5.10 A SYSTEMATIC REVIEW OF INTERVENTIONS TO ENHANCE ADHERENCE AND PERSISTENCE WITH ADHD PHARMACOTHERAPY

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Objectives: Although high rates of poor adherence/persistence have been documented in ADHD, there is limited research targeting the problem. This systematic review evaluated interventions that have attempted to address poor adherence/persistence to ADHD pharmacotherapy, with the aim of guiding the development of future interventions.

Methods: An extensive search was conducted including Embase, PubMed, PsycINFO, Cumulative Index to Nursing and Allied Health Literature (CINAHL), the Cochrane Library, and Web of Science from January 1980 to January 2021. Only published studies in the English language with full text were included. The impact of interventions on adherence/persistence and clinical outcomes in ADHD pharmacotherapy was evaluated. Studies were also reviewed for quality.

Results: Thirteen intervention studies were identified involving psychoeducation, behavioral therapy, combined psychoeducation/behavioral therapy, technology-based interventions, written informed consent, and a nursing support line. All 13 studies (including 5 RCTs) reported improvement in adherence/persistence, and 5 studies (including 4 RCTs) also reported improvement in ADHD ratings. Almost all studies involved interventions utilizing a form of education. Three RCTs of psychoeducation alone were included, with 2 of the 3 studies reporting adherence benefits at 3 and 12 months, respectively. The third RCT was terminated early due to poor recruitment. A behavioral intervention RCT reported improved adherence 6 months postintervention (but not at 12 months), although a substantial dropout rate was observed. A final RCT included used a smartphone application and reported a short-term increase in adherence. The quality of studies was typically low. There were few RCTs, a lack of blinding, large dropout rates, poor recruitment, lack of sample size justification, limitations in control group selection, and short follow-up periods.

Conclusions: Future interventions should involve combinations of strategies, have a theoretical framework, and target the most common reasons for nonadherence. Interventions should also be integrable into routine care and include patient input to maximize sustainability. To progress adherence intervention research in ADHD, more studies are required to address the recognized limitations of the current evidence base.

ADHD, PPC, R

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5.11 POLYGENIC RISK FOR ADHD INDEXES BEHAVIOR RATINGS OF EXECUTIVE FUNCTIONS IN CHILD PSYCHIATRY OUTPATIENTS

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Objectives: The first significant genome-wide association study (GWAS) of ADHD has made it possible to quantify common genetic variation underlying the condition in individuals. Determining the clinical utility of such polygenic risk scores (PRS) awaits a better understanding of the phenotypes that these scores index in clinical samples. Parent rating scales of executive function (EF) associate with functional difficulties and capture behaviors beyond the *DSM* ADHD criteria. Thus, the extent to which EF rating scales relate to ADHD PRS has implications for clinical translation.

Methods: Subjects were 365 youth (11.4 ± 3.1 years; 35.3% girls) referred for neuropsychiatric evaluation, enrolled in the Longitudinal Study of Genetic Influences on Cognition and genotyped with the Illumina PsychChip. ADHD PRS was derived from the largest published ADHD GWAS. Parents rated EF using the Behavior Rating Inventory of Executive Function (BRIEF), which reflects behavioral and emotional regulation (BER) and metacognition (MC). Linear regression models related ADHD PRS to these constructs alone, after accounting for polygenic variation (PV) for cognitive ability (COG), and after controlling for ADHD diagnoses. Finally, using structural equation modeling (SEM), we examined the extent to which ADHD PRS and BRIEF associations were mediated by ADHD diagnoses. Analyses controlled for age, sex, medication, and the first 5 principal ancestry components. Benjamini-Hochberg False Discovery Rate (FDR) 0.05 was used to correct for multiple testing.

Results: ADHD PRS was significantly associated with BER and MC. Controlling for COG PV resulted in a smaller but significant association of ADHD PRS with BER ($\Delta R^2 = 2.40\%$; $t = 3.22$; $p = 0.0014$), but the association with MC was not significant. Controlling for ADHD only yielded a significant association with BER ($\Delta R^2 = 2.41\%$; $t = 3.27$; $p = 0.0012$). SEM indicated a partial mediation effect for the model for BER, with a significant indirect effect of ADHD PRS via ADHD ($b = 0.02$; $z = 2.13$; $p = 0.0335$) and a direct effect ($b = 0.16$; $z = 3.32$; $p = 0.0009$). In contrast, the association between ADHD PRS and MC was fully mediated by ADHD status.

Conclusions: ADHD PRS influence behavioral and emotional regulation indirectly via ADHD as well as directly, suggesting that the risk score captures variation relevant to functional outcome beyond the traditional ADHD diagnosis.

COG, GS, ADHD

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5.12 RELATIONSHIP BETWEEN POLYPHARMACY AND CLINICAL FUNCTIONING IN PATIENTS WITH ADHD: A RETROSPECTIVE ANALYSIS OF REAL-WORLD DATA

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Objectives: Polypharmacy is common in the treatment of ADHD, but little is known about its relation to clinical functioning. The primary objective of this analysis was to use a large real-world data (RWD) source derived from electronic health records to examine this relationship in patients with ADHD across the life span. Notably, this RWD source includes information regarding both medications and clinical functioning, measured with a clinician-rated Clinical Global Impression-Severity (CGI-S) score.

Methods: The NeuroBlu™ database includes deidentified data from more than 550,000 unique patients over 20 years, including CGI-S scores. Data were from US sites using a common electronic health record system. All patients with an *ICD* diagnosis of ADHD were included. Additional inclusion criteria included: ≥3 clinical visits within a 12-month period, CGI-S recorded at initial visit, and prescription medication information. Cohorts were defined by the maximum number of simultaneous medications prescribed in a 12-month time frame and included patients prescribed 0, 1, 2, 3, 4, and 5 or more medications at a single time point. Mean and median CGI-S scores at initial ADHD diagnosis were compared across cohorts. Cohorts were further stratified for children (aged 0-12 years), adolescents (aged 13-17 years), and adults (aged 18 years and older).

Results: Of 53,744 patients with ADHD, 31,824 met the eligibility criteria; 59% were White, and 58% were male. The proportion of patients included in each of the polypharmacy cohorts was as follows: 0 (6%); 1 (21%); 2 (24%); 3 (19%); 4 (13%); and 5+ (18%). Patients on 0-4 medications had a median CGI of 4, and those with 5+ medications had a median CGI of 5. Although there was a statistically significant difference across cohorts with respect to mean CGI-S score, the clinical significance of this difference was small. Pairwise comparisons indicated that there were no differences in CGI-S scores between patients receiving 0, 1, or 2 medications and only a nominal difference between those receiving 0 and 3 medications. Results were similar when examined across age groups.

Conclusions: Polypharmacy practices in patients with ADHD may not be meaningfully associated with clinical functioning. Findings highlight the need

for additional research with RWD sources to better understand these prescribing practices.

ADHD, PPC, IMP

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5.13 THE EXPERIENCE OF CHILDREN AND ADOLESCENTS WITH ADHD AND THEIR CAREGIVERS DURING THE COVID-19 PANDEMIC: THE UNCOVER STUDY

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Objectives: The challenges of the COVID-19 pandemic on patients (pts) with mental health disorders are complex and not fully understood. This study surveyed parents/guardians of pediatric pts with ADHD in the United States to better understand the impact of the pandemic on their disorder and quality of life.

Methods: A 39-question cross-sectional survey was conducted (March 10, 2021 to April 2, 2021) via the PatientsLikeMe (PLM) health tracking platform within an online social network. Participants were US-resident PLM members who were caregivers of dependents aged 6 to 18 years with ADHD. Data related to the impact on treatment, medical care access, symptoms, and ADHD management goals are reported.

Results: The cohort comprised 37 adult caregivers. Twenty children were currently taking prescription medication (Rx) for ADHD (treated-pts), and 16 were not (untreated-pts). An 11% decrease in Rx use status was reported during the pandemic. In treated-pts, 25% had ≥1 switch in ADHD Rx type and 40% had an Rx dosage change. Compared to before the pandemic, 37% of the caregivers of treated-pts reported difficulty in adhering to ADHD Rx use as prescribed. Of the 79% of caregivers of treated-pts who reported a pandemic-related negative impact on their daily ADHD Rx routine, 67% reported interference in their structured routine and 53% reported changes in their virtual learning environment as the main reasons. Regarding telehealth and medical care access, 38% of caregivers reported having ≥1 telehealth visit (24% treated-pts vs 15% untreated-pts); 27% of caregivers reported not wanting to use telehealth. On a 4-point scale (none, minor, moderate, major), caregivers of untreated-pts reported a major impact of the pandemic on ADHD-related medical care (12%, vs treated-pts, 0%; $p = 0.04$). Caregivers of treated-pts were more likely to agree that ADHD symptoms were well managed during the pandemic (21%, vs untreated-pts, 6%). Regardless of treatment status, 53% of dependents had an ADHD management goal; of those, all reported a negative impact of the pandemic on their goal.

Conclusions: Compared with the prepandemic period, children/adolescents with ADHD experienced a higher disease burden that translated into a negative impact on their lives and that of their caregivers. The effect of the COVID-19 pandemic appears to have been more pronounced in pts not treated with ADHD medications during this period.

ADHD, SAC, R

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5.14 EFFICACY OF COMPUTER GAME–BASED EXECUTIVE FUNCTIONING/ATTENTION TRAINING IN CHILDREN AND ADOLESCENTS WITH ADHD: A SYSTEMATIC REVIEW

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Objectives: ADHD is common among children and adolescents, affecting 5% to 7% of the population worldwide. The core symptoms of ADHD are inattentiveness, hyperactivity, and impulsivity. Recent studies discovered that ADHD patients have impairment in executive functioning associated with goal setting and planning, which are essential for school performance and social functioning. Although medications effectively reduce ADHD core symptoms, due to stigma, side effects, and medication cost, medication adherence is low in this population. This systematic review focused on determining the effectiveness of computer games–based training programs as a treatment modality for children and adolescents with ADHD.

Methods: We followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, searching 5 databases from inception to 2021 for relevant studies. From 563 original studies on computerized executive functions/attention intervention on pediatric patients aged 6 to 17 years old with ADHD, 28 studies met the inclusion of systematic review. Two researchers independently reviewed each study, and the results were analyzed using Review Manager 5.4.

Results: A total of 1980 participants were recruited in 28 studies. Of the 28 studies, 22 are randomized controlled trials, 1 is a case study, and 5 are non–randomized controlled trial cohort studies. Fifteen of 28 studies reported improved ADHD symptoms after intervention, but only 5 studies reported the significant difference between the intervention group and the control group. Less than 50% of included studies provided details of allocation concealment, and were blinded, which increased the risks of biases.

Conclusions: There is some ADHD symptom improvement observed after the interventions. A meta-analysis should be conducted to examine the effect size of training effectiveness.

ADHD, P, COMP

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5.15 INFLUENTIAL FACTORS IN ADHD DIAGNOSIS AND TREATMENT IN BLACK AND WHITE YOUTH

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Objectives: To help resolve inconsistencies in the literature, this study aimed to: 1) examine race-related disparities between Black and White youth in ADHD diagnosis, severity, parenting support, and treatment; and 2) assess the role of insurance type.

Methods: Using the 2017-2019 National Survey of Children's Health (NSCH), which is a nationally representative and cross-sectional survey of parents, racial disparities were considered in ADHD diagnosis and treatment type. Health insurance type, severity, and use of informal social supports were considered as potential mediators of the relationship between race and ADHD treatment. Race was examined as a moderator of the influence of severity and type of support on treatment type.

Results: ADHD prevalence rates were comparable between Black (13.2%) and White (12.0%) youth aged 6 to 17 years ($M_{age} = 11.52$). In multivariate models that included demographic characteristics, race remained nonsignificant. However, the association between race and lifetime ADHD diagnosis became significant when the insurance type was added, indicating a suppression effect of insurance type. Once insurance type is controlled, Black youth are less likely to ever be diagnosed with ADHD ($p < 0.05$). Among those with a current ADHD diagnosis, a significant bivariate association emerged between race and severity ($p = 0.002$); Black youth were significantly more likely to have both moderate and severe parent-reported ADHD symptoms. However, after controlling for demographic and socioeconomic variables, no significant race-related difference in ADHD severity remained. With respect to treatment: 1) neither race nor informal support was associated with treatment type, but severity predicted all treatment types; 2) parents who reported place-of-worship support were more likely to access medical treatment only; and 3) race moderated the influence of severity and type of support in models controlling for demographic and socioeconomic variables, including insurance type.

Conclusions: Race-related disparities in lifetime ADHD diagnosis do not emerge until insurance type is considered. Then, Black youth are less likely to ever be diagnosed, yet they have more severe ADHD symptoms. This finding