

**Table F-2. Key findings in studies of methylphenidate**

<p><b>Author, Year Study Design</b></p> <p><b>Groups (dose), N enrollment / N final</b></p> <p><b>Treatment duration/Follow-up timepoint post-treatment</b></p> <p><b>Risk of Bias</b></p>	<p><b>Mean age, years ± SD</b></p>	<p><b>Outcome measure/Baseline scores, mean ±SD</b></p>	<p><b>Outcome measure/Post- treatment scores, mean ± SD</b></p>
<p><b>Mean IQ ±SD</b></p>			
<p>RUPP 2005<sup>33-36</sup> RCT</p> <p>G1: Methylphenidate - low dose (0.125 mg/kg), 66/45 G2: Methylphenidate - medium dose (0.250 mg/kg), 66/52 G3: Methylphenidate - high dose (0.500 mg/kg), 66/33 G4: Methylphenidate - optimal dose (NA), 66/58 G5: Placebo (NA), 66/46</p> <p>13 weeks/EOT</p> <p>Low RoB</p>	<p>Age G1+G2+G3+G4+ G5: 7.5</p> <p>IQ NR</p>	<p><b>Overall ratings:</b> CGI severity sub- scale rating, n (%): Moderately ill: 20 (30.3)</p> <p>Markedly ill: 35 (52.0)</p> <p>Severely ill: 11 (16.7)</p> <p><b>Educational/cog- nitive/academic attainment:</b> Slosson IQ, mean ± SD (range): 62.6 ± 32.9 (16-135)</p> <p><b>Social skills:</b> VABS score, mean ± SD (range):†</p> <p>Socialization: 61.7 ± 16.7 (20-109)</p> <p><b>Communication/ language:</b> VABS Communication: 62.8 ± 21.8 (20-126)</p> <p><b>Adaptive behavior:</b> VABS composite: 56.2 ± 21.0 (20-109)</p> <p>VABS Daily living skills: 54.4 ± 19.8 (20-110)</p> <p><b>Problem behavior:</b> ABC score, parent- rated, mean ± SD (range):†</p> <p>Irritability: 16.9 ± 10.1 (0-41)</p> <p>Lethargy/social withdrawal: 12.1 ± 8.9 (0-33)</p>	<p><b>Overall ratings:</b> Responded to treatment, sub- jects completing cross-over phase, n (%): Total: 44 (76)</p> <p>Optimal/best treatment:† Placebo: 9 (20) Low: 11 (25) Medium: 14 (32) High: 10 (23)</p> <p>Response rate, by dose, n (%):† <b>G1:</b> 20/61 (33) <b>G2:</b> 27/77 (35) <b>G3:</b> 18/47 (38) <b>G5:</b> 12/61 (20) <b>G1/G5:</b> <i>P</i> = 0.18 <b>G2/G5:</b> <i>P</i> = 0.05 (including first medium dose) <b>G2/G5:</b> <i>P</i> = 0.06 (including first and second medium dose when applicable) <b>G3/G5:</b> <i>P</i> = 0.07</p> <p><b>Social skills:</b>^ Joint attention (n=33), mean ± SD</p> <p>Initiations: <b>G1:</b> 23.29 ± 16.62 <b>G2:</b> 20.85 ± 13.01 <b>G3:</b> 19.27 ± 14.23 <b>G4:</b> 25.09 ± 15.55 <b>G5:</b> 18.59 ± 12.03 <b>G1/G5:</b> <i>P</i> &lt; 0.05 <b>G2/G5:</b> <i>P</i> = NS <b>G3/G5:</b> <i>P</i> = NS</p>

<p>Author, Year Study Design</p> <p>Groups (dose), N enrollment / N final</p> <p>Treatment duration/Follow-up timepoint post-treatment</p> <p>Risk of Bias</p>	<p>Mean age, years ± SD</p> <p>Mean IQ ±SD</p>	<p>Outcome measure/Baseline scores, mean ±SD</p>	<p>Outcome measure/Post- treatment scores, mean ± SD</p>
		<p>Stereotypy: 7.6 ± 5.9 (0-21)</p> <p>Hyperactivity: 33.2 ± 8.7 (2-47)</p> <p>Inappropriate speech: 6.0 ± 4.1 (0-12)</p> <p>ABC score, teacher- rated, mean ± SD (range):†</p> <p>Irritability: 16.1 ± 9.4 (0-43)</p> <p>Lethargy/social withdrawal: 15.5 ± 10.9 (0-42)</p> <p>Stereotypy: 7.6 ± 5.1 (0-19)</p> <p>Hyperactivity: 30.9 ± 7.9 (16-45)</p> <p>Inappropriate speech: 5.8 ± 3.6 (0-12)</p> <p>SNAP-IV, parent- rated, mean ± SD:* ADHD: 39.82 ± 8.09</p> <p>Inattention: 20.21 ± 5.17</p> <p>Hyperactivity/ impulsivity: 19.61 ± 4.22</p> <p>Oppositional defiant disorder: 9.61 ± 6.19 SNAP-IV, teacher- rated, mean ± SD:*</p> <p>ADHD: 37.23 ± 7.04</p> <p>Inattention:</p>	<p><b>G4/G5: P &lt; 0.05</b></p> <p>Responses: <b>G1: 2.48 ± 1.45</b> <b>G2: 1.69 ± 1.42</b> <b>G3: 1.93 ± 1.48</b> <b>G4: 2.24 ± 1.69</b> <b>G5: 1.90 ± 1.71</b> <b>G1/G5: P &lt; 0.01</b> <b>G2/G5: P = NS</b> <b>G3/G5: P = NS</b> <b>G4/G5: P = NS</b></p> <p>Requesting: G1: 4.04 ± 2.25 G2: 3.81 ± 2.65 G3: 3.69 ± 3.27 G4: 4.13 ± 2.58 G5: 3.67 ± 2.40 G1/G5: P = NS G2/G5: P = NS G3/G5: P = NS G4/G5: P = NS</p> <p>Competing demands task (n=33), mean ± SD: Self-regulating behavior: G1: 19.77 ± 10.89 G2: 16.21 ± 9.03 G3: 15.80 ± 12.65 G4: 16.47 ± 13.91 G5: 12.47 ± 11.29 G1/G5: P = 0.09 G2/G5: P &lt; 0.01 G3/G5: P = NS G4/G5: P = 0.09</p> <p>Regulated affective state: G1: 12.91 ± 4.98 G2: 12.96 ± 3.85 G3: 11.67 ± 5.53 G4: 12.47 ± 4.99 G5: 9.57 ± 6.72 G1/G5: P = NS G2/G5: P &lt; 0.05</p>

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		<p>19.30 ± 4.32</p> <p>Hyperactivity/ impulsivity: 17.93 ± 4.81</p> <p>Oppositional defiant disorder: 8.83 ± 5.19</p> <p>CYBOCS-PDD, clinician-rated, mean ± SD:* 13.30 ± 3.74</p> <p>VABS Maladaptive behaviors total: 29.2 ± 9.2 (13-51)</p> <p>Motor skills: 69.2 ± 17.8 (44-113)</p>	<p>G3/G5: P &lt; 0.05 G4/G5: P = 0.09</p> <p>Clean-up task (n=33), mean ± SD: Compliance behaviors: G1: 3.67 ± 4.87 G2: 3.67 ± 5.64 G3: 4.06 ± 4.55 G4: 3.94 ± 4.88 G5: 3.47 ± 5.41 G1/G5: P = NS G2/G5: P = NS G3/G5: P = NS G4/G5: P = NS</p> <p>Regulated affective state: G1: 8.10 ± 5.18 G2: 6.88 ± 4.86 G3: 6.65 ± 6.03 G4: 7.42 ± 5.05 G5: 7.33 ± 4.86 G1/G5: P = NS G2/G5: P = NS G3/G5: P = NS G4/G5: P = NS</p> <p>Repetitive behavior:† See notes Problem behavior: ABC- hyperactivity subscale score, mean ± SD:† Parent-rated: G1: 23.0 ± 11.29 G2: 20.6 ± 10.27 G3: 22.1 ± 9.67 G4: 17.2 ± 9.87 G5: 26.0 ± 9.90 G1/G5: P = 0.03 (es = 0.29) G2/G5: P &lt; 0.001 (es = 0.54) G3/G5: P = 0.003 (es = 0.40) G4/G5: P &lt;</p>

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			<p>0.001 (es = 0.89)</p> <p>Teacher-rated: G1: 22.9 ± 12.84 G2: 23.6 ± 12.53 G3: 20.3 ± 11.94 G4: 20.1 ± 12.40 G5: 26.0 ± 11.66 G1/G5: P = 0.03 (es = 0.25) G2/G5: P = 0.008 (es = 0.20) G3/G5: P = 0.002 (es = 0.48) G4/G5: P &lt; 0.001 (es = 0.48)</p> <p>SNAP-IV inatten- tion, mean ± SD:*</p> <p>Parent-rated: G1: 14.58 ± 6.56 G2: 13.38 ± 6.48 G3: 14.30 ± 6.35 G4: 11.83 ± 6.02 G5: 15.59 ± 6.51 G1/G5: P = 0.15 (es = 0.15) G2/G5: P &lt; 0.001 (es = 0.34) G3/G5: P = 0.06 (es = 0.20) G4/G5: P &lt; 0.001 (es = 0.60)</p> <p>Teacher-rated: G1: 15.24 ± 6.34 G2: 14.27 ± 6.93 G3: 14.67 ± 6.88 G4: 13.98 ± 6.46 G5: 16.15 ± 6.10 G1/G5: P = 0.21 (es = 0.15) G2/G5: P &lt; 0.001 (es = 0.29) G3/G5: P = 0.02 (es = 0.23) G4/G5: P = 0.003 (es = 0.35)</p> <p>SNAP-IV</p>

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			<p>hyperactivity/ impulsivity, mean ± SD:* Parent-rated: G1: 13.39 ± 5.87 G2: 12.19 ± 6.06 G3: 13.49 ± 6.41 G4: 10.80 ± 5.99 G5: 15.33 ± 5.81 G1/G5: P = 0.02 (es = 0.33) G2/G5: P &lt; 0.001 (es = 0.53) G3/G5: P = 0.01 (es = 0.30) G4/G5: P &lt; 0.001 (es = 0.77)</p> <p>Teacher-rated: G1: 12.76 ± 6.84 G2: 13.00 ± 6.71 G3: 11.45 ± 7.01 G4: 11.26 ± 6.26 G5: 14.41 ± 6.095 G1/G5: P = 0.08 (es = 0.24) G2/G5: P = 0.01 (es = 0.21) G3/G5: P = 0.005 (es = 0.42) G4/G5: P = 0.005 (es = 0.48)</p> <p>SNAP-IV oppositional defiant disorder, mean ± SD:* Parent-rated: G1: 6.77 ± 5.62 G2: 7.02 ± 5.90 G3: 7.53 ± 5.90 G4: 5.86 ± 4.70 G5: 7.69 ± 5.80 G1/G5: P = 0.14 (es = 0.16) G2/G5: P = 0.25 (es = 0.12) G3/G5: P = 0.66 (es = 0.03) G4/G5: P &lt; 0.001 (es = 0.35)</p>

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			<p>Teacher-rated: G1: 5.89 ± 5.43 G2: 6.65 ± 5.10 G3: 6.75 ± 5.63 G4: 5.61 ± 4.85 G5: 7.02 ± 5.80 G1/G5: P = 0.11 (es = 0.20) G2/G5: P = 0.17 (es = 0.07) G3/G5: P = 0.35 (es = 0.05) G4/G5: P = 0.04 (es = 0.26)</p> <p>CYBOCS-PDD, clinician-rated, mean ± SD:* G1: 12.82 ± 4.15 G2: 12.31 ± 4.27 G3: 13.02 ± 4.11 G4: 12.13 ± 4.22 G5: 13.05 ± 3.46 G1/G5: P = 0.90 (es = 0.06) G2/G5: P = 0.21 (es = 0.19) G3/G5: P = 0.80 (es = 0.01) G4/G5: P = 0.08 (es = 0.24)</p> <p>Commonly occurring co- morbidities: SNAP-IV ADHD, mean ± SD:* Parent-rated: G1: 27.97 ± 11.62 G2: 25.57 ± 11.66 G3: 27.79 ± 11.63 G4: 22.63 ± 11.19 G5: 30.92 ± 11.55 G1/G5: P = 0.04 (es = 0.25) G2/G5: P &lt;</p>

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			<p>0.001 (es = 0.46) G3/G5: P = 0.02 (es = 0.27) G4/G5: P &lt; 0.001 (es = 0.73)</p> <p>Teacher-rated: G1: 28.00 ± 12.12 G2: 27.27 ± 12.21 G3: 26.12 ± 12.64 G4: 25.24 ± 11.53 G5: 30.57 ± 11.84 G1/G5: P = 0.10 (es = 0.21) G2/G5: P = 0.001 (es = 0.27) G3/G5: P = 0.005 (es = 0.36) G4/G5: P = 0.003 (es = 0.46)</p>
<p>Pearson et al., 2013<sup>37</sup> RCT</p> <p>G1: Methylphenidate - low dose (0.14-0.21 mg/kg), 24/24 G2: Methylphenidate - medium dose (0.24-0.35 mg/kg), 24/24 G3: Methylphenidate - high dose (0.27-0.48 mg/kg), 24/24 G4: Placebo (NA), 24/24</p> <p>4 weeks/EOT</p> <p>Low RoB</p>	<p>Age G1+G2+G3+G4: 8.8 ± 1.6 IQ NR</p>	<p><b>Parent Ratings</b> CPRS NR</p> <p>CPRS-ADHD scale G1+G2+G3+G4: 76.4 ± 6.7</p> <p>SNAP-IV NR</p> <p>ACTeRS NR</p> <p>ABC NR</p> <p>SCQ NR</p> <p><b>Teacher Ratings</b> CTRS NR</p> <p>CTRS-ADHD scale G1+G2+G3+G4: 67.2 ± 8.7</p> <p>SNAP-IV NR</p>	<p><b>EOT Parent Ratings</b> CPRS – CGI Total G1: 61.9 ± 11.7 G2: 59.9 ± 9.8 G3: 55.8 ± 9.3 G4: 66.8 ± 12.7 G4 vs G2, p&lt;0.05 G4 vs G3, p&lt;0.05 G1 vs G3, p&lt;0.05 CPRS – Oppositional G1: 53.1 ± 15.3 G2: 53.8 ± 12.4 G3: 49.8 ± 11.4 G4: 59.2 ± 16 ANOVA p-value for all groups, p&lt;0.05 CPRS – Cognitive</p>

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		<p>ACTeRS NR</p>	<p>Problems/Inattention G1: 67.7 ± 11.6 G2: 63.9 ± 12.5 G3: 60 ± 11.7 G4: 70.3 ± 12.8 G4 vs G2, p&lt;0.05  G4 vs G3, p&lt;0.05  G1 vs G3, p&lt;0.05  CPRS – Hyperactivity G1: 62.6 ± 12.2 G2: 62.1 ± 12 G3: 58.3 ± 10.2 G4: 70.8 ± 15.2 G4 vs G2, p&lt;0.05  G4 vs G3, p&lt;0.05  CPRS – ADHD Index G1: 64.9 ± 9.3 G2: 62.3 ± 10 G3: 59.9 ± 10.5 G4: 70.1 ± 11.9 G4 vs G2, p&lt;0.05  G4 vs G3, p&lt;0.05  SNAP-IV – Inattentive/Hyper active G1: 26 ± 11.1 G2: 22.8 ± 9.6 G3: 21.6 ± 9.6 G4: 31.6 ± 11 G4 vs G2, p&lt;0.05  G4 vs G3, p&lt;0.05  ACTeRS – Attention G1: 12.4 ± 5.3 G2: 13.4 ± 5</p>



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			<p>G3: 14 ± 4.2 G4: 10.9 ± 4.7 G4 vs G3, p=ns</p> <p>ACTeRS – Hyperactivity G1: 13.3 ± 4.5 G2: 12 ± 4 G3: 12 ± 4.3 G4: 15.7 ± 4.5 G4 vs G2, p&lt;0.05</p> <p>G4 vs G3, p&lt;0.05</p> <p>ACTeRS – Social Skills G1: 13.3 ± 4.4 G2: 12 ± 3.7 G3: 14 ± 4.3 G4: 12.8 ± 4.5 G2 vs G3, p&lt;0.05</p> <p>ACTeRS – Oppositional G1: 7.8 ± 5.6 G2: 6.8 ± 4 G3: 6.6 ± 2.6 G4: 8.4 ± 5.3 G4 vs G2, p&lt;0.05</p> <p>ABC-Irritability G1: 10 ± 9.2 G2: 8.2 ± 8.1 G3: 7.2 ± 6.9 G4: 12.6 ± 10.4 G4 vs G3, p&lt;0.05</p> <p>ABC-Social Withdrawal/Leth argy G1: 7.3 ± 5.6 G2: 8.1 ± 5.9 G3: 8.5 ± 6.6 G4: 9.3 ± 8.1 p=ns</p> <p>ABC-Stereotypy G1: 4.3 ± 4.5 G2: 4 ± 3.8 G3: 3.5 ± 3.8</p>

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			<p>G4: 4.9 ± 5.4 p=ns</p> <p>ABC- Hyperactivity G1: 18.1 ± 10.5 G2: 14.5 ± 7.7 G3: 14.5 ± 9.2 G4: 24.1 ± 13 G4 vs G2, p&lt;0.05</p> <p>G4 vs G3, p&lt;0.05</p> <p>ABC- Inappropriate Speech G1: 4.3 ± 3.2 G2: 4 ± 3.1 G3: 3.9 ± 3.1 G4: 5.2 ± 3.1 G4 vs G2, p&lt;0.05</p> <p>G4 vs G3, p&lt;0.05</p> <p>SCQ – Total G1: 14.2 ± 6.6 G2: 15.2 ± 6.2 G3: 13.4 ± 6.2 G4: 15.5 ± 6.1 ANOVA p-value for all groups, p&lt;0.05</p> <p><b>Teacher Ratings</b> CTRS – CGI- Total G1: 63.4 ± 12.8 G2: 62.4 ± 12.5 G3: 59.3 ± 12.7 G4: 75.6 ± 11.5 G4 vs G2, p&lt;0.05</p> <p>G4 vs G3, p&lt;0.05</p> <p>G1 vs G3, p&lt;0.05</p> <p>CTRS- Oppositional</p>

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			<p>G1: 56.6 ± 13.2 G2: 58.1 ± 15.4 G3: 55.1 ± 13.5 G4: 65.1 ± 19.5 p=ns</p> <p>CTRS-Cognitive Problems/Inatten tion G1: 58.3 ± 10.7 G2: 57.8 ± 9.5 G3: 59.3 ± 11.1 G4: 63 ± 11.2 G4 vs G2, p&lt;0.05 G4 vs G3, p&lt;0.05 G1 vs G3, p&lt;0.05</p> <p>CTRS- Hyperactivity G1: 59.9 ± 13.6 G2: 59.9 ± 11.4 G3: 57.7 ± 11.3 G4: 70.3 ± 13.5 G4 vs G2, p&lt;0.05 G4 vs G3, p&lt;0.05 G1 vs G3, p&lt;0.05</p> <p>CTRS-ADHD Index G1: 63.1 ± 11.2 G2: 63.6 ± 10.4 G3: 61.5 ± 13 G4: 72.8 ± 12 G4 vs G2, p&lt;0.05 G4 vs G3, p&lt;0.05 G1 vs G3, p&lt;0.05</p> <p>SNAP-IV – Inattentive/Hyper active G1: 24.7 ± 10.9</p>

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			<p>G2: 23.7 ± 11.1 G3: 21.8 ± 11.6 G4: 32.7 ± 12.4 G4 vs G2, p&lt;0.05</p> <p>G4 vs G3, p&lt;0.05</p> <p>G1 vs G3, p&lt;0.05</p> <p>ACTeRS – Attention G1: 14.3 ± 6.2 G2: 13.7 ± 5.5 G3: 15.9 ± 8.5 G4: 11.3 ± 4 G4 vs G3, p&lt;0.05</p> <p>ACTeRS – Hyperactivity G1: 11.8 ± 5.6 G2: 12.8 ± 5.5 G3: 11.2 ± 5 G4: 18.7 ± 5.2 G4 vs G2, p&lt;0.05</p> <p>G4 vs G3, p&lt;0.05</p> <p>G1 vs G3, p&lt;0.05</p> <p>ACTeRS – Social Skills G1: 19.2 ± 4.2 G2: 16.7 ± 4 G3: 18.5 ± 5.8 G4: 15.8 ± 3.6 p=ns</p> <p>ACTeRS – Oppositional G1: 7.6 ± 3.5 G2: 9.2 ± 5.5 G3: 7.1 ± 2.1 G4: 10.6 ± 5.8 G4 vs G3, p&lt;0.05</p> <p>CGI-Severity (clinician 1) G1: 4 ± 0.81</p>

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			<p>G2: 3.8 ± 0.82 G3: 3.8 ± 0.74 G4: 4.8 ± 0.61 G4 vs G2, p&lt;0.05</p> <p>G4 vs G3, p&lt;0.05</p> <p>G1 vs G3, p&lt;0.05</p> <p>CGI- Improvement (clinician 1) G1: 2.8 ± 1.3 G2: 2.4 ± 1.3 G3: 2.1 ± 1.2 G4: 4 ± 0.81 G4 vs G2, p&lt;0.05</p> <p>G4 vs G3, p&lt;0.05</p> <p>G1 vs G3, p&lt;0.05</p> <p>CGI-Severity (clinician 2) G1: 4 ± 0.72 G2: 4 ± 0.62 G3: 3.9 ± 0.74 G4: 4.7 ± 0.76 G4 vs G2, p&lt;0.05</p> <p>G4 vs G3, p&lt;0.05</p> <p>G1 vs G3, p&lt;0.05</p> <p>CGI- Improvement (clinician 2) G1: 2.8 ± 1.4 G2: 2.6 ± 1.3 G3: 2 ± 1 G4: 4.1 ± 0.95 G4 vs G2, p&lt;0.05</p> <p>G4 vs G3, p&lt;0.05</p> <p>G1 vs G3,</p>

<b>Author, Year Study Design</b>  <b>Groups (dose), N enrollment / N final</b>  <b>Treatment duration/Follow-up timepoint post-treatment</b>  <b>Risk of Bias</b>	<b>Mean age, years ± SD</b>  <b>Mean IQ ±SD</b>	<b>Outcome measure/Baseline scores, mean ±SD</b>	<b>Outcome measure/Post- treatment scores, mean ± SD</b>
			p<0.05

ABC-Aberrant Behavior Checklist; CGI-Clinical Global Impression; VABS-Vineland Adaptive Behavior Scale; CYBOCS-PDD-Children's Yale-Brown Obsessive Compulsive Scale Modified for Pervasive Developmental Disorder; EOT-End of Treatment; VBS-Visual Analog Scale; CGAS-Children's Global Assessment Scale; SNAP-IV- ; ADHD-Attention Deficit/Hyperactivity Disorder; CPRS-Conners Parent Rating Scale; ACTeRS-ADD-H Comprehensive Teacher Rating Scale; CTRS-Conners Teacher Rating Scale; SCQ-Social Communication Questionnaire