Table C.2. KQ2 evidence table

| **Intervention** | **Study:**  Author, Year;  Multiple Publications;  Trial ID;  Study Design;  Sites;  Study Size;  Location  Setting | **Population:**  Setting;  Study Target;  ADHD Presentation;  Diagnosis;  Comorbidity;  % Female;  Age Mean;  Minimum Age;  Maximum Age;  Ethnicity | **Comparison:**  Intervention;  Control;  Comparator;  Follow-Up | **Outcome and Results** |
| --- | --- | --- | --- | --- |
| CAM | Aviv, 2021128  ID: ID NA  RCT  Single center  N = 123  Israel  Setting: Community | **Target:** Children with ADHD currently taking stimulant medication; those with co-occurring psychological disorders excluded  **Other:** Parents reported some outcomes  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV-TR by pediatric neurologist  **Comorbidity:** N/A  **Female:** 27.7 %  **Age mean:** 8.97 (1.68)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  Other : 100% Israeli | **Intervention:** Horseback riding sessions plus medication (not further specified), 30-min therapeutic sessions, after completing each activity with the horse, the instructors and the children analyzed the children’s and the horse’s behaviors to strengthen the riders’ monitoring abilities by teaching them to observe and analyze their actions using the horse’s reactions as a feedback and to correct their behaviors accordingly, for 20 weeks  **Control:** Wait list  Wait list plus medication (not further specified)  **Comparator:** NA  **Follow-up:** 8 months | Conners’ Parent Rating Scales, Revised (CPRS-R) emotional regulation scale  Lower scores in the intervention group.  Behavior Rating Inventory of Executive Functions (BRIEF): Behavioral Regulation Index score - Intervention 54.02 (9.46) Control 63.85 (9.94); Meta-cognition score - Intervention 86.03 (15.63); Control 99.57 (11.65). Lower is better., statistical significance not reported. |
| CAM | Binesh, 2020150  Research Institute for Islamic and Complementary Medicine, 2019998  ID: IRCT20090527001957N9  RCT  Single center  N = 50  Iran  Setting: N/A | **Target:** Children with ADHD according to DSM-5 criteria, Child Severity Inventory-4 score, clinical judgment of a psychiatrist, and a family physician; Child Severity Inventory-4 questionnaire scores for the attention deficit section >6 and the hyperactivity section >5  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-V  **Comorbidity:** N/A  **Female:** 18.2 %  **Age mean:** 9.8 (2)  **Minimum age:** 6  **Maximum age:** 14  **Ethnicity:**  N/A | **Intervention:** Auricular therapy was performed at six ear acupoints, stimulated bilaterally for20 sec at each point, each participant evaluated and received stimulation for 15 min, each point labeled with small sections of adhesive tape that contained a small granule (Vaccaria seeds), participants’ supervisors were asked to apply medium pressure once a day for 1 min on each of the seeds after stimulation, repeated once a week for 6 weeks  **Control:** Attention-matched control  Nonacupuncture points were not electrically stimulated and only the seedless adhesive tapes were attached, adhesive replacement was performed once a week for 6 weeks  **Comparator:** NA  **Follow-up:** 2.5 months | Hyperactivity Scores, Comprehensive Behavior Rating Scale, Parent’s version  Hyperactivity impulsiveness, and anger improvement improvement, investigator evaluation  Patients exhibited significantly greater improvement after receiving auricular therapy than did children in the sham control group (p < .05). |
| CAM | Frei, 2001279  ID: NA  Clinical trial  Single center  N = 115  Switzerland  Setting: Specialty care | **Target:** Participants with ADHD with a Clinical Global Impressions of 14 or higher  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 20 %  **Age mean:**  mean age 8.3  **Minimum age:** 3  **Maximum age:** 17  **Ethnicity:**  N/A | **Intervention:** Homeopathic liquid LM-potencies (LM-3 to LM-30) every day or every second day, used for 4 weeks, moving on to the next higher level (eg LM-6) after a treatment free interval of several days to one week, total duration of 3 months  **Control:** NA  **Comparator:** MedicationMethylphenidate for patients who did not reach sufficient clinical improvement, or whose behavior remained unacceptable despite a certain response to homeopathy after reevaluation, optimal dosage was adjusted over 3 months  **Follow-up:** 3 months | CGI (Clinical Global Impression) scale  During homeopathic treatment the mean CGI rating fell to 9.27 corresponding to an amelioration of 55%, and with MPD to 10.96, corresponding to an amelioration of 48%. |
| CAM | Frei, 2005278  ID: NA  Crossover trial  Single center  N = 83  Switzerland  Setting: Specialty care | **Target:** Children with ADHD with neuropsychological correlates, the necessity for treatment, and absence of any chronic physical, neurological or psychiatric disorders  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV by neuropsychologist  **Comorbidity:** N/A  **Female:** 12.8 %  **Age mean:**  Arm A: 10 (range 7–15); Arm B: 10 (range 7–15)  **Minimum age:** 6  **Maximum age:** 16  **Ethnicity:**  N/A | **Intervention:** Verum homeopathic treatment daily for 6 weeks  **Control:** Placebo  Placebo  **Comparator:** NA  **Follow-up:** 5.5 months | Conners’ Global Index (CGI)  Intervention group had significantly more improvement than control group (p=0.0479). |
| CAM | Hong, 2016332  Trial registration, 2010719  ID: KCT0000019  RCT  Single center  N = 93  Korea  Setting: Specialty care | **Target:** Participants with an ADHD diagnosis (of any subtype) receiving any intervention (pharmacological, psychosocialtherapy, educational, occupational therapies etc.) without change in ADHD treatments/ symptoms for last 2 weeks or no current treatment; no diagnosis of mental retardation or pervasive developmental disorders, past history of epilepsy or other neurotic disorder, pregnancy, change in medications during the course of the study  **Other:** Parent reported some outcomes  **ADHD presentation:** N/A : Mean Hyperactivity/Impulsivity score = 11.0 in each group.  **Diagnosis:** Confirmation by specialist  DSM IV criteria  **Comorbidity:** N/A  **Female:** 18.7 %  **Age mean:** 11.0 (2.8)  **Minimum age:** 7  **Maximum age:** 18  **Ethnicity:**  % Asian : 100 | **Intervention:** Acupuncture treatment for twenty minutes, twice per week for six weeks  **Control:** Wait list  Wait list  **Comparator:** NA  **Follow-up:** 1.5 months | Child Behavior Checklist (CBCL), change from baseline  No significant difference between groups (p = 0.393).  ADHD-RS change  Change in score did not differ significantly between groups (p = 0.561).  3 headaches in acupuncture group, none in control group; no other adverse events reported. |
| CAM | Zhuo, 2022646  ID: NCT03917953  RCT  Single center  N = 78  China  Setting: Specialty care | **Target:** Children with ADHD; those with other mental or neurodevelopmental disorders, use of ADHD medication, or prior acupuncture were excluded  **Other:** Parents and teachers provided one outcome each  **ADHD presentation:** inattentive : 46.2,hyperactive : 0,combined : 53.8  **Diagnosis:** Confirmation by specialist  DSM V by two experienced child psychiatrists  **Comorbidity:** N/A  **Female:** 17.9 %  **Age mean:** 8.3 (1.33)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % Asian : 100 | **Intervention:** Transcutaneous electrical acupoint stimulation, acupuncture points selected according to theory that Yin-Yang disharmony is implicated in the development of ADHD, acupoints were located on the midsagittal line at the intersection of a line connecting the ear apices as well as two acupoints are located on the dorsum and medial side of the foot, 8 sessions, 20 min per session, 2-3 day interval between each pair of sessions per week for 4 weeks  **Control:** Attention-matched control  Sham transcutaneous electrical acupoint stimulation, group stimulated at the same acupuncture points as those used in intervention group, 8 sessions, 20 min per session, 2-3 day interval between each pair of sessions per week  **Comparator:** NA  **Follow-up:** 1 month | Conners Parent Rating Scale, Revised  CGI-I improved  CGI-I: Significantly greater % of intervention group improved (p 0.005), improvement in CPRS-R and CTRS-R (teacher rating) not significantly differently between groups.  Improvement in accuracy for go/no-go trials, a computerized task that measures inhibition control, was larger for intervention group (p 0.049).  Any adverse event  2 members of intervention group and 1 in control group reported an adverse events, none were serious. |
| Cognitive training | Azami, 2023129  ID: NCT02780102  RCT  Single center  N = 48  Iran  Setting: Specialty care | **Target:** Male children with ADHD; those with comorbid psychiatric disorders, epileptic seizures in the last 2 years, motor disability, and other medical conditions were excluded  **Other:** Parents reported symptom outcomes  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  psychiatrist clinical interview, rating scales, parental clinical interview  **Comorbidity:** N/A  **Female:** 0 %  **Age mean:**  Intervention 10.37 (0.88), sham 10.37 (1.15), medication 10.12 (1.02)  **Minimum age:** 9  **Maximum age:** 12  **Ethnicity:**  N/A,Other : Persian | **Intervention:** Cognitive motor rehabilitation, computerassisted, 20 group sessions (3 per week, 5 participants); 1‑hour sessions of 5 min of warm‑up, 5 min of cool‑down, and 50 min of performing progressive associative tasks, for 7 weeks  **Control:** Attention-matched control  Sham cognitive motor rehabilitation, 20 group sessions (3 one-hour sessions per week)  **Comparator:** MedicationMethylphenidate 2–3 tablets of 10 mg (immediate release) per day; medication stopped 24 hour before follow‑up assessment  **Follow-up:** 3 months | SNAP IV, parent report, ADHD-C score  Cognitive motor training group improved significantly more than sham or medication group (p<0.05) on all SNAP IV scales.  RASS (symptoms during academic assignments) negative scores  Significant effect of the interventions compared to sham training (p0.003).  Cognitive motor rehabilitation outperformed methylphenidate on dictation (p < 0.01) . |
| Cognitive training | Benzing, 2019139  Universität Bern, 20161125  ID: KEK 393/15, DRKS00010171  RCT  Single center  N = 51  Switzerland  Setting: Other | **Target:** Children diagnosed with ADHD based upon the ICD‐10; no neurological disorder, Tourette syndrome, or an epileptic disorder  **Other:**  **ADHD presentation:** N/A : Scores entered above reflect dimensional ADHD-RS symptoms, not ADHD subtypes  **Diagnosis:** Confirmation by specialist  ICD-10  **Comorbidity:** N/A  **Female:** 17.6 %  **Age mean:** 10.63 (1.32)  **Minimum age:**  **Maximum age:**  **Ethnicity:** | **Intervention:** Kinect exergaming training for Xbox, 3 times a week for at least 30 minutes for 8 weeks  **Control:** Wait list  Waitlist control, no intervention  **Comparator:** NA  **Follow-up:** 2 months | Conners-3 Scale, German version, Global Index Score, parents  Significant effects favoring the intervention were detected on the total global index score (p=0.022).  ADHD symptoms (DSM-IV-TR scales)  No significant group effects (p > .05).  For the Motor ability - German Motor test the intervention group showed a significantly better total performance than the control group (p=0.008). |
| Cognitive training | Bigorra, 2016148  Bigorra, 2016687  ID: ISRCTN00767728  RCT  Single center  N = 66  Spain  Setting: Specialty care | **Target:** Children with ADHD, comorbidity with other disruptive behavior disorders accepted, diagnoses were confirmed using the semi-structured Kiddie-Schedule for Affective Disorders and Schizophrenia, Present and Lifetime Version interview; T scores on the Conners ADHD index for parents and teachers >70 at the time of diagnosis; no previous psychological or pharmacological treatment for ADHD  **Other:**  **ADHD presentation:** combined : 100  **Diagnosis:** Confirmation by specialist  DSM-IV-TR by clinician  **Comorbidity:** N/A  **Female:** 55 %  **Age mean:** 8.92 (1.75)  **Minimum age:** 7  **Maximum age:** 12  **Ethnicity:**  % Hispanic or Latino : 95.4 | **Intervention:** Cogmed Working Memory Training adaptive training, visual-spatial, auditory,and location memory and tracking of moving visual objects as working memory tasks, each training session included 90 trials and had a duration of 30–45 min, participants attended a total of 25 sessions 5 sessions per week, for 5 weeks  **Control:** Placebo  Control group (non-adaptive training) engaged in the MegaMemo, which consists of the same working memory tasks but without the adjustment for difficulty, i.e. they performed simpler tasks  **Comparator:** NA  **Follow-up:** 6 months | Behaviour Symptoms Index (mean parent, teacher)  On adjusted multiple linear regression analysis, there were no significant improvements in the outcome measures.  ADHD Composite Index (Conners, SDQ)  A significant improvement was noted for the intervention group compared to the control group (p 0.01).  Weiss Functional Impairment Rating Scale (WFIRS-P)- Parent  Significant improvements for the intervention group compared to the control group were registered on the school learning behavior subscale (p 0.02) but not on any other subscale.  With respect to executive functions scales (BRIEF), the the experimental group improved significantly more than the control group (p 0.01). No statistically significant differences between the groups for Theory of Mind composite score were recorded at any point in time (p 0.57). |
| Cognitive training | Bikic, 201856  Region Syddanmark, 2012996  ID: NCT01752530  RCT  Multicenter  N = 78  Denmark  Setting: Mixed | **Target:** Children fulfilling DSM-IV criteria for ADHD; no diagnosis of comorbid conduct disorder, autism spectrum disorders, depression or schizophrenia; no medical history of head injury or a verified neurological disorder; IQ>80; no motor or perceptual handicaps which would interfere with computer use; no medical condition requiring primary treatment; and no informed consent from custody  **Other:** Parents  **ADHD presentation:** inattentive : 42.6,hyperactive : 5.7,combined : 50  **Diagnosis:** Confirmation by specialist  interviewed by one of three trained psychologists, to confrm the ADHD diagnosis, using the ADHD section of the Kiddie-Schedule for Afective Disorders and Schizophrenia (K-SADS)  **Comorbidity:** N/A  **Female:** 16 %  **Age mean:** 9.95 (1.7)  **Minimum age:** 6  **Maximum age:** 13  **Ethnicity:**  N/A | **Intervention:** Computer program ACTIVATE 6 times a week plus ADHD treatment as usual, for 8 weeks  **Control:** Other  Treatment as usual alone, which consisted of diagnostic and cognitive assessment, psycho-education, pedagogical counseling, and questionnaires for parents and teachers, home and school visits and, for some children, medical treatment  **Comparator:** NA  **Follow-up:** 5.8 months | ADHD-RS-IV (ADHD-Rating Scale-IV), parent rating  There was no significant effect for training (p-0.69).  Weiss functional impairment rating scale-parent report form (WFIRS-P)  There were no significant differences between the intervention and the control group (p=0.54).  No significant effect of training on sustained attention, parent-rated-BRIEF, or teacher-rated-BRIEF. |
| Cognitive training | Bul, 2016166  Bul, 2018698  ID: ISRCTN62056259  RCT  Multicenter  N = 170  Multiple countries  Setting: Mixed | **Target:** Children stable on pharmacological and/or psychological treatment for ADHD 8 weeks before baseline  **Other:**  **ADHD presentation:** inattentive : 22.4,hyperactive : 3.5,combined : 74.1  **Diagnosis:** Confirmation by specialist  DSM-IV-TR by psychologist  **Comorbidity:** N/A  **Female:** 19.4 %  **Age mean:** 9.85 (1.26)  **Minimum age:** 8  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Game intervention plus treatment as usual, maximum of 65 minutes approximately 3 times per week for 10 weeks  **Control:** TAU  Treatment as usual for the first 10 weeks and the crossed over to the serious game intervention in addition to treatment as usual for the subsequent 10 weeks  **Comparator:** NA  **Follow-up:** 5 months | Behavior Rating Inventory of Executive Function (BRIEF, subscale Plan/Organized) showed significantly greater improvements (p=0.004).  10 adverse events that could be related to the intervention, all were mild or moderate severity, including pain in the fingers, irritability, and headache, one participant did not want to paly the game anymore because he could not concentrate during his s |
| Cognitive training | Denton, 2020221  University of Texas, 20101117; Dvorsky, 2021750  ID: NCT01133847  RCT  Multicenter  N = 222  US  Setting: School | **Target:** Patients with ADHD and a standard score ≤ 25th percentile on either the Woodcock-Johnson III Letter-Word Identification or Word Attack subtests or the Basic Reading Skills composite  **Other:** Parents received training and provided some outcomes  **ADHD presentation:** inattentive : 46.1,combined : 53.9  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** Learning disability  **Female:** 39.0 %  **Age mean:** 8.8 (1.3)  **Minimum age:** 5  **Maximum age:** 7  **Ethnicity:**  % Black/African American : 72.1  % White : 19.6  % Multiracial : 6.4 | **Intervention:** Reading intervention plus medication plus parent training; the reading interventionwas provided individually or in groups of two students in 45- minute lessons, 4 days per week; medication treatment in children typically began with a low dose of extended-release methylphenidate, which was titrated up in weekly visits to a dosage at which the child had a satisfactory response with limited side effects for a total of 12 weeks; the behavioral parent training consisted of 9 group sessions over 10 weeks, topics included psychoeducation about ADHD and evidence-based strategies for behavior management, a possible total of 64 lessons over 16 weeks  **Control:** Other  Parent training plus medication only; treatment typically began with a low dose of extended-release methylphenidate, which was titrated up in weekly visits to a dosage at which the child had a satisfactory response with limited side effects; the behaviora  **Comparator:** NA  **Follow-up:** 4 months | Inattention, SNAP (Swanson, Nolan, and Pelham Checklist for DSM-IV), parent rating  Combined intervention group improved more than group receiving reading instruction alone. Same for SNAP Parent Rating of Hyperactivity-Impulsivity, SNAP- Teacher Rating of Inattention, and SNAP- Teacher Rating of Hyperactivity-Impulsivity.  Test of Word Reading Efficiency (TOWRE) Phonemic Decoding Efficiency: combined intervention (p 0.03) and reading group alone (p 0.007) had significantly higher posttest means than medication and parent treatment alone. Improvement in WIAT-3 Reading Comprehension means was superior for medication plus parent training group compared to both groups receiving a reading intervention (p 0.008). |
| Cognitive training | Dentz, 2020222  Université du Québec a Montréal, 20171126  ID: NCT03335748  RCT  Single center  N = 52  Canada  Setting: Other | **Target:** Youths diagnosed with ADHD combined type with comorbid learning disability, oppositional defiance disorder, or Tourette syndrome, and under stable pharmacological treatment for ADHD for at least the past 2 months  **Other:** Parents provided outcomes  **ADHD presentation:** combined : 100  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** Other : either learning disabled, ODD, or Tourette's  **Female:** 13 %  **Age mean:**  Intervention: 10.44 (1.18), control: 9.60 (2.08)  **Minimum age:** 7  **Maximum age:** 13  **Ethnicity:**  % White : 86.5 | **Intervention:** Cogmed program plus ADHD medication, cognitive training software targeting verbal and visuospatial components of working memory, each training session 30-45 min, at least 5 sessions per week for 5 weeks  **Control:** Attention-matched control  Comparison version of the Cogmed program with a low and invariable level of difficulty, which was expected to dampen the program's effects plus ADHD medication  **Comparator:** NA  **Follow-up:** 2.5 months | Conners, parent report, attention score  No significant between group difference in parent rated attention or hyperactivity scores.  WIAT Reading  No significant difference between groups in WAIT reading or math scores.  No significant difference between groups in behavior rating inventory of executive function (BRIEF) score, continuous performance test (CPT) which measures attentional functions and inhibition., or working memory. |
| Cognitive training | Dong, 2022227  ID: ID NA  RCT  Multicenter  N = 850  China  Setting: Other | **Target:** Kindergarteners with ADHD, with sibling in Grade 7 or 8  **Other:** Parents or siblings participated  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  Diagnosed by licensed clinical psychologists per DSM  **Comorbidity:** N/A  **Female:** 50.3 %  **Age mean:** 5.35 (0.20)  **Minimum age:**  **Maximum age:**  **Ethnicity:**  % Asian : 100 | **Intervention:** Dialogic reading with parent 25 minutes twice per week; a shared bookreading approach where parent engages in dialog with the child through interactive question and answer communication while reading picture books together, for 12 weeks  **Control:** Attention-matched control  Reading books with parent 25 minutes twice per week for 12 weeks, but without dialogic reading  **Comparator:** Cognitive trainingDialogic reading with older sibling 25 minutes twice per week for 12 weeks; a shared book reading approach where parent engages in dialog with the child through interactive question and answer communication while reading picture books together  **Follow-up:** 3 months | Group interaction effects on recep­tive vocabulary, expressive vocabulary, character reading, morpho­logical awareness, phonological awareness, listening comprehension, and reading interest were significant (p < .001) in favor of the dialog reading groups over the control reading group; sibling dialog reading was significantly superior to parent dialog reading regarding expressive vocabulary, character reading , morphological awareness, phono­logical awareness, and reading interest (p < .001 for all) but inferior regarding improvement in listening comprehension (p < .001). |
| Cognitive training | Dovis, 2015229  Dovis, 2015742  ID: NTR2728  RCT  Multicenter  N = 89  Netherlands  Setting: Specialty care | **Target:** Participants with DSM-IV-TR diagnosis of ADHD combined type diagnosed by a child psychologist or child psychiatrist, score on Disruptive Behavioral Disorder Rating Scale (Dutch translation) in 9th to 100th percentile for both parent and teacher version ADHD scale, met criteria for ADHD combined type on ADHD section of Diagnostic Interview Schedule for Children, parent version; IQ score greater than or equal to 80 on Dutch Wechsler Intelligence Scale for Children-III; no conduct disorder, autism spectrum disorder, neurological disorder, sensory or motor impairment reported by parents, medications other than methylphenidate or dextroamphetamine  **Other:** Parents & teachers provided some outcomes  **ADHD presentation:** combined : 100  **Diagnosis:** Confirmation by specialist  DSM IV TR  **Comorbidity:** N/A  **Female:** 20 %  **Age mean:**  Full-active intervention 10.6 (1.4), partially-active intervention 10.3 (1.3), control (sham) group 10.5 (SD 1.3)  **Minimum age:** 8  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Executive functioning training on computer ("Braingame Brian"), total of 25 training sessions, each session taking between 35-50 minutes, all tasks were in training mode and level is adjusted to child's level of performance for 5 weeks  **Control:** Attention-matched control  Braingame Brain in sham condition: working memory, inhibition, and cognitive-flexibility tasks were presented in the same way as training mode except the stop-trials and switch-trials were replaced by go-trials and non-switch trials and difficulty level w  **Comparator:** Cognitive trainingPartially-active condition in which the working memory tasks were in sham mode which did not adjust difficultly to performance while the inhibition and cognitive-flexibility tasks were in training mode  **Follow-up:** 4.25 months | Disruptive Behavior Disorder Rating Scale (DBDRS), Inattention scale, parent report  No effect of treatment group on parent or teacher Disruptive Behavior Disorder Rating Scale (DBDRS)  No signifcant difference of treatment outcome on any executive function measures |
| Cognitive training | Egeland, 2013243  Hovik, 2013840  ID: ISRCTN19133620  RCT  Single center  N = 75  Norway  Setting: School | **Target:** Children in treatment for ADHD, IQ>=70; no comorbid diagnosis of Pervasive Developmental Disorders, Tourette’s Disorder, evidence of psychosis or Bipolar Disorder and Conduct Disorder  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  F-90 ICD-10 Hyperkinetic Disorder (equivalent to DSM-IV)  **Comorbidity:** N/A  **Female:** 24 %  **Age mean:** 10.4 (0.7)  **Minimum age:** 10  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Working Memory training (RoboMemo) performed on a daily basis at school, sessionslast for 30–45 minutes, for 5–7 weeks  **Control:** Wait list  Offered the possibility to train after the completion of the study  **Comparator:** NA  **Follow-up:** 8 months | ADHD-RS-IV (ADHD-Rating Scale IV), parent  There was no significant difference between groups.  Strengths & Difficulties Questionnaire (SDQ), parent  There was no significant difference between groups.  Training group had significant gains in working memory performance measures. |
| Cognitive training | Estrada-Plana, 2019258  ID: NA  RCT  Single center  N = 29  Spain  Setting: Other | **Target:** Children with ADHD; without having any other mental disorders; IQ>80  **Other:**  **ADHD presentation:** inattentive : 23.1,hyperactive : 76.9  **Diagnosis:** Confirmation by specialist  Psychiatrists or Clinical Psychologists  **Comorbidity:** N/A  **Female:** 46.2 %  **Age mean:** 9.46 (1.20)  **Minimum age:** 8  **Maximum age:** 12  **Ethnicity:**  % Hispanic or Latino : 97  Other : Does not specify the other 3% | **Intervention:** Cognitive training based on board games, closed groups of 6-8 participants, 60 minutes each, 1 game per week, for 5 weeks  **Control:** Wait list  Wait-list control group  **Comparator:** NA  **Follow-up:** 1 month | Conners CPRS-48 Conduct Problems Subscale  There was no significant difference between groups for Conners CPRS-48.  Hyperactivity Index, Conners CPRS-48 (CPRS-48)  Strengths and Difficulties Questionnaire (SDQ)  Intervention participants showed lower conduct problems in the SDQ subscale compared to control group participants (p<0.001).  Number of participants with adverse events  No patients with adverse events.  No adverse effects were found during the intervention. |
| Cognitive training | Hahn-Markowitz, 2020313  Hahn-Markowitz, 2017814; Hadassah Medical Organization, 2013811  ID: NCT01792921  Crossover trial  Multicenter  N = 107  Israel  Setting: Mixed | **Target:** Children with ADHD  **Other:** Parents and teachers provided some outcomes  **ADHD presentation:** inattentive : 48.6,hyperactive : 4.7,combined : 46.7  **Diagnosis:** Confirmation by specialist  DSM-IV, assessed by a certified pediatric neurologist/psychiatrist, including a semi-structured interview with the child and parents, medical/neurological/psychiatric examination, and completion of a ADHD diagnostic questionnaire  **Comorbidity:** N/A  **Female:** 38 %  **Age mean:** 8.5 (0.85)  **Minimum age:** 7  **Maximum age:** 10  **Ethnicity:**  N/A | **Intervention:** Cog-Fun: integrative intervention using effortful executive strategies and supplemented by environmental adaptations, weekly 1-hr sessions with child and parent over 12  weeks  **Control:** Wait list  Wait list which crossed over to intervention after first group finished.  **Comparator:** NA  **Follow-up:** 3 months | CPRS-R (Conners’ Parent Rating Scales–Revised), global index total  Greater improvement in intervention group compared to control group (p <.01) .  BRIEF Global Executive Composite, completed by parents: intervention group superior (p < .01). No significant group difference s in changes in BRIEF Global Executive Composite completed by teachers (p = .73)  No adverse events or side effects occurred among participants in either group. |
| Cognitive training | Kim, 2022367  ID: ID NA  RCT  Single center  N = 30  Korea  Setting: Specialty care | **Target:** Children with ADHD; those with symptoms other than ADHD symptoms and those with medical conditions that affect use of intervention were excluded  **Other:** Parents reported some outcomes  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM V by psychiatrist via K-SADS-PL  **Comorbidity:** N/A  **Female:** 23.3 %  **Age mean:** 9.1 (1,77)  **Minimum age:** 6  **Maximum age:** 13  **Ethnicity:**  % Asian : 100 | **Intervention:** Attention and working memory improvement training program, AI-based (NeuroWorld DTx), game-based cognitive therapy software, plus conventional medication (not described) for 4 weeks  **Control:** Other  Conventional medication (not described)  **Comparator:** NA  **Follow-up:** 1 month | Child Behavior CheckList (CBCL), Total Behavior Problems  No difference between groups (p 0.349 )  K-ARS (Korean ADHD RS)  No difference in improvement between groups (p 0.795).  Likelihood of re-participation  80% of participants would participate again in the intervention. |
| Cognitive training | Kofler, 2020368  ID: NA  RCT  Single center  N = 54  US  Setting: Other | **Target:** Children with ADHD and clinical/borderline elevations on at least 1 parent and one teacher ADHD rating scale, or previous psychoeducational evaluation documenting cross-informant symptoms; pretreatment working memory test scores not in the average range or higher  **Other:**  **ADHD presentation:** inattentive : 27.7,hyperactive : 3.7,combined : 68.5  **Diagnosis:** Confirmation by specialist  DSM-5 by clinical psychologist based on K-SADSK-SADS  **Comorbidity:** N/A  **Female:** 22 %  **Age mean:** 10.41 (1.46)  **Minimum age:** 8  **Maximum age:** 12  **Ethnicity:**  % Hispanic or Latino : 11  % Black/African American : 9  % White : 74  % Multiracial : 6 | **Intervention:** Inhibitory control training, web-based, weekly in-office sessions with the child (1 hour), combined with parent-supervised in-home training (15-min/day, 2–3 days/week), for 10 weeks  **Control:** NA  **Comparator:** Cognitive trainingWeb-based central executive training (CET) targeting central executive working memory deficits; identical to ICT in terms of website address, name, art, animations, storylines, layouts, interfaces, and use of adaptive training algorithms to maximize inte  **Follow-up:** 2.5 months | ADHD-RS-5, parent and teacher reports  Both interventions were equivalent for parent-reported Hyperactivity/Impulsivity (p = 0.89) and Attention Problems (p = 0.47); executive function training was superior for teacher-reported ADHD-RS-5 Attention Problems (p = 0.01).  Parent satisfaction  ICT and CET did not differ in parent-reported post-treatment satisfaction (p=.22)  Central executive training was superior for improving phonological (p < .001) and visuospatial (p = 0.01) working memory and go/no-go (inhibitory control) (p = 0.0.1), but not stop-signal inhibition (p = 0.08). |
| Cognitive training | Kollins, 2020372  Akili Interactive Labs, Inc., 2016658  ID: NCT02674633  RCT  Multicenter  N = 348  US  Setting: Other | **Target:** Children with ADHD according to DSM-5; IQ>=80; no significant comorbid psychiatric diagnoses and no use of ADHD medications that could not be discontinued  **Other:** Parents  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  Participants diagnosis of ADHD according to DSM-5 criteria was confirmed.  **Comorbidity:** N/A  **Female:** 28.7 %  **Age mean:**  Intervention 9.7 (1.3), control 9.6 (1.3)  **Minimum age:** 8  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Digital therapeutic AKL-T01 delivered through a video game-like interface via at-home play for 25 min per day, 5 days per week for 4 weeks  **Control:** Attention-matched control  Control was designed to match AKL-T01 on expectancy, engagement, and time on task in the form of a challenging and engaging digital word game, targeting cognitive domains not targeted by the AKL-T01 intervention and not primarily associated with ADHD; th  **Comparator:** NA  **Follow-up:** 1 month | CGI (Clinical Global Impressions) scoring 2 or more  No difference in improvement between groups.  ADHD-RS-IV, number with at least 30% improvement  No difference in improvement between groups (p = 0.23).  Impairment Rating Scale improved by 1 point  Marginal effect on impairment (p 0.049).  No significant difference in improvement between groups in working memory (p 0.62) or inhibit (p 0.75) scales.  Participants experiencing intervention emergent adverse events  The rate was 7% in the intervention compared to 2% in the control group.  There were no serious intervention-related adverse events or discontinuations due to adverse events in either group. |
| Cognitive training | Nejati, 2021456  Nejati, 2020955  ID: NA  RCT  Single center  N = 30  Iran  Setting: Specialty care | **Target:** Children with ADHD and no psychiatric comorbidities  **Other:**  **ADHD presentation:** inattentive : 16.7,hyperactive : 23.3,combined : 60.0  **Diagnosis:** Confirmation by specialist  Diagnosis by psychiatrist via DSM-V  **Comorbidity:** N/A  **Female:** 47 %  **Age mean:** 10.74 (1.81)  **Minimum age:** 8  **Maximum age:** 14  **Ethnicity:**  N/A,Other : Presumably 100% Persian | **Intervention:** Cognitive training with paper and pencil tasks, twelve to fifteen sessions of intervention,each session took about 40− 50 minutes, 3 per week for 4–5 weeks  **Control:** No intervention  No intervention.  **Comparator:** NA  **Follow-up:** 1.25 months | ADHD score, SNAP IV  There was no significant difference.  No effect of group on Persian Attention Registration Test, total time (p = .744) or .Stroop Test, Selective Attention Index (p =.285) or Trail Making Test. |
| Cognitive training | Nejati, 2022457  ID: ID NA  RCT  Multicenter  N = 35  Iran  Setting: School | **Target:** Children with ADHD  **Other:** Blinded parents completed outcome instruments  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM V  **Comorbidity:** N/A  **Female:** 13.3 %  **Age mean:** 6.23 (0.32)  **Minimum age:** 6  **Maximum age:** 7  **Ethnicity:**  N/A | **Intervention:** Attentive Rehabilitation of Inhibition and Selective Attention program, 6 progressive computerized tasks targeting 3 types of inhibitory control, 10-12 sessions, each 30-45 minutes, for 4-5 weeks  **Control:** Attention-matched control  Story telling group with opportunity for intervention after study ended  **Comparator:** NA  **Follow-up:** 1.5 months | Child Behavior Checklist total  Significant (p 0.001) intervention effect compared to control.  SNAP-IV ADHD scale  Significant (p 0.001) intervention effect compared to control.  Flanker test (assessing selective attention) scores favor intervention (p = .05 ) .Go/No-go task (measuring prepotent inhibition) scores favor intervention (p = .001). |
| Cognitive training | Raghuveer, 2020489  ID: NA  RCT  Multicenter  N = 70  India  Setting: School | **Target:** Children with ADHD who were not on medication; children with learning disabilities, autism spectrum disorders, musculoskeletal impairments, developmental delay, visual or audio impairments were excluded  **Other:** Therapists or parents  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV criteria per clinician interview  **Comorbidity:** N/A  **Female:**  % N/A  **Age mean:** 4.5 (1.06)  **Minimum age:** 3  **Maximum age:** 6  **Ethnicity:**  N/A | **Intervention:** Structured games which utilize visual-spatial sketch pad and phonological loop, 4 sessions per week for 5 weeks  **Control:** NA  **Comparator:** Parent trainingTraining of one or both parents on behavioral controls strategies including praising, organizing the child's possessions (toys, clothing, etc.) and keep a routine schedule. One session of training was providing. Parents received a list of do's and don'ts  **Follow-up:** 1.25 months | Intervention group performed significantly better (p <0.05) on the Sequin Form Board Test Time. |
| Cognitive training | Tamm, 2013578  ID: ID NA  RCT  Single center  N = 105  US  Setting: Specialty care | **Target:** Children with ADHD; exclusion criteria included IQ <85, history of head injury, history of prenatal drug exposure, diagnosis of other neurological conditions, and participating in other non-pharmacological interventions for ADHD  **Other:** Parents and teachers provided some outcomes  **ADHD presentation:** inattentive : 39,hyperactive,combined : 59,N/A : 2  **Diagnosis:** Confirmation by specialist  DSM IV based on interviews  **Comorbidity:** N/A  **Female:** 32.4 %  **Age mean:** 9.3 (1.35)  **Minimum age:** 7  **Maximum age:** 15  **Ethnicity:**  % Hispanic or Latino : 11.4  % Black/African American : 4.8  % Asian : 4.8  % White : 70.5  % Multiracial : 8.6 | **Intervention:** Attention training, bi-weekly sessions of Pay Attention!; materials are designed to train sustained, selective, alternating, and divided attention using visual and auditory stimuli, for 8 weeks  **Control:** Wait list  Wait list  **Comparator:** NA  **Follow-up:** 3 months | Behavioral Assessment System for Children, Second Edition (BASC-II), parent rating, Behavioral Symptoms Index  No significant differences between groups in BASC II parent or teacher rating scales (externalizing, behavioral symptoms, hyperactivity, attention problems) except for parent reported attention problems where intervention was superior at follow up (p 0.01  CGI (Clinician Global Impairment rating) severity  Clinician ratings indicated lower severity and greater improvement for the intervention than the waitlist control group.  Swanson, Nolan, and Pelham (SNAP-IV) inattention scale, parent report  Intervention group improved more on parent-rated SNAP IV Inattention (p<0.001) and Hyperactivity/Impulsivity (p 0.007) scores. Similar results for clinician rated SNAP IV scores; no difference in teacher rated SNAP IV scores.  Behavior Rating Inventory of Executive Function (BRIEF): No significant difference in any teacher-rated scale. Intervention group improved more in all but one parent rated scale (emotional regulation). |
| Cognitive training | van der Donk, 2015595  van der Donk, 20201138  ID: NA  RCT  Single center  N = 105  Netherlands  Setting: School | **Target:** Children with ADHD, some with comorbid learning disabilities and/or oppositional defiant disorder  **Other:**  **ADHD presentation:** inattentive : 25.0,combined : 64.0,N/A : not specified- 11%  **Diagnosis:** Confirmation by specialist  Parents were also asked to send a copy of the diagnostic psychiatric report of their child to establish the subtype of ADHD and rule out other potential psychiatric problems  **Comorbidity:** N/A  **Female:** 28.0 %  **Age mean:** 9.9 (1.3)  **Minimum age:** 8  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Working memory and compensatory training (Paying Attention in Class), participants trained individually outside the classroom, 5 times a week, 45 min a day for 5 weeks  **Control:** NA  **Comparator:** Cognitive trainingCogmed Working Memory Training is a computerized training program consisting of a variety of game format tasks. 5 weeks, five times a week, about 45 min a day  **Follow-up:** 6 months | CBCL (Child Behavior Checklist), parent report  There were no significant differences between groups for either subscale (attention problems, p=0.593, externalizing problems, p=0.243).  No significant differences between groups at follow-up for BRIEF, Behavioral Regulation Index, parent report (p 0.46), BRIEF ( Behavioral Regulation Index, teacher report; p 0.217) and Learning efficiency quotient, word reading fluency score. |
| Cognitive training | Wennberg, 2018613  ID: NA  RCT  Multicenter  N = 46  Sweden  Setting: N/A | **Target:** Children and adolescents with ADHD and parent-reported difficulties with daily time management, despite medication for ADHD; no autism spectrum disorder; no IQ<70  **Other:** Parents of children with ADHD  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  ADHD diagnosis was determined in accordance with DSM-IV criteria by an experienced clinician  **Comorbidity:** N/A  **Female:** 26 %  **Age mean:**  Intervention group mean age (11.7) and SD (1.83). Control group mean age (11.1) and SD (1.71).  **Minimum age:** 9  **Maximum age:** 15  **Ethnicity:**  N/A | **Intervention:** Training in time-processing ability, compensation and remediation plus ADHD medication: compensation were 1.5-hour sessions with 3-4 sessionsin the study period, remediation training sessions 3 times per week with 20 minutes per day assigned outside of sessions, for of 12 weeks  **Control:** TAU  Standard methods of care alone including ADHD medication  **Comparator:** NA  **Follow-up:** 8 months | The Kit for assessing time-processing ability (KaTid) assesses time perception, time orientation and time management. The intervention group improved more on total score (p = 0.019), time perception score (p = 0.046), time orientation (p = 0.010), but not time management (p = 0.764). |
| Cognitive training | Wu, 2023628  ID: ID NA  Clinical trial  Single center  N = 127  China  Setting: Specialty care | **Target:** Children with ADHD; those with serious medical conditions, neuropsychiatric diseases, or on any ADHD medication excluded  **Other:** Parents reported outcomes  **ADHD presentation:** inattentive\_other : Mean ADHD-RS inattention score: intervention 17.3 (4.50), comparator 18.2 (3.79),hyperactive\_other : Mean ADHD-RS hyperactivity score: intervention 13.9 (5.30), comparator 13.8 (6.09)  **Diagnosis:** Confirmation by specialist  DSM IV by child psychiatrists, via K-SADS-PL  **Comorbidity:** N/A  **Female:** 15 %  **Age mean:** 8.35 (1.26)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % Asian : 100 | **Intervention:** Cognitive training, ADHD-specific executive function training, computer-based batteryof several digital cognitive trainings designed to improve impaired executive functions; training tasks were adapted from N-back task, visual-spatial memory task, Schulte Grid, Go/ No-go task, and mental calculation; difficulty is automatically adjusted to match participants’ progressive skills; participants were required to complete 48 training sessions within 2 months  **Control:** NA  **Comparator:** Cognitive trainingCognitive training, general executive function training, a multiple component training targeting cognitive functions which are not closely associated with ADHD, such as processing speed, reasoning, and planning; participants were required to complete 48 t  **Follow-up:** 2 months | ADHD-RS total, parent report  No significant difference in improvement  No significant difference in improvement on Behavior Rating Inventory of Executive Function (BRIEF)—Parent scores or Cambridge Neuropsychological Test Automated Battery (CANTAB) scores |
| Combined pharmacological + behavioral | Abikoff, 2004107  Hechtman, 2004826; Klein, 2004888  ID: N/A  RCT  Multicenter  N = 103  Multiple countries  Setting: Mixed | **Target:** Children with ADHD free of conduct and learning disorders, who responded to short-term methylphenidate who had a current or had a previous positive response to methylphenidate  **Other:** Parents  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-III-R criteria by child psychologists  **Comorbidity:** N/A  **Female:** 7 %  **Age mean:** 8.2 (0.8)  **Minimum age:** 7  **Maximum age:** 9  **Ethnicity:**  % Hispanic or Latino : 2  % Black/African American : 13  % White : 84 | **Intervention:** Multimodal treatment plus methylphenidate, intensive multimodal psychosocial treatment, methylphenidate maximum dose design up to maximum 50mg/day divided 3 times per day, multimodal treatment modules manual-based delivered once weekly during the first year (requiring 2 clinic visits per week) and once monthly during the second year (requiring 2 clinic visits per month), for 2 years  **Control:** Other  Methylphenidate alone, no other intervention (except for crisis sessions when required); after the child was stabilized on medication, children and parents were  seen once per month by a child psychiatrist; the dose was maintained, precluding side effects  **Comparator:** Medication + behavioralAttention control psychological treatment plus methylphenadate  **Follow-up:** 24 months | Observation with Classroom Observation Code during academic classes  Classroom behaviors yielded no significant group or interaction effects.  C-GAS (Children’s Global Assessment Scale)  There was no significant difference between groups.  Mean number of ADHD symptoms at school  ADHD diagnosis  Significant improvements occurred across all treatments.  Social functioning  No advantage was found on any measure of social functioning for the combination treatment over methylphenidate alone or methylphenidate plus attention control; significant improvement occurred across all treatments and continued over 2 years.  Combination treatment did not facilitate methylphenidate discontinuation. |
| Combined pharmacological + behavioral | Coelho, 2017201  ID: NA  Crossover trial  Unclear/Not reported  N = 67  Brazil  Setting: Specialty care | **Target:** Participants with ADHD as a primary disorder and no signs of neurodevelopmental delay, epilepsy, genetic syndromes, HIV, hydrocephalus, brain damage, and not currently taking other medications  **Other:**  **ADHD presentation:** inattentive : 47,combined : 54  **Diagnosis:** Confirmation by specialist  DSM-4, clinicians who specializes in diagnosing children and adolescents with neurodevelopmental disorders  **Comorbidity:** N/A  **Female:** 25 %  **Age mean:** 10.2 (2.0)  **Minimum age:** 7  **Maximum age:** 14  **Ethnicity:**  % White : 100 | **Intervention:** CBT plus medication, group cognitive-behavioral therapy prolonged-release methylphenidate20mg, group cognitive-behavioral therapy attended by parents and children, 40 min family sessions, 80 min children sessions; intervention for 20 weeks  **Control:** Other  Prolonged-release methylphenidate 20 mg for 20 weeks alone  **Comparator:** NA  **Follow-up:** 5 months | CBCL (Child Behavior Checklist), total problems  Cognitive and behavioral outcome measures showed no differences between treatment groups.  On social skills, multimodal showed more improvement in frequency indicators on empathy, assertiveness, and self-control subscales and in the difficulty on assertiveness and  self-control subscales |
| Combined pharmacological + behavioral | David, 2021216  Babes-Bolyai University, 2018670  ID: ISRCTN92640175  RCT  Single center  N = 59  Romania  Setting: Specialty care | **Target:** Children diagnosed with ADHD by a child psychiatrist and/or certified psychologist, IQ score of at least 80 on Colored Raven Matrices, and no previous treatment for ADHD received  **Other:**  **ADHD presentation:** inattentive : 22.0,hyperactive : 15.3,combined : 62.7  **Diagnosis:** Confirmation by specialist  Structured Clinical Interview for DSMIV Childhood Diagnoses (KID-SCID) by clinician  **Comorbidity:** N/A  **Female:** 20.3 %  **Age mean:** 8.46 (1.57)  **Minimum age:** 6  **Maximum age:** 11  **Ethnicity:** | **Intervention:** CBT and rational emotive behavior therapy plus pharmacological non-stimulant treatment, cognitive-behavioral psychological treatment, 0.8 mg/kg/day and 1.2 mg/kg/day of atomoxetine; weekly psychotherapy session with parents alone (30 min) and with child alone (30 min), for 16 weeks  **Control:** Other  Pharmacotherapy non-stimulant treatment atomoxetine alone, once daily in the morning, began treatment at 0.5 mg/kg/day with weekly increases to a dose of 0.8 mg/kg/day and 1.2 mg/kg/day, unless side effects were reported by patients (maximum increase 1.8  **Comparator:** NA  **Follow-up:** 4 months | ADHD-RS-IV (ADHD-rating scale IV-Home Version Romanian)  Clinician rated ADHD diagnosis at posttreatment  Combined treatment seems to be superior to the medication alone on parent ratings on ADHD symptoms (p=0.01) but no significant differences between groups regarding ADHD diagnosis at posttreatment were found (p=0.329).  No significant differences were found on internalizing problems reported by teachers (effect size−0.32, CI −0.33, 0.97).  Appetite decrease  Rates were similar.  None of the participants reported severe side effects and none discontinued for adverse events. None of the patients reported suicidal ideation. Some participants reported mild side-effects. |
| Combined pharmacological + behavioral | FIU, 2015275  ID: NCT02502799  RCT  Unclear/Not reported  N = 158  US  Setting: Specialty care | **Target:** Adolescents with ADHD at elevated risk for substance use disorder; those with substance use disorder or on any psychiatric medications were excluded  **Other:** None  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM V  **Comorbidity:** Other : high risk for SUD  **Female:** 25.9 %  **Age mean:** 13.94 (1.38)  **Minimum age:** 12  **Maximum age:** 16  **Ethnicity:**  % Hispanic or Latino  % Black/African American : 8.9  % American Indian or Alaska Native  % Asian : 0.6  % Native Hawaiian or Pacific Islander : 0  % White : 78.5  % Multiracial : 9.5 | **Intervention:** Brief early intervention plus parent training and adolescent cognitive behavioral therapy plus methylphenidate; designed to strengthen problem-solving, resisting peer pressure, and coping with emotions, 5 individual sessions received by adolescents; parents joined portions of 3 sessions, then participated in behavioral parent training and adolescents participated in cognitive behavioral therapy to reduce substance use  **Control:** No intervention  Monitoring only, no further intervention  **Comparator:** NA  **Follow-up:** 6 months | Disruptive Behavior, Deviant Behavior Scale, youth self-report  Higher score in the intervention group, significance unclear.  Functional Impairment self report  Higher score in the intervention group, significance unclear.  Adverse events  Hospitalizations unrelated to the intervention.  No all cause mortality across groups. |
| Combined pharmacological + behavioral | Jensen, 2007343  No author, 2011669; Abikoff, 2001649; Acosta, 2016651; Arnold, 1997664; Arnold, 1997665; Arnold, 2004666; Arnold, 2003667; Babinski, 2019671; Brinkman, 2018695; Carey, 2000700; Conners, 2001724  ID: NCT00000388 (MTA)  RCT  Multicenter  N = 579  US  Setting: N/A | **Target:** Children with ADHD combined type  **Other:**  **ADHD presentation:** combined : 87.5,N/A : comm control 79.5  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:**  **Female:** 21 %  **Age mean:** 11.8 (0.95)  **Minimum age:** 11  **Maximum age:** 13  **Ethnicity:**  % Hispanic or Latino : 36  % Black/African American : 20.2  % White : 61.7  Other : 10.7% | **Intervention:** Multimodal Treatment Study of Children With ADHD (MTA), intensive multicomponent behavior therapy consisting of medication management and behavior modification, for 14 months, afterwards the families were free to choose their own treatment  **Control:** TAU  Usual community care  **Comparator:** NA  **Follow-up:** 36 months | Oppositional defiant disorder symptoms, SNAP parent and teacher average rating  Ratings were similar across groups.  SWAN  Both groups improved from baseline.  CIS (Columbia Impairment Scale)  No significant moderator effects of comorbidity were found in the treatment comorbidity group interactions (p 0.21).  Wechsler Individual Achievement Test (WIAT)  Both groups improved from baseline.  None of the treatment groups differed significantly on the social skills rating system (SSRS).  After 14 months, children treated with methylphenidate had gained less height and less weight (-1.23 cm per year and -2.48 kg per year) than untreated children669; Followup into young adulthood (25 yo) within naturalistic subgroups of ADHD cases, ext  Children with ADHD and manic symptoms respond robustly to methylphenidate during the first month of treatment and are not more likely to have an adverse response to methylphenidate.785 |
| Combined pharmacological + behavioral | Karakaya, 2019357  ID: NA  RCT  Single center  N = 41  Turkey  Setting: Specialty care | **Target:** Adolescents receiving treatment ADHD, on medication, residing in the city center  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  diagnosed prior to study; were already receiving medication tx through clinic  **Comorbidity:** N/A  **Female:** 19.5 %  **Age mean:** 13.2 (1.25)  **Minimum age:** 12  **Maximum age:** 18  **Ethnicity:**  N/A | **Intervention:** Solution-focused approach comprised of 6 sessions, each 45-60 minutes, individually and face-to-face, in addition to ADHD medication treatment with psychostimulants and clinic follow-up, 1 session per week for 6 weeks  **Control:** Other  No intervention, but ADHD medication treatment with psychostimulants as usual  **Comparator:** NA  **Follow-up:** 3 months | General Self-Efficacy Scale (GSE) evaluates the extent to which individuals perceive themselves as adequate in coping with difficulties. Intervention group score was higher at follow up ( p<0.001). |
| Combined pharmacological + behavioral | Perez-Alvarez, 2009474  ID: NA  RCT  Single center  N = 96  Spain  Setting: Specialty care | **Target:** Children and adolescents with Swanson, Nolan, and Pelham Questionnaire-IV teacher rating scores of at least 2.5 and parent ratings of at least 1.8, planning dysfunction according to planning, attention, successive and simultaneous scales; no medical and psychiatric comorbidities  **Other:** Parents and teachers provided some outcome data  **ADHD presentation:** inattentive : 79,hyperactive : 0,combined : 21  **Diagnosis:** Confirmation by specialist  ADHD diagnostic interview schedule for children module was completed face-to-face with the child ’ s principal caregiver by trained research interviewers.  **Comorbidity:** N/A  **Female:** 20 %  **Age mean:**  ADHD-Combined 9 (2), ADHD-Inattentive 12 (3)  **Minimum age:** 7  **Maximum age:** 15  **Ethnicity:**  N/A | **Intervention:** Humanistic intervention plus methylphenidate; extended release methylphenidate hydrochlorideadministered at an optimal dose plus humanistic psychological intervention conducted as 24 sessions, 1 every 15 days, for 12 months  **Control:** Other  Extended release methylphenidate hydrochloride alone  **Comparator:** NA  **Follow-up:** 12 months | Swanson, Nolan, and Pelham scale 18 (SNAP-IV-18), number in remission (score <= 1.0)  Combined intervention scored better than humanistic intervention alone and slightly better than medication alone.  PASS (planning, attention, successive, and simultaneous processes) cognitive assessment: only significant difference at follow-up was for planning scale; intervention group improved more (p <.05). |
| Combined pharmacological + behavioral | Riggs, 2011497  University of Cinncinnati, 20061129  ID: NCT00264797  RCT  Multicenter  N = 303  US  Setting: Specialty care | **Target:** Adolescents meeting DSM-IV criteria for current ADHD and at least one non-tobacco substance user disorder; no current or past psychotic disorder, bipolar disorder, suicide risk, opiate dependence, methamphetamine abuse or dependence, cardiac illness or serious medical illness, pregnancy, past month use of psychotropic medications or participation in other substance or mental health treatment  **Other:**  **ADHD presentation:** inattentive : 28.1,hyperactive : 2.6,combined : 68.6  **Diagnosis:** Confirmation by specialist  DSM-IV per Schedule for Affective Disorders and Schizophrenia for School-Age Children-Epidemiologic Version (K-SADS-E)  **Comorbidity:** Other : SUD  **Female:** 21.1 %  **Age mean:** 16.5 (1.3)  **Minimum age:** 13  **Maximum age:** 18  **Ethnicity:**  % Hispanic or Latino : 15.2  % Black/African American : 23.2  % White : 61.7 | **Intervention:** CBT plus OROS, cognitive behavioral therapy, osmotic-release methylphenidate 72mg once daily and manual-standardized, individual CBT using motivational enhancement approaches, for 16 weeks  **Control:** Other  Cognitive behavioral therapy plus matching placebo, manual-standardized, individual CBT using motivational enhancement approaches  **Comparator:** NA  **Follow-up:** 4 months | Treatment responders based on CGI-I (score of 1 or 2)  Rates of treatment response were not significantly different (P=0.418) between treatment (23.4%) and control (19.1%).  ADHD-RS  There were no group differences on reduction in ADHD-RS scores.  Substance use in the past 28 days: there was no between-group difference (p 0.321). Adolescents treated with OROS-MPH + CBT had significantly more negative urine drug screens compared to participants treated with placebo + CBT (p 0.05).  Treatment-emergent study-related adverse events  Participants treated with OROS-MPH reported more treatment-emergent study-related AEs than control group (p=0.02).  No statistically significant differences between groups on self-reported medication abuse (taking more medication than prescribed, 4.8% vs 2.8%, p>0.05) or diversion (selling medication to others, 2.1% vs 1.4%, p>0.05; letting others take your medication, |
| Combined pharmacological + behavioral | Sprich, 2016560  Massachusetts General Hospital, 2009911  ID: NCT01019252  Crossover trial  Single center  N = 46  US  Setting: Specialty care | **Target:** Adolescents with ADHD and no change in dose for at least 2 months of medication without severe comorbid disorders, active suicidality, conduct disorder, active substance abuse or dependence, organic mental disorder, mental retardation, pervasive developmental disorder, or prior CBT for ADHD  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  Kiddie-Schedule for Affective Disorders and Schizophrenia-Epidemiologic Version No  **Comorbidity:** N/A  **Female:** 21.7 %  **Age mean:**  Intervention 15.17 (1.01), control 15.09 (1.11)  **Minimum age:** 14  **Maximum age:** 18  **Ethnicity:**  % Black/African American : 2.17  % Asian : 0  % Native Hawaiian or Pacific Islander : 2.17  % White : 93.5 | **Intervention:** CBT plus medication, 7 modules of cognitive behavioral therapy over 12 sessions; 10 were one-on-one, two also included parent; all patients were also on an FDA-approved medication; average duration of 17 weeks  **Control:** Wait list  Wait list received no psychosocial treatment for 4 months but continued to receive FDA-approved medication  **Comparator:** NA  **Follow-up:** 4 months | CGI (Clinical Global Impression) score  Favored intervention (p <.01).  ADHD-RS (ADHD Rating Score) total, parent report  Both parent reported (p <.01) and patient reported ADHD RS (p < .01) favored intervention group.  No study related serious adverse events. |
| Combined pharmacological + behavioral | Tutty, 2003589  ID: ID NA  RCT  Single center  N = 100  US  Setting: Specialty care | **Target:** Children newly diagnosed with ADHD initiating stimulant treatment in primary care; those with conduct disorders, oppositional defiant disorder, Tourette syndrome, affective disorders, active alcohol or other substance abuse during the previous 90 days, or a chronic medical illness were excluded  **Other:** Parents received education and provided some outcomes  **ADHD presentation:** inattentive : 41,combined : 59  **Diagnosis:** Confirmation by specialist  DSM-IV by staff pediatrician  **Comorbidity:** N/A  **Female:** 25 %  **Age mean:** 9.2 (1.25)  **Minimum age:** 5  **Maximum age:** 12  **Ethnicity:**  % Hispanic or Latino : 1  % Black/African American : 6  % Asian : 6  % White : 87 | **Intervention:** Behavioral and social skills class plus stimulant medication, class for children and their parents, 1 session per week for 8 weeks  **Control:** TAU  All children were on stimulant medication as selected by their healthcare provider  **Comparator:** NA  **Follow-up:** 6 months | ADHD RS, parent report  Intervention group improved more (p 0.00).  No significant between-group differences in psychostimulant use (52.94% vs 39.02%; p 0.184). |
| Combined pharmacological + behavioral | van der Oord, 2007597  ID: ID NA  RCT  Multicenter  N = 50  Netherlands  Setting: Specialty care | **Target:** Children with ADHD with no prior use of methylphenidate  **Other:** Parents & teachers received training and provided outcomes  **ADHD presentation:** inattentive : 32,hyperactive : 6,combined : 62  **Diagnosis:** Confirmation by specialist  DSM IV per Diagnostic Interview Schedule for children (DISC-IV)  **Comorbidity:** N/A  **Female:** 10 %  **Age mean:** 9.9 (1.2)  **Minimum age:** 8  **Maximum age:** 12  **Ethnicity:**  % Black/African American : 2  % White : 89  % Multiracial : 9 | **Intervention:** Multimodal child and parent behavioral therapy and teacher behavioral training plus methylphenidate, therapy integrated family-based and school-based interventions with cognitive behavior therapy for the child; parent intervention was weekly sessions of 90 min group training based on Barkley’s training for defiant children; teacher training was a 2-hour workshop where psycho-education on ADHD, structuring the classroom environment, implementing contingency management in the classroom, and a daily report card system, for 10 weeks  **Control:** Other  Methylphenidate only for 10 weeks  **Comparator:** NA  **Follow-up:** 2.5 months | Disruptive Behavior Disorder Rating Scale, ADHD symptom scale, parent report  Groups did not differ in improvement on parent or teacher report.  Groups did not differ in improvement in parent or teacher reported social skills (SSRS) or child reported anxiety (State Trait Anxiety Inventory for Children). |
| FDA-approved pharmacological | Abikoff, 2007109  Greenhill, 2006800; Ghuman, 2007793; Swanson, 20061105; Wigal, 20061175; Kollins, 2006889  ID: ID NA  RCT  Multicenter  N = 114  US  Setting: School | **Target:** Children with ADHD and an impairment scale score of less than or equal to 55 on the Children Global Assessment Scale who had not responded to 10 weeks of parent training; no prior use of stimulants for > 5 weeks, major psychological or medical co-morbidities  **Other:** Parents and teachers  **ADHD presentation:** inattentive : 0,hyperactive : 29.51,combined : 70.49  **Diagnosis:** Confirmation by specialist  DSM-IV, psychiatrists interview  **Comorbidity:** N/A  **Female:** 19.67 %  **Age mean:** 4.39 (0.72)  **Minimum age:** 3  **Maximum age:** 5.5  **Ethnicity:**  % Hispanic or Latino : 19.67  % Black/African American : 19.67  % White : 59.02 | **Intervention:** Methylphenidate (immediate-release), 1.25, 2.5, 5, or 7.5 mg 3 times per day for 4 weeks  **Control:** Placebo  Placebo treatment, 3 times per day for 4 weeks  **Comparator:** NA  **Follow-up:** 1 month | CGI-S (Clinical Global Impression-Severity)  Proportion of excellent responders  Scale scores were significantly better for children in the treatment group compared to the placebo group (p < 0.0001) but only 21% on best-dose MPH and 13% on placebo  achieved MTA-defined categorical criterion for remission set for school-age children wit  SWAN (Strengths and Weaknesses of ADHD-Symptoms and Normal Behaviors), parent  There was no significant difference between treatment group and placebo group for parent or teacher report  Social Skills Rating System (Parent) (SSRS-P), measures social function  Treatment effect not statistically significant.  There was no significant difference in parental stress across the treatment and placebo groups.  Growth rates  During methylphenidate treatment, annual growth rates for completers were 20.3% less than expected for height and 55.2% less for weight  There were eight serious adverse events, but only one, a possible seizure, was thought to be related to medication. There were no episodes of mania, hypomania, depression, or suicidality |
| FDA-approved pharmacological | Abikoff, 2009108  NA  ID: ID NA  Crossover trial  Single center  N = 19  US  Setting: Specialty care | **Target:** Medication naive children with ADHD who had problems with organization, time management, and planning  **Other:** Parents and teachers provided outcome data  **ADHD presentation:** inattentive : 58,hyperactive : 0,combined : 42  **Diagnosis:** Confirmation by specialist  DSM IV criteria based on Diagnostic Interview Schedule for Children IV (DISC-IV)-Parent version  **Comorbidity:** Other : impaired organizational skills per Children's Organizational Skills Scale  **Female:** 21 %  **Age mean:** 10.05 (1.62)  **Minimum age:** 8  **Maximum age:** 13  **Ethnicity:**  N/A | **Intervention:** Methylphenidate OROS (osmotic-release oral system), 48.3 mg (range 18-54 mg) daily for 2 weeks, 4 weeks total  **Control:** Placebo  Placebo  **Comparator:** NA  **Follow-up:** 2 months | SNAP IV (Swanson, Nolan, and Pelham, Version IV) total score, parent rating  Mean SNAP IV parent rating , total score, and mean SNAP IV teacher rating, total score, were significantly lower in intervention group at follow-up (p < .005 for both outcomes). Lower is better.  Mean Children’s Organizational Skills Scale (COSS) total score, teacher rating, was significantly higher at follow-up for the intervention group (p < .01). Mean Children’s Organizational Skills Scale (COSS) total score, parent rating, was also significantly higher at follow-up for the intervention group (p < .05). Higher is better. |
| FDA-approved pharmacological | Allen, 2005118  ID: NA  RCT  Multicenter  N = 148  US  Setting: Mixed | **Target:** Children with ADHD according to DSM-IV and concurrent Tourette syndrome or chronic motor tic disorder, scores on the Attention Deficit/Hyperactivity Disorder Rating Scale-IV-Parent Version: Investigator Administered and Scored at least 1.5 standard deviations above the age and sex norm, have scores of at least 5 on the Yale Global Tic Severity Scale; no Children’s Yale–Brown Obsessive Compulsive Scale total score larger or equal to 15, have a Children’s Depression Rating Scale–Revised total score of larger than 40, history of bipolar disorder or psychosis, seizure disorder, or current use of any psychotropic medication other than study drug  **Other:**  **ADHD presentation:** inattentive : 35.8,hyperactive : 3.4,combined : 60.8  **Diagnosis:** Confirmation by specialist  Schedule for Affective Disorders and Schizophrenia for School-age Children–Present and Lifetime Version16 (K-SADSPL)  **Comorbidity:** Tic disorder  **Female:** 11.5 %  **Age mean:** 11.2 (2.5)  **Minimum age:** 7  **Maximum age:** 17  **Ethnicity:**  % Hispanic or Latino : 6.1  % Black/African American : 4.7  % Asian : 0.7  % White : 87.8  Other : Other: 4/148 (2.7%) | **Intervention:** Atomoxetine 0.5 to 1.5 mg/kg/day administered daily as a divided dose in the morning and late afternoon for approximately 18 weeks  **Control:** Placebo  Matching placebo 2 times a day for 18 weeks  **Comparator:** NA  **Follow-up:** 5 months | ADHD-RS Total  Significant treatment effects were obtained on all ADHD measures.  Reduction in Yale Global Tic Severity Scale total score between placebo and atomoxetine is not statistically significant (p = 0.063).  Decreased appetite  Decrease appetite was reported in 15.9% of intervention and 2.8% of placebo participants.  Discontinuations due to an adverse were 2 in the atomoxetine group (headache, vomiting) and 1 in the placebo group (upper abdominal pain); none was evaluated as serious. |
| FDA-approved pharmacological | Ashkenasi, 2011127  ID: N/A  RCT  Single center  N = 26  US  Setting: Other | **Target:** Children who met the DSM IV Edition criteria for attention deficit hyperactivity disorder (any subtype) and who demonstrated difficulty sleeping; no previous intolerance, adverse response, or allergy to methylphenidate or skin sensitivity to the methylphenidate transdermal system, and those with severe comorbid psychiatric disorders  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 27 %  **Age mean:**  9.8 (1.8), 9.6 (1.8), 7.5, 10.3 (1.8) across groups  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Methylphenidate transdermal patch sequence of 9 hours, 10 hours, 11 hours, and 12hours patch wear times maintained Monday through Thursday of each week, alternating wear times across 4 consecutive weeks with standard 9-hour wear time schedule Friday through Sunday, for duration of 4 weeks  **Control:** NA  **Comparator:** MedicationMethylphenidate transdermal 12 hours, 11 hours, 10 hours, 9 hours for 4 weeks, patch wear times maintained Monday through Thursday of each week, alternating wear times across 4 consecutive weeks with standard 9-hour wear time schedule Friday through Sunda  **Follow-up:** 1 month | Connor’s Global Impression-Parent  There was no significant difference between groups (p=0.114).  ADHD-RS-IV (Attention Deficit Hyperactivity Disorder Rating Scale-IV)  There was no significant difference between groups (p=0.466).  No significant effects of patch wear time on sleep latency (p=0.558) or total sleep time (p=0.382) were evident.  No adverse event related treatment discontinuations were evident and no individuals reported a reaction greater than dark red and itchy. |
| FDA-approved pharmacological | Banaschewski, 2013131  Coghill, 2013 720; Coghill, 2014721; Coghill, 2021723; Shire, 20081047; Soutullo, 20131084; Setyawan, 20151034; Coghill, 2014722  ID: NCT00763971  RCT  Multicenter  N = 336  Multiple countries  Setting: Mixed | **Target:** Children and adolescents who meet DSM-IV criteria for ADHD diagnosis, with baseline ADHD-Rating Scale-IV total score of 28 or higher; no failure to respond to a previous course of OROS-MPH, no presence of a comorbid psychiatric diagnosis with significant symptoms (not including oppositional defiant disorder), effective control of ADHD symptoms with medications of acceptable tolerability  **Other:** Parents reported some outcomes  **ADHD presentation:** inattentive : 15.96,hyperactive : 3.01,combined : 80.72  **Diagnosis:** Confirmation by specialist  DSM-IV-TR  **Comorbidity:** N/A  **Female:** 19.3 %  **Age mean:**  LDX 10.9 (2.9), placebo 11.0 (2.8), OROS-MPH 10.9 (2.6)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % Hispanic or Latino : 1.20  % Black/African American : 0.30  % Asian : 0.30  % White : 97.0  Other : 2.41 | **Intervention:** Lisdexamfetamine dimesylate once daily (30, 50, or 70 mg/day) for 7 weeks  **Control:** Placebo  Placebo pill identical to study drugs given daily at 07:00 to participants  **Comparator:** MedicationOsmotic-release oral system methylphenidate (OROS) once daily, 18, 36, or 54 mg/day dose  **Follow-up:** 2 months | CPRS-R (Conners Parent Rating Scale-Revised) change  The intervention and comparator groups had significantly more improvement than the placebo group (p<0.001).  ADHD-RS-IV change  The intervention and comparator groups had significantly more improvement than control group (p<0.001).  Weiss Functional Impairment Rating Scale-Parent Report (WFIRS-P)  The intervention and comparator groups had significantly more improvement than control group (p<0.001).  Decreased appetite  Active treatments reported more appetite suppression than placebo, no difference between treatment medications.720  Participants experiencing treatment emergent adverse events  The rate was 72.1% for LDX, 64.9% for OROS-MPH, and 57.3% for placebo.720  The proportion of patients who reported serious treatment emergent adverse events were low across all groups.720 |
| FDA-approved pharmacological | Bangs, 2007132  ID: N/A  RCT  Multicenter  N = 142  US  Setting: N/A | **Target:** Adolescents who met the criteria for both ADHD and major depressive disorder per DSM–IV; no beginning structured psychotherapy for ADHD and/or depression less than 1 month before trial entry  **Other:**  **ADHD presentation:** inattentive : 57,combined : 43  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** Mood disorder  **Female:** 27 %  **Age mean:**  ATX 14.6 (1.8), placebo 14.2 (1.5)  **Minimum age:** 12  **Maximum age:** 18  **Ethnicity:**  N/A | **Intervention:** Atomoxetine 1.2-1.8 mg/kg per day for 9 weeks  **Control:** Placebo  Placebo once daily  **Comparator:** NA  **Follow-up:** 2 months | ADHD-RS-IV-Parent: Inv scale  Mean decrease was significantly greater in the intervention group (p=0.001).  There were no significant differences between treatment groups in Children’s Depression Rating Scale–Revised total scores at any time point.  Decreased appetite  Nausea and decreased appetite occurred significantly more often during the acute phase in the ATX treatment group compared with the placebo group.  One serious adverse event, worsening of depression, occurred during the acute treatment phase in the placebo group and led to the patient discontinuing the study due to lack of efficacy. |
| FDA-approved pharmacological | Bangs, 2008133  ID: ID NA  RCT  Multicenter  N = 226  Multiple countries  Setting: Specialty care | **Target:** Children with ADHD and oppositional defiance disorder; those with serious psychiatric disorders or medical conditions were excluded  **Other:** Parents reported some outcomes  **ADHD presentation:** inattentive : 9.7,hyperactive : 5.8,combined : 84.5  **Diagnosis:** Confirmation by specialist  DSM IV by an investigator's clinical assessment via structured interview (Kiddie Schedule for Affective Disorders and Schizophrenia for School Aged Children-Present and Lifetime Version)  **Comorbidity:** ODD : 100% ODD  **Female:** 6.6 %  **Age mean:** 9.6 (1.9)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % White : 95.2 | **Intervention:** Atomoxetine, 1.2 mg/kg per day for 8 weeks  **Control:** Placebo  Placebo daily for 8 weeks  **Comparator:** NA  **Follow-up:** 2 months | CGI-S (Clinical Global Impression - Severity)  Atomoxetine group improved more on CGI-I (p 0.037) and CGI-Severity (p 0.013).  ADHD impact module (child)  Mean improvement in SNAP-IV ODD total score was not significantly different between groups (p 0.252). Mean improvement in SNAP-IV Combined, Inattentive, and Hyperactivity score was significantly greater in the intervention groups ( p < 0.001, p < 0.001, a  Decreased appetite  Significantly more atom­oxetine patients reported decreased appetite (p < .001).  Nausea and fatigue were significantly higher for atomoxetine than for placebo (p= 0.033 and p = 0.021, respectively). |
| FDA-approved pharmacological | Bedard, 2015137  Mount Sinai, 2005847  ID: NCT00183391  Crossover trial  Unclear/Not reported  N = 102  US  Setting: Other | **Target:** Youth with ADHD as the primary diagnosis; no IQ below 75, non-English speaking parent or child, neurological dysfunction, systemic medical illness, uncorrected sensory impairments, and history of psychosis or bipolar disorder, comorbid conditions did not require medication treatment; nonresponders to atomoxetine and methylphenidate and must not have experienced disabling adverse effects with either medication  **Other:**  **ADHD presentation:** inattentive : 37,hyperactive : 3,combined : 60  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 25 %  **Age mean:** 10.5 (2.7)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % Hispanic or Latino : 20  % Black/African American : 31  % Asian : 1  % White : 36  % Multiracial : 12 | **Intervention:** Atomoxetine 0.5 mg/kg, 1.0 mg/kg, 1.4 mg/kg, 1.8 mg/kg, administered each morning for 4-6 weeks  **Control:** NA  **Comparator:** MedicationMethylphenidate, 2 capsules of OROS MPH administered each morning, 18 mg, 36 mg, 54 mg, 72 mg  **Follow-up:** 3.5 months | ADHD-RS  Both medications produced significant improvement (p<0.001).  For commission errors, there were no significant main effects of Drug or Time, and the Drug by Time was not significant. For omission errors, there was a significant Drug by Time interaction and a significant main effect of Time with no main effect of Drug, significant reduction in omission errors following MPH (p 0.001) but not ATX (p 0.69). There was a significant Drug by Time interaction such that youth treated with MPH had a greater speeding of RT than those treated with ATX. There was no main effect of Drug, but there was a main effect of Time. A post hoc paired t-test showed no significant change in RT for ATX (p = .99). There were main effects for Time and Drug on reaction time variability. There was also a significant Drug by Time interaction. MPH had a significantly larger impact than ATX. |
| FDA-approved pharmacological | Biederman, 2007144  Childress, 2014713; New River Pharmaceuticals986  ID: NCT00556296  RCT  Multicenter  N = 290  US  Setting: N/A | **Target:** Children with inadequate treatment or no previous treatment of ADHD and an ADHD Rating Scale version IV score greater than or equal to 28  **Other:**  **ADHD presentation:** hyperactive : 4,combined : 96  **Diagnosis:** No  Unspecified interviewer  **Comorbidity:** N/A  **Female:** 30.7 %  **Age mean:** 9 (1.8)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % Hispanic or Latino : 17  % Black/African American : 24  % American Indian or Alaska Native : 0.7  % Asian : 1  % Native Hawaiian or Pacific Islander : 0.3  % White : 53 | **Intervention:** Lisdexamfetamine dimesylate 70mg orally once per day for 4 weeks  **Control:** Placebo  Placebo  **Comparator:** MedicationLisdexamfetamine dimesylate 30mg orally once per day for 4 weeks  **Follow-up:** 1 month | Clinical Global Impression (CGI) scale  Ratings were either very much improved or much improved in over 70% of patients in the active treatment groups, compared with 18% in the placebo group.  ADHD Rating Scale  The 70mg group had the greatest symptom improvement compared to the placebo (p<0.001).  Decreased appetite  Rates were 49.3% in the 70mg, 36.6% in the 30mg, 31.1% in the 50mg, and 4.2% in the placebo group (p<0.05).  Number of participants that experienced any adverse events  Rates were 83.6% in the 70mg, 67.6% in the 50mg, 71.8% in the 30mg, and 47.2% in the placebo group.  Statistically significant different adverse events in treatment groups vs. placebo: decreased appetite, insomnia, irritability, vomiting, weight loss, dry mouth. |
| FDA-approved pharmacological | Biederman, 2008145  Shire, 20031053  ID: NCT00152009  RCT  Multicenter  N = 345  US  Setting: N/A | **Target:** Children with ADHD; no current, uncontrolled, comorbid psychiatric diagnosis (except oppositional defiant disorder) with significant symptoms, or when other symptomatic manifestations would contraindicate guanfacine extended release treatment or confound efficacy or safety assessments; patients who weighed<55 lb or were morbidly overweight or obese, pregnant, lactating, or hypertensive excluded; no QTc interval of >440 milliseconds, history of seizure during the past 2 years, tic disorder; family history of Tourette’s disorder, positive urine drug screen, abnormal thyroid function not adequately treated, any cardiac condition or family history of cardiac condition , investigational drug use within 28 days, BP or heart rate medications, or were taking other medications that have central nervous system effects or affect performance  **Other:**  **ADHD presentation:** inattentive : 26.1,hyperactive : 2,combined : 71.9  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 25.5 %  **Age mean:**  10.5 (6.0–17.0)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % Hispanic or Latino : 9.9  % Black/African American : 13.3  % American Indian or Alaska Native : 0.3  % Asian : 0.6  % White : 70.1  Other : 5.8 | **Intervention:** Guanfacine extended release 4 mg/day for 8 weeks  **Control:** Placebo  Matching placebo tablet  **Comparator:** MedicationGuanfacine extended release 2mg/day group, began dosing at 1 mg/day, escalated weekly in 1-mg increments  **Follow-up:** 2 months | CGI-I (Clinical Global Impression of Improvement) significant improvement  Significant improvement in CGI-I scores at end point was shown in 25.64%, 55.95%, 50.00%, and 55.56% of patients in the placebo and GXR 2-mg, 3-mg, and 4-mg groups.  ADHD-RS-IV (Attention-Deficit/Hyperactivity Disorder Rating Scale IV) total score  Least-squares mean changes from baseline to the end point in Attention-Deficit/Hyperactivity Disorder Rating Scale IV total scores were significant in all groups of children taking guanfacine extended release compared with the placebo group.  Appetite decreased  The rate was 5.8% in the intervention, 2.3% in the placebo, 5.7% in the 2mg, and 9.3% in the 3mg group.  Participants experiencing treatment emergent adverse events  The rate as 87.2% in the intervention, 64% in the placebo, 77.0% in the 2mg and 88.4% in the 3mg group.  Most of the commonly reported adverse events were mild or moderate in intensity. Severe treatment emergent adverse events were experienced by 24 patients, all of whom received GXR (sedation (n=7), somnolence (n=6), fatigue (n=4), headache (n=2), vomiting |
| FDA-approved pharmacological | Block, 2009154  ID: N/A  RCT  Single center  N = 288  US  Setting: Primary Care | **Target:** Children who met DSM-IV-TR criteria for ADHD  **Other:**  **ADHD presentation:** inattentive\_other : 16-26 across arms,hyperactive\_other : 1-3% across arms,combined\_other : 68-76% across arms  **Diagnosis:** Confirmation by specialist  clinical interview  **Comorbidity:** N/A  **Female:** 30 %  **Age mean:**  Across arms 8.8 (1.7), 9.1 (1.6), 8.9 (1.7)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  Other : 62-70% across arms | **Intervention:** Atomoxetine 1.25mg/kg/day each morning for 6 weeks  **Control:** Placebo  Placebo in the morning or evening for 6 weeks  **Comparator:** MedicationEvening dosing, 1.26mg/kg/day of atomoxetine for 6 weeks  **Follow-up:** 1.5 months | Daily Parent Rating of Evening and Morning Behavior–Revised (DPREMB-R)  AM atomoxetine and PM atomoxetine showed significantly greater efficacy overall compared with placebo (p=0.048, p=0.004).  CGI-ADHD-S  Response rate CGI-ADHD-S decrease of 2 or more  Morning dosing produced a 49% response rate compared with 32% for evening dosing and 22% for placebo (p<0.001).  ADHD-RS-IV (Attention-Deficit/Hyperactivity Disorder Rating Scale IV)–Parent Version, investigator administered and scored  Response rate (at least 25% decrease on ADHD-RS total score)  Significantly greater improvement on the ADHD RS Total score (effect size 0.7) was observed for AM atomoxetine compared with placebo; evening-dosed atomoxetine also significantly decreased core ADHD symptoms relative to placebo; AM vs PM atomoxetine was e  Significantly greater improvement on the CGIP-Evening Total (single-item rating of the clinician’s assessment of the severity of ADHD symptoms) score (effect size 0.6) was observed for AM atomoxetine compared with placebo.  Decreased appetite  Decreased appetite were reported more often with AM atomoxetine than with placebo.  Participants reporting at least 1 adverse event  The rate was higher with AM atomoxetine than with PM atomoxetine or placebo (74.0%, 48.9%, 43.5%; p<0.001 for AM vs PM; p<0.001 for AM vs placebo; P = .552 for PM vs placebo).  Abdominal pain, vomiting, somnolence, nausea, and stomach discomfort were reported more often with AM atomoxetine than with placebo; vomiting was reported more often with PM atomoxetine than with placebo; no significant differences between AM and PM atomo |
| FDA-approved pharmacological | Brams, 2018161  Shire, 20151051  ID: NCT02466425  RCT  Multicenter  N = 264  US  Setting: Specialty care | **Target:** Children with ADHD  **Other:** Clinician reported outcomes  **ADHD presentation:** inattentive : 23.2,hyperactive : 1.1,combined : 75.7  **Diagnosis:** Confirmation by specialist  DSM IV plus ADHD Rating Scale IV (ADHD-RS-IV) total scores >=28  **Comorbidity:** N/A  **Female:** 38 %  **Age mean:** 12.5 (3.24)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % Black/African American : 28.5  % Asian : 0.3  % White : 61.2  % Multiracial : 8.0 | **Intervention:** Amphetamine, SHP465 mixed amphetamine salts (12.5 or 25 mg) for 4 weeks  **Control:** Placebo  Placebo  **Comparator:** NA  **Follow-up:** 1 month | CGI-I (Clinical Global Impressions-Improvement)  Intervention group improved significantly more than placebo group (p < 0.001).  ADHD-RS-IV change  Change from baseline significantly favored intervention over placebo (p<0.001).  Appetite decrease  Significantly more participants in the intervention group experienced decreased appetite than control group participants.  Participants with any adverse event  The rate was 67% for intervention and 47% for control.  The frequency of treatment-emergent adverse events leading to discontinuation was greater with the intervention treatment than with placebo. |
| FDA-approved pharmacological | Buitelaar, 2007164  Trzepacz, 20111122; Michelson, 2004926  ID: N/A  RCT  Multicenter  N = 163  Multiple countries  Setting: Other | **Target:** Children with ADHD and without bipolar disorder or psychotic illness or unstable medical illness or conditions requiring ongoing administration of a psychoactive medication (other than atomoxetine)  **Other:**  **ADHD presentation:** inattentive : 22.9,hyperactive : 4.5,combined : 72.6  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 10.6 %  **Age mean:** 10.6 (2.3)  **Minimum age:** 6  **Maximum age:** 15  **Ethnicity:**  N/A | **Intervention:** Atomoxetine 0.5-1.8 mg/kg/d for 6 months  **Control:** Placebo  Placebo-controlled  **Comparator:** NA  **Follow-up:** 12 months | CGI-S (Clinical Global Impressions–Severity of Illness) change  Statistically significant difference favoring atomoxetine (p 0.003).  ADHD-RS-IV Total Score  Relapse rate  Atomoxetine was superior to placebo in maintaining symptom response (p 0.001). The relapse rate was 2.5% for atomoxetine and 12.2% for placebo.  CHQ (Child Health Questionnaire) Psychosocial Summary Score  No difference between groups.  Effects on sexual development: Tanner stage: No statistically significant differences were observed between treatment groups either in sexual development (mean time, in days, to the first Tanner stage change, p=0.33) or in the duration of treatment exposure ( p= 0.90).1122  Weight increase in weight percentile  Both groups showed an increase in weight percentile, but the increase was greater in the placebo group (p 0.001).  Participants reporting at least 1 new or worsened adverse event  The rate was 65.6% (intervention) vs 53.7% (placebo).  Two adverse events were reported in more than 5% of subjects in both treatment groups, headache (atomoxetine, 8 [10.1%]; placebo, 7 [8.6%]) and nasopharyngitis (atomoxetine, 6 [7.6%]; placebo, 7 [8.6%]); all other adverse events were reported by <= 5% of |
| FDA-approved pharmacological | Cetin, 2015175  ID: N/A  RCT  Single center  N = 145  Turkey  Setting: Specialty care | **Target:** Patients with ADHD without any comorbid psychopathologies  **Other:**  **ADHD presentation:** inattentive : 12.6,hyperactive : 0,combined : 87.4  **Diagnosis:** Confirmation by specialist  DSM-IV-TR by child psychiatrists  **Comorbidity:** N/A  **Female:** 18.4 %  **Age mean:** 9.47 (2.32)  **Minimum age:** 7  **Maximum age:** 16  **Ethnicity:**  Other : Ethnicity, Turkish patients but not sure of race | **Intervention:** Atomoxetine, mean dose 1.14±0.13 mg/kg/day, for 6 months  **Control:** NA  **Comparator:** MedicationOsmotic release oral system methylphenidate (OROS), mean dose of 0.73±0.22 mg/kg/day for 10 weeks  **Follow-up:** 6 months | Conners Comprehensive Behavior Rating Scale-Behavior Problems, teacher  There was no significant difference between groups (p=0.720).  Weight loss  The rate was 1.6% in both groups.  Adverse effects  The rate was 31.1% in the OROS-MPH and 27.1% in the ATX group.  The most commonly encountered adverse effect was anorexia in both groups, and it was seen in 19.6% of the patients in the OROS- MPH group and 13.5% of the patients in the ATX group. |
| FDA-approved pharmacological | Childress, 2009195  ID: ID NA  RCT  Multicenter  N = 253  US  Setting: Specialty care | **Target:** Children with ADHD, drug naıve or not treated with any methylphenidate-related medication in the month prior to the study; those with serious psychological disorders were excluded  **Other:** Parents and teachers provided outcome information  **ADHD presentation:** inattentive : 21.7,hyperactive : 2.8,combined : 73.9  **Diagnosis:** Confirmation by specialist  DSM-IV-TR based on a psychiatric examination and K-SADS PL  **Comorbidity:** N/A  **Female:** 35.6 %  **Age mean:** 8.7 (1.84)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % Black/African American  % Asian : 0.8  % White : 57.7  Other : Other 12.6% | **Intervention:** Dexmethylphenidate hydrochloride extended-release (d-MPH XR; Focalin XR) methylphenidate, 30 mg extended release daily for 5 weeks  **Control:** Placebo  Placebo capsule daily  **Comparator:** MedicationDexmethylphenidate hydrochloride extended-release (d-MPH XR; Focalin XR), 10 mg extended release daily, for 5 weeks  **Follow-up:** 1 month | Clinical Global Impression - Improvement (CGI-I), number improved  Significantly greater percentage of medication patients improved on CGI-I (p < . 001 for both groups). CGI-Severity ratings of each medication group was significantly better (p < 0.001) than placebo group.  Conners’ ADHD DSM-IV Scales (CADS), teacher report  Patients in medication groups demonstrated a significant improvement as compared to placebo (p<0.001) on both CADS-T and CADS-P (parent report).  Weight decrease  Significantly more medication patients experienced appetite decease.  Any adverse event  Overall incidence of adverse events was generally higher in medication groups.  Adverse events were mild to moderate in severity. |
| FDA-approved pharmacological | Childress, 2022194  Shire, 20171052  ID: NCT03260205  RCT  Multicenter  N = 199  US  Setting: N/A | **Target:** ADHD diagnoses per DSM-IV, baseline scores of 28 (boys) or 24 (girls) on the parent reported ADHD Rating Scale-IV Preschool version total scores and 4 on the Clinical Global Impression–Severity scale, undergone nonpharmacologic treatment or to have had symptoms severe enough to warrant enrollment without prior nonpharmacologic treatment, engaged in structured group activities that allowed for assessment of ADHD symptoms and impairment outside of the home, Peabody Picture Vocabulary Test standard score 70 and to have lived with the same parent/legally authorized representative for 6 months; no medications for central nervous system, concurrent illness, disability or comorbidity  **Other:**  **ADHD presentation:** combined : 91.6  **Diagnosis:** No  **Comorbidity:** N/A  **Female:** 32.3 %  **Age mean:** 5.1 (6.54)  **Minimum age:** 4  **Maximum age:** 5  **Ethnicity:**  Other : depends on tx/placebo/pooled | **Intervention:** Lisdexamfetamine 30 mg/day for 6 weeks  **Control:** Placebo  Matching placebo for 6 weeks  **Comparator:** MedicationTreatment with 5 mg lisdexamfetamine for 6 weeks  **Follow-up:** 1.5 months | CGI Global Impression scale  Rates were 41.7% across all active treatment groups and 24.3% with placebo (p 0.0857).  ADHD-RS-IV-PS  Scores decreased more with lisdexamfetamine than placebo (p 0.0074, effect size –0.52).  Results for the sleep diary were variable across treatment groups, with no notable trends indicative of differential changes between active treatment and placebo.  Decreased weight  Weight decreased for two patients with 20 mg LDX but in no other group.  Any treatment-emergent adverse event  The rates were 57.9% in the intervention receiving 30mg, 33.3% in the 5mg group, 52.9% in the 20mg group, and 42.2% in the placebo group.  Safety and tolerability assessments included treatment-emergent adverse events and changes in pulse (greater in all treatment group vs placebo) and blood pressure (greater in all treatment groups vs placebo). |
| FDA-approved pharmacological | Cho, 2011196  ID: N/A  RCT  Multicenter  N = 153  Korea  Setting: N/A | **Target:** Children with a diagnosis of ADHD as defined by DSM-IV-TR, did not take any medication for ADHD treatment at least 2 weeks prior to randomization and at least 1 week prior to obtaining baseline ADHD-Rating Scale-IV-Parent: Investigator Rated and Clinical Global Impressions-Severity scores, had no significant laboratory abnormalities or clinical conditions that would preclude participation at study entry, had no impairment in intelligence as assessed clinically by the investigator, and were able to keep appointments for clinic visits and all examinations  **Other:**  **ADHD presentation:**  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 16.3 %  **Age mean:** 9.8 (2.4)  **Minimum age:** 6  **Maximum age:** 18  **Ethnicity:**  % Asian : 100 | **Intervention:** Atomoxetine 0.5-1.2 mg/kg/day for 6 weeks  **Control:** NA  **Comparator:** MedicationAtomoxetine at a target dose of 0.5 mg/kg/day and patients, 6 weeks total  **Follow-up:** 1.5 months | CGI-S and CGI-I  Atomoxetine 1.2 mg/kg/day was associated with greater improvement compared with atomoxetine 0.2 mg/kg/day (p 0.0025).  ADHD-RS-IV-Parent:Inv total score  The ANCOVA model for demonstrated a significantly greater improvement in mean change for atomoxetine 1.2 mg/kg/day in a pairwise comparison with atomoxetine 0.2 mg/kg/day (p=0.006).  Decreased appetite  Rates were 12.5% in the intervention vs 7.41% in the comparator group.  Participants with at least one treatment emergent adverse event  The rates were 58.33 in the intervention and 40.74 in the comparator.  The majority of these events were mild or moderate, and no events related to suicide ideation or self-harm were reported. |
| FDA-approved pharmacological | Coghill, 2014202  Banaschewski, 2014673; Shire, 20091049  ID: NCT00784654  RCT  Multicenter  N = 157  Multiple countries  Setting: Specialty care | **Target:** All patients had ADHD of at least moderate severity, defined as an ADHD-Rating Scale-IV total score of 28 or higher at baseline  **Other:**  **ADHD presentation:** inattentive : 17.3,combined : 82.2,combined\_other : 0.5%  **Diagnosis:** Confirmation by specialist  DSM-IV-TR by clinician  **Comorbidity:** N/A  **Female:** 21.7 %  **Age mean:**  6-12 years 66.9%; 13-17years 33.1 %  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % White : 94.9 | **Intervention:** Lisdexamfetamine dimesylate optimal dose orally for up to 6 weeks  **Control:** Placebo  Placebo identical in appearance for 6 weeks orally  **Comparator:** NA  **Follow-up:** 8.25 months | CGI-S treatment failure (at least 2-point increase)  The rate was 17.1% in the intervention compared to 68.8% in the placebo group.  ADHD-RS-IV Total Score  Treatment failure (50% or greater increase in ADHD-RS-IV and 2-point increase in CGI-S)  Significantly less participants in the intervention group met criteria for treatment failure compared to those in the control group (p<0.001).  The difference between the LDX and placebo groups changes from baseline to endpoint was significant (p<0.001).  CHIP-CE: PRF T-scores deteriorated in all domains in the placebo group, but not in the lisdexamfetamine dimesylate group.  Weight, kg  Decreased appetite  The rate was 3.8% in the intervention compared to none in the placebo group.  Participants with any treatment-emergent adverse events  The rate was 39.7% in the intervention compared to 25.3% in the placebo group. |
| FDA-approved pharmacological | Concordia, 2011205  ID: NCT01439126  RCT  Multicenter  N = 135  US  Setting: Mixed | **Target:** Children and adolescents who meet DSM-IV-TR criteria for primary diagnosis for ADHD, IQ at least 70 or higher; no comorbid psychiatric conditions, other significant health conditions, pharmaceuticals used for ADHD treatment prior to 30 days before begin of study  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  Kiddie-Schedule for Affective Disorders and Schizophrenia-Present and Lifetime (MINI-Kid)  **Comorbidity:** N/A  **Female:** 30.4 %  **Age mean:** 10.8 (2.88)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % Hispanic or Latino : 23.7  % Black/African American : 27.4  % American Indian or Alaska Native : 0.0  % Asian : .7  % Native Hawaiian or Pacific Islander : 0.0  % White : 64.4  % Multiracial : 7.4 | **Intervention:** Clonidine hydrochloride 0.1 mg, 0.2 mg, 0.3 mg, or 0.4 mg taken daily for 26 weeks  **Control:** Placebo  Tapered off their optimal dose of KAPVAY at weekly intervals in decrements of 0.1 mg/day until reaching the dose of 0 mg/day, and then received only placebo for the remainder  **Comparator:** NA  **Follow-up:** 6.5 months | CGI (Clinical Global Impressions-Severity of Illness)  Intervention scores improved (mean 0.4, SD 1.40) when compared to placebo (mean 0.9, SD 1.28)  ADHD-RS-IV (ADHD-Rating Scale-4th Edition)  Intervention scores improved more (mean 3.0, SD 10.75) than the control (mean 7.0, SD 12.30).  Weiss Functional Impairment Rating Scale-Parent (WFIRS-P)  N/A  Change in Epworth Sleepiness Scale for Children (ESS-C) from randomization to end of study period (mean, SD): intervention, -0.6 (3.18), placebo, -0.6 (4.09)  Number of subjects that responded "Yes" to the question "Do you have a wish to be dead" in Columbia Suicide Severity Rating Scale (C-SSRS) at Visit 20; intervention 0 count, placebo 1 count  Participants with at least 1 treatment emergent adverse event  The rate was 50% for intervention and 46% for control. |
| FDA-approved pharmacological | Connor, 2010207  Shire, 20061045  ID: NCT00367835  RCT  Multicenter  N = 217  US  Setting: Specialty care | **Target:** Children with ADHD and oppositional symptoms and no other psychiatric co-morbidities  **Other:** Parents provided some outcome data  **ADHD presentation:** inattentive : 12.6,hyperactive : 3.3,combined : 84.1  **Diagnosis:** Confirmation by specialist  DSM-IV-TR per Kiddie Schedule for Affective Disorders and Schizophrenia - Present and Lifetime  **Comorbidity:** ODD  **Female:** 31.3 %  **Age mean:** 9.4 (1.84)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % Hispanic or Latino : 16.8  % Black/African American : 22.4  % American Indian or Alaska Native : 2.8  % Native Hawaiian or Pacific Islander : 0.5  % White : 66.4  Other : 7.9% other | **Intervention:** Guanfacine extended release 1- 4 mg per day for 9 weeks  **Control:** Placebo  Placebo  **Comparator:** NA  **Follow-up:** 2 months | CGI-S  A higher percentage of patients in the intervention group had improved on the CGI-S (p < .001).  ADHD-RS-IV (ADHD Rating Scale IV) total score change, clinician rating  Reduction in ADHD-RS-IV greater in intervention group than placebo group (p < .001).  Medication Satisfaction Survey (MSS, number satisfied overall - agree or strongly agree)  Greater percentage of intervention patients satisfied with treatment (p<0.001).  Participants with any treatment emergent adverse event  The rate was 83.8% in the intervention and 57.7% in the placebo group.  Adverse events were more common in the intervention group. A higher percentage of intervention patients reported somnolence, sedation, dizziness, abdominal pain, fatigue, and irritability. |
| FDA-approved pharmacological | Daviss, 2008217  Palumbo, 2008976; University of Cincinnati, 19991130  ID: NCT00031395  RCT  Multicenter  N = 122  US  Setting: Other | **Target:** Participants of any ADHD subtype who had a designated parent in daily contact, had previously used methylphenidate or clonidine; with no history of tic disorder, major depression, pervasive developmental disorder, autism, psychosis, mental retardation, anorexia nervosa, bulimia, a serious cardiovascular or other medical disorder  **Other:**  **ADHD presentation:** inattentive : 19.9,hyperactive : 4.1,combined : 76.0,N/A  **Diagnosis:** Confirmation by specialist  DSM-IV by investigator  **Comorbidity:** N/A  **Female:** 19.7 %  **Age mean:** 9.5 (1.6)  **Minimum age:** 7  **Maximum age:** 12  **Ethnicity:**  % Hispanic or Latino : 7  % Black/African American : 11  % White : 78  Other : 4 | **Intervention:** Clonidine plus methylphenidate adjusted to optimal doses and continued, doses were titrated up to 0.6mg/day for clonidine and 60mg/day for methylphenidate in divided doses (up to four times per day for clonidine and up to three times per day for methylphenidate) for 8 weeks  **Control:** Other  Methylphenidate alone  **Comparator:** NA  **Follow-up:** 4 months | Childrens Global Assessment Scale (CGAS)  Clonidine was not found to improve ADHD symptoms, whereas subjects treated with methylphenidate showed significant improvement compared to those not treated with methylphenidate.  Conners Abbreviated Symptom Questionnaire for Teachers (ASQ-Teacher)  Patients treated with clonidine had greater improvements compared with patients not treated with clonidine.976  Pittsburgh Side Effect Scale (Drowsiness): Clon and Clon+MPH experienced initial drowsiness relative to others not taking clonidine. However, levels reached equivalent to those in placebo and MPH only. Quality of Life, as measured by Daily Hassles and Impact on Family instruments: in a general linear model repeated measures analysis, treatment groups improved compared to placebo; all treatment groups were combined for this analysis.  Weight, kg  All groups had mean weight gains during the 16 weeks period, but theses gains were significantly less when taking Methylphenidate than those that did not (p 0.0007).217  Participants with any adverse event  Rate was 75% in the combination group, 83.6% in the clonidine group, 58.6% in the methylphenidate group, and 40% in the placebo group.Subjects taking clonidine had higher rates of any AE reported (75%) than those not treated with clonidine (41%; p 0.0006  Bradycardia on ECG (HR<60 bpm) significantly higher in subjects treated with clonidine than in subjects not treated with clonidine (p=0.02), somnolence: subjects treated with clonidine experienced higher rates of somnolence than subjects not treated with |
| FDA-approved pharmacological | Dell'Agnello, 2009220  ID: NA  RCT  Multicenter  N = 139  Italy  Setting: Specialty care | **Target:** Children with ADHD with oppositional defiant disorder  **Other:** Parents and teachers provided some outcome data  **ADHD presentation:** inattentive : 5.8,hyperactive : 5.1,combined : 89.1  **Diagnosis:** Confirmation by specialist  DSM-IV, in addition to Kiddie Schedule for Affective Disorders and Schizophrenia for School Aged Children-Present and Lifetime Version (K-SADS-PL)  **Comorbidity:** ODD  **Female:** 7.1 %  **Age mean:**  mean 9.9  **Minimum age:** 6  **Maximum age:** 15  **Ethnicity:**  N/A | **Intervention:** Atomoxetine 1.2 mg/kg/day for 6 weeks  **Control:** Placebo  Placebo, once per day  **Comparator:** NA  **Follow-up:** 2 months | CGI-ADHD-S score  Significant improvement in the intervention compared to control (p<0.001).  ADHD subscale SNAP-IV (Swanson, Nolan and Pelham IV)  Swanson, Nolan and Pelham (SNAP) IV ADHD subscale, at least 25% response  Intervention group improved more (p < 0.001). A higher percentage of the intervention group had at least a 40% improvement (18.1% vs. 3.1%, p= 0.043).  Children's Depression Rating Scale-Revised (CDRS-R), mean changes: Intervention -0.5 (4.4), Control -0.1 (5.0). Screen for Child Anxiety Related Emotional Disorders (SCARED)-Parent Version, mean changes: Intervention −2.1 (7.6), Control −1.7 (6.5). Health Related Quality of Life (HRQOL): Intervention 30.7, Control 28.2. SDs not reported. Higher score is better. p values not reported.  Anorexia  Small increase (+0.5 kg) in body weight with placebo and a small decrease (−1.2 kg) with atomoxetine (p , 0.001). Mean height increased more in placebo group (+ 1.5 cm) than in atomoxetine group (+1.0 cm) (p= 0.021). |
| FDA-approved pharmacological | Diamond, 1999224  ID: ID NA  RCT  Unclear/Not reported  N = 91  Canada  Setting: N/A | **Target:** Children with pervasive ADHD (8 or more of the 14 DSM-III-R criteria for ADHD in one setting and at least 5 criteria in another setting), history of ADHD for more than 6 months and beginning before the age of 7, estimated Full Scale IQ greater than 80, no primary anxiety or affective disorder  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** No  DSM-III-R, methods only state "interviewer"  **Comorbidity:** Mood disorder  **Female:** 0.2 %  **Age mean:**  8.65 (1.8) and 8.07 (1.3)  **Minimum age:**  **Maximum age:**  **Ethnicity:**  N/A | **Intervention:** Methylphenidate (immediate release) 0.7 mg/kg twice daily with parental training/support for 4 months  **Control:** Placebo  Placebo with parental training/support  **Comparator:** NA  **Follow-up:** 4 months | Telephone interview probe oppositional behavior, parent rating  No statistically significant differences.  No difference in the development of clinically significant side effects, only 1 or 2 children in each group developed those. |
| FDA-approved pharmacological | Dittmann, 2011226  ID: NA  RCT  Multicenter  N = 181  Germany  Setting: N/A | **Target:** Children with ADHD; no history of bipolar I or II disorder, psychosis, pervasive developmental disorder, or seizure disorder, at serious suicidal risk, or likely to require psychotropic medications or a structured psychotherapy  **Other:**  **ADHD presentation:** inattentive : 19.4,hyperactive : 5,combined : 75.6  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** ODD  **Female:** 15.6 %  **Age mean:**  ATX 10.9(3.1), placebo 11.1 (2.8)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  N/A | **Intervention:** Atomoxetine fast titration, 0.5 mg/kg for 7 days, then 1.2 mg/kg once daily in the morning for 8 weeks  **Control:** Placebo  Placebo once daily for 9 weeks  **Comparator:** MedicationAtomoxetine-slow 7 days each at 0.5 and 0.8 mg/kg, then 1.2 mg/kg; once daily for 9 weeks  **Follow-up:** 2.25 months | Attention-Deficit and Disruptive Behavior Disorders (ADDB-Inv), disruptive behavior  The intervention group had significantly reduced scores compared to the control group (p <0.001). There was no significant difference between intervention and comparator.  CGI-Severity for ADHD  ATX was significantly superior to placebo.  ADHD Score SNAP-IV  Intervention and comparator groups were significantly superior to the control group (p <0.001). There was no significant difference between intervention and comparator.  The most commonly reported treatment-emergent AEs during intervention were fatigue (ATX-fast/slow 35.0%/21.3%; vs. placebo 10.2%), nausea (21.7/19.7% vs. 5.1%), headache (25.0/14.8% vs. 15.3%), vomiting (15.0/18.0% vs. 5.1%), upper abdominal pain (15.0/13 |
| FDA-approved pharmacological | Dittmann, 2013225  Shire, 2010 1050; Dittmann, 2014738;  ID: NCT01106430  RCT  Multicenter  N = 267  Multiple countries  Setting: Mixed | **Target:** Male and female children and adolescents who satisfied DSM-IV-TR criteria for a primary diagnosis of ADHD of at least moderate severity as shown by a baseline ADHD Rating Scale IV total score of 28 or higher  **Other:**  **ADHD presentation:** inattentive : 16.8,hyperactive : 3.4,combined : 79.9  **Diagnosis:** Confirmation by specialist  Yes - DSM-IV, Kiddie-Schedule for Affective Disorders and Schizophrenia for School Age Children—Present and Lifetime (KSADS-PL)  **Comorbidity:** N/A  **Female:** 24.81 %  **Age mean:** 10.65 (2.79)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % Hispanic or Latino : 18.7  % White : 88.95 | **Intervention:** Atomoxetine, mean optimal dose 40.2 mg/day (SD 20.05) for 9 weeks  **Control:** NA  **Comparator:** MedicationLisdexamfetamine dimesylate, 30, 50 or 70 mg once daily for 9 weeks  **Follow-up:** 2.25 months | CGI-I (Clinical Global Impressions-Improvement), days to first clinical response  The median time to first clinical response was significantly shorter for patients in the lisdexamfetamine group than those in the atomoxetine group (p= 0.001)  ADHD-RS-IV total score  Improvement in ADHD-RS-IV from baseline to follow-up was significantly greater in the LDX group compared to the ADX group (p < 0.001).  Decreased appetite  The rate was 26.8% in the lisdexamfetamine dimesylate and 10.4% in the atomoxetine group.  Any treatment-emergent adverse event  The rate was 71.9% in the lisdexamfetamine dimesylate and 70.9% in the atomoxetine group.  No deaths or serious treatment-emergent adverse event were reported. |
| FDA-approved pharmacological | Duke University, 2009235  ID: NCT00889915  RCT  Unclear/Not reported  N = 228  US  Setting: N/A | **Target:** Children with diagnosis of ADHD according to DSM-IV criteria, English-speaking, with no history cardiovascular diseases, may receive other medicinal and/or psychosocial interventions for other comorbid disorders; not inpatient status, cannot take another medication for ADHD (psychostimulant, atomoxetine, bupropion), no psychosis or autism spectrum disorder  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM IV  **Comorbidity:** N/A  **Female:** 31.6 %  **Age mean:** 10.3 (3.1)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  N/A | **Intervention:** Mixed amphetamine salts extended release (Adderall) for 6 weeks  **Control:** NA  **Comparator:** MedicationMethylphenidate (Concerta, Osmotic-release Oral System Methylphenidate)  **Follow-up:** 1.5 months | Weight loss  The rate for weight loss was 5.66% for concerta and 5.13% for adderall.  MAS 48% with events, concerta 34%. |
| FDA-approved pharmacological | Duke University, 2009b236  ID: NCT00889915  RCT  Unclear/Not reported  N = 228  US  Setting: N/A | **Target:** Children with diagnosis of ADHD according to DSM-IV criteria, English-speaking, with no history cardiovascular diseases, may receive other medicinal and/or psychosocial interventions for other comorbid disorders; not inpatient status, cannot take another medication for ADHD (psychostimulant, atomoxetine, bupropion), no psychosis or autism spectrum disorder  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM IV  **Comorbidity:** N/A  **Female:** 31.6 %  **Age mean:** 10.3 (3.1)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  N/A | **Intervention:** Lisdexamfetamine dimesylate (vyvanse) for 6 weeks  **Control:** NA  **Comparator:** MedicationMethylphenidate transdermal system, optimal dose received for 6 weeks  **Follow-up:** 1.5 months | Weight loss  The rate for weight loss was 6.06% for transdermal system and 4.48% for lisdexamfetamine.  Lisdexamfetamine dimesylate rate of other adverse events was 49% vs 49% methylphenidate transdermal system. |
| FDA-approved pharmacological | Eli Lilly, 2004247  ID: NCT00192023  RCT  Single center  N = 139  Italy  Setting: Specialty care | **Target:** Children and adolescents with ADHD and comorbid Oppositional Defiant Disorder, no history of bipolar, psychosis or pervasive development disorder  **Other:** Parents and teachers provided some outcomes.  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** ODD : 100% with ODD  **Female:** 7.3 %  **Age mean:** 9.8 (2.3)  **Minimum age:** 6  **Maximum age:** 15  **Ethnicity:**  % White : 97 | **Intervention:** Atomoxetine 0.5 mg per kg per day for 1 week, then 1.2 mg/kg/day for 7 weeks  **Control:** Placebo  Placebo, daily for 8 weeks  **Comparator:** NA  **Follow-up:** 2 months | Clinical Global Impressions (CGI) Severity  Greater improvement for intervention group ( p<0.001) as measured by both CGI-S and Conners' Parent Rating Scale-Revised: Short Form, ADHD Index.  Swanson, Nolan and Pelham Questionnaire (SNAP-IV)  Intervention group improved more (p<0.001).  Children's Depression Rating Scale-Revised: No difference in improvement between groups (p = 0.870).  Decreased appetite  Significantly higher proportion of intervention group experienced appetite decrease, anorexia, and weight loss.  Adverse events  Rate was 73.83% in the atomoxetine and 37.50 in the placebo group.  No serious adverse events in either group. |
| FDA-approved pharmacological | Eli Lilly, 2006248  N/A  ID: NCT00406354  RCT  Multicenter  N = 181  Germany  Setting: Specialty care | **Target:** Participants with ADHD and ODD, normal intelligence and able to swallow capsules  **Other:**  **ADHD presentation:** inattentive : 19.4,hyperactive : 5,combined : 75.6  **Diagnosis:** Confirmation by specialist  DSM-IV criteria by unknown source  **Comorbidity:** ODD  **Female:** 15.6 %  **Age mean:** 11.0 (3.01)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % Black/African American : 1  % White : 99 | **Intervention:** Atomoxetine 0.5 milligram per kilogram (mg/kg) daily dose taken orally for 1 week, then 1.2 mg/kg daily dose taken orally for 8 weeks  **Control:** Placebo  Matching placebo daily dose taken orally  **Comparator:** MedicationAtomoxetine Slow Titration arm: 0.5 mg/kg daily dose taken orally for 1 week, then 0.8 mg/kg daily dose taken orally for 1 week, then 1.2 mg/kg daily dose taken orally for 7 weeks  **Follow-up:** 2.25 months | Investigator-Rated Individual Target Behaviors (ITB-Inv): Intensity Score  Intervention and comparator performed better than control group (p=0.010).  CGI-S (Clinical Global Impressions - Severity) ADHD Score  Intervention and comparator performed better than control group (p<0.001).  ADHD Combined Score SNAP-IV (Swanson, Nolan & Pelham Rating Scale - Revised)  Intervention and comparator scored better than control group (p<0.001).  decreased appetite  Participants with non-serious adverse events  The rate was 80% for intervention, 54% for control and 70% for comparator. |
| FDA-approved pharmacological | Eli Lilly249  ID: NCT00568685  RCT  Multicenter  N = 153  Korea  Setting: N/A | **Target:** Patients with ADHD, based on the accepted criteria for that disease, must not have taken any medication used to treat ADHD for at least 2 weeks prior to study treatment, must be able to swallow capsules  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** No  **Comorbidity:** N/A  **Female:** 55.6 %  **Age mean:** 9.41 (1.64)  **Minimum age:** 6  **Maximum age:** 18  **Ethnicity:**  N/A | **Intervention:** Atomoxetine hydrochloride for 6 weeks total, 0.5 mg/kg/day orally in 2 divided doses for 7 days, then 0.8 mg/kg/day orally in 2 divided doses for 7 days, then 1.2 mg/kg/day orally in 2 divided doses for 28 days  **Control:** NA  **Comparator:** MedicationAtomoxetine 0.2 mg/kg/day orally in 2 divided doses for 6-weeks  **Follow-up:** 1.5 months | CGI-S (Clinical Global Impressions-ADHD Severity Scale) change  The intervention group had more improvement than comparator group (p=0.0048).  ADHD-RS-IV-Parent Total Score change  The intervention group had more improvement than comparator group (p=0.024).  No incidence of suicide or self-harm in either group.  Decreased appetite  Decreased appetite was more common in the high dose group.  Participants with reported adverse events  The rate was 56.25% in the higher dose compared to 29.41% in the lower dose.  8% irritability rate in high dose group, 4% in low dose group, 8% abdominal pain rate in high dose group, 0 in low dose group. |
| FDA-approved pharmacological | Findling, 2001271  ID: ID NA  RCT  Single center  N = 177  US  Setting: Specialty care | **Target:** Children and adolescents with ADHD  **Other:** Parents and teachers provided outcomes  **ADHD presentation:** inattentive : 46.9,hyperactive : 0,combined : 53.1  **Diagnosis:** Confirmation by specialist  a computerized version of the Diagnostic Interview Schedule for Children and clinical interviews with a psychologist and a psychiatrist  **Comorbidity:** N/A  **Female:** 29.4 %  **Age mean:**  Age mean by age group; <8 years 6.35, 8-10.99 years 9.47, 11-17.59 years 13.64  **Minimum age:** 4  **Maximum age:** 17  **Ethnicity:**  N/A | **Intervention:** Mixed amphetamine salts (Adderall), best dose (could be 5 mg, 10 mg or 15 mg per dose) for 4 weeks  **Control:** Placebo  Placebo in white gelatin capsules identical to the medication  **Comparator:** MedicationMethylphenidate (5 mg, 10 mg, or 15 mg per dose) twice per day (in the morning and at lunch)  **Follow-up:** 1 month | ASQ (Connors Abbreviated Symptoms Questionnaire), Parent and Teacher versions  Similar efficacy was observed between the medications.  Of the 195 youths who entered into this trial, 11 had their participation terminated because of adverse events. Dosage levels that led to discontinuation included placebo (n = 1), 5 mg (n = 3), 10 mg (n = 5), and 15 mg (n = 2). All youths who withdrew pre |
| FDA-approved pharmacological | Findling, 2008273  Noven Therapeutics, 2004964; Findling, 2009776; Findling, 2010773  ID: NCT00444574  RCT  Unclear/Not reported  N = 282  US  Setting: N/A | **Target:** Children who were diagnosed with ADHD according to DSM-IV-TR criteria (predominantly hyperactive/impulsive, inattentive, or combined type)  **Other:**  **ADHD presentation:** inattentive\_other : 11-26% across groups,hyperactive\_other : 1-2% across groups,combined\_other : 71-86% across groups  **Diagnosis:** Confirmation by specialist  inclusive who were diagnosed with ADHD according to Diagnostic and Statical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR)  **Comorbidity:** N/A  **Female:** 33.7 %  **Age mean:** 8.7 (1.94)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Methylphenidate transdermal system 10, 15, 20, or 30 mg/9 hours (dose-optimized) plus placebo capsule for 7 weeks  **Control:** Placebo  Placebo capsule plus placebo patch  **Comparator:** Medication18mg OROS capsules plus placebo patch for 5 weeks  **Follow-up:** 1.25 months | CPR-S-R (Connors Parent Rating Scale-Revised Short Form)  PGA (Parent Global Assessment) rated as improved  Compared with placebo, both active treatments showed significant improvements (p<0.0001).  ADHD-RS-IV  The average magnitude of changes from baseline was a 2-fold greater improvement in active treatments compared to placebo.  Compared with placebo, both active treatments showed significant improvements in ADHD-RS-IV scores (p<0.0001).  Decreased appetite  The rate of decreased appetite was 25.5% in the intervention, 18.7% in the OROS and 4.7% in the placebo group.  Participants with at least 1 adverse event  The rate was 75.5% for the intervention, 69.2% for the OROS, and 57.6% for the placebo group.  The majority of treatment-emergent adverse events were mild or moderate. |
| FDA-approved pharmacological | Findling, 2010272  ID: N/A  RCT  Multicenter  N = 217  US  Setting: Mixed | **Target:** Adolescent with diagnosis of ADHD according to DSM -IV-TR, total score of >=26 on the ADHD-Rating Scale-IV scale at baseline, IQ of >= 80; no conduct disorder or comorbid psychiatric illnesses that contraindicated treatment with methylphenidate transdermal system, history of cardiac problems, history of substance abuse, history of being nonresponsive to psychostimulant treatment; no clonidine, atomoxetine, antidepressants, sedatives, antipsychotics, anxiolytics, P450 enzyme altering agents, or other investigational medications within 30 days prior to screening  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  Schedule for Affective Disorders and Schizophrenia for School-Age Children– Present and Lifetime Version  **Comorbidity:** N/A  **Female:** 25.3 %  **Age mean:** 14.6 (1.3)  **Minimum age:** 13  **Maximum age:** 17  **Ethnicity:**  % Black/African American : 40  % American Indian or Alaska Native : .5  % Asian : .5  % White : 77  Other : Other: 3.7% | **Intervention:** Methylphenidate transdermal system, patches applied to hips once daily (alternatinghips each day), worn for 9 hours per day, titrated to an optimal dose (10,15,20,30 mg) of medication (week 1-5) followed by a 2-week maintenance period, for total of 7 weeks  **Control:** Placebo  Matching placebo  **Comparator:** NA  **Follow-up:** 2 months | CGI-I (Clinical Global Impressions-Improvement) very much improved or much improved  Intervention group had significantly more participants that improved compared to control group (p<0.001).  ADHD-RS-IV (ADHD Rating Scale-IV)  Intervention group had significantly more improvement compared to control group (p<0.001).  Decreased appetite  The rate was 25.5% in the intervention and 1.4% in the control group.  Participants with treatment-emergent adverse events during the study period  Adverse events were reported in 77.2% of intervention and 55.6% of placebo participants.  A total of three serious adverse events were reported by two participants, one in each treatment group discontinued from the study due to the events (two episodes of syncope,  both judged to be of moderate severity and related to study treatment by the inv |
| FDA-approved pharmacological | Findling, 2011270  Shire, 20081046  ID: NCT00735371  RCT  Multicenter  N = 314  US  Setting: N/A | **Target:** Children with ADHD; no conduct disorder or a comorbid psychiatric diagnosis requiring medication, a concurrent chronic/acute medical condition that might confound efficacy/safety assessments or pose a safety risk, history of seizures, tic disorder or family history of Tourette disorder, family history of sudden cardiac death or arrhythmia, abnormal thyroid function, glaucoma, or those considered a suicide risk; BMI not in 5th or 97th percentile for age and gender; no positive test on urine drug screen (except current stimulant therapy) or recent history of suspected substance abuse; no pregnant/lactating females, with clinically significant electrocardiogram findings, who required medications with central nervous system effects, with failure to respond to and/or intolerance of amphetamine therapy, and/or who were well controlled on current ADHD medication with acceptable safety and efficacy  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  ADHD-RS-IV  **Comorbidity:** N/A  **Female:** 29.7 %  **Age mean:** 14.6 (1.31)  **Minimum age:** 13  **Maximum age:** 17  **Ethnicity:**  % Hispanic or Latino : 14.8  % Black/African American : 14.8  % White : 79 | **Intervention:** Lisdexamfetamine dimesylate 70 mg/d for 4 weeks  **Control:** Placebo  Placebo for 4 weeks  **Comparator:** MedicationLisdexamfetamine dimesylate 30 mg/d for 4 weeks  **Follow-up:** 1 month | CGI-I (Clinical Global Impressions–Improvement) score of 1 or 2  A higher number of participants in the intervention and comparator groups were improved versus participants on placebo (p < 0.0001).  ADHD-RS-IV  A higher number of participants in the intervention and comparator groups were improved versus participants on placebo (p < 0.0001).  YQOL-R changes at endpoint scores for LDX groups versus placebo were not significant.  Decreased appetite  The rate was 37.2% in the 70mg, 37.2% in the 30mg, and 2.6% in the placebo group.  Participants with any treatment emergent adverse event  The rate was 71.8% in the 70mg, 65.4% in the 30mg, and 58.4% in the placebo group.  Commonly reported treatment emergent adverse events greater than or equal to 5% across all doses were decreased appetite, headache, insomnia, decreased weight, and irritability. |
| FDA-approved pharmacological | Fuentes, 2013281  Eli Lilly and Company, 2007754  ID: NCT00447278  RCT  Multicenter  N = 398  Multiple countries  Setting: Mixed | **Target:** Patients had to be pharmacologically naive for ADHD treatment  **Other:** Parents provided some outcomes  **ADHD presentation:** inattentive : 18.8,hyperactive : 2.8,combined : 78.4  **Diagnosis:** Confirmation by specialist  ADHD-RS-IV  **Comorbidity:** N/A  **Female:** 20.6 %  **Age mean:** 9.3 (2.60)  **Minimum age:** 6  **Maximum age:** 16  **Ethnicity:**  N/A | **Intervention:** Atomoxetine oral once or twice daily, starting dose 0.5 mg/kg per day increasing to recommended target dose of 1.2 mg/kg per day, not exceeding a maximum dose of 1.8 mg/kg per day for 12 months  **Control:** NA  **Comparator:** MedicationThe OEST group defined as any ADHD medication except ATX, including long- and short-acting MPH and antidepressants; allowed switching between different formulations of a specific medication, specific doses were not mandated in the study protocol, but inve  **Follow-up:** 12 months | Weiss Functional Impairment Rating Scale, Parent (WFIRS-P)  There was no significant difference between groups (p=0.166).  Significantly more patients of the ATX group reported fatigue (11.6% ATX vs 2.5% OEST; p= 0.001), somnolence (6.5% vs 1.0%; p = 0.006), and sedation (3.5% vs 0%; p = 0.015). In the OEST group, insomnia (12.6% OEST vs 2.0% ATX; p = 0.001) and irritability |
| FDA-approved pharmacological | Gard, 2014286  ID: CTRI/2011/08/001981  RCT  Single center  N = 84  India  Setting: Specialty care | **Target:** Children diagnosed with ADHD and have moderate to severe illness as assessed by Clinical Global Impressions Severity Scale  **Other:**  **ADHD presentation:** inattentive : 21.7,hyperactive : 8.7,combined : 69.6  **Diagnosis:** No  Not reported  **Comorbidity:** N/A  **Female:** 18.8 %  **Age mean:**  8.47 (2.22) for methylphenidate, 8.66 (2.44) for atomoxetine  **Minimum age:**  **Maximum age:**  **Ethnicity:**  N/A | **Intervention:** Atomoxetine 1.2 mg/kg/day, once or twice daily based on response and tolerability for 8 weeks  **Control:** NA  **Comparator:** MedicationMethylphenidate (immediate release) 1 mg/kg/day  **Follow-up:** 2 months | Clinical Global Impressions Severity Scale (CGI-S)  Scores significantly improved for both groups, but there was no statistically significant difference between the groups (p=0.997).  VADPRS (Vanderbilt ADHD Diagnostic Parent Rating Scale)  Scores significantly improved for both groups, but there was no statistically significant difference between the two groups (p=0.500) in the parent or the teacher ratings.  Decreased appetite  Rate 33.3% in the atomoxetine, 43.8% in the methylphenidate group.  Side effects  56% in the atomoxetine group developed side effects, 55% of the methylphenidate group (n.s.).  3 patients in each group dropped out due to adverse events. |
| FDA-approved pharmacological | Gau, 2006289  ID: N/A  RCT  Single center  N = 64  Taiwan  Setting: Mixed | **Target:** Participants with diagnosis of ADHD, taking MPH on a total daily dose of 10-40 mg for the past 3 months; no significant gastrointestinal problems, a history of hypertension, known hypersensitivity to MPH, a co-existing medical condition or concurrent medication likely to interfere with the safe administration of MPH, glaucoma, Tourette’s Syndrome, an active seizure disorder, a psychotic disorder, or girls who had reached menarche  **Other:** Parents were also asked questions about the treatment and usage of ADHD within their children, but were not actively experimented on.  **ADHD presentation:** inattentive : 18.8,hyperactive : 3.1,combined : 78.1  **Diagnosis:** Confirmation by specialist  Chinese Kiddie-Schedule for Affective Disorders and Schizophrenia  **Comorbidity:** N/A  **Female:** 9.4 %  **Age mean:** 10.5 (3.2)  **Minimum age:** 6  **Maximum age:** 13  **Ethnicity:**  N/A : Taiwanese children | **Intervention:** Methylphenidate OROS (Osmotic Release Oral System) with the treatment doses 18 mg or 36mg once daily for 28 days  **Control:** NA  **Comparator:** MedicationInstant release MPH at two different doses (5/10 mg/day)  **Follow-up:** 1 month | CGI-I rating of 1 or 2  The OROS-MPH group had a significantly greater proportion of subjects being very much or much improved in the CGI-I scale than the IR MPH group (p = 0.014).  ADHD Index Score Conner’s Teacher Rating Scale-Revised: Short Form-C change  Compared to the IR MPH group, the OROS MPH group showed a significantly greater slope of reductions in ADHD symptoms.  SKAMP (Chinese Version of the Swanson, Kotin, Agler, M-Flynn, and Pelham Rating Scale) Attention score mean change (SD) from baseline at endpoint  Difference in SKAMP Attention score mean change (SD) from baseline between OROS and IR MPH groups is statistically significant (p < 0.01). Difference in SKAMP Deportment score mean change (SD) from baseline between OROS (-4.65 SD 5.53) and IR (-4.41 SD 6.  Decreased appetite  The rate of decreased appetite was 46.9% in the OROS and 59.4% in the immediate release group (p=0.316).  There was no difference in the rates of side effects between the two groups. |
| FDA-approved pharmacological | Gau, 2007288  ID: N/A  RCT  Multicenter  N = 106  Taiwan  Setting: Other | **Target:** Children with ADHD, no ADHD treatment medication, or completion of the washout procedures before entering this study; did not weigh less than 20 kg or more than 60 kg; no serious medical illness, history of bipolar I or II disorder, psychosis, pervasive developmental disorder, anxiety disorder, history of any seizure disorder or prior EEG abnormalities related to epilepsy, or taking anticonvulsants for seizure control, history of alcohol or drug abuse within the past 3 months, or if they might have to use psychoactive medications  **Other:**  **ADHD presentation:** inattentive : 27,combined : 73  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 11 %  **Age mean:**  Atomoxetine 9.1 (2.0), placebo 9.5 (2.4)  **Minimum age:** 6  **Maximum age:** 16  **Ethnicity:**  N/A | **Intervention:** Atomoxetine once daily in the morning, maximal dose of 1.8 mg/kg per day, for 6 weeks  **Control:** Placebo  Placebo once daily in the morning  **Comparator:** NA  **Follow-up:** 1.5 months | CGI-S (Clinical Global Impressions–ADHD–Severity)  Scores significantly decreased (mildly ill to moderately ill) for the atomoxetine group and (moderately ill to markedly ill) for the placebo group (p<0.001).  ADHD-RS-IV (ADHD Rating Scale-IV Parents Version: Investigator Administered and Scored) total score change  Mean total scores were significantly lower for the atomoxetine than placebo group (p<0.001).  Decreased appetite  The rate was 36.1% in the intervention compared to 17.4% in the control group.  There was no other significant difference between the two treatment groups in the occurrence of adverse events other than decreased appetite, and no drug-related severe adverse event was reported. |
| FDA-approved pharmacological | Geller, 2007292  ID: N/A  RCT  Multicenter  N = 176  US  Setting: Specialty care | **Target:** Children with ADHD according to DSM-IV and separation anxiety disorder, generalized anxiety disorder, or social phobia  **Other:** Parents or legal representatives  **ADHD presentation:** inattentive : 23.0,hyperactive : 1.2,combined : 75.9  **Diagnosis:** Confirmation by specialist  Used the DSM-IV standard. "ADHD diagnoses were confirmed clinically, and anxiety and ADHD diagnoses were confirmed using the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version (K-SADS-PL; Univers  **Comorbidity:** Mood disorder  **Female:** 37.9 %  **Age mean:**  Intervention 12.2 (2.8), placebo 11.8 (2.5)  **Minimum age:** 8  **Maximum age:** 17  **Ethnicity:**  Other : intervention 79% white, control 82% | **Intervention:** Atomoxetine 0.8-1.8 mg/kg/day divided into two doses daily for 12 weeks  **Control:** Placebo  Placebo has the same measurements as the treatment dosage  **Comparator:** NA  **Follow-up:** 3 months | CGI (Clinical Global Impression - Severity of Illness) change  CGI results indicated overall symptom improvement.  ADHD-RS-IV-P (Attention-Deficit/Hyperactivity Disorder Rating Scale-IV Parent Version)  The mean change scores showed greater improvement with atomoxetine relative to placebo (p<0.001).  Significant reduction in Multidimensional Anxiety Scale for Children (p 0.009).  Decreased appetite  Statistically significant decreased appetite associated with the intervention (p=0.025).  No statistically significant difference in incidence of headache, upper abdominal pain, vomiting, irritability, nasopharyngitis, nausea, cough, influenza, sinusitis across groups. |
| FDA-approved pharmacological | Greenhill, 2006305  ID: ID NA  RCT  Multicenter  N = 103  US  Setting: Mixed | **Target:** Children and adolescents with ADHD, attending school in a classroom setting with the same teacher for the duration of the study; no significant abnormalities in vital signs, physical examinations, or laboratory tests, no history of seizures or use of anticonvulsant medication, comorbid psychiatric conditions, any medical condition that could interfere with study participation or assessments or that may pose a danger with administration of methylphenidate, psychotropic medications, initiated psychotherapy within the past 3 months, positive urine drug screen or history of poor response or intolerance to methylphenidate  **Other:** Teachers and parents provided outcomes  **ADHD presentation:** inattentive : 21.4,hyperactive : 1.9,combined : 76.7  **Diagnosis:** Confirmation by specialist  DSM IV per Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version)  **Comorbidity:** N/A  **Female:** 35.9 %  **Age mean:**  Intervention 9.76 (2.75), placebo 10.4 (2.70)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % Black/African American : 23.3  % White : 60.2  Other : 16.5% other | **Intervention:** Dexmethylphenidate extended release, dose finding phase, 5, 10, 15, 20, or 30 mg/day once daily for 2 weeks, 7 weeks total  **Control:** Placebo  Placebo pills once daily  **Comparator:** NA  **Follow-up:** 2 months | Clinical Global Impressions - Improvement (CGI-I), number much improved or very much improved  Significantly more medication group participants improved.  Conners ADHD/DSM-IV Scale-Teacher version total score  Statistically significant difference between groups favoring medication (p<0.001), effect size 0.79.  Decreased appetite, number with  The rate of decreased appetite was 30.2% in the intervention and 8.5% in the control group (p = 0.007)  Participants with at least one adverse event reported  The rate was 75.5% in the intervention and 57% in the placebo group; difference not statistically significant  There were no deaths or serious adverse events |
| FDA-approved pharmacological | Griffiths, 2018306  ID: ANZCTR 12607000535471  Crossover trial  Multicenter  N = 136  Australia  Setting: School | **Target:** Participants with ADHD, no current stimulant use, no contraindications to atomoxetine, no substance or alcohol abuse  **Other:**  **ADHD presentation:** inattentive : 45,hyperactive : 4,combined : 67  **Diagnosis:** Confirmation by specialist  Patients were evaluated at the beginning of the study using the DSM-IV criteria  **Comorbidity:** N/A  **Female:** 20 %  **Age mean:** 11.29 (2.5)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  N/A | **Intervention:** Atomoxetine dose based on body mass as per prescribing guidelines (mean dose was 1.35 mg.kg−1; range 1.0–1.4 mg.kg−1) taken daily for 6 weeks  **Control:** Placebo  Placebo, both groups switched and were evaluated again  **Comparator:** NA  **Follow-up:** 1.5 months | ADHD-RS  Atomoxetine resulted in significant improvement of response inhibition (p<0.001) and fear identification (p<0.04), but not for sustained attention (p<0.06). The treatment improved ADHD symptoms (p<0.001) as well as anxiety symptoms (p<0.043).  Atomoxetine significantly improved response inhibition, assessed using the Go-NoGo test (p<0.001; effect size 0.42). Atomoxetine was associated with significantly reduced symptom severity for anxiety (p=0.043). |
| FDA-approved pharmacological | Harfterkamp, 2012317  ID: NCT00380692  RCT  Multicenter  N = 97  Netherlands  Setting: Specialty care | **Target:** Children and adolescents dually diagnosed with autism spectrum disorders and ADHD  **Other:** Teachers provided some outcomes  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM IV\_TR  **Comorbidity:** Autism  **Female:** 14.4 %  **Age mean:** 9.9 (10.8)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % Black/African American : 1.0  % White : 99.9 | **Intervention:** Atomoxetine titrated in 3 weeks to a fixed once daily dose of 1.2 mg/kg for 8 weeks  **Control:** Placebo  Placebo capsules identical to medication  **Comparator:** NA  **Follow-up:** 2 months | CGI-ADHD-I, number classified as much or very much improved  Total ADHD score was not statistically difference between groups (p = 0.077); difference in those categorized as improved was not significant (p= 0.14).  Decreased appetite  The rate was 27.1% in the atomoxetine and 6.1% in the placebo group.  At least one adverse event  The rate was 81.3% in the intervention vs 653% in the placebo group.  None of the patients had a serious adverse event. |
| FDA-approved pharmacological | Hazell, 2003321  ID: NA  RCT  Unclear/Not reported  N = 67  Australia  Setting: N/A | **Target:** Children with diagnosis of ADHD and comorbid Oppositional Defiant Disorder or Conduct Disorder based on DSM-IV, T scores for Attention problems and Aggressive behavior on the Child Behavior Checklist of ≥70, who had been treated for a minimum of 3 months with methylphenidate or dexamphetamine, IQ at least 70  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  ADHD Rating Scale, assessment interviews by a qualified health professional  **Comorbidity:** ODD  **Female:** 8.96 %  **Age mean:**  112.9 (19.8) and 125.4 (23.2)  **Minimum age:** 6  **Maximum age:** 14  **Ethnicity:**  N/A | **Intervention:** Clonidine added to ongoing psychostimulant therapy (either methylphenidate or dexamphetamine), 0.05 to 0.10 mg morning and evening for 6 weeks  **Control:** Placebo  Placebo syrup added to ongoing psychostimulant therapy, 0.05 mg during week 1; if the child is not experiencing daytime sedation or symptomatic hypotension at end of Week 1, dosage of placebo increased to 0.10 mg morning and evening for 5 more weeks; if  **Comparator:** NA  **Follow-up:** 1.5 months | Parent report conduct symptoms  Number of patients achieving 38% reduction from baseline in conduct symptoms  Results favored clonidine (p<0.01).  Hyperactive index, parent report  Number achieving 43% reduction from baseline  There was no statistically significant difference between the groups (p = .16)  A significant difference in Parent report conduct symptoms—no. achieving 38% reduction from baseline (p<.01)  A significant difference in Parent report conduct symptoms—no. achi  Mean height  There were no statistically significant differences between groups.  Transient increase in side effects in the clonidine-treated group compared with the control group for drowsiness and dizziness. |
| FDA-approved pharmacological | Hervas, 2014326  ID: n/a  RCT  Multicenter  N = 338  Multiple countries  Setting: N/A | **Target:** Male and female children/adolescents with a diagnosis of ADHD of at least severity by a baseline ADHD-Rating Scale-IV with a total score of 32 or higher and a minimum Clinical Global Impression Severity score of 4; intellectual functioning, blood pressure measurements within the 95th percentile for age, sex and height; and the ability to swallow tablets or capsules  **Other:** Parent/legal guardian had to be willing, able and likely to fully comply with the study procedures and restrictions  **ADHD presentation:** inattentive : 10.7,hyperactive : 4.1,combined : 84.9  **Diagnosis:** No  **Comorbidity:** N/A  **Female:** 25 %  **Age mean:** 10.8 (2.8)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  N/A | **Intervention:** Guanfacine (extended release), dose-optimized taken once daily in the morning for 6 weeks  **Control:** Placebo  Placebo tablets provided taken once daily, at a similar time, each morning for 6 weeks  **Comparator:** MedicationAtomoxetine capsules for 6 weeks  **Follow-up:** 2.25 months | Patients showing an improvement (CGI-I, very much improved or much improved)  Compared with placebo, the difference in the percentage of patients showing improvement was significant for guanfacine (p<0.001) and atomoxetine (p 0.024).  ADHD-RS-IV  The change from baseline was greater for guanfacine and atomoxetine compared with placebo.  Decreased appetite  The rate was 13.2% in the guanfacine, 27.7% in the atomoxetine, and 10.8% in the placebo group.  Treatment-emergent adverse events  The rate was 77.2% in the guanfacine, 67.9% in the atomoxetine, and 65.8% in the placebo group.  Three (1.1%) serious adverse events were reported: one in the placebo group (syncope [considered treatment related]) and two in the guanfacine group (syncope [considered treatment related] and appendicitis [occurred prior to randomization and not treatmen |
| FDA-approved pharmacological | Ichikawa, 2020337  Ichikawa, 2020848  ID: NA  RCT  Multicenter  N = 76  Japan  Setting: N/A | **Target:** Children with ADHD per DSM-V; ADHD Rating Scale-IV total score>=28; without serious disorders of the blood or bone marrow, heart, kidneys, liver, lungs; psychiatric comorbidity (e.g., bipolar disorder, schizophrenia); Conduct Disorder (excluding Oppositional Defiant Disorder); current tics; history of seizures; low or high bodyweight; hypertension; QTc interval (Fridericia adjusted; QTcF) >430 mseconds; substance use disorder; and pregnancy or lactation  **Other:**  **ADHD presentation:** inattentive : 2.6,hyperactive : 34.2,combined : 63.2  **Diagnosis:** Confirmation by specialist  DSM V plus ADHD-RS-IV  **Comorbidity:** N/A  **Female:** 17.1 %  **Age mean:** 10.0 (2.8)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  N/A | **Intervention:** Lisdexamfetamine, 70 mg/day for 4 weeks, 1 week placebo, and 1 week of follow-up  **Control:** Placebo  Placebo pill  **Comparator:** MedicationLisdexamfetamine 30 mg/day for 4 weeks  **Follow-up:** 1 month | ADHD-RS-IV total score, parent, change from baseline  All dosages had significantly greater improvements from baseline to all time points than placebo (p<0.0001).  Participants with any adverse event  The rate was 70% for intervention, 42% for control, and 68% for comparator. |
| FDA-approved pharmacological | Jain, 2011341  Addrenex Pharmaceuticals, 2007653  ID: NCT00556959  RCT  Multicenter  N = 236  US  Setting: N/A | **Target:** Patients with a diagnosis of ADHD of the hyperactive or combined inattentive/hyperactive subtype, minimum score of 26 on the ADHD Rating Scale–IV, good health, be able to swallow tablets, be mentally competent, having a body mass index of at least the fifth percentile for the patients’ age group, and having concomitant diagnosis of tics or oppositional defiant disorder eligible; no clinically significant illness or abnormality that would increase the safety risk of clonidine or if they had a clinically significant abnormality on electrocardiographic readings that were interpreted by a single entity, having a concomitant diagnosis or history of a psychiatric disorder that required psychotropic medication, and having a history of conduct disorders, syncopal episodes, or seizures  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 28 %  **Age mean:**  9.4 (6–16), 9.6 (6–17) , 9.4 (6–17)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % Hispanic or Latino : 8  % Black/African American : 27  % White : 59 | **Intervention:** Clonidine hydrochloride extended release tablets of 0.4 mg/day: dose-escalating titration schedule of 0.1 mg/day per week to achieve the target dose for the patient (i.e., 0.2 mg/day at week 2 or 0.4 mg/day at week 4), followed by dose tapering in 0.1-mg/day/week intervals until cessation of treatment at the end of week 8  **Control:** Placebo  Placebo for 8 weeks followed the same procedure as the intervention group  **Comparator:** MedicationClonidine hydrochloride extended release 0.2 mg/day, forced dose-escalating titration schedule of 0.1 mg/day per week to achieve the target dose for the patient (i.e., 0.2 mg/day at week 2 or 0.4 mg/day at week 4), followed by dose tapering in 0.1-mg/day/  **Follow-up:** 2 months | Clinical Global Impression of Improvement (CGI-I)  Significant improvement in both treatment groups versus placebo (p=0.0032).  ADHD-RS-IV  Statistically significant improvements in the intervention groups compared to control.  Participants that reported an adverse event  83% of both intervention groups and 72% of placebo patients reported an adverse event.  Adverse events that led to discontinuation occurred in 1% of patients in the placebo group, 7% of patients in the 0.2-mg/day group, and 19% in the 0.4-mg/day group. The most common reasons for discontinuation were somnolence and fatigue. |
| FDA-approved pharmacological | Johnson, 2020348  Supernus Pharmaceuticals, 20161095  ID: NCT02633527  RCT  Multicenter  N = 234  US  Setting: Mixed | **Target:** Children with ADHD per the DSM, medically healthy ,free of ADHD medication for at least 1 week prior to baseline, no history or presence of neuropsychiatric disease other than ADHD as the primary diagnosis, no history or presence of systemic diseases or other neurologic or psychiatric diseases, no history of suicidal attempt or ideation 6 months prior to screening or at screening  **Other:**  **ADHD presentation:** inattentive\_other : placebo 21.9 (4.7); 100mg/day: 22.1 (3.9); 200mg/day: 22.2 (3.6); 300mg/day 21.8 (3.8); 400mg/day: 21.0 (4.7),hyperactive\_other : hyperactive/impulsivity mean(sd) for 4 groups: placebo: 20.5 (4.4); 100mg/day: 20.3 (5.2); 200mg/day: 21.  **Diagnosis:** Confirmation by specialist  MINI-KID  **Comorbidity:** N/A  **Female:** 33 %  **Age mean:**  Median 9.0 across all groups except 100mg group (median 8.0 years)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % Black/African American : 38.3  % American Indian or Alaska Native : 0.97  % Asian : 0.97  % White : 56.8  % Multiracial : 2.43 | **Intervention:** Viloxazine (SPN-812) , 400 mg/day of extended-release viloxazine for 8 weeks  **Control:** Placebo  Placebo titrated for the same period as the highest dose group  **Comparator:** MedicationViloxazine (SPN-812), 100 mg/day of extended-release viloxazine for 8 weeks  **Follow-up:** 2 months | CGI-I  Intervention scores but not comparator scores improved significantly compared to control (p<0.05).  ADHD-RS-IV responders  Percent responders were 68.2% in 400mg group, 60% in 100mg group, and 45.8% in placebo.  Decreased Appetite Adverse Event  All groups had at least one participant experience decreased appetite as an adverse event.  No deaths or serious treatment emergent adverse events were reported at any point during the study. |
| FDA-approved pharmacological | Kelsey, 2004361  ID: ID NA  RCT  Multicenter  N = 197  US  Setting: N/A | **Target:** Children with ADHD; serious medical illness, a history of psychosis, or bipolar disorder were excluded  **Other:** Parents provided some outcomes  **ADHD presentation:** inattentive : 27.4,hyperactive : 3.6,combined : 69.0  **Diagnosis:** Confirmation by specialist  DSM IV per Kiddie Schedule for Affective Disorders and Schizophrenia for School-Aged Children-Present and Lifetime Version  **Comorbidity:** N/A  **Female:** 29.4 %  **Age mean:** 9.5 (1.8)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % White : 72.6 | **Intervention:** Atomoxetine once per day in the morning (max 1.8 mg/kg per day, 120mg per day) for 8 weeks  **Control:** Placebo  Placebo once per day in the morning, for 8 weeks  **Comparator:** NA  **Follow-up:** 2 months | Conners' Global Index, Parent  Significantly greater improvement in atomoxetine group.  ADHD RS, parent  ADHD RS, at least 25% re­duction from baseline  Significantly greater improvement in atomoxetine group (62.7% vs 33.3%, p<0.001).  Decreased appetite  A significantly greater proportion of amoxetine patients experienced decreased appetite (17.6% vs 6.3%).  4.5% of atomoxetine and 1.6% of placebo patients discontinued as the result of adverse events. |
| FDA-approved pharmacological | Kollins, 2011374  Shire, 20051055  ID: NCT00150592  RCT  Multicenter  N = 182  US  Setting: N/A | **Target:** Participants without any current comorbid psychiatric diagnosis (except oppositional defiant disorder), weight <25 kg (55 lb), cardiac conditions that might have increased the safety risk to the subject, or a Pediatric Daytime Sleepiness Scale score 22 at screening and/or baseline  **Other:**  **ADHD presentation:** inattentive : 23.6,hyperactive : 1.7,combined : 74.7  **Diagnosis:** Confirmation by specialist  DSM-IV-TR  **Comorbidity:** N/A  **Female:** 30.3 %  **Age mean:** 12.6 (2.81)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % Hispanic or Latino : 12.4  % Black/African American : 16.3  % White : 66.9 | **Intervention:** Guanfacine extended release, optimal dose (1, 2, or 3mg/day) found in 3 week dose-findingphase, maintained for 2 weeks of maintenance; total duration of 5 weeks  **Control:** Placebo  Matching placebo  **Comparator:** NA  **Follow-up:** 2.5 months | CGI-I scale much improved or very much improved  A significantly greater percentage in the intervention group was rated ‘much improved’ or ‘very much improved’ compared with placebo (p<0.007).  ADHD-RS-IV total scores  Reductions were significantly greater in the intervention than in the placebo group (p< 0.001).  Reaction time as measured by the Choice Reaction Time (CRT) test indicated that treatment did not impair psychomotor functioning or alertness compared with placebo.  Participants with treatment emergent adverse events reported  Rate was 79.3% in intervention, 70.2% in placebo group.  The majority of adverse events were mild to moderate; there were 2 serious events severe asthma and moderate loss of consciousness (neither was judged to be related to GXR). |
| FDA-approved pharmacological | Kollins, 2011373  Addrenex Pharmaceuticals, Inc., 2008654  ID: NCT00641329  RCT  Multicenter  N = 198  US  Setting: N/A | **Target:** Children with inadequate stimulant medication response, total score 26 on the ADHD-Rating Scale-IV questionnaire after a minimum of 4 weeks on a stable stimulant regimen, estimated IQ to be 80, BMI in the 5th percentile for the patient’s gender and age; no current diagnosis or history of a psychiatric disorder that required psychotropic medication or severe comorbid Axis I or Axis II disorder, history of conduct disorder, history of syncopal episodes or seizures (except for febrile seizures), current or past drug abuse, history of clonidine intolerance, or used any investigational drug within 30 days of the study initiation or had a positive drug test (except for ADHD medication)  **Other:** Parents provided some outcomes  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 26 %  **Age mean:**  Intervention 10.4 (2.5), control 10.5 (2.5)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % Hispanic or Latino : 11  % Black/African American : 27  % White : 54  Other : 8 | **Intervention:** Clonidine hydrochloride extended-release tablets plus stimulant (methylphenidateor amphetamine): total daily doses of 0.1 to 0.4 mg per day, concomitant stimulant medication was prescribed by the patient’s regular physician and was obtained from the patient’s usual pharmacy, for duration of 8 weeks  **Control:** Placebo  Placebo plus stimulants for 8 weeks; methylphenidate or amphetamine prescribed by the patient’s regular physician and was obtained from the patient’s usual pharmacy  **Comparator:** NA  **Follow-up:** 1.25 months | CGI-I change from baseline  Intervention group had greater improvement than the control group (p=0.006).  ADHD-RS-IV (ADHD Rating Scale IV), change  Intervention group had greater improvement than the control group (p=0.009).  Participants with at least one treatment emergent adverse event  Rate was 45% in the intervention and 41% in the concomitant placebo group. Statistical significance not reported.  Somnolence, headache, fatigue, upper abdominal pain, and nasal congestion were the most commonly reported event in the CLON-XR plus stimulant group. Of the 96 patients in the placebo plus stimulant group, 3 (3%) discontinued because of TEAEs (ie, increase |
| FDA-approved pharmacological | Kratochvil, 2002376  ID: NA  RCT  Multicenter  N = 228  US  Setting: N/A | **Target:** Participants that were not girls older than 9 years or had history of bipolar or psychotic disorders, motor tics or a family history of Tourette syndrome, substance abuse, nonresponse to a previous trial of methylphenidate, and serious medical illness  **Other:**  **ADHD presentation:** inattentive : 23,hyperactive : 1,combined : 76  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 7 %  **Age mean:** 10.4 (2.1)  **Minimum age:** 7  **Maximum age:** 15  **Ethnicity:**  % White : 77 | **Intervention:** Atomoxetine 1-2 mg/kg per day administered as a divided dose in the morning and late afternoon for 10 weeks  **Control:** NA  **Comparator:** MedicationMethylphenidate was dosed beginning at 5 mg from one to three times daily with an ascending dose titration based on the investigator’s assessment of clinical response and tolerability, total daily dose was not to exceed 60 mg, concomitant use of other psy  **Follow-up:** 2.5 months | CGI ADHD Severity  Both groups improved.  ADHD-RS-IV  No statistically significant differences between treatment groups (p = .66).  Weight loss  The rate of weigh loss was 2.7% in the atomoxetine and 5% in the methylphenidate group (p=0.611).  Both atomoxetine and methylphenidate were well tolerated, with no statistically significant differences in discontinuations due to adverse events (atomoxetine 5.4%, methylphenidate 11.4%; p=.18); all atomoxetine patients who discontinued due to an adverse |
| FDA-approved pharmacological | Kratochvil, 2011378  University of Nebraska, 20071133  ID: NCT00561340  RCT  Unclear/Not reported  N = 101  US  Setting: Other | **Target:** Young children with ADHD; no concurrent use of psychotropic or other medications with significant central nervous system effects, current effective treatment with atomoxetine, medical contraindication to atomoxetine, current diagnosis of adjustment disorder, autism, psychosis, bipolar disorder, or significant suicidality, history of abuse that may confound symptoms of ADHD, and failure to respond to an adequate previous trial of atomoxetine  **Other:**  **ADHD presentation:** inattentive : 8,hyperactive : 9,combined : 82  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 32 %  **Age mean:**  Placebo 6.1 (0.5) , Atomoxetine 6.1 (0.6)  **Minimum age:** 5  **Maximum age:** 6  **Ethnicity:**  % Black/African American : 1  % Native Hawaiian or Pacific Islander : 3  % White : 86 | **Intervention:** Atomoxetine 0.5-1.8 mg/kg per day for 8 weeks  **Control:** Placebo  Placebo controlled  **Comparator:** NA  **Follow-up:** 2 months | CGI-I scores of very much improved or much improved rate  40% of atomoxetine and 22% of placebo participants had CGI-I scores of 1 (very much improved) or 2 (much improved) relative to baseline, which was not a significant difference after adjustment for age and study center (p = .1). A total of 62% of subjects  ADHD-RS total score, parent  Significant mean decreases in parent (P = .009) and teacher (P = .02) ADHD–IV Rating Scale scores with atomoxetine compared with placebo.  Decreased appetite  The rate was 30% in the intervention compared to 8% in the placebo group.  There were no significant differences in the mean change in systolic blood pressure with atomoxetine treatment compared with placebo (p=.09) , in the change in diastolic blood pressure (p=.8), or heart rate (p=.07) with atomoxetine. There was a significan |
| FDA-approved pharmacological | Kurowski, 2019383  Childrens Hospital Medical Center, Cincinnati, 2013709  ID: NCT01933217  Crossover trial  Single center  N = 26  US  Setting: Specialty care | **Target:** Children with hospital admission for blunt head trauma and confirmed diagnosis of moderate to severe traumatic brain injury (Glasgow Coma Scale≤ 8); at least 6 of 9 current symptoms on at least one subscale of the Vanderbilt Attention Deficit Hyperactivity Disorder Parent Diagnostic Rating Scale; no preinjury diagnoses of developmental or neurological disorders, hospitalization for psychiatric reasons in the past 12 months; not involved in active behavioral and/or medication treatments for attention problems and/or who had contraindications to methylphenidate use or were on medications that had potentially severe interactions with methylphenidate  **Other:**  **ADHD presentation:** inattentive : 69.2,hyperactive : 7.7,combined : 23.1,N/A  **Diagnosis:** Confirmation by specialist  K-SADS-P/L  **Comorbidity:** Other : Traumatic brain injury  **Female:** 23.1 %  **Age mean:** 11.5 (2.8)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % White : 73.1 | **Intervention:** Methylphenidate long-acting (Concerta), initial dose of 18 mg, subsequent 3 weeks, titrated based on response and side effects for week 4; <25kg = 18mg (low), 27mg (medium), and 36mg (high) dosages, 25kg = 18mg (low), 36mg (medium), 54mg (high) dosages; total duration of 4 weeks  **Control:** Placebo  Identical capsules filled with placebo (inert white capsules) for 4 weeks, then switching to the intervention drug  **Comparator:** NA  **Follow-up:** 2 months | ADHD total symptom score VADPRS (Vanderbilt ADHD Parent Diagnostic Rating Scale)  On optimal dose of medication, greater reductions were found for the medicated condition than for placebo (p 0.022, effect size 0.59).  Mean number of participants with change in appetite side effect  Compared to the placebo condition, the medication condition was associated with lower weight at the second, third, and fourth week (p<.0001).  Methylphenidate was associated with weight loss (~ 1 kg), increased systolic blood pressure (~3–6 point increase), and mild reported changes in appetite versus the placebo condition. At the last visit, suicidal ideation was reported by one participant whi |
| FDA-approved pharmacological | Law, 1999387  ID: ID NA  RCT  Single center  N = 91  Canada  Setting: Other | **Target:** Children with pervasive ADHD, estimated IQ greater than 80, no primary anxiety or affective disorder; no history of prior treatment for ADHD or tics, severe motor or vocal tic disorder or Tourette's disorder, regularly received medication for a medical problem, had a chronic medical condition, or attended a full time residential or day treatment program  **Other:** Parents, teachers, and research assistants; research assistants were trained to achieve high consistency in measurements of tics under supervision of study psychiatrist  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-III-R  **Comorbidity:** N/A  **Female:** 18.68 %  **Age mean:**  MPH group 8.4 (1.6), Placebo group 8.3 (1.5)  **Minimum age:**  **Maximum age:**  **Ethnicity:**  N/A | **Intervention:** Methylphenidate (immediate release) 0.7mg/kg twice daily for 1 year  **Control:** Placebo  Placebo  **Comparator:** NA  **Follow-up:** 12 months | Onset or worsening severity of tics: clinically significant tics developed in 19.6% of the subjects without preexisting tics receiving MPH and in 16.7% of those receiving the placebo (p 0.59); deterioration of tics was observed in 33% of subjects with pre |
| FDA-approved pharmacological | Lilly, 2008250  ID: NCT00760747  RCT  Multicenter  N = 112  Multiple countries  Setting: Mixed | **Target:** Children 6-16 years old who meet DSM-IV diagnostic criteria for ADHD and unsatisfactory symptom response to stimulant therapy or experience of adverse events while on stimulant therapy; no previous participation in an atomoxetine study and not taking anticonvulsants, antihypertensive agents, medication with sympathomimetic activity, psychotropic medications, monoamine oxidase inhibitor  **Other:**  **ADHD presentation:** inattentive : 28.2,hyperactive : 3.6,combined : 66.7,combined\_other : Not categorized: 1/111  **Diagnosis:** No  Not mentioned  **Comorbidity:** N/A  **Female:** 16.2 %  **Age mean:** 11.5 (2.38)  **Minimum age:** 6  **Maximum age:** 16  **Ethnicity:**  % Hispanic or Latino : 18,9  % Black/African American : 0.9  % White : 80.2 | **Intervention:** Slow switching group (switch from full stimulant dose to atomoxetine, 1.2 mg/kg/day, orally, during 10 weeks then continue treatment up to 1.8 mg/kg/day, to 14 weeks  **Control:** NA  **Comparator:** MedicationFast switching group (switch from full stimulant dose to atomoxetine 1.2 mg/kg/day, PO, during 2 weeks then continue treatment up to 1.8 mg/kg/day, PO to 14 weeks  **Follow-up:** 2.5 months | CGI-S (Clinical Global Impression Severity) rating scale change  There was no significant difference between groups (p=0.898).  ADHD-RS-IV (Attention Deficit Hyperactivity Disorder-Rating Scale) Parent Version change  There was no significant difference between groups (p=0.692).  Treatment Satisfaction Preference  Serious adverse events  The rate was 1.8% in the intervention group and 1.9% for comparator group. |
| FDA-approved pharmacological | Martenyi, 2010414  Eli Lilly and Company, 2004751  ID: NCT00386581  RCT  Multicenter  N = 105  Russia  Setting: N/A | **Target:** Participants with a DSM-IV diagnosis of ADHD, a minimum score of 25 for boys and 22 for girls, or > 12 for their diagnostic subtype on the Attention-Deficit/Hyperactivity Disorder Rating Scale-IV-Parent Version: Investigator-Administered and Scored, score of >= 4 on Clinical Global Impressions-ADHD Severity scale, had not taken any medications for ADHD; excluded weight <20 kg or >60 kg, history of bipolar disorder, anxiety disorder, psychosis, developmental disorder, or suicidal  **Other:**  **ADHD presentation:** inattentive : 22.9,hyperactive : 4.8,combined : 72.4  **Diagnosis:** Confirmation by specialist  Kiddie Schedule for Affective Disorders and Schizophrenia for School-aged Children-Present and Lifetime Version (K-SADS-PL)  **Comorbidity:** N/A  **Female:** 14.3 %  **Age mean:** 9.8 (2.8)  **Minimum age:** 6  **Maximum age:** 16  **Ethnicity:**  % White : 100 | **Intervention:** Atomoxetine 1.2 mg/(kg/day) as a single dose in the morning for 6 weeks  **Control:** Placebo  Identical placebo treatment  **Comparator:** NA  **Follow-up:** 1.5 months | CGI-ADHD-S (Clinical Global Impression-ADHD-Severity) change  The intervention group had significantly more improved scores compared to control group (p=0.035).  ADHD-RS-IV (Attention-Deficit/Hyperactivity Disorder Rating Scale-IV-Parent Version) change  The intervention group had significantly more improved scores compared to control group (p=0.013).  Weight loss  Rate was 8.3 in the intervention group with none in placebo.  Treatment emergent signs and symptoms  Rate was 41.9% in the intervention and 33.3% in the control group.  No serious adverse events (including deaths or suicidal ideation) were reported in either treatment group. One patient (in the atomoxetine group) discontinued the study due to an adverse event (mild skin itch and eruptions). |
| FDA-approved pharmacological | Matthijssen, 2019418  ID: 5252 Dutch trial registry  RCT  Multicenter  N = 94  Netherlands  Setting: Mixed | **Target:** Children using methylphenidate as prescribed in clinical practice in any dosage or form for 2 years or longer; if the period of not using methylphenidate had not exceeded 2 continuous months during the past 2 years  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  ADHD-RS  **Comorbidity:** N/A  **Female:** 22 %  **Age mean:**  13.8 (2.2) and 13.6 (2.2)  **Minimum age:** 8  **Maximum age:** 18  **Ethnicity:**  % White : 98.9 | **Intervention:** Gradual withdrawal of methylphenidate OROS (osmotic-controlled release oral delivery system) to placebo over a 3-week period followed by 4 weeks of complete placebo, total study of 7 weeks  **Control:** NA  **Comparator:** MedicationContinued extended-release methylphenidate OROS (osmotic-controlled release oral delivery system) for 7 weeks, 54 or 36 mg/day  **Follow-up:** 2.75 months | CGI-I (Clinical Global Impressions improvement scale) not worsened  CGI-I indicated worsening in 40.4% of the discontinuation group compared with 15.9% of the continuation group.  ADHD-RS (ADHD Rating Scale)  A significant between-group difference in change over time of in favor of the group that continued methylphenidate treatment.  Strengths and Difficulties Questionnaire (SDQ), total score, parent, change from baseline  The intervention group improved significantly compared to comparator group (p=0.03).  Change in appetite  The rate of patients with changes in appetite was 9.6% in the discontinuation group and 7.4% in the continuation group.  Participants with at least one adverse event reported  In the discontinuation group, 13.5% reported at least one adverse event, compared with 10.6% in the continuation group (p=0.46).  None of the participants had a serious adverse event. |
| FDA-approved pharmacological | Mattingly, 2020419  Shire, 20171059  ID: NCT03325881  RCT  Multicenter  N = 89  US  Setting: Specialty care | **Target:** Children with Diagnostic and Statistical Manual of Mental Disorders, Fifth edition—defined ADHD; baseline ADHD-Rating Scale, Fifth Edition, Child, Home Version total scores ≥ 28 and baseline Clinical Global Impressions-Severity scores ≥ 4  **Other:**  **ADHD presentation:** inattentive : 13.6,hyperactive : 13.6,combined : 72.8  **Diagnosis:** Confirmation by specialist  ADHD-Rating Scale, Fifth Edition, Child, Home Version  **Comorbidity:** N/A  **Female:** 40 %  **Age mean:** 8.8 (2.20)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % Black/African American : 24.4  % American Indian or Alaska Native : 0  % White : 66.7  % Multiracial : 8.9 | **Intervention:** Mixed amphetamine salts extended-release (SHP465), 6.25 mg once daily for 4 weeks  **Control:** Placebo  Placebo capsules were identical in appearance to maintain blinding  **Comparator:** NA  **Follow-up:** 1 month | CGI-I (Clinical Global Impressions-Improvement)  Difference between groups was not statistically significant (p=0.597).  ADHD-RS-5-HV-TS (ADHD-Rating Scale, Fifth Edition, Child, Home Version total scores, hyperactivity/impulsivity and inattention)  Difference between groups was not statistically significant.  Decreased appetite  The rate was 2.2% in the intervention and 4.7% in the placebo group.  Participants with treatment emergent adverse events  The rate was 16.3% in the placebo and 24.4% in the treatment group.  There were no serious or severe treatment emergent adverse events, nor events or leading to discontinuation or death. |
| FDA-approved pharmacological | McCracken, 2016425  Bilder, 2016688; Sayer, 20161022; University of California, Los Angeles, 20071128  ID: NCT00429273  RCT  Single center  N = 212  US  Setting: Specialty care | **Target:** Male or female individuals; DSM-IV ADHD (any subtype) diagnosed by Kiddie-Schedule for Affective Disorders and Schizophrenia -Present and Lifetime version and clinical interview and Clinical Global Impression Severity score 4 for ADHD  **Other:**  **ADHD presentation:** inattentive : 44,hyperactive : 2,combined : 51  **Diagnosis:** Confirmation by specialist  DSM-IV ADHD by clinician  **Comorbidity:** N/A  **Female:** 32 %  **Age mean:** 10.0 (2.1)  **Minimum age:** 7  **Maximum age:** 14  **Ethnicity:**  % Hispanic or Latino : 21.3  % Black/African American : 17  % Asian : 8  % White : 69  Other : 6 | **Intervention:** Guanfacine (1-3 mg/day) plus d-methylphenidate extended-release (5-20 mg/day), with fixed-flexible dosing, for 8 weeks  **Control:** Placebo  Placebo plus d-methylphenidate extended-release (5-20 mg/day)  **Comparator:** NA  **Follow-up:** 2 months | CGI-I treatment response (very much improved or much improved)  There were significant differences in treatment response for the 3 treatment sequences, with rates of 81% for methylphenidate alone, 69% for guanfacine alone, and 91% for guanfacine plus methylphenidate ( p 0.01).  ADHD-RS-IV (ADHD-Rating Scale-IV) total score  Guanfacine plus methylphenidate showed superiority versus guanfacine alone (p 0.049), but did not differ statistically from methylphenidate (p 0.066).  Any adverse event  The rate was 98.6% for the combination, 95.7% for DMPH, and 97.1% for guanfacine. |
| FDA-approved pharmacological | Michelson, 2001432  Matza, 2004913  ID: NA  RCT  Multicenter  N = 297  US  Setting: Other | **Target:** Children with ADHD from the DSM-IV by clinical assessment and structured interview  **Other:**  **ADHD presentation:** inattentive : 31,hyperactive : 2,combined : 67  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** ODD  **Female:** 29 %  **Age mean:** 11.2 (2.3)  **Minimum age:** 8  **Maximum age:** 18  **Ethnicity:**  % Hispanic or Latino : 2  % Black/African American : 17.9  % Asian : 1  % White : 75.8 | **Intervention:** Atomoxetine 1.8 mg/kg/day for 8 weeks  **Control:** Placebo  Placebo-controlled  **Comparator:** MedicationAtomoxetine 0.5 mg/kg/day  **Follow-up:** 2 months | Behavior rating, Psychological Summary Score  Atomoxetine groups were statistically significantly better than placebo.  CGI-S  Outcomes in the 1.2 and 1.8 mg/kg/day groups were superior to placebo on almost all measures but for the 0.5 mg/kg/day group CGI-S scale outcomes were not statistically significantly different from those of the placebo group.  ADHD-RS, parent  Atomoxetine groups were statistically significantly better than placebo.  Psychosocial summary score  Atomoxetine groups were statistically significantly better than placebo.  Reduction in affective symptoms, as measured by the CDRS-R, was greater among those in the 2 higher dose groups of atomoxetine compared with placebo.  Anorexia  The rate of anorexia was 12% in the high dose, 6.8% in the low dose, and 4.8% in the placebo group.  Atomoxetine was well tolerated at all doses. No adverse event was statistically significantly more frequent among either of the 1.2 mg/kg/day or 1.8 mg/kg/day atomoxetine dose groups compared with placebo. |
| FDA-approved pharmacological | Michelson, 2002431  ID: NA  RCT  Multicenter  N = 171  US  Setting: Specialty care | **Target:** Children and adolescents with ADHD  **Other:** Parents and teachers provided outcome data  **ADHD presentation:** inattentive : 40.6,hyperactive : 1.8,combined : 57.6  **Diagnosis:** Confirmation by specialist  DSM-IV, assessed by clinical interview and confirmed by Schedule for Affective Disorders and Schizophrenia for School-aged Children (K-SADS-PL)  **Comorbidity:** N/A  **Female:** 29.4 %  **Age mean:** 10.3 (2.4)  **Minimum age:** 6  **Maximum age:** 16  **Ethnicity:**  N/A | **Intervention:** Atomoxetine 1-1.5 mg/kg per day at 4 weeks  **Control:** Placebo  Placebo, once per day  **Comparator:** NA  **Follow-up:** 1.5 months | CGI-S  Intervention group improved more (p < .001).  ADHD-RS-IV (ADHD Rating Scale IV), total score, parent report  Intervention group improved more (p < .001).  Decreased appetite  More intervention patients reported decreased appetite (p=0 .02). |
| FDA-approved pharmacological | Montoya, 2009442  Escobar, 2009761  ID: NCT00191945  RCT  Multicenter  N = 151  Spain  Setting: Specialty care | **Target:** Medication naive children and adolescents with ADHD and no psychiatric comorbidities  **Other:** Parents provided some outcome data  **ADHD presentation:** inattentive : 32.9,hyperactive : 4.0,combined : 63.1  **Diagnosis:** Confirmation by specialist  Diagnosed per DSM-IV-TR). Confirmed by Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime version (K-SADS-PL).  **Comorbidity:** N/A  **Female:** 20.5 %  **Age mean:** 10.3 (2.5)  **Minimum age:** 6  **Maximum age:** 15  **Ethnicity:**  % Hispanic or Latino : 3.3  % Black/African American : 0.7  % White : 96 | **Intervention:** Atomoxetine, target dose of 1.2 mg/kg/day taken once daily for 12 weeks  **Control:** Placebo  Placebo  **Comparator:** NA  **Follow-up:** 3 months | CPRS-R:S (Conners’ Parent Rating Scale-Revised: Short Form), Total  CGI-S (Clinical Global Impression - Severity) severely ill  Total Conners score was significantly lower in intervention group at 12 weeks. A significantly lower percentage of intervention group participants were determined to be 'severely ill' compared to the control group.  ADHD-RS-IV (ADHD-Rating Scale-IV) total score, parent report  Statistically significant improvements with atomoxetine compared to placebo from baseline to follow up on total and subscale scores of the ADHD- RS-IV (p < .001).  Atomoxetine improved Health Related Quality of Life risk avoidance (p < .001) and achievement (p = .042) domains compared to placebo, as assessed by parents. Difference in satisfaction, comfort, and resilience domains not statistically significant.  Number with decreased appetite  Significantly lower percentage of placebo patients experienced appetite decrease (p = 0.006).  Participants with at least one adverse event  The rate was 65% for intervention and 37% for control. |
| FDA-approved pharmacological | Morell, 2019504  ID: ID NA  RCT  Single center  N = 45  Spain  Setting: Specialty care | **Target:** Children with ADHD and poor performance in executive functions or delay aversion; IQ ≥85; absence of sensory, psychiatric and/or other neurological disorders; no previous ADHD medications; absence of concomitant psychotropic medication  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 26 %  **Age mean:**  Intervention: 10.46 (0.66), comparator: 10.0 (0.40)  **Minimum age:** 9  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Atomoxetine, effective clinical dose, titration initiated with a standard dose based on weight (0.8–1.5 mg /kg/day for ATX) and adjusted by clinical response until an optimal clinical response with minimum side effects was reached, mean dose 40 mg/day, for 6 months  **Control:** NA  **Comparator:** MedicationModified-release methylphenidate (long-acting), dose titration initiated with a standard dose based on weight (1 mg/kg/day for MPH) and adjusted by clinical response until an optimal clinical response with minimum side effects was reached, mean dose was 3  **Follow-up:** 6 months | Risk taking behavior evaluated by the Cambridge Gambling Task  No significant difference between groups.  Both MPH and ATX significantly improved scores in verbal working memory, spatial working memory, planning, decision making, and inhibition, but difference between groups was not significant. No beneficial effect on delay aversion and risk taking was found with MPH or ATX.  No ADHD participant dropped out due to adverse effects or other any other reason. |
| FDA-approved pharmacological | Mount Sinai, 2012539  N/A  ID: NCT01678209  RCT  Single center  N = 127  US  Setting: Specialty care | **Target:** Children and adolescents with primary diagnosis of ADHD, any subtype, determined by Kiddie Schedule for Affective Disorders and Schizophrenia for School-Aged Children-Present and Lifetime Versions, ADHD Rating Scale-IV-Parent Version: Investigator Administered total score ≥ 1.5 SD above age and gender means for subtype, Clinical Global Impressions-ADHD-Severity score > 4, Wechsler Intelligence Scale for Children ≥ 75, treatments offered in the study must not be contraindicated for the comorbid disorder  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  Diagnosis of ADHD, any subtype, determined by Kiddie Schedule for Affective Disorders and Schizophrenia for School-Aged Children-Present and Lifetime Versions (K-SADS-PL)  **Comorbidity:** N/A  **Female:** 27.3 %  **Age mean:** 11 (2.94)  **Minimum age:** 7  **Maximum age:** 17  **Ethnicity:**  % Hispanic or Latino : 56.8  Other : 43.2 not Hispanic or Latino | **Intervention:** Atomoxetine, flexible-dose titration for 6-8 weeks  **Control:** NA  **Comparator:** MedicationMethylphenidate, flexible-dose titration with Concerta for 6-8 weeks  **Follow-up:** 1.5 months | CGI-S (Clinical Global Impressions-Severity)  Intervention scores improved when compared to comparator.  ADHD-RS  Intervention scores improved compared to comparator.  Percentage of correct inhibition in the Go-No go task favored methylphenidate (81.81%) compared to atomoxetine (80.72%).  Decreased appetite  The rate was 9.09% for atomoxetine and 18.18 for methylphenidate.  Participants with adverse events  The rate was 27.7% for atomoxetine and 18.18% for methylphenidate. |
| FDA-approved pharmacological | Nasser, 2020453  Supernus Pharmaceuticals, 20171096  ID: NCT03247530  RCT  Single center  N = 477  US  Setting: Other | **Target:** Children with ADHD according to the DSM-5, no diagnosis of a major psychiatric/neurologic disorder other than ADHD (excluding oppositional defiant disorder, or major depressive disorder if the subject was free of major depressive episodes both currently and for the 6 months before screening), significant systemic disease, history of allergic reaction to viloxazine, any food allergy or intolerance that can impede treatment, and/or evidence of suicidality within 6 months of screening  **Other:**  **ADHD presentation:** inattentive\_other : mean(sd) 22.7 (3.5),hyperactive\_other : hyperactive/impulsivity mean(sd) 21.5 (4.9)  **Diagnosis:** Confirmation by specialist  DSM-5, MINI-KID  **Comorbidity:** N/A  **Female:** 37 %  **Age mean:** 8.5 (1.7)  **Minimum age:** 6  **Maximum age:** 11  **Ethnicity:**  % Black/African American : 43.7  % American Indian or Alaska Native : 0.4  % Asian : 0.2  % White : 51.3  % Multiracial : 4.3 | **Intervention:** Viloxazine (SPN-812) 200 mg/day, viloxazine extended-release daily in the morning, with or without food, for 6-weeks  **Control:** Placebo  Placebo, 2 capsules daily for 6 weeks  **Comparator:** MedicationViloxazine (SPN-812), one 100-mg SPN-812 and one placebo capsule daily for 6 weeks  **Follow-up:** 1.5 months | Conners-3 Composite Score (inattention, hyperactivity, learning problems, executive functioning, defiance/aggression, peer relations), parent  Significant improvement for Conners 3-PS Composite T-score (P =0.0003 and P =0.0002) when compared to placebo.  ADHD-RS-5  Statistically significant improvements in ADHD-RS-5 Total score were observed in both the 100- and 200-mg/day SPN-812 treatment groups compared to placebo at week 1 of treatment (P=0.0004 and P=0.0244, respectively), which was maintained through EOS (P=0.  Weiss Functional Impairment Rating Scale - Parent, change from baseline  Significant improvement was shown in both the intervention and comparator groups compared to the placebo (p=0.0019 for comparator, p=0.0002 for intervention).  Decreased appetite  There was no incidence of decreased appetite in the placebo group but a rate of 7.5 in the 200mg group and 4.5 in the 100mg group.  Participants with at least 1 adverse event  The rate was 48% for intervention, 30% for control, and 48% for comparator  Discontinuations due to AEs were infrequent with 1.3% in the placebo, 1.2% in the 200mg, and 3.2% in the 100mg group discontinuing the trial. |
| FDA-approved pharmacological | Nasser, 2021454  Supernus Pharmaceuticals, 20171100  ID: NCT03247556  RCT  Multicenter  N = 297  US  Setting: Mixed | **Target:** Adolescents with diagnosis of ADHD according to DSM-5, weight>= 35 kg, have an ADHD-Rating Scale-5 Total score >= 28, and a Clinical Global Impression-Severity of Illness score >= 4, without a current diagnosis of a major psychiatric disorder, no major neurological disorder, no significant systemic disease, no evidence of suicidality, no intolerance or allergic reaction to viloxazine, not received any investigational drugs within 30 days of trial  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID)  **Comorbidity:** N/A  **Female:** 32.2 %  **Age mean:** 13.8 (1.6)  **Minimum age:** 12  **Maximum age:** 17  **Ethnicity:**  % Hispanic or Latino : 33.2  % Black/African American : 29.1  % American Indian or Alaska Native : 0.7  % Native Hawaiian or Pacific Islander : 0.3  % White : 66.1  % Multiracial : 3.8 | **Intervention:** Viloxazine extended-release (SPN-812), 600 mg/day group, one 200-mg capsule and two placebo capsules daily during week 1, two 200-mg capsules and one placebo capsule daily during week 2, followed by three 200-mg capsules daily for the remaining 5 weeks  **Control:** Placebo  Three placebo capsules daily for 7 weeks  **Comparator:** MedicationViloxazine, 400-mg/day viloxazine extended-release taken daily for 7 weeks  **Follow-up:** 2 months | CGI-I (Clinical Global Impression- Improvement)  There was a higher proportion of responders for each week of treatment in both the intervention and comparator groups compared to the placebo group. This difference was statistically significant in the intervention group at Week 3 and in the comparator g  ADHD-RS-5 (ADHD Rating Scale-5) change  ADHD-RS-5 responders  The difference in mean improvement was statistically significant for comparator vs control group (p<0.05), as was the proportion of responders (p < 0.0340).  Weiss Functional Impairment Rating Scale (WFIRS-P), parent, change from baseline  Total scores were improved in intervention and comparator groups compared to the placebo group, but this difference was not statistically significant for either the 600-mg/  day or 400-mg/day SPN-812 treatment arms (p = 0.9756 and p =0.0698, respectively).  Stress Index for Parents of Adolescents (SIPA) scores were lower in the comparator arm compared to placebo (p 0.1259).  Appetite changes  The rate was 6.1% in the intervention, 6.0% in the comparator, and 2.1% in the control group.  Participants with at least one adverse event  The rate was 55.6% in the intervention, 58.0% in the comparator, and 40.2% in the placebo group.  The most common treatment-related adverse events that occurred in at least 5% of subjects in any of the active treatment groups were somnolence (15.1%), fatigue  (10.6%), headache (8.0%), nausea (6.5%), and decreased appetite (6.0%), |
| FDA-approved pharmacological | Nasser, 2021455  Supernus Pharmaceuticals, Inc., 20171101  ID: NCT03247543  RCT  Multicenter  N = 313  US  Setting: Mixed | **Target:** Male and female children with a body weight of at least 20 kg and a primary diagnosis of ADHD as defined in the DSM-5, confirmed using the Mini International Neuropsychiatric Interview for Children and Adolescents, and an ADHD-Rating Scale-5 score of at least 28 and a Clinical Global Impression-Severity of Illness score of at least 4  **Other:** Parents/guardians of children with ADHD completed parent rating scales and clinicians completed clinician rating scales  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  primary diagnosis of ADHD as defined in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5), confirmed using the Mini International Neuropsychiatric Interview for Children and Adolescents, and an ADHD-RS-5 score of 28 or higher  **Comorbidity:** N/A  **Female:** 35.5 %  **Age mean:** 8.4 (1.7)  **Minimum age:** 6  **Maximum age:** 11  **Ethnicity:**  % Hispanic or Latino : 30.2  % Black/African American : 41.5  % American Indian or Alaska Native : 1.0  % Asian : 0.3  % White : 52.8  % Multiracial : 4.3 | **Intervention:** Viloxazine, 400 mg FDA-approved viloxazine extended-release, once daily for 8 weeks (including 3 weeks titration period)  **Control:** Placebo  Four matching placebo capsules daily  **Comparator:** MedicationViloxazine, 200 mg mg FDA-approved viloxazine extended-release, once daily for 8 weeks (including 3 weeks titration period)  **Follow-up:** 2 months | CGI-I (Clinical Global Impression-Improvement)  Intervention and comparator groups had significantly more improvement compared to the control group (p=0.009, p=0.0028).  ADHD-RS-5 (ADHD Rating Scale -5)  ADHD-RS-5 responders (patients who had a reduction in total score of 50%  Intervention and comparator groups had significantly more improvement compared to the control group (p=0.0063, p=0.0038).  Weiss Functional Impairment Rating Scale-Parent (WFIRS-P)  There was no significant difference between comparator and placebo (p=0.065) or between intervention and placebo (p=0.168).  Decreased Appetite Treatment Related Adverse Event  Both intervention and comparator group participants had a higher percentage of participants experiencing decreased appetite compared to control group participants.  No participants in any treatment group were noted to misuse or overuse medication.  The rate of discontinuations due to adverse events in both SPN- 812 treatment groups combined was <5%. All groups had at least 1 or greater adverse events that led to discontinuation of the study. |
| FDA-approved pharmacological | Nasser, 2021452  Supernus Pharmaceuticals, Inc., 20161099  ID: NCT03247517  RCT  Multicenter  N = 310  US  Setting: N/A | **Target:** Participants with ADHD-Rating Scale-5 Total score ≥28 and a Clinical Global Impression—Severity of Illness core ≥4; refrain from taking other ADHD medications for a minimum of 1 week before randomization and for the study duration; considered medically healthy via assessment of physical examination, medical history, clinical laboratory tests, vital signs, and electrocardiogram; females of childbearing potential had to either be sexually inactive (abstinent) or agree to use one of the acceptable birth control methods beginning 30 days before the first dose and throughout the study  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-V  **Comorbidity:** N/A  **Female:** 32.4 %  **Age mean:**  200mg 13.9 (1.48), 400mg 14.0 (1.59)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  Other : Reported for 200mg= 28.7% / 400mg=31.1%  Other : Reported for 200mg=39.4% / 400mg=40.8%  Other : reported for 200mg= 1.1% / 400mg=1.9%  Other : Reported for 200mg=1.1% / 400mg=1.0%  Other : Reported for 200mg=56.4% / 400mg=53.4%  Other : reported for 200mg= 2.1% / 400mg=2.9% | **Intervention:** Viloxazine, 400 mg viloxazine extended-release capsules, taken once daily for 6 weeks; one 200-mg Viloxazine extended-release capsule and one placebo capsule daily during week 1, followed by two 200-mg capsules daily for the remaining 5 weeks  **Control:** Placebo  Capsules were identical in appearance, 2 placebo capsules daily for 6 weeks  **Comparator:** MedicationViloxazine, 200-mg viloxazine extended-release capsules for 6 weeks  **Follow-up:** 3 months | CGI-I  The scores were significantly better in each VLX-ER treatment group compared with placebo (p<0.05).  ADHD-RS-5 (ADHD Rating Scale Edition 5)  At least 50% reduction ADHD-RS-5  Intervention and comparator groups had significantly greater improvement compared to the control group (p<0.05).  Weiss Functional Impairment Rating Scale—Parent (WFIRS-P)  There were no significant differences between groups.  Decreased appetite  The rate was 8.6% in the 400mg, 5.1% in the 200mp, and 0 in the placebo group.  Participants with at least 1 adverse event  The rate was 53.3% in the 400mg, 43.4% in the 200mg, and 36.5% in the placebo group.  The most common treatment-related adverse events were somnolence, headache, decreased appetite, nausea, and fatigue. The adverse event–related discontinuation rates were <5% in all groups. |
| FDA-approved pharmacological | Newcorn, 2005461  ID: NA  RCT  Multicenter  N = 297  US  Setting: Mixed | **Target:** Children and adolescents with clinical diagnosis of ADHD according to DSM-IV, have a symptom severity score of >=1.5 standard deviations above age and gender norms on the Attention-Deficit/Hyperactivity Disorder Rating Scale-IV-Parent version, have a IQ >= 80 according to the full Wechsler Intelligence Scale for Children-III; no serious medical illness, comorbid psychosis or bipolar disorder, history of a seizure disorder, or ongoing use of psychoactive medications other than the study drug  **Other:**  **ADHD presentation:** inattentive : 31.4,hyperactive : 1.7,combined : 66.9  **Diagnosis:** Confirmation by specialist  Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime versions (K-SADS-PL)  **Comorbidity:** N/A  **Female:** 28.3 %  **Age mean:**  ODD 11.2 (2.1), non-ODD 11.1 (2.4)  **Minimum age:** 8  **Maximum age:** 18  **Ethnicity:** | **Intervention:** Atomoxetine 1.8 mg/kg/day administered equally divided doses in themorning and late afternoon for 8 weeks  **Control:** Placebo  Matching placebo for 8 weeks  **Comparator:** MedicationAtomoxetine 1.2 mg/kg/day  **Follow-up:** 2 months | CGI-S (Clinical Global Impressions of Severity)  Tests for a linear dose-response showed a statistically significant effect, suggesting increased efficacy as a function of increasing atomoxetine dose.  ADHD-RS-IV-Parent, investigator rated and scored  Atomoxetine at 1.8 mg/kg/day, but not 1.2 mg/kg/day, was superior to placebo in reducing symptoms of ADHD among youths with ADHD and ODD, effect sizes were ADHD + ODD (placebo versus ATMX1.2 = 0.49; placebo versus ATMX1.8 = 0.69; placebo versus ATMX1.2 +  CHQ Psychosocial Summary scale  Changes in ADHD and oppositional symptoms were associated with improvements in broader functioning for youths with ADHD with and without ODD.  There was significant improvement on the CPRS-R:S Oppositional subscale for patients with ADHD and ODD receiving atomoxetine doses 0.5 and 1.8 mg/kg/day (effect sizes, ODD: placebo versus ATMX1.2 = 0.39; placebo versus ATMX1.8 = 0.68; placebo versus ATMX1.2 + ATMX1.8 = 0.56; non-ODD: placebo versus ATMX1.2 = 0.55; placebo versus ATMX1.8 = 0.40; placebo versus ATMX1.2 + ATMX1.8 = 0.46. |
| FDA-approved pharmacological | Newcorn, 2008460  ID: ID NA  Crossover trial  Multicenter  N = 516  US  Setting: N/A | **Target:** Children and adolescents with ADHD; no seizures, bipolar disorder, a psychotic illness, a pervasive developmental disorder or who were taking concomitant psychoactive medications, anxiety and tic disorders, nonresponders to methylphenidate or amphetamine or had intolerable adverse events; other concurrent psychiatric diagnoses permitted as long as ADHD was the primary diagnosis  **Other:** Parents provided some outcomes  **ADHD presentation:** inattentive : 28,hyperactive : 2,combined : 70  **Diagnosis:** Confirmation by specialist  DSM-IV via KSADS-PL  **Comorbidity:** N/A  **Female:** 26 %  **Age mean:**  Atomoxetine: 10.3 (2.2) Osmotically Released Methylphenidate: 10.2 (2.5) Placebo: 10.1 (2.7)  **Minimum age:** 6  **Maximum age:** 16  **Ethnicity:**  N/A | **Intervention:** Atomoxetine 0.8–1.8 mg/kg per day for 6 weeks  **Control:** Placebo  Placebo - identically appearing capsules  **Comparator:** MedicationOsmotically released methylphenidate, 18–54 mg/day, initiated at 18 mg/day, with increases to 36 mg and 54 mg allowed at the first and second visits  **Follow-up:** 1.5 months | Daily Parent Ratings of Evening and Morning Behavior—Revised, Evening score, change from baseline  There was no difference between comparator and intervention (p=0.21).  CGI ADHD severity scale, change in  Patients on methylphenidate changed more than patients on atomoxetine (p = 0.004) or placebo  ADHD-RS (ADHD Rating Scale) total score, change in  Osmotically released methylphenidate group improved more than atomoxetine group (p=0.02)  Change in weight (kg)  Difference from placebo was statistically significant for both active interventions (p<0.05).  Adverse events occurring in at least 5% of the patients in any group or that occurred significantly more often for either drug than for placebo: Insomnia was more common for patients assigned to methylphenidate than for those taking placebo; Somnolence wa |
| FDA-approved pharmacological | Newcorn, 2016459  Shire, 20101057  ID: NCT01081145  RCT  Multicenter  N = 316  Multiple countries  Setting: Mixed | **Target:** Primary diagnosis of ADHD, any subtype, based on a detailed psychiatric evaluation by a licensed clinician using the ADHD-Rating Scale-IV and the Kiddie Schedule for Affective Disorders and Schizophrenia Present and Lifetime version who had age-appropriate intellectual functioning  **Other:**  **ADHD presentation:** inattentive : 12.1,hyperactive : 3.8,combined : 84.1  **Diagnosis:** Confirmation by specialist  DSM-IV-TR detailed psychiatric evaluation by a licenced clinician  **Comorbidity:** N/A  **Female:** 25.7 %  **Age mean:** 10.8 (2.67)  **Minimum age:**  **Maximum age:**  **Ethnicity:**  % White : 79.5  Other : 20.5 | **Intervention:** Guanfacine hydrochloride extended-release 1-7 mg/day for 13 weeks before withdrawal for 26 weeks  **Control:** Placebo  Placebo  **Comparator:** NA  **Follow-up:** 9 months | CGI-S, rated as normal or bordeline mentally ill  A larger proportion of participants in the GXR group was rated as normal or borderline mentally ill compared with placebo (p = 0.001).  ADHD-RS-IV (ADHD Rating Scale-IV) total score  The difference between GXR and placebo was significant (p < 0.001), indicating that the effect of treatment was better maintained with GXR than placebo.  Weiss Functional Impairment Rating Scale, Parent (WFIRS-P)  There was no difference between groups in global domain score.  Treatment failure (defined as (≥50% increase in ADHD Rating Scale version IV total score and ≥2-point increase in Clinical Global Impression-Severity compared with baseline) occurred in 49.3% of the GXR and 64.9% of the placebo group(p = 0.006).  Treatment-emergent adverse events  The rate was 56.7% in the intervention, and 48.1% in the placebo group.  TEAEs led to discontinuation in 1.9% in the GXR group (grand mal convulsion, sedation, somnolence) and 1.3% in the placebo group (one with irritability, the other with chest pain, dizziness, dyspnoea, nausea and tremor). Six participants (GXR, n = 2; plac |
| FDA-approved pharmacological | Prasad, 2007481  ID: NA  RCT  Multicenter  N = 201  UK  Setting: Specialty care | **Target:** Children and adolescents with ADHD; no history of bipolar disorder, psychotic disorders, pervasive development disorder, any seizure disorder or alcohol/drug abuse, with significant prior/current medical conditions or at serious suicidal risk, or taking medication that could potentially interfere with study outcomes  **Other:** Parents supplied some outcome data  **ADHD presentation:** inattentive : 7.5,hyperactive : 2.0,combined : 90.5  **Diagnosis:** Confirmation by specialist  DSM‑IV criteria by clinical investigator and confirmed by the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Aged Children-Present and Lifetime Versions (K‑SADS‑PL)  **Comorbidity:** N/A  **Female:** 11.4 %  **Age mean:** 10.9 (2.2)  **Minimum age:** 6.9  **Maximum age:** 15.9  **Ethnicity:**  % Black/African American : 0.5  % Asian : 0.5  % White : 99.0 | **Intervention:** Atomoxetine 0.5 to 1.8 mg/kg/day for 10 weeks  **Control:** TAU  Standard current therapy  **Comparator:** NA  **Follow-up:** 2.5 months | CGI-I (Clinical Global Impression Improvement) much improved  The intervention group had significantly more improvement compared to the control group (p<0.001).  ADHD-RS (ADHD Rating Scale), investigator rated  ADHD RS, number showing at least 25% improvement  Percent improving at least 25% on investigator-rated ADHD‑RS total score was statistically superior for atomoxetine group (p< 0.001).  Weight decreased, number  No statistical differences in percent with weight decrease or decreased appetite.  There were no deaths and no serious adverse events. |
| FDA-approved pharmacological | Sallee, 2009511  Shire, 20041054  ID: NCT00150618  RCT  Multicenter  N = 324  US  Setting: Specialty care | **Target:** Children with ADHD; no co-morbid psychological disorders (other than Oppositional Defiant Disorder), medications that might affect blood pressure, morbid obesity or abnormal vital signs, or prior treatment with guanfacine  **Other:**  **ADHD presentation:** inattentive : 26,hyperactive : 2,combined : 73  **Diagnosis:** Confirmation by specialist  DSM IV - TR per psyc evaluation  **Comorbidity:** N/A  **Female:** 28 %  **Age mean:** 11 (3.0)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % Hispanic or Latino : 9  % Black/African American : 17  % American Indian or Alaska Native : 0.003  Other : 0.3% Asian or Pacific Islander  % White : 67  Other : "Other" 4.3% | **Intervention:** Guanfacine extended-release (SPD503) 4 mg g for 9 weeks  **Control:** Placebo  Placebo  **Comparator:** MedicationGuanfacine extended-release (SPD503) 1 mg g for 9 weeks  **Follow-up:** 4 months | Child Health Questionnaire-Parent Form (CHQ-PF50), psychosocial score  CGI-I (Clinical Global Impressions-Improvement) showing clinical improvement  Intervention and comparator groups had significantly more improvement compared to control group (p = 0.0237).  ADHD-RS-IV total score change, parent report  Intervention and comparator groups had significantly more improvement compared to control group (p 0.003, p 0.01).  Medication was not associated with abnormal changes in height or weight. No specific data or p value reported.  Adverse events occurring in 5% or greater in participants taking medication were somnolence, headache, fatigue, sedation, dizziness, irritability, upper abdominal pain, and nausea. |
| FDA-approved pharmacological | Sangal, 2006512  ID: NA  Crossover trial  Multicenter  N = 85  US  Setting: Other | **Target:** Children with ADHD and no pre-existing sleep disorders or serious medical conditions  **Other:**  **ADHD presentation:** inattentive : 29.8,hyperactive : 2.4,combined : 67.9  **Diagnosis:** Confirmation by specialist  DSM IV diagnosis a. Diagnosis per investigator’s clinical evaluation and by the administration of several modules of the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version structured interview  **Comorbidity:** N/A  **Female:** 24.7 %  **Age mean:** 10.1 (2.0)  **Minimum age:** 6  **Maximum age:** 14  **Ethnicity:**  % White : 72.9  Other : 27.1% non-white | **Intervention:** Atomoxetine 1.0-1.8 mg/kg/day divided into twice daily doses for 7 weeks  **Control:** NA  **Comparator:** MedicationMethylphenidate, three times per day  **Follow-up:** 1.8 months | Daily Parent Ratings of Evening and Morning Behavior (DPREMB)  There were statistically significant differences in favor of atomoxetine (p=0.003).  Clinical Global Impression-Severity (CGI-S)  There was no significant difference between groups at follow up.  ADHD-RS-IV (ADHD rating scale-IV), parent report  There was no significant difference between groups (p = 0.427).  Methylphenidate increased sleep-onset latency significantly more than did atomoxetine (p<0.001). Child diaries indicated better sleep (p=0.045), ease to get up in the morning (p=0.004), and less time to fall asleep (p=0.001) with atomoxetine.  Number of patients with decreased appetite  Greater incidence of decreased appetite with methylphenidate (p=0.03).  No significant difference in percent reporting headache, irritability, congestion, cough, and intestinal pain. More methylphenidate patients reported insomnia (p < .001). |
| FDA-approved pharmacological | Seattle Children's, 2015193  ID: NCT02293655  RCT  Multicenter  N = 109  US  Setting: Specialty care | **Target:** Children with ADHD with normal physical exam and ECG findings; those with serious psychological co-morbidities or participating in ADHD-related behavioral interventions were excluded  **Other:** Parents and teachers provided some outcomes  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-V  **Comorbidity:** N/A  **Female:** 33.9 %  **Age mean:**  all 18 or under  **Minimum age:** 7  **Maximum age:** 11  **Ethnicity:**  % Hispanic or Latino : 8.3  % Black/African American : 7.3  % American Indian or Alaska Native : 0  % Asian : 2.8  % Native Hawaiian or Pacific Islander : 0  % White : 80.7  % Multiracial : 9.2 | **Intervention:** Methylphenidate, OROS, 4-week titration, followed by 4-week MPH maintenance phase, followedby 4-week MPH continuation phase; total duration of 8 weeks  **Control:** Placebo  Methylphenidate titration 4-weeks, followed by 4-week MPH maintenance phase, followed by 4-week MPH discontinuation phase using placebo  **Comparator:** NA  **Follow-up:** 1 month | ADHD RS, Total, parent report  Maintenance group had lower symptoms than discontinuation group (p 0.01)  Inhibitory Control Reaction Time, measured by Go-No Go test: discontinuation group scored significantly worse (p 0.001). Math Computation - Number of Problems Completed Correctly: no significant difference (p 0.07).  Decreased appetite  Sustained MPH patients had higher rate of decreased appetite.  1 discontinuation patient had a serious adverse event (suicidal ideation). |
| FDA-approved pharmacological | Shang, 2020525  Shang, 20151037; Wu, 20211180; Shih, 20191041; Hospital, National Taiwan University, National Science Council, 2009953  ID: NCT00916786  RCT  Single center  N = 168  Taiwan  Setting: Specialty care | **Target:** Drug naive children with ADHD; no comorbid psychiatric conditions, including psychosis, bipolar disorders, autism spectrum disorders, substance use disorders, intellectual disability (IQ<80), or had a history of major medical or neurological problems  **Other:** Parents  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DMS IV, Chinese version of the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children– Epidemiological Version (K-SADS-E) to confirm ADHD  **Comorbidity:** N/A  **Female:** 13 %  **Age mean:** 8.7 (2.56)  **Minimum age:** 7  **Maximum age:** 16  **Ethnicity:**  % Asian : 100 | **Intervention:** Atomoxetine: an initial dosage of 0.5 mg/(kg per day), administered as once-daily dose, titrated at visits 2–7 (weeks 2–24) according to clinical response and adverse effects; max dose 1.2 mg/kg daily, total duration of 24 weeks  **Control:** NA  **Comparator:** MedicationMethylphenidate, initial dosage of 18 mg/day, administered as a single morning dose, titrated at visits 2–7 (weeks 2–24) according to clinical response and adverse effects, max dose 54 mg/day  **Follow-up:** 8 months | Home Behaviors subcale of the Social Adjustment Inventory for Children and Adolescents (SAICA), parent, change from baseline  There was no significant difference between groups (p=0.097).  CBCL (Child Behavior Checklist)  The intervention group improved more on aggressive behavior subscale ( p = 0.032) and somatic complaint subscale (0.008) than the comparator group but none of the other subscales.  Both treatment groups showed improvement in executive functions (p-value <0.05 for the major indices of each domain). Magnitude of increasing detectability (p< 0.01) and reducing commission errors (p<0.05) was significantly greater in the intervention group vs comparator group. |
| FDA-approved pharmacological | Shaywitz, 2017526  Eli Lilly and Company, 2008755  ID: NCT00607919  RCT  Multicenter  N = 124  US  Setting: Other | **Target:** Children with ADHD per DSM-IV-TR criteria; met criteria for dyslexia; IQ>=80; no history of bipolar I or bipolar II disorder, psychosis, autism, Asperger’s syndrome, or pervasive developmental disorder, or were currently taking anticonvulsants for seizure control  **Other:**  **ADHD presentation:** inattentive : 46,hyperactive : 2.4,combined : 51.6  **Diagnosis:** Confirmation by specialist  DSM-IV-TR criteria for ADHD diagnosis confirmed during the first screening visit  **Comorbidity:** Learning disability : Dyslexia alone group and dyslexia + ADHD subgroup  **Female:** 36.3 %  **Age mean:**  Intervention mean age 12.2, control mean age 12.3  **Minimum age:** 10  **Maximum age:** 17  **Ethnicity:**  % Hispanic or Latino : 15.3  % Black/African American : 13  % Asian : 2.4  % White : 69.4 | **Intervention:** Atomoxetine 1.0–1.4mg/[kg\*day] once daily for 16 weeks  **Control:** Placebo  Placebo once daily for 16 weeks  **Comparator:** NA  **Follow-up:** 4 months | ADHD-RS-IV-Parent:Inv scores  ADHD symptom decreases were significantly greater for patients treated with atomoxetine.  Reading abilities change from baseline measured using Gray Oral Reading Tests-4. N of participants intervention group (51). Academic rating scale least-squares mean change scores intervention group (-2.19). N of participants control group (55). Academic r |
| FDA-approved pharmacological | Simonoff, 2013538  ID: N/A  RCT  Single center  N = 122  UK  Setting: Specialty care | **Target:** Children with a diagnosis of ICD-10 hyperkinetic disorder and a full-scale IQ of 30–69  **Other:**  **ADHD presentation:** N/A : 100% with a diagnosis of ICD-10 hyperkinetic disorder  **Diagnosis:** Confirmation by specialist  Diagnosis of hyperkinetic disorder was made using the Child and Adolescent Psychiatric Assessment  **Comorbidity:** Learning disability : Full-scale IQ of 30–69  **Female:** 30 %  **Age mean:** 13.4 (28)  **Minimum age:** 7  **Maximum age:** 15  **Ethnicity:** | **Intervention:** Methylphenidate (equasym), dose titration comprised at least 1 week each of low (0.5 mg/kg/day), medium (1.0 mg/kg/day) and high dose (1.5 mg/kg/day), taken for 16 weeks  **Control:** Placebo  Placebo medication, offered active medication after the trial  **Comparator:** NA  **Follow-up:** 4 months | CGI-I improved  40% of participants receiving methylphenidate compared to 7% of placebo were rated as improved.  ADHD Index Conners Rating Scale-Short Version-Parent  Methylphenidate was superior to placebo for the parent Conners ADHD index.  Methylphenidate was superior to placebo for the teacher Conners ADHD index.  Poor appetite  15% of patients receiving methylphenidate compared to 2% on placebo reported poor appetite.  16 withdrew from the trial, 5 were due to adverse events following methylphenidate; 21% vs 3% had trouble getting to sleep (P<0.01) but there was no difference in looks sad/miserable, crying, looks anxious, meaningless repetitive behavior, talks less with |
| FDA-approved pharmacological | Singer, 1995540  ID: N/A  RCT  Single center  N = 37  US  Setting: N/A | **Target:** Children with Tourette's Syndrome and ADHD of normal intellect  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** Tic disorder  **Female:** 8 %  **Age mean:**  mean age 10.6  **Minimum age:** 7  **Maximum age:** 13  **Ethnicity:**  % Black/African American : 3  % White : 89 | **Intervention:** Clonidine 0.05 mg 4 times daily for 6 weeks  **Control:** Placebo  Uniform-appearing capsule  **Comparator:** MedicationDesipramine (25 mg four times daily), each child started with one capsule per day (evening) and added 1 additional capsule every week to a maximum daily dose of one capsule 4 times a day; patients then were maintained on the highest daily dose for an addi  **Follow-up:** 1.5 months | Hyperactivity scale CBCL (Child Behavior Checklist)  Desipramine was significantly better than placebo and clonidine (p <0.05).  A global linear analogue comparing the child’s current tics to tics anytime in the past, showed a statistically significant drug effect (P < .05), with orthogonal contrasts demonstrating that desipramine was superior to clonidine (P < .01). Results with clonidine did not differ from placebo, whereas desipramine significantly reduced tics compared to placebo (P <.05).  Participants with at least one drug-related problem  The rate was 82% for intervention, 44% for control, and 76% for comparator. |
| FDA-approved pharmacological | Spencer, 2002554  ID: Study 1  RCT  Multicenter  N = 144  US  Setting: Specialty care | **Target:** Children with ADHD, patients who weighed less than 55 pounds, were on psychoactive medication, or had a history of psychosis or bipolar disorder were excluded; those who were prognosed to be poor metabolizers of medication based on a genetic test were excluded  **Other:** Parents provided some outcomes  **ADHD presentation:** inattentive : 18,hyperactive : 1,combined : 81  **Diagnosis:** Confirmation by specialist  DSM IV assessed by clinical interview and the Kiddie Schedule for Affective Disorders & Schizophrenia  **Comorbidity:** N/A  **Female:** 20.6 %  **Age mean:** 9.8 (1.55)  **Minimum age:** 7  **Maximum age:** 12  **Ethnicity:** | **Intervention:** Atomoxetine 3 times per day, drug dosage based on weight, for 12 weeks  **Control:** Placebo  Placebo 3 times per day, for 12 weeks  **Comparator:** NA  **Follow-up:** 2 months | CGI-Severity  Significantly greater mean improvement in CGI-S scores (p<0.001) and Conners Parent Rating Scale in atomoxetine patients than placebo patients.  ADHD RS total, mean improvement  ADHD RS, response (25% decrease in total score)  Atomoxetine patients had greater mean improvement than placebo patients (p<0.001) and a significantly greater rate of response. |
| FDA-approved pharmacological | Spencer, 2002555  ID: Study 2  RCT  Multicenter  N = 147  US  Setting: Specialty care | **Target:** Children with ADHD, stimulant naive patients, who weighed less than 55 pounds, were on psychoactive medication, or had a history of psychosis or bipolar disorder were excluded; those who were prognosed to be poor metabolizers of medication based on a genetic test were excluded  **Other:** Parents provided some outcomes  **ADHD presentation:** inattentive : 18,hyperactive : 1,combined : 81  **Diagnosis:** Confirmation by specialist  DSM IV assessed by clinical interview and the Kiddie Schedule for Affective Disorders & Schizophrenia  **Comorbidity:** N/A  **Female:** 20.6 %  **Age mean:** 9.8 (1.55)  **Minimum age:** 7  **Maximum age:** 12  **Ethnicity:** | **Intervention:** Atomoxetine 3 times per day, drug dosage based on weight, for 12 weeks  **Control:** Placebo  Placebo 3 times per day, for 12 weeks  **Comparator:** MedicationMethylphenidate in the morning and midday and placebo dose in the evening, titrated to 1.5 mg/kg/day or total daily dose of 60mg, based on therapeutic response, for 12 weeks  **Follow-up:** 2 months | CGI-Severity  Significantly greater mean improvement in CGI-S scores (p<0.001) and Conners Parent Rating Scale in atomoxetine patients than placebo patients.  ADHD RS total, mean improvement  ADHD RS, response (25% decrease in total score)  Atomoxetine patients had greater mean improvement than placebo patients (p<0.001) and a significantly greater rate of response. |
| FDA-approved pharmacological | Spencer, 2006557  ID: NA  RCT  Unclear/Not reported  N = 287  US  Setting: Specialty care | **Target:** Adolescents with ADHD, known to be nonresponsive to stimulants or naive to stimulant treatment; no comorbid psychiatric diagnosis except oppositional defiant disorder, hypertension, history of seizure disorder within the last 2 years, tic disorder, Tourette's syndrome, abnormal thyroid function, cardiac disorder, and significant laboratory abnormalities  **Other:**  **ADHD presentation:** inattentive : 41.0,hyperactive : 2.5,combined : 56.5  **Diagnosis:** Confirmation by specialist  DSM-IV-TR  **Comorbidity:** N/A  **Female:** 34.5 %  **Age mean:** 14.2 (1.2)  **Minimum age:** 13  **Maximum age:** 17  **Ethnicity:**  % Hispanic or Latino : 6.8  % Black/African American : 15.8  % White : 73.7  Other : Other 3.6 | **Intervention:** Mixed amphetamine salts extended release 40 mg per day for 4 weeks  **Control:** Placebo  Placebo  **Comparator:** MedicationMixed amphetamine salts extended release (Adderall MX) 10 mg per day  **Follow-up:** 1 month | CGI-I (Clinical Global Impression – Improvement scale) improved  A higher percentage of patients in the medication groups were considered improved compared with those receiving placebo (p< 0.001).  ADHD-RS-IV (Attention-Deficit/Hyperactivity Disorder Rating Scale-IV)  Statistically significant (p < 0.001) improvement in mean ADHD-RS-W total scores in medication groups compared with placebo.  Anorexia/decreased appetite, number of patients  Significantly more medication patients experienced decreased appetite and weight loss compared to placebo patients. p value not reported.  Insomnia and abdominal pain more prevalent in medication patients. p value not reported. |
| FDA-approved pharmacological | Spencer, 2008556  ID: N/A  RCT  Multicenter  N = 117  US  Setting: N/A | **Target:** Children with Tourette's syndrome and scoring 1.5 standard deviations above sex norm for their diagnostic subtype at enrollment and at randomization for the Attention-Deficit/Hyperactivity Disorder Rating Scale-IV-Parent version  **Other:**  **ADHD presentation:** inattentive : 30.8,hyperactive : 3.4,combined : 65.8  **Diagnosis:** Confirmation by specialist  met the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for ADHD and concurrent TS. Subjects’ scores on the Attention-Deficit/Hyperactivity Disorder Rating Scale- IV-Parent Version:Investigator-administered and -scored (ADHDRS-IV-P  **Comorbidity:** Tic disorder  **Female:** 12.8 %  **Age mean:** 11.2 (2.4)  **Minimum age:** 7  **Maximum age:** 17  **Ethnicity:**  % Hispanic or Latino : 4.3  % Black/African American : 4.3  % Asian : 0.9  % White : 88.0 | **Intervention:** Atomoxetine 0.5-1.5 mg/kg/day, as a divided dose, for 15 weeks  **Control:** Placebo  Placebo  **Comparator:** NA  **Follow-up:** 3 months | CGI-ADHD/Psych-S  ADHD-RS-IV, parent  Intervention participants showed significantly greater improvement compared to controls (p=0.011).  The intervention group showed a significantly greater decrease from baseline in tic severity relative to control (p=0.027).  Body weight change  Decreased appetite  The rate was 18% in the atomoxetine vs 10.3% in the placebo group.  Discontinuations because of an adverse event were rare, with 2 in the atomoxetine group (headache, vomiting) and 1 in the placebo group (upper abdominal pain). |
| FDA-approved pharmacological | Steele, 2006561  ID: n/a  RCT  Multicenter  N = 147  Canada  Setting: Specialty care | **Target:** Children with ADHD; medication naïve, Clinical Global Impression Severity score of 4 or greater and with behavioral difficulties  **Other:** Parents reported some outcomes  **ADHD presentation:** inattentive : 18.37,hyperactive : 2.04,combined : 78.23  **Diagnosis:** Confirmation by specialist  DSM IV by clinical and structural interview  **Comorbidity:** N/A  **Female:** 16.6 %  **Age mean:**  9.0 (2.1) and 9.1 (1.8)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % Black/African American : 3.4  % Asian : 0.6  % White : 85.7  Other : 8.8% other | **Intervention:** Methylphenidate OROS (osmotic release oral system), 18-54 mg once daily for 8 weeks  **Control:** NA  **Comparator:** MedicationImmediate release methylphenidate initiated at what ever dose the clinician felt was appropriate and over the weeks each individual dose was titrated weekly by 5mg or 10mg increments, according to manufacturer's recommendations and the investigator's clin  **Follow-up:** 2 months | Homework visual analog scale  There was no statistically significant difference between groups  CGI-I Clinical Global Severity, change  Statistically significant difference favoring intervention group (p < .001)  SNAP-IV, 26 item score, parent report, reduction  There was a statistically significant reduction in scores favoring OROS (p = .004)  Parent satisfaction with current ADHD medication  There was a statistically significant difference in parent satisfaction favoring OROS (p = 0.003)  Parent Stress Index scores showed significant differences in favor or OROS (p = 0.008)  Decreased appetite  Rates were similar in both groups.  Participants with any adverse event  The rate was 82% for both intervention and comparator.  Adverse events (any possible medication related event, headache, insomnia, abdominal pain, nervousness, emotional lability, agitation, fatigue, flu-like symptoms, sleep disorder) were similar between groups. |
| FDA-approved pharmacological | Su, 2016568  Peking University, 2010980; Yang, 20121183  ID: NCT01065259  RCT  Single center  N = 237  China  Setting: N/A | **Target:** Youth with ADHD, either treatment naive or untreated for at least 6 months; no history of poor response with adequate treatment or intolerance to either treatment medication; no medical contraindications to stimulants or who had seizure disorder or an abnormal EEG associated with epilepsy, bipolar disorder, psychosis, anxiety disorder, depression disorder, tic disorder, pervasive developmental disorder, or an IQ less than 70, children taking concomitant psychoactive medications including dietary supplements with central nervous system activity in the past 30 days  **Other:**  **ADHD presentation:** inattentive : 48,hyperactive : 3,combined : 49  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 17 %  **Age mean:** 9.5 (1.9)  **Minimum age:** 6  **Maximum age:** 16  **Ethnicity:**  N/A | **Intervention:** Atomoxetine initiated at a dose of 0.5 mg/kg/day, which could increase to 0.8mg/kg/day for week 2, and 1.2mg/kg/day for weeks 3 and 4; initially administered once daily in the morning and could be switched to being administered twice daily when adverse events were intolerable, with follow-up up to 1 year  **Control:** NA  **Comparator:** MedicationOsmotic Release Oral System Methylphenidate optimized dose (18, 36, or 54 mg/day) for 4 weeks  **Follow-up:** 12 months | CGI-ADHD-S Remission Rate  There was no significant difference between groups (0.972).  ADHD-RS Remission Rate  There was no significant difference between groups (p 0.777).  Both OROS-MPH and ATX significantly improved the parent- and teacher-rated BRIEF and the groups did not differ significantly.  Appetite change  No statistically significant differences between the two groups (p=0.455).  Adverse events rated as severe occurred in 14% of the OROS MPH group and 18.7% of the ATX group (p > 0.05). |
| FDA-approved pharmacological | Svanborg, 2009573  Svanborg, 20091102  ID: NA  RCT  Single center  N = 92  Sweden  Setting: Specialty care | **Target:** Male and female children and adolescents that met the criteria for ADHD of the DSM- IV  **Other:**  **ADHD presentation:** inattentive\_other : 18.2% across all arms,hyperactive\_other : 4% across all arms,combined\_other : 77.8% across all arms  **Diagnosis:** Confirmation by specialist  clinical interview  **Comorbidity:** N/A  **Female:** 19.2 %  **Age mean:**  Mean 12.8  **Minimum age:** 7  **Maximum age:** 15  **Ethnicity:**  Other : 0-1%across all arms  Other : 3% across all arms  Other : 93.9% across all arms  Other : 2.2% across all arms | **Intervention:** Atomoxetine plus psychoeducation for caregivers, 1.2 mg/kg day (70 kg) or 80 mg/day (>70 kg) for 10 weeks  **Control:** Placebo  Placebo capsules plus psychoeducation for caregivers for 10 weeks  **Comparator:** NA  **Follow-up:** 2.75 months | CGI-I (Clinical Global Impression Improvement), change from baseline  An improvement was observed in the atomoxetine group whereas in the placebo group the score changed only slightly (p < 0.001).  ADHD-RS-IV (Attention-Deficit/Hyperactivity Disorder Rating Scale IV)–Parent Version: Investigator Administered and Scored  Treatment responders  Statistically significant between-treatment differences in favor of atomoxetine at each visit (P < 0.001) from visit 4 (week 3) onwards.  The global parental assessment of most aspects of psychoeducation was very positive; items were mostly rated as very good/very satisfied or rather good/satisfied.  Decreased appetite  The rate was 6.1% in the intervention and 0 in the placebo group (p 0.117).  Patients with at least 1 treatment emergent adverse event  The rate was 89.8% in the intervention, and 74% in the placebo group (p 0.066).  No serious adverse events occurred in either group. |
| FDA-approved pharmacological | Takahashi, 2009575  ID: NA  RCT  Multicenter  N = 245  Japan  Setting: Mixed | **Target:** Children and adolescents with DSM-IV diagnosis of ADHD, Clinical Global Impressions-ADHD-Severity score of >= 3, have symptom severity score at least 1.5 standard deviations above Japanese pediatric age and gender norms on the Attention-Deficit-Hyperactivity Disorder Rating Scale-IV–Parent Version: Investigator Administered and Scored, IQ >= 80; no antipsychotic medication within 26 weeks of study visit 1, history of bipolar disorder or psychosis, or at suicidal risk  **Other:**  **ADHD presentation:** inattentive : 61.2,hyperactive : 4.5,combined : 34.5  **Diagnosis:** Confirmation by specialist  Kiddie Schedule for Affective Disorders and Schizophrenia for School- Aged Children–Present and Lifetime Versions (KSADS-PL)  **Comorbidity:** N/A  **Female:** 14.7 %  **Age mean:** 10.53 (2.52)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % Asian : 100 | **Intervention:** Atomoxetine 1.8 mg/kg per day for 8 weeks  **Control:** Placebo  Placebo pills 2 times a day for 8 weeks  **Comparator:** MedicationAtomoxetine 0.5 mg/kg per day for 8 weeks  **Follow-up:** 2 months | ADHD RS-IVJ:I (Attention-Deficit Hyperactivity Disorder Rating Scale-IV–Parent Version: Investigator Administered and Scored-Translated and Validated in Japanese)  1.8 mg per day atomoxetine was superior to placebo (p 0.010).  Decreased appetite  The rate was 21.3% in the intervention, 4.8% in the comparator, and 3.2% in the placebo group.  Participants with one or more treatment-emergent adverse event  The rate was 78.7% for the intervention, 79.0% for the comparator, and 69.4% for placebo.  Two serious adverse events occurred, both in the same patient in the intervention group (hospitalization due to headache and vomiting). |
| FDA-approved pharmacological | Tris Pharma, 2014588  ID: NCT02083783  RCT  Multicenter  N = 108  US  Setting: Other | **Target:** Children with ADHD who require pharmacologic treatment for ADHD, no other serious illnesses or conditions that would put the patient at particular risk for safety events or would interfere with treatment/assessment of ADHD  **Other:**  **ADHD presentation:** inattentive : 20,hyperactive\_other : impulsive 1,combined : 78  **Diagnosis:** No  **Comorbidity:** N/A  **Female:** 31 %  **Age mean:** 9.4 (1.86)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % Hispanic or Latino : 39  % Black/African American : 34  % White : 55  % Multiracial : 10 | **Intervention:** TRI102 formulation containing active moiety (amphetamine), i.e amphetamine extended-release oral suspension, 10 to 20 mg/day for 5 weeks  **Control:** Placebo  Placebo formulation without active moiety  **Comparator:** NA  **Follow-up:** 1.25 months | Swanson, Kotkin, Agler, M-Flynn, and Pelham Scale (SKAMP), change from baseline  The intervention significantly improved compared to control group (p<0.0001).  PERMP (Permanent Product Measure of Performance) - The PERMP consists of 400 math questions and each are scored. PERMP scores are expressed as the number of questions correct. Predose PERMP Tests are compared with post-dose PERMP scores at prespecfied tim  Significant improvement compared to placebo (p<0.0001).  In the intervention group, 3.85% reported pain in the upper abdomen, 3.85% epistaxis,3.85% rhinitis; only one person (2.08%) in the placebo group reported pain in the upper abdomen. |
| FDA-approved pharmacological | TS SG, 2002380  ID: NA  RCT  Multicenter  N = 65  US  Setting: N/A | **Target:** Children meeting the DSM-IV criteria for ADHD and for Tourette disorder, chronic motor tic disorder or chronic vocal tic disorder; excluded if there was evidence of secondary tic disorder, major depression, pervasive developmental disorder, autism, psychosis, mental retardation, anorexia nervosa, bulimia, a serious cardiovascular or other medical disorder that would preclude the safe use of the medication, impaired renal function, or pregnancy  **Other:**  **ADHD presentation:** inattentive : 71,hyperactive : 2,combined : 27  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** Tic disorder  **Female:** 15 %  **Age mean:**  Placebo 9.7 (1.8), Combination 10.6 (1.9)  **Minimum age:** 7  **Maximum age:** 14  **Ethnicity:**  % White : 72 | **Intervention:** Methylphenidate plus alpha agonist, 60mg/day ritalin plus 0.6mg/day clonodine for 8 weeks  **Control:** Placebo  Placebo  **Comparator:** Medication  **Follow-up:** 4 months | Classroom observation disruptive behavior  MPH (but not CLON) improved “on task” behavior.  CGI (Clinical Global Impression) investigator judged improvement of ADHD  Combined intervention had 87.5% improvement, placebo 32.3%.  Children’s Global Assessment Scale (C-GAS)  Intervention and comparator groups significantly improved over control group (p 0.002, p 0.0005).  A similar pattern of treatment effects was found when analyzing secondary outcome measures for ADHD, including Iowa Conners.  20% with MPH reported a worsening of tics as an adverse event (8 when used alone, 6 when given in combination with CLON) compared with 26% treated with CLON alone and 22% receiving placebo. Tics were reported to limit further dosage increases more often f |
| FDA-approved pharmacological | TS SG, 2002b381  ID: ID NA  RCT  Multicenter  N = 71  US  Setting: N/A | **Target:** Children meeting the DSM-IV criteria for ADHD and for Tourette disorder, chronic motor tic disorder or chronic vocal tic disorder; excluded if there was evidence of secondary tic disorder, major depression, pervasive developmental disorder, autism, psychosis, mental retardation, anorexia nervosa, bulimia, a serious cardiovascular or other medical disorder that would preclude the safe use of the medication, impaired renal function, or pregnancy  **Other:**  **ADHD presentation:** inattentive : 71,hyperactive : 2,combined : 27  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** Tic disorder  **Female:** 15 %  **Age mean:**  MPH 10.7 (2.0), CLON 9.7 (1.8)  **Minimum age:** 7  **Maximum age:** 14  **Ethnicity:**  % White : 72 | **Intervention:** Clonodine (alpha agonist), 0.6mg/day for 8 weeks  **Control:** NA  **Comparator:** MedicationMethylphenidate, 60mg/day ritalin for 8 weeks  **Follow-up:** 4 months | Classroom observation disruptive behavior  MPH but not CLON improved “on task” behavior.  CGI (Clinical Global Impression) investigator judged improvement of ADHD  MPH 80.6%, CLON 60.6% improvement.  Children’s Global Assessment Scale (C-GAS)  Intervention and comparator groups significantly improved over control group (p 0.002, p 0.0005).  A similar pattern of treatment effects was found when analyzing secondary outcome measures for ADHD, including Iowa Conners.  20% with MPH reported a worsening of tics as an adverse event (8 when used alone, 6 when given in combination with CLON) compared with 26% treated with CLON alone. Tics were reported to limit further dosage increases more often for subjects assigned to MP |
| FDA-approved pharmacological | van Stralen, 2020598  JPM van Stralen Medicine Professional, 2013872  ID: NCT01985581  Crossover trial  Single center  N = 50  Canada  Setting: Specialty care | **Target:** Children with a diagnosis of inattentive, hyperactive, or combined subtype of ADHD, being treated with stimulant medication and presenting with suboptimal executive function  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV-TR diagnosed via clinical assessment and ADHD-RS-IV  **Comorbidity:** N/A  **Female:** 16.0 %  **Age mean:**  Meds then placebo group; 9.4 (1.6) / Placebo then meds; 9.0 (1.4)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Guanfacine extended-release 4 mg/day plus usual stimulant therapy for 8 weeks  **Control:** Placebo  Placebo plus usual stimulant therapy  **Comparator:** NA  **Follow-up:** 2 months | CGI-S (Clinical Global Impressions - Severity)  Intervention group had significantly lower severity at follow-up (p =.0007).  ADHD-RS-IV, total score  Intervention had significantly lower symptom score at follow-up (p < .001).  Participants with any adverse event  The rate was 87% in the intervention and 85% in the control group.  Intervention group reported more abdominal pain, fatigue, affect lability, and somnolence. |
| FDA-approved pharmacological | Wang, 2007604  ID: N/A  RCT  Multicenter  N = 330  Multiple countries  Setting: N/A | **Target:** Eligible participants included outpatient children and adolescents, 6-16 years of age, weighing between 20 and 60 kg with a symptom threshold of >=25 for boys or >=22 for girls, or >12 for a specific subtype, on the Attention Deficit Hyperactivity Disorder Rating Scale-IV-Parent Version: Investigator-Administered and -Scored, as well as a Clinical Global Impressions Attention Deficit Hyperactivity Disorder-Severity (CGI-ADHD-S) score of >=4. Exclusion criteria included any history of bipolar, psychotic or pervasive developmental disorders; suicidal risk; or ongoing use of psychoactive medications other than the study drug. Patients with motor tics, a diagnosis or family history of Tourette’s syndrome or those who met DSM-IV criteria for anxiety disorder as assessed by the investigator and confirmed by the K-SADS-PL were also excluded  **Other:**  **ADHD presentation:** inattentive : 38,hyperactive : 3,combined : 59  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 18 %  **Age mean:**  Atomoxetine 9.4 (2.0) Methylphenidate 9.9 (2.3)  **Minimum age:** 6  **Maximum age:** 16  **Ethnicity:**  % Hispanic or Latino : 8  % Asian : 92 | **Intervention:** Atomoxetine 0.8-1.8 mg/kg/day for 8 weeks  **Control:** NA  **Comparator:** MedicationMethylphenidate, began therapy at 0.2 mg kg^(-1) day^(-1) administered twice daily (in the morning and at lunch), which was titrated to 0.4 mg kg^(-1) day^(-1) on Day 5, and could be either maintained or titrated upward or downward within the final range  **Follow-up:** 2 months | CGI-ADHD-S ( Clinical Global Impressions-Attention Deficit Hyperactivity Disorder-Severity) scale  Both groups improved.  ADHD-RS-IV (Attention Deficit Hyperactivity Disorder Rating Scale-IV-Parent Version), investigator-administered, change  Similar improvement between the treatment groups.  Weight loss  Decreased appetite  The rate for appetite suppression was 28% in the atomoxetine and 19% in the methylphenidate group (p 0.070). Atomoxetine reported -1.2 kg vs. methylphenidate -0.4 kg weight loss (p 0.001).  Participants experiencing treatment emergent adverse events  A significantly greater percentage of patients in the atomoxetine treatment group (87%) experienced events compared with methylphenidate (67%; p<0.001).  No deaths were reported, a simple partial seizure was reported for a patient in the atomoxetine group (discontinued from the study). |
| FDA-approved pharmacological | Wehmeier, 2012608  Eli Lilly and Company, 2007753  ID: NCT00546910  RCT  Multicenter  N = 128  Germany  Setting: Mixed | **Target:** Girls and boys with a diagnosis of ADHD according to the DSM 4th edition TR  **Other:**  **ADHD presentation:** inattentive : 22.4,hyperactive : 7.2,combined : 70.4  **Diagnosis:** Confirmation by specialist  **Comorbidity:** N/A  **Female:** 22.4 %  **Age mean:** 9.0 (1.79)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % White : 99.2 | **Intervention:** Atomoxetine 0.5-1.2 mg/kg per day once daily in the morning for 8 weeks  **Control:** Placebo  Placebo-controlled  **Comparator:** NA  **Follow-up:** 2 months | Weekly Ratings of Evening and Morning Behavior (WREMB)  The severity of ADHD symptoms was reduced to a statistically significantly greater degree in the treatment group compared to placebo ( p<0.001).  CGI-S  The severity of ADHD symptoms was reduced to a statistically significantly greater degree in the treatment group compared to placebo (p<0.001).  ADHD-RS-IV  The severity of ADHD symptoms was reduced to a statistically significantly greater degree in the treatment group compared to placebo (p<0.0001).  Treatment was significantly superior to placebo in reducing hyperactivity, inattention, and impulsivity as measured by q-scores of 10 primary variables of the cb-CPT/MT (infrared motion-tracking devise).  Decreased appetite  The rate of decreased appetite was 1.6 in the intervention and 3.2 in the placebo group.  Participants with treatment emergent adverse events  The rate of participants with adverse events was 51% in the intervention and 44% in the control group.  No serious treatment emergent adverse event or death occurred. |
| FDA-approved pharmacological | Weiss, 2005611  Brown, 2006696  ID: N/A  RCT  Multicenter  N = 153  Multiple countries  Setting: Mixed | **Target:** Children with a standard deviation score of 1.0 for ADHD-Rating Scale-IV-Teacher Version and score at least 1.5 standard deviations above age and sex norm for the Conners Parent Rating Scale-Revised: Short Form ADHD Index  **Other:** Teachers had to be available for telephone interviews and updates on the progress  **ADHD presentation:** inattentive : 26.8,hyperactive : 0.7,combined : 72.5  **Diagnosis:** Confirmation by specialist  Followed the DSM-IV: "Diagnostic criteria were evaluated by clinic assessment and confirmed using a structured parent interview, the behavioral module of the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime V  **Comorbidity:** N/A  **Female:** 19.6 %  **Age mean:** 9.9 (1.3)  **Minimum age:** 8  **Maximum age:** 12  **Ethnicity:**  N/A : Not mentioned or brought up. | **Intervention:** Atomoxetine up to 1.8 mg/kg/day for 7 weeks  **Control:** Placebo  Identical in appearance, once-daily for 7 weeks  **Comparator:** NA  **Follow-up:** 1.75 months | Connors Global Index-Teacher, change from baseline  Statistically significant change favored the treatment group change compared to the placebo group (p=0.008).  ADHD-RS-IV-Teacher (Attention-Deficit/Hyperactivity Disorder Rating Scale-IV-Teacher) total score change  Only the standardized symptoms scores for the continuous data is available.  Treatment group responded with a reduction in score by 20% compared to the placebo group (Fisher exact test p 0.003).  Decreased appetite  Decreased appetite was 24.0% vs 3.8% (p 0.001).  5.9% in the atomoxetine group discontinued due to adverse events, including abdominal pain, emotional disturbance, feeling abnormal, irritability, and vomiting; no patients in the placebo group discontinued due to adverse events. |
| FDA-approved pharmacological | Weiss, 2007610  ID: N/A  Crossover trial  Multicenter  N = 90  Canada  Setting: Mixed | **Target:** Children with ADHD, score of 1.5 or greater standard deviation from the norm on the Conners’ ADHD Index; no allergy to methylphenidate or amphetamines or history of serious adverse reactions to methylphenidate or lack of response to methylphenidate, serious or unstable medical illness, co-morbid psychiatric illness of sufficient severity to require treatment, or currently receiving psychotropic medications or herbal treatments, a history of drug abuse, alcohol abuse, disorders of the sensory organs, autism, psychosis, or any unstable psychiatric conditions  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 18 %  **Age mean:** 11.0 (2.5)  **Minimum age:** 6.4  **Maximum age:** 17.5  **Ethnicity:**  % Black/African American : 6  % Asian : 4  % White : 83  Other : 7 | **Intervention:** Methylphenidate long-duration multilayer-release, once daily based on weight (10 mg for 20 kg, 20 mg for between 20 and 35 kg, and 30 mg for greater than 35 kg) for 2 weeks  **Control:** Placebo  Placebo in the morning and at midday  **Comparator:** MedicationImmediate-release MPH administered daily at 08:00 hour +/- 1 hour and 12:00 hour +/- 1 hour, initial daily dose was based on body weight (10 mg for <= 20 kg, 20 mg for between 20 and 35 kg, and 30 mg for greater than 35 kg), daily dose was titrated in 10-  **Follow-up:** 2.75 months | Home Situations Questionnaire (HSQ), number of problem situations  Both groups improved significantly form baseline but there was no difference between groups.  CGI (Clinical Global Impressions), investigator rating  No difference between active groups.  ADHD Index, CPRS (Conners’ Parent and Teacher Rating Scales)  Both active groups improved compared to baseline (p<0.05).  PSS (Parent Satisfaction Survey), satisfied or very satisfied with treatment  77% of parents were satisfied or very satisfied with MLR-MPH treatment and 82% with IR-MPH.  Decrease in ADHD Index and oppositional scales, which was of similar magnitude for MLR- and IR-MPH in patients.  Decreased appetite  There was no statistically significant difference between active treatment groups.  There were no significant differences between treatments in the adverse effects. |
| FDA-approved pharmacological | Weiss, 2021612  Rhodes Pharmaceuticals, 20141000; Rhodes Pharmaceuticals, 20141001  ID: NCT02139111, NCT02168127  RCT  Multicenter  N = 367  Multiple countries  Setting: Specialty care | **Target:** Children diagnosed with of any presentations of ADHD (hyperactive/impulsive, inattentive, or combined); either treatment naıve or dissatisfied with their current ADHD pharmacotherapy; age-appropriate intellectual functioning (IQ ≥80 based on the Wechsler Abbreviated Scale of Intelligence or Kaufman Brief Intelligence Test); provide a negative pregnancy test (if female); demonstrate that they could successfully swallow the largest capsule size  **Other:**  **ADHD presentation:** inattentive : 26.2,hyperactive : 1.9,combined : 71.5  **Diagnosis:** Confirmation by specialist  DSM-5 criteria by clinician  **Comorbidity:** N/A  **Female:** 33.0 %  **Age mean:** 14.2 (1.58)  **Minimum age:** 12  **Maximum age:** 17  **Ethnicity:**  N/A | **Intervention:** Methylphenidate long-acting formulation (PRC-063, Adhansia) 85 mg/day for 4 weeks  **Control:** Placebo  Identical in appearance  **Comparator:** MedicationLong-acting methylphenidate formulation (PRC-063, Adhansia) 25 mg/day for 4 weeks  **Follow-up:** 1 month | CGI-I (Clinical Global Impression-Improvement) responders (much or very much improved)  About 52.7% of participants randomized to PRC-063 were responders versus 32.4% on placebo (p 0.0004).  ADHD-5-RS  Treatment groups showed a statistically significant improvement compared to placebo.  Decreased appetite  Across doses, 20.1% of participants reported decreased appetite (none in placebo).  Participants with any treatment related adverse event  Across doses, the rate was 48.6% for placebo and 65.6% across all doses.  Two serious adverse events (both during the open-label study), one of which (aggressive behavior) was assessed as related to study drug. |
| FDA-approved pharmacological | Wietecha, 2009616  Saylor, 20101023; Eli Lilly and Company, 2004752  ID: NCT00191035  RCT  Multicenter  N = 267  US  Setting: Mixed | **Target:** Adolescents who met DSM-IV criteria for ADHD, score of at least1.5 standard deviation above age and gender normative sample for ADHD-Rating Scale-IV Parent version, score of 70 or more on Kaufman Brief Intelligence Test; no patients currently taking psychotropic medications, have a history of bipolar disorder, psychosis, autism, Asperger’s syndrome, pervasive developmental disorder, patients who previously participated in a study of atomoxetine  **Other:**  **ADHD presentation:** inattentive : 49.8,hyperactive : 2.2,combined : 47.9  **Diagnosis:** Confirmation by specialist  DSM-IV-TR via Kiddie Schedule for Affective Disorders and Schizophrenia for School Aged Children-Present and Lifetime Version (K-SAD-PL: Behavioral)  **Comorbidity:** N/A  **Female:** 35.95 %  **Age mean:** 14,6  **Minimum age:** 13  **Maximum age:** 16  **Ethnicity:**  % Hispanic or Latino : 7.49  % Black/African American : 12.0  % White : 74.5  Other : Other: 5.62% | **Intervention:** Atomoxetine slow titration group had starting dose 0.5 mg/kg/day for 7–9 days, followed by 1.0 mg/kg/day for 7–9 days, then 1.2 mg/kg/day for remainder of the 8-week period; fast titration group received atomoxetine at starting dose of 0.5 mg/kg/day for a minimum of 3 days followed by 1.2 mg/kg/day for the remainder of the 8-week study period; all received low dose of 0.8 mg/kg/day for 40 week maintenance  **Control:** NA  **Comparator:** MedicationAtomoxetine slow titration group had starting dose 0.5 mg/kg/day for 7–9 days, followed by 1.0 mg/kg/day for 7–9 days, then 1.2 mg/kg/day for remainder of the 8-week period; fast titration group received atomoxetine at starting dose of 0.5 mg/kg/day for a  **Follow-up:** 12 months | Youth Risk Behavior Surveillance (YRBS)  Total scores of the highest quartile patients did not improve significantly from baseline (p=0.116)  CGI-ADHD-S (Clinical Global Impressions-Attention-Deficit-Hyperactivity Disorder-Severity), clinician  Significant benefit was demonstrated with both titration schedules (p <0.001) and there was no significant difference between groups (p=0.205).  ADHD-RS (ADHD Rating Scale), clinician rating  Significant benefit was demonstrated with both titration schedules and there was no significant difference between groups.  Decreased appetite (8 week acute period)  No statistically significant differences were observed in any of the vital signs or in weight between the 0.5=1.2 mg=kg=day and 0.5=1.0=1.2 mg=kg=day groups. |
| FDA-approved pharmacological | Wigal, 2004617  ID: NA  RCT  Multicenter  N = 132  US  Setting: Specialty care | **Target:** Children with ADHD, female subjects were premenarche, without other psychological disorders, not taking antidepressants, sedatives/hypnotics, neuroleptics/antipsychotics, mood stabilizers, anticonvulsants, beta-blockers, α2-agonists, thyroid medications, and chronic oral steroids  **Other:**  **ADHD presentation:** inattentive : 34.8,hyperactive : 0.8,combined : 64.4  **Diagnosis:** Confirmation by specialist  DSM IV diagnosis, confirmed by NIMH Diagnostic Interview Schedule for Children (DISC-IV) administered to parents  **Comorbidity:** N/A  **Female:** 12 %  **Age mean:** 9.8 (2.65)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % Black/African American : 13.6  % White : 78.0  Other : Other race: 8.3 | **Intervention:** Dexmethylphenidate hydrochloride (d-MPH, Focalin) twice daily, withtitration of the dose based on weekly clinic visits, a maximum of 10 mg twice daily for 4 weeks  **Control:** Placebo  Placebo, twice daily for 4 weeks.  **Comparator:** Medicationd,l-threo-Methylphenidate Hydrochloride twice daily for 4 weeks, with titration of the dose based on weekly clinic visits.  **Follow-up:** 1 month | CGI-I, proportion much improved or very much improved  The percentage of patients with a therapeutic response was significantly higher in the group treated with d-MPH (p = .0010) and the group treated with d,l-MPH (p = .0130) than placebo.  SNAP-ADHD (abbreviated version of the full SNAP-IV Rating Scale) change, teacher reported  Treatment with either d-MPH (p = .0004) or d,l-MPH (p = .0042) significantly improved Teacher SNAP ratings compared with placebo. The d-MPH group showed significant improvements compared with placebo on afternoon Parent SNAP ratings (p = .0003) as did the  Anorexia  4 intervention patients, 2 placebo patients, and 6 comparator patients had clinically significant weight losses ranging from 5% to 18% of baseline values. Four intervention patients, 0 placebo patients, and 5 comparator patients had anorexia. P values n  70% of patients experienced at least one adverse event, more medication patients experienced headache and nausea. |
| FDA-approved pharmacological | Wigal, 2011618  Ortho-McNeil Janssen Scientific Affairs, 2008972  ID: NCT00799409  Crossover trial  Multicenter  N = 78  US  Setting: School | **Target:** Participants receiving medication to treat their ADHD exhibited an inadequate response to stimulant dose, completed a washout equivalent to 5 half-lives of the given medication before completing baseline assessments, attendance of regular school, the ability to read and understand English; no history or current diagnosis of epilepsy, severe anxiety, conduct, psychotic disorders, pervasive developmental, eating, obsessive compulsive, sleep, major depressive, bipolar, chronic tic, or disorders  **Other:**  **ADHD presentation:** inattentive : 19,hyperactive : 0,combined : 81  **Diagnosis:** Confirmation by specialist  K-SADS-PL  **Comorbidity:** N/A  **Female:** 30 %  **Age mean:** 10.1 (1.08)  **Minimum age:** 9  **Maximum age:** 12  **Ethnicity:**  % Black/African American : 28  % White : 58  Other : Other: 14% | **Intervention:** Methylphenidate OROS (Osmotic-Release Oral System) optimized dose of 18, 36,or 54 mg/day for 6 weeks  **Control:** Placebo  In the crossover design, subjects who completed both laboratory school assessments served as their own control and provided data for both OROS MPH and placebo  **Comparator:** NA  **Follow-up:** 1.5 months | Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP) - Composite score  Intervention group had significantly better scores than control group (p<0.0001).  Permanent Product Measure of Performance (PERMP) - Correct Answers  Intervention group had significantly better scores than control group (p<0.0001).  Children taking OROS MPH had significantly better scores than placebo-treated children on the Reaction Time, and Reaction Time Variability scores of the TOVA (p< 0.0001 for all). OROS MPH significantly improved performance on tests of visual working memory as demonstrated on both the Finger Windows forward and backward subtests.  Overall, 20 participants had appetite loss. The study reported only the overall number of adverse events .  A total of 39 subjects (50%) reported at least one treatment-emergent AE during the study. The types of AEs reported were consistent with those previously reported with the use of stimulant medications in the management of ADHD. There were no deaths or se |
| FDA-approved pharmacological | Wilens, 2005621  ID: N/A  RCT  Unclear/Not reported  N = 138  US  Setting: Specialty care | **Target:** Participants with IQ score ≥ 80; blood pressure measurements within the 95th percentile for age, gender, and height; electrocardiogram findings within the normal range; history of response to stimulant medication  **Other:**  **ADHD presentation:** N/A : for 6 months open-label MAS XR arm  **Diagnosis:** Confirmation by specialist  DSM-IV by either a child psychiatrist or psychologist  **Comorbidity:** N/A  **Female:** 29 %  **Age mean:**  Open-label mixed amphetamine salts extended release (MAS XR) mean age (year) at 14.4. No SD provided.  **Minimum age:** 13  **Maximum age:** 17  **Ethnicity:**  % White : 72.0  N/A : no other info provided | **Intervention:** Mixed amphetamine salts extended-release 50mg per day for 6 months  **Control:** Placebo  Placebo, no other description noted.  **Comparator:** Medication60 mg of MAS XR (mixed amphetamine salts extended-release)  **Follow-up:** 6 months | Changes in BP and QTcB (Bazett's formula) intervals at 4 weeks with MAS XR were not significantly different from the placebo group. Pulse increased by 5.0 and 8.5 bpm after 3 weeks with MAS XR 20 and 50 mg/day, respectively (P<.002). After 6 months of ope |
| FDA-approved pharmacological | Wilens, 2008619  Noven Therapeutics, 2005965  ID: NCT00151970  Crossover trial  Multicenter  N = 117  US  Setting: Specialty care | **Target:** Children with ADHD; no children with conduct disorder or comorbid illnesses that contraindicated or could confound medication treatment, or a history of failing to respond to psychostimulant treatment  **Other:** Parents provided some outcomes  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  Diagnosed per DSM-IV-TR criteria. Schedule for Affective Disorders and Schizophrenia for School Age Children-Present and Lifetime Version interview was also conducted  **Comorbidity:** N/A  **Female:** 35.9 %  **Age mean:** 8.8 (0.2)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % Black/African American : 15.4  % American Indian or Alaska Native : 0  % Asian : 0  % Native Hawaiian or Pacific Islander : 0  % White : 63.2 | **Intervention:** Methylphenidate transdermal patch, 6 hour patch, dose optimized over 5 weeks  **Control:** Placebo  Placebo transdermal patch  **Comparator:** MedicationMethylphenidate transdermal patch, dose optimized over 5 weeks, 4 hour patch  **Follow-up:** 2 months | CPRS-R (Conners Parent Rating Scale-Revised)  Mean total score decreased by >67% from baseline to follow-up when patients wore the patch (p <.0001).  ADHD-RS-IV (Attention-Deficit/Hyperactivity Disorder Rating Scale-IV) change, clinician rating  Mean total score decreased at follow-up when patients wore the patch (p <.0001).  Permanent Product Measure of Performance (PERMP) math problem score  A significant increase in the number of attempted math problems was seen during the 4- and 6-hour medicated patch wear times compared with placebo patch (p < .0001). Correct scores for the 4- and 6-hour medicated patch wear times were significantly high  326 treatment-emergent adverse events were reported during the entire study for subjects in the safety population, majority were mild (62%) or moderate (37%) in intensity; there were no serious adverse events. |
| FDA-approved pharmacological | Wilens, 2012622  Wilens, 20171176; Shire, 20081048  ID: NCT00734578  RCT  Multicenter  N = 461  US  Setting: Specialty care | **Target:** Children and adolescents with ADHD with suboptimal but partial response to stimulant medication  **Other:** Parents provided some outcome data  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV-TR per Kiddie Schedule for Affective Disorder - Present and Lifetime (K-SADS-PL)  **Comorbidity:** N/A  **Female:** 28.4 %  **Age mean:** 10.8 (2.4)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % Hispanic or Latino : 13.4  % Black/African American : 22.0  % American Indian or Alaska Native : 0.2  % Asian : 1.3  % Native Hawaiian or Pacific Islander : 0.7  % White : 67.7 | **Intervention:** Guanfacine extended release 1-4mg in morning as adjunct to usual stimulant medication for 9 weeks  **Control:** Placebo  Placebo plus usual stimulant medication daily  **Comparator:** MedicationGuanfacine extended release in evening plus usual stimulant medication  **Follow-up:** 2 months | Oppositional symptoms, measured by oppositional subscale of the Conners' Parent Rating Scale-Revised: Long Form (CPRS-R:L)  GXR + stimulant taken in AM (p<0.001) or PM (p<0.003) led to significantly greater improvement in oppositional symptoms than versus placebo + psychostimulant.  CGI-I (Clinical Global Impression - Improvement) much or very much improved  A higher proportion of intervention and comparator group aprticipants classified as much or very much improved on compared to placebo group (p =0.024 and p = 0.003).  ADHD-RS-IV (Attention Deficit Hyperactivity Disorder Rating Scale IV) , clinician rating  The intervention and the comparator group had greater decrease in ADHD symptoms at follow up than placebo (p 0.002 and p 0.001).  Before-School Functioning Questionnaire (BSFQ)  Participants who received GXR + psychostimulant showed significantly greater improvement compared with participants who received placebo + psychostimulant (p 0.002).  Participants with decreased appetite  Significantly more patients in the medication groups experienced appetite decrease compared to the placebo group.  Participants reporting any adverse event  The rates were 77.3% in the AM, 76.3% in the PM, and 63.4% in the placebo group.  Similar findings for somnolence, headache, abdominal pain, and fatigue. |
| FDA-approved pharmacological | Wilens, 2015623  Shire, 20111058  ID: NCT01081132  RCT  Multicenter  N = 314  US  Setting: Mixed | **Target:** Adolescents with ADHD; no co-morbid psychological disorder other than ODD or serious medical issues  **Other:** Parents reported function outcome  **ADHD presentation:** inattentive : 29.17,hyperactive : 2.89,combined : 67.95  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:**  **Female:** 35.03 %  **Age mean:** 14.5(1.39)  **Minimum age:** 13  **Maximum age:** 17  **Ethnicity:**  % Black/African American : 16.88  % American Indian or Alaska Native : 0.63  % Asian : 1.59  % White : 72.29  Other : 8.0% other | **Intervention:** Guanfacine extended-release once-daily less than or equal to 7mg for 13 weeks  **Control:** Placebo  Placebo ratio 1:1 same as baseline of 1 mg depending on weight group and was allowed to increase 1mg weekly  **Comparator:** NA  **Follow-up:** 3 months | CGI-S, number responded (score = 1 or 2)  More intervention participants showed improvement than control participants (p=0.01).  ADHD-RS-IV  Intervention participants showed improvement compared to control group (p<0.001).  Weiss Functional Impairment Rating Scale, parent (WFIRS-P)  No significant difference between groups.  Treatment emergent adverse events  Proportion of adverse events was 93.6% in the intervention and 77.4% in the placebo group  No clinically meaningful differencew between intervention and placebo on hematology, clinical chemistry, or urine analyses |
| FDA-approved pharmacological | Wolraich, 2001626  Faraone, 2005767; Spencer, 20061085; Baren, 2000675  ID: N/A  RCT  Multicenter  N = 282  US  Setting: Specialty care | **Target:** Children with ADHD who were taking methylphenidate or had taken it in the past; a total daily methylphenidate dose of at least 10 mg but not more than 60 mg; no glaucoma, Tourette’s syndrome, an ongoing seizure disorder, or a psychotic disorder, no girls who had reached menarche  **Other:** Parents and teachers provided outcome data  **ADHD presentation:** inattentive : 19.5,hyperactive : 7.1,combined : 73.4  **Diagnosis:** Confirmation by specialist  DSM diagnosed confirmed by Diagnostic Interview Schedule for Children (Version 4)  **Comorbidity:** N/A  **Female:** 17.4 %  **Age mean:** 9.0 (1.8)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % Hispanic or Latino : 3.5  % Black/African American : 7.4  % Asian : 0.4  % White : 84.4  Other : Other 4.3% | **Intervention:** Methylphenidate extended-release OROS tablets, 18 to 54 mg per day for 28 days  **Control:** Placebo  Placebo  **Comparator:** MedicationImmediate release methylphenidate, 5 to 15 mg per day  **Follow-up:** 1 month | CGI (Clinical Global Impression) much improved or very much improved  Both medications groups had more improvement in mean teacher (p < .05) and parent (p < .05) Conners ratings than placebo group. OROS MPH and immediate release MPH did not differ significantly (p < .539).  Inattention SNAP-IV, teacher report  The medication groups improved more than the placebo on SNAP-IV Inattention - Teacher Report, SNAP-IV Hyperactivity/Impulsivity - Teacher Report, SNAP-IV Inattention - Parent report and SNAP-IV Hyperactivity/Impulsivity - Parent Report p < .001 for all s  Proportion of patients eating less than usual  The percentage of patients eating less than usual was significantly higher (p < .001) for the 2 medication groups compared with placebo. There was not difference between the medication groups.  Participants experiencing at least one adverse event  The rate was 43% for intervention, 35% for control, and 47% for comparator. |
| FDA-approved pharmacological | Young, 2014634  Newcorn, 2013959; Stein, 20151087  ID: N/A  RCT  Multicenter  N = 340  Multiple countries  Setting: N/A | **Target:** Children with a primary diagnosis of ADHD according to DSM-IV-TR; a baseline ADHD-RS-IV total score 28 and a Clinical Global Impressions–Severity of Illness Scale score 4; no current diagnosis of controlled or uncontrolled comorbid psychiatric disorders; no previous or present risk for suicide; no history or active presence of cardiac abnormalities or a primary sleep disorder  **Other:** Parents  **ADHD presentation:** inattentive : 2.1,hyperactive : 1.8,combined : 96.1  **Diagnosis:** Confirmation by specialist  ADHD diagnosis according to DSM-IV-TR based on psychiatric assessment  **Comorbidity:** N/A  **Female:** 29.4 %  **Age mean:**  Intervention 9.1 (1.77), control 8.9 (1.78), comparator 9.3 (1.76)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % Black/African American : 36  % American Indian or Alaska Native : 0.3  % Asian : 0.6  % White : 57.1 | **Intervention:** Guanfacine extended release administered in the morning and placebo administeredin the evening, 1-4 mg/day based on dose optimization, for 8 weeks  **Control:** Placebo  Placebo administered in the morning and evening for 8 weeks  **Comparator:** MedicationGuanfacine extended release administered in the evening and placebo administered in the morning for 8 weeks; 5 week dose-optimization period, 3 week dose-maintenance period, and 9 day dose-taper period, dose optimization starting dose of 1 mg/day was titr  **Follow-up:** 2 months | CPRS-RS total score  Intervention group and comparator group had a significantly greater improvement from baseline in total score than control group (p<0.001).  ADHD-RS-IV score  At end of treatment, participants receiving guanfacine had a significantly greater reductions in mean ADHD-RS-IV total scores compared with the placebo group, regardless of the time of administration (p < .001 for all intervention groups versus placebo).  Weiss Functional Impairment Rating Scale–Parent Report (WFIRS-P)  Both medication groups showed significantly greater improvement in mean WFIRS-P Total scores versus placebo (p < 0.001).  No significant correlations were found between change from baseline to last visit in pediatric daytime sleepiness scale (PDSS) total scores by treatment group.  Decreased appetite  Rate of decreased appetite was 4% in the active arms and 2.7% in the placebo arm.  Participants with treatment-emergent adverse events  The rate of events was 79% in the active groups and 57% in placebo.  4.1% reported severe adverse events (4 in the AM, 5 in the PM group, 0 in placebo). |
| FDA-approved pharmacological | Zhu, 2017645  ID: ID NA  RCT  Single center  N = 104  China  Setting: Other | **Target:** Patients who met the ADHD diagnostic criteria of the DSM5, fourth edition  **Other:**  **ADHD presentation:** inattentive : 49.03,hyperactive : 29.80,combined : 21.15  **Diagnosis:** Confirmation by specialist  Confirmed by clinician using DSM 5.  **Comorbidity:** N/A  **Female:** 20.19 %  **Age mean:**  Atomoxetine 9.92 (2.98), methylphenidate 9.75 (3.14)  **Minimum age:** 6  **Maximum age:** 14  **Ethnicity:**  N/A | **Intervention:** Atomoxetine with initial dose 0.5 mg/kg per day then gradually increased to 1.2 mg/kg according to the participant's condition and tolerance, taken after breakfast for 2 months  **Control:** NA  **Comparator:** MedicationMethylphenidate with initial dose 0.2 mg/kg per day and then gradually increased to 0.5 mg/kh., taken after breakfast every day for 2 months  **Follow-up:** 2 months | CGI-ADHD-S  Both groups improved but there was no statistical significance in difference values between the two groups.  ADHD-RS (ADHD rating scale for parent version) total score  At the end of treatment, a significant decrease from baseline was observed in two groups in scores of ADHDRS-IV-Parent: Inv, 2 subscales and CPRS-R: S (ADHD index, learning problems, hyperactivity-impulsion and confrontation), with considerable clinical s  Loss of appetite  There was no statistically significant difference in loss of appetite between groups (p=0.239).  The incidence of lethargy of atomoxetine group was significantly higher than that of methylphenidate group (p=0.027). |
| Neurofeedback | Arnold, 2022126  Kerson, 2020880  ID: ID NA  RCT  Multicenter  N = 144  US  Setting: Specialty care | **Target:** Children with ADHD; comorbid diagnoses were allowed if they did not require psychiatric medication; exclusions were serious physical illness, convergence insuf­ficiency, vitamin D deficiency/insufficiency, more than 5 previous neurofeedback sessions, seizures, sleep apnea, restless legs, or current/recent psychoactive drug use other than stimulants for ADHD  **Other:** Parents and teachers provided outcomes  **ADHD presentation:** inattentive : 37.5,combined : 62.5  **Diagnosis:** Confirmation by specialist  DSM per Child Interview for Psychiatric Syndromes (CHIPS)  **Comorbidity:** N/A  **Female:** 23.3 %  **Age mean:** 8.6 (1.14)  **Minimum age:** 7  **Maximum age:** 10  **Ethnicity:**  % Hispanic or Latino : 10.83  % Black/African American : 7.63  % Asian : 4.24  % White : 76.3  % Multiracial : 8.47  Other : Other: 3.39 | **Intervention:** Theta-beta ratio neurofeedback protocol in which theta power was down-trained and beta power was reinforced at scalp site Cz or Fz, 38 sessions total, at 3 times per week for 13 weeks  **Control:** Placebo  Treatment of identical appearance, intensity/frequency, and duration, differing only in that reinforcement for controls was based on a pre­recorded EEG of another child  **Comparator:** NA  **Follow-up:** 25 months | Aggression, parent rating  Aggression score were more reduced in the intervention than control group.  Clinical Global Impression (CGI) global index, parent  Clinical Global Impression (CGI) - Severity >2  The proportion of scores above 2 was 78% in the intervention and 86% in the control group.  ADHD Symptom Remission  Decreases in both groups.  Functional Assessment Checklist, teacher rating  Function improved in both groups without statistical difference between them.  Percentage of participants with ADHD medication decrease/discontimuation was 7.1% for neurofeedback and 4.0% for control. |
| Neurofeedback | Bakhshayesh, 2011130  ID: NA  RCT  Unclear/Not reported  N = 35  Germany  Setting: N/A | **Target:** Children with a primary diagnosis of hyperkinetic disorder (disturbance of activity and attention (ICD-10:F90.0); or attention deficit without hyperactivity (ICD-10:F98.8); an IQ of >80; no known neurological or gross organic diseases, hyperkinetic conduct disorders (ICD-10:F90.1) or pervasive developmental disorders  **Other:** Parents, teachers; assessed the behavior of pre-and post-treatment  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  ICD-10:F90.0; (ICD-10:F98.8  **Comorbidity:** N/A  **Female:** 26 %  **Age mean:** 9.34 (1.92)  **Minimum age:** 6  **Maximum age:** 14  **Ethnicity:**  N/A | **Intervention:** EEG neurofeedback: each session lasted 30 min with a 30-s break between the different games, each game consisted of three trials lasting 3 min each, total of 30 sessions over 10-15 weeks  **Control:** NA  **Comparator:** OtherEMG biofeedback (BF) aiming at forehead muscle relaxation: Both groups experienced similar treatment conditions except for the location of electrodes. Children received instructions on a computer screen to familiarize them with the exercises based on thei  **Follow-up:** 6 months | FBB-HKS (German ADHD rating scales) total scores, parent report  Improvement of the NF group in total score was superior to EMG group and approached statistical significance (p=0.062; effect size -.77); no significant differences between treatment groups in teacher ratings  Computer Continuous Performance Test: Commission Errors: No significant difference between groups |
| Neurofeedback | Bluschke, 2022156  ID: ID NA  Clinical trial  Single center  N = 129  Germany  Setting: Specialty care | **Target:** Children and adolescents with ADHD according to ICD-10 criteria  **Other:** Parents reported one outcome measure  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  determined according to standard clinical guidelines by a team of experienced child and adolescent psychiatrists and psychologists  **Comorbidity:** N/A  **Female:**  % N/A  **Age mean:** 10.76 (0.37)  **Minimum age:**  **Maximum age:**  **Ethnicity:**  N/A | **Intervention:** Neurofeedback, downregulation of theta and upregulation of beta, 2 one-hours sessions per week for 8 weeks  **Control:** No intervention  No neurofeedback  **Comparator:** NeurofeedbackNeurofeedback, upregulation of beta, 2 one-hours sessions per week for 8 weeks  **Follow-up:** 2 months | ADHD Symptom Checklist inattention scale, parent rating  No significant difference in effect by group.  Flanker test: the no neurofeedback group demonstrated significantly faster reaction times than those in the intervention (p=0.007) or comparator (p=0.033) group. |
| Neurofeedback | Dashbozorgi, 2021215  Faculty of Rehabilitation, 2018764  ID: IRCT20160717028964N2  RCT  Single center  N = 40  Iran  Setting: Specialty care | **Target:** Male elementary school children with ADHD with IQ>90, no history of cerebral trauma/injuries, learning disability, and behavioral disorders, taking a stable dose of psychostimulant under the supervision of a child psychiatrist, no history of receiving any other types of non-medical therapies  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV per Child Psychiatrist  **Comorbidity:** N/A  **Female:** 0 %  **Age mean:** 11.17 (0.97)  **Minimum age:**  **Maximum age:**  **Ethnicity:**  N/A,Other : 100% Persian | **Intervention:** Neurofeedback 60 minute training sessions, twice a week, for a total of 12 sessions, for 6 weeks  **Control:** Placebo  Sham neurofeedback group that watched animations which had no therapeutic potency; they waited to receive neurofeedback training sessions after the study  **Comparator:** NA  **Follow-up:** 1.5 months | Buss-Perry Aggression Questionnaire (BPAQ)  Intervention group had significantly greater decrease in aggression (p=0.01)  BIS (Barrat Impulsiveness Scale)  Intervention group (NF) had significantly greater decrease in impulsivity (p=0.01) |
| Neurofeedback | Duric, 2017240  Duric, 2014748  ID: NCT01252446  RCT  Unclear/Not reported  N = 130  Norway  Setting: N/A | **Target:** Children with ADHD using the ICD-10 criteria; IQ>70; no involvement in another intervention group, including CBT and Stop Now And Plan; no co-morbid disorders other than Oppositional Defiant Disorder or anxiety disorder; no presence of a neurological and/or cardiovascular condition  **Other:** Parents, teachers  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  Child psychiatrist using ICD-10 diagnostic criteria consistent with DSM-IV  **Comorbidity:** N/A  **Female:** 20 %  **Age mean:**  11.2 (2.8), 11.4 (3.1), 10.9 (2.4) across groups  **Minimum age:** 6  **Maximum age:** 18  **Ethnicity:**  N/A | **Intervention:** Neurofeedback plus methylphenidate, 3 times a week, at a dosage of 1mg/kg/day in the form of long-acting methylphenidate capsules between 20–60mg, with a total of 30 sessions for 3 months  **Control:** Other  Methylphenidate, 3 times a week, of 1mg/kg/day in the form of long-acting methylphenidate capsules between 20–60mg, for 6 months  **Comparator:** NA  **Follow-up:** 6 months | ADHD core symptoms, Barkley’s Defiant Children rating scale, parent  All groups improved over time but no difference was found between groups (p=0.385).  School performance in the neurofeedback group did show a significant improvement (mean difference 1.5, CI 0.1 to 0.29). |
| Neurofeedback | Fuchs, 2003280  ID: ID NA  Cohort study  Single center  N = 34  Germany  Setting: Specialty care | **Target:** Treatment naive children with ADHD, Wechsler intelligence quotient >80; and at least one substandard score(<85) on the Test of Variables of Attention  **Other:** Teachers and parents reported outcomes  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV by : a child neurologist or pediatrician and a psychologist specialized in child and adolescent clinical psychology  **Comorbidity:** N/A  **Female:** 2.9 %  **Age mean:** 9.7 (1.25)  **Minimum age:** 8  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** EEG neurofeedback, 3 training sessions per week using the Neurocybernetics EEG BiofeedbackSystem; neurofeedback training consisted of 30–60 min of visual and auditory feedback per session, interrupted for short breaks if required; for 12 weeks  **Control:** NA  **Comparator:** MedicationMethylphenidate on school days only, dosages were adjusted during the treatment period and varied between 10 and 60 mg/day, for 12 weeks  **Follow-up:** 3 months | Conners Behavior Rating Scale, total, parent report  No significant difference in effect between groups on parent or teacher ratings.  No main effects of group or interactions for the three subscales of the d2 Attention Endurance Test. No main effect of group on Variables of Attention (TOVA). No effect of group on Wechsler Intelligence Scale for Children-Revised. |
| Neurofeedback | Gelade, 2017291  Gelade, 2016788; Janssen, 2016857; Janssen, 2016858; Janssen, 2017859; Janssen, 2020860; Gelade, 2018789; van Mourik, 2011 1140; van Mourik, 20101140  ID: NCT01363544  RCT  Multicenter  N = 112  Netherlands  Setting: Specialty care | **Target:** Children with confirmed ADHD, free of stimulant use for 1 month, IQ>80, no comorbidity restrictions  **Other:** Parents and teachers provided outcome data  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV-TR diagnosis required; parent- and teacher ratings on the Disruptive Behavior Disorders Rating Scale (DBDRS) confirmed diagnosis  **Comorbidity:** N/A  **Female:** 24.1 %  **Age mean:** 9.63 (1.76)  **Minimum age:** 7  **Maximum age:** 13  **Ethnicity:**  N/A | **Intervention:** Theta/beta neurofeedback training with the aim to inhibit theta (4–8 Hz) andreinforce beta (13–20 Hz) activity at Cz, three 45 minute individual training sessions a week, for 10–12 weeks  **Control:** Attention-matched control  Physical activity consisting of three 45 minute individual training sessions a week, over a period of 10–12 weeks  **Comparator:** MedicationShort-acting methylphenidate; during the 4 weeks titration phase, children received in pseudo-random order 5 mg, 10 mg, 15 mg, 10 mg MPH, or placebo for 1 week, twice daily  **Follow-up:** 6 months | Inattention score, SWAN, parent report  SWAN Inattention score, Parent report: MPH group had better score at follow-up than neurofeedback (p = .002).  SWAN Hyperactivity / Impulsivity score, Parent report: MPH group had better score at follow-up than neurofeedback (p = .005).  SWAN Inattention sc  Response speed at follow-up as measured by stop-signal reaction time (SSRT) and mean reaction time (MRT) was better for intervention compared to neurofeedback and physical activity ( p < .001 for all). |
| Neurofeedback | Gevensleben, 2010294  Gevensleben, 2009790; Wangler, 20111161  ID: ISRCTN87071503  RCT  Multicenter  N = 102  Germany  Setting: Specialty care | **Target:** Children with ADHD; vast majority (over 90%) were medication naive; included comorbid conduct disorder, emotional disorders, tic disorder, and dyslexia; lacked gross neurological, other organic disorders, and comorbidities not specified above  **Other:** Parents provided some outcome data  **ADHD presentation:** inattentive : 29.8,combined : 70.2  **Diagnosis:** Confirmation by specialist  Diagnoses were based on a semi-structured clinical interview (CASCAP-D [6]) and confirmed using the Diagnostic Checklist for Hyperkinetic Disorders/ADHD [7] by a child and adolescent psychiatrist or a clinical psychologist  **Comorbidity:** N/A  **Female:** 18.1 %  **Age mean:** 9.9 (1.25)  **Minimum age:** 8  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Neurofeedback system SAM (‘self-regulation and attention management’) with 36 units of 50 minutes each, divided in two blocks of 18 units, the units were combined in 9 sessions which took place 2-3 times a week, break of 2–3 weeks between the two treatment blocks over 8-11 weeks  **Control:** NA  **Comparator:** Cognitive trainingComputerized attention skills training which primarily exercises visual and auditory perception, vigilance, sustained attention, and reactivity; 36 units of 50 minutes each, divided in 2 blocks of 18 units; the units were combined in 9 sessions which too  **Follow-up:** 6 months | Problem behavior during homework, Homework Problem Checklist  No statistically significant difference.  FBB-HKS (German ADHD rating scale) total score  At one week post 8 week treatment, improvement in German ADHD rating scale (FBB-HKS) total score , parent rating, was greater for neurofeedback group compared to attention training group (p < .005). Improvement in teacher rating was also greater for neur  SDQ (Strength and Difficulties Questionnaire)  Effect size was 0.32 indicating a small positive effect of the intervention.  For the problem situations in family (HSQ-D) questionnaire, no significant effects were seen. |
| Neurofeedback | Gonzalez-Castro, 2016302  ID: ID NA  Clinical trial  Unclear/Not reported  N = 131  Spain  Setting: Mixed | **Target:** Children with ADHD and an IQ of 80 or higher  **Other:** Parents report ADHD symptoms outcome  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  Neuro-pediatrician  **Comorbidity:** N/A  **Female:** 37 %  **Age mean:** 9.61 (1.11)  **Minimum age:** 8  **Maximum age:** 11  **Ethnicity:**  N/A | **Intervention:** Neurofeedback plus pharmacological support, neurofeedback consisted of a 15 minsession, 3 days per week, methylphenidate administered according to neuropediatricians' recommendations, for 3 months  **Control:** Other  Pharmacalogical support, methylphenidate administered according to neuropediatricians' recommendations  **Comparator:** NA  **Follow-up:** 3 months | ADHD Scale of Assessment of Attention Deficit with Hyperactivity (EDAH)  Significant difference between neurofeedback plus pharma vs pharma alone.  Test of Variables of Attention (TOVA): Differences between combined intervention group and the pharmacological support only group were statistically significant (p 0.005) |
| Neurofeedback | Hasslinger, 2021320  Karolinska Institutet, 2013875  ID: NCT01841151  RCT  Single center  N = 217  Sweden  Setting: Other | **Target:** Individuals with ADHD as primary diagnosis, IQ>80, had sufficient Swedish proficiency, and stable pharmacologic treatment  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  Kiddie Schedule for Afective Disorders and Schizophrenia Interview  **Comorbidity:** N/A  **Female:** 24 %  **Age mean:**  12.21 and 12.61 (2.30 and 2.74)  **Minimum age:** 9  **Maximum age:** 17  **Ethnicity:** | **Intervention:** Slow cortical potentials neurofeedback plus pharmacotherapy, intentionally creating negative or positive slow cortical potentials, each trial lasted 10s, each session consisted of 144 trials split into 4 blocks (36 trial per block), lasted around 60 min, 5 sessions per week for 5 weeks  **Control:** TAU  Treatment as usual in accordance with regional guidelines for treatment of ADHD, pharmacotherapy, many of the children’s parents underwent psychoeducational parent group-training  **Comparator:** Cognitive trainingWorking Memory Training plus pharmacotherapy, computerized software program with visuospatial and auditory tasks called Minneslek Flex (based on CogMed); participants could choose between a Junior and a Senior version that differed in the thematic content  **Follow-up:** 6 months | Inattention, Conners 3 Swedish Version, parent  Intervention and comparator were significantly superior to control. There were no significant differences between intervention and comparator. Live Z-score neurofeedback outperformed slow cortical potential for teacher-rated hyperactivity (p 0.028; effect  No severe adverse events were reported during the trial, whereas transient stress-related problems were quite frequent. |
| Neurofeedback | Korfmacher, 2022375  ID: NCT 01879644  RCT  Single center  N = 115  Germany  Setting: Specialty care | **Target:** Children with ADHD; disorders or conditions that may mimic ADHD such as autism, brain disorders, epilepsy, hyperthyreosis, and any genetic or medical disorder associated with externalizing behavior were excluded  **Other:** Parents and teachers provided some outcomes  **ADHD presentation:** inattentive : 34,hyperactive : 11,combined : 55  **Diagnosis:** Confirmation by specialist  DSM-III-R and DSM-IV via semi-structured diagnostic interview (K-SADS-PL)  **Comorbidity:** N/A  **Female:** 23 %  **Age mean:**  mean 9.1  **Minimum age:** 7.0  **Maximum age:** 11.8  **Ethnicity:**  N/A | **Intervention:** Slow cortical potential neurofeedback training aims at first learning to controland self-regulate certain brain activity parameters (via real-time feedback and operant principles), and as the next step utilizing this ability (by transfer) to improve everyday life functioning; 3 booster sessions 6 months after end of therapy; 3 training sessions per week over 3 months  **Control:** NA  **Comparator:** BehavioralSelf management training addressing selective attention, inhibitory control, and self-regulation (e.g., stopping and checking), planning skills, and self-instruction; 3 sessions per week over 3 months; 3 booster sessions 6 months after end of therapy  **Follow-up:** 12 months | Conners Parent Rating Scale  No significant differences between groups in any Conner's Parent or Teacher Rating Scales (p > 0.34).  Conners parent-rated ADHD-index  Qb-Test (quantified behavior test) for core ADHD symptoms  Self-management decreased ADHD-index more than neurofeedback. No differences between the groups in the Qb subscales.  Quality of life assessed via KINDL-R self-report showed SMT superior to neurofeedback regarding quality of life in school. |
| Neurofeedback | Lim, 2019398  National Healthcare Group, Singapore, 2011951  ID: NCT01344044  RCT  Single center  N = 172  Singapore  Setting: Specialty care | **Target:** Children with ADHD; without intellectual disability, epilepsy and severe sensorineural deficits or co-existing psychiatric disorder  **Other:** One parent and one clinician per child completed outcome assessments  **ADHD presentation:** inattentive : 41.7,combined : 58.3  **Diagnosis:** Confirmation by specialist  Computerized Diagnostic Interview Schedule for Children Version IV (CDISC-IV)  **Comorbidity:** N/A  **Female:** 15.3 %  **Age mean:** 8.6 (1.54)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Brain-computer interface-based attention training program, first 8 weeks 3 sessions per week, next 12 weeks 4 sessions per week, each training session consists of 10 minutes gameplay, 10 minutes break, 10 minutes game play (30 minutes total), for 20 weeks  **Control:** Wait list  Wait list who received the intervention after the first group  **Comparator:** NA  **Follow-up:** 6 months | CBCL (Child Behavior Checklist) - Externalizing reduction  The intervention group had significantly greater reductions than the control group (p<0.001).  ADHD-RS, clinician-rated  The intervention group had significantly greater reductions on the inattentive symptom score on the clinician-rated ADHD-RS than control group (p=0.017).  A total of 11 children across groups reported at least one adverse event. Only 1 participant reported 2 different adverse events–headache and trouble paying attention/concentrating–on one occasion. None of these adverse events required medical treatment o |
| Neurofeedback | Luo, 2022409  ID: ChiCTR 1900021891  RCT  Single center  N = 121  China  Setting: Specialty care | **Target:** Children with ADHD, those with other serious neuropsychiatric diseases or IQ<80 were excluded  **Other:** Parents provided outcomes  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSMIV criteria by a qualifed psychiatrist  **Comorbidity:** N/A  **Female:** 20 %  **Age mean:**  8.8 (1.5), 8.8 (1.2), 9.1 (1.0) in the different groups  **Minimum age:** 7  **Maximum age:** 12  **Ethnicity:**  % Asian : 100,Other : assumed; conducted in China | **Intervention:** Neurofeedback plus computerized cognitive training; Focus Pocus training program includes neurofeedback games and cognitive training games, each training session consisted of 14 randomly ordered mini-games, each 1 min, total time per session 15 minutes; neurofeedback games to promote awareness and control of brain activity with EEG recorded via a portable Bluetooth device that provided the participant with real-time feedback; cognitive training games to train and improve inhibitory control and working memory abilities; 3-5 sessions per week online at home, for 3 months  **Control:** Other  Computerized cognitive training only; cognitive training games to train and improve inhibitory control and working memory abilities; 3-5 sessions per week online at home, for 3 months  **Comparator:** NA  **Follow-up:** 3 months | ADHD Rating Scale IV (ADHD-RS IV), parent  All groups improved; no significant difference in change among groups.  Weiss Functional Impairment Scale-Parent Report  All groups improved; no significant difference in change among groups.  Behavior Rating Inventory of Executive Function (BRIEF): no significant difference in change among groups. |
| Neurofeedback | Minder, 2018435  Zuberer, 20181194; University of Zurich, 20151135  ID: NCT02358941  RCT  Multicenter  N = 102  Switzerland  Setting: Mixed | **Target:** Children with ADHD, with or without hyperactivity; no severe comorbidities, autism, tics, or other psychiatric disorders; medication dose kept stable over duration of study  **Other:** Parents and teachers provided outcomes  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 35 %  **Age mean:**  Mean (SD) by group: 10.58 (2.3), 11.37 (1.7), 10.40 (2.0), 10.83 (1.8)  **Minimum age:** 8  **Maximum age:** 15  **Ethnicity:**  N/A | **Intervention:** Slow cortical potential neurofeedback with the Theraprax training device where patients were supposed to steer a feedback item on the screen downward or upward by changing brain activity; in 50% of the trials, the task was to decrease brain activity and in the other 50% to increase brain activity; in school setting, training began with two to three double sessions (2 × 45–60 min) per week and continued with one to two sessions per week, over a period of 10–14 weeks; in clinical setting, daily double sessions over 2 weeks, usually followed by a short therapy break and five double sessions over 5–8 weeks  **Control:** NA  **Comparator:** Cognitive trainingCognitive training with CogniPlus, a software program developed for the rehabilitation of neurological patients consisting of adaptive game-like training tasks that target neuropsychological functions such as alertness, sustained attention, working memory  **Follow-up:** 3.5 months | Conners-3 ADHD DSM–IV inattention, parent report  Conners-3 ADHD DSM-IV indices responder rate  Parent rated inattention score improved significantly more in cognitive training group than neurofeedback group. No significant differences between groups in other Conners scores. % responding: A greater % of neurofeedback patients "responded" - improve  BRIEF indices of Metacognition and Behavior Regulation, parent & teacher report: no significant differences in effect between intervention and comparator. |
| Neurofeedback | NF Coll. Group, 2021458  Ohio State University, 2014969  ID: NCT02251743  RCT  Multicenter  N = 144  US  Setting: N/A | **Target:** Children with ADHD and IQ>=80; an eyes-open theta/beta power ratio greater than or equal to 4.5 at Cz or Fz; stimulants discontinued for 5 days before major assessments; no comorbid disorder requiring psychoactive medication other than psychostimulant; no medical disorder requiring systemic chronic medication with confounding psychoactive effects  **Other:**  **ADHD presentation:** inattentive : 35.9,combined : 64.1  **Diagnosis:** Confirmation by specialist  DSM-V  **Comorbidity:** N/A  **Female:** 21.8 %  **Age mean:** 8.58 (1.14)  **Minimum age:** 7  **Maximum age:** 10  **Ethnicity:**  % Black/African American : 7.9  % Asian : 3.6  % White : 76.3  % Multiracial : 9.4 | **Intervention:** EEG biofeedback treatment, 5 training periods per training session, each period lasted 5 minutes at the beginning and gradually increased to 9 minutes per period in later sessions, 38 sessions in 14 weeks  **Control:** Placebo  Prerecorded electroencephalograms instead of the live electroencephalograph to determine rewards; participants were also counseled about the importance of sleep and nutrition, especially breakfast, and were given an “Eat Smart” list of recommended breakfa  **Comparator:** NA  **Follow-up:** 13 months | Conners 3 Aggression, teacher rating  The difference between groups was not statistically significant.  CGI-I (Clinical Global Impression-Improvement) improvement of more than 2  Responders were 61% in the intervention and 54% in the control group (p =0.36).  DSM Inattentive Symptoms on Conners 3 Long Version (average of teacher and parent ratings), change from baseline  Both groups improved and there was no significant difference between groups (p 0.412)  Functional assessment checklist, parent rating  The difference between groups was not statistically significant.  Appetite decrease  The rate was 26.2% in the intervention and 13.8% in the control group.  Adverse events that were possibly attributable to treatment were distributed proportionally between the treatments, with no significant difference in any. |
| Neurofeedback | Purper-Ouakil, 2021483  Mensia Technologies SA, 2016920  ID: NCT02778360  RCT  Multicenter  N = 186  Multiple countries  Setting: Mixed | **Target:** Children diagnosed with an inattentive or combined presentation of ADHD; without established diagnosis of autism, schizophrenia, severe generalized anxiety disorder, major depression, tics, epilepsy, or other neurological disorders; no antecedents of treatment with neurofeedback or medications for ADHD; no systemic chronic medication; IQ>80  **Other:**  **ADHD presentation:** N/A : Inattentive and combined presentation but no breakdown  **Diagnosis:** Confirmation by specialist  Made by a clinician using Kiddie-SADS (K-SADS)  **Comorbidity:** N/A  **Female:** 15.3 %  **Age mean:** 9.8 (1.8)  **Minimum age:** 7  **Maximum age:** 13  **Ethnicity:**  N/A | **Intervention:** At-home neurofeedback training consisted of five 4-minute-long active blocks (withreal-time feedback) and two 2.5 minute-long transfer blocks (with only intermittent feedback), 2 treatment phases of 16 to 20 sessions (4 per week), for 90 days  **Control:** NA  **Comparator:** MedicationMethylphenidate, open titration period of 3 weeks and a treatment period with titration started at 10 mg of extended-release methylphenidate per day and a maximum possible dose of 60 mg/day; treatment lasted 2 months  **Follow-up:** 3 months | CGI improvement  The comparisons between neurofeedback and medication were significant, indicating a better CGI Improvement in the medication group; 76.3% were much or very much  improved with medication and 21.1% with neurofeedback.  ADHD-Rating Scale-Clinician-rated total score  The study failed to demonstrate noninferiority of neurofeedback vs methylphenidate (mean between-group difference 8.09; 90% CI 8.09, 10.56).  Executive functions (BRIEF) showed significant decreases in both groups, the comparison showed greater effects in the medication group (p=0.002).  Participants with spontaneous reporting or Pediatric Adverse Event Rating Scale adverse events  91% of patients in the MPH group versus 21.6% in the NF group had at least one adverse event related to treatment with a significant between-group difference (chi-square test (1) = 80.71, p < .0001);  Severe adverse events occurred in 20.9% of patients in the MPH vs 29.7% in the NF group (p=0.195). |
| Neurofeedback | Qian, 2018484  ID: ID NA  RCT  Single center  N = 29  Singapore  Setting: Specialty care | **Target:** ADHD participants who had combined or inattentive subtypes on medicine after at least 1 month of washout  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 0 %  **Age mean:**  9 (1.5) and 9.45 (1.29) in the groups  **Minimum age:**  **Maximum age:**  **Ethnicity:**  N/A | **Intervention:** Brain-computer-interface training: each session lasting 30 minutes with breaks included,3 sessions per week for 8 weeks  **Control:** No intervention  MRI scan and clinical assessment were performed in the control group although no intervention was done  **Comparator:** NA  **Follow-up:** 2 months | CBCL (Child Behavior Checklist)  The reduction of internalizing problems in the intervention group was slightly greater than that in the control group, but not significant (p = 0.44).  ADHD-RS, clinician rated inattention  The intervention group had significantly greater reduction in the ADHD-RS clinician inattention scores compared to the control group (p=0.038). |
| Neurofeedback | Rahmani, 2022490  ID: IRCT20190602043790N1  RCT  Single center  N = 112  Iran  Setting: Specialty care | **Target:** Children with ADHD; those with serious medical conditions or using psychotropic medication were excluded  **Other:** Parents and teachers provided outcomes  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM V by psychiatrist  **Comorbidity:** N/A  **Female:**  % N/A  **Age mean:** 11.3 (1.94)  **Minimum age:** 6  **Maximum age:** 15  **Ethnicity:**  N/A | **Intervention:** Neurofeedback, one 30-min session 2 days per week, for 12 weeks  **Control:** No intervention  No intervention  **Comparator:** NA  **Follow-up:** 3 months | ADHD-RS-IV, total, parent rating  Effect was more significant in the intervention group (p<0.001). ADHD-RS-IV, total, teacher rating showed similar results (p<0.05).  The rate of reported side effects was not different across all groups for 12 weeks. No dangerous side effect was reported in any of the patients during 12 weeks. All reported side effects ranged from mild to moderate. |
| Neurofeedback | Rajabi, 2020492  ID: ID NA  RCT  Single center  N = 32  Iran  Setting: School | **Target:** Children diagnosed with ADHD, IQ > 85, no comorbid disorder other than oppositional defiant disorder, depression, and anxiety disorder  **Other:**  **ADHD presentation:** inattentive : 15.6,hyperactive : 25.0,combined : 59.4  **Diagnosis:** Confirmation by specialist  DSM-V  **Comorbidity:** N/A  **Female:** 0 %  **Age mean:**  intervention 10.20 (1.3), control 10.05 (0.83)  **Minimum age:**  **Maximum age:**  **Ethnicity:**  N/A | **Intervention:** Monopolar neurofeedback training, 3 times a week during thirty 45-min sessions, for 3 months  **Control:** Wait list  Waiting list control  **Comparator:** NA  **Follow-up:** 2.5 months | Attention, CPRS-R (Conners Parent Rating Scales-Revised)  There was a statistically significant effect favoring the intervention group.  The intervention significantly improved total attention and total response control (impulsivity) measured by the Integrated Visual and Auditory Continuous Performance compared to the control group (p <0.05). |
| Neurofeedback | Steiner, 2014562  Steiner, 20141088; Tufts Medical Center, 20121124  ID: NCT01583829  RCT  Multicenter  N = 104  US  Setting: School | **Target:** Children with ADHD, IQ of 80 or higher; with no coexisting diagnosis of conduct disorder, autism spectrum disorder, or other serious mental illness  **Other:** Parents provided some outcome data  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  clinical diagnosis of ADHD made by the child’s clinician,  **Comorbidity:** N/A  **Female:** 26.0 %  **Age mean:** 8.57 (1.0)  **Minimum age:** 7  **Maximum age:** 10  **Ethnicity:**  % Black/African American : 6.7  % Asian : 18.3  % White : 73.1 | **Intervention:** Neurofeedback training (Play Attention) in-school 45- minute intervention sessions 3 times per week, monitored by a trained research assistant for 40 sessions over 5 months  **Control:** No intervention  No intervention  **Comparator:** Cognitive trainingCognitive training via computer (Captain’s Log, BrainTrain) with 14 auditory and visual exercises targeting areas of attention and working memory; each exercise is interactive and lasts ∼5 minutes; in-school 45- minute intervention sessions 3 times per we  **Follow-up:** 6 months | Behavioral Observation of Students in Schools (BOSS), Off-task, teacher  Significant improvements were found in the intervention condition compared with the control (p 0.04) but there were no differences found between the intervention and comparator.  Inattention score Conners 3, parent report  Intervention participants had significantly greater than gains than control group on the Connor's 3 Inattention, Executive Functioning and Hyperactivity/Impulsivity scales (p < .01 for all).  Swanson, Kotkin, Agler, M-Flynn and Pelham scale (SKAMP) total score  No significant differences between groups in SKAMP total score at follow up.  Intervention (neurofeedback) group had greater improvement at follow-up compared to control group on the following Behavior Rating Inventory of Executive Function (BRIEF) rating summary scales: Behavior Regulation (p < .03), Metacognition (p < .04), and Global Executive Composite (p < .01).  No adverse side effects of either intervention were reported on the standardized session checklists. |
| Neurofeedback | Strehl, 2017567  Holtmann, 2014837; Aggensteiner, 2019657  ID: ISRCTN76187185  RCT  Multicenter  N = 150  Germany  Setting: School | **Target:** Children diagnosed with ADHD combined type according to the DSM-IV; no diagnosis of bipolar disorder, obsessive compulsive disorder, psychosis, chronic severe tics, Tourette syndrome, major physical or neurological illness, and IQ of less than 80  **Other:**  **ADHD presentation:** combined : 100  **Diagnosis:** Confirmation by specialist  Diagnosis confirmed by licensed psychologist/clinical psychiatrists  **Comorbidity:** N/A  **Female:** 16.7 %  **Age mean:**  mean (SD) Neurofeedback group 8.6 (0.92), EMG feedback 8.57 (0.88)  **Minimum age:** 7  **Maximum age:** 9  **Ethnicity:**  N/A | **Intervention:** Neurofeedback where participants were prompted to either produce negative (reducingthe excitability threshold of the underlying cortex) or positive shifts (inhibition of excitation) in a randomized order; after session 12, ratio of negativity to positivity trials increased from 50 to 80%, total of 25 training sessions with 2-3 sessions per week, for 3 months  **Control:** Placebo  Semi-active control condition EMG feedback of coordination in the supraspinatus muscles where participants were instructed either to contract or to relax the left relative to the right supraspinatus muscle to induce differential EMG control corresponding  **Comparator:** NA  **Follow-up:** 6 months | ADHD Symptom Severity, parent-rated  Neurofeedback showed a significant superiority over EMG (treatment difference 0.17, 95% CI 0.02–0.3, p = 0.02); yielding an effect size (ES) of d = 0.57 without and 0.40 with baseline observation carried forward (BOCF); the sensitivity analysis confirmed  In the safety population (N = 140) 119 AE were reported.; at least one AE was reported in 33% of NF participants and 35% of EMG participants; children reported headaches (N = 4, both groups), skin reactions (n = 3, NF), myalgia (n = 1, EMG), and nausea (n |
| Neurostimulation | Schertz, 2022517  ID: MOH\_2018-07-24\_002209  RCT  Single center  N = 27  Israel  Setting: Specialty care | **Target:** Children with ADHD; those with history of seizure or presence of brain implant device or score above 70 on the anxiety/depression subtest of the Child Behavior Checklist were excluded  **Other:** Parents provided some outcomes  **ADHD presentation:** inattentive : 56,hyperactive : 12,combined : 32  **Diagnosis:** Confirmation by specialist  DSM -V by a specialist in pediatric neurology and child development or a pediatrician with formal training  **Comorbidity:** N/A  **Female:** 28 %  **Age mean:** 10.83 (1.79)  **Minimum age:** 8  **Maximum age:** 16  **Ethnicity:**  N/A : Israel | **Intervention:** Transcranial Direct Current Stimulation, 12 sessions, 20 minutes each, combined with cognitive therapy 3 times per week, for 4 weeks  **Control:** Other  Sham Transcranial Direct Current Stimulation, 12 sessions, 20 minutes each, combined with cognitive therapy 3 times per week, for 4 weeks  **Comparator:** NA  **Follow-up:** 2 months | Child Behavior Checklist (CBCL) overall score  No significant difference in total score or any subscore other than social problems (p 0.035).  Vanderbilt ADHD Rating Scales total score, parent report  Group difference not significant (p 0.475).  No effect of group on Cambridge Neuropsychological Test Automated Battery (CANTAB).  Any adverse event  No group differences in number of adverse events.  3 children, all receiving active stimulation, reported notable headaches, resulting in removal from the study for one child and temporary suspension of intervention for two children. |
| New pharmaceutical agent | Aevi Genomic Medicine, 2016113  ID: NCT02777931  RCT  Single center  N = 101  US  Setting: Specialty care | **Target:** Children and adolescents with diagnosis of ADHD based on DSM-V criteria, ADHD-Rating Scale-5 score > 28 at baseline, IQ at least 79, have disruptive mutations in genes within the glutamate receptor metabotropic-network, no substance use, no comorbid psychiatric disorders, no serious chronic or physical health conditions  **Other:** Parent reported symptoms outcome  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM V  **Comorbidity:** Other : Genetic disorders  **Female:** 37.1 %  **Age mean:** 14.1 (1.58)  **Minimum age:** 12  **Maximum age:** 17  **Ethnicity:**  % Black/African American : 29.9  % American Indian or Alaska Native : 2.1  % Asian : 1.0  % White : 56.7  % Multiracial : 9.3  Other : Unknown: 1 count (1.0%) | **Intervention:** NFC-1 (Fasoracetam) 100-400 mg twice daily as capsules (size 2 hard gelatin capsules);dosing was be optimized during the first 4 weeks of treatment, based on clinical response and tolerability, and maintained for an additional 2 weeks; total duration of 6 weeks  **Control:** Placebo  Matching placebo capsules  **Comparator:** NA  **Follow-up:** 1.5 months | CGI-S, number responding (Very much improved" or Much improved")  Intervention group performed better than placebo.  ADHD-RS-5, parent report, decrease from baseline  Symptoms were reduced more in the intervention group compared to control.  Non serious adverse events, number with  The rate was 70% for intervention and 56% for control. Statistical tests not conducted.  No serious adverse events in either group. |
| New pharmaceutical agent | Aevi Genomic Medicine, 2018114  ID: NCT03609619  RCT  Multicenter  N = 108  US  Setting: Mixed | **Target:** Children with diagnosis of ADHD according to DSM-V criteria, minimum score of 28 on ADHD-Rating Scale-5; those with autism spectrum disorder or significant cardiovascular conditions, any of the specific gene mutation of interest implicated in glutamatergic signaling and neuronal connectivity; no other medications except for medications intended to treat ADHD within 28 days prior to screening visit  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM V  **Comorbidity:** N/A  **Female:** 35.2 %  **Age mean:** 10.4 (2.86)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % Hispanic or Latino : 18.5  % Black/African American : 14.8  % American Indian or Alaska Native : 0.9  % Asian : 0.00  % White : 75.9  % Multiracial : 4.6  Other : Not reported: 4/108 (3.7%) | **Intervention:** AEVI-001 (fasoracetam monohydrate) 100 mg, 200 mg or 400 mg administered orally twice daily for 6 weeks  **Control:** Placebo  Oral doses of placebo administered twice daily  **Comparator:** NA  **Follow-up:** 1.5 months | CGI-I (Clinical Global Impression) - Global Improvement scale, response (very much improved or much improved)  No significant difference between groups.  ADHD-RS-5 (Attention Deficit Hyperactivity Disorder Rating Scale) change  No difference in rates of improvement.  Non serious adverse events  The intervention rate was 6% and the comparator rate was 17%.  No serious adverse events in both treatment groups. |
| New pharmaceutical agent | Amiri, 2008122  ID: N/A  RCT  Single center  N = 60  Iran  Setting: Other | **Target:** Children with ADHD; no history or current diagnosis of pervasive developmental disorders, schizophrenia or other psychiatric disorders, any current psychiatric comorbidity that required pharmacotherapy, any evidence of suicide risk and mental retardation (I.Q.<70), a clinically significant chronic medical condition, current abuse or dependence on drugs within 6 months, hypertension, hypotension and habitual consumption of more than 250 mg/day of caffeine  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV-TR  **Comorbidity:** N/A  **Female:** 22 %  **Age mean:**  Modafinil 9.20 (2.53), methylphenidate 8.96 (2.34)  **Minimum age:** 6  **Maximum age:** 15  **Ethnicity:**  N/A | **Intervention:** Modafinil film coated tablet in doses of 200–300 mg/day depending on weight (200 mg/day for <30 kg and 300 mg/day for >30 kg) for 6 weeks  **Control:** NA  **Comparator:** MedicationMethylphenidate (in doses of 20–30 mg/day) depending on weight (20 mg/day for <30 kg and 30 mg/day for >30 kg), titrated up: week 1: 10 mg/day (5 mg in the morning and 5 mg at midday); week 2: 20 mg/day (10 mg in the morning and 10 mg at midday) and week  **Follow-up:** 1.5 months | ADHD-RS-IV (ADHD Rating Scale-IV) parent and teacher report  Responders (at least 40% decrease in ADHD-RS scores)  Both groups showed a significant improvement over the 6 weeks of treatment for the parent and teacher ratings.  Decreased appetite  Observed more frequently in the methylphenidate group (p 0.03).  Ten side effects were observed over the trial that all of them were mild to moderate and tolerable. The difference between the modafinil and methylphenidate groups in the frequency of side effects was not significant except for decreased appetite and diff |
| New pharmaceutical agent | Biederman, 2005147  ID: NA  RCT  Multicenter  N = 248  US  Setting: Mixed | **Target:** Patients with ADHD according to DSM-IV, have a Clinical Global Impressions-Severity rating of 4 or higher, have a teacher-/investigator-rated Attention-Deficit/ Hyperactivity Disorder Rating Scale-IV School Version total and/or subscale score at least 1.5 standard deviations above normal values for age and gender, between 5-9th percentile for weight and health, IQ of at least 80 based on Wechsler Intelligence Scale for Children–Third Edition, and have a score of at least 80 on the Wechsler Individual Achievement Test–Second Edition–Abbreviated; no history or current diagnosis of pervasive developmental disorder, schizophrenia, DSM IV Axis I disorders, evidence of suicide risk, current psychiatric comorbidity that required pharmacotherapy, have well-controlled ADHD, history of substance abuse  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  Psychiatric/clinical evaluation and the Diagnostic Interview Schedule for Children, Fourth Edition  **Comorbidity:** N/A  **Female:** 29.3 %  **Age mean:**  Modafinil 10.4 (6-17), placebo 10.1 (6-17)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  N/A | **Intervention:** Modafinil film–coated tablets 170-425 mg/day for 9 weeks  **Control:** Placebo  Matching placebo pills for 9 weeks  **Comparator:** NA  **Follow-up:** 2.5 months | CGI-I (Clinical Global Impressions Scale-Improvement) responders  Proportion of participants who were classified as responders based on CGI-I rating (rating of 1 or 2) at final visit between modafinil and placebo groups were statistically significant (p<0.0001). Modafinil showed significantly greater improvement than pa  ADHD-RS-IV School Version total score  Difference between Modafinil and placebo groups in ADHD-RS-IV School Version total score at final visit was statistically significant (p < 0.0001).  Decreased appetite  The rate was 16% in the intervention and 4% in the placebo group (p=<0.05).  Serious adverse events were reported for 2 patients in the modafinil group (Stevens-Johnson syndrome possibly related to study; duodenitis, peptic ulcer, and hypertonia unrelated to study drug). |
| New pharmaceutical agent | Biederman, 2006146  ID: NA  RCT  Multicenter  N = 248  US  Setting: N/A | **Target:** Children with diagnosis of ADHD according to DSM-IV, stimulant-naive or who had manifested an unsatisfactory response to stimulant therapy, IQ of at least 80, a score of 80 or higher on the screener version of the Wechsler Individual Achievement Test, Clinical Global Impressions-Severity score of 4 or more at baseline visit  **Other:**  **ADHD presentation:** inattentive : 20.6,hyperactive : 2.0,combined : 76.6  **Diagnosis:** Confirmation by specialist  Psychiatric evaluation and the Diagnostic Interview Schedule for Children, Fourth Edition  **Comorbidity:** N/A  **Female:** 26.6 %  **Age mean:**  8.8 (2.0), 8.8 (2.1), 9.2 (2.1), 10.5 (1.6), 8.9 (2.0) across groups  **Minimum age:** 6  **Maximum age:** 13  **Ethnicity:**  % White : 81.5  Other : Other: 46/248 (18.5%) | **Intervention:** Modafinil 400 mg total, 200mg twice daily (morning and midday) for 4 weeks  **Control:** Placebo  5 placebo pills daily  **Comparator:** MedicationModafinil 100 mg followed by 200 mg at midday (modafinil 100/200-mg divided dose)  **Follow-up:** 1 month | CGI-I (Clinical Global Impressions of Improvement) much improved or very much improved  The intervention and comparator groups had significantly greater improvement compared to the control group (p=0.04 and p=0.01). Both the intervention and comparator groups had a higher percentage of participants rated as improved compared to the placebo,  ADHD-RS-IV (ADHD Rating Scale-IV), school version  The intervention group had significantly greater improvement compared to the control group (p=0.006).  Decreased appetite  The rates were 2% in the intervention and the placebo group and 12% in the comparator.  Insomnia was the only adverse event that occurred with significantly greater prevalence in a group assigned to modafinil (200/100-mg divided dose) than in the placebo group (p 0.03). One child who received modafinil 400 mg experienced serious dehydration, |
| New pharmaceutical agent | Blader, 2021151  Joseph Blader, 2008870  ID: NCT00794625  RCT  Multicenter  N = 175  US  Setting: Specialty care | **Target:** Children with ADHD (any subtype) and either oppositional defiant disorder or conduct disorder according to DSM-IV-TR; Retrospective Modified Overt Aggression Scale total score >24; recent or current treatment with stimulant medication at a minimum daily total dose equivalent of 30 mg of immediate-release methylphenidate for at least 30 days; no current or previous major depressive disorder, bipolar I or II disorder, Tourette’s disorder, autism spectrum disorder, or any psychotic disorder as defined by DSM-IV-TR; IQ>=70; no seizure disorders; no pregnancy; no contraindications to treatment with stimulants  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  Completion of the Schedule of Affective Disorders and Schizophrenia for School-Age Children (K-SADS) with a parent and the child by a clinical child psychologist or a child and adolescent psychiatrist. A second clinician (child and adolescent psychiatrist  **Comorbidity:** ODD  **Female:** 19 %  **Age mean:** 9.63 (2.02)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % Hispanic or Latino : 30.29  % Black/African American : 16.57  % White : 46.29  Other : 6.86 other | **Intervention:** Stimulant medication and behavioral therapy plus risperidone, dose started at 0.25 mg each evening for 3 days, with a morning dose of 0.25 mg added on the fourth day, dose adjustments were elective and based on response and tolerability, duration of 8 weeks  **Control:** Placebo  Stimulant medication and behavioral therapy plus placebo  **Comparator:** Medication + behavioralStimulant medication and behavioral therapy plus divalproex sodium, aimed to achieve approximately 18 mg/kg by the end of the first week; when permitted by valproic acid level, dose increases by 125 mg or 250 mg occurred based on clinical response through  **Follow-up:** 2 months | Retrospective Modified Overt Aggression Scale (R-MOAS), parent  % in remission from aggression (R-MOAS <15)  Intervention and comparator had larger reductions in aggression relative to the placebo group (risperidone p <0.003; divalproex sodium p<0.046). Percent in remission from aggression-remission was met by 69% of the risperidone group, 40% of the divalproex  There were no instances of serious adverse events. |
| New pharmaceutical agent | Blumer, 2009155  Sanofi, 20061021  ID: NCT00318448  RCT  Multicenter  N = 201  US  Setting: Other | **Target:** Patients with latency to persistent sleep of 30 minutes and a sleep disturbance not attributable to direct physiologic effects of an abused drug or misused prescription medication, no other sleep disorders diagnosed with baseline polysomnography, other major psychiatric disorders (but not obsessive-compulsive disorder), or a history of substance abuse and/or dependence, no previous adverse experience with zolpidem, no use of pharmacologic sleep aids that the patient was unwilling to discontinue or current use of rifampicin and/or sertraline  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:**  % N/A  **Age mean:**  N/A  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  N/A | **Intervention:** Zolpidem, recommended dose of 0.25 mg/kg, prepared as an oral formulation at 2.5 mg/mL, once per day at night for 8 weeks  **Control:** Placebo  Placebo was matched with respect to color and flavor  **Comparator:** NA  **Follow-up:** 2 months | CGI-I (Clinical Global Impressions Scale), parent  There was no significant difference between groups (p=0.076).  ADHD Rating Scale-IV  Baseline-adjusted mean changes did not differ between groups.  No significant difference between treatment groups in latency to persistent sleep of more than 30 minutes was detected.  Participants with at least one treatment emergent adverse event  Rate of 62.5% in treatment and 47.7% in placebo group.  Administration was terminated because of adverse events for 7.4% in the intervention and none in the placebo group; the main reason was hallucination. |
| New pharmaceutical agent | Bostic, 2000158  ID: N/A  Crossover trial  Unclear/Not reported  N = 21  US  Setting: Other | **Target:** Children with ADHD and no clinically significant medical conditions or abnormal baseline laboratory liver function tests, mental retardation, organic brain disorders, unstable psychiatric conditions, bipolar disorder, psychosis, drug or alcohol abuse or dependence within the prior 6 months, or active pregnancy or nursing  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 14 %  **Age mean:** 14.14 (1.6)  **Minimum age:** 12  **Maximum age:** 17  **Ethnicity:**  % White : 90 | **Intervention:** Pemoline, morning and after school dosing as 18.75-mg and 37.5-mg tablets(3mg/kg/day) for 4 weeks  **Control:** Placebo  Identical appearing and tasting 18.75-mg and 37.5-mg tablets morning and after school dosing  **Comparator:** NA  **Follow-up:** 2.5 months | CGI score very much improved or much improved  A significantly higher proportion experienced improvement on pemoline relative to placebo (60% versus 11%, p 0.013).  Hyperactivity, Inattentiveness, Impulsivity, DSM-IV-derived ADHD rating scale  Progressive improvement in the intervention group compared to placebo (p 0.001).  Using standard cutoff points for depression (HAM-D . 16, BDI . 19) and anxiety (HAM- A.21), no subjects had scores indicative of clinical depression or anxiety. Furthermore, none of the three depression or anxiety measures changed to a clinically or statistically significant degree over the course of this study (all p . 0.05).  Loss of appetite  Rates were 38% in intervention and 10% in placebo (p 0.014).  The only adverse effects specifically associated with pemoline relative to placebo were mild insomnia (62% versus 5%, p < 0.001) and mild loss of appetite (38% versus 10%, p 0.014). |
| New pharmaceutical agent | Buitelaar, 1996165  ID: N/A  Crossover trial  Unclear/Not reported  N = 52  Netherlands  Setting: N/A | **Target:** Children with ADHD according to DSM-III-R criteria, scores in the clinical range on both the Child Behavior Checklist and Conners' Teacher Rating Scale hyperactivity factors, deficits in attention performance on either a reaction-time task or a continuous performance task; no previous treatment with psychotropic medication, a clinical indication for drug treatment, diagnosis of tic disorder or pervasive developmental disorder, a family history of tic disorder, and the usual contra-indications for treatment with j9-blockers such as cardiac diseases, hypotension, obstructive pulmonary diseases, and insulin-dependent diabetes  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 12 %  **Age mean:**  109.8 (20.2) and 113.2 (19.1)  **Minimum age:** 6  **Maximum age:** 13  **Ethnicity:**  N/A | **Intervention:** Pindolol 20 mg twice per day for 4 weeks  **Control:** Placebo  Matching placebo administered at breakfast and at noon  **Comparator:** MedicationMethylphenidate 10 mg b.i.d, during the first 3 days a single dose of 10 mg, then treated in a fixed-dosage schedule 10 mg b.i.d at breakfast and at noon  **Follow-up:** 1 month | CGI-S  No difference between the two active treatments  Hyperactivity scale CPRS (Conners Parent Rating Scale)  No difference between groups.  Anorexia  The rate was 15% for pindolol, 24% for methylphenidate, and 25% for placebo.  Paresthesias were significantly more often reported with pindolol than with methylphenidate or with placebo; for all other adverse effects the frequencies did not differ significantly across drug status. |
| New pharmaceutical agent | Ceresoli-Borroni, 2021174  Supernus Pharmaceuticals, 20111098  ID: NCT01364662  RCT  Multicenter  N = 121  US  Setting: Specialty care | **Target:** ADHD participants with persistent impulsive aggression  **Other:**  **ADHD presentation:** N/A : aggressive subtype 100%  **Diagnosis:** Confirmation by specialist  DSM-4 by psychiatrist investigator  **Comorbidity:** ODD  **Female:** 12.9 %  **Age mean:** 9.0 (0.34)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % Hispanic or Latino : 16.9  % Black/African American : 30.5  % White : 63.6  N/A : 6.0 | **Intervention:** Molidone SPN-810, extended-release, 36mg/54mg, alongside existing monotherapy (stimulants/nonstimulants) and behavioral therapy, ~2.5-week titration, 3-week maintenance; total duration of 6.5 weeks  **Control:** Placebo  Placebo  **Comparator:** MedicationSPN-810, 12 mg/18 mg extended-release molindone (low dose)  **Follow-up:** 1.5 months | Rate of remission for aggressive behavior (Retrospective-Modified Overt Aggression Scale (R-MOAS) scale score ≤. 10)  Rates of remission for aggressive behavior were greater in intervention and comparator groups compared with placebo.  CGI Global Impression scale  There was no significant difference between any groups.  Weight and BMI  All treatment groups exhibited increases in mean weight and BMI.  Participants with adverse events  The intervention group had 68% of participants with any adverse events, the comparator group had 38%, and the placebo group had 58%. |
| New pharmaceutical agent | Conners, 1996206  ID: ID NA  RCT  Multicenter  N = 109  US  Setting: Specialty care | **Target:** Children with ADHD in good physical health with no lab abnormalities  **Other:** Parents and teachers provided data  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM III  **Comorbidity:** N/A  **Female:** 10.0 %  **Age mean:**  66% in 3rd grade or lower  **Minimum age:**  **Maximum age:**  **Ethnicity:**  % White : 75 | **Intervention:** Bupropion 50 mg or 75 mg, depending on body weight, twice daily at 7 AM and 7 PM. for 4 weeks  **Control:** Placebo  Placebo tablet  **Comparator:** NA  **Follow-up:** 1 month | Clinical Global Impression  The pooled results from the sites failed to demonstrate a significant treatment effect.  Conners Parent Questionnaire, hyperactive-immature, restless-impulsive, and conduct disorder  Improvements in the intervention group.  Significant treatment effects for the continuous performance test and memory retrieval.  Bupropion appeared to be well tolerated in most children; dermatological reactions were twice as frequent in the drug group than the placebo group with 4 reactions prompting discontinuation. |
| New pharmaceutical agent | Dehbozorghi, 2019219  Roozbeh Psychiatric Hospital, 20181016  ID: IRCT20090117001556N108  RCT  Unclear/Not reported  N = 53  Iran  Setting: N/A | **Target:** Participants with the diagnosis of ADHD based on DSM-5, the Kiddie Schedule for Affective Disorders and Schizophrenia 25, and medical history; patients with history or current diagno­sis of a psychiatric comorbidity except for oppositional defiant disor­der, pervasive develop mental disorders, mental retardation; history or allergy to tipepidine or methylphenidate hydrochloride; use or any medication or supplement for psychotropic disorders; presence or uncontrolled seizures; abnormal systolic blood pressure, resting pulse rate, or liver function; neurological or cardiac disorders were excluded  **Other:**  **ADHD presentation:** inattentive\_other : Intervention: 19.54 (5.83); Control: 18.89(5.35),hyperactive\_other : Intervention: 18.00(5.18); Control: 18. 22(5.00)  **Diagnosis:** Confirmation by specialist  DSM-V  **Comorbidity:** N/A  **Female:** 25 %  **Age mean:** 8.57(1.81)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Tipepidine (Asverin) at a dose of 15- 30 mg/day divided into 3 doses before breakfast, supper, and bedtime plus 0.3-1.5 mg/kg/day of methylphenidate hydrochloride divided into two separate doses at 30 min before breakfast and lunch, treatment over a period of 8 weeks  **Control:** Placebo  Starch as placebo (at a dose or 15- 30 mg/day) for 8 weeks  **Comparator:** NA  **Follow-up:** 2 months | CGI-S Score  The effect for time by treatment interaction was not significant (p=0.182).  ADHD-IV-RS, parent  On general linear model repeated measures analysis a significant effect was seen for time by treatment interaction (p=0.049).  Increased appetite  The rate was 4.16% in the intervention compared to none in the control group.  The frequencies of adverse events were similar between the groups. |
| New pharmaceutical agent | Dreakhshanpour, 2022232  ID: IRCT2015123025768N1  RCT  Single center  N = 55  Iran  Setting: Specialty care | **Target:** Children with ADHD; those with morbid obesity, excessive polyphagia, or unstable physical conditions that prevented drug intake, using any psychotropic drug during the two prior weeks or with co-psychiatric disorders such as bipolar mood disorder, mental retardation, and autism excluded  **Other:** Parents provided some outcomes  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM V TR  **Comorbidity:** N/A  **Female:** 23.6 %  **Age mean:** 3.98 (0.93)  **Minimum age:** 3  **Maximum age:** 6  **Ethnicity:**  N/A | **Intervention:** Risperidone daily, started at 0.25 mg/day in 1 dose and increased based on response and tolerance by 0.25 mg weekly increments, to a maximum dose of 1.25 mg/day for 12 weeks  **Control:** NA  **Comparator:** OtherAripiprazole started at 2.5 mg per day and gradually increased by 1.25 mg every week based on response and tolerance, to a maximum dose of 6.25 mg/day for 12 weeks  **Follow-up:** 3 months | Strengths and Difficulties Questionnaire (SDQ), pro-social behavior  Aripiprazole group improved more than risperidone group (p 0.031).  ADHD-RS, parent report  Aripiprazole group improved more than risperidone group (p 0.019).  No difference in improvement in emotional symptoms or peer problems based on the SDQ score.  No statistically significant differences between the adverse effects of the two drugs. |
| New pharmaceutical agent | Farmer, 2017264  Aman, 2008952; Findling, 2017775; Joseph, 2019871; Grondhuis, 2020806; Farmer, 2015770  ID: NCT00796302  RCT  Unclear/Not reported  N = 165  US  Setting: N/A | **Target:** Children with a DSM-4 diagnosis of any subtype of ADHD and evidence of severe physical aggression, either conduct disorder or oppositional defiant disorder, and a Clinical Global Impressions Severity score >=4, IQ >70, no condition that was a contraindication for medication, no family history of type-2 diabetes, not using any psychotropic medications that would cause risk to the participant if stopped, no suicidal ideation, eating disorder, autism disorder diagnosed using the DSM-4 criteria, or a mood disorder  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-4 diagnosis was required for participation  **Comorbidity:** ODD  **Female:** 22 %  **Age mean:** 8.94 (2.01)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % Black/African American : 41  % White : 61  Other : Non-Hispanic 93% | **Intervention:** Risperidone plus psychostimulant (usually osmotic release oral system [OROS] methylphenidate) titrated to an optimal dose for 6 weeks  **Control:** Other  Psychostimulant alone (usually osmotic release oral system [OROS] methylphenidate; STIM) plus placebo for 6 weeks titrated to an optimal dose  **Comparator:** NA  **Follow-up:** 2.25 months | No difference in h Conners’ Continuous Performance Test (CPT-II) or Digit Span performance was observed between groups. |
| New pharmaceutical agent | Findling, 2019269  Sunovion, 20151094; Sunovion, 20151093  ID: NCT02457819, NCT02428088  RCT  Multicenter  N = 342  US  Setting: N/A | **Target:** Children meeting DMS-V criteria, ADHD Rating Scale version IV-Home Version score >28, Clinical Global Impression-Severity Scale score >4; without bipolar or major depressive disorder, conduct disorder, obsessive compulsive disorder, disruptive mood dysregulation disorder, intellectual disability, psychosis, autism, Tourette's syndrome, central nervous system disorder, or any other unstable medical condition  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  participants were evaluated based on the DSM-V criteria at the beginning of the trial  **Comorbidity:** N/A  **Female:** 33.3 %  **Age mean:**  2mg/day dose 8.9 (1.7), 4mg/day dose 9.1 (1.9), placebo 9.2 (2.1)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % Black/African American : 29.5  % White : 62.9  % Multiracial : 7.6 | **Intervention:** Dasotraline 4 mg administered once-daily in the morning for 6 weeks  **Control:** Placebo  Placebo for 6 weeks  **Comparator:** MedicationDasotraline 2 mg administered once-daily in the morning for 6 weeks  **Follow-up:** 1.5 months | CGI Severity  The reduction compared to placebo was statistically significant for the 4mg (p 0.04) but not the 2mg dose (n.s.).  ADHD-RS-IV (ADHD Rating Scale-IV) Home Version total score change  There was a significant difference in 6 week change from baseline between the placebo and 4mg/day group (p<0.001), but not when compared to the 2mg/day. This significance was also observed between the placebo and 4mg/day groups in the CGI-S score (p 0.04)  Weight change  Decreased appetite  The rate was 21.7% in the 4mg, 15.3% in the 2mg, and 4.3% in placebo.  Discontinuation rates were higher in the 4mg/day (12.2%) than 2mg/day (6.3%) and placebo (1.7%) groups. Psychosis symptoms were reported in 7 participants. For events with a higher incidence on dasotraline compared with placebo, the most frequent were ins |
| New pharmaceutical agent | Greenhill, 2006304  ID: NA  RCT  Multicenter  N = 200  US  Setting: Mixed | **Target:** Participants with clinical diagnosis of ADHD, a Clinical Global Impressions-Severity rating of 4+, weight and height between 5-95th percentile, IQ at least 80, no learning disabilities, attending school full-time, have a investigator-rated ADHD-Rating Scale-IV School Version score of at least 1.5 standard deviations above the norm for the patient's age and gender; no history or current diagnosis of pervasive developmental disorder, schizophrenia, DSM-IV axis I disorder, any current psychiatric comorbidity that required pharmacotherapy, presence of suicide risk, ADHD symptoms well controlled on current therapy with tolerable side effects, or failed 2+ courses of stimulant therapy for ADHD  **Other:**  **ADHD presentation:** inattentive : 23.7,hyperactive : 5.1,combined : 70.2  **Diagnosis:** Confirmation by specialist  the National Institute of Mental Health Diagnostic Interview Schedule for Children, Fourth Edition (DISC-IV) was used to establish the patients’ diagnosis of ADHD using the full DSM-IV diagnostic criteria.  **Comorbidity:** N/A  **Female:** 27.3 %  **Age mean:**  Modafinil 9.9 (6-16), placebo 9.9 (6-16)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % Black/African American : 18.2  % White : 71.7  Other : Other: 20/198 (10.1%) | **Intervention:** Modafinil film-coated tablets 170-425mg once daily in the morning for 9 weeks  **Control:** Placebo  Matching placebo tablets once daily in the morning for 9 weeks  **Comparator:** NA  **Follow-up:** 2.5 months | CGI-I rated 1 or 2  52% of modafinil and 18% of placebo met criteria for responder on the CGI-I (p<0.0001).  ADHD-RS-IV School Version change  Modafinil produced significant reductions in ADHD-RS-IV total scores at school compared with placebo (p<0.0001).  Decreased appetite  The rate of decreased appetite as 18% in the intervention and 3% in the placebo group.  Modafinil was associated with significantly more insomnia, headache, decreased appetite, and weight loss than placebo, but discontinuation attributed to adverse events did not differ statistically between treatment groups (modafinil, 5%; placebo, 6%). |
| New pharmaceutical agent | Kahbazi, 2009354  ID: NA  RCT  Single center  N = 46  Iran  Setting: Specialty care | **Target:** Children newly diagnosed with ADHD; no history or current diagnosis of pervasive developmental disorders, schizophrenia, or other psychiatric disorders or a clinically significant chronic medical condition  **Other:** Parents and teachers provided outcome data  **ADHD presentation:** combined : 100  **Diagnosis:** Confirmation by specialist  DSM-IV-TR diagnosis confirmed by psychiatrist  **Comorbidity:** N/A  **Female:** 23.9 %  **Age mean:** 9.07 (2.03)  **Minimum age:** 6  **Maximum age:** 15  **Ethnicity:**  N/A | **Intervention:** Modafinil, 200–300 mg/day (once daily) depending on weight for 6 weeks  **Control:** Placebo  Placebo  **Comparator:** NA  **Follow-up:** 1.5 months | ADHD-RS-IV (ADHD Rating Scale-IV) change, parent report  ADHD Rating Scale-IV (ADHD-RS-IV), parent report, % responding (at least 40% decrease in score)  Change in ADHD Rating Scale-IV (ADHD-RS-IV) total, teacher report favored intervention (p < 0.001), as did ADHD-RS-IV total score, parent report (p < 0.001).  The difference in % responding (at least 40% decrease in score) was significantly higher in the  Decreased appetite  More children in the modafinil group reported decreased appetite (p=0.05).  No statistically significant differences between groups regarding abdominal pain, anxiety or nervousness, sadness, difficulty falling asleep, weight loss, nausea, dry mouth , irritability, or headaches. |
| New pharmaceutical agent | Kratochvil, 2005377  ID: ID NA  RCT  Multicenter  N = 173  US  Setting: Mixed | **Target:** Children and adolescents with ADHD and comorbid anxiety or depression symptoms; no history of psychosis, bipolar disorder, serious medical illness, or history of substance abuse  **Other:**  **ADHD presentation:** inattentive : 23.2,hyperactive : 2.9,combined : 73.8  **Diagnosis:** Confirmation by specialist  DSM IV Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime version  **Comorbidity:** Mood disorder  **Female:** 27.7 %  **Age mean:**  Atomoxetine + Fluoxetine 11.2 (2.7), Atomoxetine + Placebo 11.6 (2.4)  **Minimum age:** 7  **Maximum age:** 17  **Ethnicity:**  % White : 83.8  Other : Other: 16.2% | **Intervention:** Fluoxetine 20 mg administered once daily plus atomoxetine 1.8mg/kg/dayevenly divided into two doses for the final 5 weeks of treatment for total of 8 weeks  **Control:** Other  Atomoxetine alone plus placebo, after 3 weeks of placebo, atomoxetine was added for the final 5 weeks of treatment, initiated at 0.5 mg/kg/day and increased at weekly intervals to 0.8 mg/kg/day and then to 1.2 mg/kg/day; maximum dose of atomoxetine up to  **Comparator:** NA  **Follow-up:** 2 months | CGI-S (Clinical Global Impressions- Severity) change  Difference in CGI-S score mean change from baseline between groups were not statistically significant (p 0.065).  ADHD-RS-IV (Attention-Deficit/Hyperactivity Disorder Rating Scale-IV) total, change  Difference in ADHD-RS-IV Total T-score mean change from baseline between groups was not statistically significant (p 0.121); difference in ADHD-RS-IV Total score mean change from baseline not significant (p =0.101)  Children’s Depression Inventory (CDI) score mean (SD) change from baseline favors intervention group (p =0.043)  CDRS-R (Children’s Depression Rating Scale-Revised) total score mean (SD) change from baseline - group difference not significant (p =0.342)  Multidimensional Anxiety Scale for Children (MASC) score mean (SD) change from baseline: - group difference not significant (p =0.489).  Decreased appetite  The rate was 20% in intervention vs 6.8% in placebo approaching significance (p=0.055); patients in the combined treatment group also experienced greater weight loss (mean [SD] weight change in kilograms: A/F –1.0 [1.7], A/P –0.4 [1.3], p = .009).  The proportion of patients who discontinued because of an adverse event was low and similar between groups (A/F 2.4%, A/P 2.2%);  Mean heart rate increased more in the A/F group as compared with the A/P group (mean [SD] change in beats/minute: A/F 11.9 [11 |
| New pharmaceutical agent | Lin, 2014399  Eli Lilly and Company, 2009756  ID: NCT00922636  RCT  Multicenter  N = 340  Multiple countries  Setting: N/A | **Target:** Female and male patients with ADHD  **Other:**  **ADHD presentation:** inattentive : 24.16,hyperactive : 3.68,combined : 72.18  **Diagnosis:** Confirmation by specialist  DSM-IV-TR  **Comorbidity:** N/A  **Female:** 29 %  **Age mean:**  mean age 11.46  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % White : 72.6% | **Intervention:** Edivoxetine 0.3mg/kg administered daily for 8 weeks  **Control:** Placebo  Placebo-controlled  **Comparator:** MedicationOROS MPH was administered at the label-recommended doses  **Follow-up:** 2 months | Clinical Global Impressions-Attention-Deficit/Hyperactivity Disorder-Improvement (CGI-ADHD-I): Scores at the end-point for the edivoxetine 0.3 mg/kg/day arm was significantly lower relative to the placebo arm (lower score indicating greater clinical impro  ADHD-RS-IV  The edivoxetine 0.2 mg/kg/day and 0.3 mg/kg/day arms had statistically significantly greater improvement than the placebo arm in mean ADHD-RS total score change at end-point (placebo - 10.35; edivoxetine 0.2 mg/kg/day - 16.09, p < 0.010; edivoxetine 0.3 m  Statistically significant differences relative to placebo were observed for all edivoxetine dose arms with respect to changes in weight. (p< 0.05)  Edivoxetine dose arms demonstrated statistically significantly greater mean increases in sitting heart rates, and sitting systolic and diastolic blood pressure, than the placebo arm (p<0.05). Edivoxetine and placebo treatment arms did not differ in the nu |
| New pharmaceutical agent | Mohammadi, 2010439  Tehran University, 20101113  ID: NCT01099059  RCT  Single center  N = 40  Iran  Setting: Mixed | **Target:** Participants with a diagnosis of ADHD based on DSM-IV criteria, have ADHD-Rating Scale-IV School version score of at least 1.5 SD above the norm for patient's gender and age; no history of pervasive developmental disorders, schizophrenia or other psychiatric disorders, any current psychiatric comorbidity that required pharmacotherapy, IQ <70, have a significant chronic medical condition  **Other:**  **ADHD presentation:** combined : 100  **Diagnosis:** Confirmation by specialist  Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime diagnostic interview  **Comorbidity:** N/A  **Female:** 30 %  **Age mean:**  Amatadine 9.60 (1.98), methylphenidate 9.25 (1.80)  **Minimum age:** 6  **Maximum age:** 14  **Ethnicity:**  N/A | **Intervention:** Amantadine, dose of 100–150 mg/day depending on weight, 50 mg twiceper day for <30 kg and 50 mg three times per day for >30 kg, for 6 weeks  **Control:** NA  **Comparator:** MedicationMethylphenidate at a dose of 20–30 mg/day depending on weight (20 mg/day for <30 kg and 30 mg/day for >30 kg), titrated up: week 1: 10 mg/day (5 mg in the morning and 5 mg at midday); week 2: 20 mg/day (10 mg in the morning and 10 mg at midday) and week 3  **Follow-up:** 1.5 months | ADHD-RS (ADHD Rating Scale) Total Score change, parent rating  No significant differences were observed between the two groups on the Parent and Teacher Rating Scale scores.  Decreased appetite  The rate was 45% in the amantadine group and 84% in the methylphenidate group (p=0.01).  All side effects were mild to moderate and tolerable. The difference between the amantadine and methylphenidate groups in the frequency of side effects was not significant  except for decreased appetite and restlessness that were observed more frequently i |
| New pharmaceutical agent | Saito, 2020507  Taisho Pharmaceutical, 20161111  ID: JapicCTI-163244  RCT  Multicenter  N = 216  Japan  Setting: N/A | **Target:** Children with ADHD according the DSM-5; a total ADHD Rating Scale-IV score ≥23; Clinical Global Impressions severity score of ≥3; no history or current diagnosis of schizophrenic disorder or any psychiatric disorder (diagnosed by DSM-5), comorbid of reactive attachment disorder, and intellectual disabilities (IQ <70 )  **Other:**  **ADHD presentation:** inattentive : 41.2,hyperactive : 0.5,combined : 58.3  **Diagnosis:** No  Any existing diagnosis was required but nothing was done in the trial  **Comorbidity:** N/A  **Female:** 15.2 %  **Age mean:** 9.5 (2.3)  **Minimum age:** 6  **Maximum age:** 16  **Ethnicity:**  N/A | **Intervention:** Tipepidine, 60 mg twice a day of tipepidine hibenzate (Asverin, non-opioid antitussive), 2 weeks of observation with 8 weeks of treatment  **Control:** Placebo  Placebo dose  **Comparator:** MedicationTipepidine, 30mg/day tipepidine hibenzate (Asverin)  **Follow-up:** 16 months | ADHD RS-IV-J:I (ADHD Rating Scale IV Japanese version) Mean Changes  No significant difference was observed between the placebo and treatment groups, and no dose-response was observed; 30mg vs placebo (p=0.183) 120mg (p=0.748)  No clinically significant changes in body weight were observed  Adverse Events Total Count  Incidence of AEs: 36.5% (placebo); 51.9% (30mg); 46.2 (60mg); 49.1% (120mg); no significant differences amongst treatment groups (p= 0.420)  Incidence of side-effects: 3.8% (placebo); 5.6% (30mg); 17.3% (60mg); 3.8% (120mg); no significant differences (p= 0.050). No clinically significant changes in laboratory tests or vital signs were observed amongst treatment groups. |
| New pharmaceutical agent | Salardini, 2016508  ID: NA  RCT  Single center  N = 54  Iran  Setting: Specialty care | **Target:** ADHD patients with blood pressure, pulse rate, and liver function tests within clinically normal range  **Other:**  **ADHD presentation:** combined : 100  **Diagnosis:** Confirmation by specialist  ADHD-RS-IV diagnosed by psychiatrist  **Comorbidity:** N/A  **Female:** 22 %  **Age mean:** 10.47 (2.13)  **Minimum age:** 6  **Maximum age:** 15  **Ethnicity:**  % White : 100 | **Intervention:** Agomelatine was started as 15 mg/day in participants with weight 30 kg and 25 mg/day in patients with weight 45 kg in the morning and followed by placebo at lunch time for 6 weeks  **Control:** NA  **Comparator:** MedicationRitalin (methylphenidate hydrochloride) 10 mg tablet twice daily for 6 weeks, participants who weighed more than 30 kg received a 10 mg methylphenidate hydrochloride tablet thrice daily  **Follow-up:** 1.5 months | ADHD-RS-IV, parent, change from baseline  Changes from baseline were not significantly different between the agomelatine group and the MPH group (p=0.44).  The frequency of side effects was not significantly different between the agomelatine and MPH groups. |
| New pharmaceutical agent | Sangal, 2014513  Sunovion, 20091091; Sunovion, 20091092  ID: NCT00856973, NCT00857220  RCT  Multicenter  N = 486  US  Setting: Specialty care | **Target:** Children and adolescents with ADHD and insomnia; exclused another primary sleep disorder, other major psychiatric disorders, alcohol or substance abuse, and nicotine use  **Other:** Parents supplied some outcome data  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV criteria and confirmed by the M.I.N.I. Inter­national Neuropsychiatric Interview for Children and Adolescents  **Comorbidity:** Sleep  **Female:** 36.2 %  **Age mean:** 11.4 (3.0)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % Hispanic or Latino : 15.5  % Black/African American : 19.3  % White : 74.5 | **Intervention:** Eszopiclone high dose (2 mg for children, 3 mg for ado­lescents), participantscontinued on whatever stimulant medication they were on prior to trial enrollment, for duration of 12 weeks  **Control:** Placebo  Placebo plus whatever stimulant medication patients were on prior to trial enrollment  **Comparator:** MedicationEszopiclone low dose (1 mg for children, 2 mg for ado­lescents), patients also continued on whatever stimulant medication they were on prior to trial enrollment  **Follow-up:** 3 months | CGI, parent  The intervention group improved significantly over the control group (p=0.009), but the comparator did not (p=0.238).  Inattention score, Conners Comprehensive Behavior Rating Scale (CBRS) change, parent report  No significant difference between groups (p 0.238 for high dose vs placebo, p 0.352 for low dose vs placebo).  No significant differences between intervention, comparator, and placebo group in change from baseline to week 12 in latency to persistent sleep based on polysomnography ( p 0.375 for high dose, p 0.999 for low dose).  Participants with any adverse event  The rate was 61% for intervention, 59.5% for comparator, and 46% for placebo.  A dose-response relationship was observed for dysgeusia, abdominal discomfort, dizziness, and nasal congestion. |
| New pharmaceutical agent | Supernus, 2016572  ID: NCT02618408  RCT  Multicenter  N = 333  US  Setting: Specialty care | **Target:** Children with ADHD and comorbid impulsive aggression already using monotherapy treatment with FDA-approved optimized ADHD medication, no current or lifetime diagnosis of epilepsy, major depressive disorder, bipolar disorder, schizophrenia or a related disorder, personality disorder, Tourette's disorder, or psychosis  **Other:** Parents provided some outcomes.  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-5 confirmed by the Schedule for Affective Disorders and Schizophrenia for School-aged Children - Present and Lifetime Version 2013  **Comorbidity:** ODD : Impulsive agression  **Female:** 24.9 %  **Age mean:** 9.0 (1.84)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % Hispanic or Latino : 14.2  % Black/African American : 26.5  % American Indian or Alaska Native :  2.2  % Asian :  0.3  % White : 65.8  Other : Categories not mutually exclusive | **Intervention:** Molindone Hydrochloride Extended-Release (SPN-810) high dose (36 mg) twice each day, in the morning and in the evening, in addition to usual ADHD medication, for total of 7 weeks  **Control:** Placebo  Placebo twice each day, in the morning and in the evening, in addition to usual ADHD medication  **Comparator:** MedicationMolindone Hydrochloride Extended-Release (SPN-810) 18 mg twice each day, in the morning and in the evening, in addition to usual ADHD medication  **Follow-up:** 1 month | Clinical Global Impression-Improvement (CGI-I) Scale Investigator Rated  No significant difference (p = 0.0742) in improvement measured by investigator rated CGI-I or CGI-S (p = 0.1729). Significantly greater improvement on parent rated CGI-I for high dose medication group (p = 0.0384).  Swanson, Nolan, Pelham Rating Scale- Revised (SNAP-IV) Rating Scale, parent  No significant difference between groups (p= 0.1418).  Increased appetite  None of 65 low dose patients experienced appetite increase, compared to 9 of 137 high dose patients. and 6 of 126 in placebo group.  Adverse events  Rates were 18.98% in the high dose, 15.38% in the low dose, and 14.29% in the placebo group.  2/13 participants experienced a serious adverse event (eye disorder, appendicitis perforated) in the high dose group, none in the other groups. |
| New pharmaceutical agent | Swanson, 2006574  ID: N/A  RCT  Multicenter  N = 190  US  Setting: Specialty care | **Target:** Participants with ADHD; Clinical Global Impressions-Severity of Illness scale rating of 4 or higher, total and/or subscale scores on the Attention-Deficit/Hyperactivity Disorder Rating Scale-IV School Version 22 at least 1.5 standard deviations above norm, and IQ of at least 80 as estimated by the Wechsler Intelligence Scale for Children-Third Edition, and a score of at least 80 on the Wechsler Individual Achievement Test, Second Edition, Abbreviated  **Other:**  **ADHD presentation:** inattentive : 27,hyperactive : 6,combined : 67  **Diagnosis:** Confirmation by specialist  DSM-IV-TR  **Comorbidity:** N/A  **Female:** 30 %  **Age mean:** 11.6 (2.6)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:** | **Intervention:** Modafinil 340 or 425 mg/day (depending on weight) for 7 weeks  **Control:** Placebo  Placebo  **Comparator:** NA  **Follow-up:** 2.25 months | ADHD-RS-IV (Attention-Deficit/ Hyperactivity Disorder Rating Scale-IV) Home Version  Modafinil significantly improved symptoms of ADHD as shown by reductions in ADHD-RS-IV School Version total scores compared with placebo at all visits (p ≤ .009), including the final visit of the double-blind phase (p < .0001).  Decreased appetite  The rate was 14% in the intervention vs 2% in the placebo group.  Two patients receiving modafinil experienced 3 serious adverse events (asthma attack, influenza syndrome, dehydration), these events resolved spontaneously and were considered to be not related or unlikely related to the study medication. |
| New pharmaceutical agent | Wilens, 2011105  ID: NCT00640419  RCT  Multicenter  N = 121  US  Setting: N/A | **Target:** Participants with DSM-IV diagnosis of any ADHD subtype, confirmed by the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version 15 and a rating of 4 or higher on the Clinical Global Impression-ADHD-Severity Scale; no history of current or past diagnosis of bipolar I, II, or not otherwise specified disorder; psychotic disorder; autism, Asperger’s syndrome or pervasive developmental disorder; tics or Tourette syndrome; seizure disorder; traumatic brain injury; current diagnosis of obsessive-compulsive disorder, eating disorder, anxiety disorder, or depressive disorder requiring treatment of any kind; psychotropic medications within 14 days or 5 half-lives (7 days for stimulants)  **Other:**  **ADHD presentation:** inattentive,inattentive\_other : %s broken down by meds,hyperactive,hyperactive\_other : %s broken down by meds,combined,combined\_other : %s broken down by meds  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 33 %  **Age mean:** 8.5  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  Other : % race is broken down by med dosage | **Intervention:** ABT-089 (neuronal nicotinic receptor partial agonist) 1.4 mg/kg taken daily for 6 weeks  **Control:** Placebo  Placebo  **Comparator:** MedicationABT-089 (neuronal nicotinic receptor partial agonist) 0.7 mg/kg taken daily for 6 weeks  **Follow-up:** 1.5 months | CGI-ADHD-S  There was no statistically significant difference between any ABT-089 dose and placebo for the mean change from baseline to final evaluation for the CGI-ADHD-S (Table 2), or on the mean change from baseline to each evaluation.  ADHS-RS-IV  There was no statistically significant difference between ABT-089 and placebo in the primary efficacy analysis of mean change from baseline to final evaluation of the ADHD-RS-IV (HV) Total Score (Table 2), or on the secondary analysis of mean change from  Any adverse event  The rates were 60% in the intervention, 69% in the placebo, and 67.6% in the low dose group. |
| New pharmaceutical agent | Willens, 2011620  ID: NCT00528697  RCT  Multicenter  N = 278  US  Setting: N/A | **Target:** Participants with DSM-IV diagnosis of any ADHD subtype, confirmed by the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version, a rating of 4 or higher on the Clinical Global Impression-ADHD-Severity Scale; no history of current or past diagnosis of bipolar I, II, or not otherwise specified disorder, psychotic disorder, autism, Asperger’s syndrome or pervasive developmental disorder, tics or Tourette syndrome, seizure disorder, traumatic brain injury, current diagnosis of obsessive-compulsive disorder, eating disorder, anxiety disorder, or depressive disorder requiring treatment of any kind, psychotropic medications within 14 days or 5 half-lives (7 days for stimulants), atomoxetine within 3 months of randomization or not a suitable candidate to receive atomoxetine  **Other:**  **ADHD presentation:** inattentive\_other : %s broken down by meds,hyperactive\_other : %s broken down by meds,combined\_other : %s broken down by meds  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 33 %  **Age mean:**  mean 8.6  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:** | **Intervention:** ABT-089 of 0.085 mg/kg, 0.260 mg/kg, 0.520 mg/kg, or 0.700 mg/kg once per day, treatment period of 8 weeks  **Control:** Placebo  Placebo  **Comparator:** MedicationAtomoxetine 1.2 mg/kg/day once per day, treatment period of 8 weeks  **Follow-up:** 2 months | CGI-ADHD-S  There was no statistically significant difference between any ABT-089 dose and placebo for the mean change from baseline to final evaluation for the CGI-ADHD-S, or on the mean change from baseline to each evaluation, with the exception of the 0.520 mg/kg  ADHD-RS-IV  There was no statistically significant difference between ABT-089 and placebo in the primary efficacy analysis of mean change from baseline to final evaluation of the ADHD-RS-IV (HV) Total Score, or on the secondary analysis of mean change from baseline t  In the atomoxetine group, mean weight and BMI decreased by 0.1 kg and 0.2 kg/m2 (mean difference from placebo −1.3 CI-1.99, −0.69 and −0.6 CI −0.96, −0.19]  Any adverse event  The rate were 82% in the intervention, 76.1% in the placebo, and 82% in the atomoxetine group.  ABT-089 was generally safe and well tolerated, with no statistically significant difference between any ABT-089 dose and placebo in the overall incidence of any specific AE, and no clinically significant changes in other safety measures |
| New pharmaceutical agent | Zarinara, 2010636  ID: N/A  RCT  Single center  N = 38  Iran  Setting: Other | **Target:** Children with combined subtype of ADHD and newly diagnosed (drug naive); no history or current diagnosis of pervasive developmental disorders, schizophrenia or other psychiatric disorders, any current psychiatric comorbidity that required pharmacotherapy, any evidence of suicide risk, mental retardation (IQ<70), clinically significant chronic medical condition, seizures or current abuse or dependence on drugs in the last 6 months, hypertension or hypotension  **Other:**  **ADHD presentation:** combined : 100  **Diagnosis:** Confirmation by specialist  DSM-IV-TR  **Comorbidity:** N/A  **Female:** 29 %  **Age mean:**  9.42 (2.19) and 9.57(1.86)  **Minimum age:** 6  **Maximum age:** 13  **Ethnicity:**  N/A | **Intervention:** Venlafaxine (antidepressant) at doses of 50–75 mg/day depending on weight (25 mg twice per day for <30 kg and 25 mg three times per day for >30 kg), treatment for 6 weeks  **Control:** NA  **Comparator:** MedicationMethylphenidate at a dose of 20–30 mg/day depending on weight, titrated up: week 1: 10 mg/day (5 mg in the morning and 5 mg at midday); week 2: 20 mg/day (10 mg in the morning and 10 mg at midday); and week 3: 30 mg/day for children >30 kg (10 mg in the m  **Follow-up:** 1.5 months | ADHD-RS-IV, parent rating  Responder (at least 40% decrease in ADHD-RS-IV)  No significant difference was observed in the two groups (p 0.33).  No significant difference was observed on the reduction of scores of the Teacher ADHD Rating Scale (p 0.30).  Decreased appetite  The reported rates were 10.52% in the venlafaxine and 10.52% in the methylphenidate group.  Nine side effects were observed over the trial, but all of them were mild to moderate and tolerable. The difference between the venlafaxine and methylphenidate groups in the frequency of side effects was not significant except for headaches and insomnia t |
| New pharmaceutical agent | Zavadenko, 2019637  NA  ID: NA  RCT  Multicenter  N = 100  Russia  Setting: Mixed | **Target:** Children with ADHD diagnosis based on ICD-10 criteria, presence of hyperdynamic (hyperkinetic) syndrome with attention deficit; severity of ADHD on the Clinical Global Impressions-Severity scale of 3–6 points; total score on the ADHD-DSM-IV scale is at least 25 for boys and 22 for girls; patients with comorbid diseases that would require the use of barbiturate, anticonvulsants, or any other nootropic agents were excluded  **Other:**  **ADHD presentation:** inattentive : 61.8,hyperactive : 7.9,combined : 30.3  **Diagnosis:** No  **Comorbidity:** N/A  **Female:** 18.0 %  **Age mean:**  Intervention 8.7 (2.1). placebo 8.24 (1.63)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Hopantenic acid (pantogam) was given as tablets containing 250 mg at the pediatric therapeutic dose of 30 mg/kg, divided into two split doses taken after meals, for 4 months  **Control:** Placebo  Placebo as tablets with external appearance, packaging, and labeling identical to those of the study drug, taken in two split doses after meals, for 4 months  **Comparator:** NA  **Follow-up:** 4 months | CGI-S (Clinical Global Impressions Scale- Severity)  The intervention produced a decrease in disease severity from the placebo level (p=0.014).  Proportions of patients with clinical improvements (decreases in total points scores on the DSM-IV ADHD scale by 25% or more from baseline)  There was no significant difference between groups.  Weiss Functional Impairment Rating Scale (WFIRS-P); Family Section-Parent  There were significant decreases in impairment in the intervention compared to the control (p<0.01).  Total adverse events  The rate was 68% for intervention and 48% for control.  Statistical analysis did not identify any significant differences between groups in clinical or biochemical blood tests or measures of urinalysis; results of clinical and neurological examination, the state of major organs or organ systems revealed no sig |
| Nutrition, supplements | Abbasi, 2011104  ID: N/A  RCT  Single center  N = 40  Iran  Setting: Other | **Target:** Children with combined subtype of ADHD and newly diagnosed (drug naive); no history or current diagnosis of pervasive developmental disorders, schizophrenia or other psychiatric disorders, any current psychiatric comorbidity that required pharmacotherapy, any evidence of suicide risk, mental retardation (IQ<70), clinically significant chronic medical condition, seizures or current abuse or dependence on drugs in the last 6 months, hypertension or hypotension  **Other:**  **ADHD presentation:** combined : 100  **Diagnosis:** Confirmation by specialist  DSM-IV-TR  **Comorbidity:** N/A  **Female:** 30 %  **Age mean:**  8.84(2.03) and 8.36(1.53)  **Minimum age:** 7  **Maximum age:** 13  **Ethnicity:**  N/A | **Intervention:** Acetyl-L-Carnitine plus methylphenidate, doses ranging from 500 to 1,500 mg/day depending on the weightof the child (13.5–30 kg = 0.5 g twice per day;>30–50 kg = 1.0 g twice per day; and >50 kg = 1.5 g twice per day) plus methylphenidate at a dose of 20–30 mg/day depending on weight (20 mg/day for <30 kg and 30 mg/day for>30 kg), treatment for 6 weeks  **Control:** Placebo  Placebo plus methylphenidate at a dose of 20–30 mg/day depending on weight (20 mg/day for <30 kg and 30 mg/day for >30 kg). Methylphenidate was titrated up: week 1: 10 mg/day (5 mg in the morning and 5 mg at midday), week 2: 20 mg/day (10 mg in the mornin  **Comparator:** NA  **Follow-up:** 1.5 months | ADHD-RS-IV, parent rating  The difference between groups was not significant (p 0.74).  The difference between the two protocols was not significant for the teacher ratings (p 0.63).  Decreased appetite  The rate was 35% in the intervention and 40% in the control group.  Fourteen side effects were observed, all mild to moderate and tolerable. The difference in the frequency of side effects was not significant except for headache and irritability that were observed more frequently in the methylphenidate plus placebo group. |
| Nutrition, supplements | Akhondzadeh, 2004116  ID: ISRCTN64132371  RCT  Single center  N = 44  Iran  Setting: Specialty care | **Target:** Children with newly diagnosed with ADHD combined subtype and had not yet received any stimulant medication prior to enrollment  **Other:**  **ADHD presentation:** combined : 100.0  **Diagnosis:** Confirmation by specialist  Diagnosed by psychiatrist  **Comorbidity:** N/A  **Female:** 40.9 %  **Age mean:** 7.88 (1.67)  **Minimum age:** 5  **Maximum age:** 11  **Ethnicity:**  Other : Persian: 100% | **Intervention:** Zinc sulfate 55 mg/day (15mg elemental zinc) plus methylphenidate 1 mg/kg/day twice daily for 6 weeks  **Control:** Other  Methylphenidate 1 mg/kg/day twice daily  **Comparator:** NA  **Follow-up:** 1.5 months | Parent ADHD rating scale  Both groups showed significant improvement and the zinc+methylphenidate group improved significantly more than the placebo+methylphenidate group (p<0.001).  Decreased appetite  No difference between groups.  Metallic taste was experienced more in the zinc group (p=0.0001). |
| Nutrition, supplements | Arnold, 2007125  ID:  RCT  Multicenter  N = 112  US  Setting: N/A | **Target:** Children with ADHD  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** No  **Comorbidity:** N/A  **Female:** 26 %  **Age mean:**  placebo mean 8.3 (2.2), ALC mean 8.4 (2.3)  **Minimum age:** 5  **Maximum age:** 12  **Ethnicity:**  % White : 68.75 | **Intervention:** Acetyl-L-Carnitine, metabolite necessary for energy metabolism and essential fatty acid anabolism, 500-1500mg depending on weight, for 16 weeks  **Control:** Placebo  Identical-appearing and tasting  **Comparator:** NA  **Follow-up:** 4 months | CGI-I responder  17% improved in the interention, 14% in the placebo group.  Conners'-Revised  Both groups improved (p 0.291)  Height  Hight increased more in placebo group. |
| Nutrition, supplements | Baziar, 2019136  Tehran University of Medical Sciences, 20171114  ID: IRCT201701131556N94  RCT  Single center  N = 54  Iran  Setting: Other | **Target:** Children with a subscale scores on Attention-Deficit/Hyperactivity Disorder Rating Scale-IV of at least 1.5 standard deviations above norms; exclusion criteria were psychiatric comorbidities, mental retardation, clinically significant chronic medical condition, systolic blood pressure over 125 mmHg and/or resting pulse below 60 or over 110 beats/min, history of allergy to saffron, psychotropic medication use in the past 2 weeks, females who were likely to go through pregnancy or lactation, use of any medication that might have adverse reactions with saffron, and patients who were going to undergo surgery within 36 hours to 14 days  **Other:**  **ADHD presentation:** N/A : Baseline ADHD-RS-IV Parent version total, mean(SD): Control=34.20(4.69) Intervention=33.56(6.48) Baseline ADHD-RS-IV Teacher version total, mean(SD): Control=24.16(8.32) Intervention=23.64(8.16)  **Diagnosis:** Confirmation by specialist  DSM-V  **Comorbidity:** N/A  **Female:** 20 %  **Age mean:**  Intervention 9.08 (2.23), control 8.28 (1.59)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  N/A | **Intervention:** Saffron (crocus sativus L.) capsules at a dosage of 20–30 mg/d depending on weight (20 mg/d for <30 kg and 30 mg/d for >30 kg) for 6 weeks  **Control:** NA  **Comparator:** MedicationMethylphenidate (ritalin), 0.3–1 mg/(kg\*d), titrated up during the trial: 10 mg/d (5 mg in the morning and 5 mg at midday) in week 1; 20 mg/d (10 mg in the morning and 10 mg at midday) in week 2; 20 mg/d for children <30 kg and 30 mg/d for children >30 kg  **Follow-up:** 1.5 months | ADHD-RS-IV total, parent and teacher  No significant difference between the two groups on Parent and Teacher Rating Scale scores.  Decreased appetite  The rate of decreased appetite was 8% in the saffron group compared to 20% in the methylphenidate group.  No serious adverse event was observed in any of the patients and all noticed adverse effects were mild to moderate and tolerable, the frequency of side effects was not significantly different between the saffron and MPH groups. |
| Nutrition, supplements | Behdani, 2013138  ID: ID NA  RCT  Single center  N = 75  Iran  Setting: Specialty care | **Target:** Children and adolescents with ADHD; those with co-morbid psychological diagnoses or serious medical conditions were excluded  **Other:** Teachers and parents reported outcomes  **ADHD presentation:** inattentive : 21.7,hyperactive : 37.7,combined : 40.6  **Diagnosis:** Confirmation by specialist  DSM-IV-TR by board-certified psychiatrists  **Comorbidity:** N/A  **Female:** 20.3 %  **Age mean:** 8.7 (1.7)  **Minimum age:** 7  **Maximum age:** 15  **Ethnicity:**  Other : 100% Persian | **Intervention:** Omega 3 plus methylphenidate, final dose of 1mg/kg (maximum dose 60mg/day), in 2or 3 divided doses, plus Omega-3, two 1000-miligram capsules (containing 240 mg of DHA and 360 mg of EPA), per day in 2 divided doses for 8 weeks  **Control:** Placebo  Placebo plus methylphenidate; final dose of 1mg/kg (maximum dose 60mg/day), in 2or 3 divided doses plus placebo  **Comparator:** NA  **Follow-up:** 2 months | ADHD Rating Scale-IV, parent  Difference between groups in terms of parent’s and teacher’s ADHD rating scale scores were not significant.  1/75 dropped out due to side effects of omega 3, including nausea, vomiting, and abdominal pain. |
| Nutrition, supplements | Bilici, 2004149  ID: N/A  RCT  Single center  N = 400  Turkey  Setting: Specialty care | **Target:** Children with ADHD who have no other mental or medical illness  **Other:** Teachers supplied some outcomes  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV by psychiatrists, pediatrician, and psychologist  **Comorbidity:** N/A  **Female:** 20 %  **Age mean:** 9.4 (1.5)  **Minimum age:** 6  **Maximum age:** 14  **Ethnicity:**  Other : Turkish | **Intervention:** Zinc sulfate (150 mg/day) for 12 weeks  **Control:** Placebo  Placebo (sucrose, 150 mg) for 12 weeks  **Comparator:** NA  **Follow-up:** 3 months | ADHDS (Attention Deficit Hyperactivity Disorder Scale) change  Therapeutic response  Intervention patients showed greater improvement than placebo patients (p=.002). Intervention group also showed significantly more improvement in ADHDS-H (p=.01), ADHDS-I (p=.03), and ADHDS-S (p = .03) subscales compared with placebo groups. Therapeutic  Significantly more intervention patients than placebo patients reported metallic taste (p = .01). No significant difference in nausea, vomiting, abdominal pain, and diarrhea. |
| Nutrition, supplements | Carucci, 2022171  ID: ID NA  RCT  Multicenter  N = 160  Italy  Setting: Specialty care | **Target:** Drug naive children with mild to moderate ADHD-inattentive type; those with serious medical or serious psychiatric conditions were excluded  **Other:** Parents reported some outcomes  **ADHD presentation:** inattentive : 100  **Diagnosis:** Confirmation by specialist  DSM IV based on psychiatric evaluation and Schedule for Afective Disorders and Schizophrenia for school-age children-present and lifetime version  **Comorbidity:** N/A  **Female:** 26 %  **Age mean:** 9.7 (1.9)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Omega 3/6, 2 capsules containing 279 mg EPA, 87 mg DHA, 30 mg GLA (gamma linolenic acid) per day, to be taken with a meal for 6 months  **Control:** Placebo  Placebo, 2 capsules per day, to be taken with a meal  **Comparator:** NA  **Follow-up:** 6 months | Clinical Global Impression, Severity score (CGI-S)  No significant differences between the two groups in CGI-S or Conner’s Parent and Rating Scale‑Revised.  ADHD RS IV, total, clinician administered  ADHD-RS- Inattention score, number "responders"  Intervention group improved more than control on total score (p 0.036); no significant difference in the percent categorized as responders on Inattention scale.  No effect was found on mood and anxiety symptoms measured by Multidimensional Anxiety Scale for Children (MASC).  Number reporting an adverse event  2 in intervention group reported diarrhoea, 3 on placebo reported one each respectively abdominal pain, itch, and somnolence.  No severe adverse events. |
| Nutrition, supplements | Chang, 2019178  Hospital, China Medical University, National Science Council, 2016715  ID: NCT03542643  RCT  Single center  N = 103  Taiwan  Setting: Specialty care | **Target:** Children and adolescents with ADHD who were drug naïve or had no medication for the past 6 months, without comorbid psychiatric disorders, such as autism spectrum disorder, anxiety disorder, and conduct disorder  **Other:** ADHD symptoms were rated by parents and teachers  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM V diagnoses were confirmed by a child and adolescent psychiatrist  **Comorbidity:** N/A  **Female:** 14.1 %  **Age mean:** 9.49 (3.05)  **Minimum age:** 6  **Maximum age:** 18  **Ethnicity:**  % Asian : 100 | **Intervention:** Omega 3 eicosapentaenoic acid (EPA) 1.2 g per day for 12 weeks  **Control:** Placebo  Placebo  **Comparator:** NA  **Follow-up:** 3 months | SNAP IV total score, parent version  There was no difference between groups in changes in parent or teacher reported inattention (p=.072, .066), hyperactivity (p=.075, .766) and ODD (p=.207, .759) subscale scores.  Continuous Performance Test (CPT) variability score (measures focused attention). Intervention group had significantly greater decrease from baseline to 12 weeks (p = 0.041). |
| Nutrition, supplements | Cornu, 2018209  ID: ID NA  RCT  Multicenter  N = 162  France  Setting: Specialty care | **Target:** Children and adolescents with hyperactivity-impulsivity symptoms for 6 months or more and/or at least one of six inattention symptoms for six months or more, with certain symptoms which were present before age 7 and with a functional impairment in 2 or more environments and clinically significant alteration in social, school, or family functioning  **Other:** Staff, parents  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  child psychiatrist  **Comorbidity:** N/A  **Female:** 0 %  **Age mean:** 6.9 (2.9)  **Minimum age:** 6  **Maximum age:** 15  **Ethnicity:**  N/A | **Intervention:** Omega 3 dietary supplement, aged 6–8 eicosatetraenoic acid 336mg, aged 9–11 eicosatetraenoic acid 504mg, aged 12–15 eicosatetraenoic acid 672mg, capsules also contained 100 µg vitamin A, 1.25 µg vitamin D, and 3.5 mg vitamin E, during which other hyperactivity treatments and other omega-3 supplements or psychotropic drugs were not allowed, for 3 months  **Control:** Placebo  Placebo capsules indistinguishable from active capsules, composedof olive oil, the same amount of vitamin A, D, and E, with traces of marine lipid concentrate: EPA (18%), DHA (12%), totaling 4.83 mg, to give the capsules a similar taste and smell and stra  **Comparator:** NA  **Follow-up:** 3 months | Connors total score  No beneficial effect of omega-3 supplement.  ADHD-RS-IV  No beneficial effect of omega-3 supplement.  There was no significant change in reading skills (L'Aloutte) in both groups (p=0.28).  Participants experiencing adverse events  15% vs 11% adverse events favoring placebo.  2/80 patients in the DHA–EPA group experienced a severe adverse event (hospitalisation for worsening ADHD symptoms). |
| Nutrition, supplements | Crippa, 2019212  Crippa, 2018726; IRCCS Eugenio Medea, 2012849  ID: NCT01796262  RCT  Single center  N = 50  Italy  Setting: Specialty care | **Target:** Children with ADHD who were drug-naïve and had not consumed omega-3/omega-6 supplements during the 3 months prior to the recruitment  **Other:**  **ADHD presentation:** inattentive : 15.7,hyperactive : 33.3,combined\_other : 51  **Diagnosis:** Confirmation by specialist  DSM-IV by child neuropsychiatrist  **Comorbidity:** N/A  **Female:** 8.7 %  **Age mean:** 11.1 (1.85)  **Minimum age:** 7  **Maximum age:** 14  **Ethnicity:**  % White : 100 | **Intervention:** Omega 3 supplement of 500 mg algal docosahexaenoic acid (DHA) per day for 6 months  **Control:** Placebo  Placebo, 2 pearls per day of 500mg wheat germ oil, stabilized with low concentration of Vitamin E  **Comparator:** NA  **Follow-up:** 6 months | Behavior in Child Health Questionnaire  Only the intervention group improved.  CGI-S  Difference between groups was not significant (p > 0.05).  ADHD-RS-IV (ADHD rating scale IV) Parent Version, total  Difference between groups was not significant (p>0.05).  Word Reading Accuracy (errors) difference between groups was not significant (p>0.05). Higher impact of symptoms on functioning evaluated by SDQ in DHA group (p=0.045).  Participants with adverse events  No adverse events in both groups.  Over the course of the 6 months, no instances of either major or minor adverse events were reported. |
| Nutrition, supplements | Fallah, 2018262  Shahid Sadoughi University of Medical Sciences, 20161036  ID: IRCT201604212639N18  RCT  Single center  N = 56  Iran  Setting: Specialty care | **Target:** Children with ADHD and refractory epilepsy  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** Other : Epilepsy  **Female:** 41.0 %  **Age mean:** 9.24 (0.15)  **Minimum age:** 7  **Maximum age:** 11  **Ethnicity:**  % White : 100 | **Intervention:** Omega 3 plus risperidone, plus antiepileptic drug, 1000 mg of omega 3 fish oil, 180 mg of eicosapentaenoic acid and 120 mgdocosahexaenoic acids) 1 capsule per day plus 0.5 mg of risperidone per day and an antiepileptic drug for 3 months  **Control:** Other  Risperidone 0.5 mg and an antiepileptic drug alone  **Comparator:** NA  **Follow-up:** 6 months | Monthly seizure frequency was lower in intervention group compared to control group (p=0.03). The rate of good response, defined as a 50% decrease in seizures, was higher in the intervention group (p 0.001).  Participants with side effects  No significant difference between groups (p 0.50). |
| Nutrition, supplements | Ghajar, 2018295  ID: IRCT201601031556N84  RCT  Single center  N = 56  Iran  Setting: Specialty care | **Target:** Participants who met criteria of DSM-V, no previously diagnosed psychiatric comorbidity (except for Oppositional Defiant Disorder) or developmental or physiological disorders, IQ>70, without receiving any supplemental medication, or having an allergy to L-carnosine or methylphenidate  **Other:**  **ADHD presentation:** combined : 100  **Diagnosis:** No  **Comorbidity:** N/A  **Female:** 16 %  **Age mean:** 9.12 (2.18)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  Other : All patients were reported as persian | **Intervention:** L-carnosine (800mg/d) plus methylphenidate hydrochloride (20 mg/d in 2 divided doses, 30 mg/d in three divided doses) for 8 weeks  **Control:** Other  Methylphenidate alone, 0.5-1.5mg;/kg, titrated up: 10mg/d (2 divided doses) for the first week followed by 20mg/d (2 divided doses) from the second week till the rest of the trial; weight >30kg received 30mg/d (3 divided doses) from the third week of the  **Comparator:** NA  **Follow-up:** 2 months | ADHD-RS-IV  Significant time by treatment interaction on total and inattention subscales indicating beneficial effects of the adjunct.  Seven side effects were recorded during the course of the study; no serious adverse event was observed in any of the patients; the most common side effects were abdominal pain (28%), headache (20%), and insomnia (16%) in the l-carnosine group; and abdomi |
| Nutrition, supplements | Ghanizadeh, 2015296  ID: IRCT201311303930N29  RCT  Single center  N = 106  Iran  Setting: Specialty care | **Target:** Children with ADHD; those with serious medical conditions were excluded  **Other:** Parents  **ADHD presentation:** inattentive\_other : Mean inattentiveness score at basline = 15.75 on ADHD Checklist  **Diagnosis:** Confirmation by specialist  DSM-IV diagnostic criteria supported by KSADS  **Comorbidity:** N/A  **Female:** 26.4 %  **Age mean:** 8.45 (2.1)  **Minimum age:** 5  **Maximum age:** 14  **Ethnicity:**  Other : 100% Persian | **Intervention:** Dietary recommendations plus methylphenidate, mean dose 12.7(5.4) mg/day. parents received a lists of foods which were recommended (diary, homemade fruit juices, vegetables, low-fat meat) and another list of the foods which were recommended to be eaten as less as possible; parents were encouraged to provide their children with 3 regular meals per day, for 1 month  **Control:** Other  Methylphenidate alone, mean dose 11.9(4.6) mg/day  **Comparator:** NA  **Follow-up:** 1 month | ADHD Checklist, Hyperactivity / Impulsivity Score  No significant difference between groups. |
| Nutrition, supplements | Gustafsson, 2010310  Hela Pharma AB, 2004828  ID: EudraCT No. 2004-003853-13  RCT  Multicenter  N = 92  Sweden  Setting: Specialty care | **Target:** ADHD patients with no medical conditions requiring intervention and no neurological or psychological comorbidity  **Other:** Parents and teachers provided outcomes  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:**  % N/A  **Age mean:**  NA  **Minimum age:** 7  **Maximum age:** 12  **Ethnicity:**  % White : 100 | **Intervention:** Omega 3, one eicosapentaenoic acid capsule PlusEPA, 500 mg EPA +2.7 mg DHA and 10 mg Vitamin E mixed tocopheroles, 1 capsule per day for 15 weeks  **Control:** Placebo  Placebo, mixture of rape seed oil and medium-chain triglycerides containedin a capsule identical to the PlusEPA containing <10% of the PlusEPA content of omega-3 LCPUFA  **Comparator:** NA  **Follow-up:** 3.75 months | Conners Rating Parent rating scale total  No significant difference between groups (p > .05).  There were only mild adverse events observed, most of them classified as not related or unlikely to have been related to the drug. Events possibly related to drug treatment, such as abdominal symptoms and nose bleeding did not differ between groups. |
| Nutrition, supplements | Hariri, 2012318  ID: N/A  RCT  Single center  N = 120  Iran  Setting: Other | **Target:** ADHD patients taking Ritalin with Conners’ Abbreviated Questionnaires scores for hyperactivity greater than 14; no infectious diseases, diabetes, hyperthyroidism, convulsion, epilepsy and consumption of n-3 fatty acids supplements  **Other:** Parents provided outcomes  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  Conners’ Abbreviated Questionnaires (ASQ-P)  **Comorbidity:** N/A  **Female:** 38 %  **Age mean:** 7.90 (1.5)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:** | **Intervention:** Omega 3 plus ritalin (any dose); soft gel capsules of n-3 fatty acids with a total daily dose of 900mg n-3 fatty acids (635mg eicosapentaenoic acid, 165mg docosahexaenoic acid and 100mg other n-3 fatty acids), for 8 weeks  **Control:** Other  Placebo plus ritalin (any dose), olive oil capsules  **Comparator:** NA  **Follow-up:** 2 months | ASQ-P (Conners’ Abbreviated Questionnaires)  Intervention group improved more than control group (p < .001).  2 intervention group patients withdrew because of steatorrhoea. |
| Nutrition, supplements | Hemamy, 2021324  Hemamy, 2020829  ID: ID NA  RCT  Single center  N = 66  Iran  Setting: Mixed | **Target:** Children with serum level of 25-hydroxyvitamin D3 less than 30 ng/dL, a diagnosis of ADHD based on the presence of at least 6 out of 9 cases of inattention and also at least 6 out of 9 cases of hyperactivity based on DSM IV and serum magnesium levels less than 2.3 mg/dL  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV diagnosed by unknown source  **Comorbidity:** N/A  **Female:** 30.3 %  **Age mean:** 9.06 (1.76)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % White : 100 | **Intervention:** Vitamin D (50,000 IU/week with lunch meal) and an oral tablet of magnesium (6 mg/kg/day with lunch meal) for a duration of 8-weeks  **Control:** Placebo  Placebo, similar in appearance, color, and taste to the supplements (edible paraffin oil as a placebo for vitamin D, microcrystalline cellulose, and stearic acid as a placebo for magnesium)  **Comparator:** NA  **Follow-up:** 2 months | Conduct problems  Significant reduction in conduct problems (p 0.0002).  Strength and difficulties questionnaire (SDQ), total difficulties  The intervention group showed a significant reduction in total difficulties compared to control group (p 0.001).  Significant reduction in emotional problems (p 0.001), peer problems (p 0.001), prosocial score (p 0.007), externalizing score (p 0.001), and externalizing score (p 0.001) compared with placebo.  No adverse effects of Vitamin D and magnesium supplementation were reported at the end of this study. |
| Nutrition, supplements | Hirayama, 2014328  ID: ID NA  RCT  Single center  N = 36  Japan  Setting: Community | **Target:** Children with ADHD  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  diagnosed by child's own psychiatrist  **Comorbidity:** N/A  **Female:** 5.6 %  **Age mean:**  9.1 (1.7) for intervention group; 8.7 (3.0) for placebo group  **Minimum age:**  **Maximum age:**  **Ethnicity:**  N/A | **Intervention:** Phosphatidylserine (soy-derived) 100mg chewable tablet, 2 chews per day for 2 months  **Control:** Placebo  Identical-appearing placebo chewable tablets, 2 chews per day  **Comparator:** NA  **Follow-up:** 2 months | Inattention Go/No-Go task  No difference between groups (p 0.29).  DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 4th edition) criteria score  ADHD symptoms were statistically significantly lower in the phosphatidylserine treated group compared to the placebo group (p<0.01).  Working memory: phosphatidylserine 0.3, placebo -0.7 (n.s.). |
| Nutrition, supplements | Johnson, 2009349  ID: N/A  RCT  Multicenter  N = 75  Sweden  Setting: Specialty care | **Target:** Children and adolescents with ADHD; no autism, psychosis, bipolar disorder, mental retardation, uncontrolled seizure disorder, hyper- or hypothyroidism, significant other medical conditions, weight below 20 kg, alcohol or drug abuse, or the use of any psychoactive drugs or omega 3 preparations in the past 3 months  **Other:** Parents reported some outcomes  **ADHD presentation:** inattentive : 53,combined : 47  **Diagnosis:** Confirmation by specialist  DSM-RS-IV  **Comorbidity:** N/A  **Female:** 15 %  **Age mean:**  Intervention 11.8 (2.14), control 12.2 (2.19)  **Minimum age:** 8  **Maximum age:** 18  **Ethnicity:**  N/A | **Intervention:** Omega 3/6 in a dose of three capsules twice daily, corresponding to a daily dose of 558 mg eicosapentaenoic acid, 174 mg docosahexaenoic acid (both are omega-3 fatty acids), 60 mg gamma linoleic acid (an omega 6 fatty acid), and 10.8 mg Vitamin E for 3 months  **Control:** Placebo  Placebo, identical capsules containing olive oil  **Comparator:** NA  **Follow-up:** 3 months | CGI (Clinical Global Impression) scale change  Intervention group improved more than placebo group (p 0.02).  ADHD-RS-IV (ADHD Rating Scale IV), parent reported change  Number responding (defined as 25% improvement in ADHD symptoms on ADHD RS IV)  Difference in mean improvement at follow-up not significant. Higher percentage of intervention group classified as responders.  11 (3 active, 8 placebo) withdrawals during Study Period (7 were unmotivated to continue or had problems swallowing the capsules [1 active, 6 placebo], 3 had side effects in the form of dyspepsia, vomiting, or diarrhea [2 active, 1 placebo]), and 1 patien |
| Nutrition, supplements | Johnstone, 2022350  Johnstone, 2019869; Oregon Health Science University, 2018971  ID: NCT03252522  RCT  Multicenter  N = 135  US  Setting: Specialty care | **Target:** Children with ADHD not on medication; exclusion criteria were neurological disorders, serious medical conditions, and known allergy to any ingredient in either intervention  **Other:** Parents provided outcome data  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-V  **Comorbidity:** N/A  **Female:** 27 %  **Age mean:** 9.8 (1.7)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % Black/African American : 3  % Asian : 3  % White : 88 | **Intervention:** Vitamins and known essentialminerals, amino acids and antioxidants, total of 9 to 12 capsules per day accumulated to doses above the recommended dietary allowance but below the upper tolerable intake level, for 8 weeks  **Control:** Placebo  Visually identical placebo capsules containing cellulose filler and 0.1 mg of riboflavin per capsule to mimic the color of urine as when supplemented with B-vitamins  **Comparator:** NA  **Follow-up:** 2 months | CGI-S severity reduced  56% of micronutrient group vs 22% of placebo group had illness severity reduced by at least 1 category (p < .001).  Inattention CASI-5 (Child and Adolescent Symptom Inventory-5), parent-rated  Between-group difference was not significant.  Impairment scale CASI teacher rating  No statistically significant difference between groups (p=0.22).  Height (cm)  Intervention patients gained more height (p 0.002).  Participants with any adverse event  Rate was 32% in the intervention and 45% in the placebo group.  No between-group differences for treatment-emergent adverse events were detected. |
| Nutrition, supplements | Katz, 2010360  Etz-HaChayim Clinic (Israel), 2007762  ID: ISRCTN10628149  RCT  Single center  N = 120  Israel  Setting: Specialty care | **Target:** Treatment naïve children with ADHD and without medical conditions, psychiatric comorbid conditions, or ongoing use of any medications  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 15 %  **Age mean:**  Intervention 9.72 (1.58), control 9.20 (1.82)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** PaeoniaeAlba, Withania Somnifera , Centella Asiatica, Spirulina Platensis, Bacopa Monieri, and Mellissa Officinalis compound herbal preparation, 3 ml of the compound herbal preparation taken 3 times daily before meals diluted in 50 to 60 ml of water for 4 months  **Control:** Placebo  Placebo home administered by parents who were instructed how to prepare (dilute in water) the daily dosage for the entire day  **Comparator:** NA  **Follow-up:** 4 months | Test of Variables of Attention (TOVA), composite score  Improvement for overall TOVA (p < .001) as well as omission (p = .016), commission (p = .026), response time (p < .001) and variability (p < .001) scales was greater for intervention group than placebo group.  Decreased appetite  Decreased appetite reported by 2 people in the control group and only 1 in the intervention group.  No serious adverse events were reported, and the rate of even mild adverse events among intervention patients was less than that of placebo. None of the adverse events were more frequent in the intervention than in the placebo group. |
| Nutrition, supplements | Khaksarian, 2021363  Khoram-Abad University of Medical Sciences, 2020882  ID: IRCT20190602043790N2  RCT  Single center  N = 70  Iran  Setting: Specialty care | **Target:** Children and adolescents with ADHD  **Other:** Parents and teachers provided outcomes  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM V by Child Psychiatrist  **Comorbidity:** N/A  **Female:**  % N/A  **Age mean:**  Methylphenidate group: 11.03 (2.31) and for Methylphenidate and Saffron group: 10.57 (2.56)  **Minimum age:** 6  **Maximum age:** 16  **Ethnicity:**  N/A | **Intervention:** Saffron plus methylphenidate: 20 mg/d (for <30 kg and 30 mg/d for > 30 kg, 10 mg for morning, midday, and evening equally) plus 20-30 mg/d saffron capsules according to the BMI (20 and 30 mg/d for <30kg and > 30kg), for 8 weeks  **Control:** Other  Methylphenidate alone; in week one, initial dose 10mg/d (5mg for morning and midday equally); week 2 dose 20 mg/d (10 mg for morning and midday equally), 20 mg/d (for <30 kg and 30 mg/d for > 30 kg, 10 mg for morning, midday, and evening, for 8 weeks  **Comparator:** NA  **Follow-up:** 2 months | ADHD-IV (Attention-Deficit/Hyperactivity Disorder Rating Scale-IV) scores, total, parent report  Intervention group improved more on all ADHD IV parent and teacher reported scales (p < .001).  No significant difference between groups in side effects. |
| Nutrition, supplements | Khoshbakht, 2021364  Nutrition and Food security research center, 2018966  ID: IRCT20130223012571N6  RCT  Single center  N = 86  Iran  Setting: Specialty care | **Target:** Treatment naive children with ADHD  **Other:** Parents and teachers provided outcomes  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV by psychiatrist  **Comorbidity:** N/A  **Female:** 0 %  **Age mean:**  N/A  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Dietary Approaches to Stop Hypertension (DASH) diet, dietcontains higher amounts of whole grains, fruits, vegetables, low-fat dairy products, nuts, and beans, as well as low amounts of saturated fats, cholesterol, refined grains, sweets, and red meat, for 3 months (12 weeks)  **Control:** Attention-matched control  Control diet was similar to the usual diet of Iranian children, allowing for refined grains, full-fat dairy, and meats; it had lower amounts of fruits and vegetables, simple sugars were also allowed  **Comparator:** NA  **Follow-up:** 3 months | SNAP-IV, combined, parent report  Intervention group improved more on both parent reported SNAP IV (p = 0.007) and teacher reported SNAP IV (p = 0.03).  SDQ-P (strengths and difficulties questionnaire, parent reported) total score  After adjustment for confounders, parent, teacher, and child reported SDQ hyperactivity, emotional symptoms, and total scores significantly improved in the DASH group compared with the control group (p < 0.05). |
| Nutrition, supplements | Manor, 2012411  Manor, 2012908; Enzymotec, 2007760  ID: NCT00418184  RCT  Single center  N = 200  Israel  Setting: Specialty care | **Target:** Participants with confirmed DSM-IV-ADHD diagnosis, no girls who reached menarche, no history or current diagnosis of any serious systemic or neurological condition, no pervasive developmental disorder or nonverbal learning disability, no psychotic disorder, no current psychiatric comorbidity that required psychiatric pharmacotherapy, no history of alcohol or substance abuse.  **Other:** Parents, teachers reported outcomes  **ADHD presentation:** inattentive : 32,hyperactive : 2,combined : 66  **Diagnosis:** Confirmation by specialist  DSM-IV ADHD diagnosis confirmed  **Comorbidity:** N/A  **Female:** 29.3 %  **Age mean:** 9.2 (1.9)  **Minimum age:** 6  **Maximum age:** 13  **Ethnicity:**  N/A | **Intervention:** Omega 3, 4 capsules (2 capsules twice a day) of Phosphatidylserine-Omega3daily; daily dosage provided 300 mg of Phosphatidylserine, 120 mg of Eicosapentaenoic acid + Docosahexaenoic acid (Eicosapentaenoic acid/Docosahexaenoic acid ratio of 2:1); for duration of 15 weeks  **Control:** Placebo  Placebo, 4 capsules (2 capsules twice a day) of cellulose as placebo, for 15 weeks  **Comparator:** NA  **Follow-up:** 4 months | CTRS/L (Conners’ Teacher Rating Scale Revised Long-Hebrew Version)  No significant difference between the intervention and control group (p=0.898).  Strengths and Difficulties Questionnaire (SDQ)  No significant difference between the intervention and control group.  BMI change following 15 weeks of treatment  P=0.301  Participants with adverse events  No significant differences were detected between the placebo and the intervention group in the incidence or number of adverse events recorded (p = 0.848 and p = 0.982, respectively). |
| Nutrition, supplements | Mohammadi, 2012440  ID: N/A  RCT  Single center  N = 50  Iran  Setting: N/A | **Target:** Children diagnosed with ADHD (combined form) by a child and adolescent psychologist, no use any confounding drugs or supplements; no history of major prenatal complications such as prematurity, low birth weight, any past or present psychosis, comorbid Tourette syndrome, celiac, phenylketonuria, autism, other persistent developmental disorders, or narcotics use  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 28 %  **Age mean:**  Intervention 9.57(1.65), control 8.83(1.82)  **Minimum age:** 7  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Melatonin (3 or 6mg) plus methylphenidate (ritalin) (1mg/kg) for 8 weeks  **Control:** Placebo  Placebo plus methylphenidate (ritalin) (1mg/kg) for 8 weeks  **Comparator:** NA  **Follow-up:** 2 months | ADHD-RS (ADHD Rating Scale)  The mean attention deficiency scores of two groups based on ADHD rating scale at 8 weeks after the treatment showed no statistically significant difference (p=0.974; mean for melatonin was 11.11 and mean for placebo was 11.29).  SDSC (Sleep Disturbance Scale for Children): The mean sleep latency and total sleep disturbance scores were reduced in melatonin group, while the scores increased in the placebo group (p≥0.05).  Loss of appetite  The rates were 70% in the melatonin and 61% in the placebo group.  Mean scores of side effects based on the stimulant drug side effects questionnaire were 11.35 (SD 8.81) in melatonin group and 10.16 (SD 9.05) in placebo group (p=0.686). |
| Nutrition, supplements | Mohammadzadeh, 2019441  Kurdistan University of Medical Sciences, 2017891  ID: IRCT2016060128182N2  RCT  Single center  N = 66  Iran  Setting: Specialty care | **Target:** Children with ADHD, no omega-3 use in at least the last6 months, without any physical illness or psychological disorder  **Other:** Parents provided some outcomes  **ADHD presentation:** N/A : "Patients were from all ADHD subtypes and new ones."  **Diagnosis:** Confirmation by specialist  DSM-IV-TR, diagnosis made by a child & adolescent psychiatrist  **Comorbidity:** N/A  **Female:** 25.8 %  **Age mean:**  Methylphenidate + placebo: 8.20 (1.72), Methylphenidate + omega-3: 7.7 (1.65)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Omega-3 plus methylphenidate, eicosapentaenoic acid capsules (180 mg) and docosahexaenoic acid (120mg) plus optimal dose of methylphenidate up to 30 mg, supplement and medication taken twice a day for 8 weeks  **Control:** Other  Placebo plus methylphenidate for 8 weeks  **Comparator:** NA  **Follow-up:** 2 months | ADHD-RS-IV (ADHD Rating Scale-IV parents), total score  There was no statistically significant difference between groups (p=0.75). There were also no significant intergroup differences between the Inattention (p=0.48) and hyperactivity/impulsivity (p=0.80) subscale scores on the Parents ADHD Rating Scale.  Anorexia  No difference between groups (p>0.05).  There was no statistically significant difference in incidences of nausea, vomiting, diarrhea, stomach ache, dry mouth, drowsiness, insomnia, anxiety, restlessness, irritability, or seizure between the groups. |
| Nutrition, supplements | Mostajeran, 2020443  Mostajeran, 20181186  ID: IRCT20180303038930N1  RCT  Single center  N = 64  Iran  Setting: Specialty care | **Target:** Children with ADHD on medication; no significant physical impairment, history of a pervasive developmental disorder, schizophrenia, bipolar disorder, severe depressive episode, epilepsy or heart disease  **Other:** Parents provided some outcomes  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  Pediatrician by DSM-V  **Comorbidity:** N/A  **Female:** 12.5 %  **Age mean:** 9.38 (2.18)  **Minimum age:** 6  **Maximum age:** 13  **Ethnicity:**  N/A | **Intervention:** Ma’aljobon (whey protein) powder plus medication, 25 g in 100 cc water, once daily after breakfast, participants continued their previous standard conventional ADHD medications, for 2 months  **Control:** TAU  Medication alone, standard conventional ADHD medications continued  **Comparator:** NA  **Follow-up:** 2 months | Hyperactivity scale Strengths and Difficulties Questionnaire (SDQ), parent-report  Intervention group improved more on hyperactivity scale (p = 0.04). No significant difference in improvement on emotional symptoms (p= .88), conduct problems (p = .55), peer problems (p = .66), or prosocial behavior (p = .62). Regarding teacher report SD |
| Nutrition, supplements | Motaharifard, 2019444  Vice Chancellor for research of Tehran university of Medical Sciences, 20151142  ID: IRCT2015050922165N1  RCT  Single center  N = 59  Iran  Setting: Primary Care | **Target:** Children diagnosed with mild or moderate ADHD according to DSM-5, no significant chronic medical condition, no development disorders, no other psychiatric disorders, no intellectual disabilities (IQ<70), not clinically current drug abusers or dependent on drugs within the last 6 months  **Other:** Parents and teachers of children with ADHD  **ADHD presentation:** combined : 100  **Diagnosis:** Confirmation by specialist  Child and adolescent psychiatrist confirmed diagnosis of ADHD according to DSM-5  **Comorbidity:** N/A  **Female:** 34 %  **Age mean:** 7.1 (1.36)  **Minimum age:** 6  **Maximum age:** 14  **Ethnicity:** | **Intervention:** Sweet almond syrup 5 cc/day three times a day for 8 weeks  **Control:** NA  **Comparator:** MedicationMethylphenidate 1 mg/kg/day, dose 5 mg twice daily in the first week, followed by a 10-mg tablet twice daily, participants weighing beyond 30 kg received a 10-mg tablet thrice daily from the third week of the study, tablets mixed into 5 cc/day of therapeu  **Follow-up:** 2 months | ADHD-RS-IV (ADHD Rating Scale-IV), parent- Hyperactivity Subscale  There was no significant difference between groups (p=0.78).  Decreased appetite  Intervention group had significantly more participants with decreased appetite (p<0.001).  Reported side effects of sweet almond syrup: insomnia 8%; increased sleep 16%; difficulty falling asleep 12%; abdominal pain 8%; impulsiveness 4%) irritability 4%; nausea 4%. Side effects of MPH: insomnia 24%; increased sleep 4%; difficulty falling asleep |
| Nutrition, supplements | Pelsser, 2011472  Wageningen University (The Netherlands), 20081147  ID: ISRCTN76063113  Crossover trial  Unclear/Not reported  N = 100  Netherlands  Setting: Mixed | **Target:** Children with ADHD; not receiving drugs or behavioural therapy for ADHD, children already following a diet, or family circumstances that were likely to prevent completion of the study  **Other:** Parents & teachers supplied some outcomes.  **ADHD presentation:** inattentive : 6,hyperactive : 9,combined : 85  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 14 %  **Age mean:** 6.9 (1.3)  **Minimum age:** 4  **Maximum age:** 8  **Ethnicity:** | **Intervention:** Elimination diet, individually designed, consisting of the few­ foodsdiet (ie, rice, meat, vegetables, pears, and water) complemented with specific foods such as potatoes, fruits, and wheat for 5 weeks  **Control:** Attention-matched control  Healthy food advice according to the guidelines of the Dutch NutritionCentre. Parents continued to keep an extended diary until the end of the trial  **Comparator:** NA  **Follow-up:** 3 months | ADHD-RS (ADHD rating scale), total score, teacher report  Intervention group improved more than control group on both teacher (p < .001) and parent (p < .001) scales. |
| Nutrition, supplements | Pongpitakdamrong, 2021478  ID: ID NA  RCT  Single center  N = 52  Thailand  Setting: Specialty care | **Target:** Children and adolescents with ADHD and iron deficiency treated with a steady dosage of methylphenidate for at least 1 month  **Other:** Parents & teachers supplied outcomes  **ADHD presentation:** inattentive : 21.2,hyperactive : 1.9,combined : 76.9  **Diagnosis:** Confirmation by specialist  DSM-V  **Comorbidity:** Other : Iron deficiency  **Female:** 13.5 %  **Age mean:** 9.6 (2.0)  **Minimum age:** 6  **Maximum age:** 18  **Ethnicity:**  % Asian : 100 | **Intervention:** Iron in the form of ferrous fumarate, 200mg capsules of ferrous fumarate, participantswho weighed less than or equal to 30kg received 1 capsule of ferrous fumarate per day, participants who weighed > 30kg received 2 capsules per day (2–4 mg of elemental iron/kg/d), methylphenidate continued as already prescribed; duration of 12 weeks  **Control:** Placebo  Placebo that tasted and looked similar to the ferrous fumarate capsules, participants who weighed less than or equal to 30kg received 1 capsule of placebo per day for 12 weeks, whereas participants who weighed >30kg received 2 capsules per day for 12 wee  **Comparator:** NA  **Follow-up:** 3 months | Vanderbilt ADHD total score  Intervention group improved more (p 0.037). No significant difference between groups regarding change in teacher ADHD RS total score.  Participants with any adverse event  No reported adverse events in either group. |
| Nutrition, supplements | Rafeiy-Torghabeh, 2021488  Roozbeh Psychiatric Hospital, 20181015  ID: IRCT20090117001556N115  RCT  Single center  N = 66  Iran  Setting: Specialty care | **Target:** Children 6 to 12 with ADHD per DSM 5; excluded if any psychiatric comorbidity except oppositional defiant disorder  **Other:** Guardians (usually parents) and teachers  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM 5  **Comorbidity:** N/A  **Female:** 28.3 %  **Age mean:** 8.7 (1.7)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Antioxidant resveratrol 250mg two times a day in addition to methylphenidate 20mg/day, participants weighing more than 30kg received methylphenidate 30mg/day for 8weeks  **Control:** Placebo  Placebo plus methylphenidate 20mg/day for 8 weeks, participants weighing more than 30kg received methylphenidate 30mg/day  **Comparator:** NA  **Follow-up:** 2 months | ADHD-RS-IV parent version  Significant of intervention on parent ADHD-RS (total p 0.015; inattention p 0.032; hyperactivity/impulsivity p 0.036). No significant differences on teacher version of ADHD-RS (total p 0.401; inattention p 0.507; hyperactivity/impulsivity p 0.466).  Reduced appetite  No group difference in decreased appetite ( p = 0.76).  The frequencies of adverse events in the groups were similar. |
| Nutrition, supplements | Rucklidge, 2018505  ID: ACTRN12613000896774  RCT  Single center  N = 93  New Zealand  Setting: Specialty care | **Target:** Medication-free children with ADHD  **Other:** Parents and teachers provided some outcome data  **ADHD presentation:** inattentive : 28.0,hyperactive : 5.4,combined : 66.6  **Diagnosis:** Confirmation by specialist  DSM IV plus Kiddie Schedule for Affective Disorders and Schizophrenia Lifetime Version (KSADS-PL) plus parent and teacher Conners Rating Scales (CRS-R:L; T score > 65 on parent form and >60 on teacher form)  **Comorbidity:** N/A  **Female:** 23.7 %  **Age mean:** 9.75 (1.5)  **Minimum age:** 7  **Maximum age:** 12  **Ethnicity:**  % Native Hawaiian or Pacific Islander : 21.5%,Other info : Maori or Tongan  % White : 78.5% | **Intervention:** Vitamin capsules, multivitamin containing a comprehensive range of micronutrients (13 vitamins, 17 minerals, and four amino acids), 15 capsules a day for 10 weeks  **Control:** Placebo  Placebo  **Comparator:** NA  **Follow-up:** 2.5 months | SDQ - Conduct problems, teacher  No statistically significant difference between groups (p=0.055).  CGI-I (Clinical Global Impressions-Improvement)  CGI-I improved or very much improved  Intervention group had greater improvement in mean score (p=0.029) and had a higher percentage showing improvement (p<0.05).  ADHD-RS-IV, clinician report  No between-group differences (p=0.415).  Intervention group improved more on Teacher BRIEF–Behavioural Regulation Index (p 0.05) and BRIEF emotional control scale (p 0.01). No difference in Child Mania Rating Scale -Parent report (p 0.10). No difference in Strengths and Difficulties Questionnaire (SDQ) total problem score as reported by parents (p 0.062) or teachers (p 0.064). Intervention group scored better on SDQ conduct problems scale in the parent (p 0.015) but not teacher report (p 0.055).  Weight (kg) change from baseline  The change in weight was not statistically significant (p=0.6.08).  Across a large number of assessed outcomes, micronutrients had minimal side effects. |
| Nutrition, supplements | Salehi, 2010509  Roozbeh Psychiatric Hospital, 20091014  ID: IRCT138711151556N6  RCT  Single center  N = 50  Iran  Setting: Specialty care | **Target:** Children with ADHD; no comorbid psychiatric diagnosis that would contraindicate guanfacine extended-release treatment or confound efficacy or safety assessments  **Other:** Parents & teachers provided outcomes  **ADHD presentation:** combined : 100  **Diagnosis:** Confirmation by specialist  Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime diagnostic interview  **Comorbidity:** N/A  **Female:** 22 %  **Age mean:**  Ginko 9.12 (1.61), methylphenidate 9.61 (2.26)  **Minimum age:** 6  **Maximum age:** 14  **Ethnicity:**  Other : Persian | **Intervention:** Ginkgo biloba dose of 80–120 mg/day depending on weight, 40 mg twice per day for < 30 kg and 120 mg three times per day for > 30kg, treatment for 6 weeks  **Control:** NA  **Comparator:** MedicationMethylphenidate 20–30 mg/day depending on weight (20 mg/day for < 30kg and 30 mg/day for > 30 kg) for 6 weeks; titrated in week 1: 10 mg/day (5 mg in the morning and 5 mg at midday), week 2: 20 mg/day (10 mg in the morning and 10 mg at midday) and week 3:  **Follow-up:** 1.5 months | ADHD-RS-IV Total Score changes, parent  MPH group improved more on parent (p=0.047) and teacher (p =0.05) ADHD-RS-IV total score.  Decreased appetite, number of patients  Decreased appetite more common in MPH group (p = 0.0002).  Side effects were mild to moderate and tolerable, the difference in the frequency of side effects was no significant except for decreased appetite, headache, and insomnia that were more frequent in the methylphenidate group. |
| Nutrition, supplements | Salehi, 2016510  ID: IRCT20110416201N1  RCT  Single center  N = 150  Iran  Setting: Specialty care | **Target:** Children with ADHD with no history of psychiatric drug usage and no history of other psychiatric disorders, no limitation or sensitivity for the use of zinc sulfate and omega‑3, and absence of mental retardation  **Other:** Parents & teachers supplied outcomes  **ADHD presentation:** inattentive : 28.7,hyperactive : 29.3,combined : 42  **Diagnosis:** Confirmation by specialist  Psychiatrist DSM-IV-TR  **Comorbidity:** N/A  **Female:** 26 %  **Age mean:** 9.07 (2.13)  **Minimum age:** 6  **Maximum age:** 15  **Ethnicity:**  Other : Persian | **Intervention:** Omega 3 plus methylphenidate, eicosapentaenoic fatty acid (100 mg for children <25 kg, 200 mg for 26–35kg, and 400 mg for children >35 kg/day) with daily methylphenidate, prescribed based on child’s weight (10 mg daily for children under 20 kg; 10 mg, twice a day for children over 20 kg) for 8 weeks  **Control:** Other  Placebo plus methylphenidate, whitish color capsule containing sugar, as the sameshape and volume of omega‑3 capsules  **Comparator:** Nutrition, supplementsZinc sulfate capsule (containing 22 mg zinc sulfate) administered with daily MPH  **Follow-up:** 2 months | Conners’ Parent and Teacher Rating Scales average  No difference among groups (p=0.581). |
| Nutrition, supplements | Tan, 2016579  ID: NCT01855984  RCT  Multicenter  N = 146  Malaysia  Setting: Specialty care | **Target:** Children with ADHD; those with syndromes, inborn errors of metabolism, structural brain lesions, co-existing chronic liver disease and those on concurrent anticoagulants or antiplatelet drugs were excluded as were children who were unable to swallow the capsule  **Other:** Parents and teachers provided outcomes  **ADHD presentation:** inattentive : 10.3,hyperactive : 0,combined : 89.7  **Diagnosis:** Confirmation by specialist  DSM-IV by physicians  **Comorbidity:** N/A  **Female:** 15 %  **Age mean:** 9.4 (1.8)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % Asian : 100,Other : Malaysian | **Intervention:** Antioxidant tocotrienol-rich fractions (from the natural Vitamin E family), 2 softgel capsules containing 100 mg per day, for 6 months  **Control:** Placebo  Two placebo capsules per day for 6 months  **Comparator:** NA  **Follow-up:** 6 months | Vanderbilt ADHD Parent Rating Scale, Total  No significant group differences in parent or teacher ratings.  There were 14 adverse events in the intervention and 24 in the placebo group, all were mild. |
| Nutrition, supplements | Trebaticka, 2006586  Chovanova, 2006716  ID: NA  RCT  Single center  N = 61  Slovakia  Setting: Specialty care | **Target:** Children with ADHD with at least 6 months of symptoms, general disposition as restless, inattentive, distractible and disorganized; acute inflammatory diseases, renal and cardiovascular disorders, diabetics, and co-morbid psychiatric conditions were excluded  **Other:** Parents and teachers provided some outcomes  **ADHD presentation:** N/A  **Diagnosis:** No  ADHD according to ICD-10 with following diagnoses: Hyperkinetic Disorder, Hyperkinetic Conduct Disorder, Attention Deficit without Hyperactivity  **Comorbidity:** N/A  **Female:** 18 %  **Age mean:**  mean 9.5  **Minimum age:** 6  **Maximum age:** 14  **Ethnicity:**  N/A : Slovakian | **Intervention:** Pycnogenol (extract from the bark of the French maritime pine, consisting of phenolic acids, catechin, taxifolin and procyanidins), 1 mg/kg/day for 4 weeks  **Control:** Placebo  Placebo  **Comparator:** NA  **Follow-up:** 1 month | CAP (Child Attention Problems), teacher  Intervention group scores improved significantly compared to placebo on hyperactivity (p=0.044) and inattention (p= 0.0067) scores.  CPRS (Conner’s Parent Rating Scale)  No significant difference in reduction between intervention and placebo. |
| Nutrition, supplements | Tzang, 2016590  Mackay Memorial Hospital, 2012905  ID: NCT01725737  RCT  Single center  N = 116  Taiwan  Setting: Primary Care | **Target:** Children with a clinical diagnosis of ADHD as defined by DSM-IV; children were deemed healthy by means of medical history, physical examination, vital-sign measurements, and laboratory assessments; children had to be naïve to all treatments for ADHD  **Other:**  **ADHD presentation:** inattentive : 34.5,hyperactive\_other : Treatment: 14.0%; Placebo 15.1%,combined : 65.5,N/A : ODD comorbidity in treatment group: 72.4% and placebo: 74.1%  **Diagnosis:** Confirmation by specialist  The diagnoses of ADHD and other mental disorders were confirmed by a child-and adolescent psychiatrist by using a structured parent interview according to the National Institute of Mental Health Diagnostic Interview Schedule for Children (version 4.0).  **Comorbidity:** N/A  **Female:** 44.8 %  **Age mean:**  Treatment group: 9.3 (2.7) Placebo Group: 9.0 (2.2)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Sarcosine (dietary supplement, glycine transporter-1 inhibitor), 0.3 g of 1 capsule daily if body weight 10±5 kg, twice a day for 20±5 kg, thrice a day for 30±5 kg, or 2 capsules twice a day for 40±5 kg, no other psychotherapy was provided, including family or group therapy, for 6 weeks  **Control:** Placebo  Identically appearing capsules of placebo  **Comparator:** NA  **Follow-up:** 6 months | SNAP ODD: Swanson, Nolan, Pelham oppositional defiance disorder scores  The sarcosine group had lower mean values on all three subscales compared to placebo.  Decreased appetite  The difference between groups was not significant (p=0.677).  Rates of adverse events |
| Nutrition, supplements | Van der Heijden, 2007596  ID: ISRCTNR47283236  RCT  Multicenter  N = 107  Netherlands  Setting: Specialty care | **Target:** Children with diagnosed ADHD and chronic sleep-onset insomnia  **Other:**  **ADHD presentation:** inattentive : 21.0,hyperactive : 3.8,combined : 73.3  **Diagnosis:** Confirmation by specialist  Psychologist and psychiatrist  **Comorbidity:** Sleep : chronic sleep-onset insomnia  **Female:** 25.7 %  **Age mean:**  9.1 (2.3) treatment, 9.3 (1.8) placebo  **Minimum age:**  **Maximum age:**  **Ethnicity:**  N/A | **Intervention:** Melatonin, fast-release, 3mg if body weight <40mg, 6mg if body weight > 40kg for 4 weeks  **Control:** Placebo  Identical-appearing placebo tablets  **Comparator:** NA  **Follow-up:** 1 month | CBCL (Child Behavior Checklist)  The melatonin group had significantly smaller improvements compared to the placebo group.  TACQOL-P (TNO-AZL Questionnaire for Children's Health-Related Quality of Life, Parent form) showed no statistically significant changes in scores between groups.  Adverse events  There were no statistically significant differences between the intervention and placebo group (p=1.00) |
| Nutrition, supplements | Voigt, 2001601  ID: ID NA  RCT  Single center  N = 63  US  Setting: Specialty care | **Target:** Children with ADHD treated with stimulant medication; no treatment with other psychotropic medications, diagnosis of other childhood psychiatric disorders, use of dietary supplements other than vitamins, occurrence of a significant life event within 6 months, a history of head injury or seizures, receipt of special education services for mental retardation or a pervasive developmental disorder, premature birth, exposure to tobacco, alcohol, or other drugs in utero, chronic medical condition  **Other:** None  **ADHD presentation:** inattentive : 9.4,combined : 90.6  **Diagnosis:** Confirmation by specialist  DSM-IV per diagnostic interview with a neurodevelopmental pediatrician  **Comorbidity:** N/A  **Female:** 22 %  **Age mean:** 9.3 (1.9)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % White : 92.5 | **Intervention:** Omega 3 plus stimulant medication, docosahexaenoic acid (DHA), algae-derived triglyceride capsule, 345mg DHA per day for 4 months  **Control:** Placebo  Placebo plus stimulant medication, 1 capsule once a day for 4 months  **Comparator:** NA  **Follow-up:** 4 months | Test of Variables of Attention (TOVA), a computer administered measure of sustained attention: No significant difference in improvement in any of the four TOVA scores (errors of omission, errors of commission, total response time, response time variability).  No participant withdrew because of adverse effects of treatment. |
| Nutrition, supplements | Weber, 2008606  National Center for Complementary and Integrative Health (NCCIH), 2004950  ID: NCT00100295  RCT  Single center  N = 54  US  Setting: Other | **Target:** Children and adolescents with ADHD that scored more than 1.5 standard deviations above age and sex norms on the ADHD Rating Scale-IV; no psychiatric co-morbidities  **Other:** Parents  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM IV criteria based on the Kiddie Schedule for Affective Disorders and Schizophrenia–Epidemiologic Version (K-SADS)  **Comorbidity:** N/A  **Female:** 37 %  **Age mean:** 9.8 (2.0)  **Minimum age:** 6  **Maximum age:** 17  **Ethnicity:**  % Hispanic or Latino : 14.8  % Black/African American : 0  % American Indian or Alaska Native : 1.9  % Asian : 0  % White : 85.2  % Multiracial : 13.0 | **Intervention:** St. John's wort, 300 mg of H perforatum standardized to 0.3% hypericin 3 timesdaily for 8 weeks  **Control:** Placebo  Placebo 3 times daily  **Comparator:** NA  **Follow-up:** 2 months | CGI-I (Clinical Global Impression - Improvement Scale) much or very much improved  There was no significant difference between groups (p=0.59).  ADHD RS-IV (ADHD Rating Scale–IV), parent report  No significant difference between the 2 groups in the change in scores from baseline to follow up (p = 0.68).  No significant difference was seen in change in height between the groups during the 8-week trial.  Participants with any adverse event  The rate was 41% for intervention and 44% for comparator, which was no significantly different between groups. |
| Parent education | Abikoff, 2015110  NYU Langone Health, 2011968  ID: NCT01320098  RCT  Single center  N = 164  US  Setting: Specialty care | **Target:** Preschool, daycare or nursery school students diagnosed with ADHD, not currently taking medication for ADHD  **Other:** Parents were trained  **ADHD presentation:** inattentive : 33.5,hyperactive : 15.2,combined : 50.6  **Diagnosis:** Confirmation by specialist  DSM IV diagnosis confirmed by confirmed by clinical evaluation conducted by a psychologist with child and parent  **Comorbidity:** N/A  **Female:** 26.2 %  **Age mean:**  N/A  **Minimum age:** 3  **Maximum age:** 4  **Ethnicity:**  % Hispanic or Latino : 25.6  % Black/African American : 16.4  % Asian : 8.8  % White : 69.2 | **Intervention:** New Forest Parenting Package, weekly 1-to-1.5-hour sessions, home-based intervention which fosters constructive parenting to target ADHD-related dysfunctions in attention and impulse control for 8 weeks  **Control:** Wait list  Wait list  **Comparator:** Parent trainingHelping the Noncompliant Child, clinic-based parenting intervention for treating noncompliant behavior  **Follow-up:** 24 months | New York Parent Rating Scale - Physical Aggression Subscale, parent, post-tx  Comparator group participants, but not intervention group, were rated better than control (p < 0.003) at 6 months. There was no significant difference between intervention and comparator at 2 years.  CPRS (Conners Parent Rating Scale) total  Intervention and comparator groups significantly improved score compared to control (p <. 001); there was no significant difference between intervention and control .  Parent treatment satisfaction  Treatment satisfaction was equally high for intervention and comparator. P value not reported.  There were no adverse effects with either NFPP or HNC. |
| Parent education | Chacko, 2009176  ID: NA  RCT  Single center  N = 120  US  Setting: Other | **Target:** Children living with single mothers  **Other:** Single mothers of children with ADHD  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  diagnosis was determined through completion of parent and teacher rating scales of DSM IV, completion of semistructured interviews with the parent, and assessment of cross-situational impairment through completion of parent and teacher rating scales (Imp  **Comorbidity:** N/A  **Female:** 29.3 %  **Age mean:** 7.85 (2.14)  **Minimum age:** 5  **Maximum age:** 12  **Ethnicity:**  % Hispanic or Latino : 12.7  % Black/African American : 21.0  % White : 53.3  % Multiracial : 13.0 | **Intervention:** Strategies to Enhance Positive Parenting (STEPP), a manualized, program heldfor 2.5 hours each week, for 9 weeks  **Control:** Wait list  Wait list  **Comparator:** Parent trainingTraditional manualized behavioral parent training program; meets for one 2.5 hour session per week for 9 weeks; sessions included videotapes of parenting errors whereby  single mothers identified these errors and then formulated alternative parenting strat  **Follow-up:** 3 months | Inattentive score, Disruptive Behavior Disorders rating scale  Benefits of the combined parent training groups compared to the waitlist control group were observed on on DBD ODD symptoms (p < .009) at treatment end but not follow-up. No significant differences in Disruptive Behavior Disorders Inattentive and Hype  Impairment Rating Scale (IRS)  The intervention group was significantly more improved than the control group, while the comparator group was not significantly different from the control group. |
| Parent education | Churchill, 2018200  ID: ID NA  RCT  Unclear/Not reported  N = 174  US  Setting: Other | **Target:** Children and adolescents with ADHD; child must live with mother or primary female caregiver; English or Spanish speaking; lack of comorbid intellectual disability, autism, or psychosis  **Other:** Mother or primary female caregiver of child with ADHD  **ADHD presentation:** inattentive : 16.7,hyperactive : 23.55,combined : 33.35,combined\_other : % unknown 26.4  **Diagnosis:** Confirmation by specialist  Diagnosed by County Health Department, unclear method  **Comorbidity:** N/A  **Female:** 33.9 %  **Age mean:**  Intervention group mean age (10.6) and SD (3.2). Control group mean age (10.8) and SD (3.4).  **Minimum age:** 4  **Maximum age:** 18  **Ethnicity:**  % Hispanic or Latino : 8.6  % Black/African American : 14.35  % American Indian or Alaska Native : 7.5  % Asian : 6.95  % White : 79.35 | **Intervention:** In-home nurse visits with families with variable frequency based onparticipant family needs, participant families given a resource guide and received a newsletter every 6 months with up-to-date information about ADHD, duration of 1 year  **Control:** NA  **Comparator:** Parent trainingParenting book on ADHD and same newsletter every 6 months with up-to-date information about ADHD  **Follow-up:** 18 months | CBCL (Child Behavior Checklist)  No significant difference between groups (p=0.374).  Longitudinal family function: Family Systems Scale  No difference between groups (p = 0.154). |
| Parent education | Dose, 2017228  University of Cologne, Shire, 20121131  ID: NCT01660425  RCT  Single center  N = 103  Germany  Setting: Other | **Target:** Children with ADHD taking methylphenidate for at least 2 months and had to show functional impairment in at least 1 of the domains of the Weiss Functional Impairment Rating Scale – Parent Report  **Other:** Parents were the intervention target and provided some outcome data  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  Diagnosis by psychologist or psychiatrist required.  **Comorbidity:** N/A  **Female:** 18.5 %  **Age mean:** 9.78 (1.60)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Telephone-assisted self-help program for parents, reading 8 self-helpbooklets, then parents receive 10 telephone consultations of about 30 min each during the first 6 months and four booster telephone consultations during the second 6-month period; children received also methylphenidate but no specific dose was required, duration of 1 year  **Control:** TAU  Usual care plus children received methylphenidate, but no specific dosage was required  **Comparator:** NA  **Follow-up:** 12 months | FBB-ADHS (German symptom checklist for ADHD), total score  No difference in German ADHD scale, total score, at follow-up (p = 0.12). Intervention group performed better on German symptom checklist for Oppositional Deviant Disorder at follow-up (p = .03).  Weiss Functional Impairment Rating Scale – Parent Report  There was no significant difference between groups (p = 0.30). |
| Parent education | Ercan, 2014257  ID: NA  Clinical trial  Single center  N = 120  Turkey  Setting: Specialty care | **Target:** Children diagnosed with ADHD and oppositional defiant disorder or conduct disorder by psychiatrists, no other comorbid disorders  **Other:** Parents, teachers  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM IV per KSADS-PL  **Comorbidity:** ODD  **Female:** 31.7 %  **Age mean:** 9.07 (1.92)  **Minimum age:** 6  **Maximum age:** 13  **Ethnicity:**  N/A | **Intervention:** Parent-training program plus methylphenidate, optimal methylphenidate dose takendaily, parent-training program consisted of 4 consecutive weekly meetings that started at the beginning of the 2nd month and 10 monthly meetings that took place during the remaining 10 months of the treatment with each parent-training group consisted of 10 to 15 members, total duration of 12 months  **Control:** Other  Methylphenidate only, initial dose was 7.5 mg/day for children between 7 and 10 years of age and 10 mg/day for children between 11 and 13, dose was adjusted in response to continuous feedback from the parents, mean (SD) dose throughout the 12-month study  **Comparator:** NA  **Follow-up:** 12 months | CPRS (Conners’ Parent Rating Scale)  No significant effect of parent training on CPRS or Conners’ Teacher Rating Scale.  Hyperactivity-impulsivity scale, T-DSM-IV-S, parent rating  No significant effect of group on T-DSM-IV-S Hyperactivity / Impulsivity - Parent (p = .60), T-DSM-IV-S Attention - Parent (p = .89), T-DSM-IV-S OD - Parent (p = .39), or T-DSM-IV-S CD - Parent (p = .39). No significant effect of group on T-DSM-IV-S |
| Parent education | Ferrin, 2014265  ID: N/A  RCT  Single center  N = 81  Spain  Setting: Other | **Target:** Female and male participants with diagnosis of ADHD any subtype according to the DSM-IV; the diagnosis was confirmed by clinical interview with a child psychiatrist, supplemented with structured interview using the validated Spanish version of the semi-structured clinical interview of the Schedule for Affective Disorders and Schizophrenia for school age children, clinical ADHD symptoms stabilization for at least 1 month before entering the study  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  KSADS-PL  **Comorbidity:** N/A  **Female:** 20 %  **Age mean:**  Intervention 11.25(2.96), control 9.94(3.04)  **Minimum age:** 5  **Maximum age:** 18  **Ethnicity:**  N/A | **Intervention:** Psychoeducation program composed of 5 successive groups of 8–10 families who received 90 min weekly sessions for 12 weeks  **Control:** NA  **Comparator:** Parent trainingParent counselling and support intervention, 5 successive groups of 8–10 families who received 12-week 90 min weekly sessions, families were reunited and encouraged to comment on their thoughts and share their experiences in a nondirective, nonthreatening  **Follow-up:** 12 months | ADHD Index, CPRS-R (Conners’ Parent Rating Scale Revised 27-items), parent  There was no significant difference between groups.  Strengths and Difficulties Questionnaire (SDQ), parent  There was no statistically significant interaction effect of time by group. |
| Parent education | Ferrin, 2020266  ID: ISRCTN 26270684  RCT  Single center  N = 69  UK  Setting: Specialty care | **Target:** Children and adolescents with ADHD on stabilizing medication for 1 month prior to baseline assessment, without severe learning disabilities (IQ <70), autistic spectrum disorder as primary diagnosis, any clinically significant or unstable medical or psychiatric condition, and children whose families had received any similar school-based individual and/or group treatments at any point in time  **Other:** Parents  **ADHD presentation:** combined : 69.6  **Diagnosis:** Confirmation by specialist  DSM-IV confirmed by clinical interview with a child psychiatrist  **Comorbidity:** N/A  **Female:** 13 %  **Age mean:**  Intervention 10.86 (3.04), control 10.56 (3.20)  **Minimum age:** 5  **Maximum age:** 18  **Ethnicity:**  % Black/African American : 10.14%  % White : 50.7%  % Multiracial : 24.6 | **Intervention:** Psychoeducation with 5 successive groups of 7-10 families who received six sessionsof 2 hr at weekly intervals; a handout was delivered and parents were assigned some short additional homework to prepare for the next session, total duration of 6 weeks  **Control:** TAU  Treatment as usual group, families continued routine medical care as usual with their clinicians; they were offered the opportunity to join the psychoeducation group once their collaboration with the study had ended; control participants received monthly  **Comparator:** NA  **Follow-up:** 6 months | CGI-I (Clinical Global Impression - Improvement) change, clinician rating  Intervention improved significantly more than control (p=.038)  ADHD Index, Conners’ Parent Rating Scale: Short Form (CPRS-R:S)  Intervention group improved more than control on overall Index (p = .034) and cognitive/inattention (p = .037) and the hyperactive/impulsive (p = .025) subdomains. Difference on Conners Teacher Rating Scale, total, not statistically significant (p = .210  Strengths and Difficulties Questionnaire, teacher rating  No statistically significant differences (p=0.67) in teacher rating, parent rating, or child rating.  There were no statistically significant differences in parental stress across groups (p=0.521). |
| Parent education | Herbert, 2013325  ID: ID NA  RCT  Single center  N = 31  US  Setting: Specialty care | **Target:** Preschool age children with developmentally deviant levels of hyperactivity /impulsivity; children with mental retardation, autism, Asperger's, or cerebral palsy were excluded  **Other:** Parents  **ADHD presentation:** hyperactive : 100  **Diagnosis:** Confirmation by specialist  DISC-IV  **Comorbidity:** N/A  **Female:** 25.8 %  **Age mean:** 4.42 (0.90)  **Minimum age:** 2  **Maximum age:** 6  **Ethnicity:**  % Hispanic or Latino : 3.2  % Black/African American : 6.5  % White : 83.9  % Multiracial : 6.5 | **Intervention:** Parenting Your Hyperactive Preschooler pro­gram delivered via one 90-minute sessionper week; first 8 sessions focus on traditional parenting strategies shown to be effective in managing child behavior and tailoring these strate­gies for use with hyperactive preschoolers; the last 6 sessions focus on emotion socialization strategies designed to improve children's emotion regulation; for duration of 14 weeks  **Control:** Wait list  Wait list  **Comparator:** NA  **Follow-up:** 3 months | DBRS (Disruptive Behavior Rating Scale), hyperactivity-impulsivity  Intervention group improved more on DBRS hyperactivity/ impulsivity (p 0.008), inattention (p 0.002), and oppositional defiance disorder (p 0 .046) scales.  Behavior Assessment System for Children 2 (BASC 2), Parent Report , externalizing behavior scale  Intervention group improved more on BASC-2 externalizing scale (p 0.035) but not on internalizing scale (p 0.203). |
| Parent education | Hosainzadeh Maleki, 2014333  ID: ID NA  RCT  Single center  N = 36  Iran  Setting: Specialty care | **Target:** Children with ADHD taking ritalin  **Other:** One group received parent training; all had parents report some outcomes  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-TR by child psychiatrist  **Comorbidity:** N/A  **Female:**  % primarily boys  **Age mean:**  mean N/A  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  Other : 100% Persian | **Intervention:** Barkley’s parent training plus children's working memory training plus ritalin, 10 training sessions for mothers, a coupon-based economy at home for behavior modification, child computer working memory training and learning strategies and feedback from a therapist, 1 session for mothers and 1 for the children per week for 8 weeks  **Control:** Other  Working memory training plus ritalin alone, computerized, for child, for 8 weeks  **Comparator:** NA  **Follow-up:** 2 months | SNAP IV total score  Intervention group (combined treatment) improved most (p<0.001). |
| Parent education | Lange, 2018384  University of Aarhus, 20121127  ID: NCT01684644  RCT  Multicenter  N = 164  Denmark  Setting: Specialty care | **Target:** Children with clinical ADHD diagnosis supported by the Development and Well-Being Assessment; Danish as a first language spoken at home; IQ>=70; no autism spectrum disorder diagnosis; not in receipt of pharmacologic or psychosocial treatment for ADHD; no severe parental psychiatric disorder; no severe social adversity in the home  **Other:** Parents and teachers of children with ADHD  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  ADHD diagnosis was made by specialist child and adolescent psychiatrists based on results from all clinical assessments and Development and Well-Being Assessment profiles, which were conducted by trained raters. Development and Well-Being Assessment desig  **Comorbidity:** N/A  **Female:** 27 %  **Age mean:**  57% of children were aged 3-5; 43% of children were aged 6-7  **Minimum age:** 3  **Maximum age:** 7  **Ethnicity:**  N/A | **Intervention:** New Forest Parenting Programme consisted of personalized weekly homework assignments and 8 2-hour sessions (6 sessions in the clinic and 2 in the home), includes 5 elements: psychoeducation to enhance parents’ understanding of child’s behavior, scaffolding to help parents work from the child’s level of development, enhancing parent-child interaction, relieving the child’s ADHD symptoms through play and games, guiding parents in use of behavioral strategies; intervention for 12 weeks  **Control:** TAU  Treatment as usual typically consisted of a package of psychoeducation delivered to groups of individual parents by specialized staff; information about ADHD as a developmental disorder; how ADHD symptoms affect normal play and the development of preschoo  **Comparator:** NA  **Follow-up:** 9 months | Directly observed ADHD behaviors during solo play “index of attention/ engagement” using the Child Solo Play instrument  No significant difference.  ADHD-RS-IV (ADHD Rating Scale) symptom severity, parent ratings  After treatment, the parent training program was superior to treatment as usual on parent-rated ADHD symptoms (p=0.009; effect size d=0.30).  The parent training program was superior to treatment as usual on parenting self-efficacy and family strain. |
| Parent education | Mehri, 2020428  Department of Research and Technology, 2013734  ID: IRCT2013042112990N1  RCT  Single center  N = 56  Iran  Setting: Specialty care | **Target:** Children with ADHD, only taking methylphenidate for 6 months prior to study, with a fixed dose of drug in the last 30 days prior to start of study; at least one sleeping issue; no physical or mental comorbidities  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  diagnosed by psychiatrist based on DSM-IV criteria  **Comorbidity:** Sleep  **Female:** 14.3 %  **Age mean:** 8.50 (1.79)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Behavioral parental training on sleep problems, including information, sleep hygiene and nutrition health, control of environmental stimuli, cognitive behavioral therapy strategies, conducted in 2 groups of 14 parents per week in week 1, 3, and 5 of the study; children also received methylphenidate treatment; for 5 weeks  **Control:** Other  Methylphenidate treatment only  **Comparator:** NA  **Follow-up:** 2 months | Intervention group experienced a significantly greater improvement in total sleep scores compared to the control group (p = 0.03). Also the intervention group had a significantly greater decline in total sleep problem compared to the control group (p = 0.01). |
| Parent education | Schorr-Sapir, 2021520  ID: ID NA  RCT  Unclear/Not reported  N = 101  Israel  Setting: Mixed | **Target:** Children with primary DSM-5 ADHD diagnosis and scores above 55 on the Conners’ Scale for ADHD; no psychotic symptoms and no concurrent psychotherapy  **Other:** Parents  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-5  **Comorbidity:** N/A  **Female:** 21 %  **Age mean:** 8.8 (1.77)  **Minimum age:** 5  **Maximum age:** 13  **Ethnicity:**  Other : 100% Jewish | **Intervention:** Nonviolent resistance parent training with clinical psychologist,12 sessions (1 involving the parents and members of the school staff); 2 weekly telephone conversations with undergraduate student; special emphasis was given to psychoeducation on ADHD, parental emotion regulation and self-control, and the development of a collaborative relationship with the school; for 4 months  **Control:** Wait list  Waiting period is 12 weeks, given nothing during waiting period  **Comparator:** NA  **Follow-up:** 4 months | Child Behavior Checklist (CBCL), Externalizing symptoms  Difference in externalizing symptoms not significant (p<0.08); significant difference in internalizing symptoms (p<0.001).  Conners’ Rating Scale - ADHD index, parent  Difference between groups not statistically significant (p<0.08) |
| Parent education | Smit, 2021544  Mikami, 2020928  ID: NA  RCT  Multicenter  N = 172  Canada  Setting: Specialty care | **Target:** Children with ADHD who children scored ≥3 on parent or teacher reports on the Strengths and Difficulties Questionnaire Peer Problems subscale  **Other:** Parents were trained to coach children in friendship skills  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM V diagnosis required. Children required to have ≥6 symptoms of inattention and/or hyperactivity/impulsivity endorsed by either the parent on the K-SADS (Kiddie-Schedule for Affective Disorders and Schizophrenia) or the teacher on the CSI ( Child Sympt  **Comorbidity:** N/A  **Female:** 30 %  **Age mean:** 8.54 (1.55)  **Minimum age:** 6  **Maximum age:** 11  **Ethnicity:**  % Hispanic or Latino : 1.2  % Black/African American : 0.6  % Asian : 5.8  % White : 72.7  % Multiracial : 18.6 | **Intervention:** Parental Friendship Coaching: behavioral parent training where parents learn to be friendship coaches by teaching their children friendship skills and facilitating opportunities for children to make real-life friends; weekly, 90-min sessions for parents over 10 weeks  **Control:** NA  **Comparator:** Parent trainingPsychoeducation and social support (Coping with ADHD through Relationships and Education), weekly, 90-min sessions for parents over 10 weeks  **Follow-up:** 8 months | Child Behavior Checklist (CBCL) - Aggressive Behavior Subscale, parent and teacher score composite  There were no significant differences between treatment and comparator groups.  Intervention group had greater score improvement than comparator for Child Behavior Checklist (CBCL) - Withdrawn / Depressed Subscale, parent and teacher score composite |
| Parent education | Sonuga-Barke, 2001550  ID: N/A  RCT  Single center  N = 78  UK  Setting: Community | **Target:** Children born between January 1992 and September 1993, parents had to take the Parental Account of Childhood Symptoms examination  **Other:** Parents  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  They followed the American Psychiatric Association, DSM-IV standard.  **Comorbidity:** N/A  **Female:** 38.5 %  **Age mean:**  All age 3  **Minimum age:** 3  **Maximum age:** 3  **Ethnicity:**  N/A | **Intervention:** Parent training group received coaching in child management techniques, 1-hour weekly sessions for 8 weeks  **Control:** Wait list  Waiting-list control  **Comparator:** Parent trainingParent counseling and support, non-directive support and counseling for parent of children with ADHD  **Follow-up:** 3.75 months | Observation of ADHD behavior during 10 minute play with multipurpose toy  Significant effects seen for the intervention in direct observation measures (p<.05).  Parental Account of Childhood Symptoms (PACS) to assess core symptoms of ADHD, parent  Recovery (Jacobson & Truax criteria)  Significant effects were seen for the intervention (p<0.001). |
| Parent education | Sonuga-Barke, 2004551  Sonuga-Barke, 20021083  ID: NA  RCT  Unclear/Not reported  N = 89  UK  Setting: Other | **Target:** Children with ADHD  **Other:** Parents receiving training and providing outcome measures  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  Children met cut-offs on the Werry-Weiss-Peters Activity Scale and the Parental Account of Childhood Symptoms Structured Clinical Interview and their parents reported significant clinical impairment.  **Comorbidity:** N/A  **Female:**  % N/A  **Age mean:**  3 years old at time of enrollment  **Minimum age:** 3  **Maximum age:** 3  **Ethnicity:**  N/A | **Intervention:** Parent training of mothers, conducted in home with 1 hour per week for 8 weeks  **Control:** Wait list  Wait list  **Comparator:** NA  **Follow-up:** 3.75 months | BCL (Behaviour checklist)  Difference in Behavior Checklist not significant between intervention and control.  AD/HD score PACS (Parental Account of Childhood Symptoms)  No difference in follow-up ADHD symptoms between intervention and control groups. |
| Parent education | Sonuga-Barke, 2018552  ID: NA  RCT  Multicenter  N = 307  UK  Setting: Mixed | **Target:** Children positive for ADHD symptoms (score≥ 20) on the Werry-Weiss-Peters Activity Rating Scale, were given an ADHD research diagnosis of any sub-type based on the parent Diagnostic Interview Schedule for Children-IV-ADHD Scale; not taking ADHD medication  **Other:** Parent and/or caregiver aged 18 years or over  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  Werry-Weiss-Peters Activity Rating Scale and DISC-IV-ADHD Scale  **Comorbidity:** N/A  **Female:** 27 %  **Age mean:**  mean 42.7 (6.75) months  **Minimum age:** 3  **Maximum age:** 5  **Ethnicity:**  N/A | **Intervention:** New Forest Parenting Programme parent training intervention delivered at home for 1.5 hour sessions for 12 weeks  **Control:** TAU  Standard patterns of preschool ADHD care available in the parents' region; in two regions, there was little provision for preschool ADHD while in one region provision might include parenting education and training  **Comparator:** Parent trainingIncredible Years, developmentally based interventions, delivered weekly for 12 weeks, sessions were 2-2.5 hours long  **Follow-up:** 6 months | Directly Observed Attention  No difference between arms.  SNAP-IV (Swanson Nolan and Pelham - IV - Parent)  Small, non-significant, benefits of New Forrest program over TAU were seen (p 0.053).  Slightly better results for Incredible Years compared to New Forrest. No difference between active programs and treatment as usual.  One adverse event was reported—an accidental minor head injury in the New Forrest program. |
| Parent education | Sugaya 2022569  ID: NCT02807870  RCT  Single center  N = 153  Brazil  Setting: Specialty care | **Target:** Children with moderate or severe ADHD; those with affective, psychotic, or autism spectrum disorders, used psychotropic medications during the previous 30 days, a major clinical condition; a history of neurological disorder or head trauma with loss of consciousness were excluded  **Other:** Parents provided outcomes - one group of parents received training  **ADHD presentation:** inattentive : 7,hyperactive : 22,combined : 71  **Diagnosis:** Confirmation by specialist  DSM V by psychiatrists experienced in preschool mental health  **Comorbidity:** N/A  **Female:** 16 %  **Age mean:** 5.0 (0.63)  **Minimum age:** 3.0  **Maximum age:** 5.9  **Ethnicity:**  N/A | **Intervention:** Parent behavioral training session, Helping the Noncompliant Child based on social learning and behavior modification principles designed to teach parents how to manage children’s behavior, improve parent–child relationships, and parental competencies one 90 minute session per week for 8 weeks  **Control:** Placebo  Placebo plus sham parent behavioral training for 8 weeks  **Comparator:** MedicationMethylphenidate plus sham parent training (education), immediate release, for 8 weeks  **Follow-up:** 2 months | Multidimensional Assessment Profile of Disruptive Behavior (MAP-DB)  Time-by-group interaction significant only for Temper Loss scale: methylphenidate plus sham intervention vs placebo plus behavioural parent training group (p = 0.026); placebo plus behavioural parent training vs placebo plus sham intervention group (p=0·  Clinical Global Impressions Severity (CGI-S) scale  Significant difference between methylphenidate plus sham intervention and placebo plus sham intervention group (p 0·0088).  SNAP-IV, average scores across parent and teacher ratings  Significant difference between methylphenidate plus sham intervention and placebo plus sham intervention groups (p 0·049).  Conners Kiddie Continuous Performance Test (KCPT-2), a cognitive measure: detectability and hit reaction time results were superior for methylphenidate plus sham intervention compared to both placebo plus behavioural parent training and placebo plus sham intervention.  Decreased appetite  Significantly more common in more frequently in the methylphenidate plus sham intervention group than in the other two groups.  Number with any adverse event  No significant difference among groups.  Insomnia occurred more frequently in the methylphenidate plus sham l intervention group than in the other two groups, |
| Parent education | Tiwawatpakorn, 2021585  ID: TCTR20180516002  RCT  Unclear/Not reported  N = 80  Thailand  Setting: Other | **Target:** Participants diagnosed with ADHD by a developmental behavioral pediatrician or child and adolescent psychiatrist, receiving stable medication for at least 3 months, and living with their primary caregivers for at least 5 days a week  **Other:** Parents  **ADHD presentation:** inattentive\_other : Intervention: 1.7 (0.6); Control: 1.6 (0.6),hyperactive\_other : 1.8 (0.6); Control: 1.6 (0.8)  **Diagnosis:** Confirmation by specialist  Vanderbilt ADHD Diagnostic Parent Rating Scale (VADPRS)  **Comorbidity:** N/A  **Female:** 18 %  **Age mean:** 8.3 (1.1)  **Minimum age:**  **Maximum age:**  **Ethnicity:** | **Intervention:** Parental training plus routine clinical care, routine clinical care included psychoeducation, problem-oriented counseling, prescription of standard medications, and child evaluation, visits were scheduled every 3–6 months and took 15–30 minutes for each visit, parenting training consisting of six 120-minute weekly sessions consisting of general knowledge about ADHD and quality time, functional behavioral analysis, effective communication, positive and negative reinforcement, punishment, and time and school management; for 6 weeks  **Control:** Other  Routine clinical care only: psychoeducation, problem-oriented counseling, prescription of standard medications, and child evaluation, visits were scheduled every 3–6 months and took 15–30 minutes for each visit  **Comparator:** NA  **Follow-up:** 2 months | VADPRS (Vanderbilt ADHD Diagnostic Parent Rating Scale) subscales  The scores of inattention, hyperactivity/impulsivity, and oppositional-defiant behavior showed a noticeable reduction in both groups; no significant interactions were found between time and treatment arm (P > 0.05) indicating that the improvement in score  Treatment arm was not associated with changes in parenting style. |
| Parent education | Vaidyanathan, 2023593  ID: ID NA  RCT  Single center  N = 56  India  Setting: Specialty care | **Target:** Children with ADHD per DSM-5, without visual and hearing impairment, comorbid autism spectrum disorder, or social quotient under 50  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  Diagnosis was made by the team in the clinic consisting of a paediatrician, child psychiatrist, and senior resident in child psychiatry based on the DSM-5 criteria  **Comorbidity:** N/A  **Female:** 16.1 %  **Age mean:**  mean 57.82 (15.12) months  **Minimum age:** 2.5  **Maximum age:** 6  **Ethnicity:**  N/A | **Intervention:** Behavior parent training in groups of 4-8 members per group, educating parents about their child's disorder, necessary investigations as planned by the treating team, if indicated: pharmacotherapy, occupational therapy, speech therapy; training for 12 weeks  **Control:** NA  **Comparator:** Parent trainingBehavior parent training on an individual basis, plus educating parents about their child's disorder, necessary investigations as planned by the treating team; if indicated: pharmacotherapy, occupational therapy, speech therapy  **Follow-up:** 3 months | Conner's abbreviated behaviour rating scale  Both groups improved from baseline (p<0.001) and there was no significant interaction between group and time (p 0.468). |
| Physical exercise | Chang, 2022180  ID: ID NA  RCT  Multicenter  N = 48  Taiwan  Setting: School | **Target:** Children with ADHD and handwriting difficulties; those with history of any medical, neurological, or pervasive developmental disorders were excluded, as were those taking medication other than stimulant for ADHD  **Other:** None  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  **Comorbidity:** N/A  **Female:** 18.8 %  **Age mean:**  mean 8.36  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % Asian : 100 | **Intervention:** Table tennis training designed to improve to general executive attention with a special focus on short- and long-duration visuomotor control, 3 one-hour sessions per week for 12 weeks  **Control:** No intervention  No intervention  **Comparator:** Physical exerciseSimulated table tennis training with Nintendo Wii Sport, 3 one-hour sessions per week for 12 weeks  **Follow-up:** 3 months | Wisconsin Card Sorting Test, total errors: Intervention group improved more than comparator or control groups (p <0.01). No differences in improvement in Stroop Color Test among groups, intervention and comparator groups improved more than control group on Stroop Word test (p 0.017). |
| Physical exercise | Durgut, 2020239  University, Bezmialem Vakif, University, Medipol, 2018683  ID: NCT03469180  RCT  Single center  N = 30  Turkey  Setting: Specialty care | **Target:** Treatment naive children with ADHD; without history of chronic and severe systemic disease or a seizure-like neurological disorder or vision, speech and hearing problems; any contraindications for physical activity; comorbid conditions such as autism spectrum disorders or intellectual disability  **Other:** Teachers and parent provided some outcome data  **ADHD presentation:** inattentive : 16.7,hyperactive : 3.3,combined : 80.0  **Diagnosis:** Confirmation by specialist  diagnosed by psychiatrists via DSM V  **Comorbidity:** N/A  **Female:** 20 %  **Age mean:** 8.13 (1.19)  **Minimum age:** 7  **Maximum age:** 11  **Ethnicity:**  N/A | **Intervention:** Treadmill training plus whole body vibration training 3 days per week, treadmill training for 45 minutes, 5 minutes rest, whole body vibration training for 15 minutes, for 8 weeks  **Control:** Other  Treadmill training alone  **Comparator:** NA  **Follow-up:** 2 months | CPRS-R/L (Conners’ Parent Rating Scale-Revised/Long Form)  Intervention group had more improvement in CPRS-R/L-total (parent report) but did not reach statistical significance (p = .055). Intervention group had significantly more improvement in CTRS-R/L-total (teacher report) p = .041.  No difference between groups in Behavior Rating Inventory of Executive Function (BRIEF) - Parent report (p = 0.816) at follow-up. Intervention groups scored significantly better on BRIEF- teacher report (p = 0.023). |
| Physical exercise | Ji, 2023345  ID: KCT0008239  RCT  Single center  N = 30  Korea  Setting: Specialty care | **Target:** Children with mild to moderate ADHD, absence of diseases other than ADHD, right-hand dominance, normal or corrected-to-normal vision, and the absence of  physical impairment to perform exercise  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** No  Korean Attention-Deficit/Hyperactivity Disorder Diagnostic Scale  **Comorbidity:** N/A  **Female:** 13 %  **Age mean:**  Intervention: 9.00 (1.46), Comparator: 8.85 (1.63)  **Minimum age:** 8  **Maximum age:** 12  **Ethnicity:**  % Asian : 100 | **Intervention:** Exergaming using using ExerHeart devices consisting of a running or jumping board with a connected screen; participants run or jump in place with their avatars,  using the front, back, left, and right sensors on the mat to avoid obstacles and acquire items; 3 days/week, 50 min/day, for 4 weeks  **Control:** Attention-matched control  Attention matched control - stationary bike exercise using commercial Fit Elite-Whole body exerciser 1000, with resistance  of 0.5~3 kiloponds; 3 days/week, 50 min/day, for 4 weeks  **Comparator:** NA  **Follow-up:** 1 month | FAIR (Frankfurt Attention Inventory)  Both groups increased selective attention and continuous attention (p<.001) and self-control (p<.05) but no significant difference between groups.  No significant group × time interaction on the changes in Response Time to Go and No-go stimulations. |
| Physical exercise | Kadri, 2019353  University of Genova, 20181132  ID: NCT03678844  RCT  Single center  N = 40  Tunesia  Setting: Other | **Target:** Children with ADHD, no consumption of any diet supplements or drugs; no history of chronic disease, bronchospasm or atopy; not color blind or vision-impaired  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** No  Participants with ADHD were recruited from Tunis and Sidi Bouzid mental centers, but DSM criteria not mentioned.  **Comorbidity:** N/A  **Female:** 10 %  **Age mean:**  Intervention group 14.5 (3.5), control group 14.2 (3.0)  **Minimum age:**  **Maximum age:**  **Ethnicity:** | **Intervention:** Taekwondo exercises practiced for 50-minutes twice weekly, 10-minute general warm-up before each session and 10-minute recovery after each session, for a year and a half  **Control:** Other  Engaged in physical activities, including athletics, handball and gymnastic, during two sessions of physical education per week at school  **Comparator:** NA  **Follow-up:** 18 months | Processing speed measured using total time in seconds to complete the Ruff’s test 2 and 7; intervention mean 240.3 (SD 19.7), control group 288.1 (SD 12.5). |
| Physical exercise | Liang, 2022396  ID: ChiCTR2200056126  RCT  Single center  N = 80  China  Setting: Specialty care | **Target:** Children with ADHD without comorbid psychological disorders  **Other:**  **ADHD presentation:** inattentive : 51.25,hyperactive : 16.25,combined : 32.5  **Diagnosis:** Confirmation by specialist  DSM 5 by psychiatrist using K-SADS-PL  **Comorbidity:** N/A  **Female:** 22.6 %  **Age mean:** 8.46 (1.5)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % Asian : 100 | **Intervention:** Aerobic and neurocognitive exercise, 3 sessions per week, 60-minutes per session, for 12 weeks  **Control:** Wait list  Wait list control group  **Comparator:** NA  **Follow-up:** 3 months | Intervention group decreased reaction time as measured by Arrow Flanker Task for Inhibitory Control, compared to wait list group. Intervention group also increased working memory as measured by the Tower of London task, compared to wait list group. Intervention group also improved cognitive flexibility measured by the Trail Making Test for Cognitive Function compared to the wait list group. Sleep quality also improved significantly. However, the significant differences in all measures disappeared 1 month after intervention ended. |
| Physical exercise | Ludyga, 2022406  ID: DRKS00020125  RCT  Multicenter  N = 63  Multiple countries  Setting: Community | **Target:** Right-handed children with ADHD undergoing pharmacotherapy with methylphenidate or dexamphetamine for at least three months  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-5  **Comorbidity:** N/A  **Female:**  % N/A  **Age mean:** 10.4 (1.2)  **Minimum age:** 8  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Judo training in a group setting, 2 weekly 60-min sessions per week, for 3 months  **Control:** Wait list  Wait list  **Comparator:** NA  **Follow-up:** 3 months | No group difference in Movement Assessment Battery for Children-2. Intervention group performed better on a Change Detection Task (p 0.003). |
| Physical exercise | Rothe, 2023503  ID: ID NA  Cohort study  Single center  N = 58  Germany  Setting: Specialty care | **Target:** Children with ADHD, majority with below average motor skills; those with neurological disorders, head injury, metabolic disorder or below average intelligence (IQ<85) were excluded  **Other:** None  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  by child and adolescent psychiatrists/psychotherapist  **Comorbidity:** Coordination disorder : majority had below average motor coordination  **Female:** 17.2 %  **Age mean:** 9.52 (1.91)  **Minimum age:**  **Maximum age:**  **Ethnicity:**  N/A | **Intervention:** Physiotherapeutic treatment designed to treat and train children’s fine and grossmotor skills, 2 sessions per week with physiotherapist, for8 weeks  **Control:** NA  **Comparator:** MedicationMethylphenidate, 10–40 mg per day, for 8 weeks  **Follow-up:** 2 months | General motor testing (handwriting, drawing movements) no significant differences among groups. |
| Provider | Elmaadawi, 2022252  ID: ID NA  Cohort study  Single center  N = 136  US  Setting: Specialty care | **Target:** Children and adolescents with ADHD  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM IV by board certified child psychiatrists  **Comorbidity:** N/A  **Female:**  % N/A  **Age mean:** 13.8 (3.6)  **Minimum age:** 4  **Maximum age:** 18  **Ethnicity:**  N/A | **Intervention:** Pharmacogenetic testing to enable genomically assisted prescribing for 6 months  **Control:** TAU  Treatment as usual, without genetic testing or treatment guidance  **Comparator:** NA  **Follow-up:** 6 months | Clinical Global Impression Scale­, Improvement Component (CGl-I)  Significantly more improvement in intervention group.  Intervention group required almost twice as many medication changes compared to control (1.8 changes vs 1.1 in control; p<0.001). |
| Provider | Enns, 2017254  ID: NA  Cohort study  Single center  N = 2369  Canada  Setting: Community | **Target:** Children and adolescents with ADHD  **Other:**  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  Manitoba Population Research Data Repository  **Comorbidity:** N/A  **Female:** 15.37 %  **Age mean:**  16% of the intervention cohort were 6 years old or younger, 13% were 13 years old or older; 17% of the control cohort were 6 years old or younger, 10% were 13 years old or older  **Minimum age:** 5  **Maximum age:** 17  **Ethnicity:**  N/A | **Intervention:** ADHD intervention service, participants and their families receive a range of servicesthat can include assessment, treatment, and consultative services (e.g. individual therapy, parent support, group therapy, education, and medication management) from multiple providers; the typical participation length in the program ranges from 3-6 months (extended based on participant needs)  **Control:** No intervention  No contact with the ADHD Service matched on age, sex, year of ADHD diagnosis, and income quintile; matches were identified separately in urban and rural income quintiles  **Comparator:** NA  **Follow-up:** 24 months | Adjusted rate ratios (95% CI) for health and social services use outcomes for intervention (n =485) and control (n = 1884):  Hospital admissions (rate of): 1.29 (0.68 to 2.46) (p = 0.43)  Visits to emergency department (rate of): all 1.03 (0.75 to 1.41) (p = 0.87), injury-related 1.00 (0.68 to 1.46) (p =1.00)  Medication use (proportion of participants who were dispensed 1 or more medications): 1.21 (1.08 to 1.36) (p < 0.01)  Medication adherence (proporton of participants who have a medication possession ratio of at least 0.8): 1.42 (1.03 to 1.96) (p < 0.05)  Children with child welfare contact: 1.34 (0.54 to 3.35) (p = 0.53)  Children in age-appropriate grade: 1.33 (1.09 to 1.63) (p < 0.01). |
| Provider | Epstein, 2007256  ID: NA  Cluster RCT  Multicenter  N = 377  US  Setting: Primary Care | **Target:** Children who met DSM-IV criteria for ADHD, stimulant-naive  **Other:** Pediatricians and associated healthcare professionals (27 men, 25 women) from 12 practices  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  Conners Rating Scale  **Comorbidity:** N/A  **Female:** 36.3 %  **Age mean:** 7.8 (1.5)  **Minimum age:** 6  **Maximum age:** 10  **Ethnicity:**  % Hispanic or Latino : .68  % Black/African American : 16.4  % American Indian or Alaska Native : .68  % White : 79.5  % Multiracial : .68 | **Intervention:** Collaborative consultation services: pediatricians were encouraged to and assisted in using titration trials to determine optimal dosages, taught to prescribe 4 different weekly dosages of methylphenidate hydrochloride during a titration trial (placebo, 18 mg, 36 mg, 54 mg) and the order of weekly dosages was blinded but standardized across all patients (week 1, 18 mg; week 2, placebo; week 3, 36 mg; week 4, 54 mg); participants followed for 12 months  **Control:** TAU  Patients in control group received treatment as usual alone, practices assigned to control group do not have access to consultative services  **Comparator:** NA  **Follow-up:** 12 months | DSM-IV symptomatology, Conners Parent Rating Scale  Children in the intervention group demonstrated a 27% reduction in DSM-IV symptomatology compared with an 18% reduction in the control group (p=.008). |
| Provider | Epstein, 2016255  Childrens Hospital Medical Center, Cincinnati, 2010710  ID: NCT01143701  Cluster RCT  Multicenter  N = 577  US  Setting: Primary Care | **Target:** Children presenting for ADHD evaluation, ADHD medication naive  **Other:** Pediatric practices with ≥2 physicians, uses an electronic billing system, office has Internet access, must not have co-located mental health care  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV by research staff  **Comorbidity:** N/A  **Female:** 29.5 %  **Age mean:** 7.8 (1.4)  **Minimum age:**  **Maximum age:**  **Ethnicity:**  Other : 36.7% were Non-white - unspecified | **Intervention:** Training sessions for providers, office flow modification, guided quality improvement, and an ADHD Internet portal to assist with treatment monitoring, for at least 4 weeks  **Control:** No intervention  Control practices  **Comparator:** NA  **Follow-up:** 12 months | ADHD symptoms parent ratings  Intent-to-treat analyses examining outcomes of all children assessed for ADHD were not significant (P=0.08) but among the 373 children prescribed ADHD medication, there was a significant intervention effect (P=0.04) indicating greater reductions in parent  ADHD treatment care around medication was significantly better at intervention practices compared with control practices. |
| Provider | Guevara, 2021308  Children’s Hospital of Philadelphia, 2016712  ID: NCT02716324  RCT  Multicenter  N = 303  US  Setting: Primary Care | **Target:** Participant had an ADHD diagnosis code (InternationalClassification of Diseases, Ninth Revision [ICD-9] code 314) recorded at an ambulatory visit in the past year  **Other:**  **ADHD presentation:**  **Diagnosis:** Confirmation by specialist  International Classification of Diseases, Ninth Revision  **Comorbidity:** N/A  **Female:** 31 %  **Age mean:** 8.5  **Minimum age:** 5  **Maximum age:** 12  **Ethnicity:**  % Hispanic or Latino : 5  % Black/African American : 45.9  % White : 26.4  Other : 9.2 | **Intervention:** Portal combined with an ADHD care manager to enhance communication and promote greater shared decision-making ; designed to (1) collect and share patient and family treatment preferences and goals with a clinician; (2) trend ADHD symptoms, performance impairment ratings, medication side effects, treatment receipt, and medication side effects by using electronically submitted parent and teacher reports; (3) provide a repository of ADHD educational materials; and (4) support information sharing between parents and teachers. ADHD care managers were bachelor’s-trained individuals who were responsible for communicating information and facilitating coordination of care; total duration of 12 months  **Control:** Other  Electronic Health Record portal alone  **Comparator:** NA  **Follow-up:** 9 months | ADHD symptoms VPRS (Vanderbilt Parent Rating Scale)  In multivariate models, VPRS scores decreased over time (Adjusted b 5 .015; 95% confidence interval 0.023 to 0.07) in both groups, but there were no intervention-by-time effects (Adjusted b 5 .000; 95% confidence interval 0.011 to 0.012) between groups.  There were no adverse effects from either intervention identified, and interactions of intervention by race or income were not significant, suggesting no heterogeneity of treatment effects. |
| Provider | Kolko, 2020371  University of Pittsburgh, 20081134  ID: NCT00600470  Cluster RCT  Multicenter  N = 411  US  Setting: Primary Care | **Target:** Children diagnosed with ADHD based on DSM-IV criteria  **Other:** Parents  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  At intake, parents and children participated in a diagnostic/clinical interview based on the DSM-IV criteria to identify formal diagnoses.  **Comorbidity:** N/A  **Female:** 31 %  **Age mean:** 8.0 (1.9)  **Minimum age:** 5  **Maximum age:** 12  **Ethnicity:**  % White : 70  N/A : No other race info reported outside of White | **Intervention:** Collaborative care, care manager delivered content modules which taught behavioral strategies to manage ADHD with caregivers and ADHD "survival skills" with participants in 3 to 4 1-hr sessions for 6 months  **Control:** NA  **Comparator:** ProviderEnhanced usual care; families received a referral to a mental health provider and could receive services for ADHD from their primary care provider and/or a community mental health provider  **Follow-up:** 6 months | Vanderbilt ADHD Diagnostic Parent Rating Scale (VADPRS) change from baseline for intervention group compared to comparator group slope (−3.31) was significant (p 0.02).  Collaborative care showed greater acute improvement in individualized ADHD treatment goals and follow-up improvements in quality of life and ADHD and oppositional defiant disorder goals. |
| Provider | Lavigne, 2011386  Childrens Hospital of Chicago, 2005661  ID: NCT00179894  Cluster RCT  Multicenter  N = 270  US  Setting: Specialty care | **Target:** Participants must have a diagnosis of ADHD according to DSM-IV criteria, IQ >= 70; no comorbidity of ASD, Tourette, other major health conditions, not taken ADHD medications in the past 2 months, or taking medications incompatible with stimulants  **Other:** Physicians from 24 Chicago-area pediatric practices  **ADHD presentation:** inattentive : 41.2,hyperactive : 9.8,combined : 49.0  **Diagnosis:** Confirmation by specialist  Diagnostic Interview Schedule for Children IV-Parent  **Comorbidity:** N/A  **Female:** 23.0 %  **Age mean:**  Specialized care SC: 8.25 (SD = 1.38, n = 138), treatment as usual TAU: 8.19 (SD = 1.62, n = 133)  **Minimum age:**  **Maximum age:**  **Ethnicity:**  % Hispanic or Latino : 12.2  % Black/African American : 2.5  % White : 81.5 | **Intervention:** Derived medication management procedures: physicians received 2 hours of office-based training in using stimulant medications and atomoxetine, an ADHD specialist provided 1 hour of training to office staff in the use of software (Focus on ADHD Medication Management Program), and returned to the office/practice for the first 3 patients per physician to ensure that staff understood program use; follow treatments for up to 9 months  **Control:** Other  Pediatricians in treatment as usual group provided treatment per their usual procedure  **Comparator:** NA  **Follow-up:** 12 months | ADHD-RS total scale, parent report  Children in both specialized care and treatment-as-usual groups improved on the ADHD Rating Scales and SNAP-IV, and there were no group differences in improvement rates.  There were no differences on the Barkley adverse effects scale between groups at 4, 9, or 12 months. |
| Provider | Myers, 2015451  Rockhill, 20161009; Myers, 2013947; Vander Stoep, 20171141; Rockhill, 20201008; Seattle Children’s Hospital, 20091031  ID: NCT00830700  RCT  Multicenter  N = 223  US  Setting: Other | **Target:** Children with ADHD in rural underserved communities  **Other:** Parents received behavior training; parents and teachers provided outcome data  **ADHD presentation:** N/A : Percentages above do not add to 100 because they are not mutually exclusive (caregiver ratings, not clinician diagnosed)  **Diagnosis:** Confirmation by specialist  Children scoring >= 65 on the Child Behavior Checklist (CBCL) ADHD diagnostic subscale online were eligible. Clinician then confirmed in person via DSM-IV criteria  **Comorbidity:** N/A  **Female:** 26 %  **Age mean:** 9.25 (2.0)  **Minimum age:** 5  **Maximum age:** 12  **Ethnicity:**  % Hispanic or Latino : 13.0  % Black/African American : 0.9  % American Indian or Alaska Native : 2.7  % Asian : 0.9  % Native Hawaiian or Pacific Islander : 1.8  % White : 80.7 | **Intervention:** Telehealth intervention combining pharmacotherapy and caregiver behavior training; 6 sessions, 3-4 weeks apart over 22 weeks  **Control:** NA  **Comparator:** OtherChildren remained under care of their primary care providers and received a single consultation with a tele-psychiatrist, who shared treatment recommendations with the referring provider; providers were not restricted from referring to other resources  **Follow-up:** 6 months | Vanderbilt ADHD Parent Rating Scale  Number meeting parent-reported diagnostic criteria on Inattention subscale of the Vanderbilt Attention-Deficit/Hyperactivity Disorder (ADHD) Rating Scale, 25 weeks  The percent of participants with at least 50% reduction in ADHD symptoms was significantly higher in the intervention group (p = 0.000). Lower proportions of children in the intervention arm met diagnostic criteria on the VADRS-Caregiver: inattention, hy  Columbia Impairment Scale-Parent Version (CIS-P)  Children assigned to the intervention improved significantly more than children in the comparator group (p<0.001). |
| Provider | Oppenheimer, 2019466  Boston Childrens Hospital, 2014691  ID: NCT02097355  Cluster RCT  Multicenter  N = 518  US  Setting: Specialty care | **Target:** Children receiving ongoing treatment for ADHD, prescribed ADHD medication, parents and children proficient in English  **Other:** Clinicians providing ADHD care  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  Neurology department clinician  **Comorbidity:** N/A  **Female:** 24.3 %  **Age mean:**  Intervention 9.85 (3.21), control 11.09 (3.24)  **Minimum age:**  **Maximum age:**  **Ethnicity:**  % Hispanic or Latino : 5.8  % White : 78.4,Other : 406 | **Intervention:** Trigger algorithm and alert resolution process, web-based platform that enables clinicians to administer online clinical questionnaires to parents and teachers to monitor patients remotely between visits, data collected for 13 months  **Control:** No intervention  Non-alert group  **Comparator:** NA  **Follow-up:** 15 months | CGI-S scores  Alert group patients had lower scores than non-alert group patients indicating worse global functioning.  Vanderbilt scores  Alert group patients had higher Vanderbilt scores at time 2 than the non-alert group indicating a worse ADHD severity (p<0.001). |
| Psychological or behavioral | Abikoff, 2013106  ID: N/A  RCT  Multicenter  N = 158  US  Setting: Other | **Target:** Children with ADHD and organizational deficits  **Other:** Parents received training and provided some outcome data  **ADHD presentation:** inattentive : 55.7,hyperactive : 0,combined : 44.3  **Diagnosis:** Confirmation by specialist  DSM IV diagnosis confirmed by clinical evaluation required  **Comorbidity:** Other : Organizational deficits  **Female:** 35.4 %  **Age mean:** 9.04 (0.82)  **Minimum age:** 7  **Maximum age:** 11  **Ethnicity:**  % Hispanic or Latino : 13.9  % Black/African American : 14.6  % White : 69.6 | **Intervention:** Organizational skills training; session time is spent working with the child, with parents joining during the last 10 minutes; 20 hour long in-clinic sessions held twice-a-week after school over 10-12 weeks  **Control:** Wait list  Wait list  **Comparator:** OtherPerformance-based intervention that precluded skills, training motivates children by training teachers and parents to establish specific, individualized goals for children on written charts completed daily and to prompt, monitor, and praise/reward childre  **Follow-up:** 24 months | Clinical Global Impression-Improvement (CGI-I)  Responder rates were significantly better for OST (85.3%) and PATHKO (86.9%) than waitlist (0%), overall p<0.0001).  Children’s Organizational Skills Scale, parent  The intervention group performed better than the comparator group (p < 0.02).  Teachers and parents were satisfied with treatments, with no significant differences by treatment tgroupype. p value not reported.  Academic Performance Rating Scale (APRS)  No significant difference in academic outcomes at 2 years (p value not reported).  There were no significant group differences for any other event. |
| Psychological or behavioral | Antshel, 2003123  ID: ID NA  RCT  Single center  N = 120  US  Setting: Specialty care | **Target:** Children with Inattentive type or Combined type ADHD taking a stimulant or SSRI  **Other:** Parents  **ADHD presentation:** inattentive : 49.2,combined : 50.8  **Diagnosis:** Confirmation by specialist  DSM-IV per Diagnostic Interview for Children & Adolescents - Revised  **Comorbidity:** N/A  **Female:** 25 %  **Age mean:** 9.95 (1.1)  **Minimum age:** 8  **Maximum age:** 12  **Ethnicity:**  % Hispanic or Latino  % Black/African American : 5.0  % Asian : 1.7  % Native Hawaiian or Pacific Islander  % White : 93.3 | **Intervention:** Social skills group training for children plus parent sessions; one 90 minute sessionper week, each week children were given a homework assignment to practice a skill, parents attended their own sessions on week 1, 4, and 8, for 8 weeks  **Control:** Wait list  Wait list  **Comparator:** NA  **Follow-up:** 3 months | No significant differences between groups on parent ratings for Cooperation, Responsibility, and Self-Control scores; no significant differences between groups on child ratings for Cooperation, Empathy, and Self-Control scores; intervention group improved significantly more on both parent and child Assertion scales (p = .001). |
| Psychological or behavioral | Boyer, 2016160  Boyer, 2015692  ID: NTR2142  RCT  Multicenter  N = 159  Netherlands  Setting: Specialty care | **Target:** Adolescents with a prior DSM-IV-TR diagnosis of ADHD by a child psychiatrist or certified psychologist, a confirmed ADHD diagnosis on the ADHD sections of the diagnostic interview schedule for children for DSM-IV parent version; no alternative non-pharmacological treatment between pre- and post- participant assessment, alternative treatments stopped until post-test, no autism spectrum disorder, no predominant addiction, depression with suicidal ideations, acute familial crisis or conduct disorder, no pharmacological treatment with Atomoxetine  **Other:**  **ADHD presentation:** inattentive : 70,hyperactive : 5,combined : 25  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 26 %  **Age mean:**  Intervention 14.4(1.2), control 14.4(1.3)  **Minimum age:** 12  **Maximum age:** 17  **Ethnicity:**  N/A | **Intervention:** Cognitive behavioral treatment (Plan my life), 8 adolescent sessions and 2 parental sessions of 45–60 min, 1 session per week for 10 weeks  **Control:** NA  **Comparator:** BehavioralSolution-focused treatment, consisting of eight individual adolescent sessions and two parental sessions (between adolescent session 2 and 3, and between adolescent session 5 and 6) of 45–60 min. At every session the adolescent discussed a problem he/she  **Follow-up:** 3 months | ADHD-RS (ADHD-Rating Scale), parent-rated  Marginally significant differences were found in favor of the intervention. At 12 months there no significant differences.  Overall impairment, parental report  There was a significant time x treatment effect . Executive function, teacher rated, significantly improved over time. At 1 year, no differences between groups.  Attendence  Intervention group showed significantly higher attendance rates than comparator (p = .03).  At 1 year, no differences in effect on depression, anxiety, parent-adolescent conflict, or neurological tasks. |
| Psychological or behavioral | Chu, 2021199  Shanghai Children’s Hospital, 20211038  ID: ChiCTR2100052803  RCT  Single center  N = 145  China  Setting: Specialty care | **Target:** Children with ADHD, IQ at least 70, with parents or primary caregivers who did not want child to receive drug therapy; without autism spectrum disorder, schizophrenia, epilepsy, head injury, or verified neurological disorder, intellectual disability, sensory impairment (hearing/vision problems) or receiving other ADHD treatments  **Other:** Parents & teachers provided outcomes; intervention group received parent training  **ADHD presentation:** inattentive : 60,hyperactive : 14,combined : 26  **Diagnosis:** Confirmation by specialist  DSM-V  **Comorbidity:** N/A  **Female:** 25 %  **Age mean:**  Intervention: 7.10 (0.47)  Waitlist: 7.04 (0.61)  **Minimum age:** 6  **Maximum age:** 8  **Ethnicity:**  % Asian : 100  Other : Chinese | **Intervention:** Multimodal treatment for children and parents, TEAMS training (Training Executive, Attention, and Motor Skills), executive function training program hospital-based, 90 minute sessions, and online parent training program, each session 30 minutes long, for 8 weeks  **Control:** Wait list  Wait list  **Comparator:** NA  **Follow-up:** 2 months | SNAP- IV total score (Chinese version), parent  Difference in parent score approached significance (p = 0.07); difference in teacher score was significant, favoring intervention group (p < 0.001).  Weiss Functional Impairment Scale, parent  The intervention had significantly greater improvement compared to control (p = 0.009).  The intervention group had greater reduction in the scores of BRIEF behavioral regulation index (inhibition, emotional control) and metacognition index (working memory, planning/organization, monitoring) in executive function than those in the control group (p < 0.05). |
| Psychological or behavioral | Coles, 2020204  ID: NA  RCT  Single center  N = 127  US  Setting: Mixed | **Target:** Unmedicated children with ADHD  **Other:** Parents of the children  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV diagnosis required. A Ph.D.-level clinician conducted interview with parents and reviewed symptom rating and impairment scales (DBD-RS)  **Comorbidity:** N/A  **Female:** 16 %  **Age mean:** 9.3 (2.0)  **Minimum age:** 5  **Maximum age:** 13  **Ethnicity:**  % Hispanic or Latino : Not reported  % Black/African American : 13  % Asian : Not reported  % White : 79 | **Intervention:** Behavioral consultation with school and home components (high or low intensity); behavioral treatment summer block; 3 initial teacher visits to set up Daily Report Card with home-based rewards, bank of 3 additional consultation visits throughout year; 1 initial home visit to establish a homebased Daily Report Card, bank of 3 additional consultation visits throughout year, option to attend monthly group parent training booster sessions; total duration of 1 year  **Control:** No intervention  No behavioral consultation  **Comparator:** NA  **Follow-up:** 9 months | Inattention/Overactivity, Conners Score, parent report  No difference in teacher or parent reported Conners Score, Oppositional/Defiant subscale or Inattention/ Overactivity subscale between children receiving or not receiving the behavioral consultation.  Children who received the intervention were about half as likely those who did not to initiate medication use each week at school or home and used lower doses when medicated at school, 63% of the control group was medicated at home at endpoint compared to 26% of the intervention group (p < .01). |
| Psychological or behavioral | Fabiano, 2016261  ID: NA  RCT  Unclear/Not reported  N = 172  US  Setting: Mixed | **Target:** Adolescents with ADHD-Combined Type  **Other:** Parents and teachers  **ADHD presentation:** combined : 100  **Diagnosis:** Confirmation by specialist  DSM IV per Disruptive Behavior Disorder (DBD) rating scales of ADHD symptoms and DSM scale on the Child Behavior Checklist and Teacher Report Form  **Comorbidity:** N/A  **Female:** 27.4 %  **Age mean:**  16.98 (0.70) and 16.88 (0.65)  **Minimum age:** 16  **Maximum age:** 18  **Ethnicity:**  % Black/African American : 11  % White : 85.5  % Multiracial : 1  Other : Other: 2% | **Intervention:** Supporting the Effective Entry to the Roadway (STEER), parent-teen intervention of weekly sessions divided into two 45-minute meetings with the first half including individual parent and teen meetings that occur in parallel and the second half including a joint activity, adjunct to drivers ed program which control group also received, for 8 weeks  **Control:** Attention-matched control  Driver education driver practice program, 10-week diver education co.urse with 30 hours of classroom instruction and 10 45-minute individual driving lessons  **Comparator:** NA  **Follow-up:** 12 months | Treatment satisfaction  No difference between groups.  Compared to the driver education practice program, the teens in the supporting the effective entry to the roadway group reported lower levels of risky driving behavior at the six-month (p=0.03) but not the 12-month follow-up (p= 0.07); there was also no significant differences for observed positive parenting. |
| Psychological or behavioral | Geissler, 2020290  Jans, 2015856; Hage, 2018812; Jaite, 2019854; Hautmann, 2018822  ID: CCT-ISRCTN73911400  RCT  Multicenter  N = 144  Germany  Setting: Specialty care | **Target:** Children diagnosed with ADHD and their mothers also diagnosed with ADHD; not currently receiving psychopharmacotherapy, or their medication had been stable for at least 4 weeks prior to baseline assessment  **Other:**  **ADHD presentation:** combined : 52,combined\_other : 52% children / 66% mothers  **Diagnosis:** Confirmation by specialist  DSM-IV specially trained expert clinicians at each study centre’s Department of Child and Adolescent Psychiatry European Child & Adolescent Psychiatry (assessment and treatment of children; PCT) or Department of Psychiatry (assessment and treatment of  **Comorbidity:** N/A  **Female:** 26.5 %  **Age mean:**  Mean age 9.4  **Minimum age:**  **Maximum age:**  **Ethnicity:**  N/A | **Intervention:** Parent-child training program comprised a structured and modular behavioral psychotherapy program with methylphenidate medication for mothers with ADHD (1 appointment/4 week), behavioral group psychotherapy for mothers who were also offered methylphenidate for 12 weeks, then 6 months of maintenance of all previous interventions; total duration 12 months  **Control:** NA  **Comparator:** Parent trainingIndividual non-specific counseling for mothers, seven 4-weekly sessions, 2 booster parent-child therapy sessions  **Follow-up:** 12 months | Home Situations Questionnaire (HSQ), externalizing problem behavior in the family  There were no differences between groups (p 0.62).  ADHD symptoms, Schedule for Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL)  No statistically significant difference between groups (p 0.35)  Strength and Difficulties Questionnaire global score  There was no significant difference between groups (p=0.54)  No difference in Strengths and Difficulties Questionnaires rated by teachers (p=0.73). |
| Psychological or behavioral | Hiscock, 2019329  Murdoch Childrens Research Institute, 2014945  ID: ISRCTN50834814  RCT  Multicenter  N = 361  Australia  Setting: Other | **Target:** Children who met full DSM-5 diagnostic criteria for ADHD; had a moderate to severe parent-rated sleep problem; met the International Classification of Sleep Disorders – 3rd edition criteria for chronic insomnia disorder or delayed sleep wake phase disorder, or had sleep-related anxiety  **Other:** Parents  **ADHD presentation:**  **Diagnosis:** Confirmation by specialist  DSM-5 diagnostic criteria for ADHD  **Comorbidity:** Sleep  **Female:** 25.1 %  **Age mean:** 9.6 (1.7)  **Minimum age:** 5  **Maximum age:** 13  **Ethnicity:** | **Intervention:** Sleep intervention, 2 face-to-face sessions with the parent and child approximately 2 weeks apart,each session 3.5 hours, parents completed a sleep diary, the second consultation and followup telephone call were used to review the sleep diary, reinforce suggested strategies, and troubleshoot any problems; clinician provided information about normal sleep, sleep cycles, and sleep hygiene strategies, and formulated a behavioral sleep management plan, follow up phone call a further 2 weeks later, min 4 weeks  **Control:** TAU  Families in the control group could access care as usual from their pediatrician, which does not typically include assessment and management of child sleep problems  **Comparator:** NA  **Follow-up:** 6 months | Children’s Sleep Habits Questionnaire: proportion of children with moderate to severe sleep problems was lower in the intervention (28.0%, 35.8%) compared with usual care group (55.4%, 60.1%). |
| Psychological or behavioral | Hogue, 2020330  National Center on Addiction and Substance Abuse at Columbia University, 20151115  ID: NCT02420990  Cluster RCT  Multicenter  N = 145  US  Setting: Specialty care | **Target:** Adolescents with ADHD  **Other:** Parents involved with intervention  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  Yes, however only 77% of the sample met full diagnostic criteria for ADHD based on researcher administered interviews; per the study eligibility criteria, the remaining 23% were enrolled based on already being treated for ADHD  **Comorbidity:** N/A  **Female:** 28 %  **Age mean:** 14.8 (1.95)  **Minimum age:** 12  **Maximum age:** 18  **Ethnicity:**  % Hispanic or Latino : 37  % Black/African American : 15  % White : 42  % Multiracial : 6 | **Intervention:** Changing Academic Support in the Home for Adolescents with ADHD, a 3-module protocol that utilizes family and individual sessions to improve school performance, flexible protocol that do not prescribe a fixed number of sessions or intervention sequences, one year of observation  **Control:** NA  **Comparator:** Medication + behavioralMedication program is a family-based protocol designed to integrate medication services into behavioral treatment planning for adolescents with ADHD; contains 5 modular tasks: ADHD Assessment & Medication Consult, ADHD Psychoeducation & Client Acceptance,  **Follow-up:** 12 months | National Youth Survey Self-Report Delinquency Scale, Delinquency  Among adolescents who engaged in any delinquency, CASH-AA + MIP clients showed greater declines in delinquent acts than CASH-AA Only clients.  Inattentive/Disorganized and Hyperactive/Impulsive subscale, Mini-International Neuropsychiatric Interview (MINI)  There was a significant association between intervention group and fewer Inattentive symptoms (self report) in a quadratic equation controlling for age, race, sex, and baseline substance use. Effects on self-reported hyperactivity symptoms were not sign  School functioning  Association with grades, academic self-efficacy, problems with homework, and time spent on homework were not statistically significant in models controlling for age, sex, race, and baseline substance abuse. |
| Psychological or behavioral | Huang, 2015335  ID: N/A  Clinical trial  Single center  N = 97  Taiwan  Setting: N/A | **Target:** Boys and girls with ADHD and without autism and mental retardation  **Other:** Parents and teachers provided outcome data  **ADHD presentation:** inattentive : 19.6,combined : 80.4  **Diagnosis:** Confirmation by specialist  DSM-IV-TR  **Comorbidity:** N/A  **Female:** 17.5 %  **Age mean:** 8.4 (0.9)  **Minimum age:** 7  **Maximum age:** 10  **Ethnicity:**  N/A | **Intervention:** Social skill training combined with parent training, 7 consecutive behavioral-basedgroup sessions, 80-minute group sessions during consecutive weeks teaching social skill modules using didactic instructions, modeling, role-play activities, behavior rehearsal, homework was assigned for each week for 8 weeks  **Control:** No intervention  Recruited from referral as a control group, motivated for group therapy but could not find a mutually available time  **Comparator:** NA  **Follow-up:** 4 months | Change in Delinquent Behavior, Child Behavior Check List (CBCL)  No statistically significant group effect (p=0.38).  Inattention scale SNAP-IV (Swanson, Nolan, and Pelham, version IV) change, parent  There was no significant difference between groups on parent SNAP IV inattention (p=.41) or hyperactive/impulsivity (p = .13) scales. Significant effect of intervention on oppositional scale (p = .04). No significant effect of group on any teacher SNAP I  Teacher version of modified social skill rating system (SSRS): intervention group improved more on Active Participation scale (p = .03) but not on Cooperative Behavior, Self Assertion, Self Control or Conflict Coping scales. For child report SSRS, difference in Self Control favored intervention (p = .03). |
| Psychological or behavioral | Huang, 2021334  Fujian Maternity and Child Health Hospital, 2022782  ID: ChiCTR2100049863  RCT  Single center  N = 201  China  Setting: Other | **Target:** Treatment naive children with ADHD, IQ >=75, no history of seizures or psycho-morbidities  **Other:** Parents provided some outcome information  **ADHD presentation:** inattentive : 62.7,hyperactive : 13.9,combined : 23.4  **Diagnosis:** Confirmation by specialist  2 independent providers used DSM V  **Comorbidity:** N/A  **Female:** 29.4 %  **Age mean:** 5.6 (0.65)  Preschool  **Minimum age:**  **Maximum age:**  **Ethnicity:**  % Asian : 100 | **Intervention:** Behavioral therapy, attention training (twice per day), relief therapy and game therapy, and parental training (1 hour weekly sessions) plus conventional therapy (biofeedback and a health education booklet), for 1 year  **Control:** TAU  Conventional treatment (biofeedback and a health education booklet)  **Comparator:** NA  **Follow-up:** 18 months | Impulsivity/ hyperactivity scale, Conners parent symptom questionnaire  Significant effect of intervention (p < .001). Intervention effect on hyperactivity index was also significant (p < .001).  Significant effect of intervention on full-scale attention quotient (FAQ; p < .001) and full-scale response control quotient (FRCQ, p = 0.014) from integrated visual and auditory comprehensive continuous performance tests. |
| Psychological or behavioral | Kareem, 2021358  ID: ID NA  RCT  Single center  N = 50  Egypt  Setting: Specialty care | **Target:** Children recently diagnosed with ADHD  **Other:** Parents provided outcome data  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-V  **Comorbidity:** N/A  **Female:** 24 %  **Age mean:**  Intervention: 10.44 (1.18) Control: 9.60 (2.08)  **Minimum age:** 7  **Maximum age:** 13  **Ethnicity:**  N/A | **Intervention:** Attention span training, time table activities and homework, 12 sessions, 30-45 min with 5 children and their parents, 1 session per week, for 12 weeks  **Control:** No intervention  No intervention  **Comparator:** NA  **Follow-up:** 2.5 months | Restless in the squirmy sense  Intervention group improved significantly but not the control group, |
| Psychological or behavioral | Li, 2022392  ID: ID NA  RCT  Single center  N = 180  China  Setting: Specialty care | **Target:** Children with ADHD without co-morbid serious psychological disorders or medical conditions  **Other:** Parents reported some outcomes  **ADHD presentation:** inattentive : 38.3,hyperactive : 30.6,combined : 31.1  **Diagnosis:** Confirmation by specialist  DSM IV  **Comorbidity:** N/A  **Female:** 47.8 %  **Age mean:** 5.01 (0.36)  **Minimum age:** 3  **Maximum age:** 7  **Ethnicity:**  % Asian : 100 | **Intervention:** Theme building block games to promote psychological and behavioral development, 2-3 children per group, once a week, interactive environment for children, research instructor gives specific instructions (e.g., we are going to build a castle today), for 8 weeks  **Control:** Attention-matched control  Attention matched control, children play with blocks with 2 to 3 children per group, once a week for 8 weeks  **Comparator:** NA  **Follow-up:** 2 months | Behavior, PHCSS (Piers-Harris Children's Self-concept Scale)  Scores were significantly (p 0.05) higher in the intervention compared to the control group.  Child Behavior Check List (CBLC)  For boys, intervention group improved more than control group on CBCL Discipline violation, Hostility, Compulsion, Immaturity, Bad communication, Schizoid, and Physical complaint scales. For girls, intervention group improved more than control group on CB  Swanson, Nolan, and Pelham, Version IV total score, parent  Intervention showed significantly more improvement (p<.05). |
| Psychological or behavioral | Lv, 2023 410  ID: China research registry 8696  RCT  Single center  N = 90  China  Setting: Specialty care | **Target:** Children with ADHD; patients with mental retardation, character disorder, mood disorder, tic disorder, childhood autism, and schizophrenia were excluded  **Other:** Parents provided some outcomes; some underwent parent training  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM 5  **Comorbidity:** N/A  **Female:** 18.9 %  **Age mean:**  pharma intervention 9.03 (1.78), non-pharma intervention 9.23 (1.65)  **Minimum age:** 6  **Maximum age:** 18  **Ethnicity:**  % Asian : 100 | **Intervention:** Behavior modification, sensory integration therapy, sand tray therapy with parent training; parent training involved four sessions, including disease awareness, pros and cons of drugs, parent-child relationship, and methods to improve attention span; behavior modification involved two major courses covering the positive reinforcement method of behavior modification, temporary isolation method, fading method, demonstration method, cognitive behavior therapy, and applied behavior analysis; sensory integration therapy involved 45–60 min of training per session, including warm-up, vestibular sensory, proprioception, balance, hand-eye coordination, sedation, and fine motor; Sand tray therapy involved 10–12 sessions with a unified sand tray therapist, with each session lasting about 40–60 minutes, including instructional language, familiarization with the environment, feeling the sand, creating a sand tray, playing with the sand tray, dialogue and communication, dismantling the work, and discussion and analysis with parents; homeopathy Tiaoshen Yizhi Decoction powder dissolved in water taken every morning and evening, for 3-6 months  **Control:** NA  **Comparator:** MedicationMethylphenidate and atomoxetine, dosage not described; participants also received homeopathy Tiaoshen Yizhi Decoction powder dissolved in water taken every morning and evening for 6 months  **Follow-up:** 6 months | Swanson, Nolan, and Pelham, Version IV (SNAP-IV)  No significant difference in improvement.  Weiss Functional Impairment Rating Scale (WFIRS), family subscore  Non-pharma group improved more on family function, life skills, and self concept scores (p < 0.05); no difference between groups regarding learning/school, social activities, and risk-taking activities. |
| Psychological or behavioral | McGrath, 2011426  ID: NA  RCT  Single center  N = 72  Canada  Setting: Other | **Target:** Children with ADHD, able to speak and understand English; no co-intervention (within 6 months) and disorder severity, involvement with child protection authorities, autism, schizophrenia, or other psychosis, complex comorbidity, and serious cognitive delay  **Other:** Parents  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV, K-SADS-PL  **Comorbidity:** N/A  **Female:** 25 %  **Age mean:** 8.89 (1.92)  **Minimum age:** 8  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Strongest Families intervention, skill-focused learning, anxiety program consisted of 11 sessions and the behavior programs had 12 sessions (Parenting the Active Child, positive parenting strategies), weekly coach session calls were on average 40 minutes, for 12 weeks  **Control:** No intervention  Control participants received one call from the coach to review the randomization placement results and to inform the parent that the next contact from study staff would be at the 120-day follow-up time point to collect assessment data only  **Comparator:** NA  **Follow-up:** 12 months | % recovered, Schedule for Affective Disorders - Present and Lifetime (K-SADS-PL)  The percent successful rate (no diagnosis according to K-SADS-PL) was higher for the treatment group than for the control group for 8 months (p=0.05) and 12 months (p=0.04) . |
| Psychological or behavioral | Meyer, 2021430  Uppsala County Council, 20161136  ID: ISRCTN17366720  RCT  Multicenter  N = 184  Sweden  Setting: Specialty care | **Target:** Adolescents with ADHD; without severe depression, suicidality, psychosis, or bipolar disorder without stable medication, mental retardation, autism, current substance abuse  **Other:** Parents reported some outcomes.  **ADHD presentation:** inattentive : 25.6,combined : 70.7,N/A : Unspecified: 3.7  **Diagnosis:** Confirmation by specialist  DSM V per Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID)  **Comorbidity:** N/A  **Female:** 63.9 %  **Age mean:**  SSTG 16.46 (0.88), control 16.71 (0.94)  **Minimum age:** 15  **Maximum age:** 18  **Ethnicity:**  N/A | **Intervention:** Dialectical behavioral therapy, age-adapted structured skills training group program, manualized consisting of 14 weekly 2-hour sessions where each session focused on a specific theme; the program includes elements of DBT, psychoeducation and strategies for managing difficulties related to ADHD; total of 14 weeks  **Control:** NA  **Comparator:** OtherManual-based psychoeducational group program of three 2-hour sessions focusing on psychoeducation about ADHD, including information about ADHD symptomatology, strengths and challenges with ADHD, sleep and diet; the participants also received a book descri  **Follow-up:** 6 months | ASRS-A (ADHD Self-Report Scale for Adolescents) - Self-rating  No group effect on patient or parent reported symptoms.  Child Sheehan Disability Scale (CSDS), adolescent report  No difference in effect on patient or parent report.  No significant group differences regarding acceptability.  No difference in effect on Quality of Life or Impact of ADHD Symptoms (IAS) on well-being.  No difference in effect on Hospital Anxiety and Depression Scale (HADS). |
| Psychological or behavioral | Pelham, 2016471  ID: ID NA  Crossover trial  Single center  N = 152  US  Setting: Mixed | **Target:** Children clinically diagnosed ADHD; should not have (1) IQ<70; (b) history of seizures or other neurological problems; (c) history of other medical problems; (d) childhood history or concurrent diagnosis of pervasive developmental disorder, schizophrenia or other psychotic disorders, sexual disorder, organic mental disorder, or eating disorder; (e) lack of functional impairment; and (f) placement in special education classrooms  **Other:** Parents, teachers  **ADHD presentation:** inattentive\_other : mean score: Medication First: 7.6 (1.9); Behavioral First: 8.1 (1.5),hyperactive\_other : mean score Hyperactivity/Impulsivity: Medication First: 7.1 (2.2); Behavioral First: 6.8 (2.1)  **Diagnosis:** Confirmation by specialist  DSM-IV by clinicians  **Comorbidity:** N/A  **Female:** 24 %  **Age mean:**  Medication first 8.3 (2), behavioral first 8.5(1.8)  **Minimum age:** 5  **Maximum age:** 12  **Ethnicity:**  % Black/African American : 12.3  % White : 80.1 | **Intervention:** Behavioral first intervention, social skills training sessions for children, parenttraining (8 group sessions), and brief teacher consultation to establish a daily report card, report cards were sent home each day and parents provided rewards for good performance, monthly parent-training booster session for 8 weeks, case manager communicated with teacher monthly for 1 school year  **Control:** NA  **Comparator:** MedicationMedication first intervention, extended-release methylphenidate (equivalent to .15 mg/kg/dose bid)  **Follow-up:** 4 months | Classroom rule violations  The behavior management intervention exhibited significantly fewer classroom rule violations per hour than the comparator of medication intervention (incidence rate ratio 0.66, p<0.01).  ADHD, Disruptive Behavior Disorders Rating Scale  No difference between groups (effect size -0.01).  Social Skills Total Score SSRS, parent  There was no significant difference between groups for the Social Skills Total Score.  67% of the children who began treatment with behavioral interventions required additional treatment by the end of the school year compared with 47% of the children who began the school year receiving a low dose of medication (OR 2.23). Survival analyses indicated a significant group difference (p < .01). |
| Psychological or behavioral | Pfiffner, 2014476  Tran, 20181120; Haack, 2017808; Rooney, 20181013; Adalio, 2018652  ID: N/A  RCT  Multicenter  N = 199  US  Setting: Specialty care | **Target:** Children with ADHD-inattentive type and IQ > 80, living with at least one parent for the past year, attending school full time in a regular classroom  **Other:** Parents received training and provided some outcomes  **ADHD presentation:** inattentive : 100  **Diagnosis:** Confirmation by specialist  DSM-IV diagnosis confirmed by the KSADS-PL by clinician  **Comorbidity:** N/A  **Female:** 42 %  **Age mean:** 8.6 (1.2)  **Minimum age:** 7  **Maximum age:** 11  **Ethnicity:**  % Hispanic or Latino : 17  % Black/African American : 5.0  % Asian : 8.0  % White : 54.0  % Multiracial : 17.0 | **Intervention:** Child Life and Attention Skills (CLAS) program included three manualized coordinated components: (a) ten 90-minute parent group meetings, along with up to six 30-minute family meetings (parent, child, and therapist); (b) ten 90-minute child group meetings; and (c) teacher consultation, which included one 30-minute orientation meeting involving the teacher and therapist and up to five subsequent 30-minute meetings with the parent, child, teacher, and therapist and booster sessions, treatment occurred over a 10- to 13-week period  **Control:** TAU  Treatment as usual did not receive either study intervention; families received a written diagnostic report based on the assessment conducted at baseline, a list of community treatment providers, but no specific treatment recommendations; families were o  **Comparator:** BehavioralParent-focused treatment included parent training teaching parent skills but did not receive specific training in how to work with teachers and were not informed about the child skills taught in the CLAS condition; families received the same number of par  **Follow-up:** 7 months | Clinical Global Impression (CGI) - I, parent report  Intervention and comparator performed better than control. No group differences on teacher reported CGI-I.  Inattentive symptoms CSI (Child Symptom Inventory), parent rating  Responders (mean parent rated CSI inattention symptom severity score fell within 1 SD of norms)  At follow-up according to parents, 63.0% of CLAS, 52.7% of PFT, and 36.2% of control were positive responders (p=0.016); the difference between CLAS and control was significant (p=0.004), but not between CLAS and PFT (p>.05). At follow-up according to tea  IRS (Impairment Rating Scale)  Teachers did not report differences across groups regarding overall impairment.  Parent and teacher satisfaction  Parent and teacher satisfaction with CLAS was very high; >95% of parents rated the child and parent skills taught as useful or very useful, 94% of teacher rated the classroom challenge as helpful or very helpful. Parent satisfaction with the comparator in |
| Psychological or behavioral | Power, 2012480  ID: N/A  RCT  Single center  N = 199  US  Setting: Specialty care | **Target:** Children meeting criteria for ADHD, Combined Type or ADHD, Inattentive Type who are enrolled in school and scored at or above 0.75 of a standard deviation above the mean on the Homework Problem Checklist; children scoring at or above an estimated IQ of 75 on the 2-subtest version of the Wechsler Abbreviated Scale of Intelligence  **Other:** Parents, teachers  **ADHD presentation:** inattentive : 51.8,combined : 48.3  **Diagnosis:** Confirmation by specialist  Parent-report on the Schedule for Affective Disorders and Schizophrenia for School Age Children - DSM IV by clinician  **Comorbidity:** Learning disability : homework problems,N/A  **Female:** 32 %  **Age mean:**  Grade level (M and SD) 3.5 (1.2)  **Minimum age:** 7  **Maximum age:** 10  **Ethnicity:**  % Hispanic or Latino : 7.1  % Black/African American : 22.2  % Asian : 2.0  % White : 72.4  % Multiracial : 3.5 | **Intervention:** Family-School Success, which included 6 groupsessions (90 minutes each), 4 individualized family sessions (60 minutes each), and 2 school-based consultations (45 minutes each), over the course of 12 weekly sessions  **Control:** NA  **Comparator:** BehavioralCoping with ADHD through Relationships and Education (CARE) included 11 group sessions and 1 family-school meeting, which were held on consecutive weeks. The initial session was conducted on a Saturday for 3 hours and subsequent meetings were 75 minutes (  **Follow-up:** 3 months | SNAP-P (Swanson, Nolan, and Pelham Questionnaire), parent-report  There was no intervention effect on ADHD and ODD symptoms, as assessed by parent and teacher ratings on the SNAP-IV.  parent-rated Treatment Acceptability Questionnaire (TAQ)  Tx acceptance significantly higher for intervention (p = .006).  Academic Performance Rating Scale (APRS)  Group had no effect on improvement. |
| Psychological or behavioral | Qian, 2021485  ZIli Fan, 20161191  ID: NCT02656758  Crossover trial  Unclear/Not reported  N = 70  China  Setting: Specialty care | **Target:** Children with ADHD who received initial training approximately 14 ± 7 months before the current study; no history of head injury; no diagnosis of other congenital or acquired neurological conditions; estimated full‐scale IQ>=80; no diagnosis of autism spectrum disorders, psychosis, or an emergent psychiatric condition that needed immediate medication  **Other:** Parents  **ADHD presentation:** inattentive : 51.43,hyperactive : 4.29,combined : 44.29  **Diagnosis:** Confirmation by specialist  DSM‐IV criteria based on parent ratings of the ADHD‐rating scale‐IV and was then confirmed by a semi‐structured interview conducted by experienced pediatric psychiatrists using the clinical diagnostic interview scale.  **Comorbidity:** N/A  **Female:** 23 %  **Age mean:** 9.24 (1.04)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:** | **Intervention:** Ecological executive skills training which includes child training program and parent self-help group, multiple-family role-play component, and behavior parent training group, each session lasting 120 minutes, consisted of 12 weekly sessions  **Control:** Wait list  12-week waitlist, after which group received intervention  **Comparator:** NA  **Follow-up:** 3 months | ADHD-RS-IV (ADHD Rating Scale IV) scores  Intervention group improved more (group x time p = 0.004). Same for inattention (p =0.007) and hyperactivity (p = 0.020) subscales.  WEISS Function Impairment Scale-Parent report, total  There was no significant difference between groups.  Behavior Rating Scales of Executive Function (BRIEF) : no effect of group on any subscales. |
| Psychological or behavioral | Schramm, 2016521  ID: NA  RCT  Single center  N = 113  Germany  Setting: Specialty care | **Target:** Participants with ADHD and not meeting the criteria for severe comorbid disorders  **Other:**  **ADHD presentation:**  **Diagnosis:** Confirmation by specialist  DSM-IV-TR by dministered by a clinical psychologist under supervision of a board-certified child and adolescent psychotherapist  **Comorbidity:** N/A  **Female:** 15 %  **Age mean:** 13.99 (1.44)  **Minimum age:** 12  **Maximum age:** 17  **Ethnicity:**  N/A : Germans | **Intervention:** Learning Skills Training for Adolescents With ADHD, manualized, multimodal intervention combining an adolescent-direct training approach (maximum of 20 sessions of 60 mins each) with a behavioral training component in methods of contingency management for parents and teachers (3 sessions of 90 mins each) for average duration of 6 months  **Control:** Wait list  Waiting list controls were invited twice for data collection with an average interval of 5.76 (SD 1.65) months in between and expected to start intervention after post-measurement  **Comparator:** OtherProgressive muscle relaxation training, adolescents met in groups of 4-5 twice-weekly for 12–15 sessions (60 mins) and were trained by 2 BA-level students followed by playtime; the students did not mention or talk about ADHD or related problems with the a  **Follow-up:** 6 months | Inattention, FBB-HKS (Fremdbeurteilungsbogen für Hyperkinetische Störungen), parent report  The training significantly reduced ADHS symptoms and parent- and teacher-rated internalizing problems and increased teacher rated academic enablers compared to waiting list controls.  The training significantly reduced parent- and teacher-rated internalizing problems and increased teacher rated academic enablers compared to waiting list controls. |
| Psychological or behavioral | Schuck, 2018522  Schuck, 20181027  ID: NA  RCT  Single center  N = 88  US  Setting: Community | **Target:** Children with ADHD Combined Type  **Other:** Parents  **ADHD presentation:** combined : 100  **Diagnosis:** Confirmation by specialist  DSM-IV confirmed by Kaufman-Schedule for Affective Disorders and Schizophrenia for School-Age Children: Present and Lifetime Version (K-SADS-PL)  **Comorbidity:** N/A  **Female:** 28.5 %  **Age mean:** 7.65 (0.75)  **Minimum age:** 7  **Maximum age:** 9  **Ethnicity:**  % Hispanic or Latino : 29.5  % Black/African American : 1.5  % Asian : 12.5  % Native Hawaiian or Pacific Islander : 1.5  % White : 62  % Multiracial : 20.5 | **Intervention:** Canine assisted psychosocial intervention, weekly 2-hour sessions for 12 weeks  **Control:** Wait list  Wait list condition  **Comparator:** BehavioralBehavioral parent training plus social skills training, parents participated in 12 weekly 2-hour sessions of group Behavioral Parent Training emphasizing positive reinforcement strategies and nonphysical discipline  **Follow-up:** 3 months | Social Skills Improvement System (SSIS) Problem Behaviors scale  A significant interaction of group by time (p 0.002) was found at treatment completion for problem behaviors.  ADHD-RS-IV (Attention-Deficit/Hyperactivity Disorder Rating Scale, 4th Edition) total score, parent report  Ratings were significantly lower in the intervention group than control group but the difference was borderline significant (p 0.06).  Self esteem was measured by the Self-Perception Profile for Children and children’s self-perceptions in the domains of behavioral conduct, social, and scholastic competence, were significantly increased from baseline to post-treatment in intervention group (p 0.021, p 0.008, and p 0.011) while the control group did not experience significant increases.  Participants with adverse events  There were no adverse events across seven cohorts of treatment. |
| Psychological or behavioral | Sciberras, 2020523  Murdoch Childrens Research Institute (MCRI) (Australia), 2010946; Hiscock, 2015834; Sciberras, 20101029  ID: ISRCTN68819261  RCT  Multicenter  N = 244  Australia  Setting: Mixed | **Target:** Children with ADHD and behavioral sleep disorder or experiencing significant bedtime anxiety leading to insomnia, parents needed to rate as moderate/severe sleep problem  **Other:** Parents  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** Sleep  **Female:** 14.7 %  **Age mean:** 10.1 (2.0)  **Minimum age:** 5  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Sleep intervention for family, 2 face to face, fortnightly consultations about sleep witha trained clinician; clinician assessed the child’s sleep problem, elicited parent goals for sleep management, provided information about normal sleep, sleep cycles, and sleep hygiene strategies, and formulated a behavioral sleep management plan tailored to the child’s sleep problem; parents were asked to complete a sleep diary; the second consultation and a follow-up telephone call were used to review the sleep diary, reinforce suggested strategies, and troubleshoot any problems; total duration of 4 weeks  **Control:** TAU  Families allocated to ‘usual care’ accessed care from their child’s pediatrician, which does not usually involve the assessment and treatment of sleep problems  **Comparator:** NA  **Follow-up:** 12 months | Strengths & Difficulties Questionnaire (SDQ) conduct problems, teacher report  No difference in improvement in conduct reported by parent (p 0 .17) or teacher (p 0 .11) adjusted for confounding variables.  ADHD-RS-IV (ADHD rating scale IV), total score, parent  Intervention group improved more on parent rating (p = .001) but not teacher rating (p = 0.91).  Daily Parent Rating of Evening and Morning Behavior (DPREMB)  The intervention group improved more than control group (p = .001).  Child sleep habits questionnaire—total score: Intervention group improved more than control (p < .02). |
| Psychological or behavioral | Shuai, 2020530  Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, 20181181  ID: NCT03515135  RCT  Unclear/Not reported  N = 96  China  Setting: N/A | **Target:** Native Chinese speaking preschool children with DSM-V diagnosed ADHD, no major sensory-motor disorders, no history of brain damage, epilepsy, no diagnosis of autism spectrum disorder, no IQ score <80, and no pharmacological or nonpharmacological treatment  **Other:** Parents  **ADHD presentation:** inattentive : 8.3,hyperactive : 19.8,combined : 71.9  **Diagnosis:** Confirmation by specialist  Parents of the children were interviewed by two independent psychiatrists to confirm DSM-V diagnosed ADHD  **Comorbidity:** N/A  **Female:** 18.75 %  **Age mean:**  Intervention group age mean in months (61.78) and SD (6.67). Waitlist group age mean in months (59.09) and SD (6.62).  **Minimum age:** 4  **Maximum age:** 5  **Ethnicity:**  Other : Presumably 100% Chinese | **Intervention:** Psychotherapy (Executive Function Training for Preschool), structured program, 90-min sessions (60-min for children, 30-min for parents), sessions contain 4 parts: tasks and games aiming to practice executive function (40min), paper-pencil tasks (15min), relaxation (5 min) for children; parents received session on guiding their child (30 min); sessions once a week for 8 weeks  **Control:** Wait list  Put on waitlist and received treatment as usual  **Comparator:** NA  **Follow-up:** 2 months | SNAP-IV (Swanson, Nolan, and Pelham Rating Scale Chinese version)  The intervention group had significnatly reduced ODD symptoms compared to control group (p=.02), but differences in inattention scores were not significant (p=0.24).  Differences in BRIEF-P scores between intervention group and control group were not significant (p=0.47). |
| Psychological or behavioral | Sibley, 2016533  ID: NA  RCT  Multicenter  N = 128  US  Setting: School | **Target:** Children with ADHD with significant academic impairment and without autism spectrum disorder  **Other:** Parents were involved in intervention and supplied some outcome data  **ADHD presentation:** inattentive : 39.1,combined : 60.9  **Diagnosis:** Confirmation by specialist  Phone screen containing the DSM-IV-TR ADHD symptoms and questions about impairment was administered to the primary caretaker. Then in person parent structured interview (Computerized-Diagnostic Interview Schedule for Children) and symptom assessment con  **Comorbidity:** N/A  **Female:** 35.2 %  **Age mean:** 12.7 (0.86)  **Minimum age:** 11  **Maximum age:** 15  **Ethnicity:**  % Hispanic or Latino : 78.5  % Black/African American : 10.8  % White : 7.7 | **Intervention:** Supporting Teens’ Academic Needs Daily (STAND) consists of ten 50-minute manualized family therapy sessions attended by the parent and teen, uses motivational interviewing, for a total of 10 weeks  **Control:** TAU  Treatment as usual, without intervention  **Comparator:** NA  **Follow-up:** 6 months | Disruptive behavior, parent report  Group by time effects were nonsignificant (p=0.343).  ADHD Symptom Severity, Disruptive Behavior Disorder Rating Scale (DBD), parent report  The intervention group improved compared to the control group (p < .001).  Cumulative GPA  There were no significant differences between intervention and comparator group (p=0.265). |
| Psychological or behavioral | Sibley, 2020534  Sibley, 20161067  ID: NA  RCT  Unclear/Not reported  N = 123  US  Setting: School | **Target:** Adolescents with ADHD, without any history of autism, intellectual disability or IQ<70  **Other:** Parents provided outcome data  **ADHD presentation:** inattentive\_other : Dyadic, 49.2% / Parent-Teen Group, 58.3%,combined\_other : Dyadic, Parent-Teen 50.8% / Group, 41.7%  **Diagnosis:** Confirmation by specialist  DSM 5 via Diagnostic Interview Schedule for Children  **Comorbidity:** N/A  **Female:** 19.6 %  **Age mean:**  Dydactic 13.63 (1.49), Parent-teen group 13.59 (1.78)  **Minimum age:** 11  **Maximum age:** 17  **Ethnicity:**  Other : Dyadic, 85.7% / Parent-Teen Group, 85%  Other : Dyadic, 4.8% / Parent-Teen Group, 5%  Other : Dyadic, 7.9% / Parent-Teen Group, 8.3% | **Intervention:** Supporting Teens' Autonomy Daily (STAND), manualized parent-teen dyadic, ten 60-minweekly sessions attended by the participant and a parent, skill instruction blended with motivational interviewing and parent-teen behavioral contracting, for total 10 weeks  **Control:** NA  **Comparator:** BehavioralGroup Supporting Teens' Autonomy Daily (STAND), manualized, eight 90-min weekly group sessions, teens and parents meet in separate groups for the first 75 minutes and meet for the final 15 minutes  **Follow-up:** 6 months | ADHD symptoms inattention, parent rating  No difference in parent reported inattention (p = 0.61) or hyperactivity (p=0.37 ) scores. No difference in teacher reported inattention (p = 0.07 ) or hyperactivity (p= 0.50) scores.  Organization, time management, and planning impairment, skills applied to homework, school, and chores, parent report  There was no difference across groups in either parent (p=0.84) or teacher (p=0.23) reported.  Teen treatment satisfaction  No significant differences in treatment satisfaction (p = 0.81) or percentage of treatment attended (p=0.16).  Grade Point Average (GPA)  No difference between groups (p = 0.50). |
| Psychological or behavioral | Sibley, 2021532  Bickman, 20211062; Florida International University, 2016777  ID: NCT02694939  RCT  Multicenter  N = 278  US  Setting: Community | **Target:** Adolescents with ADHD; without diagnosis of autism spectrum disorder or intellectual disability  **Other:** Parents involved in intervention. Parents & teachers provided some outcomes  **ADHD presentation:** inattentive : 52.2,combined : 47.8  **Diagnosis:** Confirmation by specialist  DSM-5  **Comorbidity:** N/A  **Female:** 29.5 % STAND 29.7, usual care 29.3  **Age mean:**  13.97 (1.51) and 14.08 (1.50)  **Minimum age:** 11  **Maximum age:** 17  **Ethnicity:**  % Hispanic or Latino : 81.7  % Black/African American : 13.3  % White : 4.7  % Multiracial : 0.7 | **Intervention:** Supporting Teens' Autonomy Daily (STAND) consisting of weekly 60-minute motivationalinterviewing-enhanced behavior therapy sessions attended by dyads of teens and parents for 10 weeks  **Control:** No intervention  No intervention, controls continued with any already existing treatment as usual  **Comparator:** NA  **Follow-up:** 9.8 months | Number of disciplinary incidents  No difference in number of disciplinary incidents (p 0.063).  Inattention, DSM score, parent report  No difference in parent rated inattention score (p = .162), teacher rated inattention score (p = .6340, parent rated hyperactivity score (p = .272), or teacher rated hyperactivity score (p = .801).  Satisfaction with treatment  No group differences in adolescent satisfaction.  Grade Point Average (GPA)  No difference (p = .904). |
| Psychological or behavioral | Siebelink, 2021535  Karakter Kinder en Jeugdpsychiatrie, 2017873; Siebelink, 20181071  ID: NCT03220308  RCT  Single center  N = 103  Netherlands  Setting: Mixed | **Target:** Dutch-speaking children and adolescents with ADHD; could use ADHD medication if stable dose was reached two weeks prior to study; no current psychosis, bipolar illness, active suicidality, untreated post-traumatic stress disorder or substance use disorder; no IQ<80  **Other:** Parents  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-4 or DSM-5 confirmed with a structured interview conducted by trained researchers  **Comorbidity:** N/A  **Female:** 30 %  **Age mean:**  Intervention 11.0 (1.8), control 11.4 (1.8)  **Minimum age:** 8  **Maximum age:** 16  **Ethnicity:**  N/A | **Intervention:** Mindfulness-based intervention for family, weekly 90-minute group sessions, followedby a booster session 8 weeks later, homework of approximately 30–45 min/day for parents and 15 min/day for children, also received care-as-usual, for 8 weeks  **Control:** TAU  Care-as-usual only  **Comparator:** NA  **Follow-up:** 8 months | Oppositional behavior scale, Conners Parent Rating Scale (CPRS)  No difference between groups.  Hyperactivity-impulsivity, SWAN (Strengths and Weaknesses of ADHD symptoms and Normal behaviour ) parent-rated  Parent-rated hyperactivity-impulsivity group differences were larger and significant in favor of intervention group (p<.05). Difference in parent-rated inattentiveness not significant. No differences in teacher reported hyperactivity-impulsivity or inatte  No difference in parent-rated self-control deficits measured using 75-item Behaviour Rating Inventory of Executive Function-Adult Version (BRIEF).  No CAU- or MBI-related Serious Adverse Events were spontaneously reported by the participants or mindfulness teachers. |
| Psychological or behavioral | Storebo, 2012565  Storebo, 2011997; Storebo, 20111089  ID: NCT00937469  RCT  Single center  N = 56  Netherlands  Setting: Specialty care | **Target:** ADHD diagnosis according to DSM, without schizophrenia or autism, no violent and criminal children, IQ of 80 or above, without having previously taken medication for ADHD  **Other:**  **ADHD presentation:** inattentive : 29.1,hyperactive : 3.9,combined : 58  **Diagnosis:** Confirmation by specialist  DSM-IV by psychologists from the Clinic  **Comorbidity:** N/A  **Female:** 30 %  **Age mean:** 10.4 (1.31)  **Minimum age:** 8  **Maximum age:** 12  **Ethnicity:**  N/A | **Intervention:** Social skills training offered weekly, 90 minute sessions, in additionto standard treatment that encompassed offer of medical treatment for the child following a medication protocol, treatment started with the first choice: methylphenidate; the second choice: dexamphetamine; and atomoxetine was considered in patients where there was a suspicion of abuse of dexamphetamine or a significant anxiety component change; standard treatment involved an educational parent group, where the parents met 3 times during the 8 week trial and received general information about ADHD, duration of 8 weeks  **Control:** TAU  Standard treatment encompassed family was offered medical treatment for the child following a medication protocol, treatment started with the first choice: methylphenidate; the second choice: dexamphetamine; and atomoxetine was considered in patients wher  **Comparator:** NA  **Follow-up:** 6 months | Hyperactivity-impulsivity subindex Conner’s 3rd Edition Rating Scale  Social skills training plus parental training did not show any significant benefit for children with attention deficit hyperactivity disorder when compared with standard treatment.  Academic performance based on Conners-3 and CBRS  No difference between groups.  Participants with adverse events  No adverse events were observed. |
| Psychological or behavioral | Valero, 2021594  ID: NA  RCT  Unclear/Not reported  N = 30  Spain  Setting: Community | **Target:** Children with ADHD  **Other:** Parents also received mindfulness training  **ADHD presentation:** inattentive : 30,hyperactive : 13,combined : 57  **Diagnosis:** Confirmation by specialist  Diagnosis had to be performed by a specialist—psychologist, neuro-pediatrician, or psychiatrist—at least 2years prior to participation. ADHD confirmed by parent version of Conners—3rd Edition  **Comorbidity:** N/A  **Female:** 23.3 %  **Age mean:** 10.6 (1.69)  **Minimum age:** 9  **Maximum age:** 14  **Ethnicity:**  N/A | **Intervention:** Mindfulness training, children's sessions were1 hour long, parent sessions were1.5 hours, 8 sessions over 8 weeks  **Control:** Wait list  Wait list  **Comparator:** NA  **Follow-up:** 6 months | Conners—3rd Edition, aggressive behavior scale  Intervention group had less aggression at follow-up (p = .045).  Inattention score, Conner’s Version 3, parent report  At follow-up, intervention group showed less inattention compared to the wait-list group (p=.0324). There was no difference in hyperactivity/impulsivity score p = (.103).  Conners Version 3, parent report, executive function, intervention group had better executive function (p=.002). |
| Psychological or behavioral | Wilkes-Gillan, 2016624  Barnes, 2017676  ID: ACTRN12614000973617  Crossover trial  Single center  N = 31  Australia  Setting: Mixed | **Target:** Children with ADHD with co-morbid difficulties; no other major developmental disorders  **Other:** Parents, plus a "typical" friend of each child  **ADHD presentation:** inattentive : 38,hyperactive : 3,combined : 59  **Diagnosis:** Confirmation by specialist  DSM-IV by pediatrician or psychiatrist  **Comorbidity:** Learning disability  **Female:** 13 %  **Age mean:** 8.4 (1.6)  **Minimum age:** 5  **Maximum age:** 11  **Ethnicity:**  N/A | **Intervention:** Play-based intervention, 1-hour sessions for 10 weeks  **Control:** Wait list  No treatment for 10 weeks, after which the group crossed over to the 10-week play-based intervention. Outcomes reported pre-crossover.  **Comparator:** NA  **Follow-up:** 2.5 months | The change in play scores for the intervention-first group was significantly greater than the change in the control-first group during their 10 week wait period (p < .001). One year follow up did not have adequate power. |
| Psychological or behavioral | Zhu, 2022643  ID: ID NA  RCT  Single center  N = 120  China  Setting: N/A | **Target:** Children with ADHD, not on medication, without co-occurring psycological or medical problems  **Other:** Parents provided some outcomes  **ADHD presentation:** inattentive : 33.3,hyperactive : 27.5,combined : 37.5  **Diagnosis:** Confirmation by specialist  DSM IV  **Comorbidity:** N/A  **Female:** 34.2 %  **Age mean:** 4.28 (0.38)  **Minimum age:** 2  **Maximum age:** 7  **Ethnicity:**  % Asian : 100 | **Intervention:** Musicotherapy combined with cognitive behavioral intervention: behavioral intervention provided basic attention training in the auditory and visual senses, 5 times every week, 60 minutes per session, while musicotherapy was provided once per weeks to groups of 5 children, for 16 weeks  **Control:** Wait list  Intervention provided after completion of the study  **Comparator:** NA  **Follow-up:** 4 months | ADHD RS IV, total score, parent report  Intervention group improved more (p<0.05).  Numerical cross-attention test: Intervention group improved more than control group (p<0.05). |
| Teacher, school environment | Breaux, 2018163  Langberg, 2018893; Smith, 20201078; Breaux, 2019694  ID: ID NA  RCT  Multicenter  N = 222  US  Setting: School | **Target:** Children with ADHD; intelligence quotient of 80 or above; no pervasive developmental disorder, bipolar disorder, or psychosis  **Other:** School mental health professionals, parents of children with ADHD, teachers of children with ADHD  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-IV-TR per psychologist  **Comorbidity:** N/A  **Female:** 28 %  **Age mean:** 12.00 (1.02)  **Minimum age:**  **Maximum age:**  **Ethnicity:**  % Hispanic or Latino : 9  % Black/African American : 28  % White : 56  % Multiracial : 12  Other : 4% other/did not report | **Intervention:** Homework, Organization, and Planning Skills (HOPS) is skills-based treatment that focuses on teaching organization and planning skills that are important for homework completion; 2 parent/family meetings focused on promoting generalization; 16 sessions delivered during the school day; sessions conducted with individual students; first 10 sessions occurred twice weekly and final 6 sessions occurred once per week; also two 1-hour sessions with provider and family, families left first session with formal written monitoring and behavior rewarding plan, for 11 weeks  **Control:** Wait list  Wait list  **Comparator:** Teacher, school environmentCompleting Homework by Improving Efficiency and Focus (CHIEF) is contingency management-based treatment, 16 sessions delivered during the school day, first 10 sessions occurred twice weekly and final 6 sessions occurred once per week, also included two 1-  **Follow-up:** 6 months | Parent satisfaction, 5 point Likert scale  No significant difference between groups.  Grade Point Average (GPA)  No difference among groups (p 0.236). |
| Teacher, school environment | Corkum, 2019208  Dalhousie University, 2012730  ID: NCT01547702  RCT  Multicenter  N = 58  Canada  Setting: School | **Target:** Children with ADHD; on a stable dose of medication for ADHD or was taking no medication, with no plan to start or change medications for the duration of the study; no Individualized Program Plan due to significant physical, behavioral, communication, or intellectual difficulties; no significant co-occurring mental health problems aside from ADHD; no moderate or severe intellectual impairment; no previous involvement with the Teacher Help for ADHD program  **Other:** Teachers of students with ADHD  **ADHD presentation:** N/A  **Diagnosis:** No  doesn't indicate confirmation, but does indicate that participants were previously diagnosed by a certified health care provider  **Comorbidity:** N/A  **Female:** 12 %  **Age mean:** 8.83 (1.72)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % White : 90  Other : 10% non-caucasian | **Intervention:** Teachers given weekly online sessions, session covered a different topicrelated to education, treatment, support and additional interventions, for total of 6 weeks  **Control:** Wait list  Waitlist group did not receive any intervention but were free to access usual care. Waitlist lasted 12 weeks  **Comparator:** NA  **Follow-up:** 6 months | ADHD Index Conners 3-T  Significant improvements based on teacher (but not parent) reports of core ADHD symptoms.  Impairment ratings score, teacher  Significant improvement associated with the intervention.  Teacher intervention satisfaction (content presented was easy to understand)  Rated 5.28 90.84) on a 6-point scale |
| Teacher, school environment | DuPaul, 2021238  Ohio University, 2020970  ID: NCT04480346  RCT  Multicenter  N = 186  US  Setting: School | **Target:** Adolescents with ADHD in school for at least half the day, an IQ of 75 for above, and not diagnosed with psychosis, bipolar, or obsessive compulsive disorder  **Other:** Parents and teacher provided some outcome data  **ADHD presentation:** inattentive,combined : 50  **Diagnosis:** Confirmation by specialist  diagnostic criteria for at leastADHD based on the Parent-Children's Interview for Psychiatric Syndromes (P-ChIPS)  **Comorbidity:** N/A  **Female:** 20 %  **Age mean:** 15 (0.8)  Grades 9 through 11  **Minimum age:**  **Maximum age:**  **Ethnicity:**  % Hispanic or Latino : 10.2  % Black/African American : 14.5  % Asian : 1.0  % White : 74  Other : Other 4.8% | **Intervention:** Multi-component training interventions: individual coaching sessions for 15–20 mintwice per week, at least monthly collaborative problem-solving between the teen and coach, ten 90-min evening group sessions at their school offered separately for adolescents and parents, duration of the academic year  **Control:** TAU  Community care, given a list of available resources in their community, including locally available providers of child and family psychosocial and pharmacological interventions. Participants in both groups were informed that they could continue with any s  **Comparator:** NA  **Follow-up:** 6 months | Tardiness frequency  There was no statistically significant Group (p=0.75) or Time (p=0.96) effect for school tardiness.  Adolescent Academic Problems Checklist Total  The intervention group had significantly fewer academic problems compared to the comparator group (p<0.01).  Children's Organization Skills Scale Task Planning showed steeper negative slopes (i.e., more improvement over time) for intervention participants than those in the community care condition. |
| Teacher, school environment | Evans, 2016259  Langberg, 2016894; Schultz, 20171028  ID: ID NA  RCT  Multicenter  N = 326  US  Setting: School | **Target:** Children had to attend one of the participating schools, met full DSM–IV–TR diagnostic criteria for either ADHD–Predominantly Inattentive Type or ADHD–Combined Type ADHD based on the Parent Children’s Interview for Psychiatric Syndromes or combined with teacher ratings on the Disruptive Behavior Disorders Rating Scale, demonstrated impairment based on parent or teacher report on the Impairment Rating Scale, IQ of 80 or above, did not meet diagnostic criteria for a pervasive developmental disorder or bipolar disorder, psychosis, or obsessive–compulsive disorder  **Other:** Parents and teachers provided data  **ADHD presentation:** combined : 49  **Diagnosis:** Confirmation by specialist  DSM-IV  **Comorbidity:** N/A  **Female:** 29 %  **Age mean:** 12.1 (1.0)  6th grade to 8th grade  **Minimum age:**  **Maximum age:**  **Ethnicity:**  % Hispanic or Latino : 3  % Black/African American : 12  % White : 70  % Multiracial : 8 | **Intervention:** Challenging Horizons Program–after school version (CHP-AS): 2 days per week for 2 hr 15 min per day for 9 months  **Control:** TAU  Community care condition received a list of available resources in their community at the start of the school year; resource lists were developed in collaboration with school staff to include locally available child and family psychosocial and pharmacolog  **Comparator:** Teacher, school environmentChallenging Horizons Program–mentoring version provided by a teacher or other staff member in their school (mentor); mentor participation was voluntary, and mentors received a small stipend ($100) for participation. Mentors agreed to meet weekly with thei  **Follow-up:** 18 months | Inattention and hyperactivity/impulsivity scale, Disruptive Behavior Disorders (DBD) Rating Scale  Challenging Horizons Program after school version is associated with moderate effect size improvements in ADHD symptoms of inattention but not hyperactive/impulsive symptoms.  IRS (Impairment Rating Scale), relation with peers scale, teacher  There were no significant differences between groups.  Classroom Performance Survey (CPS), Academic factor, teacher  There were no significant differences between groups.  Intervention group performed better than mentoring group (p = .0011) and better than community care (p = 0007). Similar results for COSS materials management scale (p=.0430 vs mentoring, p=0 .0010 vs community care). |
| Teacher, school environment | Mikami, 2013433  ID: ID NA  RCT  Single center  N = 24  US  Setting: School | **Target:** Children with ADHD who recently completed grade 1, 2, or 3, with "peer impairment" and fewer than 50% of peers rated as liking them  **Other:** 113 neurotypical children participated in programs; teachers received intervention training and provided some outcomes  **ADHD presentation:** inattentive : 25,hyperactive : 0,combined : 75  **Diagnosis:** Confirmation by specialist  DSM IV via Kiddie Schedule for Affective Disorders and Schizophrenia  **Comorbidity:** ODD : half had ODD  **Female:** 45.8 %  **Age mean:** 8.15 (0.79)  **Minimum age:** 6.8  **Maximum age:** 9.8  **Ethnicity:**  % Hispanic or Latino : 2  % Black/African American : 3  % Asian : 6  % White : 81  % Multiracial : 8 | **Intervention:** Contingency Management (COMET) plus Making Socially-Accepting Inclusive Classrooms (MOSAIC), to reduce exclusionary and increase positive peer behavior, MOSAIC teachers set explicit classroom rules for social inclusion, while teachers modeled for peers that children with ADHD were worthy of liking by developing positive relationships with children through warm, one-on-one interactions to discuss the child's personal interests; contingency management worked by providing children with specific expectations for desired behavior whereby children gained and lost points based on their compliance; to minimize social comparisons between children based on points, MOSAIC teachers provided corrections about behavior privately by calling the child aside when feasible; 4-week program (one component for 2 weeks only)  **Control:** Other  Contingency management (COMET) alone: teachers provided children with specific expectations for desired behavior whereby children gained and lost points based on their compliance, children needing extra assistance had specialized behavior plans where addi  **Comparator:** NA  **Follow-up:** 1 month | Problem behaviors, Teacher-Child Rating Scale  No main effects for treatment condition on Teacher Rating Scale for internalizing behavior, hyperactivity, inattention, or oppositional behavior, nor on observations of off-task behavior or aggressive/noncompliant behavior.  Children with ADHD displayed improved sociometric preference and more reciprocated friendships, and received more positive messages from peers, when they were in MOSAIC relative to in COMET |
| Teacher, school environment | Shen, 2021529  School of Public Health, 20181026  ID: ChiCTR1800014945  Cluster RCT  Multicenter  N = 232  China  Setting: School | **Target:** Children with ADHD; without intellectual disability (IQ <70). autistic spectrum disorder, epilepsy, schizophrenia, cerebral palsy and other nervous system diseases and mental disorders, severe heart, brain, kidney, and other organ dysfunction  **Other:** Teachers and parents received training  **ADHD presentation:** inattentive : 40.2,hyperactive : 28.9,combined : 30.9  **Diagnosis:** Confirmation by specialist  DSM 5  **Comorbidity:** N/A  **Female:** 14.2 %  **Age mean:**  Intervention 7.71 (1.22) Control 8.39 (1.38)  **Minimum age:** 6  **Maximum age:** 12  **Ethnicity:**  % Asian : 100 | **Intervention:** Primary school-based multimodal treatment for teachers and parents; 2 teacher training meetings (1 2-hrsessionand 1 30-min session), 2 group parent trainings sessions (4.5-hrs) and 2 individualized family therapy sessions (2hrs), participants also received stimulant medication prescribed by their pediatricians, for 16 weeks  **Control:** TAU  Stimulant medication prescribed by pediatricians referring to the clinical practice guidelines for ADHD children published by the American Academy of Pediatrics  **Comparator:** NA  **Follow-up:** 4 months | SNAP-IV (Swanson Nolan and Pelham version 4)  Intervention group had significantly greater improvement than control group (p < 0.05)  Treatment Acceptability Questionnaire (TAQ) scale  64.8% of the parents in the intervention group indicated that this treatment would help their children.  Academic Performance Questionnaire (APQ) change  There was no significant time by group effect (p > 0.05).  Parental stress measured with the PSI improved in both groups.  "There were no serious adverse events and adverse events reported." |
| Teacher, school environment | Sibley, 2018531  Sibley, 20201065; Sibley, 20191063  ID: NA  RCT  Single center  N = 325  US  Setting: School | **Target:** Children with ADHD that meets DSM IV criteria, displaying significant academic impairment (at least a 3 on a 0–6 teacher Impairment Rating Scale), without autism spectrum disorder  **Other:** Parents and teachers provided data  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  ADHD diagnosis was confirmed through a combination of parent structured interview (Computerized-Diagnostic Interview Schedule for Children; Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000) and parent and teacher symptom and impairment ratings. Clinic  **Comorbidity:** N/A  **Female:** 25.8 %  **Age mean:**  Rising 6th & 9th graders  **Minimum age:**  **Maximum age:**  **Ethnicity:**  % Hispanic or Latino : 72.7  % Black/African American : 17.4 | **Intervention:** Summer program between transitions from middle to highschool, 8-week intensive summer program from 8-5 pm on weekdays (45 hrper week), alternated between 30- and 50-min small- and large-group modules, parent training once per week for 1.5 hours, for 8 weeks  **Control:** No intervention  No intervention  **Comparator:** Teacher, school environmentSummer program, low intensity, organization skills group 1.5 hr per week; also parent training once per week for 1.5 hours, for 8 weeks  **Follow-up:** 12 months | School Disciplinary Incidents  There were no significant group by time interaction effects for school disciplinary incidents.  Inattention severity, Disruptive Behavior Disorder Rating Scale, parent  There were no significant Group by Time interaction effects between the groups.  Satisfaction with treatment  Both groups reported high overall satisfaction that did not significantly differ between groups.  Grade Point Average (GPA), 9th Grade  Ninth-grade intervention youth showed smaller reductions in GPA over time than ninth-grade control youth. There were no GPA effects for sixth graders. |
| Teacher, school environment | Tamm, 2017577  ID: NA  RCT  Multicenter  N = 216  US  Setting: Mixed | **Target:** Children with ADHD and word reading/decoding deficits  **Other:** Parents  **ADHD presentation:** combined : 54.6,N/A : sample included also inattentive and hyperactive presentations  **Diagnosis:** Confirmation by specialist  **Comorbidity:** Learning disability : Word-level reading difficulties or disabilities  **Female:** 38.9 %  **Age mean:** 8.8 (1.3)  Grades 2 through 5  **Minimum age:**  **Maximum age:**  **Ethnicity:**  % Hispanic or Latino : 12.0  % Black/African American : 72.2  % Multiracial : 6.5 | **Intervention:** Reading training by teachers plus medication plus parent training; 9 parent group sessions, each 1.5 hours, over 10 weeks, low dose extended release methylphenidate, atomoxetine or extended release guanfacine could be used if MPH not tolerated, reading treatment provided by teachers to one or two students at a time for 45 minutes, four days per week for 16 weeks  **Control:** Other  Parent training plus medication; parent training in behavior management, 9 group sessions conducted by clinical psychologists, each 1.5 hours, over 10 weeks; medication: open label, typically beginning with low dose extended release methylphenidate; at  **Comparator:** NA  **Follow-up:** 5 months | Inattention scale, SNAP-IV, parent rating  The medication plus parent training group (p<.012) and combined (p<.001) treatment groups were rated as significantly less inattentive than the reading treatment alone group, but did not significantly differ from one another (p=.058). The medication plu  Wechsler Individual Achievement Test, Word Reading score: the reading (p<0.001) and combined (p<0.001) treatment groups had higher phonemic decoding scores than the medication plus parent training group but did not differ from one another (p 0.65). There were not significant differences between groups on word reading at follow-up. |
| Teacher, school environment | Volpe, 2009602  Jitendra, 2007866  ID: NA  RCT  Multicenter  N = 167  US  Setting: School | **Target:** Children with ADHD who were experiencing achievement problems in either math or reading  **Other:** Teachers conducted intervention  **ADHD presentation:** combined : 65.0,N/A : sample included inattentive and hyperactive presentations  **Diagnosis:** Confirmation by specialist  Parent and teacher ratings on the ADHD Rating Scale IV and NIMH diagnostic interview scale for children IV  **Comorbidity:** Learning disability : Problems with either math or reading  **Female:** 24.0 %  **Age mean:** 8.7 (1.23)  **Minimum age:**  **Maximum age:**  **Ethnicity:**  % Hispanic or Latino : 26.9  % Black/African American : 11.4  % White : 58.0 | **Intervention:** Intensive data-based academic intervention involves ongoing feedback to teachers from consultants, individual interventions are selected based on functional and academic assessment data for 15 months  **Control:** NA  **Comparator:** Teacher, school environmentTraditional data-based academic intervention, design of intervention based on teacher choice  **Follow-up:** 12 months | Woodcock-Johnson III tests of achievement, standardized math fluency score  No differences between groups on Woodcock-Johnson tests of achievement, Curriculum based measurement (CBM) scores, Academic Competency Evaluation Scale (ACES), or Report Card grades |
| Teacher, school environment | Zheng, 2020640  ID: ID NA  Cluster RCT  Multicenter  N = 219  China  Setting: School | **Target:** Children with ADHD, IQ ≥70, and no prior ADHD medication use; no comorbidity with autism spectrum disorder, schizophrenia, epilepsy, head injury, verified neurological disorder, or sensory retardation (hearing/vision problems)  **Other:** Parents, teachers  **ADHD presentation:** N/A  **Diagnosis:** Confirmation by specialist  DSM-5  **Comorbidity:** N/A  **Female:** 15.2 %  **Age mean:**  Intervention group mean age 7.93 (1.38); Control group mean age 7.21 (1.22)  **Minimum age:** 6  **Maximum age:** 11  **Ethnicity:**  % Asian : 100 | **Intervention:** School-based teacher and parent training, teacher training was 4 weekly 2-hour sessions consisting of knowledge about ADHD, behavioral strategies to manage conduct problems, classroom behavior management, teaching how to use scaffolding to promote the development of self-regulation in children with ADHD, parent training 4 weekly 2-hour sessions addressing knowledge about ADHD, medication, behavioral strategies, how to combine procedures and behavior management techniques; medication given was either methylphenidate or atomoxetine; for 4 weeks  **Control:** Other  Methylphenidate or atomoxetine alone  **Comparator:** NA  **Follow-up:** 6 months | SNAP-IV (Chinese Version, Swanson Nolan and Pelham, Version IV)  Difference in score change was statistically significant (p 0.009), favoring intervention  Medication adherence was significantly higher (p < 0.01) in the intervention group. |

Notes: ADHD = attention deficit hyperactivity disorder; N/A = not available