

# NEWSLETTER



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## **BIBLIOGRAFIA ADHD AGOSTO 2021**

Asian J Psychiatr. 2021 Aug;62:102708.

**EXPOSURE TO GENERAL ANAESTHESIA IN CHILDHOOD AND THE SUBSEQUENT RISK OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER: A META-ANALYSIS OF COHORT STUDIES.**

**Sun JJ, Zhu CY, Jiang HY.**

**Background** The evidence for a relationship between general anaesthesia induced in childhood and the risk of attention-deficit hyperactivity disorder (ADHD) in later life is inconsistent. We systematically assessed whether such an association existed.

**Methods** We searched the PubMed and EMBASE databases for relevant cohort studies. Relative risks (RRs) and 95 % confidence intervals (CIs) were calculated to determine the relationship between induction of childhood general anaesthesia and the risk of ADHD in later life.

**Results** Seven studies (eight publications) on developmental outcomes after the induction of childhood general anaesthesia met our inclusion criteria but not our exclusion criteria. Repeat childhood general anaesthesia (RR = 1.84, 95 CI% 1.14–2.97; P < 0.001; I<sup>2</sup> = 74.8 %), but not one-off general anaesthesia (RR = 1.09, 95 CI% 0.93–1.27; P = 0.301; I<sup>2</sup> = 0%), was associated with an increased risk of ADHD in later life. The association was evident only when the total general anaesthesia exposure exceeded 90 min.

**Conclusions** Our meta-analysis indicated that the effect of general anaesthesia on the risk of ADHD is dose- or duration-dependent

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Per la ricerca degli articoli pubblicati nella letteratura scientifica nel mese in esame sono state consultate le banche dati Medline, Embase, PsycINFO e PsycArticle utilizzando le seguenti parole chiave (o i loro sinonimi): 'Attention deficit disorder', 'Attention deficit hyperactivity disorder', 'Infant', 'Child', 'Adolescent', 'Human'. Sono qui riportate le referenze considerate rilevanti e pertinenti.

Asian J Psychiatr. 2021 Aug;62:102729.

**BULLYING PERPETRATION AND VICTIMIZATION IN ELEMENTARY SCHOOL STUDENTS DIAGNOSED WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Bong SH, Kim KM, Seol KH, et al.**

Previous research has found that attention-deficit/hyperactivity disorder (ADHD) in children is related to bullying perpetration. This study examined the correlation between ADHD and bullying perpetration, and aimed to identify which factors, including bullying victimization, predicted bullying. Forty-nine elementary school students, aged 6-12, participated voluntarily in a comparative study between children with ADHD and non-ADHD control children; none of them had previously undergone psychiatric treatment. Both parents' and participants' social demographic information (gender, age) and clinical variables were obtained from self-report questionnaires. The participants' bullying victimization experience, impulsivity, and parents' history of ADHD had significant relationships with bullying. The status of ADHD and other self-reported scales had no significant relationships with bullying. The association between bullying victimization and bullying perpetration was notable among all factors examined. This was consistent with the claims of prior studies that past victimization led to perpetration of bullying. Therefore, it seems that when treating victims of bullying, care should be taken, through proper intervention, to ensure the incident is neither repeated nor replicated. Characteristics associated with ADHD, including impulsivity and parents' history of ADHD, were significantly related to bullying. However, we could not confirm our hypothesis that ADHD itself might be associated with bullying behavior

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Autism Res. 2021 Aug;14:1769-76.

**ATTENTION TRAINING IN CHILDREN WITH AUTISM SPECTRUM DISORDER IMPROVES ACADEMIC PERFORMANCE: A DOUBLE-BLIND PILOT APPLICATION OF THE COMPUTERIZED PROGRESSIVE ATTENTIONAL TRAINING PROGRAM.**

**Spaniol MM, Mevorach C, Shalev L, et al.**

Atypical attention has been reported in individuals with autism spectrum disorder (ASD) with studies pointing to an increase in attention deficit and hyperactivity disorder-like symptomatology. Individuals with ASD may also present academic difficulties and it is possible that they face a double-barrier for academic attainment from both core ASD symptomatology and from attention atypicalities, which are directly linked to academic performance. This raises the possibility that academic difficulties in ASD may benefit from cognitive training targeting attention. To test this possibility, we used the computerized progressive attentional training (CPAT) intervention in a double-blind, active control with follow-up intervention study in Brazil. The CPAT is a computerized attention training program that was recently piloted with schoolchildren with ASD in the UK. Twenty-six participants (8-14 years) with ASD in the São Paulo ASD Reference Unit were assigned to either the CPAT (n = 14) or active control group (n = 12), which were matched at baseline. Two 45-min intervention sessions per week were conducted over a 2-month period. School performance, attention, fluid intelligence, and behavior were assessed before, immediately after and 3 months following the intervention. Significant group by time interactions show improvements in math, reading, writing and attention that were maintained at follow-up for the CPAT (but not the active control) group, while parents of children from both groups tended to report behavioral improvements. We conclude that attention training has the potential to reduce obstacles for academic attainment in ASD. Combined with the previous pilot study, the current results point to the generality of the approach, which leads to similar outcomes in different cultural and social contexts.

LAY ABSTRACT: Attention difficulties tend to occur in ASD and are linked to academic performance. In this study, we demonstrate that school performance in math, reading and writing in children with ASD can improve following an intervention that trains basic attention skills (the CPAT intervention). The improvements we report are stable and were maintained 3-months following the intervention. This study, which was conducted in a public-health setting in Brazil, extends previous research in schools in the UK pointing to the cross-cultural and cross-settings efficacy of the intervention

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BMC Psychiatry. 2021 Aug;21:411.

**ASSOCIATION OF TREATMENT PROCEDURES AND RESILIENCE TO SYMPTOM LOAD THREE-YEARS LATER IN A CLINICAL SAMPLE OF ADOLESCENT PSYCHIATRIC PATIENTS.**

**Gårdvik KS, Rygg M, Torgersen T, et al.**

**Background** We aimed to examine symptom load in a clinical adolescent population at three-year follow-up and explore associations with standard care treatment procedures and resilience factors upon first presenting at Child and Adolescent Mental Health Services.

**Methods** This study is part of a prospective longitudinal cohort study: The Health Survey in Department of Children and Youth, St. Olavs hospital, Norway. A clinical population of 717 (43.5% of eligible) adolescents aged 13–18 years participated in the first study visit (T1, 2009–2011). Of these, 447 adolescents with psychiatric disorders, with treatment history from medical records and self-reported resilience factors (Resilience Scale for Adolescents; READ) at T1, reported symptom load (Achenbach System of Empirically Based Assessment - Youth Self Report; YSR) three years later aged 16–21 years (T2).

**Result** At T1, 93.0% received individual treatment. The frequency of psychotherapy and medication varied by disorder group and between genders. Overall, psychotherapy was more frequent among girls, whereas medication was more common among boys. Total READ mean value (overall 3.5, SD 0.8), ranged from patients with mood disorders (3.0, SD 0.7) to patients with Attention Deficit Hyperactivity disorder (3.7, SD 0.7), and was lower for girls than boys in all diagnostic groups. At T2, the YSR Total Problem mean T-score ranged across the diagnostic groups (48.7, SD 24.0 to 62.7, SD 30.2), with highest symptom scores for those with mood disorders at T1, of whom 48.6% had T-scores in the borderline/clinical range ( $\geq 60$ ) three years later. Number of psychotherapy sessions was positively associated and Total READ score was negatively associated with the YSR Total Problems T-score (regression coefficient  $\beta = 0.5$ , CI (0.3 to 0.7),  $p < 0.001$  and  $\beta = -15.7$ , CI (-19.2 to -12.1),  $p < 0.001$ , respectively). The subscale Personal Competence was associated with the lowest Total Problem score for both genders.

**Conclusions** Self-reported symptom load was substantial after three years, despite comprehensive treatment procedures. Higher self-reported resilience characteristics were associated with lower symptom load after three years. These results highlight the burden of adolescent psychiatric disorders, the need for extensive interventions and the importance of resilience factors for a positive outcome.

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BMC Psychiatry. 2021 Aug;21:405.

**SECULAR TRENDS AND REGIONAL VARIATIONS IN PHARMACOTHERAPY OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) AMONG CHILDREN AND ADOLESCENTS IN GERMANY.**

**Akmatov MK, Holstiege J, BÄtzing J.**

**BACKGROUND:** The study aim was to examine the secular trends and regional variations in pharmacotherapy of children and adolescents with attention-deficit/hyperactivity disorder (ADHD) in Germany.

**METHODS:** We used nationwide drug prescription data of outpatient care (2009 to 2016). The study population comprised patients aged between 5 and 14 years with the diagnoses "hyperkinetic disorders" (ICD-10 code F90) (e.g.  $n=262,766$  in 2016). The examined drugs were methylphenidate, amphetamines, atomoxetine and guanfacine.

**RESULTS:** Overall, the proportion of patients received any prescription showed a decreasing trend over years (2010, 51%; 2016, 44%). The proportion of methylphenidate prescription was higher in Western than Eastern federal states. However, atomoxetine was more often prescribed in Eastern than Western federal states. The proportion of methylphenidate prescriptions issued by pediatric psychiatrists increased from 28% (2009) to 41% (2016).

**CONCLUSION:** A decreasing trend in use of pharmacotherapy may be explained by prescription restrictions issued by the Federal Joint Committee in recent years

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BMJ Open. 2021 Aug;11:e045443.

**STUDY PROTOCOL OF A RANDOMISED TRIAL OF SUMMER STRIPES: A PEER-DELIVERED HIGH SCHOOL PREPARATORY INTERVENTION FOR STUDENTS WITH ADHD.**

**Zulauf-Mccurdy CA, Coxe SJ, Lyon AR, et al.**

**INTRODUCTION:** High schoolers with attention-deficit/hyperactivity disorder (ADHD) experience substantial impairments, particularly in the school setting. However, very few high school students with ADHD receive evidence-based interventions for their difficulties. We aim to improve access to care by adapting evidence-based psychosocial intervention components to a low-resource and novel school-based intervention model, Summer STRIPES (Students Taking Responsibility and Initiative through Peer Enhanced Support). Summer STRIPES is a brief peer-delivered summer orientation to high school with continued peer-delivered sessions during ninth grade.

**METHODS AND ANALYSIS:** Participants will be 72 rising ninth grade students with ADHD who are randomised to receive either Summer STRIPES or school services as usual. Summer STRIPES will be delivered by 12 peer interventionists in a school setting. Outcomes will be measured at baseline, start of ninth grade, mid-ninth grade and end-of-ninth grade. At each assessment, self, parent and teacher measures will be obtained. We will test the effect of Summer STRIPES (compared with school services as usual) on ADHD symptoms and key mechanisms (intrinsic motivation, extrinsic motivation, executive functions) as well as key academic outcomes during the ninth-grade year (Grade Point Average (GPA), class attendance).

**ETHICS AND DISSEMINATION:** Findings will contribute to our understanding of how to improve access and utilisation of care for adolescents with ADHD. The protocol is approved by the institutional review board at Seattle Children's Research Institute. The study results will be disseminated through publications in peer-reviewed journals and presentations at scientific conferences.

**TRIALS REGISTRATION NUMBER:** NCT04571320; pre-results

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Dev Psychopathol. 2021 Aug;33:767-77.

**INCREASED PUPIL DILATION TO HAPPY FACES IN CHILDREN WITH HYPERACTIVE/IMPULSIVE SYMPTOMS OF ADHD.**

**Kleberg JL, Frick MA, Brocki KC.**

Attention-deficit/hyperactivity disorder (ADHD) is associated with disrupted emotional processes including impaired regulation of approach behavior and positive affect, irritability, and anger. Enhanced reactivity to emotional cues may be an underlying process. Pupil dilation is an indirect index of arousal, modulated by the autonomic nervous system and activity in the locus coeruleus-noradrenergic system. In the current study, pupil dilation was recorded while 8- to 12- year old children (n = 71, 26 with a diagnosis of ADHD and 45 typically developing), viewed images of emotional faces. Parent-rated hyperactive/impulsive symptoms were uniquely linked to higher pupil dilation to happy, but not fearful, angry, or neutral faces. This was not explained by comorbid externalizing symptoms. Together, these results suggest that hyperactive/impulsive symptoms are associated with hyperresponsiveness to approach-related emotional cues across a wide range of symptom severity

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Dyslexia. 2021 Aug;27:342-54.

**THE ASSOCIATION BETWEEN ANXIETY AND ACADEMIC PERFORMANCE IN CHILDREN WITH READING DISORDER: A LONGITUDINAL COHORT STUDY.**

**Hossain B, Bent S, Hendren R.**

The purpose of this study was to examine the association between anxiety and overall academic performance (AP) in children with reading disorder (RD). This two-year longitudinal cohort study included 128 participants (aged 7-14 years) with RD. Anxiety symptoms were evaluated using the School Anxiety Scale - Teacher Report for the first year and the eight-item Spence Children's Anxiety Scale for the second year. AP was assessed by teacher ratings of progress in academic content areas, including reading, writing and math. Teachers completed evaluations every 3 months. We standardized all scores (to z scores). Multivariate linear regression models (adjusting for age, sex and Attention-Deficit/Hyperactivity Disorder symptoms) assessed the association cross-sectionally at each timepoint of survey completion. Repeated measures analysis using mixed models assessed the relationship longitudinally. Results from both univariate and multivariate

analyses showed anxiety being significantly negatively associated with AP in children with RD, both cross-sectionally and longitudinally. Importantly, increased anxiety was significantly associated with reduced AP over time within an individual (adjusted  $\beta = -0.22$ ,  $p = .002$ ). This lends support to screening for anxiety disorders in children with RD. Future research should examine the directionality of this relationship, potential mediators in the pathway and whether interventions to reduce anxiety increase AP

Indian J Ophthalmol. 2021 Aug;69:2004-11.

**PERCEPTUAL VISUAL DYSFUNCTION IN CHILDREN - AN INDIAN PERSPECTIVE.**

**Pehera NK, Dutton GN.**

Perceptual visual dysfunction (PVD) comprises a group of vision disorders resulting from dysfunction of the posterior parietal and/or temporal lobes. Often, affected children have normal/near normal visual acuities and/or visual fields, but have difficulties in activities of daily living involving the use of vision. PVDs are known to be common among children with risk factors such as a history of prematurity and/or neurodevelopmental disorders. The inferior temporal lobes and ventral stream transform visual signals into perception, while the posterior parietal lobes and dorsal stream transform visual signals to non-consciously map the scene to guide action and facilitate attention. Dysfunction of these can lead to specific visual impairments that need to be identified during history taking, triggering ascertainment of further details by a structured inventory approach. Clinical tests to elicit dorsal and ventral stream visual dysfunctions have good specificity but low sensitivity. Neuropsychologists are rarely available in the developing world to perform detailed assessments, but there are a few tests that can be used by eye care professionals with some training. Optical coherence tomography (OCT) showing thinning of the ganglion cell layer and retinal nerve fiber layer is being explored as a potential tool for rapid assessment in the clinic. The behavioral outcomes of PVD can mimic psychological conditions including autism spectrum disorder, attention deficit hyperactivity disorder, specific learning disability, and intellectual impairment, and one needs to be aware of overlap among these differential diagnoses. A practical functional approach providing working solutions for each child's set of difficulties in day-to-day activities is needed

Injury. 2021 Aug;52:2244-50.

**A RETROSPECTIVE OBSERVATIONAL COHORT STUDY: EPIDEMIOLOGY AND OUTCOMES OF PEDIATRIC UNINTENTIONAL FALLS IN US EMERGENCY DEPARTMENTS.**

**Nguyen QP, Saynina O, Pirrotta EA, et al.**

**INTRODUCTION:** The objective is to determine how outcomes from unintentional falls differ for children with and without developmental disabilities, with a sensitivity analysis specifically examining those with ADHD.

**MATERIALS AND METHODS:** This is a retrospective observational cohort study of 2010-2015 data from the Nationwide Emergency Department Sample (NEDS). The NEDS is a sampling of ED visits across 953 hospitals in 36 states. Unintentional falls for children with and without developmental disabilities were compared, adjusting for age, sex, payment source, income, mechanism, injury severity score (ISS). A sensitivity analysis was then performed for children with ADHD ( $n=139,642$ ) and those without any developmental disabilities. A priori chosen outcomes included hospital admission, length of stay, intubation, and surgery. Logistic regression analysis estimated adjusted odds ratios for outcomes.

**RESULTS:** Among children who presented to the ED with unintentional falls ( $n=13,217,237$ ), there were 223,445 (1.7%) with developmental disabilities. The majority of those with developmental disabilities were male, ages 10-14 years. Compared to children without developmental disabilities, those with developmental disabilities were more likely to have an inpatient admission ( $aOR=2.27$ , 95%  $CI=2.10-2.44$ ), length of stay more than 2 days ( $aOR=1.73$ , 95%  $CI=1.51-1.98$ ), intubation ( $aOR=4.77$ , 95%  $CI=3.62-6.27$ ) and surgery ( $aOR=2.11$ , 95%  $CI=1.93-2.32$ ). A sensitivity analysis showed that 139,642 (1%) of children ages 5-17 years had ADHD. Of those with ADHD, the majority was also male, ages 10-14 years. Compared to children without ADHD, those with ADHD had a higher odds of inpatient admission ( $aOR=1.74$ , 95%  $CI=1.58-1.91$ ), length of stay greater than 2 days ( $aOR=1.59$ , 95%  $CI=1.37-1.85$ ), intubation ( $aOR=3.96$ , 95%  $CI=2.73-5.73$ ), and surgery ( $aOR=1.82$ , 95%  $CI=1.60-2.06$ ).

**CONCLUSIONS:** Children with developmental disabilities, in particular those with ADHD, who experience falls are often older and male. They had greater odds of poor outcomes. These children need additional anticipatory guidance and attention to adequate treatment to prevent injuries from unintentional falls

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Int Braz J Urol. 2021 Sep;47:979-81.

**EDITORIAL COMMENT: ASSOCIATION BETWEEN ATTENTION DEFICIT HYPERACTIVITY DISORDER AND LOWER URINARY TRACT SYMPTOMS IN CHILDREN: DO THEY MEAN WHAT WE PRESUME THEM TO BE?**  
**Combs AJ.**

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Int Braz J Urol. 2021 Sep;47:969-78.

**ASSOCIATION BETWEEN ATTENTION DEFICIT HYPERACTIVITY DISORDER AND LOWER URINARY TRACT SYMPTOMS IN CHILDREN AND ADOLESCENTS IN A COMMUNITY SETTING.**

**Vasconcelos MMA, Bastos JN, Arana IE, et al.**

**INTRODUCTION:** The present study aims to investigate the prevalence of lower tract urinary symptoms (LUTS) and symptoms of attention-deficit/hyperactivity disorder (ADHD) in children and adolescents and their association in a community setting using validated scoring instruments.

**MATERIALS AND METHODS:** A cross-sectional study was carried out from February 2015 to December 2019, during which the parents or guardians of 431 children and adolescents from 5 to 13 years of age, attending a general pediatric outpatient clinic were interviewed.

**RESULTS:** The prevalence of ADHD symptoms and LUTS were 19.9% and 17.9%, respectively. Of the 82 children and adolescents with ADHD, 28% (23) had LUTS (OR 2.31, 95% CI 1.28 to 3.75,  $p=0.008$ ). Mean total DVSS score in children in the group of children presenting ADHD symptom was significantly higher than those without ADHD symptom ( $10.2\pm 4.85$  vs.  $4.9\pm 2.95$ ,  $p=0.002$ ). Urgency prevailed among LUTS as the most frequent symptom reported by patients with ADHD symptoms ( $p=0.004$ ). Analyzing all subscales of the DVSS, the items "When your child wants to pee, can't he wait?" "Your child holds the pee by crossing his legs, crouching or dancing?" were higher in those with ADHD symptoms ( $p=0.01$  and  $0.02$ , respectively). Functional constipation was present in 36.4% of children with LUTS and 20.7% without LUTS (OR 4.3 95% CI 1-5.3  $p=0.001$ ).

**CONCLUSION:** Children and adolescents with ADHD symptoms are 2.3 times more likely to have LUTS. The combined type of ADHD was the most prevalent among them

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Int J Clin Pract. 2021 Aug;75:e14330.

**EVALUATING THE LIKELIHOOD TO BE HELPED OR HARMED AFTER TREATMENT WITH VILOXAZINE EXTENDED-RELEASE IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Nasser A, Kosheleff AR, Hull JT, et al.**

**AIMS:** When clinicians evaluate potential medications for their patients, they must weigh the probability of a treatment's benefits against the possible risks. To this end, the present analyses evaluate the novel nonstimulant viloxazine extended-release (viloxazine ER) using measures of effect size to describe the potential benefits of its treatment in children and adolescents with attention-deficit/hyperactivity disorder (ADHD) as well as the risk of discontinuation because of intolerable adverse events.

**METHODS:** These post hoc analyses use pooled data from four pivotal Phase 3 trials in paediatric patients treated with viloxazine ER. The Likelihood to be Helped or Harmed (LHH) effect size measure was calculated to describe the probability of patients benefiting from treatment vs discontinuing. The Number Needed to Treat (NNT) was calculated from frequently used thresholds of response. The Number Needed to Harm (NNH) was calculated using discontinuations because of adverse events.

**RESULTS:** LHH values for viloxazine ER ranged from 5 to 13, suggesting that subjects were 5-13 times more likely to benefit from, rather than discontinue, viloxazine ER treatment. Specifically, NNT values for viloxazine ER treatment ranged from 6 to 7. NNH values for viloxazine ER treatment ranged from 31 to 74. By convention, single-digit NNTs ( $<10$ ) suggest the intervention is potentially useful, while NNH values  $\geq 10$  for adverse events suggest it is potentially safe or tolerable.

**CONCLUSIONS:** These results indicate that patients with ADHD are likely to benefit from treatment with viloxazine ER, and are unlikely to discontinue, as viloxazine ER treatment was associated with favourable LHH, NNT, and NNH values. Clinicaltrials.gov: NCT03247530, NCT03247543, NCT03247517, NCT03247556

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Int J Environ Res Public Health. 2021 Aug;18.

**PREDICTORS OF DEPRESSIVE SYMPTOMS IN CAREGIVERS OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A ONE-YEAR FOLLOW-UP STUDY.**

***Chou WJ, Hsiao RC, Chang CC, et al.***

This 1-year follow-up study examined the predictive values of the demographics, depressive symptoms, stress-coping orientations, and perceived family support of caregivers as well as the internalizing, externalizing and ADHD symptoms of children with attention-deficit/hyperactivity disorder (ADHD) at baseline on the depressive symptoms of the caregivers after 1 year. A total of four hundred caregivers of children with ADHD were recruited. The baseline levels of the caregivers' depressive symptoms, stress-coping orientations, and perceived family support and the internalizing and externalizing problems of the children were assessed using the Center for Epidemiological Studies Depression Scale, the Coping Orientation to Problems Experienced, Family Adaptation, Partnership, Growth, Affection, Resolve Index, and the Child Behavior Checklist For Ages 6-18, respectively. Their predictions for the caregiver's depressive symptoms 1 year after the baseline were examined using linear regression analysis. In total, 382 caregivers of children with ADHD underwent the follow-up assessment 1 year from the baseline. A marital status of being separated or divorced, less effective coping and depressive symptoms orientation, and children with internalizing problems and ADHD symptoms at baseline were positively associated with the caregivers' depressive symptoms at follow-up, whereas the caregivers' perceived family support and an emotion-focused coping orientation at baseline were negatively associated with depressive symptoms at follow-up. Multiple characteristics of the caregivers and children with ADHD at baseline predicted the caregivers' depressive symptoms 1 year later

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Int J Nurs Stud. 2021 Aug;120:103956.

**PATTERNS OF MENTAL HEALTH SERVICE USE AMONG MEDICAID-INSURED YOUTHS TREATED BY NURSE PRACTITIONERS AND PHYSICIANS: A RETROSPECTIVE COHORT STUDY.**

***Yang BK, Idzik S, Evans P.***

**BACKGROUND:** Despite the growing involvement of nurse practitioners in mental health services for children and adolescents, little is known about the patterns of mental health service use among youths treated by nurse practitioners compared to those by physicians.

**OBJECTIVES:** To identify new users of psychotropic medications initiated by nurse practitioners and physicians among Medicaid-insured youths and to assess if receiving psychosocial services prior to or concurrent with medication initiation differs among youths treated by provider and specialty type.

**DESIGN:** A retrospective cohort study.

**SETTINGS:** We used Medicaid-insurance claims data in one mid-Atlantic state in the US.

**PARTICIPANTS:** A total 12,991 Medicaid-insured youths aged 0-20 years who started psychotropic medications prescribed by nurse practitioners or physicians with primary care or psychiatric specialty during 2013-2014.

**METHODS:** Providers were grouped into nurse practitioners and physicians and into primary care and psychiatric specialty. Descriptive statistics were performed to compare each class of psychotropic medications initiated and psychiatric diagnoses of enrollees according to provider type within each specialty. Using multinomial logistic regression with psychiatrists as a reference group, we estimated the odds of having a type of prescriber for psychotropic medication initiation for youths who received psychosocial services prior to a new start of the medication and concurrently, compared to that for those who did not, after adjusting for patients' demographic characteristics and diagnosis.

**RESULTS:** Youths served by nurse practitioners resided in small and non-metropolitan areas significantly more often than those served by their physician counterparts. There was no major difference in a class of



psychotropic medications initiated by nurse practitioners and physicians within each specialty type, except a higher proportion of antidepressants (13.5% versus 10.5%) and a lower proportion of attention deficit hyperactivity disorder medications prescribed (68.8% versus 74.0%) by primary care nurse practitioners compared to their physician counterparts. Youths who received psychosocial services prior to medication initiation were less likely to have primary care physicians (Adjusted odds ratio=0.15, 95% confidence interval=0.82, 1.33) or primary care nurse practitioners (Adjusted odds ratio=0.16, 95% confidence interval=0.12, 0.20) as their initiating prescriber than those who did not.

**CONCLUSIONS:** Youths treated by nurse practitioners and physicians with or without psychiatric specialty showed unique patterns of mental health service use. Our findings can be used to build effective collaborations among provider and specialty type for quality of mental health services delivered to targeted populations in need

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Int J Pediatr Otorhinolaryngol. 2021 Aug;147:110781.

**DOES PERIOPERATIVE KETOROLAC INCREASE BLEEDING RISK AFTER INTRACAPSULAR TONSILLECTOMY?**

**Kolb CM, Jain N, Schillinger K, et al.**

**IMPORTANCE:** Conflicting evidence exists regarding the post-tonsillectomy bleed risk associated with perioperative ketorolac use in the pediatric population. Surgical technique for tonsillectomy can further confound this risk.

**OBJECTIVE:** The primary objective was to retrospectively quantify the post-tonsillectomy bleed rate after single-dose administration of ketorolac in pediatric patients following intracapsular tonsillectomy. The secondary objective was to determine if age, sex, body mass index, medical comorbidities, and indication for surgery increased post-tonsillectomy bleed risk.

**DESIGN:** Retrospective cohort study of 1920 children who underwent intracapsular tonsillectomies between January 2017 and December 2018.

**SETTING:** This study was completed at a tertiary-care pediatric referral center.

**PARTICIPANTS:** 1920 children who underwent intracapsular tonsillectomies between January 2017 and December 2018 at a single tertiary-care children's hospital.

**EXPOSURES:** Patients were divided into two cohorts: 1458 patients (75.9%) received ketorolac (K+), and 462 (24.1%) did not (NK). Age, sex, body mass index, comorbidities, and indication for surgery also were evaluated for association with post-tonsillectomy bleed risk.

**MAIN OUTCOME(S) AND MEASURE(S):** Primary study outcome for both cohorts was post-tonsillectomy hemorrhage requiring operative intervention.

**RESULTS:** 1920 study participants were included with an average age of 6.5 years; 51.5% of participants were males; and, 63.9% were white. Overall, the postoperative bleeding rate was 1.5%. However, there was no significant difference when comparing bleeding rates for the ketorolac group and the non-ketorolac group (1.4%-1.7%; P = .82) Age, chronic tonsillitis, higher body mass index Z-scores, attention-deficit/hyperactivity disorder, and behavioral diagnoses were statistically significant risk factors for post-tonsillectomy hemorrhage.

**CONCLUSIONS AND RELEVANCE:** Single-dose postoperative ketorolac does not appear to be associated with increased risk of post-tonsillectomy bleed in pediatric patients undergoing intracapsular tonsillectomy. Providers should not avoid using ketorolac in patients undergoing intracapsular tonsillectomy due to concerns over bleeding risk

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J Affect Disord. 2021 Sep;292:223-26.

**NEURAL CORRELATES OF IRRITABILITY IN A COMMUNITY SAMPLE OF CHILDREN.**

**Mulraney M, Sciberras E, Gulenc A, et al.**

Irritability has been associated with aberrant patterns of neural activation, yet little is known about structural brain correlates of irritability. As such, we aimed to investigate associations between irritability and gray matter volume (GMV) in a community sample of children enriched for irritability. The sample comprised children (n=162) aged 9-11 years with and without Attention-Deficit/Hyperactivity Disorder (ADHD), participating in a cohort study with magnetic resonance imaging data available. Mixed effects linear

regression analyses tested the associations between irritability symptoms and regional GMV (extracted using Freesurfer). Irritability was associated with smaller gray matter volume across multiple brain regions implicated in executive functioning, and emotion and reward processing including frontal regions and the cingulate

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J Am Acad Child Adolesc Psychiatry. 2021 Aug;60:952-54.

**EDITORIAL: TESTING THE VALIDITY OF THE LIMITED PROSOCIAL EMOTIONS SPECIFIER.**

**Frick PJ.**

Colins et al.(1) address a timely and important topic. Specifically, both the DSM-5 and the International Classification of Diseases, 11th edition (ICD-11) for the first time introduced a specifier (ie, with limited prosocial emotions) for the diagnosis of conduct disorder (DSM-5) or for the diagnoses of conduct-dissocial and oppositional defiant disorders (ICD-11) to designate those persons with these disorders who also show elevated levels of callous-unemotional (CU) traits. This change was based on research showing that children and adolescents with significant conduct problems who also show elevated levels of CU traits seem to be an etiologically and clinically important subgroup of persons with these disorders.(2,3) The DSM-5 chose not to conduct field trials to test the validity of new diagnoses (only reliability) and, instead, considers research on new diagnoses as the field trials for future revisions of the manual.(4) Thus, the work by Colins et al.(1) is critical for this validation process. The study by Colins et al. has a number of methodological features that make their results particularly informative.(1) The most notable feature was the use of a large nonreferred sample that was followed from 3 to 5 years of age to 11 to 13 years of age with a high retention rate. The authors also provide a nice summary of past attempts to validate the LPE specifier, which has provided mixed support at best. However, they also note that most of these studies did not use the full criteria for the LPE specifier and that this is an important limitation that Colins et al. overcome, especially given that the criteria include only 4 symptoms. Thus, the authors' findings that children with the LPE specifier and serious conduct problems exhibited more conduct disorder (CD) symptoms and comorbid problems (ie, fearlessness, symptoms of oppositional defiant disorder, and attention-deficit/hyperactivity disorder [ADHD]) and were at higher risk for future CD symptoms 3 years later are critical advances

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J Am Acad Child Adolesc Psychiatry. 2021 Aug;60:1020-29.

**THE DSM-5 LIMITED PROSOCIAL EMOTIONS SPECIFIER FOR CONDUCT DISORDER: COMORBID PROBLEMS, PROGNOSIS, AND ANTECEDENTS.**

**Colins OF, Fanti KA, Andershed H.**

**OBJECTIVE:** A limited prosocial emotions (LPE) subtype of conduct disorder (CD) has been added to the DSM-5. Empirical studies on this categorically defined subtype are scarce, and existing work is predominantly cross-sectional. Hypotheses surrounding the LPE subtype that relate to comorbidity, prognosis, and developmental antecedents, and overlap with psychopathic personality, have received no or little scrutiny.

**METHOD:** These knowledge gaps were addressed in a community sample of 1,839 children 8 to 10 years of age who were enrolled in the study in early childhood (age 3-5 years) and were followed up in early adolescence (age 11-13 years). Parents and teachers completed questionnaires that tap theoretically and clinically relevant features.

**RESULTS:** Children with the LPE subtype exhibited more CD symptoms and comorbid problems, including fearlessness, and symptoms of oppositional defiant disorder and attention-deficit/hyperactivity disorder. These children were also at higher risk for future CD symptoms at the 3-year follow-up. Additionally, fearlessness, callous-unemotional traits, interpersonal traits, and harsh parenting assessed in early childhood were identified as developmental antecedents of the LPE subtype. Findings tentatively suggest that the LPE subtype is a heterogeneous group differentiated on other psychopathic personality traits.

**CONCLUSION:** The LPE subtype appears to identify a troubled, etiologically distinct group of children with conduct problems who are at heightened risk for future maladjustment. Findings can inform the underlying mechanisms related to the LPE subtype, and can lead to the development and improvement of prevention and intervention programs for children with conduct problems

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J Atten Disord. 2021 Aug;25:1479-96.

**INTERVENTIONS FOR ADOLESCENTS WITH ADHD TO IMPROVE PEER SOCIAL FUNCTIONING: A SYSTEMATIC REVIEW AND META-ANALYSIS.**

**Morris S, Sheen J, Ling M, et al.**

**Objective:** Peer social functioning difficulties characteristic of ADHD persist into adolescence, but the efficacy of interventions for this age group remains unclear.

**Method:** A systematic search of nonpharmacological interventions for adolescents with ADHD (10-18 years) identified 11 trials addressing social functioning, of which eight were included in meta-analyses.

**Results:** Random effects meta-analyses of four randomized trials found no differences in social functioning between treatment and control groups by parent- ( $g = -0.08 [-0.34, 0.19]$ ,  $k = 4$ ,  $N = 354$ ) or teacher-report ( $g = 0.17 [-0.06, 0.40]$ ,  $k = 3$ ,  $N = 301$ ). Meta-analyses of nonrandomized studies indicated participants' social functioning improved from baseline to postintervention by parent-report, but not teacher- or self-report. All trials had a high risk of bias.

**Conclusion:** These results highlight the paucity of research in this age group. There is little evidence that current interventions improve peer social functioning. Clearer conceptualizations of developmentally relevant targets for remediation may yield more efficacious social interventions

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J Atten Disord. 2021 Aug;25:1441-54.

**DO GERMAN CHILDREN DIFFER? A VALIDATION OF CONNERS EARLY CHILDHOOD.**

**Türk S, Harbarth S, Bergold S, et al.**

**Objective:** The present study aimed to validate the German version of the Conners Early Childhood (EC)<sup>TM</sup> among German-speaking children.

**Method:** A total of 720 parental and 599 childcare provider ratings of 2- to 6-year-old children were surveyed throughout Germany. Validity was assessed by calculating exploratory factor analyses (EFAs) and confirmatory factor analyses (CFAs), and a series of multivariate analyses of variance (MANOVAs) to analyze associations between Conners EC<sup>TM</sup> symptom ratings and sociodemographic variables. In addition, parent and childcare provider ratings of Conners EC<sup>TM</sup> scales were correlated with a number of other well-validated German measures assessing preschoolers' behaviors.

**Results:** Although the EFA yielded different factors than the original scales, CFA revealed acceptable to good model fits.

**Conclusion:** Overall, we confirmed the factor structure of the Conners EC's<sup>TM</sup> American original within the German validation. The use of the American factor structure is justified and can be recommended to facilitate international research on psychopathology in early childhood

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J Atten Disord. 2021 Aug;25:1395-406.

**BEHAVIORAL AND NEURAL MARKERS OF EMOTION COMPETENCE AS PREDICTORS OF LATER PSYCHOPATHOLOGY IN CHILDREN WITH AND WITHOUT HYPERACTIVE/IMPULSIVE SYMPTOMS.**

**Brown HR, Hareli M, Breaux R, et al.**

**Objective:** We examined behavioral and neural markers of emotion competence in young children as predictors of psychopathology, and as mediators of the relation between hyperactivity/impulsivity (H/I) and psychopathology.

**Method:** At Time 1 (T1), children ( $n = 49$ ; ages 4-7 years) with and without H/I symptoms completed a frustration task. Frustration, observed emotion, and neural activity (P1, N2, and P3 event-related potentials) were measured. Symptoms of psychopathology were collected 18 months later

(Time 2; T2). **Results:** T1 lability, negative affect, and frustration predicted T2 depression and aggression symptomatology, controlling for T1 symptoms. Children with difficulty allocating neural resources during and after frustration were at risk for depression, aggression, and anxiety symptoms, controlling for earlier symptoms. P3 amplitudes during recovery mediated the relation between H/I and later depression.

**Conclusion:** Markers of emotion competence contribute to psychopathology symptoms, particularly in children at risk for attention-deficit/hyperactivity disorder (ADHD). Emotion competence skills may be useful intervention targets

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J Atten Disord. 2021 Aug;25:1384-94.

**IS THE QbMINI A VALID INSTRUMENT FOR ADHD ASSESSMENT?**

**Hamadache S, Hoberg K, Zaplana LS, et al.**

**Objective:** Few neuropsychological measurement tools of attention can assess preschoolers despite adequate instruments' potential to facilitate early diagnostic processes, which are currently demanding. This study's objective was to evaluate the QbMini, an attention-deficit hyperactive disorder (ADHD) measurement tool for preschoolers.

**Method:** QbMini performances of 37 5-year-old ADHD patients, 55 healthy controls, and 26 children with specific language impairment (SLI) were compared using univariate analyses of variance. The test's predictive power was evaluated using receiver operating characteristics (ROC) analyses and compared to a parental rating scale. Finally, the scales were compared by correlating their respective scores.

**Results:** The QbMini measures ADHD symptoms and reliably differentiates between healthy children and patients, but not between children with ADHD and children with SLI.

**Conclusion:** The QbMini can indicate presence and strength of ADHD symptoms, but fails to diagnose ADHD. It measures symptoms in a different way than parental ratings and might be stronger in distinguishing between hyperactivity and inattention

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J Atten Disord. 2021 Aug;25:1374-83.

**IMPACT OF ADHD ON HOUSEHOLD CHORES.**

**Spaulding SL, Fruitman K, Rapoport E, et al.**

**Objective:** To assess the relationship between ADHD and performance of household chores.

**Method:** A 72-question online questionnaire was developed to collect demographic/clinical information as well as parents' assessment of their child's performance of self-care (SC) and family-care (FC) chores.

**Results:** The sample consists of 797 primary caregivers of children with ADHD. The overwhelming majority of parents believed that ADHD to some extent affected their child's ability to independently and satisfactorily complete SC and FC chores. An inverse relationship was noted between parent ratings of a child's ability to do chores independently and satisfactorily and the likelihood they believed ADHD affected chore performance. There was no difference in chore performance between children with or without co-morbid oppositional defiant disorder.

**Conclusion:** Given that household routines, including chores, play an important role in children's development and psychosocial adjustment, clinicians must be sensitive to the adverse impact that ADHD may have in this regard

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J Atten Disord. 2021 Aug;25:1429-40.

**HEAD MOTION DURING MRI PREDICTED BY OUT-OF-SCANNER SUSTAINED ATTENTION PERFORMANCE IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Thomson P, Johnson KA, Malpas CB, et al.**

**Objective:** To characterize head movements in children with ADHD using an ex-Gaussian distribution and examine associations with out-of-scanner sustained attention.

**Method:** Fifty-six children with ADHD and 61 controls aged 9 to 11 years completed the Sustained Attention to Response Task (SART) and resting-state functional magnetic resonance imaging (fMRI). In-scanner head motion was calculated using ex-Gaussian estimates for mu, sigma, and tau in delta variation signal and framewise displacement. Sustained attention was evaluated through omission errors and tau in response time on the SART.

**Results:** Mediation analysis revealed that out-of-scanner attention lapses (omissions during the SART) mediated the relationship between ADHD diagnosis and in-scanner head motion (tau in delta variation

signal), indirect effect:  $B = 1.29$ , 95% confidence interval (CI) = [0.07, 3.15], accounting for 29% of the association.

**Conclusion:** Findings suggest a critical link between trait-level sustained attention and infrequent large head movements during scanning (tau in head motion) and highlight fundamental challenges in measuring the neural basis of sustained attention

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J Atten Disord. 2021 Aug;25:1347-50.

**ADHD DIAGNOSIS AND DRUG USE ESTIMATES IN FRANCE: A CASE FOR USING HEALTH CARE INSURANCE DATA.**

**Ponnou S, Haliday H.**

**Objective:** Prevalence estimates for ADHD have been debated for decades. In France, the only available study states the prevalence rate in France ranges from 3.5% to 5.6% of children aged 6 to 12. It also evaluates that 3.48% of children aged 6 to 12 are treated with psychostimulants. The article uses a different method to determine whether these estimates hold true.

**Method:** Estimating ADHD diagnosis and methylphenidate prescription rates can be done by analyzing national health care insurance system's data. We used data from the French Healthcare Insurance as reported by the National Agency for Medicines and Health Products Safety.

**Results:** We claim that an adequate estimate of the ADHD prevalence rate in France fluctuates around 0.3% of children aged 6 to 11. Discussion: Methodological biases in ADHD prevalence studies and factors contributing to the low level of prescription in France need to be assessed.

**Conclusion:** We call for supplementary investigations in health care insurance databases to conduct contradictory studies

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J Atten Disord. 2021 Aug;25:1407-16.

**PROBABILISTIC LEARNING IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Luman M, Janssen TWP, Bink M, et al.**

**Objective:** The current study examined instrumental learning in ADHD.

**Method:** A total of 58 children with ADHD and 58 typically developing (TD) children performed a probabilistic learning task using three reward probability conditions (100%, 85%, 70% reward). After a learning phase, application of what was learned was assessed in a test phase.

**Results:** Results showed that children with ADHD performed less accurate compared with TD children during the learning phase, particularly in the 100% and 85% reward probability conditions. These findings were accompanied by a blunted learning rate in the first few task trials. Furthermore, children with ADHD showed poorer application of what was learned.

**Conclusion:** To conclude, children with ADHD show initial learning problems, but increased performance in a similar manner as TD children independent of the probability of reward, although they fail to apply their knowledge. Findings are of clinical relevance as the application of knowledge is important to successfully adapt to daily challenges in life

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J Atten Disord. 2021 Aug;25:1497-505.

**PARENTAL INVOLVEMENT OF PARENTS OF CHILDREN WITH ADHD: A FIRST POPULATION STUDY.**

**Montes G, Montes SA.**

**Objective:** The purpose of the study was to create a national profile of parental involvement for parents of children with ADHD in the United States.

**Method:** Using the 2016 Parent and Family Involvement in Education Survey, parents of children with ADHD (N = 1,600) were compared with other parents (N = 11,923) on 32 distinct measures of parental involvement in education.

**Results:** Parents of children with ADHD were more likely to invest more time in communications regarding school and behavior problems, teaching their child time management skills, checking and helping with their homework, whereas they were less likely to engage in athletic sports, attend class or school events, or visit the library.

**Conclusion:** A more systematic approach to encourage and support parental involvement in education for children with ADHD is needed

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J Atten Disord. 2021 Aug;25:1455-65.

**PEER VICTIMIZATION AND POOR ACADEMIC OUTCOMES IN ADOLESCENTS WITH ADHD: WHAT INDIVIDUAL FACTORS PREDICT RISK?**

**Zendarski N, Breaux R, Eadeh HM, et al.**

**Objective:** Examine individual factors associated with peer victimization (PV) in adolescents with attention-deficit/hyperactivity disorder (ADHD) and to examine the association between PV and educational outcomes.

**Method:** Participants were 121 adolescents (M(age) = 13.62, SD = 1.03; 89% boys) with diagnosed ADHD. Using path analysis, we tested whether general adolescent factors (ADHD symptoms, comorbid autism spectrum disorder, cognitive and social functioning, and age) were associated with experiences of PV, and associations between PV and academic outcomes.

**Results:** Deficits in working memory (WM) and peer relationship problems were weakly and moderately associated with PV, respectively. PV was in turn associated with adolescents' attitudes about school, academic competence, and academic achievement.

**Conclusion:** Adolescents with poor social skills and/or WM difficulties who have ADHD may be particularly vulnerable to being victimized by peers. Failure to identify and manage PV during early adolescence may be connected to poor educational outcomes

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J Atten Disord. 2021 Aug;25:1466-78.

**ROMANTIC RELATIONSHIPS AND SEXUAL BEHAVIOR AMONG ADOLESCENTS WITH ADHD.**

**Margherio SM, Capps ER, Monopoli JW, et al.**

**Objective:** Both qualitative and quantitative analyses were used to (a) describe the romantic and sexual relationships of adolescents with ADHD and (b) examine how ADHD-related impairments (e.g., social skill deficits and emotion dysregulation [ED]) are associated with romantic relationship outcomes in this group.

**Method:** Adolescents with ADHD (N = 171; 80% male; 70% White) responded to questions about their romantic and sexual relationship experiences and ED. Parents provided ratings of ADHD symptoms, ED, and social skills.

**Results:** Adolescents with ADHD reported high rates of romantic relationship turnover and low rates of physical intimacy. More severe self-reported ED was associated with increased likelihood of engaging in romantic relationships, having more romantic relationship partners, increased likelihood of engaging in sexual intercourse, and increased likelihood of engaging in unprotected sex.

**Conclusion:** Early intervention programs that alter the developmental trajectory of romantic relationships among individuals with ADHD may benefit from targeting ED among these youth

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J Pediatr Adolesc Gynecol. 2021 Aug;34:471-76.

**PREPARING FOR PUBERTY IN GIRLS WITH SPECIAL NEEDS: A COHORT STUDY OF CAREGIVER CONCERNS AND PATIENT OUTCOMES.**

**Fei YF, Ernst SD, Dendrinios ML, et al.**

**STUDY OBJECTIVE:** To characterize the patient population with cognitive or physical impairments that presents for anticipatory guidance of puberty, evaluate caregiver concerns with respect to puberty, and describe chosen management strategies and outcomes following menarche.

**DESIGN:** Retrospective cohort study

**SETTING:** Academic tertiary care women and children's hospital

**PARTICIPANTS:** Eligible female patients with special needs up to age 26 years presenting for anticipatory guidance from 2009 to 2018

**MAIN OUTCOME MEASURES:** Primary outcomes included characterization of patients presenting for anticipatory guidance and their reasons for menstrual management. Secondary outcomes were satisfaction with menstrual management and bleeding patterns.

**RESULTS:** A total of 61 patients presented for anticipatory guidance of puberty, on average 13.5 months prior to menarche. Compared to the overall adolescent population with special needs who presented for gynecologic care, patients who had autism spectrum disorder (ASD), were nonverbal, or had attention-deficit/hyperactivity disorder (ADD/ADHD) were more likely to present for a pre-menarchal visit to discuss anticipated pubertal development ( $P < .001$ ,  $P=.009$ , and  $P=.04$ , respectively). More than half of families described potential behavioral changes as their main concern. The majority of post-menarchal patients (80%) desired hormonal management of menses, including 30% of patients who had placement of a levonorgestrel intrauterine device. In all, 96% of patients were satisfied with their final menstrual bleeding pattern; 50% achieved amenorrhea or light spotting.

**CONCLUSIONS:** This study describes the important role of pre-menarchal reproductive counseling for girls with disabilities. Anticipation of puberty causes great anxiety in families and patients, especially those with ASD, ADD/ADHD, and non-verbal status. Providers should consider initiating these conversations early in pubertal development

Lancet Psychiatry. 2021 Sep;8:774-83.

**MAPPING PHENOTYPIC AND AETIOLOGICAL ASSOCIATIONS BETWEEN ADHD AND PHYSICAL CONDITIONS IN ADULTHOOD IN SWEDEN: A GENETICALLY INFORMED REGISTER STUDY.**

**Du RE, Brikell I, Butwicka A, et al.**

**Background** Emerging evidence suggests increased risk of several physical health conditions in people with ADHD. Only a few physical conditions have been thoroughly studied in relation to ADHD, and there is little knowledge on associations in older adults in particular. We aimed to investigate the phenotypic and aetiological associations between ADHD and a wide range of physical health conditions across adulthood.

**Methods** We did a register study in Sweden and identified full-sibling and maternal half-sibling pairs born between Jan 1, 1932, and Dec 31, 1995, through the Population and Multi-Generation Registers. We excluded individuals who died or emigrated before Jan 1, 2005, and included full-siblings who were not twins and did not have half-siblings. ICD diagnoses were obtained from the National Patient Register. We extracted ICD diagnoses for physical conditions, when participants were aged 18 years or older, from inpatient (recorded 1973–2013) and outpatient (recorded 2001–13) services. Diagnoses were regarded as lifetime presence or absence. Logistic regression models were used to estimate the associations between ADHD (exposure) and 35 physical conditions (outcomes) in individuals and across sibling pairs. Quantitative genetic modelling was used to estimate the extent to which genetic and environmental factors accounted for the associations with ADHD.

**Findings** 4 789 799 individuals were identified (2 449 146 [51%] men and 2 340 653 [49%] women), who formed 4 288 451 unique sibling pairs (3 819 207 full-sibling pairs and 469 244 maternal half-sibling pairs) and 1 841 303 family clusters (siblings, parents, cousins, spouses). The mean age at end of follow-up was 47 years (range 18–81; mean birth year 1966); ethnicity data were not available. Adults with ADHD had increased risk for most physical conditions (34 [97%] of 35) compared with adults without ADHD; the strongest associations were with nervous system disorders (eg, sleep disorders, epilepsy, dementia; odds ratios [ORs] 1.50–4.62) and respiratory diseases (eg, asthma, chronic obstructive pulmonary disease; ORs 2.42–3.24). Sex-stratified analyses showed similar patterns of results in men and women. Stronger cross-disorder associations were found between full-siblings than between half-siblings for nervous system, respiratory, musculoskeletal, and metabolic diseases ( $p < 0.007$ ). Quantitative genetic modelling showed that these associations were largely explained by shared genetic factors (60–69% of correlations), except for associations with nervous system disorders, which were mainly explained by non-shared environmental factors.

**Interpretation** This mapping of aetiological sources of cross-disorder overlap can guide future research aiming to identify specific mechanisms contributing to risk of physical conditions in people with ADHD, which could ultimately inform preventive and lifestyle intervention efforts. Our findings highlight the importance of assessing the presence of physical conditions in patients with ADHD.

**Funding** Swedish Research Council; Swedish Brain Foundation; Swedish Research Council for Health, Working Life, and Welfare; Stockholm County Council; StratNeuro; EU Horizon 2020 research and innovation programme; National Institute of Mental Health

Neurology. 2021 Aug;97:S81-S90.

**RECOMMENDATIONS FOR MEASUREMENT OF ATTENTION OUTCOMES IN PRESCHOOLERS WITH NEUROFIBROMATOSIS.**

***Klein-Tasman BP, Lee K, Thompson HL, et al.***

Children with neurofibromatosis type 1 (NF1) are at increased risk for attention problems. While most research has been conducted with school-aged cohorts, preschool-aged children offer a novel developmental window for clinical studies, with the promise that treatments implemented earlier in the developmental trajectory may most effectively modify risk for later difficulties. Designing research studies around the youngest children with NF1 can result in intervention earlier in the developmental cascade associated with NF1 gene abnormalities. Furthermore, clinical trials for medications targeting physical and psychological aspects of NF1 often include individuals spanning a wide age range, including preschool-aged children. In a prior report, the REiNS Neurocognitive Subcommittee made recommendations regarding performance-based and observer-rated measures of attention for use in clinical trials and highlighted the need for separate consideration of assessment methods for young children. The observer-rated Attention-Deficit/Hyperactivity Disorder Rating Scale-Preschool version is recommended as a primary outcome measure. The NIH Toolbox Flanker, Dimensional Change Card Sort, and List Sort Working Memory tasks and Digits Forward from the Differential Ability Scales-2nd Edition (performance-based measures) are recommended as secondary outcome measures. Specific methodologic recommendations for inclusion of preschoolers in clinical trials research are also offered

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Neurosci Biobehav Rev. 2021 Sep;128:64-73.

**ASSESSING UNDERTREATMENT AND OVERTREATMENT/MISUSE OF ADHD MEDICATIONS IN CHILDREN AND ADOLESCENTS ACROSS CONTINENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS.**

***Massuti R, Moreira-Maia CR, Campani F, et al.***

A controversy exists on whether there is an over or underuse of medications for Attention-Deficit/Hyperactivity Disorder (ADHD). We conducted the first meta-analysis to estimate the rate of ADHD pharmacological treatment in both diagnosed and undiagnosed individuals. Based on a pre-registered protocol (CRD42018085233), we searched a broad set of electronic databases and grey literature. After screening 25,676 abstracts, we retained 36 studies including 104,305 subjects, from which 18 studies met our main analysis criteria. The pooled pharmacological treatment rates were 19.1 % and 0.9 % in school-age children/adolescents with and without ADHD, respectively. We estimated that for each individual using medication without a formal ADHD diagnosis, there are three patients with a formal diagnosis who might benefit from medication but do not receive it in the US. Our results indicate both overtreatment/misuse of medication in individuals without ADHD and pharmacological undertreatment in youths with the disorder. Our findings reinforce the need for public health policies improving education on ADHD and discussions on the benefits and limitations of ADHD medications

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Neurosci Biobehav Rev. 2021 Sep;128:735-48.

**THE EFFECTS OF COMBINED PHYSICAL AND COGNITIVE TRAINING ON INHIBITORY CONTROL: A SYSTEMATIC REVIEW AND META-ANALYSIS.**

***Dhir S, Teo WP, Chamberlain SR, et al.***

While strong inhibitory control is critical for health and wellbeing, there are no broadly applicable effective behavioural interventions that enhance it. This meta-analysis examined the neurocognitive rationale for combined physical and cognitive training and synthesised the rapidly growing body of evidence examining combined paradigms to enhance inhibitory control. Across the research to date, there was a small positive effect (n studies = 16, n participants = 832) of combined training on improving inhibitory control. Sub-group analyses showed small-moderate positive effects when the physical component of the combined training was moderately intense, as opposed to low or vigorous intensities; moderate positive effects were found in older adults, as compared to adolescents and adults; and healthy individuals and those with vascular cognitive impairment, as compared to ADHD, ASD, mild cognitive impairment and cancer survivors. This is the first meta-analysis to provide evidence that combined physical, specifically when moderately intense, and



cognitive training has the capacity to improve inhibitory control, particularly when delivered to healthy individuals and those experiencing age-related decline

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Neurosci Biobehav Rev. 2021 Aug;127:899-916.

**CORTISOL RESPONSE TO ACUTE PSYCHOSOCIAL STRESS IN ADHD COMPARED TO CONDUCT DISORDER AND MAJOR DEPRESSIVE DISORDER: A SYSTEMATIC REVIEW.**

**Bernhard A, Mayer JS, Fann N, et al.**

BERNHARD, A., J. S. Mayer, N. Fann, and C. M. Freitag. Cortisol response to acute psychosocial stress in ADHD compared to Conduct Disorder and Major Depressive Disorder: A systematic review. NEUROSCI BIOBEHAV REV XX(X) XXX-XXX, 2020. - Heterogeneous alterations of the cortisol stress response in Attention-deficit/hyperactivity Disorder (ADHD) were recently reported by a systematic literature review. To investigate the moderating effect of frequent psychiatric comorbidities, we systematically searched for studies on cortisol stress response to psychosocial stress in ADHD compared to Conduct Disorder (CD) and Major Depressive Disorder (MDD) following PRISMA guidelines. EBSCOhost and PubMed databases were searched in July 2020, employing relevant keywords. Nineteen studies met inclusion criteria. While blunted cortisol stress response was consistently reported in individuals with CD and/or Oppositional Defiant Disorder (ODD), alterations of cortisol stress response were less pronounced in ADHD. Consistently blunted cortisol stress response in ADHD was only found in children with comorbid CD/ODD. Results on cortisol stress response in children and adolescents with MDD were mixed, and no indication for influence of comorbid MDD on cortisol stress response in ADHD was found. Taken together, altered cortisol stress response in ADHD is driven by comorbidity with disruptive behavior disorders. Limitations of previous research and suggestions for future studies are discussed

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Nord J Psychiatry. 2021 Aug;75:437-46.

**CHANGES IN REFERRAL PATTERNS TO OUTPATIENT CHILD AND ADOLESCENT PSYCHIATRIC SERVICES FROM 2005-2018.**

**Hansen AS, Kjaersdam TuG, Lauritsen MB.**

**INTRODUCTION:** There has been a steep increase in referrals to child and adolescent psychiatric (CAP) services across Western countries. To fit CAP services to the increasing demand, it is important to gain more knowledge about the background for the increase in referrals and to investigate changes in referral patterns over time.

**METHODS:** Cross-sectional observational study comparing referrals to outpatient CAP services from 2005, 2010 and 2018 to the only CAP center in the North Denmark Region.

**RESULTS:** There was a 3.9 times increase in referrals from 2005 to 2018. Referrals for disorders with onset in early childhood (primarily autism and ADHD/ADD) increased from 2005 to 2010 but decreased from 2010 to 2018. There was an increase in the proportion of referrals for emotional disorders from 2010 to 2018. The proportion of girls referred for disorders with onset in early childhood increased from 2005 to 2018. The referral age for these disorders remained relatively high, and this was most pronounced for girls.

**CONCLUSIONS:** There has been significant changes in the referral pattern to outpatient CAP services. The increasing referral rates for girls for disorders with onset in early childhood could indicate improved ability in primary settings to recognize these symptoms in girls. However, late referral to CAP services for these disorders remains an issue. Educational services play an increasing role in referring children for these disorders, and it is important to ensure that they have the competences to identify children in need of assessment by CAP services

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Pediatrics. 2021 Aug;148.

**PRESCRIPTION DRUG DISPENSING TO US CHILDREN DURING THE COVID-19 PANDEMIC.**

**Chua KP, Volerman A, Conti RM.**

**BACKGROUND** After the US coronavirus disease 2019 outbreak, overall prescription dispensing declined but then rebounded. Whether these same trends occurred for children is unknown.

**METHODS** Using the IQVIA National Prescription Audit, which contains monthly dispensing counts from 92% of US retail pharmacies, we assessed changes in the monthly number of prescriptions dispensed to US children aged 0 to 19 years during 2018–2020. We compared dispensing totals in April to December 2020 and April to December 2019 overall, by drug class, and among drug classes that typically treat acute infections (eg, antibiotics) or chronic diseases (eg, antidepressants).

**RESULTS** Between January 2018 and February 2020, the median monthly number of prescriptions dispensed to children was 25 744 758. Dispensing totals declined from 25 684 219 to 16 742 568 between March and April 2020, increased to 19 657 289 during October 2020, and decreased to 15 821 914 during December 2020. Dispensing totals during April to December 2020 (160 630 406) were 27.1% lower compared with April to December 2019 (220 284 613). Among the 3 drug classes accounting for the most prescriptions in 2019, the corresponding percentage changes were –55.6% for antibiotics, –11.8% for attention-deficit/hyperactivity disorder medications, and 0.1% for antidepressants. Among drug classes that typically treat acute infections and chronic diseases, percentage changes were –51.3% and –17.4%, respectively.

**CONCLUSIONS** Prescription dispensing to children declined by one-quarter in April to December 2020 compared with April to December 2019. Declines were greater for infection-related drugs than for chronic disease drugs. Decreased dispensing of the latter is potentially concerning and warrants further investigation. Whether reductions in dispensing of infection-related drugs are temporary or sustained will be important to monitor going forward

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Saudi Med J. 2021 Aug;42:878-85.

**SOCIODEMOGRAPHIC, CLINICAL CHARACTERISTICS, AND SERVICE UTILIZATION OF YOUNG CHILDREN DIAGNOSED WITH AUTISM SPECTRUM DISORDER AT A RESEARCH CENTER IN SAUDI ARABIA: THE ROAD TO AUTISM SPECTRUM DISORDER DIAGNOSIS.**

*Alotaibi AM, Craig KA, Alshareef TM, et al.*

**OBJECTIVES:** To assess how clinical services are accessed and utilized by young children with suspected autism spectrum disorder (ASD) and identifying factors that prevent the early identification of developmental concerns and diagnosis.

**METHODS:** This retrospective study examined the sociodemographic and clinical characteristics of a convenience sample of children diagnosed with ASD at the Center for Autism Research, Riyadh, Saudi Arabia between 2016 and 2018. The characteristics of ASD assessment and intervention service use were examined. Additionally, we examined the association between sociodemographic, clinical, and service use variables with the child's age at the time of the parent's initial concern and first ASD diagnosis, and the time from first concern to diagnosis.

**RESULTS:** Out of 127 cases, 67 were diagnosed with ASD (mean: 46.88 months, SD: 18.88, median: 42.00, range, 19-93). Most ASD cases had one previous assessment (n=28, 41.8%). Higher sibling numbers were associated with a later age of first concern (p=0.0278). Applied behavior analysis service utilization was associated with later age of first ASD diagnosis (p=0.0336) and longer time to ASD diagnosis (p=0.0301).

**CONCLUSION:** Larger sample size is needed to further investigate whether these findings are representative of the national experience. Community-based intervention outcome studies should assess the quality of services being provided

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Scand J Psychol. 2021 Aug;62:460-67.

**SKI.**

*Lantz S, Fornwall C, LÁŕÁŕf M, et al.*

Psychoeducation is regarded as a first line of intervention for attention-deficit/hyperactivity disorder (ADHD). Previous studies have been limited to psychoeducation for adult patients or parents of children with ADHD. Therefore, the aim of the present study was to investigate the acceptability and effectiveness of a psychoeducational group intervention for children with ADHD. The two-session psychoeducational intervention, SKILLS, was completed by 125 children (6-12 years) with ADHD and their parents. Self-ratings and parental ratings of ADHD symptoms, functional impairment and attitudes to diagnosis and treatment

were collected before and after treatment. Post-treatment client satisfaction and parental responses to an open question about SKILLS were assessed. The data were analyzed using a combination of quantitative and qualitative (content analysis) methods. A majority of the participants expressed satisfaction with the group intervention. The intervention had no effect on symptoms and level of function, although the parents were more positive to their child's diagnosis after the intervention. The parents were positive to the group format and to the opportunity for their children to meet other children with similar symptoms. Parents wished for more interactive elements and more opportunities for children to share experiences. We concluded that the group intervention was accepted by most participants, although more activating exercises and opportunities for interaction between participants should be included. Since the intervention group was not compared with a control group, the results should be interpreted with caution. Future studies should use a randomized control treatment design and investigate the effect on adherence to later treatment

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Sci Rep. 2021 Aug;11:16144.

**MORE THAN 50 LONG-TERM EFFECTS OF COVID-19: A SYSTEMATIC REVIEW AND META-ANALYSIS.**

**Lopez-Leon S, Wegman-Ostrosky T, Perelman C, et al.**

COVID-19 can involve persistence, sequelae, and other medical complications that last weeks to months after initial recovery. This systematic review and meta-analysis aims to identify studies assessing the long-term effects of COVID-19. LitCOVID and Embase were searched to identify articles with original data published before the 1st of January 2021, with a minimum of 100 patients. For effects reported in two or more studies, meta-analyses using a random-effects model were performed using the MetaXL software to estimate the pooled prevalence with 95% CI. PRISMA guidelines were followed. A total of 18,251 publications were identified, of which 15 met the inclusion criteria. The prevalence of 55 long-term effects was estimated, 21 meta-analyses were performed, and 47,910 patients were included (age 17-87 years). The included studies defined long-COVID as ranging from 14 to 110 days post-viral infection. It was estimated that 80% of the infected patients with SARS-CoV-2 developed one or more long-term symptoms. The five most common symptoms were fatigue (58%), headache (44%), attention disorder (27%), hair loss (25%), and dyspnea (24%). Multi-disciplinary teams are crucial to developing preventive measures, rehabilitation techniques, and clinical management strategies with whole-patient perspectives designed to address long COVID-19 care

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Sleep Med. 2021 Aug;84:107-13.

**ASSOCIATION BETWEEN SENSORY MODULATION AND SLEEP DIFFICULTIES IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD).**

**Mimouni-Bloch A, Offek H, Engel-Yeger B, et al.**

**BACKGROUND:** Sleep difficulties have been reported in up to 85% of children with Attention Deficit hyperactivity disorder (ADHD). Children with ADHD exhibit commonly sensory modulation difficulties (SMD) and experience more significant functional difficulties. Sleep difficulties have also been associated with SMD. The aim of this study was to evaluate whether SMD are associated with sleep difficulties in children with ADHD.

**METHODS:** We assessed sleep difficulties using the Children's Sleep Habits Questionnaire, and SMD using the Short Sensory Profile (SSP) questionnaire. A total of 25 children with ADHD and atypical sensory profiles, 13 children with ADHD and typical sensory profiles and 38 children used as controls (all children aged 8-11 years) were included.

**RESULTS:** Sleep difficulties were detected in 86.4% of children with ADHD and atypical SSPs, as compared to 30.8% of children with ADHD and typical SSPs, and 16.7% of controls. A multivariate logistic regression revealed that children with ADHD and atypical SSPs had significantly increased odds for sleep difficulties as compared to controls (OR = 32.4; 95% CI 4.0-260.1, p = 0.001), while children with ADHD and typical SSPs were indistinguishable from controls. Suspected confounders (gender, age, mother's education, and stimulant therapy) did not contribute to sleep difficulties.

**CONCLUSION:** In this pilot study, SMD were associated with sleep difficulties in children with ADHD

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Soc Sci Med. 2021 Sep;284:114232.

**"WHY CAN'T YOU SIT STILL?" THE EFFECT OF DAILY PHYSICAL ACTIVITY ON CHILDHOOD INATTENTION/HYPERACTIVITY AND THE EDUCATIONAL GENDER GAP.**

**Chen K, Phipps S.**

Despite the compelling evidence of the long-run consequences of childhood inattention/hyperactivity and harmful side effects of stimulant medication, relatively little is known about accessible non-pharmacological options to reduce inattentive/hyperactive behaviours. This study evaluates the effect of daily exercise on inattentive/hyperactive behaviours among young children by leveraging evidence from a quasi-experiment generated when 3 Canadian provinces adopted mandatory requirements for all students in grades 1 through 6 to participate in 20-30 min of daily physical activity at school between 1994 and 2009. By exploiting plausibly exogenous variations in the timing of implementation and duration of physical activity mandated as well as over 20,000 observations on a sample of nationally representative children, our difference-in-differences estimates indicate that brief bouts of daily exercise at school effectively reduce inattention/hyperactivity in children - with the beneficial effect enhanced by the duration of exercise mandated. Importantly, most of the exercise effect is concentrated on boys. Since boys' higher rates of inattention/hyperactivity contribute to the explanation for boys' lagging academic motivation and achievement, we argue that providing more scope for physical activity during the school day might be a feasible policy option not only for reducing inattentive/hyperactive behaviours, but also for helping to close the educational gender gap in the longer run

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(in attuazione della D.G. sanità n. 3798 del 08/05/2014, n. 778 del 05/02/2015, n.  
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