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Treatment Maintenance of Cognitive-Behavioral Therapy for Anxiety in Youth with Autism Spectrum Disorders

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by

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Abstract

Anxiety disorders commonly co-occur in children and adolescents with an autism spectrum disorder (ASD). Recently, treatment of anxiety using cognitive behavioral therapy (CBT) has been modified and studied in youth with ASD, with results consistently demonstrating positive treatment outcomes. In typically developing populations, CBT gains are well maintained as long as 14-years post-treatment; however, maintenance of CBT has not yet been studied in anxious youth with ASD. Using a sample of 32 youth who previously completed one of three CBT for anxiety in ASD treatment studies, the present study re-assessed parent report of anxiety symptoms in youth, 12-26 months (M = 17.16 Months; SD = 4.32) following treatment completion. Retrospective data from the original studies' screening/baseline and post-treatment time points were used in combination with newly obtained follow-up data to determine treatment maintenance. Compared to baseline, follow-up scores on all measures of anxiety were associated with large effects for treatment. Compared to post-treatment, no significant differences in scores were observed; however, scores on the Pediatric Anxiety Rating Scale suggested a small effect for return in symptoms. While the percentage of individuals with remission of their primary anxiety diagnosis was identical at post-treatment and follow-up, significantly fewer individuals were rated as responders at follow-up as compared to post-treatment. Similar to CBT for anxiety in neurotypical youth, CBT for anxiety in youth with ASD appears to be relatively durable over a one to two year interval. Despite this, a significant portion of participants demonstrate some level of symptom regression. Future study should investigate factors associated with poor treatment maintenance, as well as modifications or additions to treatment protocols (e.g., booster sessions) that may help maintain treatment gains.

Treatment Maintenance of Cognitive-Behavioral Therapy for Anxiety in Youth with Autism Spectrum Disorders

A category of neurodevelopmental disorders, autism spectrum disorders (ASD) affect as many as 1 out of 150 children world-wide (Fombonne, 2009) and as many as 1 in 81 children in the United States (CDC, 2012). Autism spectrum disorders functions as an over-arching category for autistic disorder (AD), Asperger's Syndrome (AS), and pervasive developmental disorder not otherwise specified (PDD-NOS) [1]. Individuals who meet criteria for AD demonstrate significant developmental delays in social interaction and communication as well as the presence of stereotyped behavior and restricted interests (American Psychiatric Association, 2000). Comparatively, individuals diagnosed with AS demonstrate both social delays and repetitive, restricted or stereotyped behavior but do not demonstrate the same delays in cognitive ability or communication. A diagnosis of PDD-NOS is reserved for individuals whose expression of significant developmental delays is not best described by either AD or AS.

Co-occurring psychiatric/psychological disorders are common in youth with ASD with approximately 75% meeting criteria for a second disorder (De Bruin, Ferdinand, Meester, De Nijs, & Verheij, 2007; Leyfer et al., 2006; Siminoff, Pickles, Charman, Chandler, & Loucas, 2008). Intellectual disabilities (excluding Asperger's Syndrome; Matson & Shoemaker, 2009), depressive disorders (Ghaziuddin, Ghaziuddin, & Greden, 2002; Leyfer et al., 2006), tic disorders (Baron-Cohen, Mortimore, Moriarty, Izaguirre, & Robertson, 1999), and disruptive behavior disorders (e.g., oppositional defiant disorder; De Bruin et al., 2007; Leyfer et al., 2006) are all commonly diagnosed comorbid conditions. Anxiety disorders, however, have received particular attention because of their frequency and impact on overall functioning (De Bruin et al., 2007; Gillot, Furniss, & Walter, 2001; Kim, Szatmari, Bryson, Streiner, & Wilson, 2000; Russell, Mataix-Cols, Anson, & Murphy, 2005).

The present study proposes to examine the maintenance of cognitive-behavioral therapy for individuals with ASD and co-occurring anxiety. Following is a review of extant research that outlines the relationship and impact of anxiety in youth with ASD, as well as treatment of anxiety within typically

[1] The DSM-5 does not distinguish between AD, AS, and PDD-NOS, but includes all individuals under a single ASD umbrella diagnosis (American Psychiatric Association, 2013).

developing populations and those with ASD. Follow-up treatment outcomes within these populations and any previously identified predictors of treatment maintenance are also discussed.

Anxiety in Autism

Anxiety is not a criterion component for ASD, although it is clear many youth with ASD suffer from clinically significant anxiety symptoms, with severity comparable to typically developing children with clinical diagnoses (Russel & Sofronoff, 2005). While the prevalence rates of specific comorbid anxiety diagnoses have differed by study, approximate ranges for individual disorders include: 8.5-44.3% specific phobia, 7.4-29.2% social phobia, 6.4-37% obsessive compulsive disorder, 6.4-7.9% agoraphobia, 2.4-13.4% generalized anxiety disorder, 1.1-10.1% panic disorder, and 0.5-12% separation anxiety disorder (De Bruin et al., 2007; Leyfer et al., 2006; Siminoff et al., 2008).

Currently, the relationship between anxiety and ASD remains unclear (Weisbrot, Gadow, DeVincent, & Pomeroy, 2005). Etiologically, there appear to be some associations between neurobiological abnormalities associated with ASD and anxiety (Kleinhans et al., 2010; Shumann & Amaral, 2006), as well as a number of ASD related deficits (e.g., social deficits, sensory sensitivity) that may contribute to the development of anxiety within this population (Bellini, 2004; Ben-Sasson et al., 2008; Spiker et al., 2011). More generally, level of intellect and communication abilities are both predictors of anxiety severity in youth with ASD (Davis et al., 2011; Weisbrot et al., 2005) while anxiety and depressive symptoms appear to positively predict core autism symptom severity (Kelly, Garnett, Attwood, & Peterson, 2008).

Co-occurring anxiety in youth with ASD presents a serious concern for these youth and their families. Among concerns reported by parents of children with ASD, anxiety was the second most common (Mills & Wing, 2005). Increases in anxiety severity among this population appear to have a broad negative impact, with adverse outcomes in multiple symptom domains. For example, Kim et al. (2000) found that measures of anxiety and mood problems were highly correlated with scores of aggressive ($r = 0.67$, $p < .001$) and oppositional behavior ($r = 0.50$, $p < .001$). Additionally, youth with ASD and high anxiety report limited social engagement and poorer relationships with parents, teachers and peers (Kim et al., 2000), while family cohesion appears to negatively predict anxiety/depression

symptoms (Kelly et al., 2008). The number of hospitalizations and occurrences of medical illness for youth with ASD also increase with anxiety symptom severity (Gadow, DeVincent, & Schneider, 2008).

Treatment of Anxiety

For the treatment of anxiety in typically developing populations, two approaches have received empirical support, namely cognitive behavioral therapy (CBT) and pharmacotherapy using serotonin reuptake inhibitors (SRIs). Cognitive behavioral therapy has emerged as the first line treatment for childhood anxiety, over pharmacology, due in part to its comparable or superior efficacy, maintenance and safety/tolerability (Abramowitz, Whiteside, & Deacon, 2005; Cartwright-Hatton, Roberts, Chitsabesan, Fothergill, & Harrington, 2004; In-Albon & Schneider, 2007; Mancuso, Faro, Joshi, & Geller, 2010; Mitte, 2005). As an example, for the cognitive-behavioral treatment of obsessive-compulsive disorder (OCD) randomized controlled trials report that up to 85% of individuals respond to treatment and up to 50% experience clinical remission (Franklin et al., 2011; POTS, 2004; Simpson, Huppert, Petkova, Foa, & Liebowitz, 2006).

Cognitive behavioral therapy for anxiety disorders includes four primary components: psychoeducation, exposure hierarchy generation, behavioral exposures with response prevention, and cognitive therapy. Psychoeducation is typically employed at treatment outset and includes teaching patients and their families about the nature of the disorder, the etiology of anxiety and behaviors (e.g., accommodation) related to its manifestation/maintenance, how the treatment will target these problems and how treatment and homework adherence are essential to success. Following psychoeducation, therapists work with patients to develop an individually-tailored fear hierarchy which ranks stimuli according to their associated level of distress. Starting low on the hierarchy, the therapist begins behavioral exposures and response prevention, where participants confront their feared stimuli and are prevented from engaging in their prototypical response. Finally, cognitive therapy is employed to help the child recognize, examine, evaluate, and combat maladaptive anxiogenic thought patterns related to anxiety. In particular, meta-analytic data suggests behavioral exposure and response prevention is a key component especially in the treatment of OCD and social phobia (Deacon & Abramowitz, 2004). In youth with anxiety disorders, the inclusion of family in the treatment process is recommended and appears to reduce developmentally based barriers to treatment, such as poor insight and homework compliance

(Kendall & Choudhury, 2003; Storch et al., 2007a; Wood, Piacentini, Southam-Gerow, Chu, & Sigman, 2006).

Anxiety Treatment in Autism

While the treatment of anxiety in typically developing populations has strong empirical support, only recently have studies began to examine its utility in youth with ASD and comorbid anxiety. The symptomology of ASD presents a number of potential barriers to treatment success that may include, but are not limited to: attention, social, and communication delays/deficits (Warren et al., 2011; Wood et al., 2009a), limited insight (Storch et al., 2012), disruptive behavior, and restricted interests (Wood et al., 2009a). As a result, evaluation is required to determine whether these treatment approaches, which mitigate anxiety symptomology within typically developing populations, will be associated with similar treatment outcomes within youth with ASD.

Antidepressants, typically SRIs, represent the single most prescribed medication in youth with ASD (Oswald & Sonenklar, 2007). Research support for their use is limited with inconsistent findings, poorly designed studies, safety and tolerability concerns, and either have not looked at anxiety as a target symptom or have not measured it in a methodologically rigorous way (King et al., 2009; Autism Speaks, 2009; Warren et al., 2011). While further study of SRI monotherapy in youth with ASD is still warranted, especially in regards to anxiety improvement, extant data currently do not support its use in youth with ASD and anxiety.

Nine controlled trials have been conducted examining the use of CBT-based approaches to anxiety in ASD. While the methodology of each approach has differed slightly, these treatments are based on CBT treatment for anxiety in typically developing individuals and combined with aspects of skills training/applied behavioral analysis that are commonly used in the treatment of individuals with ASD or modified to address ASD specific barriers (Lang, Regester, Lauderdale, Ashbaugh, & Haring, 2010).

Sofronoff, Attwood, and Hinton (2005) conducted the first randomized controlled trial examining a brief CBT intervention for 71 children (10-12 years old) diagnosed with AS and co-occurring anxiety symptoms. Improvements in parent-rated anxiety were significant for treatment conditions (child-focused and child and parent focused), when compared to waitlist control, at treatment end as well as at 6-week follow up. The second randomized controlled trail, conducted by Chalfant, Rapee, and Carroll (2007),

examined a 12-week individual CBT treatment for anxiety symptoms in 47 children (8-13 years old) with high functioning ASD. Of those in the CBT condition 71.4% (*n* = 20) experienced diagnostic remission of their primary anxiety diagnosis compared to 0% of those randomized to waitlist control. Compared to the waitlist condition, individuals in the CBT condition also showed significantly better symptom improvement across self, parent, and teacher reports.

Wood et al. (2009a) conducted a statistically rigorous randomized control trial with 40 children (7-11 years old) randomly assigned to either a 16-session CBT protocol or a waitlist control. Compared to previous CBT protocols, Wood et al. (2009a) put a stronger emphasis on the use of *in vivo* exposures, which are associated with greater anxiety improvements compared to other treatment components in typically developing populations (Deacon & Abramowitz, 2004) and developed and employed a number of modules aimed at targeting ASD specific deficits including social exposures and friendship development. At post-treatment, 76.5% (*n* = 13) of children in the treatment condition were rated as treatment responders with 52.9% (*n* = 9) reporting diagnostic remission of their anxiety disorder. In contrast, only 8.7% (*n* = 2) were rated as responders or experienced clinical remission in the waitlist condition. Compared to waitlist control, the treatment condition also demonstrated large effects for reductions in clinician-rated anxiety severity (*d* = 2.46) and parent-rated anxiety (*d* = 1.23).

Following the lead of these initial trials, in recent years the number of randomized controlled trials has grown significantly. Based on positive outcomes from an initial pilot study (Reaven et al., 2009), Reaven, Blakeley-Smith, Culhane-Shelburne, and Hepburn (2012) investigated a 12-week group treatment CBT protocol for 50 youth, finding a large effect for the treatment condition (*d* = 1.03) and maintenance of gains at both 3- and 6-month follow ups. In a sample of 45 youth, Storch et al. (2013) examined the Wood et al. (2009) treatment protocol and found a large treatment effect compared to a treatment as usual control (*d* = 1.03). McNally Keehn, Lincoln, Brown, and Chariva, (2013) investigated the efficacy of slightly modified version of the Coping Cat CBT program in 22 youth and found large effects compared to a waitlist control (*d* = 1.45). Sung et al. (2011) investigated CBT versus a social recreational control in a Singapore based sample of 70 youth, showing small effects for both the CBT program and control arm on child self-reports of anxiety with continued improvement through the 3- and 6-month follow-ups. The only study to include an adult population (N = 40), Russell et al. (2013)

investigated the use of exposure and response prevention for OCD in adolescents and adults with ASD compared to an anxiety management control. Results suggested the CBT condition was slightly more effective than the treatment control (*d* = 0.37). A combined CBT and social skills treatment for adolescents has also been investigated (N = 30); however, only small improvements in anxiety were noted (*d* = 0.32; White et al., 2013).

While the primary interest of the majority of these treatment protocols has been decreasing anxiety severity, Wood et al. (2009b), Drahota, Wood, Sze, and Van Dyke (2011), Storch et al. (2013) and White et al. (2013) have examined the broader improvement implications of the treatments. In addition to the reported anxiety related improvements, CBT has also been associated with significant decreases in parent-rated autism symptom severity (Wood et al., 2009: *d* = .77; Storch et al., 2013; *d* = 0.46). White et al.'s (2013) combined anxiety and social skill group protocol appeared particularly effective in improving this domain (*d* = 1.03). In addition, reports by parents indicated participants in Wood et al.'s (2009a) CBT protocol required less assistance and care on a daily basis and had demonstrated improvements in living/self-care skills over the course of treatment (Drahota et al., 2011).

Treatment Maintenance

A number of studies have examined the durability of CBT protocols for OCD and non-OCD anxiety disorders in typically developing populations. At 1-year following treatment end, gains made during treatment of non-OCD anxiety are well-maintained, with studies generally finding non-significant differences between post-treatment and follow-up, as well as large treatment effects when compared to baseline (Kendall, 1994; Spence, Holmes, March, & Lipp, 2006; Spence et al., 2011; Sportel, Hullu, de Jon, & Nauta, 2013). For example, in Spence et al., (2006) remission of primary anxiety diagnosis increased from 55% (*n* = 27) at post-treatment to 63% at 1-year follow-up (*n* = 31). Longer term follow-ups at 2-,5-, 7-, and even up to 14-years following treatment end have found similar results suggesting gains made during CBT are robust and stable over time (Durham, Chambers, MacDonald, Power, & Chambers, 2003; Garcia-Lopez et al., 2006; Kendall, Safford, Flannery-Schroeder, & Webb, 2004; Manassis, Avery, Butalia, & Mendlowitz, 2004).

For the treatment of OCD, results are similar with treatment gains comparable at 1-year follow-up as compared to post-treatment (Anand, Sudhir, Math, Thennarasu, & Reddy, 2011; Barrett, Farrell,

Dadds & Boulter, 2005; Braga, Cordioli, Niederauer, & Manfro, 2005; Jaurrieta et al., 2008). On an individual level, Barrett et al. (2005) reported that 64.6% (*n* = 31) had maintained treatment gains, 14.6% (*n* = 7) had improved from post-treatment, and 16.7% (*n* = 8) had relapsed in the 18-months since post-treatment. Like in other anxiety disorders, gains for CBT treatment of OCD appear to be relatively stable over time, with a 7-year follow-up of Barrett et al. (2005) demonstrating comparable results to the 18-month follow-up (O'Leary, Barrett, & Fjermestad, 2009), as well as an additional 7-year follow-up demonstrating that of the 20 participants who demonstrated response at post-treatment, 90% (*n* =18) had maintained treatment gains (Rufer et al., 2005).

However, the long term efficacy of CBT treatments for individuals with anxiety in ASD is currently unknown. Non-anxiety based treatment approaches for this population, such as social skills interventions, have not been particularly successful in maintaining treatment gains at follow-up, with symptom levels returning to baseline as short as 2-months after treatment end (Hwang & Hughes, 2000; Rao, Beidel, & Murray, 2008; Warren et al., 2011). However, participants in previous controlled trials for anxiety in ASD have demonstrated maintenance of treatment gains up to 6-months post-treatment (Sofronoff et al., 2005; Reaven et al., 2012; Storch et al., 2013; Wood et al., 2009a). While individuals with ASD present a number of additional treatment barriers compared to typically developing children (Wood et al., 2009) the similar level of response to CBT based treatment across both populations lends support to longer-term treatment maintenance within youth with ASD.

Predictors of Treatment Maintenance

While studies do appear to demonstrate that CBT is successfully maintained over the long-term in typically developing youth, in many of these cases it is unclear to what extent individuals have obtained additional psychological services between treatment-end and long-term follow-up. Rufer et al. (2005) noted that of their participant pool, almost all individuals obtained some form of additional treatment, and that those who had suffered from OCD longer at pre-treatment demonstrated a higher-rate of treatment usage. While it is unclear what effect it had on their reported levels of treatment maintenance, Durham et al. (2003) also found that 23% (*n* = 13) of the individuals who had received CBT indicated a "moderate" level of interim treatment and 9% (*n* = 5) obtained "a lot". These findings demonstrate the importance of assessing interim treatment usage and its relation to treatment maintenance.

In examining treatment maintenance at 2-5-year follow up, Kendall and Southam-Gerow (1996) examined whether participants could free recall a component of treatment and whether they remembered and used specifically probed factors of treatment (e.g., emotion recognition component, in vivo exposures). Their results determined that while very few perceived factors were related to outcome in a meaningful way, recall of emotion recognition steps and of relaxation exercises were associated with positive treatment effects.

In the follow-up of CBT for OCD at 12- and 18- months, Barrett et al. (2005) examined a number of pre-treatment variables, including OCD severity, self-reported depression and anxiety symptoms, and family functioning, and their relationship to treatment maintenance. In particular, the severity of obsessions, compulsions and family dysfunction were found to be significant independent predictors of poor long-term treatment outcomes while self-reported anxiety did not appear to be a beneficial predictor of outcomes. This evidence suggests that clinical factors may predict treatment outcomes, therefore in the present study, the predictive ability of various clinical factors will be examined in regards to durability of CBT in youth with ASD.

Present Study

This study focused on the extent to which gains made during the course of a CBT treatment for anxiety in youth with ASD were extended beyond treatment end. Cognitive-behavioral interventions are time and cost-intensive for both patients and practitioners and therefore determining the extent of treatment maintenance is an important component of deciding the true effectiveness of a treatment. If treatment gains were maintained well after treatment end, this would add significant validity to the usefulness of this treatment approach. If, however, they were not, it would be important for researchers to determine how the treatment could be modified or supported in order to do so (e.g., booster sessions). It was also of importance to determine what factors may predict successful, or a lack of, treatment maintenance within certain individuals so that practitioners can develop and provide the appropriate provisions to ensure the success of these individuals (e.g., extended treatment length, combined therapy).

Therefore, the current study intended to determine the maintenance of treatment gains of responders to a CBT protocol for anxiety in ASD at a 12-26 month follow-up. Based on long-term outcomes of typically developing individuals, as well as preliminary follow-ups in individuals with ASD, it

was hypothesized that gains made in treatment would be non-significantly different at long-term follow up and that the treatment gains would remain significant when compared to baseline. In addition, the current study conducted an exploratory analysis of factors which were believed to be possible predictors of maintenance (or lack there of), specifically baseline severity, primary anxiety diagnosis, number of comorbid diagnoses, presence of disruptive behavior, interim treatment obtainment and continued memory and use of treatment techniques (specifically emotion recognition/coping skills and in vivo exposure) by participants and their families.

Method

Participants

Following approval by the local institutional review board (IRB), youth were recruited from a list of participants who had previously consented/assented and completed one of three IRB-approved, funded studies, namely *Cognitive-Behavioral Treatment for Anxiety Disorders in Children with Autism Spectrum Disorders* (PI: Storch, All Children's Hospital Research Foundation; Storch et al., 2013)*, CBT for Anxiety Disorders in Autism: Adapting Treatment for Adolescents* (PI: Storch, National Institute of Health, #1R34HD065274), and *Cognitive Behavioral Therapy for Anxiety Disorders in Adolescents with Autism Spectrum Disorders* (PI: Storch, University of South Florida Research Foundation). For inclusion in any of the initial treatment trials, participants were required to meet criteria for a DSM-IV-TR diagnosis of AD, AS or PDD-NOS, have a primary anxiety diagnosis of either separation anxiety disorder (SAD), generalized anxiety disorder (GAD), social phobia, or OCD, have an IQ >70 on a standardized test, and have stable medication (if applicable) for 8-(antipsychotics, alternative medications, nutritionals or therapeutic diets) or 12-weeks (antidepressants) before study enrollment. Further, participants were excluded if they displayed suicidal behaviors within the 6 months prior to treatment start or if they had histories of bipolar, schizophrenia or schizoaffective disorders. Initial treatment eligibility was established at screening procedures by a trained independent evaluator.

All participants received a 16-session, 60-90-minute, family based CBT treatment protocol, either the *Behavioral Interventions for Anxiety in Children with Autism (BIACA;* Wood & Drahota, 2005; Wood et al., 2009a) or the slightly modified adolescent version *Anxiety-Focused Interventions for Youth with Autism* (*AFIYA;* Ehrenreich, Simpson & Wood, 2009). Both programs are based off a published family treatment manual for typically developing children (Wood & McLeod, 2008; Wood et al., 2006); though they similarly employed a number of expanded components designed to appropriately address the treatment needs and difficulties of youth with ASD. The interventions were flexible in nature, and allowed the therapist to choose appropriate modules based on the child's current needs. A minimum of three sessions addressed coping skills and a minimum of eight addressed *in vivo* exposure, with the alternative

modules focusing on positive reinforcement, social skills, and communication skills. The integrity of treatment administration was monitored through out, using the *BIACA* or *AFIYA* treatment manual, ongoing supervision and regular monitoring both of therapists and patients. While the initial studies included control conditions (treatment as usual; TAU or waitlist; WL), all participants received CBT following completion of TAU/WL, and therefore participants from both treatment arms were eligible for inclusion.

For inclusion in the current study, participants must have demonstrated some level of treatment response (score 4 or higher on the clinical global impression – improvement; CGI-Improvement; Guy, 1976) and have completed study procedures between 12-26 months prior to the follow-up assessment.[2] After eliminating individuals who did not demonstrate any treatment response or did not reach follow-up in time for inclusion, 45 participants were identified for recruitment. Of those recruited, 8.89% (*n* = 4) declined to participate and 20% (*n* = 9) could not be reached and/or scheduled. All together 32 youth (*M* =12.13, *SD* = 2.27, Range: 8-16-years old) consented and completed the study procedures (see Table 1 for demographics). No direct compensation for participation was provided; however, for those participants who requested it, anonymous donations were made to one of four possible charities and a brief research report based on the assessment was provided.

Materials

Autism Diagnosis Interview-Revised (ADI-R): The ADI-R (Lord, Rutter, Le Couteur, 1994; Le Couteur, Lord, & Rutter, 2003) is a standardized clinician administered semi-structured interview used for the assessment of the presence and severity autism. Diagnostic criteria for autism are based on the DSM-IV-TR (American Psychiatric Association, 2000). The ADI-R has well established psychometric properties including inter-rater reliability, test-retest reliability, internal consistency, and discriminative validity (Lord et al., 1994). The ADI-R was used with the Autism Diagnostic Observation Schedule (ADOS) as recommended (Le Couteur et al., 2003; Le Couteur, Haden, Hammal, & McConachie, 2008) at screening of the initial studies to determine the initial diagnosis of an ASD. The ADI-R was not re-administered as part of the present study.

[2] Data for one participant was only available from a treatment study screening that occurred 10 months following completion of treatment. In order to maximize sample size this participant's data was included.

Autism Diagnostic Observation Schedule – Module 3 (ADOS): The ADOS (Lord et al., 2000; Lord, Rutter, Di Lavore, & Risi, 2001) is a structured observational assessment used to elicit specific behaviors (e.g., social interaction, atypical use of language) important in determining differential diagnosis of ASD. The ADOS is psychometrically sound with excellent inter-rater reliability and internal consistency as well as substantial test-retest reliability (Lord et al., 2000). When used together, the ADI-R and ADOS demonstrate good discriminative ability and diagnostic utility (Bildt et al., 2004; Mazefsky & Oswald, 2006). The ADOS was used with the ADI-R as recommended (Le Couteur et al., 2003; Le Couteur et al., 2008) at screening of the initial studies to determine the initial diagnosis of an ASD. The ADOS was not re-administered as part of the present study.

Anxiety Disorders Interview Schedule for DSM-IV – Parent Version (ADIS): Based on DSM-IV-TR criteria (American Psychiatric Association, 2000) the ADIS (Silverman & Albano, 1996) is a structured interview administered by the clinician. The ADIS assesses current episodes and provides differential diagnosis of Axis I disorders reflecting parental endorsement of symptoms as well as the severity of patient impairment/distress. Final diagnoses and severity scores are determined by the clinician using a 0-8 scale, with a score of 4 or more indicating the presence of a clinically significant disorder (clinician severity rating; CSR). The ADIS has demonstrated strong psychometric properties with typically developing youth, including test-retest reliability, inter-rater reliability and concurrent validity (Silverman, Saavedra, & Pina, 2001; Wood, Piacentini, Bergman, McCracken, & Barrios, 2002), and recently was noted to have good to excellent inter-rater reliability in youth with ASD (Ung et al., 2013). While the ADIS does include a child component, youth with ASD demonstrate poor diagnostic agreement with both parents and clinicians (Storch et al., 2012). Considering its limited benefit and non-informing contribution towards diagnoses, the ADIS-child version was not employed. Retrospective ADIS scores were used from the initial trial baseline and post-treatment and the ADIS was re-administered at follow-up.

Clinical Global Impression – Severity (CGI-Severity): The CGI-Severity (National Institute of Mental Health, 1985) is a 7-point rating scale for clinicians to measure severity of general psychopathology. The CGI-Severity is used in conjunction with other test scores, and has demonstrated sound psychometric properties including convergent validity and treatment sensitivity (Storch, Lewin, De Nadai, & Murphy, 2010; Storch et al., 2007b; Zaider, Heimberg, Fresco, Schneier, & Liebowitz. 2003).

Scores range from 0 (indicating no illness) to 6 (indicating extreme severity) and was retrospectively used from initial trial baseline and post-treatment. In addition, the CGI-Severity was re-administered at follow up.

Clinical Global Impression – Improvement (CGI-Improvement): The CGI-Improvement (Guy, 1976) is a 7-point rating scale for clinicians to measure improvement of clinically significant symptoms. Used in conjuncture with other test scores, CGI-Improvement ratings range from 0 (very much worse) to 6 (very much improved). The CGI-Improvement is a psychometrically established measure and has demonstrated convergent validity and strong agreement with the CGI-Severity (Zaider et al., 2003). CGI-Improvement scores are based on the initial baseline measurement of pathology, were recorded at post-treatment and again at follow-up. All participants were required to score at least a 4 (minimally improved) at post-treatment for inclusion in the follow-up assessment, while a score of 5 or 6 is required in order to be deemed a treatment responder.

Pediatric Anxiety Rating Scale (PARS): The PARS (RUPP, 2002) is a clinician rated scale assessing both child and parent reports of child anxiety symptoms, severity, and impairment over the past week. The PARS demonstrates sound psychometric properties in typically developing youth including inter-rater reliability, test-retest reliability and both convergent and divergent validity with good sensitivity to treatment (RUPP, 2002). In youth with ASD, the PARS demonstrates high test-retest and inter-rater reliability as well as convergent validity and divergent validity adequate for assessing anxiety symptoms in this population (Storch et al., 2012). Considering the lack of insight regarding anxiety symptoms characteristic of individuals with ASD (Storch et al., 2012), only the parent report on the PARS was obtained. PARS assessment scores from initial trial baseline and post-treatment were used retrospectively. The PARS was also re-administered at follow-up.

Social Responsiveness Scale (SRS). The SRS (Constantino & Gruber, 2005) is a standardized 65-item parent-rated scale designed to assess the presence of autism spectrum symptoms (e.g., social and communication deficits, repetitive behaviors). Using 4-point likert scales, the SRS provides a flexible index that is recommend for use in measuring changes of autism symptoms (Wood, Fujii, & Renno, 2011). The SRS has demonstrated sound psychometric properties including inter-rater reliability, internal consistency, test-retest reliability and convergent validity (Constantino et al., 2003; Constantino & Gruber,

2005). As recommended, any missing items on the SRS were replaced with the median score for that item (Constantino & Gruber, 2005). The SRS was completed by parents at baseline and post-treatment and scores were used retrospectively. Parents once again completed the SRS at follow-up.

Brief Interview Based on the Service Assessment for Children and Adolescents – Service Use Scale (SACA). The SACA is a standardized and reliable interview for parents that assesses the extent to which a variety of mental health services have been obtained by the child over the past 3 months (Horwitz et al., 2001). A brief modified SACA was conducted by the clinician at follow-up to assess the extent to which mental health services had been obtained since treatment completion.

Assessment of Independent Implementation of Treatment Techniques (IITT; Appendix A). The IITT is a self-developed measure consisting of 48 questions, including likert scales and descriptive multiple-choice questions. Based on the treatment manual employed and the recommendations of therapists from the initial treatment studies, the IITT assesses the extent and reasons parents did/did not remember and employ therapeutic techniques (e.g. exposures) after treatment completion. Psychometric properties of this measure have not been established and all analysis was exploratory. Since emotion recognition and in vivo exposure were mandated parts of treatment and are the anxiety-focused components of the treatment, responses regarding these modules were chosen for analysis.

Procedure

All research procedures were reviewed and approved by the local IRB. All evaluators were extensively trained on the administration of clinician-rated measures (e.g., ADIS-P, PARS, CGI-Improvement, CGI-Severity) including instructional didactics, extensive observation of administrations by certified raters, and supervised administration of the measures. Prior to involvement in the current study, all parents provided written informed consent. Because children were not involved in this aspect of the study, child assent was not required. As part of the initial therapy delivery study, an independent evaluator administered and collected the relevant measures at baseline and post-treatment, which were used for comparison of treatment maintenance at follow-up. The post-treatment measure of those initially enrolled to the TAU condition served as their baseline measure.

Participants were contacted by the experimenter, regarding their participation in the present study, between 12-26 months following completion of CBT. For all willing participants, assessments were

administered and collected in person by the evaluator; however, individuals not available to complete the assessment in person were administered the clinician-rated assessments by phone and completed parent measures via a secure web-based survey service (i.e. checkbox). The inclusion of telephone assessments provided flexibility for participants and should not have reduced the accuracy of outcome measures in any way (Lyneham & Rapee, 2005). Those participants who had requested reports were provided them within 30 days. See Table 2 for a timeline of data used in the present study.

Data Analysis

Specific Aim 1. In order to examine whether treatment was maintained at follow-up compared to the baseline measurement, dependent samples *t*-tests were used to compare scores on continuous measures of anxiety severity (primary anxiety CSR; total anxiety CSRs; CGI-Severity; PARS). Parent-rated autism spectrum symptoms (SRS) were also examined. However, only a portion of the sample (*n* = 19) completed the measure, since completion of the assessment via telephone allowed for non-completion of the online survey based measures (SRS and IITT). Based on previous studies (e.g., Wood et al., 2009; Storch et al., 2013), baseline to post-treatment effects were expected to be large (*d* > 1.0). Therefore, the present study chose to obtain power for a medium effect, as this would represent a clinically meaningful decrease in the value of treatment/return of symptoms. Power analysis determined that given a sample of N = 32, power of .80 would be present to detect 'medium' size (*d* > 0.51) effects.

Specific Aim 2. To examine whether treatment was maintained at follow up compared to post-treatment end, dependent samples *t-tests* were used to compare scores on continuous measures of anxiety severity (primary anxiety CSR; total anxiety CSRs; CGI-Severity; PARS). Additionally, parent-rated autism spectrum symptoms (SRS) were examined in the portion of the sample who had completed the measure (*n* = 19). For categorical measures of improvement (remission of primary anxiety diagnosis; treatment response) McNemar's chi-square test was used as it is recommended for testing the equivalence of dependent groups (McNemar, 1947). With the sample size of 32 participants and power of 0.8, power analysis revealed the dependent samples *t*-test sensitive enough to detect an effect of *d* > 0.51.

To further evaluate comparability of scores and make-up of treatment maintenance, changes in participant's scores between post-treatment and follow-up were rated as either worse (0), comparable (1),

or better (2) on the CGI-Severity (<one point difference indicated change), CGI-Improvement (<one point difference indicated change), PARS (<two point difference indicated change), and total CSR (<25% difference indicated change). Summed together, change scores ranged from 0 (worse on all scales) – 8 (better on all scales), with a sum score of 0-2 indicating reductions in treatment gains, 3-5 indicating maintenance of treatment gains, and 6-8 indicating further improvement of treatment gains.

Exploratory Aim 3. To examine what factors predict maintenance of treatment gains logistic regression analysis was utilized. Using the change scores calculated for specific aim two, scores were dichotomized with individuals scoring from 0-3 categorized as non-maintainers and those scoring from 4-8 categorized as maintainers. The predictive value of baseline severity (PARS), primary anxiety diagnosis (ADIS), number of comorbid diagnoses (ADIS), presence of comorbid oppositional defiant disorder (ADIS), time to follow-up, and interim treatment obtainment (SACA). Treatment obtained during the follow-up was categorized as: A) medication usage; B) anxiety-focused psychotherapy; C) general psychotherapy; D) social skills training; E) occupational, physical and/or speech therapy; and F) in-school assistance. Continued use of treatment components (IITT) was also evaluated; however, complete data was only available for a portion of the sample (n = 12). Of the sample, 16 participants did not complete the online version of the measure, while an additional 4 participants completed the measure, bud appeared to have done so incorrectly (e.g., answered “did not complete” to all modules of treatment, including those all participants received).

Table 1: Demographic and Clinical Information.

Measure	n (%)
Child sex (male)	24 (75.0)
Study Type	
Pilot Trial	11 (34.4)
Child Study	19 (59.4)
Adolescent Study	2 (6.3)
Ethnicity/Race	
Caucasian	29 (90.6)
Latino/Hispanic	1 (3.1)
Middle Eastern	1 (3.1)
Mixed Race	1 (3.1)
Primary ASD Diagnosis	
Autistic Disorder	11 (34.4)
Asperger's Syndrome	12 (37.5)
PDD-NOS	9 (28.1)
Primary Anxiety Diagnosis	
SAD	2 (6.3)
Social Phobia	12 (37.5)
GAD	13 (40.6)
OCD	5 (15.6)
Interim Treatment	
On Medications	21 (67.7)
Anxiety-Focused Psychotherapy	4 (12.5)
General Psychotherapy	10 (32.3)
Social Skills Training	6 (18.8)
Occupational, Physical, and Speech Therapy	11 (34.4)
In-School Assistance	10 (31.3)

Table 2*:* Schedule of Measure Completion for Study Participants.

Measure	Baseline/Screening (Retrospective)	Post-Treatment (Retrospective)	Follow-Up (Active)
ADOS	X		
ADIR	X		
ADIS	X	X	X
CGI-Severity	X	X	X
CGI-Improvement		X	X
PARS	X	X	X
SRS	X	X	X
SACA			X
IITT			X

Results

Baseline Comparison

Follow-up data was compared to baseline data to determine the magnitude and significance of the treatment effects 12-26 months (M = 17.16 Months; SD = 4.32) following treatment completion. Results suggest that treatment effects were robust with large reductions in anxiety severity on all measures, including the PARS (t (31) = 5.09, p < .001; d = 1.03), CGI-Severity (t (31) = 6.78, p < .001; d = 1.43), primary anxiety CSR (t (31) = 6.36, p < .001; d = 1.38) and total anxiety CSR (t (31) = 6.41, p < .001; d = 1.07; see Table 3). Based on clinician ratings on the CGI-Improvement, 53.1% (n = 17) of the sample was considered treatment responders at follow-up, though an additional 25% (n = 8) were rated as minimally improved, with 18.8% (n = 6) rated as demonstrating no change from baseline and 3.1% (n = 1) reporting minimally worse symptoms at follow-up. In addition, approximately 46.9% (n = 15) of the sample had demonstrated remission of their primary anxiety disorder as determined at baseline. Parent-rated core autism symptoms, as measured by the SRS, also demonstrated a significant, albeit smaller, decrease in severity from baseline to follow-up (t (18) = 2.13, p < .05; d = 0.46; see Table 3).

Post-Treatment Comparison

Follow-up data was compared to post-treatment data to determine the extent to which treatment gains were maintained or had returned at 12-26 months following completion. Results suggest that treatment gains were generally well-maintained, although not for all participants. In particular, scores on the CGI-Severity (t (31) = -.34, p = .74, d = -.07) and the ADIS CSR for primary anxiety (t (31) = -.06, p = .96; d = -.01) suggested full maintenance of treatment gains. Scores on total anxiety CSR (t (31) = -.77, p = .44, d = -.15) and the PARS (t (31) = -1.58, p = .12, d = -.32) indicated a small effect towards symptom regression (see Table 3).

Regarding categorical measures of improvement, results suggested that on average treatment gains were well maintained, but that on an individual level some participants experienced symptom regression. The number of individuals demonstrating remission of their primary anxiety diagnosis did not differ from post-treatment to follow-up (46.9% vs. 46.9%; see Table 4); however, many participants

changed status between time points with 21.9% (*n* = 7) experiencing a return of their primary anxiety diagnosis and 21.9% (*n* = 7) demonstrating remission of their primary anxiety diagnosis during the follow-up period (see Table 5). Regarding response status, the percentage of individuals deemed treatment responders was significantly less at follow-up as compared to post-treatment (84.38% vs. 53.13%; McNemar X^2 = 5.56, *p* = .03). Using the procedures outlined in the data analysis section, 43.8% (*n* = 14) participants were rated as having reductions in treatment gains, 37.5% (*n* = 12) demonstrated maintenance of treatment gains, and 18.8% (*n* = 6) demonstrated continued improvement of treatment gains. Maintenance status did not appear related to post-treatment response (see Table 6). Finally, autism spectrum symptoms were non-significantly different at follow-up as compared to baseline (*t* (18) = 0.41, *p* = .69; *d* = .09; see Table 3).

Predictors of Maintenance

Though underpowered, primary anxiety diagnosis, baseline severity (PARS), comorbid ODD, length of time to follow-up, and continued use of treatment techniques (i.e., emotion recognition/coping skills, in vivo exposure) were not related to the likelihood that individuals maintained treatment gains at follow-up (see Table 7). While not statistically significant, the number of comorbid diagnoses at baseline did appear to be associated with a 36% decreased likelihood of being a treatment maintainer at follow-up (*B* = -0.44, *p* = .17, e^B = 0.64). Obtainment of treatment during the follow-up period also appeared to have an impact on treatment maintenance. Use of psychotherapy predicted non-maintenance, whether specific to anxiety (*B* = -1.01, *p* = .37, e^B = 0.33) or general (*B* = -1.14, *p* = .17, e^B = 0.32). The use of in-school assistance was highly related to treatment maintenance (*B* = 3.18, *p* < .01, e^B = 24.00), while medication usage and (*B* = .50, *p* = .52, e^B = 1.65) and the use of occupational, physical and speech therapy (*B* = -1.05, *p* = .18, e^B = 2.84) demonstrated smaller effects. Completion of social skills training did not appear related to maintenance.

Table 3: Comparisons for baseline, post-treatment and follow-up on continuous measures of symptom severity.

	Baseline Mean (SD)	Post-Treatment Mean (SD)	Baseline vs. Post-Treatment		Follow-Up Mean (SD)	Baseline vs. Follow-Up		Post-Treatment vs. Follow-Up	
			t	*d*		*t*	*d*	*t*	*d*
CGI – Severity	3.69 (.59)	2.50 (.67)	9.70**	1.89	2.56 (.95)	6.78**	1.43	-.34	-.07
PARS (5 Item)	16.41 (2.07)	11.19 (3.55)	10.05**	1.80	12.56 (4.89)	5.09**	1.03	-1.58	-.32
Primary CSR	5.44 (.80)	2.97 (2.16)	6.92**	1.52	3.00 (2.37)	6.36**	1.38	-.06	-.01
Total Anxiety CSR	14.84 (6.00)	7.69 (4.79)	7.17**	1.32	8.50 (5.89)	6.41**	1.07	-.77	-.15
SRS (19)	105.68 (18.22)	98.53 (20.52)	1.94	0.37	96.74 (20.74)	2.13*	0.46	.41	.09

** $p < .01$; $p < .05$.

Table 4: Comparisons for post-treatment and follow-up on categorical measures.

	Post- Treatment (*n*)	Follow Up (*n*)	X^2
Response Status	84.38% (27)	53.13% (17)	5.56*
Any Response	100% (32)	78.13% (25)	N/A[1]
Primary Remission	46.9% (15)	46.9% (15)	0.00

* p< .05; [1]Chi-square analyses can not be conducted if one group is a constant.

Table 5: Composition of remission status at post-treatment and follow-up.

		Post-Treatment Remission	
		Primary Diagnosis Present (17)	Primary Diagnosis Remitted (15)
Follow-Up Remission	**Primary Diagnosis Present (17)**	10	7
	Primary Diagnosis Remitted (15)	7	8

Table 6: Composition of individual change in treatment-response at post-treatment and treatment-maintenance at follow-up.

		Post-Treatment Response		
		Minimally Improved (5)	Much Improved (16)	Very Much Improved (11)
Follow-Up Status	**Regression (14)**	1	10	3
	Maintenance (12)	2	5	5
	Improvement (6)	2	1	3

Table 7: Results of logistic regressions examining predictors of treatment maintenance at follow-up.

Predictor	***B***	***SE B***	e^B	**Wald's X^2**
Primary Anxiety Diagnosis				
Social Phobia	0.20	0.73	1.22	0.08
SAD	0.13	1.46	1.14	0.01
GAD	-0.05	0.72	0.95	0.01
OCD	-0.33	0.99	0.72	0.11
Baseline Severity (PARS)	-0.00	0.17	1.00	0.00
Number of Comorbid Diagnoses	-0.44	0.32	0.64	1.92
Presence of ODD	-0.09	0.75	0.92	0.14
Time to Follow-Up	-0.00	0.00	1.00	0.09
Interim Treatment				
On Meds	0.50	0.78	1.65	0.41
Anxiety-Focused Psychotherapy	-1.01	1.22	0.33	0.82
General Psychotherapy	-1.14	0.82	0.32	1.92
Social Skills Training	-0.13	0.35	0.88	0.13
Occupational, Physical, and Speech Therapy	1.05	0.77	2.84	1.84
In-School Assistance	3.18	1.16	24.00	7.54**
Independent Implementation of Treatment Techniques				
Emotion Recognition	0.08	0.09	1.09	0.91
In Vivo Exposure	-0.00	0.09	1.00	0.00

* $p < .05$; ** $p < .01$;

Discussion

The present study examined the maintenance of CBT for anxiety in youth with ASD 12-26-months following the completion of treatment. Initial investigations have established CBT as a probably efficacious treatment for anxiety disorders in youth with ASD (e.g., Reaven et al., 2012; Storch et al., 2013); however, treatment maintenance beyond 6-months had not yet been examined. Consistent with follow-up data of CBT in neurotypical populations (e.g., Spence et al., 2006; Barrett et al., 2005), the present study found treatment improvement from CBT to be relatively well-maintained over time. On average, youth's anxiety ratings were relatively similar between follow-up and post-treatment, demonstrating a minimal decline in overall improvement. In comparison, severity levels and improvements scores at follow-up were significantly different from baseline, indicating that on average a large effect for treatment was still present. Individually, results indicated the majority of individuals had either comparable or further improvement from post-treatment with a sizable minority having demonstrated some level of symptom regression.

The results of the study support the durability of CBT for anxiety in ASD and are comparable with data in neurotypical youth. Regarding sample averages, the present study is consistent with follow-up studies of neurotypical youth (e.g., Spence et al., 2006) in finding a large effect for treatment and minimal differences between post-treatment and follow-up. This result is promising for the use of CBT in this population, as CBT is associated with a low level of risk (Walkup et al., 2008) and is generally acceptable to participants, particularly compared to psychotropic medications (Patel & Simpson, 2010; Stevens et al., 2009), to which youth with ASD may be at an increased risk for, the already frequent, adverse side effects (West, Waldrop, & Brunssen, 2009).

Despite the promising nature of the overall results categorical data from the present study suggests that when compared to neurotypical follow-up studies, a slightly larger portion of the present sample did not fully maintain treatment gains. In the present study, changes in individual status of response and remission, in both positive and negative directions, were common (see Tables 5 and 6). For example, while remission of primary anxiety diagnosis remained at 46.9% between time points, 7

individuals fell out of diagnostic criteria for their primary anxiety diagnosis during the interim, while 7 individuals who had not met diagnostic criteria for their primary anxiety diagnosis at post-treatment did again at follow-up (see Table 5). The variability in status may indicate that severity of symptoms, or degree of response, at post-treatment may not fully represent an individual's long-term clinical outcome. For example, remission of primary anxiety diagnosis and treatment response, while beneficial as outcomes for their clarity and comparability, are typically specific to the primary treatment outcome and may neglect other important factors (e.g., level of functioning, comorbidity). Further, remission and response do not account well for the potential differences between individuals who are symptom free and those are still experiencing sub-clinical symptoms. Finally, differentiating between participants who may have plateaued versus those who are continuing to improve is difficult, since remission and response do not provide a clear picture of patient trajectory.

With a significant reduction in the number of individuals considered responders between post-treatment and follow-up, and considerable movement in response status, variables were examined to explore what differentiated individuals who maintained treatment gains from those who did not. Under powered for this analysis, only one significant relationship was identified; however, a number of additional predictors demonstrated effect sizes that suggest they also were related to maintenance. First, the number of comorbid anxiety diagnoses at baseline predicted failure to maintain treatment gains. Although outcome at post-treatment has historically not been related to the number of comorbid anxiety disorders (e.g., Kendall, Brady, & Verduin, 2001; Storch et al., 2008), within the context of treatment maintenance this result is not particularly surprising. Individuals who suffer from multiple anxiety diagnoses may have a larger number of target symptoms and despite making large improvements during the course of treatment, still have more residual symptoms at post-treatment than those with a single diagnosis. Given that, by reducing anxiety temporarily, avoidance and compulsive behaviors are self-reinforcing in nature, without diligent monitoring and resisting, individuals with residual symptoms may be more likely to experience a significant return in symptoms. This is supported by research in depression, which has found residual symptoms to be associated with increased relapse and poorer long-term outcome (Kennedy & Paykel, 2004).

Second, the obtainment of additional psychological services during the interim period was associated with a decrease in treatment maintenance. This result could reflect a few potential, though differing hypotheses. For one, rather than predicting non-maintenance of treatment gains, it may indicate that those individuals who began to experience a return of symptoms sought out additional psychological services. However, if so, it is unclear why these services were not effective in returning symptoms to post-treatment levels, particularly those focused directly on anxiety. Since the quality of services provided during the interim could not be evaluated, it is possible that these individuals were not receiving empirically supported treatments for their symptoms, as is common within community care (Stein et al., 2004). If so, participants may been taught counterproductive (e.g., family accommodation, distracting oneself) or unhelpful strategies that contributed to decreased maintenance. Beyond quality of care, for those who obtained general psychological services, it could be that treatment was focused on different psychopathology than was treated in the initial trial (e.g., depression, oppositional behavior). In this case, participants may have shifted treatment focus towards these other symptoms, and as a result neglected their anxiety based strategies. Conversely, for those who received anxiety specific services, this result could suggest that if symptoms return following successful CBT treatment, these symptoms are more resistant to psychotherapy and might benefit from an alternate treatment approach. Finally, it is also possible that the negative relationship between psychological treatment and non-maintenance may be explained by non-measured mediating factors, such as poor treatment adherence in the initial study or a negative home environment. Hypothetically, these factors could contribute to patients seeking further psychotherapy while contributing to non-maintenance of gains.

As compared to psychotherapy, obtainment of non-psychological based treatments, namely occupational, physical and/or speech therapy, as well as in-school assistance, were associated with increased maintenance of treatment gains. While the direct impact of these services on anxiety is unclear, one hypothesis would be that these services help youth better manage their environment and reduce anxiety triggers/stressors. For example, school accommodations may provide structure for children, thereby reducing anxiety over uncertainty and change. Additionally, it may reduce barriers associated with the youth's ASD diagnosis, such as communication deficits or fine-motor delays, and as a result minimize anxiety specific to those situations. For example, speech therapy may reduce communication

deficits for youth, and as a result help them feel less anxious in social situations. Alternatively, this result may suggest that these services are more likely to be obtained or be beneficial when individuals have their anxiety symptoms well controlled. Youth with lower overall anxiety, may be better equipped to focus on, process, and/or take advantage of these services. For example, a child with significant social fears may not feel comfortable asking for help, even if additional help is made available; however, once overall anxiety is reduced, they may be more prepared to take advantage of those services. Finally, what may also be likely is that families that seek out these additional services and advocate for their child, are also more likely to ensure their child maintains gains during made treatment. Use of medication during the interim period had a smaller positive impact on treatment maintenance that may indicate its added benefit in maintaining treatment gains.

Even in light of the limited power for the exploratory analysis, the majority of predictors did not appear to have a relationship to treatment maintenance, including primary anxiety diagnosis, baseline anxiety severity, presence of comorbid disruptive behavior, time to follow-up, and continued use of treatment techniques. Of note, the non-predictive effect of time to follow-up may suggest that treatment maintenance is relatively stable past the 1-year time point. This is consistent with follow-up studies in neurotypical populations which have found relative consistency in follow-ups across time (e.g., O'Leary et al., 2009). While primary anxiety diagnosis may not have a direct impact on treatment, particularly considering the consistency of the treatment approach across diagnostic categories, it is also possible that the high level of comorbidity within the sample reduced the predictive impact of the primary anxiety diagnosis. Regarding treatment techniques, participants may have had difficulty recalling and differentiating between treatment modules and may have, as a result, had limited ability to report their continued usage of those techniques.

Beyond those measured, several other variables may have impacted the likelihood that individuals maintained treatment, continued to improve, or experienced a return in symptoms. For one, the nature of anxiety within individuals with ASD may be of importance. While evidence has established that individuals with ASD often experience comparable anxiety symptoms and severity levels to neurotypical youth (e.g., Russell & Sofronoff, 2005), the precise nature of anxiety in this population is less clear. Wood and Gadow (2010) suggest that anxiety may play a number of different roles in youth with

ASD. In particular, they identify anxiety as a consequence of ASD, a moderator of ASD severity, and a proxy of ASD symptoms. For many youth with ASD, anxiety symptoms are directly related to the nature of the ASD diagnosis, such as anxiety associated with rigidity, sensory sensitivity, prevention of restricted interests or repetitive behaviors, and/or social deficits (Green et al., 2011; Spiker et al., 2011; Zandt et al,. 2007). Hypothetically, this association with core ASD symptomology could result in a difference in maintenance of treatment, with individuals who experience independent comorbid anxiety demonstrating better treatment maintenance than youth with overlapping anxiety and autism symptoms. This seems particularly feasible considering that previous treatment focused on improving specific core autism symptoms (e.g., social skills training) have typically demonstrated poor treatment maintenance (Hwang & Hughes, 2000; Rao, Beidel, & Murray, 2008; Warren et al., 2011).

Autism spectrum disorders represent a diverse diagnostic category that includes a wide range of deficits and symptoms and is commonly comorbid with other psychopathology beyond anxiety disorders. While inclusion criteria mandated participants be considered “high-functioning”, participants likely still differed considerably in many of these factors. As a result, individuals may have presented with potentially different barriers to successful maintenance of treatment. For example, the extent to which social, communication, and/or cognitive deficits are present may play a part in treatment maintenance. In addition, ADHD symptoms are extremely common in youth with ASD (though technically not diagnosed due to frequency) and have been associated with reduced treatment response in neurotypical youth (e.g., Storch et al., 2008). Beyond ASD specific barriers, the extent of family accommodation (e.g., Merlo, Lehmkuhl, Geffken, & Storch, 2009), level of insight (e.g., Himle, Van Etten, Janeck, & Fischer, 2006), and treatment dose/adherence (e.g., Glenn et al., 2013) may play a role in treatment maintenance in youth with ASD, as these variables have been associated with treatment outcome of CBT for neurotypical youth. These factors may also help explain why some individuals continue to improve post-treatment even with a minimal initial response, while others experience significant relapse in symptoms. Further, the role of ASD related symptoms may partially explain the value of the use of non-anxiety focused treatments during the interim period.

The change in course across the follow-up period for many individuals may also be a function of anxiety diagnosis and/or the onset of other pathology. For example, similar to how GAD demonstrates a

modest placebo response while OCD does not (Khan et al., 2005), certain anxiety disorders could demonstrate an initial response that quickly fades, while others demonstrate slow but stable progress over time. This may be related to the natural development of the disorders. For example, even without treatment, separation anxiety often naturally remits over time (e.g., Foley et al., 2004), while GAD and OCD tend to have a more chronic course without intervention (e.g., Keller, 2001; Stewart et al., 2004). Another potential impact on course could be the onset of a new psychiatric disorder, particularly a depressive disorder. As the present study only evaluated participants for disorders endorsed at the baseline time point, it is unclear what percentage of individuals developed other conditions during the follow-up period. Considering many youth were entering adolescence during the follow-up period, onset of a depressive disorder could be possible (Lewinsohn, Clarke, Seeley, & Rohde, 1994) and impact the treatment gains made by youth.

While the results of the present study are promising for the future of CBT in youth with ASD, further refinement of, or targeted-additions to, CBT protocols for this population may be beneficial in increasing the percentage of individuals who successfully maintain treatment gains or even improve post-treatment. One consideration for future study would be to examine how ASD focused modifications play a part in the maintenance of CBT. Currently, ASD focused modifications have been included to reduce barriers to treatment present in youth with ASD; however, their value has not been directly examined. On the one hand, it is possible that the ASD modifications are successful in reducing barriers to treatment and have contributed to the largely successful maintenance of CBT in youth with ASD observed in the present study. In this case, continued focus on the use of modifications and ASD focused supplements may further improve the long-term outcome of treatment. Conversely, the inclusion of modifications to treatment may reduce the emphasis on the anxiety driven components of CBT (e.g., in vivo exposure, coping skills). It is possible that, as a result, participants did not receive as robust a treatment, and may have demonstrated slightly attenuated treatment maintenance as a result. In this case, use of non-modified standard CBT protocols would be encouraged to maximize gains.

These options are not necessarily exclusionary, as the need for modifications to treatment could be participant dependent. In this case treatment response and maintenance could be maximized by better matching and tailoring treatment to youth. Comparative study of these approaches will be necessary to

determine the respective value of these components in maintaining treatment gains. If so, a stepped care model, in which therapy is increased from least to most intensive based on the needs of the patient, may hold particular promise in a diverse patient population like youth with ASD. In neurotypical youth, stepped care has demonstrated comparable or even improved treatment response at a lower cost than standard care (Salloum, 2010; Tolin, Diefenbach, & Gilliam, 2011). As part of a stepped approach, considerations could be taken to increase the level of post-treatment contact between patients and clinicians. For example, the introduction of monthly or twice-monthly booster sessions following treatment completion may be beneficial for maintaining treatment, as it would allow families to review CBT strategies, problem-solve recent relapses and solidify continued progress. In a recent study examining the use of 9-monthly booster sessions following a full course of CBT for panic disorder, individuals who received them had significantly lower relapse rates and impairment at 21-month follow-up (White et al., 2013). Alternatively, provision of a brief overview on how to implement techniques could be a quick and cost-effective way to help remind participants and their families of ways to continue to combat anxiety symptoms. These strategies may be helpful in minimizing regression of symptoms and ensuring the largest number of youth are maintaining treatment gains.

Several limitations of the present study should be noted. First, the study included a relatively small sample that, while adequately-powered for primary analyses, was not sufficiently powered in exploring predictors of treatment maintenance. Second, the sample was self-selected, in that individuals who agreed to participate may be different (e.g., better maintainers) than those who declined or could not be reached, although the data suggests a diverse group of participants was reached. Third, for follow-up symptoms only parent-report was obtained. While this may have altered results as this did not take into account the child's perspective regarding symptoms, as discussed earlier, previous research suggests that child-report of symptoms is often poor, with clinicians more likely to base ratings off of parent-report (Storch et al., 2012). Fourth, the assessors of the present study differed from those originally used for ratings and were not blinded to participant history. However, use of different raters is typically considered a more stringent method, as it eliminates familiarity between the assessor and the participant. Fifth, the present study was a naturalistic follow-up and as a result could not control for many outside influences. While a number of factors were examined as predictors (including a general measure of use of interim

treatment), as discussed above, other non-measured variables may have contributed to maintenance or non-maintenance of treatment gains. Finally, although attempted to be measured, data regarding interim treatment and continued usage of treatment techniques was incomplete and difficult to categorize. Poor response may have been partially a result of having participants complete self-report questionnaires through a web-based service following completion of the verbal interview, as this allowed them to easily refrain from responding. As a result, the impact of these components on treatment could not be fully examined as proposed.

While the present study provides valuable information on the maintenance of CBT for anxiety in youth with ASD, future research would be beneficial in further examining this treatment and this population. In particular, further study of possible predictors of treatment maintenance may provide additional information on what participants may be at particular risk for symptom regression. In particular, factors related to ASD diagnosis (e.g., the relationship between anxiety and core ASD symptoms, level of functioning), the level of family accommodation, insight, treatment compliance, and the presence and severity of ADHD symptoms, may be worth investigation. Second, attempts to improve treatment maintenance should be made both within the context of treatment, as well as during the interim period. Within the context of treatment, future research should examine the impact of adding or removing ASD modifications, or modifying/bolstering relapse prevention material. The use of a modified time schedule that allows for treatment fading has been helpful for maintaining alternative treatments (Eyberg, Edwards, Boggs, & Foote, 1998) and may be similarly beneficial in this population. Following treatment, additional contact with participants, whether brief or in the form of a booster session, holds promise and research should investigate the ideal intensity, frequency and content of such follow-ups. Many individuals will not require additional maintenance, therefore with the help of maintenance related predictors, strategies would ideally target youth most likely to relapse, perhaps via a stepped-care approach. Finally, future randomized controlled trials that compare CBT treatment to a waitlist, treatment-as-usual, or alternative therapy controls, should consider extending the follow-up period for longer durations. This extended follow-up may provide additional information about the natural course of symptoms and reduce unexplained variance present in the current sample.

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Appendixes

Appendix A. Independent Implementation of Therapeutic Techniques (IITT)
Subject ID#: _____ Date:_____ Interviewer: _____

Description: The following questions are focused on aspects of treatment you and your child received over the course of therapy completed at the Rothman Center for Pediatric Neuropsychiatry in St. Petersburg, FL. The length of each component may have ranged from 1-10 sessions, with each family receiving a unique combination. Do not be concerned if you did not complete a component. If differences arise between your opinions and what you would believe your child's to be, please answer in a manner that best represents your family as a whole.

I. Child and Parent Focused Modules:

A. Emotion Recognition (Kick Plan): The child learns K: knowing you're anxious; I: icky thoughts; C: calming thoughts; K: keep practicing.

1. **Did your child complete the KICK Plan portion?**
    a. Yes (answer the following questions)
    b. No (skip to next page)

2. **When you and your child learned the KICK steps, how helpful did you find them to be?**

1	2	3	4	5
Not At All (no perceived benefit)		Mildly (some perceived benefit)		Extremely (key to child's success)

3. **How well do you or your child remember the KICK steps?**

1	2	3	4	5
Not At All (no aspects are recallable)		Somewhat (generally familiar)		Perfectly (vividly clear)

4. **When applicable, how often did/do you or your child employ the KICK steps?**

1	2	3	4	5
Never (was not employed at any time)		Occasionally (in certain situations)		Always (every applicable situation)

5. **How long after the last session did you or your child continue to use the KICK steps?**

1	2	3	4	5
Never used		6 months		Still Used

6. If you no longer use this treatment technique, which choice best explains your reason for discontinuing use?

a. No longer needed
b. No longer remembered
c. No longer effective
d. No longer interested
e. Other: _____

B. In Vivo Exposures: The child is exposed to things he/she fears and is prevented from using behaviors to escape (e.g. avoidance, compulsion), while parents are taught strategies to complete exposures within the home.

7. Did your child complete the exposure portion?

a. Yes (answer the following questions)
b. No (skip to next page)

8. When you and your child learned/completed exposures, how helpful did you find them to be?

1	2	3	4	5
Not At All		Mildly		Extremely

9. How well do you or your child remember how to complete exposures?

1	2	3	4	5
Not At All		Somewhat		Perfectly

10. When applicable, how often did/do you or your child employ exposures?

1	2	3	4	5
Never		Some of the time		Always

11. How long after the last session did you or your child use exposures?

1	2	3	4	5
Never Used		6 Months		Still Used

12. If you no longer use exposures, which choice best explains your reason for discontinuing use?

a. No longer needed
b. No longer remembered
c. No longer effective
d. No longer interested
e. Other: _____

C. Making Friends: The child is taught important social rules and skills and is assisted in attempts to arrange playdates.

13. Did your child complete the making friends portion?

a. Yes (answer the following questions)
b. No (skip to next page)

14. When you and your child learned skills to make friends, how helpful did you find them to be?

1	2	3	4	5
Not At All		Mildly		Extremely

15. How well do you or your child remember skills learned for making friends?

1	2	3	4	5
Not At All		Somewhat		Perfectly

16. When applicable, how often did/do you or your child employ skills learned for making friends?

1	2	3	4	5
Never		Some of the time		Always

17. How long after the last session did you or your child use skills learned for making friends?

1	2	3	4	5
Never Used		6 Months		Still Used

18. If you no longer use friend-making skills, which choice best explains your reason for discontinuing use?

a. No longer needed
b. No longer remembered
c. No longer effective
d. No longer interested
e. Other: _____

D. Social Coaching Exposure: The child is provided with social coaching immediately followed by a social interaction with another child. Parents learn appropriate ways of coaching their child for social situations.

19. Did your child complete the social coaching portion?

a. Yes (answer the following questions)
b. No (skip to next page)

20. When you and your child learned skills/completed exposures for interacting with others, how helpful did you find them to be?

1	2	3	4	5
Not At All		Mildly		Extremely

21. How well do you or your child remember skills/exposures learned for interacting with others?

1	2	3	4	5
Not At All		Somewhat		Perfectly

22. When applicable, how often did/do you or your child employ skills/exposures learned for interacting with others?

1	2	3	4	5
Never		Some of the time		Always

23. How long after the last session did you or your child use skills/exposures learned for interacting with others?

1	2	3	4	5
Never Used		6 Months		Still Used

24. If you no longer use skills/exposures related to interaction with others, which choice best explains your reason for discontinuing use?

a. No longer needed
b. No longer remembered
c. No longer effective
d. No longer interested
e. Other: _____

II. Parent-Focused Modules:

A. Rewards: Parents are taught basic ideas about rewarding children and come up with rewards that will be attractive and motivating for the child.

25. Did you or another guardian complete the rewards portion?

a. Yes (answer the following questions)
b. No (skip to next page)

26. When you or the attendee learned reward-based skills, how helpful did you find them to be?

1	2	3	4	5
Not At All		Mildly		Extremely

27. How well do you or the attendee remember skills learned for using rewards?

1	2	3	4	5
Not At All		Somewhat		Perfectly

28. When applicable, how often did/do you or the alternate guardian employ skills learned for using rewards?

1	2	3	4	5
Never		Some of the time		Always

29. How long after the last session did you or the alternate guardian continue to employ skills learned for using rewards?

1	2	3	4	5
Never Used		6 Months		Still Used

30. If you no longer use skills related to using rewards, which choice best explains your reason for discontinuing use?

a. No longer needed
b. No longer remembered
c. No longer effective
d. No longer interested
e. Other: _____

B. Advocacy: Parents are taught about and assisted in obtaining an advocacy plan specifically design to help children with an autism spectrum disorder.

31. Did you or another guardian complete the advocacy portion?

a. Yes (answer the following questions)
b. No (skip to next page)

32. When you or the attendee learned advocacy-based skills, how helpful did you find them to be?

1 2 3 4 5

Not At All Mildly Extremely

33. How well do you or the attendee remember skills learned regarding advocacy?

1 2 3 4 5

Not At All Somewhat Perfectly

34. When applicable, how often did/do you or the alternate guardian employ skills learned regarding advocacy?

1 2 3 4 5

Never Some of the time Always

35. How long after the last session did you or the alternate guardian use skills regarding advocacy?

1 2 3 4 5

Never Used 6 Months Still Used

36. If you no longer use skills related to advocacy, which choice best explains your reason for discontinuing use?

a. No longer needed
b. No longer remembered
c. No longer effective
d. No longer interested
e. Other: _____

C. Independence Encouragement: Parents learn how to help their child develop self-help skills that are appropriate considering the child's age.

37. Did you or another guardian complete the self-help skills portion?

a. Yes (answer the following questions)
b. No (skip to next page)

38. When you or the attendee learned ways of promoting self-help skills, how helpful did you find them to be?

1 2 3 4 5

Not At All Mildly Extremely

39. How well do you or the attendee remember techniques for promoting self-helps skills?

1 2 3 4 5

Not At All Somewhat Perfectly

40. When applicable, how often did/do you or the alternate guardian employ techniques for promoting self-help skills?

1 2 3 4 5

Never Some of the time Always

41. How long after the last session did you or the alternate guardian use techniques for promoting self-help skills?

1 2 3 4 5

Never Used 6 Months Still Used

42. If you no longer use techniques that promote self-help skills, which choice best explains your reason for discontinuing use?

a. No longer needed
b. No longer remembered
c. No longer effective
d. No longer interested
e. Other: _____

III. School-Focused Module:

A. Promoting Prosocial Behavior: The therapist meets with important school staff to figure out or create school-based behavioral programs that will improve a child's social abilities and reduce their negative behaviors.

43. Did your therapist and school personnel complete the school-focused portion?

a. Yes (answer the following questions)
b. No (end of questionnaire)

44. When school staff learned ways of promoting positive behavior, how helpful did you find this to be?

1 2 3 4 5

Not At All Mildly Extremely

45. How well do you believe the school staff remember learned skills for promoting positive behavior?

1 2 3 4 5

Not At All Somewhat Perfectly

46. When applicable, how often did/do the school staff employ skills for promoting positive behavior?

1 2 3 4 5

Never Some of the time Always

47. How long after the last session do you believe the school staff used skills for promoting positive behavior?

1 2 3 4 5

Never Used 6 Months Still Used

48. If you believe the school staff no longer use techniques that promote positive behavior, which choice do you believe best explains their reason for discontinuing use?

a. No longer needed
b. No longer remembered
c. No longer effective
d. No longer interested
e. Other: _____

Appendix B: Institutional Review Board Approval Letter

Institutional Review Board
All Children's Hospital
ACH Box #9496
FWA# 00000977
IRB# 00001642
727.767.4275

June 12, 2012

Robert Selles, B.A.
Rothman Center for Pediatric Neuropsychiatry.
880 6th Street South,
Suite 460,
St. Petersburg, FL 33701

Dear Mr. Selles,

Your new protocol entitled, "Treatment Maintenance of Cognitive-Behavioral Therapy for Anxiety in Youth with Autism Spectrum Disorders" IRB# 12-0491, Ref# 106751 was approved under the expedited review process pending recommended changes to the application and informed consent. Those changes have been received, reviewed and found to be appropriate. This will be reported at the 07/11/2012 meeting of the All Children's Hospital Institutional Review Board. This protocol meets the criteria 45 CFR 46.404, research not involving greater than minimal risk. This action fits the criteria for expedited review under research category 45 CFR 46.110 (b) (1).

The initial approval period is for a maximum of one year. The IRB approval for this protocol will expire on 6/11/2013. Please submit your continuation request by 5/13/2013 in order to avoid lapses in approval of your research and possible suspension of subject enrollment. If during the course of the study, there are any changes or amendments, or you decide to terminate the study, please notify the All Children's Hospital Institutional Review Board.

As Principal Investigator of this protocol, it is your responsibility to keep the necessary documentation, and not add further responsibility to the role of nurses, pharmacists or other healthcare providers not directly involved with this study.

Per Hospital Administrative Policy No. 014-0024-9581-000-A *Research Administrative Review Process*, your protocol must receive administrative approval prior to commencing the study. For administrative review questions, please contact the Department of Research Administration at (727) 767-4813.

Thank you for your participation in the All Children's Institutional Review Board process. If you have any questions, please contact the office of the ACH Institutional Review Board at (727) 767-4275.

Sincerely,

Signature applied by Dawn A. Bruton on 06/13/2012 09:02:19 AM EDT

Dawn Bruton, BSN, CCRP
Member, ACH Institutional Review Board

DB:se