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Longitudinal associations between internalizing and externalizing comorbidities and functional outcomes for children with ADHD

Original Empirical Research Article

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Abstract This study examined functional outcomes for children with ADHD by comorbidity status. Children with ADHD (5-13 years) were recruited from 21 pediatric practices and followed up 12 months later ($n=199$). Parent and teacher-reported baseline and 12 month surveys measured peer problems, daily functioning, quality of life (QoL), parent mental health, and family QoL. The Anxiety Disorders Interview Schedule for Children IV assessed mental health comorbidities at baseline. Linear regression adjusted for socio-demographics, ADHD severity, and baseline functioning (where possible). In adjusted analyses, children with ADHD and co-occurring internalizing and externalizing comorbidities had poorer QoL, greater peer problems, and poorer family QoL, compared to children with ADHD alone. The parents of children with ADHD and internalizing and externalizing comorbidities alone, also reported poorer family QoL, compared to children with ADHD alone. Children with ADHD and co-occurring internalizing and externalizing comorbidities appear particularly vulnerable to poorer functioning.

Keywords Attention-Deficit Hyperactivity Disorder; Internalizing; Externalizing; Longitudinal; Comorbidity.

Introduction

Children with Attention-Deficit/Hyperactivity Disorder (ADHD) commonly present with mental health comorbidities. About 50-70% of children with ADHD present with an externalising disorder such as Oppositional Defiant Disorder (ODD) or Conduct Disorder (CD), while up to 64% present with an internalizing disorder such as depression and anxiety [1-3]. Children with ADHD can also present with co-occurring internalizing and externalizing comorbidities in up to 22% of cases [4]. Yet, very few longitudinal studies have examined how internalizing, externalizing, and co-occurring internalizing and externalizing comorbidities uniquely influence functional outcomes for children with ADHD over time.

Many cross-sectional studies have examined how comorbidities affect the functioning of children with ADHD [5-7]. These studies have demonstrated that children with ADHD and externalizing comorbidities are at greater risk of poorer peer functioning [6, 8-10], and poorer psychosocial quality of life (QoL) [11-13]. For example, Hoza et al. [14] found evidence that externalizing comorbidities were associated with poorer peer functioning as rated by peers (e.g., lower social preference, peer rejection), when compared to children with ADHD alone. Conversely, studies examining the association between internalizing comorbidities and peer functioning of children with ADHD have produced mixed findings. Some studies have found that internalizing comorbidities are associated with poorer peer functioning [7, 15-17], while others have not [9, 14, 18, 19]. Sciberras et al. [3] recently demonstrated that children with ADHD presenting with multiple anxiety comorbidities had poorer daily functioning, behavior and QoL, compared to children with ADHD alone.

Limited research has examined the unique contribution of specific internalizing and externalizing comorbidities on the functioning of children with ADHD. In a large cross-sectional study, Booster, DuPaul, Eiraldi, and Power [19] examined the impact of internalizing and externalizing comorbidities on the functioning of children aged 5-16 years

with ADHD ($n=416$). They found that children with ADHD and an externalizing disorder had poorer social skills, compared to children with ADHD alone, while co-occurring internalizing and externalizing comorbidities were particularly associated with homework problems, compared to children with ADHD alone. However, this study did not take into account many variables, which could possibly confound the relationship between comorbidity and functioning, including socio-demographic factors, ADHD symptom severity and medication use.

Cross-sectional studies have also examined the relationship between internalizing and externalizing comorbidities in children with ADHD, and parent mental health and family functioning. Externalizing comorbidities in children with ADHD have been associated with poorer family functioning [20, 21], including strain on family activities [22], family relationships, and poorer communication and problem solving abilities within the family [23]. Internalizing comorbidities in children with ADHD have been associated with poorer child-parent relationships [24] and increase parental stress [25], anxiety [24], and depression [5]. It is important to note that the relationship between child and parent mental health is reciprocal; parent depression may be a risk factor for the development of externalizing comorbidities in some children with ADHD, while externalizing comorbidities in children with ADHD may contribute to parent depression [26, 27].

Collectively, these cross-sectional studies provide some evidence that comorbidities in children with ADHD are associated with poorer child, parent, and family outcomes. However, given that most of the research to date has been cross-sectional, it is difficult to infer directionality between comorbid status and functional outcomes. Most studies have not delineated specific comorbid categories (i.e., co-occurring internalizing and externalizing comorbidities) meaning that our understanding of the unique impact of comorbidities is limited. Further, existing research often does not account for a broad range of confounding

variables [e.g., medication use, ADHD symptom severity; 19] which may account for the relationship between comorbidities and poorer functioning.

Few longitudinal studies have examined how internalizing and externalizing comorbidity categories influence the outcomes for children with ADHD over time. Newcorn, Spencer, Biederman, Milton, and Michelson [28] found children aged 7-11 years with ADHD and both conduct disorder and an anxiety disorder were particularly vulnerable to poorer parent-reported social functioning 4-9 years later. However, this study was limited by a small sample size ($n=32$). Two longitudinal studies have also demonstrated that psychosocial QoL is poorer in children with ADHD experiencing mental health comorbidity. In an eight-week medication trial, Newcorn et al. [29] found that children with ADHD and comorbid ODD randomized to the control group had poorer psychosocial QoL (after controlling for baseline ADHD, ODD and depression symptom severity), compared to children with ADHD alone. Similarly, over a six-month period, Hakkaart-Van Roijen et al. [30] showed that ADHD and mental health comorbidities in children predicted poorer psychosocial QoL, compared to children with ADHD alone; however, the differential impact of particular comorbidities was not examined. Together, these studies provide some evidence that comorbidities contribute to poorer outcomes for children with ADHD. Nonetheless, a substantial gap remains in the literature, as few longitudinal studies have examined how specific comorbidity categories uniquely influence functional outcome for children with ADHD. Considering over a quarter of children with ADHD experience co-occurring internalizing and externalizing comorbidities, it is crucial that longitudinal research clarifies the differential impact of internalizing and externalizing comorbidities, both separately and together, to determine if functional outcomes are temporarily affected or persist over time.

The current study seeks to address these gaps by investigating, in a large clinically diverse sample of school-aged children with ADHD, the 12-month longitudinal associations

between internalizing and externalizing comorbidities and child (peer problems, psychosocial QoL, and daily functioning) and family functioning (parent mental health and family QoL). We hypothesized that compared to children with ADHD alone, children with ADHD and internalizing, externalizing, or co-occurring internalizing and externalizing comorbidities at baseline would have:

- 1) poorer functioning across all child domains, 12 months on; and,
- 2) poorer parent and family functioning as measured by parent mental health and family QoL, 12 months on.

Method

Design

We recruited children from two harmonized ADHD studies focused on sleep: (1) *Attention to Sleep* – a cohort study of children with no/mild sleep problems [31], and (2) *Sleeping Sound with ADHD* – randomized controlled trial (RCT) of a behavioral sleep intervention [32]. Children were recruited from outpatient and private pediatric practices (N=21) across the state of Victoria, including metropolitan (n=37) and regional/rural areas (n=13). Pediatricians were selected through convenience sampling. Of the 80 to be involved in recruitment, 50 decided to take part. Only children randomized to the ‘usual care’ group were included in the current study given that the sleep interventions were anticipated to improve behavioral outcomes for children with ADHD [33]. Both studies utilized identical criteria for inclusion (with the exception of sleep problem severity), exclusion, diagnostic, and outcome measures, as outlined below. The current study obtained full ethical approval from The Royal Children’s Hospital (30033 D; 31193 A) and The Victorian Department of Education and Early Childhood Development (2010_000573; 2011_001307) Human Research Ethics Committees.

Participants

Pediatricians identified children aged 5-13 with a diagnosis with ADHD, who had been seen within the past 12 months. Children needed to meet full DSM-IV-TR [34] criteria for ADHD at the time of recruitment in order to be eligible. ADHD symptom criteria were assessed using the ADHD Rating Scale IV [35]. Primary caregivers had to endorse a minimum of 6 out of 9 symptoms as occurring ‘often’ or ‘very often’, in either the inattention and/or hyperactive/impulsive domain (rated off ADHD medication). In addition, study-designed questions were used to ensure symptoms were present for 6 months or longer, that symptom onset was before the age of 7, and that the symptoms resulted in cross-situational impairment at home and at school. Children were excluded if: (1) parents could not understand English sufficiently to complete the recruitment call; (2) children were receiving sleep assistance (except from their pediatrician); (3) children suffered from a serious medical condition (e.g., severe cerebral palsy) or an intellectual disability ($IQ < 70$); and (4) if the child had suspected obstructive sleep apnea. The child’s primary caregiver, who in most cases was the mother, completed all baseline and 12 month measures reported below.

Baseline measures

Internalizing and externalizing comorbidities

The Anxiety Disorders Interview Schedule for Children IV-Parent Version [ADIS-C; 36] was telephone-administered at baseline. In order to meet criteria for a disorder, caregivers needed to endorse minimum DSM-IV-TR symptom criteria and needed to rate the symptoms as causing significant interference in daily functioning (a rating of 4 or more on an 8-point scale). The ADIS-C has excellent reliability and validity [$k=0.73$ to 0.92 ; 37, 38]. In the present study, inter-rater reliability was “good” for Obsessive-Compulsive Disorder ($k=0.69$; $p<.001$), and “excellent” for other disorders ($k=0.83$ to 1.00 ; $p<.001$).

Children were allocated into four diagnostic categories based on ADIS-C results: (1) ADHD alone: children who did not screen positive for an internalizing (according to the definition below) or externalizing comorbidities (reference category); (2) Internalizing: children who screened positive for two or more anxiety comorbidities (Generalised Anxiety Disorder, Social Phobia, Specific Phobia, Separation Anxiety Disorder, Panic Disorder, Obsessive-Compulsive Disorder, Posttraumatic Stress Disorder) or one mood disorder (Major Depressive Disorder, Dysthymic Disorder); (3) Externalizing: children who screened positive for ODD or CD; and (4) Co-occurring: children who screened positive for *both* internalizing and externalizing comorbidities. The threshold of screening positive for two or more anxiety comorbidities was chosen based on research in children with ADHD, using a similar measure (e.g., Kiddie-SADS-E), which showed that two or more anxiety disorders produced high specificity (0.67) and sensitivity (0.75) for a clinically meaningful anxiety disorder in children with ADHD [39]. Additionally, two or more anxiety disorders has been shown to be associated with poorer daily functioning, as opposed to one anxiety disorder [3].

ADHD Symptom Severity/Subtype

The ADHD Rating Scale-IV Parent Version [ADHD-RS-IV; 35] is an 18-item scale based directly on the DSM-IV-TR [34] symptom criteria for ADHD ($\alpha=0.90$). Each symptom is rated on a four-point scale from 0 “*Never or rarely*” to 3 “*Very often*”, contributing to a total symptom severity score, with higher scores reflecting greater symptom severity. Children with six or more inattention and six or more hyperactivity/impulsivity symptoms occurring often or very often were classified as ADHD combined subtype, while those with six or more inattentive or hyperactivity/impulsivity symptoms only were classified as ADHD Inattentive or ADHD Hyperactivity/Impulsivity subtype, respectively.

Socio-demographic and confounding measures

Parent-reported baseline data were collected including: child age and gender, ADHD medication use, Autism Spectrum Disorder (ASD) previous diagnosis (yes/no), and if the parent had completed high school (yes/no). Area based disadvantage was measured using the Socio-Economic Indexes for Areas Disadvantage Index (SEIFA) for the child's residential postcode. Higher scores reflect less disadvantage [$M=1000$, $SD=100$; 40, 41].

Outcome Measures (collected at baseline and 12 months, except Family QoL, which was only measured at 12 months)

Peer Functioning

The Strengths and Difficulties Questionnaire [SDQ; 42] is a five-item measure and is a valid and reliable assessment of peer functioning for children aged 4-17 years. Both parents ($\alpha=0.63$) and teachers ($\alpha=0.68$) rated the child's peer functioning (e.g., "*Has at least one good friend*") over the past month, on a three-point scale from 0 "*Not true*" to 2 "*Certainly true*", with higher scores reflecting more difficulties.

Child Daily Functioning

The Daily Parent Rating of Evening and Morning Behavior [DPREMB-R; 43] is an 11-item measure and assesses child functioning difficulties in the morning and late afternoon/evening (e.g., "*Sitting through dinner*") over the past four weeks. ($\alpha=0.84$). Items are rated on a four-point scale from 0 "*None*" to 3 "*A lot*", with higher scores reflecting poorer daily functioning.

Psychosocial Quality of Life

The Pediatric Quality of Life Inventory 4.0 [PedsQL; 44] is a 15-item psychosocial health summary score. This is a reliable and valid measure ($\alpha=0.84$), consisting of three subscales: Emotional, Social, and School Functioning. Parents rate perceived problems for

their child (e.g., “*Feeling angry*”), over the past four weeks, on a five-point scale ranging from 0 “*Never*” to 4 “*Almost always*”, with higher scores reflecting better psychosocial QoL.

Parent Mental Health

The Depression Anxiety Stress Scale [DASS; 45] is a 21-item measure and is a validated and reliable assessment of adult mental health. The current study reports on the total DASS scale ($\alpha=0.95$), which consists of three subscales: Depression, Anxiety, and Stress. Parents rate the extent to which they have experienced each symptom (e.g., “*I find it difficult to relax*”) over the past four weeks, on a four-point scale from 0 “*Not at all*” to 3 “*Most of the time*”, with higher scores reflecting poorer mental health.

Family Quality of Life

The Family Impact Scales of the Child Health Questionnaire [CHQ-PF50; 46] is a 10-item measure and is a validated and reliable assessment of the impact of a child’s health and behavior on the family over the past four weeks. Three subscales assess: (1) Parental Impact-Emotional (e.g., “*how much emotional worry or concern did your child's emotional well-being or behavior cause you?*”), rated on a five-point scale from 0 “*None at all*” to 4 “*A lot*” ($\alpha=0.65$); (2) Parental Impact- Time (e.g., “*how much emotional worry or concern did your child’s attention or learning abilities cause you?*”), rated on a four-point scale from 0 “*Yes, limited me a lot*” to 4 “*No, did not limit my time*” ($\alpha=0.67$); and (3) Family Activities Impact (e.g., “*how often has your child’s health and behaviour caused tension or conflict in the home?*”), rated on a five-point scale from 0 “*Never*” to 4 “*Very often*” ($\alpha=0.89$), with lower scores reflecting poorer family QoL.

Procedure

Pediatricians from metropolitan and regional Victoria, Australia, mailed study invitation letters to all children diagnosed with ADHD seen within the past 12 months. An “opt-out” recruitment method was used. If the family did not “opt out” within two weeks,

pediatricians provided the research team with contact details of families. The research team then contacted families who did not “opt-out” to assess eligibility and interest in participating. Eligible families were mailed a recruitment package, which included a study information letter, consent form, and baseline survey. Families were enrolled upon receipt of the completed consent form and survey. Teachers were also sent a consent form and survey if the parent provided consent for teacher participation.

Participating parents were then telephoned to complete the ADIS-C to assess internalizing and externalizing comorbidities. Researchers administering this interview ($n=8$) held a minimum fourth year degree in psychology and received formal training and supervision from an experienced clinical psychologist (ES). At 12 months post-enrolment, parent and teacher surveys were distributed to assess outcomes. Surveys were posted to all parents and were emailed (Attention to Sleep cohort) or posted (Sleeping Sound with ADHD RCT) to teachers. If surveys were not returned within two weeks parents and teachers were sent a reminder letter and replacement survey. This was followed by a reminder call and/or SMS if the survey was not received after the first reminder.

Data analysis

Examination of the distribution of study variables indicated that the DASS total score was positively skewed at baseline and 12 months. Therefore, a change score was calculated to denote the mean difference in parent mental health score from baseline to 12 months. This change score was used in analyses given that it was normally distributed.

Summary statistics were first used to describe baseline sample characteristics by comorbidity group: 1) ADHD alone; 2) internalizing alone; 3) externalizing alone; and 4) co-occurring internalizing and externalizing. For categorical variables, n 's and percentages are reported, along with χ^2 statistics and corresponding p values. One-way ANOVA examined

differences in continuous variables across comorbidity categories; means and standard deviations are reported along with *F* statistics.

Twelve month outcomes for children with internalizing, externalizing or co-occurring comorbidities at baseline, were compared to children with ADHD alone (reference group) in three hierarchical linear regression models. In Model 1, unadjusted 12 month child and parent/family outcomes for children in each comorbidity group are presented, compared to children with ADHD alone. In Model 2, analyses are repeated to adjust for a-priori confounders, including child age and gender, ADHD medication use (yes/no), ADHD symptom severity (total score), comorbid ASD (parent-reported diagnosis, yes/no), and parent high school completion (yes/no). Finally, in Model 3, analyses are repeated for all 12 month child outcomes to adjust baseline functioning on the outcome variable, in addition to a-priori confounding variables. It was not possible to examine family functioning in Model 3 given that a baseline measure was unavailable. A hierarchical approach was used in order to demonstrate how child and family characteristics (model 2), as well as baseline functioning (model 3), contribute to functioning over the 12 month period.

For Models 1 and 2 we report: 1) mean difference (and 95% CI) for each 12 month outcome between children in each comorbidity group, compared to the reference group (ADHD alone); 2) Cohen's *d* effect sizes. Effect sizes are considered as: small i.e. ~ 0.20 SD, moderate i.e. ~ 0.50 SD and large i.e. ~ 0.80 SD [47]; and 3) R^2 values representing the amount of variance explained in each analysis. For Model 3, we report Beta weights (β) and *p* values for our key independent variable (comorbidity group), all confounding variables, and baseline functioning on the outcome variable. Analyses were conducted using Stata 12.1 [48].

Results

Invitation letters were distributed to 1349 families. Five hundred and twenty two children were not assessed for eligibility (232 ‘not interested’; 192 ‘uncontactable’; 89 ‘outside age range’; 9 ‘insufficient English’). Of the 827 families assessed for eligibility, 561 were eligible. The main reasons for exclusion were not meeting ADHD DSM-IV criteria ($n=99$) or having an intellectual disability ($n=53$). Of the 392 eligible families, 244 children were recruited and had a moderate/severe sleep problems ($n=122$ were randomized and excluded as they received behavioral sleep interventions) and 148 were recruited and had no/mild sleep problems. Therefore, 270 families were recruited and eligible for follow-up. Participants who enrolled were comparable to those who did not enroll in terms of child gender or age, as well as SEIFA scores.

At baseline, the following data were available: parent surveys ($n=270$, 100%), ADIS-C data ($n=256$, 95%), and teacher surveys ($n=195$, 72%). In order to be included in this study, children were required to have ADIS-C data available and at least one parent-reported outcome measure available at 12 months, which provided a final sample of 199 children (172 male, 27 female; *mean age*=10.13, *SD*=1.82, *range*: 5.60 to 13.48 years).

Teacher data were available at 12 months for 171 children with ADIS-C data available at baseline. There were no differences between participants who took part at 12 months compared to those that did not in terms of child gender, age, or baseline internalizing or externalizing comorbidities, ADHD symptom severity, teacher- and parent-reported behavioral and emotional problems, or parental mental health and education level. They did differ, however, in terms of psychosocial QoL with non-responders scoring poorer on this measure at baseline.

Demographic and behavioral characteristics by comorbidity group

Internalizing and externalizing comorbidities were common in the sample. In terms of Internalizing Disorders, Specific Phobia, Social Phobia and Generalized Anxiety Disorder

were the most common affecting 47% ($n=93$), 45% ($n=89$) and 33% ($n=65$), respectively. Twenty-six percent ($n=51$) met criteria for Separation Anxiety Disorder, with fewer children with ADHD meeting criteria for Major Depressive Disorder ($n=17$; 8%), Dysthymic Disorder ($n=13$; 7%), Obsessive-Compulsive Disorder ($n=12$; 6%), Posttraumatic Stress Disorder ($n=10$; 5%), and Panic Disorder ($n=5$; 3%). Over half of the children with ADHD met criteria for Oppositional Defiant Disorder or Conduct Disorder ($n=112$; 56%). Overall, 17% ($n=33$) met criteria for an internalizing comorbidity alone, 21% ($n=41$) for an externalizing comorbidity alone and 36% ($n=71$) for co-occurring internalizing and externalizing comorbidities. Twenty-seven percent ($n=54$) were defined as being in the ADHD only group.

Table 1 presents sample characteristics by comorbidity group. In terms of child characteristics, child gender significantly differed across diagnostic categories; higher number of males had co-occurring comorbidity (90%), compared with ADHD alone (80%). Children with ADHD and internalizing (39%), or co-occurring (35%) comorbidity were more likely to have comorbid ASD, compared to children with ADHD alone (15%). Children with ADHD and co-occurring comorbidities were more likely to have the combined subtype (76%), than children with ADHD alone (43%). Child ADHD symptom severity differed across diagnostic categories, by parent-report but not by teacher-report. Parent-reported ADHD symptom severity was higher in children with an Externalizing Disorder ($M=35.30$, $SD=10.10$) and co-occurring comorbidities ($M=38.78$, $SD=8.65$), compared to ADHD alone ($M=29.31$, $SD=9.34$).

In terms of primary caregiver characteristics, rates of high school completion differed across diagnostic categories; fewer primary caregivers in the externalizing (50%), and co-occurring comorbidities (42%) groups had completed high school, compared to the ADHD alone group (61%). There were no significant differences in terms of primary caregiver age,

gender of the primary caregiver, or neighborhood socio-economic disadvantage (SEIFA) across groups.

Model 1: Unadjusted relationship between comorbidities and 12 month outcomes

Table 2 presents the unadjusted mean differences in 12 month outcomes for children in each comorbidity group, compared to children with ADHD alone (reference group). There was little evidence that comorbidity (any type) was associated with teacher-reported peer problems ($R^2=.002$). However, by parent-report children with externalizing ($p<.002$; effect size: 0.61) and co-occurring comorbidities had increased peer problems ($p<.001$; effect size: 0.82), compared to children with ADHD alone. Parent-reported peer problems did not significantly differ between children with internalizing comorbidities and children with ADHD alone ($p=.73$).

Children with co-occurring comorbidities had increased daily functioning difficulties and poorer quality of life, compared to children with ADHD alone (both $p<.001$). Children with externalizing comorbidities alone also had increased daily functioning difficulties, compared to children with ADHD alone ($p=.05$), however, significant differences were not observed in terms of quality of life. There was minimal evidence to suggest that internalizing difficulties alone were associated with daily functioning or quality of life.

In terms of parent and family 12 month outcomes, there was little evidence that comorbidity (any type) was associated with change in parent mental health over the 12 month period ($R^2=.03$), with the exception that parents of children with ADHD and co-occurring comorbidities reported significant improvement in mental health symptoms ($p=.04$; effect size: -0.40), compared to the ADHD alone group. The parents of children with ADHD and co-occurring comorbidity reported that their child's behavior had a significantly greater impact on family emotions ($p<.001$; effect size: -0.66), time ($p<.001$; effect size: -0.82), and

activities ($p<.001$; effect size: -0.95). Similar results were obtained for children with externalizing comorbidities alone: family emotions ($p=.001$; effect size: -0.73), time ($p=.04$; effect size: -0.45), and activities ($p=.009$; effect size: -0.56). Internalizing comorbidities alone was associated with greater impact on family activities than ADHD alone ($p=.007$; effect size: -0.57); however, there were no significant differences for family emotions or family time.

Model 2: Relationship between comorbidities and 12 month outcomes, controlling for a-priori confounding variables

Table 3 presents the 12 month outcomes for children in each comorbidity group, compared to children with ADHD alone (reference group), controlling for a-priori confounding variables (e.g., child age and gender, ADHD medication use and symptom severity, comorbid ASD, and parent high school completion). Although effects attenuated after adjustment, most findings held. At 12 months, children with co-occurring comorbidities ($p<.001$; effect size: 0.68) and externalizing comorbidity alone ($p=.006$; effect size: 0.57), continued to have greater parent-reported peer problems, compared to children with ADHD alone. Similarly, children with ADHD and co-occurring comorbidities continued to have greater daily functioning difficulties ($p=.01$; effect size: 0.46), and poorer psychosocial QoL ($p<.001$; effect size: -0.75).

Families also continued to report significantly greater impact of the child's condition on family emotions and family time if they had ADHD and externalizing (effect size: -0.64 , -0.46 , respectively) and co-occurring comorbidities (effect size: -0.49 , -0.71 , respectively), compared to families of children with ADHD alone. Greater impact on family activities was observed across all comorbidity categories, compared to families of children with ADHD alone ($R^2=.23$).

Model 3: Relationship between comorbidities and 12 month child outcomes, controlling for

a-priori confounding variables and baseline functioning

For all child 12 month outcomes, analyses were re-run, adjusting for baseline functioning on the outcome being examined. Table 4 presents the relationship between all independent variables and each child 12 month outcome examined. For each outcome domain examined (teacher-reported peer problems, parent-reported peer problems, daily functioning, quality of life), the strongest predictor of functioning at 12 months was baseline functioning on the respective outcome domain ($\beta = -.26$ to $.39$).

There was evidence that female gender ($\beta = .23$; $p = .02$) and ASD diagnosis ($\beta = .26$; $p = .008$) were associated with increased teacher-reported peer problems over the 12 month period, however, comorbid mental health difficulties were not.

Children with co-occurring comorbidities continued to have increased parent-reported peer problems ($\beta = .17$; $p = 0.04$) in the fully adjusted model. There was also tendency for internalizing comorbidities to be associated with reduced parent-reported peer problems at 12 months ($\beta = -.13$; $p = 0.07$). Interestingly, comorbid ASD diagnosis was also independently associated with increased parent-reported peer problems at 12 months ($\beta = .12$; $p = 0.05$).

Children with co-occurring comorbidities continued to have poorer quality of life ($\beta = -.22$; $p = 0.02$) in the fully adjusted model, compared to children with ADHD alone; no other independent variables significantly predicted QoL at 12 months, apart from baseline QoL. The only independent predictor of daily functioning difficulties at 12 months was baseline daily functioning difficulties.

Discussion

We aimed to examine the longitudinal associations between internalizing and externalizing comorbidities and child and family functioning for children with ADHD, over a 12 month period. Compared to children with ADHD alone, children with ADHD and co-occurring comorbidities had more peer problems, greater daily functioning difficulties and

poorer psychosocial QoL, even when taking into account key confounding variables including ADHD symptom severity. Additionally, parents of children across all comorbidity groups reported poorer family QoL, compared to parents of children with ADHD alone. There was little evidence that internalizing and externalizing comorbidities alone were associated with poorer child functioning over the 12 month period, with the exception of externalizing comorbidities, which were associated with greater peer problems. Importantly, some findings held after adjusting for baseline functioning indicating that there were instances in which comorbidities contributed to declining functioning over the 12 month period.

We aimed to examine how specific comorbidity categories (i.e., internalizing alone, externalizing alone, co-occurring internalizing/externalizing) uniquely contributed to outcomes for children with ADHD. The results suggest that children with ADHD and co-occurring comorbidities were particularly vulnerable to poorer functioning 12 months later, including greater parent-reported peer problems, and poorer QoL, greater daily functioning difficulties, and poorer family QoL. These findings held after accounting for key confounding variables including ADHD symptom severity and ASD status. These results are consistent with cross-sectional research by Booster, DuPaul, Eiraldi, and Power [19], which showed children with ADHD and co-occurring comorbidities had poorer functioning, and longitudinal research by Newcorn, Spencer, Biederman, Milton, and Michelson [29] and Hakkaart-Van Roijen et al. [30], which reported that psychosocial QoL was poorer in children with ADHD and comorbidity. These findings are unique and extend knowledge showing that, beyond the confounding effects of baseline variation in outcome and potential confounders, children with ADHD and co-occurring comorbidities have greater parent-reported peer problems and poorer QoL over time.

In contrast, there was less evidence for the unique contribution of internalizing or externalizing comorbidities alone, on child and family functioning. Consistent with previous cross-sectional research [3, 7, 15-17], there were no differences in peer problems for children with internalizing comorbidities compared to children with ADHD alone. However, in line with previous research, there was some evidence, before adjusting for baseline scores, that externalizing comorbidities were associated with poorer peer functioning [6, 8-10]. Although previous research has reported that children with ADHD and psychiatric comorbidities have poorer QoL [11, 13], we found that internalizing and externalizing comorbidities alone were not associated with poorer QoL 12 months on.

A number of studies have reported that the parents of children with ADHD experience higher stress and anxiety due to difficulties encountered managing their child's behavior [5, 24, 25]. We found that mean parental mental health scores across all diagnostic categories were higher at baseline and reduced at 12-months. This suggests that parents may have experienced more mental health problems at baseline, however through maturation effects (e.g., seeking psychological and/ or medication treatment, improvement in their child's mental health symptoms), have learnt to cope and adjust 12-months on. Alternatively, this might also be explained by "regression to the mean", a statistical phenomenon whereby an extreme value is expected to fall closer to the mean upon repeated measure by chance alone [49].

Consistent with previous research [22, 23] we found evidence that all comorbidity categories were related to poorer family QoL across one, two or all three domains 12 months later, compared to families of children with ADHD alone. This study extends previous research by demonstrating that the families of children with co-occurring comorbidities are particularly vulnerable to poorer family QoL. Our findings suggest that compared to children with ADHD alone, children with ADHD and mental health comorbidities may be more

challenging for parents to manage and may therefore more regularly interrupt family life, limit time for family activities and cause tension and conflict at home.

No differences were found in teacher-reported peer problems for children with ADHD alone versus children with ADHD and comorbidities. A number of studies have reported that children with ADHD have poorer peer functioning by teacher-report, relative to children without ADHD [6, 7, 18]. It may be that factors aside from comorbidity status (i.e., ADHD symptom severity) influence teacher ratings of peer relationship functioning. In fact, male gender and comorbid ASD were the strongest predictors of teacher-reported peer problems at 12 months. It is also possible that our longitudinal findings were unstable given that most children had different teachers complete baseline and 12 month outcome surveys. However, weak relationships were also observed between comorbidity status and teacher-reported peer problems even in unadjusted analyses, which did not take into account baseline ratings. It is important to note that only one brief teacher-reported measure of peer functioning was included; future research would therefore benefit from use of more comprehensive measures of peer and broader functioning (e.g., academic achievement).

The study strengths include the recruitment of children from a large number of pediatric clinics across metropolitan and rural areas, thereby increasing the generalizability of results to clinical practice. Well-validated measures of ADHD and comorbidities were used, with the inclusion of both parent and teacher-reported outcome measures. Outcomes associated with co-occurring internalizing and externalizing comorbidities were specifically examined in analyses, and adjusted for key confounding variables (e.g., ADHD symptom severity, ASD).

This study has several limitations. There was some sample attrition at the 12 month follow-up. Although there were no differences between participants who did and did not take part at 12 months across most baseline characteristics (e.g., gender, age, comorbidity profile,

ADHD symptom severity, behavioral and emotional problems, parental mental health etc.), non-responders did have poorer baseline psychosocial QoL. Participants were from a clinical sample referred for treatment for ADHD; therefore, results may not apply to children with milder or unrecognized ADHD. A brief 5-item scale was used to examine peer functioning, which may not have been sensitive enough to detect subtle differences in peer difficulties between comorbidity categories. Finally, the relationship between parental mental health problems and comorbidities is likely to be bidirectional. Parental mental health problems may be a risk factor for child mental health problems, and conversely, the stressful nature and severity of the child's comorbidities may contribute to parent mental health problems.

This research provides information about the short-term prognosis associated with internalizing, externalizing, and co-occurring comorbidities in children with ADHD. This research also highlights the need for clinicians to take a multidimensional view of ADHD through assessment for comorbid disorders, to facilitate the targeting of interventions for specific comorbidities that can exacerbate impairments. Specifically, clinicians should systematically assess for comorbidities, and incorporate strategies for addressing these comorbidities in their management plan.

Summary

The current study highlights the importance of assessing and managing comorbidities in children with ADHD. Children with ADHD and co-occurring comorbidities were particularly vulnerable to poorer functioning 12 months later, including greater peer problems, poorer QoL, poorer daily functioning, and poorer family QoL. These findings held after accounting for key confounding variables including ADHD symptom severity and ASD status. Children with an internalizing comorbidity alone were vulnerable to poorer family QoL, while children with an externalizing comorbidity alone had greater peer problems and poorer family QoL. Therefore, identifying comorbidities will enable clinicians to actively

recognize, plan, and manage symptoms through evidence-based interventions in order to improve the functioning of children with ADHD and comorbidities.

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Table 1

Demographics and behavioral characteristics by comorbidity group

Characteristics	ADHD Alone (<i>n</i> =54)	ADHD & Internalizing (<i>n</i> =33)	ADHD & Externalizing (<i>n</i> =41)	ADHD & Co-occurring (<i>n</i> =71)	χ^2 or <i>F</i> ^a	<i>p</i>
Child						
Male (<i>n</i> , (%))	42 (79.63)	29 (87.88)	35 (87.80)	64 (90.14)	3.08	.38
Age in years (mean (<i>SD</i>))	10.10 (1.64)	10.42 (1.52)	10.09 (2.10)	10.05 (1.92)	0.33	.81
Comorbid ASD (<i>n</i> , (%))	8 (14.81)	13 (39.39)	8 (19.51)	25 (35.21)	10.20	.02
ADHD subtype (<i>n</i> , (%))					18.64	.005
Combined	23 (42.59)	18 (54.55)	23 (56.10)	54 (76.06)		
Inattentive	27 (50.00)	15 (45.45)	15 (36.59)	13 (18.31)		
Hyperactive/Impulsive	4 (7.41)	0 (0.00)	3 (7.32)	4 (5.63)		
ADHD medication (<i>n</i> , (%))	43 (81.13)	29 (87.88)	36 (87.50)	57 (80.28)	1.74	.63
ADHD symptom severity -Parent report (mean (<i>SD</i>))	29.31 (9.34)	32.55 (9.32)	35.30 (10.10)	38.78 (8.65)	11.31	<.001
ADHD symptom severity -Teacher report (mean (<i>SD</i>))	23.14 (11.60)	23.17 (12.28)	27.83 (13.22)	29.59 (12.69)	2.66	.05
Primary caregiver/family						
Mother (<i>n</i> , (%))	50 (92.59)	31 (93.94)	40 (97.56)	64 (92.75)	5.68	.46
Age in years, (mean (<i>SD</i>))	42.08 (5.37)	42.03 (5.41)	39.93 (5.53)	41.28 (7.29)	1.11	.35
Completed high school (<i>n</i> , (%))	33 (61.11)	24 (72.73)	20 (50.00)	30 (42.25)	9.96	.02
SEIFA, (mean (<i>SD</i>))	1020.67 (60.09)	1006.95 (62.38)	1004.75 (61.12)	995.06 (62.16)	1.75	.16

^a χ^2 statistics reported for categorical outcomes. *F* statistics reported for continuous outcomes; ^b SEIFA: Socio-Economic Indexes for Areas Disadvantage Index.

Table 2

Linear regression analyses examining unadjusted mean difference in outcomes for children with ADHD alone (reference category), compared to children within each comorbidity type (Model 1)

Outcomes	ADHD Alone (<i>n</i> =54 ^a)	ADHD & Internalizing (<i>n</i> =33 ^a)			ADHD & Externalizing (<i>n</i> =41 ^a)			ADHD & Co-occurring (<i>n</i> =71 ^a)			R ²
	Mean (<i>SD</i>)	Mean difference ^b (95% <i>CI</i>)	<i>p</i>	Effect Size	Mean difference ^b (95% <i>CI</i>)	<i>p</i>	Effect Size	Mean difference ^b (95% <i>CI</i>)	<i>p</i>	Effect Size	
Child											
Peer Problems (Teacher report) ^c	3.71 (2.15)	0.19 (-0.96, 1.33)	.75	0.09	-0.08 (-1.14, 0.98)	.88	-0.04	0.12 (-1.05, 0.82)	.80	-0.05	.002
Peer Problems (Parent report) ^c	2.67 (2.09)	0.16 (-0.75, 1.08)	.73	0.07	1.35 (0.48, 2.22)	.002	0.61	1.80 (1.06, 2.55)	<.001	0.82	.13
Daily Functioning ^c	15.40 (6.28)	1.33 (-1.58, 4.24)	.37	0.19	2.75 (0.03, 5.48)	.05	0.40	5.07 (2.68, 7.46)	<.001	0.74	.09
Psychosocial QoL ^d	64.70 (16.83)	-4.23 (-10.89, 2.43)	.21	-0.26	-4.22 (-10.54, 2.10)	.19	-0.26	-15.53 (-20.95, -10.12)	<.001	-0.95	.16
Parent and Family											
Parent Mental Health ^{d,e}	3.16 (19.22)	-6.78 (-16.55, 2.99)	.17	-0.31	-5.40 (-15.00, 4.19)	.27	-0.25	-8.67 (-16.76, -0.58)	.04	-0.40	.03
Family Functioning Emotions ^d	51.85 (24.57)	-6.69 (-17.34, 3.96)	.22	-0.27	-17.64 (-27.64, -7.63)	.001	-0.71	-16.34 (-24.93, -7.63)	<.001	-0.66	.09
Time ^d	70.75 (30.30)	-9.29 (-21.87, 3.28)	.15	-0.31	-12.86 (-24.80, -0.92)	.04	-0.43	-24.62 (-34.88, -14.36)	<.001	-0.82	.11
Family Activities ^d	63.82 (21.71)	-13.60 (-23.38, -3.83)	.007	-0.57	-12.50 (-21.77, -3.22)	.009	-0.52	-22.72 (-30.68, -14.76)	<.001	-0.95	.14

^a *n* ranges between: ADHD Alone *n*=37-53, ADHD & Internalizing *n*=24-32, ADHD & Externalizing *n*=31-40, ADHD & Co-occurring *n*=53-70; ^b The mean difference represents the difference between the comorbid group and children with ADHD alone (reference group); ^c Higher scores reflect poorer functioning; ^d Lower scores reflect poorer functioning; ^e Mean difference in change from baseline to 12 months was used due to skewed data.

Table 3

Linear regression analyses examining adjusted mean difference in outcomes for children with ADHD alone (reference category), compared to children within each comorbidity type (Model 2)

	ADHD Alone (<i>n</i> =54 ^a)	ADHD & Internalizing (<i>n</i> =33 ^a)			ADHD & Externalizing (<i>n</i> =41 ^a)			ADHD & Co-occurring (<i>n</i> =71 ^a)			R ²
Outcomes	Mean (<i>SD</i>)	Adjusted mean difference ^b (95% <i>CI</i>)	<i>p</i>	Effect Size	Adjusted mean difference ^b (95% <i>CI</i>)	<i>p</i>	Effect Size	Adjusted mean difference ^b (95% <i>CI</i>)	<i>p</i>	Effect Size	
Child											
Peer Problems (Teacher report) ^c	3.71 (2.15)	0.04 (-1.10, 1.18)	.95	0.02	0.17 (-0.91, 1.26)	.75	0.08	0.10 (-0.90, 1.10)	.84	0.05	.10
Peer Problems (Parent report) ^c	2.67 (2.09)	-0.15 (-1.08, 0.77)	.74	-0.07	1.25 (0.36, 2.14)	.006	0.57	1.50 (0.66, 2.33)	<.001	0.68	.18
Daily Functioning ^c	15.40 (6.28)	0.82 (-1.96, 3.60)	.56	0.12	1.52 (-1.13, 4.16)	.26	0.22	3.14 (0.65, 5.62)	.01	0.46	.25
Psychosocial QoL ^d	64.70 (16.83)	-2.53 (-9.32, 4.26)	.46	-0.15	-2.85 (-9.35, 3.66)	.39	-0.17	-12.29 (-18.28, -6.30)	<.001	-0.75	.21
Parent and Family											
Parent Mental Health ^{d,e}	3.16 (19.22)	-4.85 (-15.06, 5.35)	.35	-0.22	-2.95 (-13.18, 7.29)	.57	-0.14	-4.43 (-13.71, 4.84)	.35	-0.20	.06
Family Functioning											
Emotions ^d	51.85 (24.57)	-5.25 (-15.90, 5.40)	.33	-0.21	-15.92 (-26.01, -5.83)	.001	-0.64	-12.25 (-21.54, -3.00)	.01	-0.49	.18
Time ^d	70.75 (30.30)	-7.07 (-20.07, 5.93)	.29	-0.24	-11.84 (-24.36, 0.68)	.06	-0.46	-21.25 (-32.78, -9.72)	<.001	-0.71	.13
Family Activities ^d	63.82 (21.71)	-10.16 (-19.94, -0.38)	.04	-0.43	-8.04 (-17.45, 1.36)	.09	-0.34	-14.81 (-23.46, -6.15)	.001	-0.62	.23

^a *n* ranges between: ADHD Alone *n*=37-53, ADHD & Internalizing *n*=24-32, ADHD & Externalizing *n*=31-40, ADHD & Co-occurring *n*=53-70; ^b The mean difference represents the difference between the comorbid group and children with ADHD alone (reference group) adjusted for child age and gender, ADHD medication use, ADHD Rating Scale total score, comorbid ASD, and parent high school completion; ^c Higher scores reflect poorer functioning; ^d Lower scores reflect poorer functioning; ^e Mean difference in change from baseline to 12 months was used due to skewed data.

COMORBIDITIES AND FUNCTIONAL OUTCOMES FOR CHILDREN WITH ADHD

Table 4

Linear regression analysis examining the relationship between comorbidity group and 12 month outcomes, adjusted for confounding variables and baseline functioning (Model 3)

Predictors	12 month outcome domain							
	Peer problems (teacher report)		Peer problems (parent report)		Daily functioning		Quality of life	
	(n=114)		(n=190)		(n= 189)		(n=192)	
	β	<i>p</i>	β	<i>p</i>	β	<i>p</i>	β	<i>p</i>
ADHD alone (ref)								
Internalizing	-.05	.63	-.13	.07	.03	.66	.007	.93
Externalizing	-.03	.81	.10	.18	.05	.47	-.04	.58
Co-occurring	-.05	.70	.17	.04	.09	.29	-.22	.02
Child age	.08	.38	-.04	.51	-.02	.70	-.01	.82
Child gender	.23	.02	.01	.83	.01	.87	.02	.72
ADHD medication use	-.001	.99	-.04	.54	.02	.75	.08	.23
ADHD symptom severity	-.02	.81	-.005	.93	.13	.13	-.08	.26
ASD diagnosis	.26	.008	.12	.05	-.07	.27	-.07	.28
Primary caregiver high school completion	.12	.21	.07	.23	.03	.56	-.04	.58
Baseline functioning on outcome variable	.26	.008	.46	<.001	.46	<.001	.34	<.001
R ²	.17		.39		.34		.29	
<i>F</i>	2.16		11.47		9.39		7.30	
Df	10, 103		10, 179		10, 178		10, 181	