebo (NA), 50/45 3 months/EOT Moderate RoB	Age G1: 5.94 ± 2.01 G2: 5.87 ± 2.12 IQ NR	CARS G1: 36.1 ± 3.7 G2: 35.3 ± 4.0 GBRS Child's General Behavior G1: 3.01 ± 1.3 G2: 3.50 ± 0.7 Nighttime sleeping G1: 3.89 ± 1.3 G2: 3.84 ± 1.0	EOT CARS G1: 31.2 ± 1.2 G2: 35.5 ± 2.8 G1 vs G2: p=0.034 GBRS Child's General Behavior G1: 5.5 ± 0.75 G2: 3.39 ± 1.01 G1 vs G2:, p<0.001 Nighttime sleeping

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Groups (dose), N enrollment / N final			
Treatment duration/Follow-up timepoint post-treatment			
Risk of Bias			
		Gastrointestinal symptoms G1: 3.79 ± 0.61 G2: 4.02 ± 0.28 Daytime wetting G1: 3.86 ± 0.67 G2: 3.92 ± 0.83 Nighttime wetting G1: 4.60 ± 0.97 G2: 3.92 ± 0.6	G1: 4.02 ± 1.20 G2: 3.98 ± 0.89 G1 vs G2: p=ns Gastrointestinal symptoms G1: 6.03 ± 0.56 G2: 4.02 ± 0.23 G1 vs G2: p<0.001 Daytime wetting G1: 3.97 ± 0.88 G2: 4.03 ± 1.04 G1 vs G2: p=ns Nighttime wetting G1: 4.23 ± 1.25 G2: 4.09 ± 0.64 G1 vs G2: p=ns
Bent et al., 2014 ⁴¹ RCT G1: Omega-3 fatty acid (1.3g/day), 29/29 G2: Placebo, 28/28 6 weeks/EOT Moderate RoB	Age, months G1: 88.2 ± 12.3 G2: 85 ± 13.2 mos IQ NR	ABC- Hyperactivity Parent Ratings G1: 28.4 ± 8.4 G2: 28.1 ± 7.6 ABC-Hyperactivity Teacher Ratings G1: 18.1 ± 12.0 G2: $14.6 \pm .4$ ABC-Irritability Parent G1: 20.0 ± 8.9 G2: 16.8 ± 8.3 ABC-Irritability Teacher G1: 14.3 ± 9.8 G2: 9.4 ± 9.3 ABC-Stereotypy Parent G1: 8.0 ± 6.0 G2: 5.4 ± 4.7 ABC-Stereotypy Teacher G1: 5.1 ± 4.8 G2: 3.7 ± 4.1 ABC-Lethargy Parent G1: 12.2 ± 8.8 G2: 8.8 ± 4.2	Mean change score ABC – Hyperactivity Parent G1: -5.3 ± 7.2 G2: -3.4 ± 7.5 G1 vs G2: p=ns ABC- Hyperactivity Teacher G1: -2.6 ± 8.0 G2: -1.0 ± 10.0 G1 vs G2: p=ns ABC-Irritability Parent G1: -2.0 ± 6.9 G2: -2.1 ± 4.4 G1 vs G2: p=ns ABC-Irritability Teacher G1: -1.3 ± 8.6 G2: -0.2 ± 6.8 G1 vs G2: p=ns ABC-Stereotypy Parent G1: -2.0 ± 3.7 G2: -0.5 ± 2.6 G1 vs G2: p=0.05 ABC-Stereotypy Teacher

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Treatment duration/Follow-up timepoint post-treatment			
Risk of Bias			
		ABC-Lethargy Teacher G1: 9.9 \pm 8.9 G2: 8.3 \pm 7.1 ABC-Inappropriate speech Parent G1: 7.0 \pm 3.4 G2: 5.8 \pm 2.8 ABC-Inappropriate speech Teacher G1: 4.2 \pm 3.9 G2: 3.1 \pm 3.3 SRS-total G1: 89.7 \pm 12.7 G2: 88.3 \pm .7 CGI-S G1: 3.8 \pm 1.0 G2: 4.0 \pm 0.79	G1: -1.0 \pm 4.2 G2: -0.7 \pm 3.2 G1 vs G2: p=ns ABC-Lethargy Parent G1: -2.1 \pm 4.2 G2: 0.1 \pm 2.6 G1 vs G2: p=0.01 ABC-Lethargy Teacher G1: -2.5 \pm 7.9 G2: -1.6 \pm 5.5 G1 vs G2: p=ns ABC-Inappropriate speech Parent G1: -0.6 \pm 2.7 G2: -0.9 \pm 2.2 G1 vs G2: p=ns ABC-Inappropriate speech Teacher G1: -1.0 \pm 2.6 G2: -0.1 \pm 5.5 G1 vs G2: p=ns SRS-total G1: -2.6 \pm 8.3 G2: -6.1 \pm 7.8 G1 vs G2:p=ns CGI-S G1: NR G2: NR
Voigt et al., 2014 ⁴² RCT G1: Docosahexaenoic acid (DHA) (500 mg/day), 24/19 G2: Placebo, 24/15 6 months/EOT Moderate RoB	Age G1: 5.8 \pm 1.8 G2: 6.5 \pm 2.2 IQ NR	CGI-I Parent NR BASC – Parent G1: 26.5 \pm 7.1 G2: 30.3 \pm 9.1 BASC – Teacher G1: 32.2 \pm 7.6 G2: 38.5 \pm 4.3	CGI-I Parent 3 months G1: 4/21 (19) G2: 5/16 (31) G1 vs G2: p=ns 6 months G1: 5/18 (28) G2: 2/13 (15) G1 vs G2: p=ns CGI-I Investigator 3 months G1: 1/17 (6)) G2: 0/13 (0) G1 vs G2: p=ns

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Risk of Bias			
			6 months G1: 0/18 (0) G2: 1/14 (7) G1 vs G2: p=ns EOT BASC – Parent G1: 26.3 ± 6.8 G2: 33.3 ± 9.7 G1 vs G2: p=0.04 BASC – Teacher G1: 33.6 ± 9.3 G2: 34.0 ± 5.6 G1 vs G2: p=0.02
Al-Ayadhi et al., 2013 ⁴³ RCT G1: Raw camel milk (500 mL/day), 24/24 G2: Boiled camel milk (500 mL/day), 25/25 G3: Cow milk (500 mL/day), 11/11 2 weeks/EOT High RoB	Age 2-12 IQ NR	CARS – total score G1: 37.63 ± 6.31 G2: 36.82 ± 3.27 G3: 34.18 ± 3.25	EOT CARS – total score G1: 34.54 ± 5.19 G2: 33.8 ± 4.91 G3: 34.41 ± 3.25 p=NR
Fahmy et al. 2013 ⁴⁴ RCT G1: Levocarnitine, 16/16 G2: Placebo, 14/14 6 months/EOT Moderate RoB	Age (months) G1: 69 (29-103) G2: 68.5 (32- 98) IQ NR	CARS – Mild/Moderate Severity G1: 1 (6.3) G2: 9 (64.3) CARS – Severe G1: 15 (93.80) G2: 5 (35.7) CARS-Total Score G1: 45.25 ± 6.191 G2: 36.71 ± 5.594	EOT Mild/Moderate Severity G1: 9 (56.3) G2: 9 (64.3) G1 vs G2, p=ns CARS – Severe G1: 7 (43.8) G2: 5 (35.7) G1 vs G2, p=ns CARS-Total Score G1: 37.06 ± 5.882 G2: 34.71 ± 4.631 G1 vs G2, p<0.001
Bent et al., 2011 ⁴⁵ RCT G1: Omega-3 fatty acid (1.3 g/day), 14/13 G2: Placebo, 13/12 12 weeks/EOT	Age, months G1: 70.2 ± 22 G2: 69.8 ± 17 IQ G1: 77.5 ± 27 G2: 77.5 ± 17	ABC –Hyperactivity G1: 16.8 ± 13 G2: 20.3 ± 8 PPVT G1: 72.2 ± 28 G2: 85.8 ± 12 EVT	Mean change score ABC – Hyperactivity G1: 2.7 ± 4.8 G2: 0.3 ± 7.2 G1 vs G2: p=ns PPVT G1: 2.7 ± 11.6 G2: 1.9 ± 12.4

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Risk of Bias			
Low RoB		G1: 70.8 \pm 33 G2: 86.4 \pm 14 SRS G1: 76.9 \pm 11 G2: 79.0 \pm BASC-Externalizing G1: 53.8 \pm 13 G2: 66.3 \pm 25 BASC- Internalizing G1: 43.3 \pm 10 G2: 50.1 \pm 9 BASC-Behavioral G1: 60.9 \pm 14 G2: 65.4 \pm 3 BASC- Adaptive skill G1: 29.8 \pm 9 G2: 31.9 \pm 9 BASC-Hyperactivity G1: 61.8 \pm 17 G2: 64.6 \pm 7	G1 vs G2: p=ns EVT G1: 2.2 \pm 7.6 G2: 5.8 \pm 5.7 G1 vs G2: p=ns SRS G1: -0.9 \pm .5 G2: 1.7 \pm 7.2 G1 vs G2: p=ns BASC-Externalizing G1: 0.1 \pm 6.7 G2: 6.6 \pm 30.4 G1 vs G2: p=ns BASC-Internalizing G1: 0.3 \pm 6.6 G2: -2.9 \pm 7.6 G1 vs G2: p=ns BASC-Behavioral G1: -1.1 \pm 6.1 G2: -2.0 \pm 4.9 G1 vs G2: p=ns BASC-Adaptive skill G1: 1.8 \pm 6.8 G2: 0.8 \pm 7.1 G1 vs G2: p=ns BASC-Hyperactivity G1: 2.1 \pm 6.3 G2: 1.2 \pm 5.8 G1 vs G2: p=ns
Geier, et al., 2011 ⁴⁶ RCT G1: Levocarnitine (50 mg/kg/day), 19/16 G2: Placebo, 11/11 3 months/EOT High RoB	Age: G1: 6.3 \pm 2.4 G2: 6.7 \pm 1.6 IQ NR	CARS G1: 35.7 \pm 5.3 G2: 38.2 \pm 6.0 CGI G1: 2.0 G2: 2.0 Hand Muscle Testing G1: 32.7 \pm 13.9 G2: 35.3 \pm 13.2 ATEC Total G1: 55.1 \pm 23.3 G2: 62.8 \pm 31.7	EOT CARS G1: 33.8 \pm 5.8 G2: 38.4 \pm 6.3 p=.02 CGI G1: 1.5 \pm 0.63 G2: 2.09 \pm 0.7 p= .03 Hand Muscle Testing G1: 34.3 \pm 16.7 G2: 35.1 \pm 7.5 p= ns

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Risk of Bias			
		ATEC Speech G1: 9.9 \pm 6.3 G2: 10.5 \pm 6.4 ATEC Sociability G1: 12 \pm 7.1 G2: 11.9 \pm 7.7 ATEC Cognitive G1: 12.7 \pm 6.1 G2: 14.4 \pm 7.6 ATEC Health/Behavior G1: 20.5 \pm 8.1 G2: 26 \pm 14.8	ATEC Total G1: 40.1 \pm 22.8 G2: 56 \pm 27.6 p= ns ATEC Speech G1: 7.8 \pm 5.9 G2: 10.9 \pm 7.2 p= ns ATEC Sociability G1: 8.3 \pm 5.9 G2: 10.8 \pm 8.4 p=ns ATEC Cognitive G1: 9.2 \pm 5.5 G2: 14.9 \pm 7.3 p=.009 ATEC Health/Behavior G1: 14.8 \pm 7.9 G2: 19.5 \pm 10.9 p=ns
Bertoglio et al., 2010 ⁴⁷ RCT G1: Methyl B12 (64.5 µg/kg) G2: Placebo Crossover design N=30 total 12 weeks/EOT Low RoB	Age G1 + G2: 3-8 IQ NR	CGIS NR	No significant group difference in behavior measures EOT CGIS Improvement (\geq 1 point) n (%) G1+G2: 9 (30) 3 received placebo first and 6 received active treatment CBCL improvement (\geq 5 points): G1+G2: 3 (10) ABC improvement (\geq 5 points): G1+G2: 5 (16.7)

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Risk of Bias			
<p>Munasinghe et al., 2010⁴⁸ RCT</p> <p>G1: Digestive enzyme supplement- Peptizyde (up to 2 capsules/day) G2: Placebo (360 mg/day) Crossover design N=43 total</p> <p>3 months/EOT</p> <p>Moderate RoB</p>	<p>Age, months G1 + G2: 5.78 \pm 1.77</p> <p>IQ NR</p>	<p>GBRS G1+G2: 4</p> <p>ARS G1+G2: 4</p> <p>LDS NR</p>	<p>EOT</p> <p>Food variety score G1: 4.42 \pm 0.62 G2: 4.06 \pm 0.45 p= 0.02</p> <p>Parent Behavior score G1: 4.29 \pm 0.79 G2: 4.11 \pm 0.73 p = ns</p> <p>GI symptoms score G1: 4.01 \pm 0.68 G2: 3.87 \pm 0.36 p = ns</p> <p>Sleep Quality score G1: 3.95 \pm 0.75 G2: 3.87 \pm 0.56 p = ns</p> <p>Therapist engagement score G1: 4.59 \pm 0.96 G2: 4.43 \pm 0.55 p = ns</p> <p>LDS Vocabulary percentile score G1: 56.95 \pm 28.6 G2: 55.59 \pm 28.6 p = ns</p> <p>LDS Sentence length percentile score G1: 62.38 \pm 26.2 G2: 63.91 \pm 24.9 p = ns</p>
<p>Hendren et al., 2016⁴⁹ RCT</p> <p>G1: Methyl B-12 (75 µg/kg every 3 days), 28/27 G2: Placebo (75 µg/kg every 3 days), 29/23</p> <p>8 weeks/EOT</p> <p>Moderate ROB</p>	<p>Age (months) G1: 67 \pm 16 G2: 58 \pm 14</p> <p>IQ-Stanford Binet G1: 64 \pm 18 G2: 67 \pm 20</p>	<p>CGI-Severity G1: 5.2 \pm 0.7 G2: 5.1 \pm 0.6</p> <p>ABC-Hyperactivity G1: 25 \pm 10.1 G2: 22.4 \pm 11.5</p> <p>ABC-Inappropriate Speech G1: 4.2 \pm 3.2 G2: 2.9 \pm 3.2</p>	<p>Change Score</p> <p>CGI-Improvement G1: 2.4 \pm 0.8 G2: 3.1 \pm 0.8 G1 vs G2, p=0.005</p> <p>ABC-Hyperactivity G1: -0.9 \pm 4.8 G2: -3.9 \pm 7.1 G1 vs G2, p=ns; ES=-0.48</p> <p>ABC-Inappropriate</p>

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		ABC-Irritability G1: 15.2 ± 10.4 G2: 11.1 ± 8.4 ABC-Social Withdrawal/Lethargy G1: 15 ± 9.1 G2: 14.2 ± 8.5 ABC-Stereotypic Behavior G1: 7.1 ± 4.6 G2: 7.4 ± 5.1 SRS-Total Score G1: 90 ± 13.7 G2: 83.5 ± 10.6	Speech G1: 0.3 ± 1.4 G2: -0.3 ± 1.6 G1 vs G2, p=ns; ES=-0.43 ABC-Irritability G1: -0.1 ± 3.7 G2: -2.6 ± 4.3 G1 vs G2, p= 0.08; ES=-0.61 ABC-Social Withdrawal/Lethargy G1: -1.9 ± 5.8 G2: -1.2 ± 7.1 G1 vs G2, p=ns; ES=0.12 ABC-Stereotypic Behavior G1: -0.3 ± 2.2 G2: 0.3 ± 3.2 G1 vs G2, p=ns; ES=0.23 SRS-Total Score G1: -1.6 ± 7.7 G2: -4.1 ± 7.7 G1 vs G2, p=ns; ES=-0.32

ABC-Aberrant Behavior Checklist; CGI-Clinical Global Impression; VABS-Vineland Adaptive Behavior Scale; EOT-End of Treatment; PDDBI-Pervasive Developmental Disorders Behavior Inventory; BASC-Behavior Assessment System for Children; CARS-Childhood Autism Rating Scale; GBRSS-Global Rating Scale; SRS-Social Responsiveness Scale; PPVT-Peabody Picture Vocabulary Test; EVT-Expressive Vocabulary Test; ATEC-Autism Treatment Evaluation Checklist; CGIS-Clinical Global Impressions Scale; CBCL-Child Behavior Checklist; GBRSS-Global Rating Scale; ARS-Additional Rating Scale; LDS-Language Development Survey