Doctoral Thesis

The Use of Cognitive Behavioural Therapy with Individuals with Autism Spectrum Disorder across the Lifespan: A Meta-Analysis

Lisa Weston

100035111

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Abstract

Background and Aims

Despite a growing interest in the use of Cognitive Behavioural Therapy with individuals with Autism Spectrum Disorders, there has been little systematic appraisal of effectiveness research in this area to date. The primary aim of the current study was to systematically appraise the evidence for using CBT in the treatment of either core features of ASD or co-occurring mental disorder in individuals with ASD across the lifespan.

Methods

A systematic search of relevant databases was conducted according to pre-defined criteria, followed by a series of random effects meta-analyses to account for the variation in outcome report type.

Results

Fifty studies met inclusion criteria and 48 studies, involving 2099 participants (1081 CBT, 1018 control) were included in the meta-analysis. CBT for the treatment of mental disorder was associated with a significant "medium" effect size, $g = .66$, for informant-reported measures, and a significant "medium" effect size, $g = .73$, for clinician-reported measures. Similarly, CBT for the treatment of core features of ASD was associated with a significant "small" effect size, $g = .48$, for informant-reported measures, a significant "medium" effect size, $g = .65$, for clinician-reported measures, and a significant "small" effect size, $g = .35$, for task-based measures. CBT was not found to be superior to control when self-reported outcome measures were utilised. Sensitivity analyses to exclude outliers and studies deemed to be at a high risk of bias generally reduced effect size magnitude. Subgroup analysis was severely limited by a lack of definitive studies and the interpretation of results was hampered by the poor methodological quality of included studies.

Conclusions

Future larger-scale clinical trials are needed to further explore the effectiveness of CBT in this client group, with well characterised samples, clearly defined primary outcome measures and adequate randomisation, allocation concealment and blinding.

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Chapter One: Introduction

1.1 Introduction to Thesis

There is a growing interest in the development of psychotherapeutic interventions for use with individuals with Autism Spectrum Disorders (ASD). Cognitive Behavioural Therapy (CBT) may be one promising treatment for use with this client group. However, there has been little systematic appraisal of effectiveness research in this area to date, particularly involving studies with adult participants and those investigating CBT targeting core features of ASD. The primary aims of the present research are therefore: (a) to systematically appraise the evidence for using CBT in the treatment of either core features of ASD or co-occurring mental disorder in individuals with ASD across the lifespan, and (b) to consider whether the effectiveness of CBT is moderated by age group or the format of CBT delivery.

1.1.1 Overview of thesis structure.

The thesis consists of four chapters. Chapter One provides an overview of ASD and CBT, in addition to briefly summarising intervention research in the area to date and highlighting the rationale for the present research. The aims and research questions are then presented.

Chapter Two provides an overview of the methods used to address the research questions, in addition to outlining the rationale for the approaches and techniques selected. A summary of the search strategy, study selection and data extraction is provided, alongside information on quality appraisal and methodology used to facilitate quantitative synthesis.

Chapter Three provides a detailed summary of the outcomes of data collection and analysis. An overview of study selection is presented, in addition to a summary of characteristics of included studies. The outcomes of the quality appraisal process are addressed and a summary of quantitative synthesis is reported in relation to each research question.

Chapter Four provides an overall discussion of the findings in relation to the research questions and background literature. Clinical and theoretical implications of the study are discussed, in addition to limitations and recommendations for future research.

1.2 Autism Spectrum Disorders

1.2.1 Diagnostic criteria and core features.

The term Autism Spectrum Disorder (ASD) has historically been used as a collective term to represent a number of neurodevelopmental conditions, including autism, atypical autism, Asperger syndrome, and pervasive developmental disorder not otherwise specified (PDD-NOS). However, the use of categories to define ASD has been widely criticised and a dimensional assessment examining the core and associated features of ASD has instead been recommended (Ousley & Cermak, 2014). The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association, 2013) has adopted this approach, abandoning diagnostic subtypes and instead providing criteria to indicate the severity level of core ASD features, in addition to the presence of intellectual impairment, language impairment and co-occurring medical, neurodevelopmental, mental or behavioural disorders. A similar approach is likely to be adopted in the eleventh edition of the International Classification of Diseases of the World Health Organisation (ICF-11). Although the ICF-11 has not yet been finalised, the proposed revision has also abandoned diagnostic subtypes; instead groups are characterised by the presence or absence of intellectual impairment and/ or impairment of functional language (ICD-11 Beta Draft; World Health Organisation, 2016).

Within DSM-5, the “core” features or criteria used to diagnose ASD are: (a) persistent deficits in social communication and social interaction across contexts, not accounted for by general developmental delays, and (b) restricted, repetitive patterns of behaviour, interests or

activities. Table 1 summarises the behavioural symptoms indicated across these core criteria or dimensions, in addition to further criteria required for an ASD diagnosis.

Table 1.

DSM-5 Behavioural Criteria for ASD Diagnosis

A) Persistent deficits in social communication and social interaction across contexts, not accounted for by general developmental delays (3 of 3 symptoms)	
Symptoms	A1. Deficits in social-emotional reciprocity
	A2. Deficits in non-verbal communicative behaviours used for social interaction
	A3. Deficits in developing and maintaining relationships appropriate to developmental level
B) Restricted, repetitive patterns of behaviour, interests or activities (at least 2 of 4 symptoms)	
Symptoms	B1. Stereotyped or repetitive speech, motor movements, or use of objects
	B2. Excessive adherence to routines, ritualized patterns of verbal or nonverbal behaviour, or excessive resistance to change
	B3. Highly restricted, fixated interests that are abnormal in intensity or focus
	B4. Hyper-or hypo-reactivity to sensory input or unusual interest in sensory aspects of environment
C) Symptoms must be present in the early developmental period	
D) Symptoms cause clinically significant impairment in important areas of current functioning	
E) Disturbances are not better explained by intellectual disability or global delay	

Whilst the move towards dimensional assessment and diagnosis has been generally welcomed, there are several limitations of the current system. It could perhaps be argued that the merging of Asperger syndrome and PDD-NOS into a general ASD diagnosis may have resulted in a loss of sensitivity and identity for individuals who would previously have

received a more specific diagnosis. Concerns have also been raised regarding the impact upon service provision and longitudinal research (Volkmar & Reichow, 2013). However, the actual impact of the changes remains to be seen, and whilst the aforementioned concerns remain speculative, clinicians and researchers need to move forward with the changes.

1.2.1 Non-diagnostic features.

The phenotype of ASD extends well beyond the aforementioned core features, encompassing a range of associated symptoms in the cognitive, behavioural, affective, motor and sensory domains (see, for example, Volkmar, Paul, Klin, & Cohen, 2005). Examples of common features of ASD not included in current diagnostic criteria include sleeping and eating difficulties, anxiety in social situations, a lack of spontaneity or initiative and poor planning and organisational skills (Baron-Cohen, 2008). Some individuals with ASD may also experience synaesthesia, a condition in which a sensation in one modality triggers a perception in another modality (Baron-Cohen et al., 2013) and an estimated ten percent of individuals with ASD have savant skills- a skill which is above average for the general population (Treffert, 2014). The presentation of ASD across individuals varies widely and the term ‘autism spectrum’ (Wing & Gould, 1979) was coined to reflect this heterogeneity in symptoms and severity of the condition. However, this notion is no longer defined by any sharp separation from “normality” (Wing, 1997), since autistic traits have been shown to be normally distributed across the whole population (Baron-Cohen, Hoekstra, Knickmeyer, & Wheelwright, 2006; Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001).

1.2.2 Epidemiology.

Whilst prevalence rates remain unclear, it has been estimated that approximately 1.1% of the population in the United Kingdom may have ASD (National Autistic Society, 2013). This estimate is based on combined epidemiological data reporting a childhood prevalence rate of 116.1 per 10000 (Baird et al., 2006) and an adult prevalence rate of 9.8 per 1000

(Brugha et al., 2011). These rates are considerably higher than those documented in the past, although it is not clear whether this reflects case finding changes or increasing incidence due to newly emerging causes (Brugha et al., 2011). Regardless, the current prevalence estimates emphasise the need for an enhanced understanding of the aetiology of ASD, in addition to the development of effective interventions.

1.2.3 Aetiology and theoretical perspectives.

As already discussed, ASD is associated with a complex spectrum of difficulties and is currently diagnosed using only behavioural criteria. Substantial research has been conducted to attempt to explain behavioural characteristics of ASD using biological, environmental and cognitive theories. Whilst a full review of this research is beyond the scope of this thesis, a critical summary of key developments will be presented in this section.

1.2.3.1 Biological factors.

It is now generally accepted that there is a considerable genetic component to ASD, with many studies indicating that the condition is highly heritable (Freitag, 2007). Family studies have suggested that the rate of recurrence in siblings of individuals with ASD is 2-8%, considerably higher than the prevalence rate in the general population (Muhle, Trentacoste, & Rapin, 2004). Twin studies have also supported the argument for heritability, with research indicating a concordance rate of more than 60% in monozygotic (MZ) twins (Bailey et al., 1995). In an extension of this study, unaffected twins were re-evaluated for broader ASD phenotypes and concordance rose to 90% (Le Couteur et al., 1996). Family studies provide similar evidence, with a 6% rate of ASD in siblings of individuals with ASD, in contrast to 0.5% in the general population (Rutter, 2005).

Despite this compelling evidence for a strong genetic influence, there is a lack of clarity regarding the genes involved. Loci on chromosomes 2 and 7 are perhaps the most widely implicated to date (Rutter, 2005), although this research is ongoing and remains

inconclusive. Further biological research has focused on the role of neurochemistry and abnormalities in brain structure in individuals with ASD. A number of transmitter systems have been reported to potentially play a role in ASD, including serotonin, dopamine and oxytocin (Lam, Aman, & Arnold, 2006). However, many studies in this area can be criticised for poor methodology, including small sample sizes and lack of control groups, hindering the validity of conclusions drawn. The heterogeneity of ASD also complicates the interpretation of research (Polšek, Jagatic, Cepanec, Hof, & Simić, 2011).

The literature base for abnormalities in brain structure in individuals with ASD is similarly inconclusive. Studies have indicated that there may be an early overgrowth in brain volume in children with ASD, followed by a rapid deceleration of growth (Carper, Moses, Tigue, & Courchesne, 2002). There is also evidence of abnormalities in the structure of basic units of cortical information processing, smaller cerebellar volume, early amygdala enlargement and impaired neural connectivity (Polšek et al., 2011). However, again much of this research is limited by small sample sizes, clinical heterogeneity and variation in methodology. A recent study using the Autism Brain Injury Data Exchange, a database of approximately 1000 datasets of participants with ASD, attempted to overcome some of these difficulties by conducting a large-scale comparison of volume, thickness and surface area measures across the brain (Haar, Berman, Behrmann, & Dinstein, 2014). The study concluded that individuals with ASD had significantly larger ventricular volumes, smaller corpus callosum volume and several cortical areas with increased thickness, whilst there was found to be no difference in intracranial, cerebellar or amygdala volume as previously reported. The sharing of data across sites and the publication of this type of study is an important step forward for the advancement of our understanding of the neurobiological basis of ASD. However, there is a clear need for replication of research in this area and further advances in methodology to overcome the current inconsistencies.

Finally, an increase in studies utilising functional magnetic resonance imaging (fMRI) has helped to inform our understanding of potential changes in brain function in individuals with ASD. A systematic review and meta-analysis in the area (Philip et al., 2012) identified a high number of studies in which reductions in neuronal connectivity were reported in individuals with ASD compared to controls. Particular difficulties in function were reported amongst neuronal areas thought to be involved in social cognition, although this is discussed in terms of a lack of preference for social stimuli rather than a primary dysfunction of these areas (Philip et al., 2012). Generally, there has been a shift towards the assumption that ASD is associated with impairment of specific brain networks rather than particular regions, with local "over-connectivity" but long-distance "under-connectivity" between distant brain regions (Parellada et al., 2014).

fMRI studies have also contributed to the theory that the mirror neurone system may be impaired in individuals with ASD. Mirror neurones have been shown in animal studies to activate during both the execution and observation of actions (Gallese, Fadiga, Fogassi, & Rizzolatti, 1996). Since the understanding of other people's intentions and mental states requires observation of others' actions, it had been proposed that the mirror neurone system may play a direct role in social cognition (Philip et al., 2012). The aforementioned systematic review and meta-analysis indicated impaired activation in brain areas thought to be involved in the mirror neurone system, including the inferior frontal gyrus, and authors interpreted this as evidence for mirror neurone dysfunction in ASD (Philip et al., 2012).

Biological and neurological research on the aetiology of ASD has developed significantly throughout the last decade, enhanced by advances in methodology. While fMRI studies have added a valuable contribution to the understanding of neurophysiology in ASD, they tend to merely demonstrate anatomical or functional differences without providing much insight into aetiology. Further, studies to date are restricted by small and unrepresentative

samples (Philip et al., 2012) and further replication is therefore necessary before firm conclusions can be drawn.

1.2.3.2 Environmental factors.

It is now widely accepted that ASD is a multifactorial disorder and it is therefore likely that environmental factors play some role in its aetiology. Early theories positing that emotional deprivation may play a causal role in the development of ASD (e.g. Bettelheim, 1967) have now been completely discounted, whilst a range of other factors have since been implicated, including intrauterine infections and toxins, obstetric complications, birth order, parental social class and postnatal infections (Rutter, 2005). It has also been argued that medication prescribing in early life may be an aetiological factor. For example, Niehus & Lord (2006) analysed infant medical records and reported that children who went on to develop ASD had significantly more ear infections and were prescribed significantly more antibiotics than typically developing children. However, much of this research is based on isolated case studies and to date there is no conclusive evidence linking any single environmental factor with an increased risk of ASD. This is therefore an important area for further research, with the study of epigenetic factors in ASD receiving an increasing amount of attention in recent years.

1.2.3.3 Cognitive theories.

Given the lack of clarity regarding both biological and environmental factors involved in the development of ASD, cognitive theories of ASD are perhaps the most well established conceptualisations of ASD to date. In the absence of clear aetiological models, cognitive theories have provided firm theoretical foundations for clinical interventions and are therefore important to consider in any intervention research in ASD. This section will provide a critical summary of the key cognitive models of ASD to date.

1.2.3.3.1 Theory of mind hypothesis.

One of the earliest and arguably most well discussed explanations of ASD posits that individuals with ASD have impaired theory of mind (Baron-Cohen, Leslie, & Frith, 1985). First defined in relation to chimpanzees as the ability to impute mental states to oneself and others (Premack & Woodruff, 1978), a theory of mind enables humans to predict other people's mental states and to understand that the beliefs and intentions of others may differ from one's own. False belief tasks, for example in which participants watch a sequence of events involving dolls and are asked to make judgements that require them to infer that a doll has a mistaken belief about the world, have indicated that typically developing children develop a theory of mind between the ages of four and six years (Wimmer & Perner, 1983). Using the same task, Baron-Cohen et al. (1985) reported that 80 percent of children with ASD aged six to sixteen were unable to impute beliefs to others, in contrast to 14 percent of a control group consisting of children with Down syndrome who had a higher level of intellectual disability. It was concluded that individuals with ASD have a cognitive deficit in theory of mind, providing an explanation for social impairment and a lack of imaginative play in this client group (Baron-Cohen et al., 1985).

This finding has been widely replicated since, and in line with the fact that failure on this type of task was not shown to be universal, the theory was modified to propose that theory of mind difficulties may develop at a later age in ASD due to developmental differences (Baron-Cohen, 1989). This was supported by a meta-analysis indicating that the probability of children with ASD passing a false belief task was highly predicted by verbal mental age (Happé et al., 1996), a finding which also provided an explanation for why individuals with higher functioning ASD were able to pass the task. Consequently, advanced tests of theory of mind have since been developed, including the "Reading the Mind in the Eyes" and "Reading the Mind in the Voice" tasks, in which individuals with ASD were reported to be significantly worse than controls at extracting mental state information from

pictures of eyes (Baron-Cohen, Jolliffe, Mortimore, & Robertson, 1997; Baron-Cohen & Wheelwright, 2001) and vocalisations (Rutherford, Baron-Cohen, & Wheelwright, 2002).

Whilst these later studies provided further support for the theory of mind hypothesis at some level, their ecological validity can be questioned since the stimuli were based on static images and recordings from scripted audiobooks. Furthermore, it has been argued that the development of these advanced tasks could be viewed as a post-hoc response to finding data anomalous to the initial theory of mind hypothesis, i.e. that some individuals with ASD passed tests of false belief (Rajendran & Mitchell, 2007). However, neuroimaging studies have also provided support for the theory by showing less activation in areas of the brain assumed to be heavily involved in the perception and understanding of social information, including theory of mind. For example, in a study using positron emission tomography (PET), Happé et al. (1996) reported that no task-related activity was found in the left medial prefrontal cortex of individuals with ASD performing a theory of mind task, an area which had previously been associated with task-related activity in a control sample.

Taken together, behavioural and biological research does appear to support the theory that impaired theory of mind is related to difficulties in social interaction and communication and imaginative play in ASD. However, non-social features of ASD, for example restricted and repetitive patterns of behaviour and interests, rigidity and difficulties in planning and organising, cannot be well explained by this theory. The theory also fails to account for areas of strength often seen in this client group. Whilst the model has certainly been influential and generated a large amount of research, it cannot account for some core aspects of ASD and this is a fundamental limitation.

1.2.3.3.2 Empathising- systemising theory.

Baron-Cohen (2002) revised and extended the theory of mind or ‘mindblindness’ hypothesis to account for some of the aforementioned difficulties. The social and

communication difficulties in ASD are explained by delays and deficits in empathy, whilst areas of strength are attributed to intact or superior skill in systemising. It is proposed that the discrepancy between empathising and systemising determines the likelihood of an individual developing ASD (Baron-Cohen, 2009).

Within this model, empathy is assumed to have two components: a cognitive aspect, the identification of mental states in oneself and others, which is discussed as analogous to theory of mind; and an affective aspect, responding to another person's thoughts and feelings with an appropriate emotional reaction (Baron-Cohen, 2009). Research has shown that adults with high-functioning ASD score lower than comparison groups on the Empathy Quotient (EQ), a questionnaire designed to assess both cognitive and affective aspects of empathy (Baron-Cohen & Wheelwright, 2004). This was replicated in a study in which parents rated their children with ASD using a modified version of the questionnaire (Auyeung, Baron-Cohen, Wheelwright, & Allison, 2008). Other areas of research have also provided support for the notion of delays and deficits in empathy in individuals with ASD. For example, Yirmiya, Sigman, Kasari, & Mundy (1992) reported that children with ASD were less able than typically developing children to label emotional states, take the perspective of another person, and respond with empathy after watching video clips of children experiencing different events and emotional responses.

Systemising has been defined as "the drive to analyse or construct systems" or trying to predict how a system will behave via the identification of rules that govern the system (Baron-Cohen, 2009). Within this model, a variety of examples of systems are given, including mechanical, abstract systems and social systems, in all of which we are assumed to systemise by identifying rules and regularities. Evidence from a variety of sources has indicated that individuals with ASD show intact or superior skills in this area. For example, adults with high-functioning ASD scored higher than comparison groups on the Systemising

Quotient (SQ), a questionnaire designed to capture drive to systemise (Baron-Cohen, Richler, Bisarya, Gurunathan, & Wheelwright, 2003). Children with ASD have been shown to be above average on a test requiring them to work out how a polaroid camera worked, whilst they had difficulties understanding other people's thoughts and feelings (Perner, Frith, Leslie, & Leekam, 1989). This experimental evidence is further supported by clinical descriptions and self-reports of individuals with ASD indicating a greater desire to learn about systems and to perform system-related behaviours than typically developing individuals (Baron-Cohen et al., 2003).

Baron-Cohen (2002) has extended the empathising-systemising theory to the extreme male brain theory of ASD. It is posited that males are naturally better systemisers, whilst females are better empathisers, and ASD is described as an extreme of the typically male profile. Scores on the EQ and SQ across typically developing men and women and individuals with ASD have supported this model (Goldenfeld, Baron-Cohen, & Wheelwright, 2005), as have other measures of empathising (Baron-Cohen, 2009). It has also been reported that brain areas such as the anterior cingulate, prefrontal cortex and thalamus, which are generally smaller in males than in females, are smaller still in individuals with ASD. A similar pattern of results has been reported for areas of the brain that are typically larger in males than in females and it has been suggested that this "hypermasculinisation" may be related to higher levels of foetal testosterone in individuals with ASD (Auyeung et al., 2009). This is an interesting area of research, although several other studies do not support this pattern and further research is necessary before firm conclusions can be drawn.

The empathising-systemising theory has several strengths. It is able to account for limitations of the theory of mind hypothesis since it can explain both social and non-social features of ASD, in addition to strengths often seen in this client group. Furthermore, a variety of interventions have been developed as a direct result of this theory, with some

promising outcomes. For example, *The Transporters* is an animation programme in which facial expressions of emotion are mapped onto mechanical systems that move in a highly predictable way, such as trams and trains. This has been shown to lead to a greater improvement in emotion recognition in children with ASD than typically developing children (Baron-Cohen, Golan, & Ashwin, 2009) and can perhaps emphasise the utility of using strong systemising skills to teach aspects of empathy. Similar results have been demonstrated in adults using computer generated emotion regulation teaching (Golan & Baron-Cohen, 2006).

However, several limitations should also be acknowledged. The majority of the aforementioned studies were conducted with high-functioning individuals and it could therefore be questioned whether the E-S theory can account for all individuals with ASD. Whilst Baron-Cohen has argued that systemising is evident in lower functioning individuals with ASD, for example via repetitive patterns of behaviour (Baron-Cohen, 2006), there is minimal experimental evidence to support this. A further limitation is that much of the evidence discussed as support for the theory is derived from results on the EQ and SQ, self-report measures from one particular research group. It is argued that independent evidence is needed to verify the E-S and extreme male brain theories, preferably using behavioural observations (Andrew, Cooke, & Muncer, 2008).

1.2.3.3.3 Executive dysfunction theory.

Some researchers (for example, Ozonoff, Pennington, & Rogers, 1991) have argued that ASD may be explained by an impairment in executive function. Executive function is an umbrella term used for cognitive functions including initiation and monitoring, planning, impulse control, inhibition, working memory and cognitive flexibility (Stuss & Knight, 2002). These functions are thought to be mediated by the frontal lobes of the brain, damage to which often leads to Dysexecutive Syndrome (Baddeley & Wilson, 1988). Symptoms of Dysexecutive Syndrome, including a lack of impulse control, perseveration, difficulty

switching attention and a need for sameness, are often seen in individuals with ASD and may therefore indicate the involvement of the frontal lobes and impaired executive function (Hill, 2004).

Studies reporting that individuals with ASD are impaired on tasks requiring executive function have been interpreted as support for this theory. For example, both children and adults with ASD have been shown to be impaired on Tower of Hanoi or Tower of London tasks which assess planning (Ozonoff & Jensen, 1999). Tasks of mental flexibility or set shifting, for example the Wisconsin card sorting task, have also been shown to be performed poorly by individuals with ASD (Hughes, Russell, & Robbins, 1994). Furthermore, neuroimaging studies have provided additional support for the theory. For example, in a study using functional MRI, Luna et al., (2002) demonstrated that individuals with ASD showed significantly less task-related activation in the dorsolateral prefrontal cortex and posterior cingulate cortex than healthy controls during a spatial working memory task.

Whilst these findings support the hypothesis that some aspects of executive function are impaired in individuals with ASD, there are a number of limitations of this theory. Research has shown that some individuals with ASD do not score poorly on tests of executive function, particularly those with average or above average IQ (Hill & Russell, 2002), indicating that difficulties with executive function do not appear to be universal in this client group. Furthermore, studies have indicated that some areas of executive function, such as inhibition measured by a Stroop task, are not impaired in individuals with ASD (Ozonoff & Jensen, 1999), although alternative tasks measuring inhibition have demonstrated impairments (Hughes & Russell, 1993). This inconsistency is also seen in research into other areas of executive function and perhaps undermines the hypothesis that executive dysfunction in ASD is comparable to that seen in Dysexecutive Syndrome. A further criticism is that executive dysfunction is found in other clinical conditions, including Attention Deficit

Hyperactivity Disorder, restricting its use as a diagnostic marker of ASD (Hill, 2004). Whilst some research has indicated that there may be a specific pattern of executive dysfunction that distinguishes ASD from other neurodevelopmental disorders (Ozonoff & Jensen, 1999; Sergeant, Geurts, & Oosterlaan, 2002), this research is certainly far from conclusive.

Despite these limitations, the executive dysfunction theory should not be discounted completely. Further research is needed to contribute to a clearer understanding of executive functioning in individuals with ASD across the lifespan and how executive dysfunction may relate to key features of ASD. At present, the theory is not able to account for several key features of ASD and is hindered by inconsistent research findings, although it may be useful when considered in parallel to other theoretical explanations of ASD.

1.2.3.3.4 Weak central coherence theory.

A final cognitive theory of ASD which warrants discussion relates to weak "central coherence", the ability to bring information together to construct higher level meaning in context (Frith, 1989). This account proposes that, whilst typically developing individuals use overall meaning to process information, individuals with ASD instead focus on small detail and process information using constituent parts rather than the whole picture (Rajendran & Mitchell, 2007).

Perceptual research involving individuals with ASD has provided support for this theory. For example, studies have shown that children with ASD score above average on the Children's Embedded Figure Test, in which participants are required to locate a hidden figure within a larger meaningful drawing (Shah & Frith, 1983). Individuals with ASD have also consistently shown superior performance on the Block Design subtest of the Wechsler Intelligence Scales, in which individual blocks are used to reconstruct a 2-D pattern from separate parts (Frith & Happé, 1994). It had previously been suggested that superior performance on this task was due to strong general spatial skills in ASD (Prior, 1979),

although Shah & Frith (1993) demonstrated that typically developing participants benefitted from pre-segmentation of the designs whilst individuals with ASD did not, concluding that their superior performance was in fact due to an ability to segment the designs cognitively. Performance on these types of task has been related to anecdotal descriptions of some features of ASD, for example the ability to quickly notice changes in familiar lay outs and patterns (Frith & Happé, 1994).

Further evidence for the weak central coherence hypothesis has been provided by studies in which individuals with ASD have been shown to perform poorly on tasks requiring the use of context or overall meaning to interpret information, for example the disambiguation of homographs. Homographs are words that share the same written form as another word but have a different meaning. Studies have shown that individuals with ASD are less able than typically developing individuals to pronounce homographs correctly when the word must be processed as part of the whole sentence meaning (Frith & Snowling, 1983; Jolliffe & Baron-Cohen, 1999), suggesting that they may not be making global connections between words or 'reading between the lines'. This finding has been replicated several times and has been discussed as an explanation for difficulties understanding communication intent often seen in individuals with ASD.

A key benefit of this theory is that it is able to account for strengths often seen in individuals with ASD, in addition to savant skills, which both the theory of mind and executive functioning theories do not. Furthermore, it is able to competently explain aspects of social communication difficulty, whilst also accounting for non-social features of ASD. As already discussed, this is an area which is often neglected by other cognitive theories which instead focus on explanations for social deficits in ASD.

However, the theory can also be criticised, particularly as there is evidence that the processing of global information is sometimes preserved in individuals with ASD (e.g.

Lopez, Donnelly, Hadwin, & Leekam, 2004). This has led to a revision of the theory to consider weak central coherence as a cognitive style rather than a deficit; individuals with ASD may be able to extract overall meaning with effort, although they are likely to be biased to attend to detail (Rajendran & Mitchell, 2007). Whilst this revision makes sense theoretically, it fails to account for studies which have found no differences at all in global processing between individuals with ASD and typically developing controls (e.g. Mottron & Belleville, 1993). There is also evidence that weak central coherence may not be universal among individuals with ASD (Jarrold & Russell, 1997) and it may also be seen in individuals with schizophrenia (Bellugi, Lichtenberger, Jones, Lai, & St. George, 2000), limiting its value as a theoretical account specific to ASD. However, this may not actually be considered as problematic by many.

1.2.4 Summary.

ASD is a neurodevelopmental condition diagnosed on the basis of difficulties in social interaction and communication across contexts, alongside restricted or repetitive patterns of behaviour and interests (American Psychiatric Association, 2013). A wide variety of other cognitive and behavioural features are also associated with ASD, including sleeping and eating difficulties, some deficits in executive function and synaesthesia. Prevalence rates remain unclear, although rates are now higher than previously documented, highlighting the need for an enhanced understanding of the aetiology of ASD, in addition to the development of effective interventions.

Aetiological research in ASD is unfortunately inconsistent, fraught with methodological limitations and further complicated by the clinical heterogeneity of ASD. Whilst there have been considerable advances in genetic and biological explanations of ASD, there is a lack of a comprehensive model of aetiology at present. Cognitive theories of ASD are similarly inconsistent, with no one model being able to account for the heterogeneous

presentation associated with ASD. Nonetheless, when considered in combination, cognitive theories can explain both core and associated features of the condition well. They also provide important theoretical foundations, with reference to which interventions can be developed and appraised.

1.3 Psychosocial Interventions to Improve Core Features of Autism Spectrum Disorders

Treatment strategies to improve core features of ASD are perhaps hindered by the fact that the biological causes of ASD remain poorly understood (Granovetter, 2013). However, a proliferation of psychosocial interventions have been developed to improve social interaction and communication, in addition to restricted or repetitive patterns of behaviour and interests. A full review of research focusing on psychosocial interventions to improve core features of ASD is beyond the scope of this thesis. However, it is important to acknowledge key interventions since the National Institute for Health and Clinical Excellence (NICE) guidelines for the diagnosis and management of adults and children with autism (NICE, 2012a, 2013) specify that individuals with ASD and coexisting mental disorders should be offered age-appropriate psychosocial interventions to help address the core features of ASD.

A huge number of interventions claiming to be effective in the treatment of core features of ASD in children are currently available, although the evidence base for many of these is poor (Matson, Adams, Williams, & Rieske, 2013). Interventions with perhaps the most solid evidence to date are based upon operant and classical conditioning, as well as social learning theory (Matson et al., 2013). Many interventions incorporating principles of Applied Behaviour Analysis (ABA; systematic observation and modification of behaviour) have been developed with promising results. For example, a recent Cochrane review investigating the effectiveness of Early Intensive Behavioural Interventions (EIBI), originating from the Lovaas method (Lovaas, 1981), concluded that there is some evidence

that EIBI is an effective treatment for some children with ASD, with improvements in adaptive behaviours, communication and social skills noted (Reichow, Barton, Boyd, & Hume, 2012). However, it was also reported that the strength of this evidence was poor, since many of the included studies were non-randomised and subject to a high risk of bias.

Unfortunately, this is also a common problem with other types of intervention for ASD. There has been some promising research into interventions teaching key skills relating to social ability, for example emotion recognition, imitation and joint attention, although again much of the research in this area is from case series and quasi-experimental designs (Simpson et al., 2004). Interventions focused on the direct teaching of social skills, for example via social skills groups, video modelling and social stories are receiving increasing attention, but again, further systematic and experimental research is required before firm conclusions can be drawn regarding effectiveness.

The investigation of psychosocial interventions for adults with ASD is even less conclusive. A recent systematic review of peer-reviewed studies in this area found only 13 relevant studies, the majority of which were case studies or non-randomised controlled trials focusing on ABA or social cognition training (Bishop-Fitzpatrick, Minshew, & Eack, 2013). Despite the fact that the quantity and quality of studies were limited, the effect sizes of those included were largely positive, demonstrating the importance of further research into psychosocial interventions for adults with ASD.

In summary, there are a wide variety of interventions designed to treat core features of ASD, although there is currently little empirical research of a high enough quality to make firm conclusions about effectiveness, particularly for interventions designed for adults with ASD. The difficulty in synthesising the evidence base is complicated by the heterogeneity in the clinical presentation of ASD and individual differences in response to treatment. This is

perhaps further complicated by the fact that ASD is associated with high levels of comorbidity, an area which will be reviewed in the following section.

1.4 Psychiatric comorbidity in Autism Spectrum Disorders

As acknowledged in diagnostic criteria, ASD commonly co-occurs with intellectual and language impairment, in addition to medical, neurodevelopmental, mental and behavioural disorders. Intellectual disability and ASD covary at high rates; it has been estimated that intellectual disability is present in 24-40% of individuals with ASD (Baird & Charman, 2000). Comorbidity with other neurodevelopmental disorders, including Attention Deficit Hyperactivity Disorder, is also high (e.g. Simonoff et al., 2008), whilst multiple psychiatric comorbidities have been shown to be common in both children and adults with ASD. The following section will review research relating to comorbid mental disorder in individuals with ASD.

1.4.1 Comorbid mental disorders.

1.4.1.1 Children and adolescents.

Several studies have indicated that children and adolescents with ASD experience high rates of mental disorders. Using an epidemiological, population-derived sample of 12 year old children, Simonoff et al. (2008) reported that 70% of participants with ASD had at least one comorbid disorder and 41% had two or more. The most common psychiatric diagnoses in this age group were anxiety disorders, attention-deficit/ hyperactivity disorder and oppositional defiant disorder. These results are consistent with other studies involving children of varying ages, with studies involving older children also reporting high levels of comorbid mood disorders (e.g. Leyfer et al., 2006). Studies of adolescents with ASD have reported increased loneliness associated with high levels of affective disorders (Attwood, 2004a).

Simonoff et al. (2013) extended their earlier study (Simonoff et al., 2008) by reassessing participants in their original sample at age 16 years. Results indicated that comorbid psychiatric disorders in individuals with ASD are persistent from childhood to adolescence. This study can be criticised for the fact that the only measure used to assess psychiatric comorbidity was the Strengths and Difficulties Questionnaire (Goodman, 1997), a screening measure that does not apply a clinical interpretation, is not validated for use with individuals with ASD and does not cover the full range of psychopathology. Additionally, no comparison group was utilised, further hindering the interpretation of results. However, the study is the first to report persistence of mental disorder in a longitudinal sample of individuals with ASD and therefore highlights the importance of targeting comorbid psychopathology during intervention with this client group.

1.4.1.2 Adults.

There is a lack of empirical evidence on the prevalence of comorbid psychiatric disorders in adults with ASD, particularly when compared to child and adolescent populations. Tsakanikos et al. (2006) and Rydén & Bejerot (2008) were the first studies to address this issue and reported mixed results, although Tsakanikos et al. (2006) did not use a typically developing control group for comparison which was a clear limitation. Both studies were further limited by the fact that unstandardised diagnostic assessments were used to assess symptoms of mental disorder.

Joshi et al. (2013) attempted to address these difficulties in a larger-scale study that compared adults with and without ASD referred to a speciality clinic for ASD. The prevalence of comorbid psychiatric disorders was assessed using structured diagnostic assessments, alongside measures of psychosocial functioning. It was reported that adults with ASD had higher levels of both lifetime and current psychiatric comorbidity, including major depressive disorder and multiple anxiety disorders. Individuals with ASD were also reported

to have a higher level of functional impairment, and were significantly more likely to have received both pharmacotherapy and counselling. Whilst further research in this area is clearly needed and the generalizability of this data may be questioned due to the fact that all participants were recruited from a specialist ASD clinic, the study supports research demonstrating high levels of psychiatric comorbidity in children with ASD. This has important implications for clinical practice and intervention.

1.4.2 Theoretical and clinical rationale for psychotherapeutic interventions.

Gaus (2007) developed a model to conceptualise difficulties commonly reported by individuals with ASD seeking psychotherapy based on empirical evidence relating to cognitive dysfunction in ASD. Within the model, information processing deficits (e.g. impaired theory of mind; dysfunctional internal feedback loops involved in self-perception and self-regulation; and weak central coherence) combine, leading to social skills deficits (e.g. poor language pragmatics and semantics) and difficulties with activities of daily living, resulting in negative social consequences, such as being ignored, rejected or ridiculed (Gaus, 2007). Difficulties with self-management and activities of daily living (e.g. inefficient task management) and a higher than average number of stressful events, increase the frequency and intensity of daily "hassles". Since both poor social support and chronic stress are known risk factors for mental health difficulties in the general population (e.g. Cohen & Wills, 1985), it is hypothesised that individuals with ASD are particularly vulnerable to the development of co-morbid mental disorders (Gaus, 2007).

Given the high level of coexisting mental disorders in both children and adults with ASD, it is unsurprising that there has been a growing interest in the development of psychotherapeutic interventions targeting co-occurring mental health difficulties in this client group. The development and use of interventions targeting psychiatric comorbidity may reduce overall impairment and improve quality of life. Indeed, the NICE guidelines for the

diagnosis and management of adults and children with autism (NICE, 2012a, 2013) specify that individuals with ASD and coexisting mental disorders should be offered psychosocial interventions informed by existing NICE guidance for the specific disorder, with adaptations to the method of delivery as appropriate. The Autism Act 2009 also states that mainstream services should offer interventions to individuals with ASD, offering reasonable adjustments where necessary.

From a public health perspective, ASD is associated with high service utilisation due to its early onset, high level of associated impairment and high level of psychiatric comorbidity (Jarbrink, Fombonne, & Knapp, 2003). The lifelong persistence of ASD adds to this picture; research has indicated that support costs for adults with ASD may be more than eight times as much as children, with the annual support cost of an adult with ASD in Great Britain estimated to be £90,000 (Knapp, Romeo, & Beecham, 2009). There is therefore a clear clinical need for research into both the clinical application and effectiveness of psychotherapeutic interventions with individuals with ASD across the lifespan. One such intervention is Cognitive Behavioural Therapy (CBT) and this will be introduced and reviewed in the following section.

1.5 Cognitive Behavioural Therapy

Cognitive Behaviour Therapy (CBT) is a short-term, structured and predominantly present-oriented psychotherapy focused on modifying dysfunctional thought patterns and behaviour (Beck, 2011). It is currently recommended by the National Institute of Health and Clinical Excellence as a first line treatment for many mental disorders, including depression, obsessive compulsive disorder, panic disorder, social anxiety disorder, schizophrenia and psychosis. There is a growing interest in the use of CBT with individuals with ASD to treat both core features of ASD and co-existing mental disorders. This section will provide an

overview of the theoretical origins of CBT, in addition to briefly describing research literature to date regarding both its effectiveness and clinical practice.

1.5.1 Theoretical background.

As implied by its name, CBT has two main theoretical influences: behavioural theories widely endorsed by the behaviourist movement in the 1950's and 1960's; and cognitive theories which dominated the 'cognitive revolution' of the 1970's (Westbrook, Kennerley, & Kirk, 2011). These theories provided the foundations for behavioural therapy and cognitive therapy respectively, both of which influenced the development of CBT.

Key figures of the behaviourist movement posited that scientific study should predominantly focus on observable behaviour rather than unobservable events that take place in the mind (Skinner, 1984). Learning theory was particularly influential, providing explanations for the learning of new associations between stimuli and responses, and these principles were used within behavioural therapy to modify emotional reactions and undesirable behaviour. For example, systematic desensitisation (Wolpe, 1958) used principles of classical conditioning (implicit learning of a response to a previously neutral stimulus by association with an unconditioned stimulus that elicits the response; Pavlov, 1927) to treat fear reactions to a stimulus by pairing positive stimuli to the fear inducer during gradual and systematic exposure. Other behavioural treatment approaches influenced by learning theories include exposure and response prevention (Meyer, 1966) and contingency management programmes (see, for example, Petry, 2006).

Whilst such approaches had rapid early success and continue to be useful in the treatment of anxiety disorders today, the attempt to describe and treat mental disorder in purely behavioural terms was widely criticised in the 1970's (Westbrook et al., 2011). Cognitive theorists argued that the omission of cognitive phenomena such as thoughts and beliefs in psychotherapies was unjust and their focus was to use experimental investigation to

"describe formally the meanings that human beings created out of their encounters with the world, and then to propose hypotheses about what meaning-making processes were implicated" (Bruner, 1990). Aaron T. Beck and others were influenced by this movement, theorising about the role of cognitive processes in emotional disorders. Indeed, Beck's cognitive theory of emotion and emotional disorders (Beck, 1976) provided a firm foundation for the development of Cognitive Behavioural Therapy and this cognitive model remains central to the practice of modern CBT.

Beck (1976) considered that dysfunctional thinking is common to all psychological disturbances and directly influenced an individual's mood, physical symptoms and behaviour. A high number of negative automatic thoughts are likely to be generated in situations in which dysfunctional assumptions, an intermediate class of beliefs, are activated. The development of such assumptions is influenced by an individual's schemas or core beliefs- fundamental, rigid and overgeneralised beliefs that are usually developed as a result of childhood or early experiences. A key component of CBT interventions is therefore the identification and modification of cognitive structures, i.e. thoughts, beliefs and schemas, to facilitate clinical improvement. This is often combined with behaviourally focused interventions, for example developing skills in identifying, planning and increasing pleasurable activities. In practice, individuals are encouraged to complete structured tasks between sessions to consolidate and practice skills and techniques introduced in therapy sessions.

1.5.2 Effectiveness in other populations.

Today, CBT is possibly the most extensively researched and widely evidenced psychotherapeutic treatment of a range of mental disorders in the general population (Hofmann, Asnaani, Vonk, Sawyer, & Fang, 2012). Since the body of effectiveness research

for CBT is so extensive, the following section will provide an overview of meta-analytical literature published in key populations.

1.5.2.1 Children and adolescents.

In a review of meta-analyses of CBT conducted with both children and adults, Hofmann et al. (2012) concluded that CBT for children and adolescents showed robust support for the treatment of internalising disorders. "Large" effect sizes have been reported for the use of CBT in the treatment of anxiety disorders (James, James, Cowdrey, Soler, & Choke, 2015; Santacruz et al., 2002), with CBT for obsessive compulsive disorder reported to have significantly better outcomes than other psychosocial treatments and medication (Guggisberg, 2005). Santacruz et al. (2002) also reported a "medium" effect size for CBT for depression in children, whilst Haby, Tonge, Littlefield, Carter, & Vos (2004) concluded that CBT was superior to the use of selective serotonin reuptake inhibitors in children and adolescents.

Hofmann et al. (2012) reported that the evidence for the use of CBT to treat externalising disorders in children and adolescents is less conclusive. Meta-analyses have indicated that CBT is more effective than no treatment or treatment as usual but no more effective than other psychosocial treatments in the reduction of violent behaviours (Ozabacı, 2011) and the treatment of juvenile sex offenders, childhood sexual abuse survivors, faecal incontinence, chronic headaches and childhood obesity (Macdonald et al., 2012; Walker, McGovern, Poey, & Otis, 2004). Van der Oord, Prins, Oosterlaan & Emmelkamp (2008) reported a moderate mean weighted effect size for ADHD outcomes following CBT, although this was deemed less effective than medication.

1.5.2.1.1 Children and adolescents with intellectual disabilities.

The research base for the effectiveness of CBT with children and adolescents with intellectual disabilities can certainly be described as in its infancy. To the best of our

knowledge no randomised controlled trials or studies adopting an independent group design have been conducted with this client group to date. In a recent review of psychological therapies in individuals with intellectual disabilities, Vereenooghe & Langdon (2013) theorised that the current lack of research may be partially explained by ethical concerns in the recruitment of young people with intellectual disabilities. This is disheartening and it is hoped that the generation of controlled outcome trials for CBT with children with intellectual disabilities will be encouraged by the publication of randomised controlled trials involving children with ASD (see Section 1.6.2.1), in addition to the growing clinical interest in the use of CBT in children and adolescents with intellectual disabilities.

1.5.2.2 Adults.

The aforementioned review of meta-analyses reporting on the effectiveness of CBT in a variety of populations concluded that the strongest support exists for CBT in adults with anxiety disorders, somatoform disorders, bulimia nervosa, anger control problems and general stress (Hofmann et al., 2012). The evidence base for CBT for anxiety in adults is particularly strong (Hofmann & Smits, 2008) and recent research has indicated that guided self-help and internet-based CBT can also be effective in the relief of anxiety symptoms (Coull & Morris, 2011), although long term maintenance of gains with this modality remains unclear. However, it should also be noted that considerable heterogeneity has been reported amongst studies reporting on CBT for anxiety disorders and standardised reporting and a more uniform approach to study design would be beneficial for future research in this area.

Although less consistent, meta-analyses for the effectiveness of CBT in other areas have also shown promising results. For example, CBT has been reported to be more effective than control conditions in the treatment of smoking cessation, positive symptoms of psychosis, depression and insomnia (Hofmann et al., 2012). Evidence for the efficacy of CBT

has also been reported in adults with substance dependence (Dutra et al., 2008), although the effect size for CBT was small in comparison to other psychosocial interventions in this study.

In summary, the evidence for the effectiveness of CBT in adults is generally strong across a range of conditions (Hofmann et al., 2012). However, despite the large literature base, Hofmann et al. (2012) highlighted that many meta-analytic studies of the effectiveness of CBT include studies with inadequate control groups and small sample sizes, emphasising the ongoing need for high-quality effectiveness studies and meta-analytic reviews in this area.

1.5.2.2.1 Older adults.

The evidence base for the effectiveness of CBT in older adults remains relatively limited compared to studies for working age adults (Whittington & Grey, 2014). However, a recent meta-analysis of CBT for late life depression concluded that CBT was more effective than waiting list or treatment as usual conditions, although no more effective than pharmacotherapy or other psychotherapies (Gould, Coulson, & Howard, 2012). The same pattern of results was found for six month follow up and other meta-analyses reporting on the effectiveness of CBT for depression in older adults have described similar results (Krishna et al., 2011; Wilson, Mottram, & Vassilas, 2008).

CBT for anxiety disorders in older adults has been shown to have mixed outcomes. A meta-analysis by Thorp et al. (2009) reported that CBT was no more effective than relaxation training, although many of the studies included in this review were uncontrolled. In an arguably more methodologically sound meta-analysis due to the more stringent inclusion criteria (Hendriks, Oude Voshaar, Keijsers, Hoogduin, & van Balkom, 2008), CBT was shown to be more effective in reducing anxiety symptoms and accompanying symptoms of worry and depression than both a waiting list control and active control conditions.

1.5.2.2.2 Adults with intellectual disabilities.

The aforementioned systematic review and meta-analysis by Vereenooghe & Langdon (2013) investigated the efficacy of psychological therapies of a variety of modalities with individuals with intellectual disabilities. Of the 22 trials deemed eligible for review, 18 reported on cognitive-behavioural interventions, some of which were excluded from the meta-analysis if data were included in a later study or if insufficient data were reported. Whilst studies involving children and adolescents were included in the systematic review, all studies included in the meta-analysis consisted of adult participants. Vereenooghe & Langdon (2013) reported that CBT for anger and aggression had an average estimated effect size of g= .827, whilst studies evaluating CBT for depression generated an effect size of g= .742. These outcomes were interpreted as "large" and "moderate to large" respectively, providing support for the use of CBT with individuals with intellectual disabilities. However, the heterogeneity of studies included in the review, in addition to the variability of methodological quality across studies may limit the validity of this conclusion. Nonetheless, Vereenooghe & Langdon (2013) provided a thorough review of research in this area to date, highlighting limitations and generating recommendations for future research, including the measurement and reporting of level of intellectual functioning to reduce heterogeneity and thorough description of methods, interventions and adaptations. Such recommendations are likely to be paramount for the development of the literature base for CBT in individuals with intellectual disabilities and may also be applicable to studies investigating the use of CBT in individuals with ASD.

1.5.3 Group versus individual Cognitive Behavioural Therapy.

There has been an increase in the clinical delivery of CBT using a group format throughout the last decade. There are clearly appealing benefits to this, including cost-effectiveness in an increasingly resource-limited NHS, although it is important to consider the evidence base for the delivery of CBT in this format. Whilst CBT may appear to lend

itself well to group sessions due to its structured, time-limited and skills-focused approach, potential impacts on effectiveness due to the considerable differences in format should be explored.

CBT delivered in a group format has generally attracted less empirical research than individualised CBT, although a number of studies have investigated its effectiveness. Jónsson, Hougaard, & Bennedsen (2011) compared 110 outpatients with OCD randomly assigned to sessions of either individual or group CBT and concluded that OCD can be treated equally as effectively across both formats, although a meta-analysis of other research in this area demonstrated that individual CBT may be slightly superior. Other meta-analyses have concluded that group CBT may be an effective treatment for post-traumatic stress disorder (Barrera, Mott, Hofstein, & Teng, 2013), depression (Feng et al., 2012) and insomnia (Koffel, Koffel, & Gehrman, 2015). These outcomes are promising and emphasise the importance of future systematic reviews of the efficacy of CBT to include an exploration of effectiveness across both individual and group formats.

1.5.4 Adaptations.

There is an increasing recognition of the need for CBT to be adapted or modified to increase its accessibility for some client groups. Perhaps the mostly widely researched groups to date in this area are children, older adults and individuals with intellectual disabilities, although a wide range of other factors may influence accessibility to CBT, including neurodevelopmental disorders, neurological disorders and sensory impairments (Rossiter & Holmes, 2013).

Common features of adaptive approaches that have been said to be associated with effectiveness include the increased use of visual resources, for example drawings, photographs and video; simplification of core concepts; the involvement of family members and carers; shorter session duration; and increased training of emotional vocabulary and

recognition (Rossiter & Holmes, 2013). Such modifications have been associated with effectiveness in CBT with children (e.g. Stallard, 2005), individuals with intellectual disabilities (e.g. Dodd, Joyce, Nixon, Jennison, & Heneage, 2011) and adults with dementia (e.g. Laidlaw, Thompson, & Gallagher-Thompson, 2004), demonstrating the flexibility of the intervention. However, very little experimental research has been conducted to systematically examine the effectiveness of modifications in individuals with ASD. It is therefore difficult to comment on whether particular adaptations to CBT cause improvements in outcome for this client group and additional research in this area would therefore be beneficial.

1.5.5 Summary.

CBT is a short-term psychotherapy influenced by cognitive and behavioural theories and focused on modifying dysfunctional thought patterns and behaviour (Beck, 2011). It has been demonstrated to be effective in the treatment of a large variety of conditions, in both individual and group formats. When considering the evidence base for CBT across such a wide range of presentations and client groups, it seems logical to explore the use of this approach with individuals with ASD. Whilst it is acknowledged that adaptations may need to be made to account for social and cognitive difficulties seen in this client group, the fact that CBT has already been shown to be successfully adapted for use with a range of client groups highlights the flexibility of this approach.

1.6 Cognitive Behavioural Therapy in Individuals with Autism Spectrum Disorders

1.6.1 Theoretical rationale.

The aforementioned model by Gaus (2007; see Section 1.4.2) emphasises the interaction between cognitive dysfunction and behavioural outcomes in individuals with ASD and may be extended to provide a theoretical rationale for the utility of CBT in this client group. Information processing deficits, social skills deficits and difficulties in daily living are likely to contribute to the development or reinforcement of negative beliefs and affect. For

example, the social consequences of being ignored or ridiculed could influence negative schemas about others and the self, subsequently increasing symptoms of low mood and anxiety. Difficulties with social cognition and cognitive rigidity can also make it more difficult for individuals with ASD to make use of contextual information and to modify existing beliefs and affect. Due to the complex nature of ASD, it could therefore be hypothesised that a therapy which aims to target behavioural, cognitive and affective skills simultaneously would be useful. Whilst many interventions focused specifically on social skills deficits have been found to effectively improve social outcomes for individuals with ASD (see Section 1.3), CBT may provide a more holistic approach as its conceptual basis assumes reciprocity between an individual's thoughts, feelings and behaviours in social situations (Beck, 2011) and interventions are therefore multifaceted. Social skills training programmes that are not specific to ASD have reported increased effectiveness in interventions incorporating CBT techniques, in contrast to those that focus on either social, cognitive or behavioural techniques independently (Bauminger, 2007). Thus, CBT can theoretically target both core features of ASD *and* symptoms of co-occurring mental disorder, making it a potentially unique and desirable intervention for use with this client group.

Given the fact that individuals with ASD have been shown to experience difficulties identifying emotions and cognitions in themselves and others, the suitability of CBT for use with this client group may logically be questioned. However, recent evidence suggests that individuals with ASD are able to accurately report their anxious and depressed cognitions (Ozsivadjian, Hibberd, & Hollocks, 2014) and it has also been reported that individuals with ASD perform comparably to typically developing individuals on tasks requiring discrimination among thoughts, feelings and behaviours and cognitive mediation (Lickel, MacLean, Blakeley-Smith, & Hepburn, 2012). Whilst it is acknowledged that this research is

currently in its infancy, it is argued that there is currently a lack of evidence to indicate that CBT should be contra-indicated in this client group.

1.6.2 Effectiveness research.

1.6.2.1 Children and adolescents.

There is an emerging literature on the effectiveness of CBT for children and adolescents with ASD. To date, the majority of these studies have reported on the use of CBT to target symptoms of anxiety (see Shaker-Naeeni, Govender, & Chowdhury, 2014, for a review), although there has been a growing interest in alternative uses of CBT with children with ASD, for example to treat anger (Sofronoff, Attwood, Hinton, & Levin, 2007), to target social and emotional understanding (Beaumont & Sofronoff, 2008) and to improve affectionate communication and friendship skills (Andrews, Attwood, & Sofronoff, 2013). Many studies have only included participants with at least average intellectual functioning, although there have also been some reports of treatment gains with individuals with mild intellectual impairment (Ames & Weiss, 2013).

Three recent narrative reviews have concluded that CBT may be an effective treatment for children and adolescents with ASD, although all have highlighted the need for further research in this area in order for firm conclusions to be drawn (Danial & Wood, 2013; Ho, Stephenson, & Carter, 2015; Shaker-Naeeni et al., 2014). To date, a further three studies have involved quantitative synthesis in the investigation of the effectiveness of CBT in children and adolescents with ASD. Sukhodolsky, Bloch, Panza, & Reichow (2013) conducted a meta-analysis of randomised controlled trials investigating CBT for anxiety in children with high-functioning autism and reported overall effect sizes for clinician- and parent-rated outcomes measures as d= 1.19 and d= 1.21 respectively. A sensitivity analysis in which outlier studies were removed reduced the magnitude of these effects to d= 0.57 for parent ratings and d= 0.89 for clinician ratings, although both remained statistically

significant. In contrast, the effect size for self-reported anxiety was considerably lower at *d*=0.17.

A similar, more recent study involved a systematic review and meta-analysis examining the efficacy of CBT for anxiety among youth with ASD (Ung, Selles, Small, & Storch, 2015). An overall treatment effect favouring CBT of *d*= 0.71 was reported, although removal of an outlier study reduced this to *d*= 0.47. Anxiety informant and treatment modality were not found to be statistically significant moderators of treatment response, although self-reported outcomes were again found to be significantly lower than informant-reported and clinician-rated outcomes (Ung et al., 2015).

Finally, and most recently, Kreslins, Robertson, & Melville (2015) conducted a systematic review and meta-analysis examining the effectiveness of psychosocial interventions for anxiety in children and adolescents with ASD. All studies included in the meta-analysis utilised both cognitive and behavioural components. In a similar pattern to results reported by Sukhodolsky et al. (2013), psychosocial interventions were shown to be superior to control conditions on clinician- (*d*= 1.05) and parent-rated (*d*= 1.00) outcomes, whilst no significant effect was found on examination of self-reported outcomes (Kreslins et al., 2015).

These are the first systematic reviews incorporating meta-analytic methods to quantitatively investigate the use of CBT in individuals with ASD and they report promising results. However, they also highlight methodological limitations of the included studies, such as a lack of matched active control groups, poor subject characterisation and poor outcome assessment.

1.6.2.2 Adults.

Whilst most of the research relating to the effectiveness of CBT in individuals with ASD has reported on child and adolescent populations, some studies have included adult

participants. This is important since ASD is a lifelong disorder and difficulties encountered as children are likely to continue into adulthood (Seltzer, Shattuck, Abbeduto, & Greenberg, 2004). A number of case studies have been published reporting clinical gains of modified CBT in adults with ASD (see, for example, Cardaciotto & Herbert, 2004; Hare, 1997; Naidu, James, Mukaetova-Ladinska, & Briel, 2006), whilst a recent randomised controlled trial concluded that CBT was effective in treating comorbid OCD in young people and adults with ASD (Russell et al., 2013) based on clinician-rated outcomes. This was the first randomised controlled trial to highlight the potential effectiveness of CBT in adults with ASD, although CBT was not shown to be any more effective than an anxiety management control group. Furthermore, in a similar pattern to studies investigating CBT for anxiety in children and adolescents with ASD (see Kreslins et al., 2015; Sukhodolsky et al., 2013; Ung et al., 2015), effect sizes for self-rated improvement were small. Several recent narrative reviews of studies reporting on the use of CBT in adults with high functioning ASD have concluded that there is preliminary evidence that CBT may decrease comorbid psychiatric symptomatology in this client group (Binnie & Blainey, 2013; Scattone & Mong, 2013; Spain, Sin, Chalder, Murphy, & Happé, 2015), although the need for increased quantitative research in this area was again highlighted.

1.6.3 Rationale for further systematic appraisal of research.

Whilst several narrative reviews have highlighted that CBT may be a promising treatment for children and adolescents (Danial & Wood, 2013; Ho et al., 2015; Shaker-Naeeni et al., 2014) and adults (Binnie & Blainey, 2013; Scattone & Mong, 2013; Spain et al., 2015) with ASD, there has been little systematic appraisal of research in this area to date that has involved quantitative synthesis. In terms of effectiveness, the three meta-analytic studies in this area to date (Kreslins et al., 2015; Sukhodolsky et al., 2013; Ung et al., 2015) focused exclusively on CBT for anxiety in children, excluding trials that included samples of

adults. Whilst it is acknowledged that there has been considerably more research involving children and adolescents with ASD, there is a growing recognition of the need for an evidence synthesis of studies involving both child and adult populations. Inclusion and consideration of the use and effectiveness of CBT across the lifespan is important since ASD is associated with atypical development and the impact of symptoms may fluctuate at different life stages, e.g. difficulties in social interaction are likely to become more profound during adolescence as social contexts increase in complexity and pose higher social expectations (Williams White, Keonig, & Scahill, 2007).

By focusing exclusively on the effectiveness of CBT for anxiety for children, Sukhodolsky et al. (2013), Ung et al. (2015) and Kreslins et al. (2015) also excluded trials investigating CBT for other mental disorders, in addition to trials reporting on the use of CBT to target core features of ASD. To the best of our knowledge, no review to date has quantitatively reviewed research in either of these areas and it is therefore argued that a meta-analysis across both areas would be both timely and clinically useful.

1.7 Aims

The aims of this study were twofold: First, to systematically appraise the evidence for using CBT in the treatment of either core features of ASD or co-occurring mental disorder in individuals with ASD across the lifespan, and second, to consider whether the effectiveness of CBT is moderated by age group or the format of CBT delivery.

1.8 Research Questions

In line with the aims outlined in section 1.7, the following research questions were generated:

Research Question 1: How effective is Cognitive Behavioural Therapy in reducing symptoms of mental disorder in individuals with Autism Spectrum Disorders?

Research Question 2: How effective is Cognitive Behavioural Therapy in the treatment of core features of Autism Spectrum Disorders?

Research Question 3: Is the effectiveness of Cognitive Behavioural Therapy with individuals with Autism Spectrum Disorders moderated by age?

Research Question 4: Is individual Cognitive Behavioural Therapy more effective than group-based Cognitive Behavioural Therapy in individuals with Autism Spectrum Disorders?

Chapter Two: Method

2.1 Introduction

This chapter provides an overview of the methods used to address the research questions, in addition to outlining the rationale for the approaches and techniques selected. The chapter begins with a summary of the search strategy used to identify potentially relevant studies, followed by a description of the eligibility criteria and screening method applied to select studies for inclusion. A clear account of procedures implemented to extract both descriptive and quantitative data from included studies is provided, alongside information on the quality assessment framework chosen to facilitate quality appraisal. The chapter concludes with a summary of methodology used to facilitate the quantitative synthesis of extracted data.

2.2 Registration of Research

The review was prospectively registered with PROSPERO, an international database of systematic reviews in health and social care, in order to provide transparency in the review process and to avoid duplication of research effort (Weston & Langdon, 2015).

2.3 Search Strategy

2.3.1 Database search.

Relevant studies were identified by systematic searches of the following electronic databases: PsycINFO; MEDLINE; CINAHL Plus and Web of Science, in addition to Google Scholar. Initial searches were conducted on 09/12/14 (see Appendix B for output summaries from the initial search for each database). Search alerts were set up to repeat the search on a weekly basis throughout the data collection period to ensure that relevant articles published after the initial search were included. The last date searched was 29/01/16. The Cochrane Library was also searched to identify any existing systematic reviews. As search tools and assigned subject headings differ across databases, the pooling of tools and terms in a

simultaneous search may reduce effectiveness, resulting in the loss of potentially relevant articles (Higgins & Green, 2008). Databases were therefore searched individually rather than using a host such as EBSCO to search across databases concurrently.

Experimental studies that reported on the effectiveness of CBT in children, adolescents and/or adults with an ASD were sought by combining key terms describing the target population and intervention (see Table 2). Terms related to study design or outcome measures were not included to prevent exclusion of studies which may have been relevant. Initial search trials resulted in a very high number of clearly irrelevant studies, for example medication trials, so exclusion terms were added to narrow the search. Terms were searched using US and UK terminology and truncation was used to ensure that all variant word endings were identified. A filter was applied to ensure that all articles retrieved were written in English. At this stage, titles and abstracts were screened by the primary author to identify potentially relevant studies and articles which were clearly not relevant were excluded.

Table 2.

Search Terms in Title and Abstract

Target Population[1]	Autism Spectrum Disorder OR ASD OR Autis* OR Asperger* OR Kanner* OR Pervasive Developmental Disorder
Intervention[2]	Cognitive Behavio* (Therap* OR Treatment OR Intervention) OR Cognitive (Therap* OR Treatment OR Intervention) OR Behavio* (Therap* OR Treatment OR Intervention) OR CBT OR Psychotherap* OR Problem Solving
Combined Terms	1 AND 2
Exclusion Terms	(Drug* OR Medication* OR Vitamin* OR Hormon* OR Pharmacotherap*) Gene* (Applied Behavio* Analysis OR ABA) (Education OR Classroom* OR School*) Epilepsy ADHD

2.3.2 Ancestry method.

In order to identify further relevant literature, the ancestry method was used to examine reference lists of articles retrieved as part of the initial search, including existing reviews. Key journals were also identified by examining journal titles of articles meeting inclusion criteria; *Autism*, *The Journal of Autism and Developmental Disorders* and *Research in Autism Spectrum Disorders* were hand searched from 2000 to present. The World Health Organisation (WHO) International Clinical Trials registry was searched for relevant ongoing studies.

2.3.3 Grey literature search.

A key source of potential bias in meta-analytic research is publication bias or the "file-drawer" problem (Rosenthal, 1979); the fact that significant findings are more likely to be published than non-significant findings. It has been reported that studies with positive outcomes are approximately seven times more likely to be published than studies supporting the null hypothesis (Coursol & Wagner, 1986). This can lead to the overestimation of population effects in meta-analytic reviews that do not include unpublished studies, since effect sizes in comparable unpublished studies are likely to be smaller (McLeod & Weisz, 2004).

Various strategies were therefore used to identify unpublished or "grey" literature and to minimise publication bias. An initial search was conducted via http://www.opengrey.eu/, a database including research reports, doctoral dissertations and conference papers. This was supplemented with searches of Dissertation Abstracts International and the British Library e-theses Online Service, in addition to the scanning of relevant conference programs online and searching trial registers for completed and ongoing studies. Authors of potentially relevant trial protocols were contacted to request a progress update and any relevant data. First authors of included studies were contacted by email to request support in identifying unpublished or ongoing research which may have been relevant (see Appendix C).

2.4 Eligibility Screening

2.4.1 Eligibility criteria.

2.4.1.1 Inclusion criteria.

Studies meeting the following criteria were included in the meta-analysis:

1. Inclusion of participants with a diagnosis of ASD (or autistic disorder, Asperger disorder, childhood disintegrative disorder or pervasive developmental disorder not otherwise specified prior to the publication of DSM-V). Diagnosis made by a qualified clinician or by the use of a standardised diagnostic assessment
2. Use of a control or comparison group design, for example waiting list or treatment as usual (TAU), with or without randomisation
3. Inclusion of a clinician-led CBT intervention, either individual or group-based, incorporating both cognitive and behavioural components and based on well-established and theoretically driven principles and techniques. Articles describing interventions in which CBT theory and principles were utilised to teach or improve behavioural patterns, for example social skills, were included providing that this was explicitly stated
4. Use of at least one validated/ standardised outcome measure of either core ASD features, i.e. difficulties in social interaction, impaired social communication or restricted or repetitive patterns of behaviour and interests, or co-occurring symptoms of mental disorder, for example anxiety, depression or psychosis
5. Written in English

2.4.1.2 Exclusion criteria.

The following exclusion criteria were applied:

1. Single case studies, case series, single case designs, qualitative studies, meta-analysis and review articles

2. Studies in which the effect of the CBT intervention could not be isolated from other treatment methods, for example psychotropic medication
3. Studies which reported on applied behavioural analysis or behaviour modification only, including behavioural activation as a stand-alone treatment
4. Studies which used the same dataset as an already included study, to avoid double counting of data, which could introduce significant bias (Senn, 2009)

No limits were applied on date of publication or completion of research due to the novelty of this review. No limits were applied on age of participants due to the nature of Research Question 3. Both published and non-published studies were included to avoid publication bias.

2.4.2 Screening method.

Literature deemed to be potentially relevant from the title or abstract was screened for eligibility by both the primary researcher and a research supervisor. Inter-rater reliability was assessed using a Kappa statistic (Altman, 1991) and final decisions on inclusion were made via discussion. Reasons for the exclusion of articles at full-text stage are reported in section 3.2.

2.5 Data Extraction

2.5.1 Data extraction method.

Information was extracted and coded from each study meeting eligibility for the meta-analysis using a predesigned data extraction form (see Appendix D). Data extraction was conducted by the primary researcher and independently checked by a research supervisor for accuracy and completeness. Any disagreements were resolved via discussion. In the event of missing or unclear information, authors of included studies were contacted via email in an attempt to obtain or clarify the data (see Appendix E for email correspondence). A summary table was completed detailing the key data extracted from each included study.

2.5.2 Non effect size data.

A unique identification number was assigned to each study and a range of descriptive data were extracted to facilitate data synthesis and quality appraisal. Excluding effect size data, the following data were extracted: full reference; year of publication and country of origin; type of report; group descriptors, for example CBT format, number and format of control group/s, duration of treatment and reported baseline differences; sample descriptors, including number and basic characteristics of participants across groups, for example mean age and age range; and design descriptors, for example randomisation, method of allocation, CBT target, outcome measures used and length of follow up.

2.5.3 Effect size data.

Calculation of effect sizes was based on data reported in research papers, in addition to responses from authors to requests for further information. If means and standard deviations were not directly reported but were possible to calculate from data included in the study, the primary author of the current research calculated these independently. The Cochrane Collaboration Review Manager software (RevMan Version 5.3; The Cochrane Collaboration, 2014) was used for effect size calculations. This software was chosen as it was freely available and had the capability to conduct all planned analytic procedures, in addition to having extensive features for collaborative management of the review (Bax, Yu, Ikeda, & Moons, 2007).

The standardised mean difference (SMD) was calculated for outcomes assessed immediately post-intervention to estimate the difference between treatment and control conditions for each study. The SMD was used rather than the weighted mean difference since outcome measures were not consistent across studies (Lipsey & Wilson, 2001). The standardized mean difference expresses the size of the intervention effect in each study relative to the variability observed in that study. Cohen's d (Cohen, 1988) was calculated by

subtracting the mean post-test score of the control group from the mean post-test score of the experimental group and dividing the result by the pooled standard deviation. Cohen's d was then transformed into Hedge's g (Hedges, 1981) using correction factor J to correct for possible positive bias due to small sample size. The magnitude of Hedges g was interpreted using Cohen's (1988) convention as "small" (0.2), "medium" (0.5), and "large" (0.8). The variance and standard error of g was also calculated for each study.

The SMD does not correct for differences in the direction of the scale. The majority of continuous outcome measures included in analysis were based on scales in which an increase in score indicated greater symptom severity. Where this was not the case, i.e. when an increase in score indicated a positive outcome, the mean values were multiplied by -1 to ensure that all scales pointed in the same direction (Deeks, Higgins, & Altman, 2011).

Data from various intervention arms were pooled when there was only one control arm to avoid double counting of data (Senn, 2009). The following formulae were used to pool means and standard deviations across intervention arms, as recommended by Higgins and Deeks (2011). This method was chosen as it produces outcomes as if the combined groups have never been divided into two, giving a more accurate estimate than standard pooling techniques.

Mean:

$$\frac{N_1M_1 + N_2M_2}{N_1 + N_2}$$

Standard Deviation:

$$\sqrt{\frac{(N_1 - 1)\,SD_1^2 + (N_2 - 1)\,SD_2^2 + \frac{N_1N_2}{N_1 + N_2}\left(M_1^2 + M_2^2 - 2M_1M_2\right)}{N_1 + N_2 - 1}}$$

In instances where data pertaining to a comparable outcome were presented in some studies as dichotomous data and in other studies as continuous data, the SMD was calculated

for continuous data and Odds Ratios (OR) were calculated for dichotomous data. The ORs were re-expressed as SMDs, allowing the data to be pooled together, using the following formula (Chinn, 2000):

$$\text{SMD} = \frac{\sqrt{3}}{\pi} \ln \text{OR}$$

The standard error (SE) of SMDs and log ORs was calculated from 95% confidence intervals using the following formula (Higgins & Deeks, 2011):

$$\text{SE} = \frac{\text{Upper limit} - \text{Lower limit}}{3.92}$$

The SE of log ORs was converted to the SE of SMDs by multiplying by the same constant; $\frac{\sqrt{3}}{\pi} = 0.5513$ (Deeks et al., 2011). All SMDs and SEs were then combined using the Generic Inverse-Variance method in RevMan (The Cochrane Collaboration, 2014).

2.5.3.1 Outcome measures

Outcome measures were validated or standardised measures of either core ASD features, for example The Social Skills Rating System (SSRS; Gresham & Elliott, 1990), or co-occurring symptoms of mental disorder, for example the Spence Children's Anxiety Scale (Spence, 1998). Outcome measures which were not appropriately validated or standardised were not included.

Measures taking the form of self-, clinician- or informant-report were included, in addition to task-based measures. Since evidence indicates that ASD may impair an individual's ability to judge their own social or communicative behaviour, due to subtle mind-reading difficulties (Baron-Cohen, 1995; Baron-Cohen et al., 1997), effect sizes were calculated individually for all report types, in the event that more than one type of measure

was reported for the same construct. This enabled comparison of effect size estimates across outcome report type. As effect sizes were calculated individually for all report types included in each study, the level of effect size data extracted varied across studies.

In instances in which more than one outcome measure was included for the same report-type, the primary outcome measure was used in analysis where this was specified. If primary outcome measures were not specified, the most commonly used measure across similar studies was selected. Where no commonalities across studies were noted, and authors failed to specify their primary outcome measure for a report-type, this was picked at random.

In instances in which the construct being measured varied considerably across report-types/s, the measures/s pertaining to the primary construct being targeted were included. Measures not pertaining to the primary construct being targeted were not included to avoid inappropriate comparisons during analysis. Outcome measures selected for each study for each report-type are documented in Table 3.

2.6 Quality Assessment Framework

Careful consideration was given to the evaluation of the validity of included studies to ensure that conclusions drawn regarding the effectiveness of the intervention were as accurate as possible. A large number of scales have been developed to quantify the quality or risk of bias in clinical trials. However, few have been validated using established criteria and the conclusions of different scales when assessing the same data have been shown to vary considerably (Juni, Witschi, Bloch, & Egger, 1999). The use of such scales is therefore discouraged in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidance (Liberati et al., 2009) and the use of a checklist or component approach to provide a framework for critical appraisal is recommended.

The NICE Quality Appraisal Checklist for Quantitative Intervention Studies (NICE, 2012b; see Appendix F) was used in the present study as it enables appraisal of internal and

external validity of both randomised and non-randomised trials. The checklist was completed for each included study by both the primary researcher and a research supervisor and inter-rater reliability was assessed using a Kappa statistic (Altman, 1991). The second rater was an expert in the content area which was felt to be important as increased knowledge of the area may result in a more consistent assessment of study validity (Jadad et al., 1996). The quality appraisal process was not blinded as it has been suggested to add little benefit (Berlin & Cirigliano, 1997; Kjaergard, Villumsen, & Gluud, 2001) and practical aspects were also a factor, i.e. most of the included studies were by this point well known to the researchers. A decision was made not to contact study authors to collect missing information in relation to quality assessment due to resource constraints, and because it has been reported that answers to these types of request are likely to be positively biased (Haahr & Hróbjartsson, 2006).

Outcomes of quality assessment are presented in section 3.4. Potential risks of bias and threats to study validity both within and across studies are narratively summarised. A decision was made not to weight studies according to their validity or risk of bias as formal statistical methods are not sufficiently well developed to allow for this (Higgins, Altman, & Sterne, 2011), and are therefore not currently recommended (Greenland & O'Rourke, 2001). Sensitivity analyses were conducted to demonstrate how conclusions may be affected if studies deemed to be at a high risk of bias were excluded from the analysis.

2.7 Data Synthesis

Meta-analysis was employed to analyse intervention effects and moderating variables using the Cochrane Collaboration Review Manager software (RevMan, Version 5.3; The Cochrane Collaboration, 2014).

2.7.1 Model.

A random-effects model was used for the following reasons: 1) heterogeneity was anticipated since the project was accumulating data from a wide variety of sources and we

could therefore not assume a common effect size, and 2) inferences made from random-effects models are unconditional and may be applied to a population of studies larger than the sample (Ellis, 2010), enabling the research questions to be addressed. Inverse variance methods were used to calculate study weight, assigning greater value to more precise studies with large samples or smaller variances.

Separate random-effects meta-analyses were conducted to account for the variation in outcome report type: self-report, informant-report, clinician-rated and task-based. Heterogeneity assessment, subgroup analysis, sensitivity analysis and exploration of publication bias were conducted for each report type.

2.7.2 Heterogeneity assessment.

It was anticipated that there may be considerable heterogeneity within the studies included in the analysis. Potential sources of heterogeneity included the method of CBT used (individual or group), the age range of participants, symptom severity at baseline and outcome measures used. Heterogeneity was explored using the I^2 statistic, which describes the percentage of variation across studies that is due to heterogeneity rather than chance (Higgins & Thompson, 2002). The I^2 statistic was chosen rather than Cochran's Q since it enabled quantification of the effect of heterogeneity, providing a measure of the degree of inconsistency in the studies' results (Higgins & Thompson, 2002) and it does not inherently depend on the number of studies included in the meta-analysis (Higgins, Thompson, Deeks, & Altman, 2003). The degree and impact of heterogeneity was assessed using the categorisation of "low" (25%), "medium" (50%) and "high" (75%) (Higgins et al., 2003), in addition to a qualitative assessment of diversity within methodology.

2.7.3 Subgroup analysis.

Subgroup analysis was conducted to evaluate the impact of potentially moderating variables and to address the research questions directly. The following planned subgroup

analyses were conducted for each of the outcome report types provided at least two studies fulfilled the requirements for meta-analysis. All subgroup analysis was conducted using RevMan.

A random-effects meta-analysis was conducted to assess potential variations of treatment effects across outcome constructs (co-occurring symptoms of mental disorder and "core" symptomatology), in line with Research Questions 1 and 2.

A second analysis was conducted to assess potential variations of treatment effects across common age groups, addressing Research Question 3. Studies were assigned to an age group on the basis of the age range of participants (children and adolescents: 4-18; adults: >18; mixed: samples including both children/ adolescents and adults).

A third analysis was conducted to assess variation of treatment effects by type of CBT (individual and group), in order to address Research Question 4.

Additional planned subgroup analysis included publication (published and non-published). However, the subgroup analysis for publication was not conducted due to the lack of unpublished trials sourced that met inclusion criteria for the study.

In addition to the planned subgroup analyses, an additional unplanned analysis was conducted. Due to the high number of studies included which specifically assessed co-occurring symptoms of anxiety, a subgroup analysis was conducted to assess potential variations of treatment effects across age groups (children and adolescents: 4-18; adults: >18; mixed: samples including both children/ adolescents and adults) within this subset of studies.

2.7.4 Sensitivity analysis.

Sensitivity analyses were undertaken to consider whether the findings were robust to the decisions made in the process of obtaining them (Higgins & Thompson, 2002). As several outlier studies with a considerably larger effect size estimate than the other studies were

identified, sensitivity analyses were conducted by removing outliers and recalculating the estimated weighted mean effect size and heterogeneity statistic.

Several pilot or feasibility studies also met inclusion criteria for the current research. Efficacy analyses in pilot trials have been shown to be vulnerable to false positive and false negative findings and can potentially be misleading (Kraemer & Kupfer, 2006). This is likely to be directly related to sample size, with smaller sample sizes in pilot trials contributing to unstable effect sizes (Leon, Davis, & Kraemer, 2011). A plan was therefore made to conduct sensitivity analysis using the above method to examine the effect of the inclusion of pilot or feasibility trials. However, during the analysis it was felt that a number of other included studies which were not defined by the authors as pilot or feasibility trials were in fact lower in quality and/or had smaller sample sizes than many pilot or feasibility trials. Quality appraisal and risk of bias was therefore considered on a study by study basis and sensitivity analysis was conducted by removing studies deemed to be at a high risk of bias rather than those defined by authors as pilot or feasibility trials.

2.7.5 Exploration of publication bias.

Publication bias was assessed graphically using funnel plots plotting effect size against sample size (Light & Pillemer, 1984) since a skewed and asymmetrical plot may indicate a publication bias (Greenhouse & Iyengar, 2009). However, funnel plots were supplemented by further analysis due to their recognised limitations; they require a large number of studies of varying sizes and their inter-rater reliability is low (Song, Hooper, & Loke, 2013), whilst publication bias is not the only source of asymmetry in funnel plots (Egger, Smith, Schneider, & Minder, 1997). For example, true heterogeneity of effect sizes, English language bias and data irregularities can also lead to asymmetry (Egger et al., 1997).

Where publication bias was detected, the fail-safe *N* (Rosenthal, 1979) was used to assess the impact of bias by calculating an estimate of the number of new studies averaging a

null result that would be required to bring the overall treatment effect to non-significance. Fail-safe *N* was calculated using an online calculator (see Rosenberg, 2005, for further details).

It is recognised that there are several limitations of this approach. The calculation of the fail-safe *N* has been criticised as different formulas for fail-safe *N* can lead to widely varying estimates and do not take information on heterogeneity or sample size into account (Becker, 2005). Results were therefore interpreted with caution.

A decision was made not to correct for detected publication bias, for example, by using the trim and fill method (Duval & Tweedie, 2000) which involves the removal of smaller studies presumed to be causing asymmetry, the estimation of the true "centre" of the funnel, and the replacement of the studies alongside artificial studies to correct the asymmetry (Sterne, Egger, & Moher, 2011). This approach has been criticised as it relies on the assumption that the 'missing' studies are those with the smallest effect sizes (Vevea & Woods, 2005) which can lead to overcorrection. In addition, it does not take into account reasons for funnel plot asymmetry other than publication bias (Sterne et al., 2011). More sophisticated methods have been devised (see Field & Gillett, 2010) but as they have only been shown to be effective in meta-analyses including a very large number of studies, they were not considered for the current research.

Chapter Three: Results

3.1 Introduction

In order to address the research questions, this chapter provides a detailed summary of the data collection and analysis. The chapter begins with an overview of the identification, screening and inclusion or exclusion of articles, supported by a PRISMA flow diagram (Moher, Liberati, Tetzlaff, & Altman, 2009). A clear summary of included studies is provided, alongside a table detailing key characteristics of all studies included in the quantitative synthesis. The outcomes of the quality appraisal process are addressed and a summary of the quantitative synthesis is reported with reference to each research question. The chapter ends with a brief discussion of the key findings.

3.2 Study Selection

Following the removal of duplicate studies by both electronic and manual screening, the systematic search of electronic databases identified 2332 potentially eligible studies, and of these, 2263 were excluded by the primary author as it was clear from the screening of titles and abstracts that they did not meet inclusion criteria. The remaining 69 studies were supplemented by 102 studies identified by the ancestry method and two studies identified during the grey literature search, giving a total of 173 studies which were retrieved and assessed for eligibility by both the primary researcher and a research supervisor. One hundred and twenty-three studies were excluded at this stage for a variety of reasons, including a lack of a control or comparison group design (107 studies), use of a dataset that had already been utilised in an included study (five studies) and a lack of both cognitive and behavioural techniques within the intervention (four studies); see Figure 1 for full list of reasons for exclusion.

Six relevant protocols were identified during the search process and authors were contacted to request a progress update and any relevant data. Two authors replied with an

update that their studies had just been accepted for publication and forwarded the manuscripts (Begeer et al., 2015; Langdon et al., 2016). These studies were included, whilst the remaining four authors did not reply and the protocols were therefore excluded.

Fifty studies met inclusion criteria for the study. However, it was not possible to include two of these studies (DeRosier, Swick, Davis, McMillen, & Matthews, 2011; Provencal, 2003) in the meta-analysis as requests to authors for data required to calculate effect sizes were unsuccessful. Forty-eight studies, involving 2099 participants (1081 CBT, 1018 control) were therefore included in the quantitative synthesis. There was very good agreement between the researchers regarding study inclusion (96.5%; Kappa 0.92; 95% CI [0.85, 0.98; see Appendix G for calculation]. Figure 1 depicts a PRISMA flow diagram (Moher et al., 2009), outlining the identification, screening and inclusion or exclusion of articles throughout the process. Reasons for article rejection are clearly indicated.

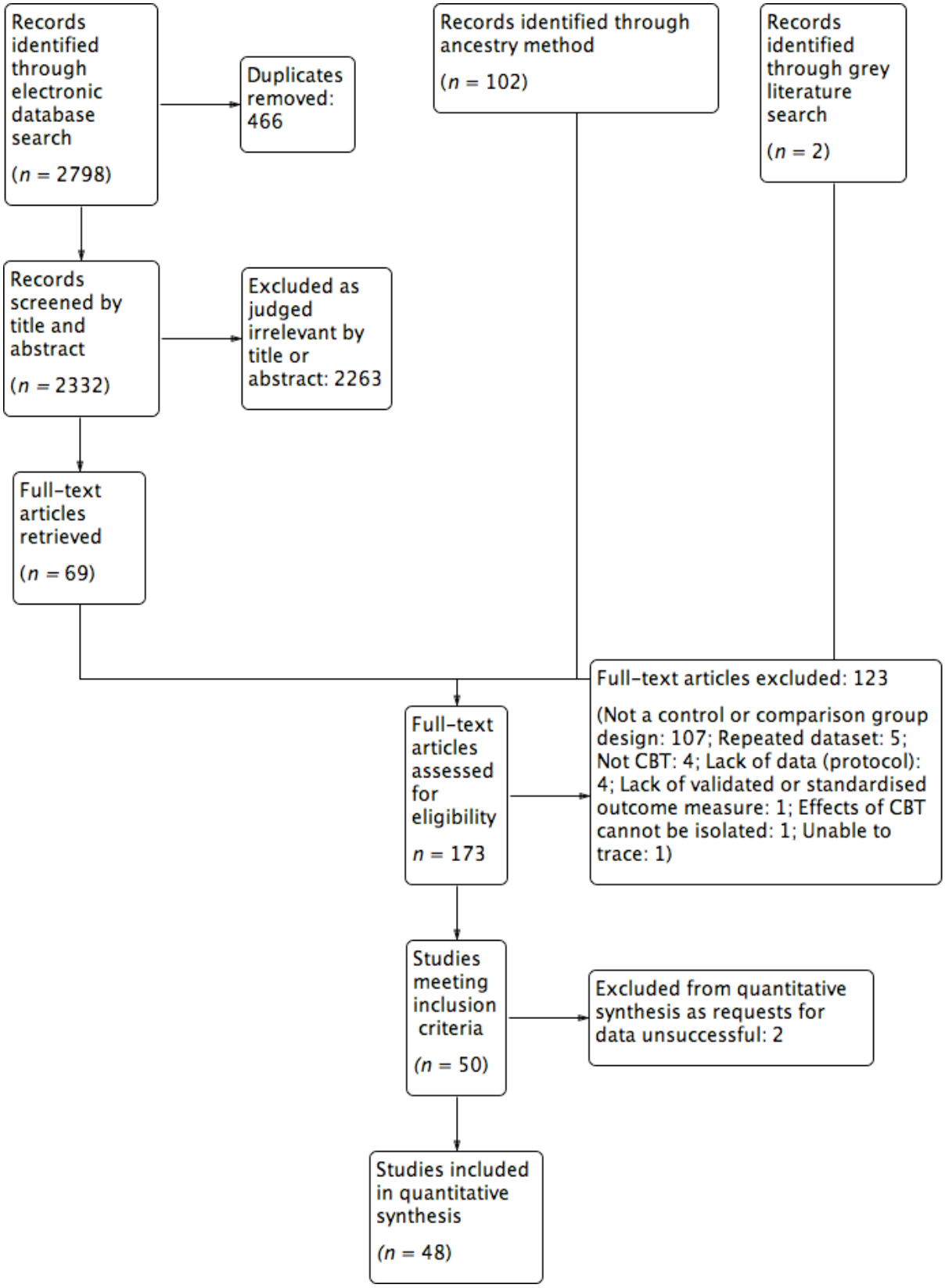

Figure 1. PRISMA flow diagram of study selection

3.3 Study Characteristics

Key characteristics of the 50 studies meeting the inclusion criteria are detailed in Table 3. Two of the included studies were unpublished; both were academic theses sourced via the grey literature search (Clarke, 2012; Provencal, 2003). The quality of these studies was assessed using the same framework as all published studies.

As indicated in Table 3, 24 of the included studies assessed the effectiveness of CBT for co-occurring symptoms of mental disorder, whilst 24 studies targeted core features of ASD. One study (White et al., 2013) investigated both social skills and anxiety. Since outcomes for both could not be included due to the high risk of bias associated with double counting of data (Senn, 2009), the data pertaining to outcomes for social skills were included as this increased the data available to evaluate the effectiveness of CBT in the treatment of core features of ASD. One study (Wood, Fujii, Renno, & Van Dyke, 2014) described the use of a CBT intervention to target both social communication and anxiety, although anxiety outcomes were reported in a separate paper (Fujii et al., 2013). The Fujii et al. (2013) study was excluded during screening of full-text articles since it used the same participants as Wood et al. (2014), again to avoid double counting of data (Senn, 2009).

3.3.1 Studies investigating the effectiveness of CBT for symptoms of mental disorder.

All 24 studies investigating the effectiveness of CBT for co-occurring symptoms of mental disorder were included in quantitative synthesis. Seventeen of the studies involved children and adolescents, whilst four included adult participants. Three studies (McGillivray & Evert, 2014; Pahnke, Lundgren, Hursti, & Hirvikoski, 2014; Russell et al., 2013) included both adolescent and adult participants and were therefore assigned to a ‘Mixed Age’ subgroup for analysis.

Fifteen of the 24 studies in the co-occurring symptoms of mental disorder group examined group-based CBT, whilst eight reported on individual CBT. The remaining study

(Langdon et al., 2016) involved 21 group sessions, in addition to 3 individual sessions prior to group entry to support socialisation to the CBT model. Since this study was predominantly group-based, the decision was made to include it in the 'group-based' subgroup when analysing mode of CBT delivery.

Fourteen of the studies targeting symptoms of mental disorder were defined by authors as randomised controlled trials, seven of which compared a CBT intervention with a waiting list control group and three of which compared CBT to treatment as usual. Three randomised controlled trials compared CBT to a non-CBT group-based treatment: either a social recreational program (Hesselmark, Plenty, & Bejerot, 2014; Sung et al., 2011) or an anxiety management group (Russell et al., 2013). The final randomised controlled trial (Cortesi, Giannotti, Sebastiani, Panunzi, & Valente, 2012) compared a CBT group to a group which received a placebo drug. This study also included a condition in which participants received melatonin and a condition in which participants received both melatonin and CBT. Participants from these intervention arms were not included as the use of a drug-based comparison group was not utilised in any other included study. Three of the 24 studies investigating the effectiveness of CBT for co-occurring symptoms of mental disorder were quasi-experimental or non-randomised (Clarke, 2012; McGillivray & Evert, 2014; van Steensel, Dirksen, & Bögels, 2014), whilst seven were defined by the authors as pilot studies. These studies were included in initial analysis but treated with caution (see Section 3.4 for further details). Three of the seven pilot studies within this group were randomised, whilst four were not, and six compared a CBT intervention to a waiting list control group, whilst one compared CBT to treatment as usual.

The majority of studies investigating the effectiveness of CBT for co-occurring symptoms of mental disorder were targeting anxiety symptoms (15 of the 24 studies). As this was such a large group, a subgroup analysis was conducted to assess potential variations of

treatment effects across age groups within this subset of studies, enabling comparison to recent meta-analytic studies which have looked specifically at the effectiveness of CBT for anxiety in individuals with ASD (Kreslins et al., 2015; Sukhodolsky et al., 2013; Ung et al., 2015). Two studies targeting symptoms of Obsessive Compulsive Disorder (Russell et al., 2013; Russell, Mataix-Cols, Anson, & Murphy, 2009) were also included within this subset, as was a study investigating depression, anxiety and rumination (Spek, van Ham, & Nyklicek, 2013) and a study investigating depression, anxiety and stress (McGillivray & Evert, 2014). In the latter two studies, only outcomes pertaining specifically to anxiety were used to reduce heterogeneity within the quantitative synthesis as much as possible. In total, 19 studies were included within the anxiety subset. Of the remaining five studies, one targeted anger (Sofronoff et al., 2007), one targeted general emotional regulation skills (Scarpa & Reyes, 2011), one targeted insomnia (Cortesi et al., 2012), one targeted self-esteem, quality of life and sense of coherence (Hesselmark et al., 2014) and one targeted stress and emotional distress (Pahnke et al., 2014).

As anticipated, there was extensive variation in the outcome measures used across studies. Many studies included outcome measures from various sources, with the most common report type being self-report within studies targeting co-occurring symptoms of mental disorder, followed closely by informant-report (usually parent) outcomes and clinician-rated outcomes. Only one study within this group used a task-based outcome measure (Cortesi et al., 2012).

There was also considerable variation in the intensity and content of intervention. The number of sessions ranged from four to 50, whilst the length of each session ranged from 40 to 180 minutes. The majority of studies investigating the effectiveness of CBT for co-occurring symptoms of mental disorder used a structured protocol (22 out of 24). In terms of content, 21 of the studies utilised “traditional” CBT methods, with common components

including role play, exposure and teaching/ rehearsal of emotional regulation skills. Common adaptations for the use of CBT in individuals with ASD included an increased emphasis on behavioural rather than cognitive components, the use of social stories and vignettes and increased involvement of family members. One of the studies (Hepburn, Blakeley-Smith, Wolff, & Reaven, 2016) piloted a videoconferencing CBT intervention designed for delivery in a small, multi-family group format, whilst another study (Spek et al., 2013) used a modified version of Mindfulness Based Therapy (Segal, Williams, & Teasdale, 2002) with cognitive elements omitted. The final study within this group (Pahnke et al., 2014) utilised a modified Acceptance and Commitment Therapy protocol (Hayes, Strosahl, & Wilson, 2003) and participants in the CBT group engaged in daily mindfulness exercises in addition to structured intervention sessions.

3.3.2 Studies investigating core features of ASD.

Of the 26 studies investigating the effectiveness of CBT for core features of ASD, 24 were included within quantitative synthesis; as previously mentioned, Provencal (2003) and De Rosier et al. (2011) were excluded as attempts to obtain data required to calculate effect sizes were unsuccessful. In a similar pattern to the above, of the 24 studies included in quantitative synthesis, 22 included children and adolescents whilst only two involved adult participants. This highlights the fact that the research base investigating the effectiveness of CBT in individuals with ASD is considerably more established within child and adolescent populations than with adults.

Twenty-one of the 24 studies in the core features group examined group-based CBT, as may be expected since the majority of studies targeted social skills. One study (Wood et al., 2014) reported on the effectiveness of individual CBT. As previously mentioned, this study examined CBT targeting both social interaction and anxiety, although anxiety outcomes are reported elsewhere (Fujii et al., 2013) and are not included in the present research to

prevent double counting of data. The remaining two studies (Beaumont & Sofronoff, 2008; White et al., 2013) involved both individual and group sessions. In both of these studies each component was reported with equal importance and they were therefore excluded from the 'CBT type' subgroup analysis.

Fourteen of the studies targeting core features were defined by authors as randomised controlled trials, one of which is the only Phase III trial in this area to date (Freitag et al., 2016). Thirteen of the RCT's compared a CBT intervention with a waiting list control group, whilst Freitag et al. (2016) compared CBT to treatment as usual. The final RCT (Soorya et al., 2015) compared CBT to an active control group structured around facilitated play. Of the remaining ten studies investigating the effectiveness of CBT for core features of ASD, three were quasi-experimental or non-randomised and seven were defined by the authors as pilot studies. Again, these studies were included in initial analysis but treated with caution (see Section 3.4 for further details). The quasi-experimental studies involved a variety of control groups: Ozonoff & Miller (1995) compared CBT to no treatment, Laugeson et al. (2012) used a waiting list control group and Laugeson et al. (2014) reported the use of an active control group based on a non-CBT social skills curriculum ('Super Skills'; Coucouvanis, 2005). Of the studies defined as pilot studies by the authors, three used a waiting list control group, two compared CBT to treatment as usual and one (Koning, Magill-Evans, Volden, & Dick, 2013) compared CBT to "no intervention". The remaining study (Baghdadli et al., 2013) reported the use of an active control group with sessions consisting predominantly of leisure activities. Six of the seven pilot studies within this group were randomised, whilst the remaining study (Turner-Brown, Perry, Dichter, Bodfish, & Penn, 2008) was quasi-experimental.

The majority of studies investigating the effectiveness of CBT for core features of ASD were targeting social skills (18 of the 24 studies included in quantitative synthesis), while of the remaining six studies, four targeted Theory of Mind (Begeer et al., 2011; Begeer

et al., 2015; Ozonoff & Miller, 1995; Solomon, Goodlin-Jones, & Anders, 2004), one targeted affectionate communication (Andrews et al., 2013) and one targeted the perception of facial emotions (Baghdadli et al., 2013). A number of studies targeted both social skills and aspects of social cognition. In these circumstances, the primary outcome measure was included. In situations in which the primary outcome measure was not specified, only outcome measures pertaining to social skills were included to avoid comparisons of different constructs across report types.

As reported in Section 3.3.1, there was also extensive variation in the outcome measures used across studies investigating the effectiveness of CBT for core features of ASD. Again, many studies included outcome measures from various sources, with the most common report type within this group being informant-report, followed by self-report. In contrast to studies investigating the effectiveness of CBT for co-occurring mental disorder, seven studies within this group utilised task-based measures, for example Theory of Mind tasks.

As in studies targeting co-occurring symptoms of mental disorder, there was again considerable variation in the intensity and content of the intervention. The number of sessions ranged from five (Andrews et al., 2013) to 70, with Laugeson et al. (2014) reporting on an intervention in which children received 30 minute sessions five days per week over a period of 14 weeks. The length of each session ranged from 30 minutes to whole day sessions. The majority of studies investigating the effectiveness of CBT for core features of ASD used a structured protocol (22 out of 24).

In terms of content, studies within this group less commonly reported “traditional” CBT methods. Some studies did not directly refer to cognitive behavioural therapy per se but they explicitly mentioned the inclusion of both cognitive and behavioural techniques in the intervention and therefore met inclusion criteria for the current study. Content commonly

included direct social skills teaching and role play, emotional identification work and problem-solving exercises or discussions. Common adaptations for the use of CBT in individuals with ASD included increased use of social stories and vignettes, increased use of role play and the involvement of family members in intervention sessions and homework activities.

Table 3.

Characteristics of Included Studies

Source	CBT Target	Methods	Participants	Intervention	Outcome Measures used in Meta-Analysis (Effect Size)	Follow Up
Studies targeting symptoms of mental disorder: Children and Adolescents						
(Sofronoff, Attwood, & Hinton, 2005)	Anxiety	- Randomised Controlled Trial - CG: WL	- IG: *N*= 48; Mean Age, 10.55; Age Range, 9-12 - CG: *N*= 23; Mean Age, 10.75; Age Range, 9-12 - Country: Australia	- Group-based - Child only or Child + Parent sessions (intervention arms pooled to prevent double counting of data) - 6 x 120 minute sessions - Original, manualised program	- Self-Report: None - Informant-Report: Spence Children's Anxiety Scale-Parent Report (0.10) - Clinician-Rated: None - Task-Based: None	- 6 week follow up
(Chalfant, Rapee, & Carroll, 2007)	Anxiety	- Randomised Controlled Trial - CG: WL	- IG: *N*= 28 - CG: *N*= 19 - TS: Mean Age, 10.8; Age Range, 8-13 - Country: Australia	- Group-based - 12 x 120 minute sessions - Adapted 'Cool Kids' program (Lyneham, Abbott, Wignall, & Rapee, 2003)	- Self-Report: Spence Children's Anxiety Scale (2.64) - Informant-Report: Spence Children's Anxiety Scale-Parent Report (4.27) - Clinician-Rated: Anxiety Disorders Interview Schedule-Child & Parent: Diagnostic Status (2.51) - Task- Based: None	- None
(Sofronoff et al., 2007)	Anger	- Randomised Controlled Trial	- IG: *N*= 24; Mean Age, 10.79; Age	- Group-based (pairs) - Parallel parent group	- Self-Report: None - Informant-Report:	- 6 week follow up

		- CG: WL	Range, 9-13 - CG: *N*= 21; Mean Age, 10.77; Age Range, 10-13 - Country: Australia	- 6 x 120 minute sessions - Original, manualised program (built on Sofronoff et al., 2005)	Children's Inventory of Anger- parent Report (0.40) - Clinician-Rated: None - Task-Based: None	(CBT group only)
(Reaven et al., 2009)	Anxiety	- Pilot study - Quasi-experimental - CG:WL	- IG: *N*= 10 - CG: *N*= 23 - TS: Mean Age, 11.8; Age Range, 8-14 - Country: USA	- Group-based - Multi-family sessions - 12 x 90 minute sessions - Original, manualised program ('Face your Fears')	- Self-Report: Screen for Child Anxiety and Related Emotional Disorders- Child Report (0.28) - Informant-Report: Screen for Child Anxiety and Related Emotional Disorders- Parent Report (0.86) - Clinician-Rated: None - Task-Based: None	- None
(Wood et al., 2009)	Anxiety	- Randomised Controlled Trial - CG: WL	- IG: *N*= 17; Mean Age, 9.18; Age Range not reported - CG: *N*= 23; Mean Age, 9.22; Age Range not reported - TS: Age Range, 7-11 - Country: USA	- Individual - Parental involvement in all sessions - 16 x 90 minute sessions (approximately 30 minutes with child and 60 minutes with parents/ family) - Modified 'Building Confidence' program (Wood & McLeod, 2008)	- Self-Report: Multidimensional Anxiety Scale for Children (-0.03) - Informant-Report: Multidimensional Anxiety Scale for Children- Parent Report (1.21) - Clinician-Rated: Anxiety Disorders	- Three month follow up (CBT group only)

					Interview Schedule-Child & Parent: Clinical Severity Rating (2.47) - Task-Based: None	
(Scarpa & Reyes, 2011)	Emotional regulation: Anxiety and Anger	- Pilot study - Randomised - CG: WL	- IG: *N*= 5; Mean Age, 5.84; Age Range not reported - CG: *N*= 6; Mean Age, 5.47; Age Range not reported - TS: Age Range, 4.5-7 -Country: USA	- Group-based - Simultaneous psycho-educational parent group - 9 x 60 minute sessions - Modified manualised program used by Sofronoff et al. (2005; Sofronoff et al., 2007) to be developmentally appropriate for younger children	- Self-Report: None - Informant-Report: Emotion Regulation Checklist- Emotion Regulation subscale (-0.09) - Clinician-Rated: None - Task-Based: None	- None
(Sung et al., 2011)	Anxiety	- Randomised Controlled Trial - CG: AP (Manualised Social Recreational Program)	- IG: *N*= 36; Mean Age, 11.33; Age Range not reported - CG: *N*= 34; Mean Age, 11.09; Age Range not reported - TS: Age Range, 9-16 - Country: Singapore	- Group-based - 16 x 90 minute sessions - Original, manualised program	- Self-Report: Spence Children's Anxiety Scale (0.07) - Informant-Report: None - Clinician-Rated: Clinical Global Impression- Severity (0.46) - Task-Based: None	- Three month follow up - Six month follow up
(Clarke, 2012)	Anxiety	- Cluster randomisation - CG: TAU	- IG: *N*= 14; Mean Age, 12.64; Age Range not reported - CG: *N*= 14; Mean Age, 12.86; Age Range not reported	- Group-based - No parental involvement in intervention - 6 x 60 minute sessions - Adapted 'Exploring Feelings' program (Attwood, 2004b)	- Self-Report: Spence Children's Anxiety Scale (0.70) - Informant-Report: Spence Children's Anxiety Scale-	- Six-eight week follow up

			- TS: Age Range not reported - Country: UK		Parent Report (0.67) - Clinician-Rated: None - Task-Based: None	
(Cortesi et al., 2012)	Insomnia	- Randomised Controlled Trial - CG: Placebo drug (Trial also included 'melatonin' condition & 'melatonin + CBT' condition)	- IG: *N*= 40; Mean Age, 7.1; Age Range not reported - CG: *N*= 40; Mean Age, 6.3; Age Range not reported - TS: Age Range, 4-10 - Country: Italy	- Individual - Family sessions (child and parents) + maintenance sessions for parents - 4 x 50 minute sessions - Original program. Unclear whether program was manualised.	- Self-Report: None - Informant-Report: Children's Sleep Habits Questionnaire- Total Score (completed by parents; 1.01) - Clinician-Rated: None - Task-Based: Actigraph data- Total sleep time (0.62)	- None
(Reaven, Blakeley-Smith, Culhane-Shelburne, & Hepburn, 2012)	Anxiety	- Randomised Controlled Trial - CG: TAU	- IG: *N*= 24; Mean Age, 10.5; Age Range, 7-13 - CG: *N*= 26; Mean Age, 10.4; Age Range, 7-14 - Country: USA	- Group-based - Multi-family sessions - 12 x 90 minute sessions - Original, manualised program ('Face your Fears'- based on 2009 pilot study)	- Self-Report: Screen for Child Anxiety and Related Emotional Disorders- Child Report (0.28) - Informant- Report: Screen for Child Anxiety and Related Emotional Disorders- Parent Report (0.45) - Clinician-Rated: Anxiety Disorders Interview Schedule-	- Three month follow up - Six month follow up (CBT group only)

					Parent: No. of Principal Anxiety Diagnoses (0.60) - Task-Based: None	
(McNally Keehn, Lincoln, Brown, & Chavira, 2013)	Anxiety	- Pilot study - Randomised - CG: WL	- IG: *N*= 12; Mean Age, 11.65; Age Range not reported - CG: *N*= 10; Mean Age, 11.02; Age Range not reported - TS: Age Range, 8-14 - Country: USA	- Group-based - 16 x 75 minute sessions - Adapted 'Coping Cat' Program (Kendall, 1994)	- Self-Report: Spence Children's Anxiety Scale (0.47) - Informant-Report: Spence Children's Anxiety Scale-Parent Report (0.91) - Clinician-Rated: Anxiety Disorders Interview Schedule-Parent: Interference Rating (1.35) - Task-Based: None	- Two month follow up (CBT group only)
(Storch et al., 2013)	Anxiety	- Randomised Controlled Trial - CG: TAU	- IG: *N*= 24; Mean Age, 8.83; Age Range not reported - CG: *N*= 21; Mean Age, 8.95; Age Range not reported - TS: Age Range, 7-11 - Country: USA	- Individual - Parallel parent sessions + parental involvement in some child sessions - 16 x 60-90 minute sessions - Manualised, modular treatment approach (Behavioural Interventions for Anxiety in Children with Autism program-BIACA; Wood & Drahota, 2005)	- Self-Report: Revised Children's Manifest Anxiety Scale- Total Anxiety: *Not included in quantitative synthesis as request for data required to calculate effect size was unsuccessful* - Informant-Report: Multidimensional Anxiety Scale for Children- Parent	- Three month follow up (CBT treatment-responders group only)

					Report (0.48) - Clinician-Rated: Anxiety Disorders Interview Schedule-Child & Parent: Highest Clinical Severity Rating (0.89) - Task-Based: None	
(McConachie et al., 2014)	Anxiety	- Pilot study - Randomised - CG: WL	- IG: *N*= 17; Mean Age, 11.7; Age Range not reported - CG: *N*= 15; Mean Age, 11.8; Age Range not reported - TS: Age Range not reported - Country: UK	- Group-based - Parallel parent group - 7 x 120 minute sessions - Slightly adapted 'Exploring Feelings' program (Attwood, 2004b) for UK use	- Self-Report: Spence Children's Anxiety Scale (0.04) - Informant-Report: Spence Children's Anxiety Scale-Parent Report (0.20) - Clinician-Rated: Anxiety Disorders Interview Schedule-Parent: Primary diagnosis Clinical Severity Rating (0.43) - Task-Based: None	- Three month follow up - Six month follow up
(van Steensel et al., 2014)	Anxiety	- Quasi-experimental - CG: TAU	- IG: *N*= 24; Mean Age, 11.0; Age Range not reported - CG: *N*= 25; Mean Age, 10.72; Age Range not reported - TS: Age Range, 8-18	- Individual - Parental attendance at all sessions - 15 sessions (length not reported) - Modified, combined version of individual and family CBT intervention (Bodden, Dirksen,	- Self-Report: None - Informant-Report: None - Clinician-Rated: Clinician-Rated: Anxiety Disorders Interview Schedule-Child & Parent:	- Three month follow up

			- Country: The Netherlands	& Bögels, 2008)	Diagnostic Status (0.44) - Task-Based: None	
(Hepburn et al., 2016)	Anxiety	- Pilot study - Quasi-experimental - CG: WL (not recruited simultaneously with CBT group)	- IG: *N*= 17; Mean Age, 11.53; Age Range not reported - CG: *N*= 16; Mean Age, 12.12; Age Range not reported - TS: Age Range not reported - Country: USA	- Group-based - 'Telehealth'/ videoconferencing intervention designed for delivery in a small, multi-family group format - Parental involvement in all sessions + parent-only time at end of sessions (20-30 minutes) - 10 x 60 minute sessions + 1 'booster' session - Modified version of 'Face Your Fears' program (Reaven, 2011; Reaven et al., 2012; Reaven et al., 2009)	- Self-Report: None - Informant-Report: Screen for Child Anxiety and Related Emotional Disorders (0.48) - Clinician-Rated: None - Task-Based: None	- None
(Storch et al., 2015)	Anxiety	- Randomised Controlled Trial - CG: TAU	- IG: *N*= 16; Mean Age, 12.75; Age Range not reported - CG: *N*= 15; Mean Age, 12.73; Age Range not reported - TS: Age Range, 11-16 - Country: USA	- Individual - Parallel parent sessions + parental involvement in majority of adolescent sessions - 16 x 60-90 minute sessions - Manualised, modular treatment approach (Developmentally modified version of Behavioural Interventions for Anxiety in Children with Autism program-BIACA; Wood & Drahota, 2005)	- Self-Report: Revised Child's Anxiety and Depression Scales (-0.12) - Informant-Report: Multidimensional Anxiety Scale for Children- Parent Report (0.09) - Clinician-Rated: Clinician-Rated: Anxiety Disorders Interview Schedule-Child & Parent:	- One month follow up (CBT treatment-responders group only)

					Primary diagnosis Clinical Severity Rating (1.38) - Task-Based: None	
(Wood et al., 2015)	Anxiety	- Randomised Controlled Trial - CG: WL	- IG: *N*= 19; Mean Age, 12.4; Age Range not reported - CG: *N*= 14; Mean Age, 12.2; Age Range not reported - TS: Age Range, 11-15 - Country: USA	- Individual - Parallel parent sessions + parental involvement in all adolescent sessions - 16 x 60-90 minute sessions - Manualised, modular treatment approach (Developmentally modified version of Behavioural Interventions for Anxiety in Children with Autism program-BIACA; Wood & Drahota, 2005)	- Self-Report: Revised Child's Anxiety and Depression Scales (-0.09) - Informant-Report: Multidimensional Anxiety Scale for Children- Parent Report (0.71) - Clinician-Rated: Anxiety Disorders Interview Schedule-Child & Parent: Primary diagnosis Clinical Severity Rating (0.39) - Task-Based: None	- One month follow up (CBT treatment-responders group only)
Studies targeting symptoms of mental disorder: Adults						
(Russell et al., 2009)	Obsessive Compulsive Disorder	- Pilot study - Quasi-experimental - CG: TAU	- IG: *N*= 12; Mean Age, 23.8; Age Range not reported - CG: *N*= 12; Mean Age, 32.1; Age Range not reported - TS: Age range not reported	- Individual sessions - Mean number of sessions: 27.5; Range: 10-50 - Treatment not manual or protocol driven	- Self-Report: Beck Anxiety Inventory (-0.39; secondary measure) - Informant-Report: None - Clinician-Report: Yale-Brown Obsessive	- None

			- Country: UK		Compulsive Scale (primary measure; -0.31) - Task-Based: None	
(Spek et al., 2013)	Depression, anxiety and rumination	- Randomised Controlled Trial - CG: WL	- IG: *N*= 20; Mean Age, 44.4; Age Range not reported - CG: *N*= 21; Mean Age, 40.1; Age Range not reported - TS: Age range not reported - Country: The Netherlands	- Group-based - 9 x 150 minute sessions - Modified version of Mindfulness Based Therapy (Segal et al., 2002)- cognitive elements omitted	- Self-Report: Symptom Checklist-90-Revised: Anxiety scale (0.85) - Informant-Report: None - Clinician-Rated: None - Task-Based: None	- None
(Hesselmark et al., 2014)	Self-esteem, quality of life and sense of coherence	- Randomised Controlled Trial - CG: AP (Recreational Activity)	- IG: *N*= 34; Mean Age, 31.9; Age Range not reported - CG: *N*= 34; Mean Age, 31.8; Age Range not reported - TS: Age Range, 19-53 - Country: Sweden	- Group-based - 36 x 180 minute sessions - Original, manualised, modular program	- Self-Report: Rosenberg Self-Esteem Scale (0.07; primary measure) - Informant-Report: None - Clinician-Rated: None - Task-Based: None	8-57 months after treatment termination
(Langdon et al., 2016)	Anxiety	- Randomised Controlled Trial - CG: WL	- IG: *N*= 26; Mean Age, 33.1; Age Range, 20-64 - CG: *N*= 26; Mean Age, 38.7; Age Range, 17-65	- Predominantly group-based - 21 x 60 minute group sessions + 3 x 60 minute individual sessions prior to group entry for socialisation to model - Original manualised program	- Self-Report: Liebowitz Social Anxiety Scale (-0.37; secondary measure) - Informant-Report: None	- Six month follow (CBT group only)

			- Country: UK		- Clinician-Rated: Hamilton Rating Scale for Anxiety (0.10) - Task-Based: None	
Studies targeting symptoms of mental disorder: Mixed (Adolescents and Adults)						
(Russell et al., 2013)	Obsessive Compulsive Disorder	- Randomised Controlled Trial - CG: AP (Anxiety Management)	- IG: *N*= 23; Mean Age, 28.6; Age Range, 14-49 - CG: *N*= 23; Mean Age, 25.2; Age Range, 14-65 - Country: UK	- Individual sessions - Up to 20 x 60 minute sessions. Mean number of sessions: 17.4 - Original manualised treatment	- Self-Report: Obsessive Compulsory Inventory-Revised (0.28; secondary measure) - Informant-Report: Children's Obsessive Compulsive Inventory- Parent Version (-0.39) - Clinician-Rated: Yale-Brown Obsessive Compulsive Scale (0.36) - Task-Based: None	- One month follow up - Three month follow up - Six month follow up - Twelve month follow up (CBT group only)
(McGillivray & Evert, 2014)	Depression, anxiety and stress	- Quasi-experimental - CG: WL	- IG: *N*= 26; Mean Age, 20.27; Age Range not reported - CG: *N*= 16; Mean Age, 20.5; Age Range not reported - TS: Age Range, 15-25	- Group-based - 9 x 120 minute sessions - Original, manualised program ('Think well, Feel well and Be well')	- Self-Report: Depression Anxiety Stress Scales-Anxiety Score (0.06) - Informant-Report: None - Clinician-Rated:	- Three month follow up - Nine month follow up

			- Country: Australia		None - Task-Based: None	
(Pahnke et al., 2014)	Stress and emotional distress	- Pilot study - Cluster randomisation - CG: WL	- IG: *N*= 15; Mean Age, 16.2; Age Range not reported - CG: *N*= 13; Mean Age, 16.8; Age Range not reported - TS: Age Range, 13-21 - Country: Sweden	- Group-based - School-based. No parental involvement in sessions - 12 x 40 minute sessions + daily 6-12 minute mindfulness exercises in classroom - Modified an Acceptance and Commitment Therapy protocol (Hayes et al., 2003)	- Self-Report: Strengths and Difficulties Questionnaire (-0.38) - Informant-Report: Strengths and Difficulties Questionnaire-Teacher Report: *Not included in quantitative synthesis as request for data required to calculate effect size was unsuccessful* - Clinician-Rated: None - Task-Based: None	- Two month follow up
Studies targeting core features of ASD: Children and Adolescents						
(Ozonoff & Miller, 1995)	Theory of Mind and social skills	- Quasi-experimental - CG: No treatment	- IG: *N*= 5; Mean Age, 13.8; Age Range, 13-14 - CG: *N*= 4; Mean Age, 13.6; Age Range, 11-16 - Country: USA	- Group-based - 14 x 90 minute sessions - Original program. Unclear whether program was manualised	- Self-Report: None - Informant-Report: None - Clinician-Rated: None - Task-Based: Theory of Mind Composite (0.64)	- None
(Provencal, 2003)	Social skills and peer	- Quasi-experimental	- IG: *N*= 10; Mean Age, 14.5; Age	- Group-based - Concurrent parent sessions	*Not included in quantitative*	- None

	relationships	- CG: TAU	Range, 12-16 - CG: *N*= 9; Mean Age, 14.2; Age Range, 12-16 - Country: USA	- 25 x 75 minute sessions (weekly for eight months) - Original program. Unclear whether program was manualised	*synthesis as request for data required to calculate effect sizes was unsuccessful*	
(Solomon et al., 2004)	Emotion recognition, theory of mind and problem solving	- Randomised Controlled Trial - CG: WL	- IG: *N*= 9; Mean Age, 9.7; Age Range, 7-12 - CG: *N*= 9; Mean Age, 9.2; Age Range, 7-11 - Country: USA	- Group-based - Concurrent parent training - 20 x 75 minute sessions - Original, modularised program. Unclear whether program was manualised	- Self-Report: None - Informant-Report: None - Clinician-Rated: None - Task-Based: Strange Stories Task (ToM; 0.24)	- None
(Beaumont & Sofronoff, 2008)	Social skills and emotion recognition	- Randomised Controlled Trial - CG: WL	- IG: *N*= 26; Mean Age, 9.64; Age Range, 7-11 - CG: *N*= 23; Mean Age, 9.81; Age Range, 8-11 - Country: Australia	- Individual sessions (computer-game based) + group sessions - Simultaneous parent training sessions + teacher handouts - 8 x 120 minute sessions - Original, manualised program ('The Junior Detective Training Program')	- Self-Report: None - Informant-Report: Social Skills Questionnaire-Parent report (1.42) - Clinician-Rated: None - Task-Based: Assessment of Perception of Emotion from Facial Expression (0.07)	- Six week follow up - Five month follow up
(Laugeson, Frankel, Mogil, & Dillon, 2009)	Social skills and friendship quality	- Randomised Controlled Trial - CG: WL	- IG: *N*= 17; Mean Age, 14.6; Age Range not reported - CG: *N*= 16; Mean Age, 14.6; Age Range not reported	- Group-based - Concurrent parent sessions - 12 x 90 minute sessions - Manualised program ('Program for the Education and Enrichment of Relational	- Self-Report: Friendship Qualities Scale (0.14) - Informant-Report: Social Skills Rating System: Social	- None

			- TS: Age range, 13-17 - Country: USA	Skills'; PEERS). Adapted from 'Children's Friendship Training' (Frankel & Myatt, 2003)	Skills Scale (0.81) - Clinician-Rated: None - Task-Based: None	
(Frankel et al., 2010)	Social skills	- Randomised Controlled Trial - CG: WL	- IG: *N*= 35; Mean Age, 8.6; Age Range not reported - CG: *N*= 33; Mean Age, 8.5; Age Range not reported - TS: Age range not reported - Country: USA	- Group-based - Concurrent parent sessions - 12 x 60 minute sessions - Manualised program: 'Children's Friendship Training' (Frankel & Myatt, 2003)	- Self-Report: The Loneliness Scale (0.67) - Informant-Report: Social Skills Rating System- Assertion Scale (0.40) - Clinician-Rated: None - Task-Based: None	- Twelve week follow up (CBT group only)
(Koenig et al., 2010)	Social skills	- Randomised Controlled Trial - CG: WL	- IG: *N*= 25; Mean Age, 9.2; Age Range not reported - CG: *N*= 19; Mean Age, 9.3; Age Range not reported - TS: Age range, 8-11 - Country: USA	- Group-based - 16 x 75 minute sessions - Original, manualised program - Inclusion of peer mentors	- Self-Report: None - Informant-Report: Social Competence Inventory (0.11) - Clinician-Rated: Clinical Global Impressions Scale-Improvement (2.43) - Task-Based: None	- None
(Lopata et al., 2010)	Social skills, face-emotion recognition, interest expansion and interpretation of non-literal language	- Randomised Controlled Trial - CG: WL	- IG: *N*= 18; Mean Age, 9.39; Age Range not reported - CG: *N*= 18; Mean Age, 9.56; Age Range not reported - TS: Age range, 7-12	- Group-based - Weekly parent training groups - Summer program: 25 whole day sessions (over 5 weeks) - Manualised program (Lopata, Thomeer, Volker, & Nida, 2006; Lopata, Thomeer, Volker, Nida, & Lee, 2008)	- Self-Report: None - Informant-Report: Social Responsiveness Scale (0.69) - Clinician-Rated: None - Task-Based: None	- None

			- Country: USA			
(Begeer et al., 2011)	Theory of Mind	- Randomised Controlled Trial - CG: WL	- IG: *N*= 19; Mean Age, 10.3; Age Range, 8-13 - CG: *N*= 17; Mean Age, 10.3; Age Range, 8-12 - Country: The Netherlands	- Group-based - Parental involvement at end of sessions + monthly training for parents - 16 x 90 minute sessions - Manualised program ('Theory of Mind Training'; Gevers, Clifford, Mager, & Boer, 2006; Steerneman, Jackson, Pelzer, & Muris, 1996)	- Self-Report: Index of Empathy for Children and Adolescents (-0.17) - Informant-Report: None - Clinician-Rated: None - Task-Based: Theory of Mind test (0.04)	- None
(DeRosier et al., 2011)	Social skills	- Randomised Controlled Trial - CG: 'Social Skills Group Intervention'- not adapted for ASD (S.S.GRIN; DeRosier, 2002, 2007)	- IG: *N*= 27; Mean Age, 10.2; Age Range not reported - CG: *N*= 28; Mean Age, 9.9; Age Range not reported - TS: Age Range, 8-12 - Country: USA	- Group-based - 15 x 60 minute sessions, including 4 joint parent-child sessions - Manualised program ('Social Skills Group Intervention- High Functioning Autism'; S.S.GRIN-HFA). Adapted from 'Social Skills Group Intervention' (S.S.GRIN; DeRosier, 2002, 2007)	*Not included in quantitative synthesis as request for data required to calculate effect sizes was unsuccessful*	- None
(Laugeson et al., 2012)	Social skills	- Quasi-experimental - CG: WL	- IG: *N*= 14; Mean Age, 15.0; Age Range not reported - CG: *N*= 14; Mean Age, 14.3; Age Range not reported - TS: Age range, 12-17	- Group-based - Concurrent parent sessions - 14 x 90 minute sessions - Modified version of 'Program for the Education and Enrichment of Relational Skills' (PEERS; Laugeson et al., 2009)	- Self-Report: Quality of Play Questionnaire: Host Score (1.07) - Informant-Report: Social Skills Rating System- Parent Report: Social Skills	- Fourteen week follow up (CBT group only)

			- Country: USA		Scale (0.94) - Clinician-Rated: None - Task-Based: None	
(Thomeer et al., 2012)	Social skills, face-emotion recognition, interest expansion and interpretation of non-literal language	- Randomised Controlled Trial - CG: WL	- IG: *N*= 17; Mean Age, 9.24; Age Range not reported - CG: *N*= 18; Mean Age, 9.39; Age Range not reported - TS: Age range, 7-12 - Country: USA	- Group-based - Weekly parent training groups - Summer program: 25 whole day sessions (over 5 weeks) - Manualised program (Lopata et al., 2006; Lopata et al., 2008; Lopata et al., 2010)	- Self-Report: None - Informant-Report: Social Responsiveness Scale (0.65) - Clinician-Rated: None - Task-Based: None	- Two-three month follow up
(Andrews et al., 2013)	Affectionate communication and friendship skills	- Randomised Controlled Trial - CG: WL	- IG: *N*= 29, Mean Age and Age Range not reported - CG: *N*= 29, Mean Age and Age Range not reported - TS: Mean Age, 9.02; Age Range, 7-12 - Country: Australia	- Group-based - 5 x 120 minute sessions - Original, manualised program	- Self-Report: None - Informant-Report: Affection for Others Questionnaire for children with Asperger's syndrome (0.43) - Clinician-Rated: None - Task-Based: None	- Three month follow up (CBT group only)
(Baghdadli et al., 2013)	Perception of facial emotions and quality of life	- Pilot study - Randomised - AP: Leisure Activities	- IG: *N*= 7; Mean Age, 10.7; Age Range not reported - CG: *N*= 7; Mean Age, 11.5; Age Range not reported - TS: Age range, 8-	- Group-based - 20 x 90 minute sessions - Original, manualised program ('Social Skills Training Group-based program; SST-GP)	- Self-Report: None - Informant-Report: None - Clinician-Rated: None - Task-Based: Diagnostic Analysis	- None

			12 - Country: France		of Non Verbal Accuracy 2 (DANVA2)- Adult facial expressions (-0.05)	
(Ichikawa et al., 2013)	Social reciprocity	- Pilot study - Randomised - CG: WL	- IG: *N*= 5; Mean Age, 5.3; Age Range, 5-5 - CG: *N*= 6; Mean Age, 5.2; Age Range, 5-5 Country- Japan	- Group-based - Concurrent parental sesssions - 20 x 120 minute sessions - Original, manualised program	- Self-Report: None - Informant-Report: Strengths and Difficulties Questionnaire (-0.44) - Clinician-Rated: Interaction Rating Scale (0.08) - Task-Based: None	- None
(Koning et al., 2013)	Social skills	- Pilot study - Randomised - CG: No intervention. Nature of control group unclear	- IG: *N*= 7; Mean Age, 10.99; Age Range not reported - CG: *N*= 8; Mean Age, 11.15; Age Range not reported - TS: Age range, 10-12 Country- Canada	- Group-based - 15 x 120 minute sessions - Original, manualised program, incorporating both structured skills building and loosely structured natural situations with fun activities	- Self-Report: None - Informant-Report: Social Responsiveness Scale (0.43) - Clinician-Rated: None - Task-Based: Child and Adolescent Social Perception Measure- Emotion score (0.61)	- None
(White et al., 2013)	Social skills and anxiety (included within core features analysis only to	- Pilot study - Randomised - CG: WL	- IG: *N*= 15; Mean Age, 14.2; Age Range not reported - CG: *N*= 15; Mean Age, 15.0; Age	- Individual therapy (up to 13 x 60-70 minute sessions) + group therapy (7 x 75 minute sessions) - Parent education and coaching	- Self-Report: None - Informant-Report: Social Responsiveness Scale (0.82)	- None

	prevent double counting of data)		Range not reported - TS: Age range not reported - Country: USA	at the end of each individual session - Original, manualised, modular program	- Clinician-Rated: Developmental Disabled Children's Global Assessment Scale (0.17) - Task-Based: None	
(Laugeson et al., 2014)	Social skills	- Quasi-experimental - CG: AP: Social skills curriculum based on 'Super Skills' (Coucouvanis, 2005)	- IG: *N*= 40; Mean Age, 12.68; Age Range not reported - CG: *N*= 33; Mean Age, 12.74; Age Range not reported - TS: Age range, 12-14 - Country: USA	- Group-based - Teacher-led - Daily 30 minute sessions x 5 days per week x 14 weeks - Manualised program ('PEERS Curriculum for School-Based Professionals'), adapted from 'Program for the Education and Enrichment of Relational Skills' (PEERS; Laugeson & Frankel, 2010)	- Self-Report: Friendship Qualities Scale (0.38) - Informant-Report: Social Responsiveness Scale- Teacher Report (-0.07) - Clinician-Rated: None - Task-Based: None	- None
(Schohl et al., 2014)	Social skills and friendship quality	- Randomised Controlled Trial - CG: WL	- IG: *N*= 29; Mean Age, 14.00; Age Range not reported - CG: *N*= 29; Mean Age, 13.31; Age Range not reported - TS: Age range, 11-16 - Country: USA	- Group-based - Concurrent parent sessions - 14 x 90 minute sessions - Manualised program ('Program for the Education and Enrichment of Relational Skills': PEERS; Laugeson & Frankel, 2010)	- Self-Report: Friendship Qualities Scale (-0.01) - Informant-Report: Social Skills Rating System: Social Skills Scale (0.44) - Clinician-Rated: None - Task-Based: None	- None
(Wood et al., 2014)	Social communication and anxiety (anxiety outcomes	- Pilot study - Randomised - CG: TAU	- IG: *N*= 7; Mean Age, 8.7; Age Range not reported - CG: *N*= 6; Mean Age, 8.8; Age	- Individual - Parental involvement in all sessions - 32 x 90 minute sessions (approximately 30 minutes with	- Self-Report: None - Informant-Report: None - Clinician-Rated: Bauminger's	- None

	reported in Fujii et al., 2013)		Range not reported - TS: Age Range, 7-11 Country- USA	child, and 60 minutes with parents/ family) - Modified 'Building Confidence' program (Wood & McLeod, 2008)	Observational Measure of Social Communication Behaviour- Positive or Appropriate Interaction with Peers (1.51) - Task-Based: None	
(Yoo et al., 2014)	Social skills	- Randomised Controlled Trial - CG: WL	- IG: *N*= 23; Mean Age, 14.04; Age Range not reported - CG: *N*= 24; Mean Age, 13.54; Age Range not reported - TS: Age Range, 12-18 - Country: South Korea	- Group-based - Concurrent parent sessions - 14 x 90 minute sessions - Modified version of 'Program for the Education and Enrichment of Relational Skills' (PEERS; Laugeson & Frankel, 2010)	- Self-Report: Korean Version of Social Skills Rating System (-0.23) - Informant-Report: Social Responsiveness Scale (0.16) - Clinician-Rated: Autism Diagnostic Observation Schedule- Reciprocal Social Interaction score (0.62) - Task-Based: None	- Three month follow up
(Begeer et al., 2015)	Theory of Mind and social skills	- Randomised Controlled Trial - CG: WL	- IG: *N*= 52; Mean Age, 9.7; Age Range, 7-12 - CG: *N*= 45; Mean Age, 9.5; Age Range, 7-12	- Group-based - 8 x 60 minutes sessions - Shortened version of ToM training program used in Begeer et al. (2011)	- Self-Report: None - Informant-Report: Theory of Mind Behaviour Checklist (0.74) - Clinician-Rated: None	- Six month follow up

			- Country: The Netherlands		- Task-Based: Theory of Mind test (0.64)	
(Freitag et al., 2016)	Social skills	- Randomised Controlled Trial - Multicentre phase-III trial - CG: TAU	- IG: *N*= 101; Mean Age, 12.7; Age Range not reported - CG: *N*= 108; Mean Age, 12.9; Age Range not reported - TS: Age Range, 8-19 - Country: Germany	- Group-based - 12 x 90 minutes sessions - 3 additional parent training sessions - Original, manualised program ('Social Skills Training Autism- Frankfurt'; SOSTA-FRA)	- Self-Report: None - Informant-Report: Social Responsiveness Scale (0.22) - Clinician-Rated: None - Task-Based: None	- Three month follow up
(Soorya et al., 2015)	Social behavioural impairments and social cognition	- Randomised Controlled Trial - CG: AP (Facilitated play)	- IG: *N*= 35; Mean Age, 10.05; Age Range not reported - CG: *N*= 34; Mean Age, 9.87; Age Range not reported - TS: Age Range, 8-11 - Country: USA	- Group-based - Concurrent parent sessions - 12 x 90 minutes sessions - Original, manualised program ('Seaver Nonverbal communication, Emotion recognition, and Theory of mind Training'; Seaver-NETT)	- Self-Report: None - Informant-Report: Social Behaviour Composite (0.48) - Clinician-Rated: None - Task-Based: None	- Three month follow up (only began part way through trial so follow up data not available for all participants)
Studies targeting core features of ASD: Adults						
(Turner-Brown et al., 2008)	Social interaction and social cognition	- Pilot study - Quasi-experimental - CG: TAU	- IG: *N*= 6; Mean Age, 42.5; Age Range, 25-55 - CG: *N*= 5; Mean Age, 28.8; Age Range, 27-29	- Group-based - 18 x 50 minute sessions - Modified version of Social Cognition & Interaction Training (SCIT; Roberts, Penn, & Combs, 2004)	- Self-Report: Social Communication Skills Questionnaire (-0.11) - Informant-Report: None - Clinician-Rated:	- None

			- Country: USA		Social Skills Performance Assessment (0.19) - None	
(Gantman, Kapp, Orenski, & Laugeson, 2012)	Social skills	- Pilot study - Randomised - CG: WL	- IG: *N*= 9; Mean Age, 19.9; Age Range not reported - CG: *N*= 8; Mean Age, 20.9; Age Range not reported - TS: Age Range, 18-23 - Country: USA	- Group-based - Concurrent caregiver sessions - 14 x 90 minute sessions - Modified version of 'Program for the Education and Enrichment of Relational Skills' (PEERS; Laugeson & Frankel, 2010)	- Self-Report: Social and Emotional Loneliness Scale for Adults (0.63) - Informant-Report: Social Responsiveness Scale (0.60) - Clinician-Rated: None - Task-Based: None	- None

IG, intervention group; CG, control group; TS, total sample (where group demographics are not reported); WL, waiting list; TAU, treatment as usual; AP, Attention Placebo

3.4 Quality Appraisal

As detailed in Chapter 2 (section 2.6), the NICE Quality Appraisal Checklist for Quantitative Intervention Studies (NICE, 2012b) was completed for each included study by both the primary researcher and a research supervisor to assess internal and external validity and identify potential sources of bias. There was 'moderate' agreement between the researchers regarding ratings for internal validity (72.0%; Kappa 0.48; 95% CI, 0.26 to 0.71; see Appendix G for calculation) and 'good' agreement regarding ratings for external validity (84.0%; Kappa 0.66; 95% CI, 0.45 to 0.86; see Appendix G for calculation). Disagreements were resolved via discussion. Table 4 summarises the final ratings given to each study, alongside key sources of bias identified.

A persistent problem across all studies was small sample size, contributing to reduced power. Freitag et al. (2016) included the highest number of participants (101 CBT, 108 control), whilst eight of the studies included in the quantitative synthesis involved less than ten participants per group. Several of these studies were defined by the authors as pilot or feasibility trials. However, it was felt that a number of other included studies which were not defined by the authors as pilot or feasibility trials were in fact lower in quality and/or had smaller sample sizes than many pilot or feasibility trials. Quality appraisal and risk of bias was therefore considered on a study by study basis and sensitivity analysis was conducted by removing studies deemed to be at a high risk of bias rather than those defined by authors as pilot or feasibility trials.

Other common problems included the lack of reporting on compliance with intervention sessions, poor reporting on missing data and minimal information on fidelity checks. Very few studies reported adequate allocation concealment and ten of the 48 studies included in quantitative analysis were non-randomised, contributing to a high risk of allocation bias. Due to the nature of the interventions involved, it was obviously not possible

for investigators to blind participants (and often informants) to intervention allocation. However, blinding of outcome assessors was possible but was not conducted in the majority of studies, contributing to detection bias.

A final common difficulty across studies was failure to specify a primary outcome measure or measures. This complicated the quantitative synthesis process, particularly in studies where a high number of outcome measures were utilised and/or in studies using different measures to assess a range of constructs. In addition, the lack of measures that are validated or norm-referenced for use with individuals with ASD was noted, although this is clearly a wider issue that needs attention. These factors will be discussed in more depth in Chapter 4, in addition to a more thorough discussion of quality issues within the included studies and implications for future research.

Table 4.

Summary of Quality Assessment

Study	External Validity	Internal Validity	Key Sources of Bias
Studies targeting symptoms of mental disorder: Children and Adolescents			
Sofronoff et al. (2005)	+	+	Small sample; No allocation concealment; Lack of blinding
Chalfant et al. (2007)	+	+	Small sample; No allocation concealment; Lack of blinding
Sofronoff et al. (2007)	+	+	Small sample; No allocation concealment; Lack of blinding; Drop outs prior to intervention not included in analysis
Reaven et al. (2009): Pilot study	-	+	Small sample; Non-randomised; No allocation concealment; Participants entered in order of expressed interest- possible confound; Lack of blinding
Wood et al. (2009)	+	+	Small sample; Lack of blinding
Scarpa & Reyes (2011): Pilot study	-	-	Very small sample; No allocation concealment; Limited information on randomisation procedure; Lack of blinding; Did not adjust for baseline differences between groups
Sung et al. (2011)	+	+	Small sample; No allocation concealment; Lack of blinding; Did not adjust for baseline differences between groups
Clarke (2012)	-	-	Small sample; Lack of individual randomisation (cluster); No allocation concealment; Lack of blinding; No formal assessment of anxiety prior to allocation
Cortesi et al. (2012)	+	+	Recruitment method unclear; Limited information on randomisation procedure
Reaven et al. (2012)	++	+	Small sample
McNally Keehn et al. (2013): Pilot study	+	+	Small sample; No allocation concealment; Lack of blinding
Storch et al. (2013)	+	+	Small sample; Simple randomisation procedure
McConachie et al. (2014): Pilot study	+	+	Small sample
Van Steensel et al. (2014)	-	+	Small sample; Non-randomised; No allocation concealment; Lack of blinding; Did not adjust for baseline differences between groups

Hepburn et al. (2016): Pilot study	-	-	Small sample; Non-randomised; No allocation concealment; Control group not recruited simultaneously with CBT group; Lack of blinding; Did not adjust for baseline differences between groups
Storch et al. (2015)	+	+	Small sample; Simple randomisation procedure
Wood et al. (2015)	+	+	Small sample
Studies targeting symptoms of mental disorder: Adults			
Russell et al. (2009): Pilot study	-	-	Small sample; Non-randomised; No allocation concealment; CBT group had more severe OCD at baseline- not adjusted for in analysis; Treatment not manualised
Spek et al. (2013)	+	+	Small sample; Lack of blinding
Hesselmark et al. (2014)	-	-	Small sample; Two participants not randomised; No allocation concealment; Lack of blinding; High amount of drop outs/ missing data; Did not adjust for baseline differences between groups
Langdon et al. (2016)	+	+	Small sample; Lack of fidelity checks
Studies targeting symptoms of mental disorder: Mixed (Adolescents and Adults)			
Russell et al. (2013)	+	+	Small sample; Possible contamination as crossover between groups and unclear when post-assessments were completed;
McGillivray & Evert (2014)	-	-	Small sample; Non-randomised; No allocation concealment; Lack of blinding; Asymptomatic participants included
Pahnke et al. (2014): Pilot study	+	+	Small sample; Lack of individual randomisation (cluster); No allocation concealment; Lack of blinding; Potential for contamination between groups as all conducted within same school
Studies targeting core features of ASD: Children and Adolescents			
Ozonoff & Miller (1995)	-	-	Very small sample; Non-randomised; No allocation concealment; Recruitment poorly described; Inappropriate analysis
Provencal (2003)	-	-	Very small sample; Non-randomised; No allocation concealment; Partial blinding; Inappropriate analysis; Did not adjust for baseline differences between groups
Solomon et al. (2004)	-	-	Very small sample; Limited information on randomisation procedure; No allocation concealment; Lack of blinding; Inappropriate analysis;
Beaumont & Sofronoff (2008)	+	+	Small sample; Lack of information on randomisation; Lack of blinding

Laugeson et al. (2009)	+	+	Small sample; No allocation concealment; Lack of blinding
Frankel et al. (2010)	+	+	Small sample; Simple randomisation; No allocation concealment; Lack of blinding
Koenig et al. (2010)	+	+	Small sample; Simple randomisation; No allocation concealment
Lopata et al. (2010)	+	+	Small sample; No allocation concealment; Lack of blinding
Begeer et al. (2011)	+	+	Small sample; Lack of information on randomisation; Lack of blinding
DeRosier et al. (2011)	+	+	Small sample; Lack of information on randomisation; No allocation concealment; Lack of blinding
Laugeson et al. (2012)	-	+	Small sample; Non-randomised; No allocation concealment; Lack of blinding
Thomeer et al. (2012)	+	+	Small sample; No allocation concealment; Lack of blinding
Andrews et al. (2013)	+	+	Small sample; No allocation concealment; Lack of blinding
Baghdadli et al. (2013): Pilot study	-	-	Very small sample
Ichikawa et al. (2013): Pilot study	-	-	Very small sample; Lack of blinding
Koning et al. (2013): Pilot study	-	-	Small sample; No allocation concealment; Lack of blinding; Lack of normed outcome measures
White et al. (2013): Pilot study	+	+	Small sample; No allocation concealment; Lack of blinding
Laugeson et al. (2014)	-	-	Small sample; Non-randomised; No allocation concealment; Lack of blinding;
Schohl et al. (2014)	+	+	Small sample; Lack of information on randomisation procedure; No allocation concealment; Partial blinding; High number of drop outs
Wood et al. (2014): Pilot study	-	-	Very small sample; Inappropriate analysis
Yoo et al. (2014)	+	+	Small sample; Lack of information on randomisation procedure; No allocation concealment; Partial blinding;
Begeer et al. (2015)	+	+	Lack of blinding
Freitag et al. (2016)	++	++	
Soorya et al. (2015)	++	+	Small sample; Use of Social Behaviour Composite as primary outcome measure- not validated
Studies targeting core features of ASD: Adults			
Turner-Brown et al. (2008): Pilot study	-	-	Very small sample; Non-randomised; No allocation concealment; Two participants changed groups; Inappropriate analysis
Gantman et al. (2012): Pilot study	-	-	Very small sample; Simple randomisation; No allocation concealment; Lack of blinding; Inappropriate analysis

++, All or most of the checklist criteria have been fulfilled; where they have not been fulfilled the conclusions are very unlikely to alter; +, Some of the checklist criteria have been fulfilled; where they have not been fulfilled, or not adequately described, the conclusions are unlikely to alter; - , Few or no checklist criteria have been fulfilled and the conclusions are likely or very likely to alter

3.5 Meta-analysis

Data were analysed in a series of meta-analyses. Outcomes relating to each research question will be presented in turn, organised by report-type. Data collected from all outcome measures deemed appropriate were included unless otherwise specified (see Section 2.5.3.1 for further information on the selection of outcome measures to include).

3.5.1 Research question 1: How effective is CBT in reducing symptoms of mental disorder in individuals with ASD?

3.5.1.1 Self-reported outcomes.

Seventeen studies, including 645 participants (329 CBT, 316 control), that investigated the effectiveness of CBT in reducing symptoms of mental disorder included appropriate self-reported outcome measures. One study (Storch et al., 2013) utilised a relevant self-reported outcome measure but it was not possible to include this in the analysis as an attempt to obtain the data necessary to calculate the effect size was unsuccessful. The outcome measures used varied considerably across studies.

As indicated in Figure 2, a random-effects meta-analysis of these trials indicated a "small" but non-significant effect favouring CBT over waiting-list, treatment as usual or active control as reported by participants (g = 0.24; 95% CI [-0.05, 0.53], z = 1.60, p = .11). The analysis indicated a significant amount of heterogeneity, with I^2 indicating that 69% of the variability in estimated treatment effect was due to heterogeneity rather than chance (p < .001).

As one study (Chalfant et al., 2007) had a SMD (g = 2.64) considerably higher than the other included studies (g ranged from -0.39 to 0.85), a sensitivity analysis was conducted to remove this outlier. Exclusion of this study resulted in no significant treatment effect (g = 0.10; 95% CI [-0.06, 0.27], z = 1.21, p = .23) and I^2 reduced markedly to 4% (p = .41), indicating the considerable impact that the inclusion of this study had on the pooled SMD. A

further sensitivity analysis to remove studies deemed to be at a high risk of bias (Clarke, 2012; Hesselmark et al., 2014; McGillivray & Evert, 2014; Reaven et al., 2009; Russell et al., 2009) resulted in a very similar effect (g = 0.09; 95% CI [-0.12, 0.30], z = 0.84, p = .40).

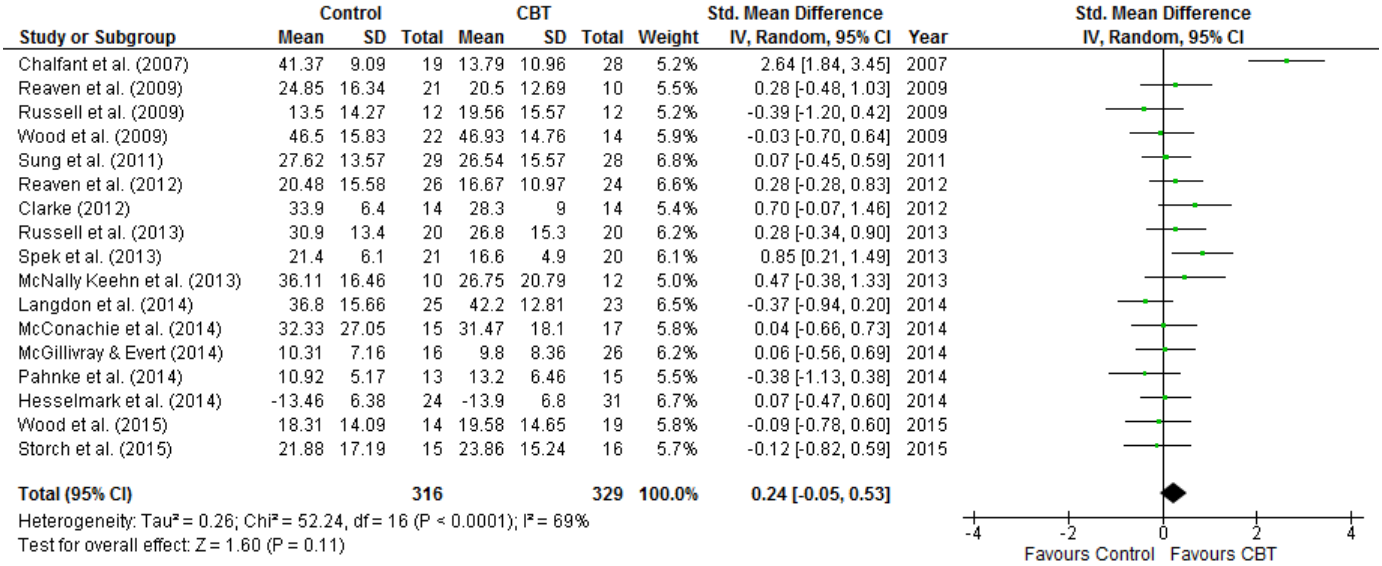

Figure 2. Forest plot showing estimated treatment effect of CBT for symptoms of mental disorder in ASD based on self-reported outcomes

3.5.1.2 Informant-reported outcomes.

Sixteen studies, including 620 participants (325 CBT, 295 control), that investigated the effectiveness of CBT in reducing symptoms of mental disorder included appropriate informant-reported outcome measures. One study (Pahnke et al., 2014) utilised a relevant informant-reported outcome measure but it was not possible to include this in the analysis as an attempt to obtain the data necessary to calculate the effect size was unsuccessful. The outcome measures used varied considerably across studies.

As indicated in Figure 3, a random-effects meta-analysis of these trials indicated a significant "medium" effect favouring CBT over waiting-list, treatment as usual or active control as reported by informants (g = 0.66; 95% CI [0.29, 1.03], z = 3.49, p < .001). The analysis indicated a significant amount of heterogeneity, with I^2 indicating that 78% of the

variability in estimated treatment effect was due to heterogeneity rather than chance (p < .001).

Chalfant et al. (2007) again had a SMD (g = 4.27) considerably higher than the other included studies (g ranged from -0.39 to 1.21) and a sensitivity analysis was therefore conducted to remove this outlier. Exclusion of this study resulted in a lower treatment effect (g = 0.47; 95% CI [0.25, 0.69], z = 4.17, p < .001), although it remained statistically significant. I^2 reduced to 38% (p = .07), again indicating the impact that the inclusion of this study had on the pooled SMD. A further sensitivity analysis to remove studies deemed to be at a high risk of bias (Clarke, 2012; Hepburn et al., 2016; Reaven et al., 2009; Scarpa & Reyes, 2011) resulted in a very similar effect (g = 0.45; 95% CI, 0.18 to 0.72, z = 3.24, p = .001).

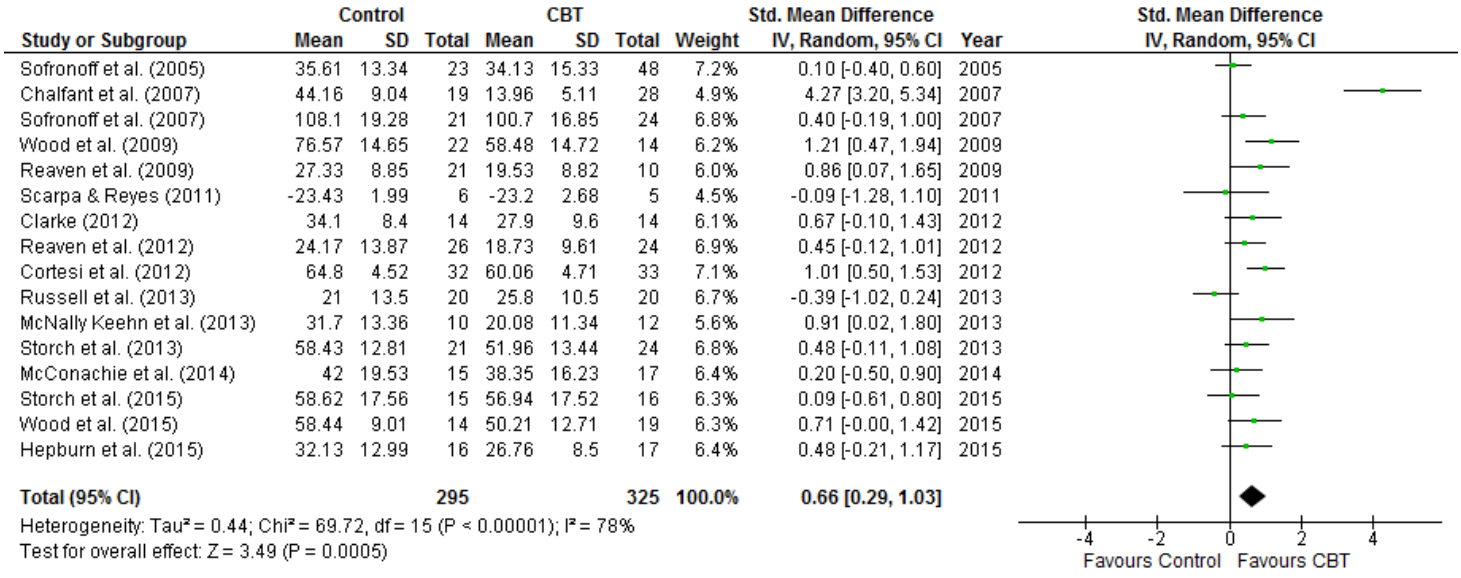

Figure 3. Forest plot showing estimated treatment effect of CBT for symptoms of mental disorder in ASD based on informant-reported outcomes

3.5.1.3 Clinician-rated outcomes.

Thirteen studies, including 514 participants (262 CBT, 252 control), that investigated the effectiveness of CBT in reducing symptoms of mental disorder included appropriate clinician-rated outcome measures. Two of these studies (Chalfant et al., 2007; van Steensel et

al., 2014) presented the outcomes as dichotomous data. In order to include these studies in a random-effects meta-analysis, the Odds Ratio was calculated and re-expressed as a SMD (Chinn, 2000; see Section 2.5.3 for further information). The outcome measures used varied considerably across studies.

A random-effects meta-analysis using the Generic Inverse Variance method was conducted as estimates of effect were calculated for the two aforementioned studies. As shown in Figure 4, analysis indicated a significant "medium" effect favouring CBT over waiting-list, treatment as usual or active control as rated by clinicians ($g = 0.73$; 95% CI [0.38, 1.08], $z = 4.05$, $p < .001$). The analysis again indicated a significant amount of heterogeneity, with I^2 indicating that 69% of the variability in estimated treatment effect was due to heterogeneity rather than chance ($p < .001$).

Two studies (Chalfant et al., 2007; Wood et al., 2009) had a SMD ($g = 2.51$ and $g = 2.47$ respectively) considerably higher than the other included studies (g ranged from -0.31 to 1.38) and a sensitivity analysis was conducted to remove these outliers. Exclusion of these studies resulted in a lower treatment effect ($g = 0.52$; 95% CI [0.27, 0.77], $z = 4.06$, $p < .001$), although it remained statistically significant. I^2 reduced to 36% ($p = .11$), again indicating the impact that the inclusion of these studies had on the pooled SMD. A further sensitivity analysis to remove studies deemed to be at a high risk of bias (Russell et al., 2009; van Steensel et al., 2014) resulted in a very similar effect ($g = 0.59$; 95% CI [0.33, 0.85], $z = 4.48$, $p = <.001$).

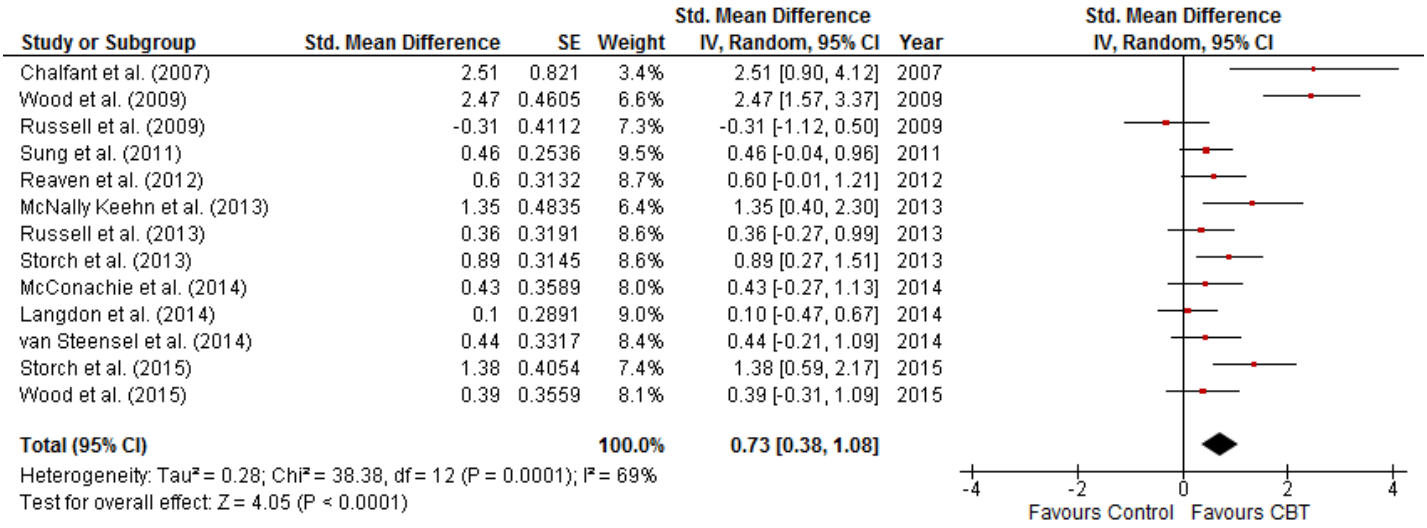

Figure 4. Forest plot showing estimated treatment effect of CBT for symptoms of mental disorder in ASD based on clinician-rated outcomes

3.5.1.4 Task-based outcomes.

Only one study that investigated the effectiveness of CBT in reducing symptoms of mental disorder included an appropriate task-based outcome measure (Cortesi et al., 2012). It was therefore not possible to calculate a pooled SMD in this area.

3.5.1.5 Summary.

Twenty-four studies that investigated the effectiveness of CBT in reducing symptoms of mental disorder in children, adolescents and adults with ASD were included within this analysis. Overall effect sizes on informant- reported and clinician-rated outcomes were *g*= 0.66 and *g*= 0.73 respectively, both of which may be interpreted as "medium". When outlying studies were removed, the magnitude of these effects reduced to *g*= 0.47 and *g*= 0.52 respectively, although they remained statistically significant. In contrast, the overall effect size on self-reported outcomes was *g*= 0.24, which may be interpreted as a "small" but non-significant effect. When an outlying study was removed, the magnitude of the effect reduced to *g*= 0.10, indicating no superiority of CBT over control on self-reported outcome measures.

Further sensitivity analysis to remove studies deemed to be at a high risk of bias did not significantly affect the results for any outcome report type.

3.5.2 Research question 2: How effective is CBT in the treatment of core features of ASD?

3.5.2.1 Self-reported outcomes.

Nine studies, including 370 participants (192 CBT, 178 control), that investigated the effectiveness of CBT in the treatment of core features of ASD included appropriate self-reported outcome measures. The outcome measures used varied considerably across studies.

As indicated in Figure 5, a random-effects meta-analysis of these trials indicated a "small" but non-significant effect favouring CBT over waiting-list, treatment as usual or active control as reported by participants (g = 0.25; 95% CI, [-0.03, 0.53], z = 1.77, p = .08). Heterogeneity was not found to be significant, although I^2 indicated that 40% of the variability in estimated treatment effect was due to heterogeneity rather than chance (p = .10).

A sensitivity analysis to remove studies deemed to be at a high risk of bias (Gantman et al., 2012; Laugeson et al., 2014; Laugeson et al., 2012; Turner-Brown et al., 2008) resulted in no significant treatment effect (g = 0.10; 95% CI [-0.24, 0.45], z = 0.58, p = .56).

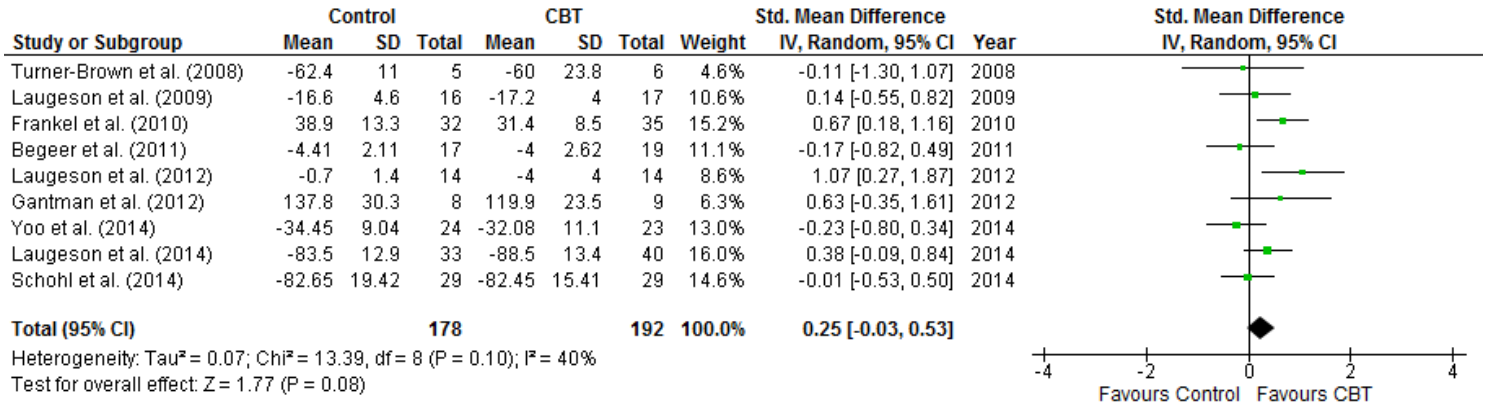

Figure 5. Forest plot showing estimated treatment effect of CBT for core features of ASD based on self-reported outcomes

3.5.2.2 Informant-reported outcomes.

Eighteen studies, including 950 participants (480 CBT, 470 control), that investigated the effectiveness of CBT in the treatment of core features of ASD included appropriate informant-reported outcome measures. The outcome measures used varied considerably across studies.

As indicated in Figure 6, a random-effects meta-analysis of these trials indicated a significant "small" effect favouring CBT over waiting-list, treatment as usual or active control as reported by informants (g = 0.48; 95% CI [0.30, 0.65], z = 5.39, p < .001). Heterogeneity was again not found to be significant, although I^2 indicated that 36% of the variability in estimated treatment effect was due to heterogeneity rather than chance (p = .06).

A sensitivity analysis to remove studies deemed to be at a high risk of bias (Gantman et al., 2012; Ichikawa et al., 2013; Koning et al., 2013; Laugeson et al., 2014; Laugeson et al., 2012) resulted in a slightly larger "medium" treatment effect (g = 0.52; 95% CI [0.34, 0.70], z = 5.63, p < .001), with a small reduction in heterogeneity (I^2 = 33%, p = .12).

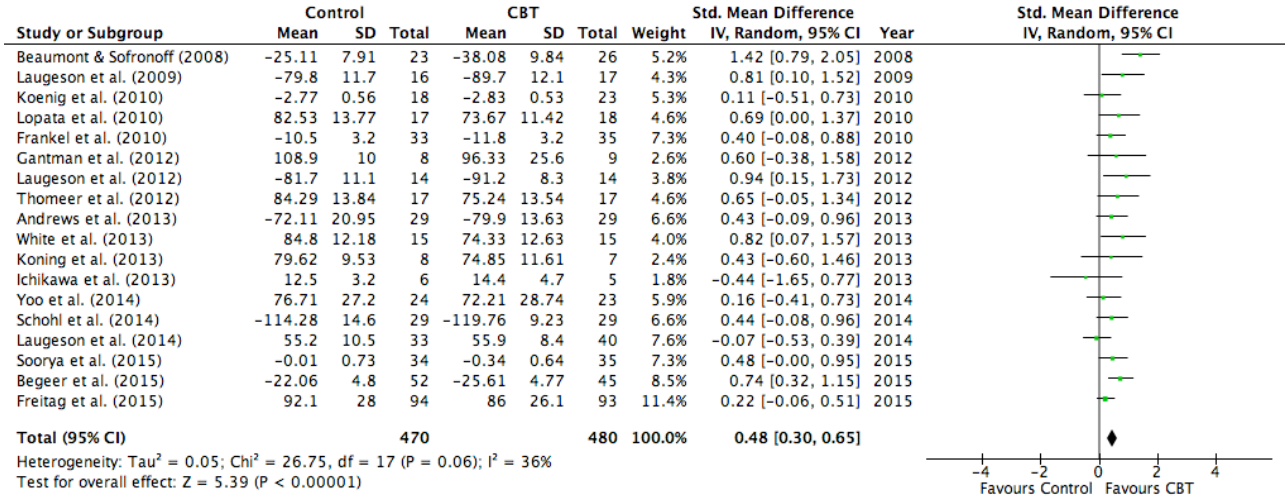

Figure 6. Forest plot showing estimated treatment effect of CBT for core features of ASD based on informant-reported outcomes

3.5.2.3 Clinician-rated outcomes.

Six studies, including 153 participants (79 CBT, 74 control), that investigated the effectiveness of CBT in the treatment of core features of ASD included appropriate clinician-rated outcome measures. One of these studies (Koenig et al., 2010) presented the outcome as dichotomous data. In order to include this study in a random-effects meta-analysis, the Odds Ratio was calculated and re-expressed as a SMD (Chinn, 2000; see Section 2.5.3 for further information). The outcome measures used varied across studies.

A random-effects meta-analysis using the Generic Inverse Variance method was conducted as an estimate of effect was calculated for Koenig et al. (2010). As shown in Figure 7, analysis indicated a significant "medium" effect favouring CBT over waiting-list, treatment as usual or active control as rated by clinicians (g = 0.65; 95% CI [0.10, 1.21], z = 2.30, p = .02). Heterogeneity was again found to be non-significant, although I^2 indicated that 47% of the variability in estimated treatment effect was due to heterogeneity rather than chance (p = .10).

One study (Koenig et al., 2010) had a SMD (g = 2.43) considerably higher than the other included studies (g ranged from 0.08 to 1.51) and a sensitivity analysis was conducted to remove this outlier. Exclusion of Koenig et al. (2010) resulted in a lower treatment effect (g = 0.47; 95% CI [0.09, 0.85], z = 2.40, p = .02), although it remained statistically significant. I^2 reduced to 1% (p = .40), indicating the considerable impact that the inclusion of this study had on the pooled SMD. A further sensitivity analysis to remove studies deemed to be at a high risk of bias (Ichikawa et al., 2013; Turner-Brown et al., 2008; Wood et al., 2014) resulted in a very similar treatment effect (g = 0.44; 95% CI [-0.01, 0.89], z = 1.90, p = .06), although this was no longer statistically significant. It is highly likely that this is because the exclusion of the above studies left only two studies in the analysis; as such, this analysis should be interpreted with marked caution, considering that it is based upon a small number of participants (N = 77).

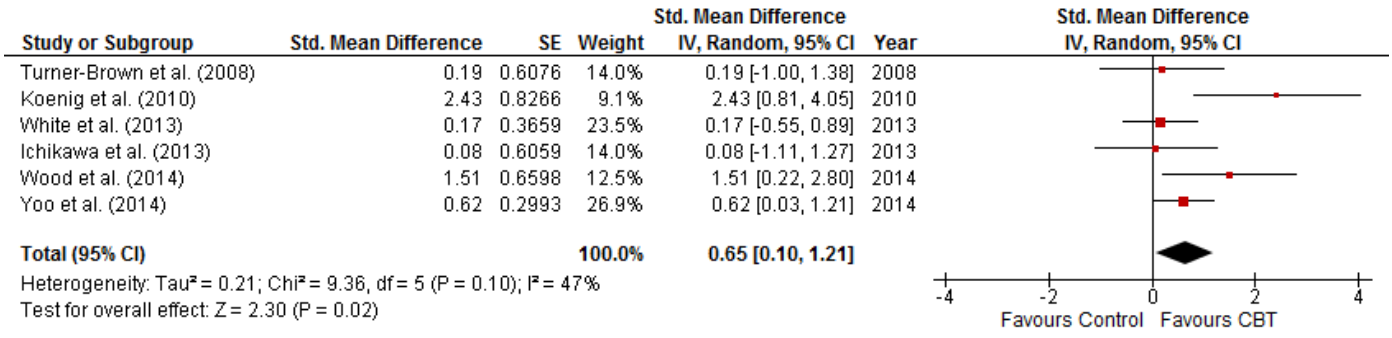

Figure 7. Forest plot showing estimated treatment effect of CBT for core features of ASD based on clinician-rated outcomes

3.5.2.4 Task-based outcomes.

Seven studies, including 237 participants (117 CBT, 120 control), that investigated the effectiveness of CBT in the treatment of core features of ASD included appropriate task-based outcome measures. The outcome measures used varied considerably across studies.

As indicated in Figure 8, a random-effects meta-analysis of these trials indicated a significant "small" effect favouring CBT over waiting-list, treatment as usual or active control on task-based measures (g = 0.35; 95% CI [0.09, 0.61], z = 2.67, p = .008). Heterogeneity was not an issue, with I^2 indicating that 0% of the variability in estimated treatment effect was due to heterogeneity rather than chance (p = .58).

A sensitivity analysis to remove studies deemed to be at a high risk of bias (Baghdadli et al., 2013; Koning et al., 2013; Ozonoff & Miller, 1995; Solomon et al., 2004) resulted in a very similar treatment effect (g = 0.30; 95% CI [-0.12, 0.72], z = 1.42, p = .16), although this was no longer statistically significant. Again, it is highly likely that this is because the exclusion of the above studies left only three studies in the analysis and this result should therefore be interpreted with marked caution, being based on studies that included N = 182 participants.

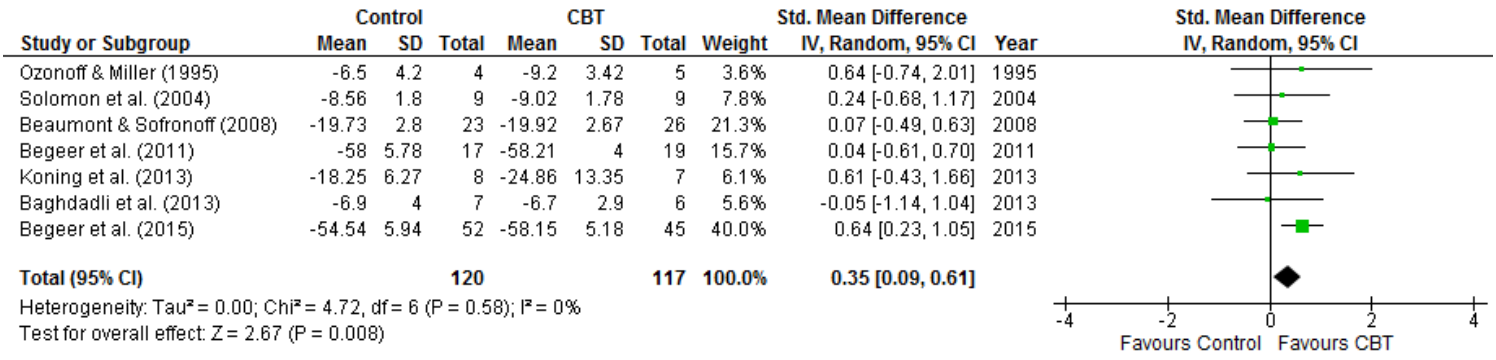

Figure 8. Forest plot showing estimated treatment effect of CBT for core features of ASD based on task-based outcomes

3.5.2.5 Summary.

Twenty-six studies that investigated the effectiveness of CBT in the treatment of core features of ASD in children, adolescents and adults with ASD were identified for potential inclusion, with twenty-four of these studies being included in the quantitative synthesis. The overall effect size on self-reported outcomes was *g*= 0.25, a "small" but non-significant effect which was reduced further when a sensitivity analysis was conducted to remove studies deemed to be at a high risk of bias. In contrast, the overall effect size on informant- reported outcomes was *g*= 0.48, a "small" but significant effect. Sensitivity analysis to remove studies deemed to be at a high risk of bias resulted in a slightly larger "medium" treatment effect (*g*= 0.52).

The overall effect size on clinician-rated outcomes was *g*= 0.65, which may be interpreted as a "medium" effect. When an outlying study was removed, the magnitude of this effect reduced to *g*= 0.47, although it remained statistically significant. However, once a further sensitivity analysis to remove studies deemed to be at a high risk of bias was completed, the magnitude of effect was no longer significant. Similarly, the overall effect size on task-based outcomes indicated a significant "small" effect favouring CBT over control (*g*= 0.35), although this was no longer statistically significant when studies deemed to

be a high risk of bias were removed. The fact that there were very few studies within the analysis for clinician-rated and task-based measures is likely to have been influential and data for these outcome types should therefore be interpreted with marked caution.

3.5.3 Research question 3: Is the effectiveness of CBT with individuals with ASD moderated by age?

3.5.3.1 Self-reported outcomes.

As reported in Sections 3.5.1.1 and 3.5.2.1, CBT was not superior to control groups on self-reported outcome measures for both studies investigating the effectiveness of CBT for co-occurring symptoms of mental disorder and studies investigating CBT targeting core features of ASD. However, subgroup analysis was conducted as planned to compare effectiveness across age groups in order to ensure that a significant effect had not become masked by the inclusion of studies from other age groups.

3.5.3.1.1 Studies investigating CBT targeting symptoms of mental disorder in individuals with ASD

Subgroup meta-analysis of studies investigating CBT targeting symptoms of mental disorder in individuals with ASD indicated no significant difference between age groups on self-reported outcomes, with I^2 indicating that 0% of the variability in effect estimates was due to genuine subgroup differences rather than sampling error (p = .43). No significant effect of CBT was found in adult studies (g = 0.05; 95% CI [-0.50, 0.60], z = 0.18, p = .86) or mixed age group studies (g = 0.03; 95% CI [-0.35, 0.41], z = 0.16, p = .87) on self-rated outcomes (see Figure 9). A "small" combined effect size favouring CBT in child and adolescent studies was found (g = 0.40; 95% CI [-0.05, 0.85], z = 1.75, p = .08), although this was non-significant and exclusion of an outlier (Chalfant et al., 2007) eliminated this effect (g = 0.15; 95% CI [-0.07, 0.38], z = 1.34, p = .18).

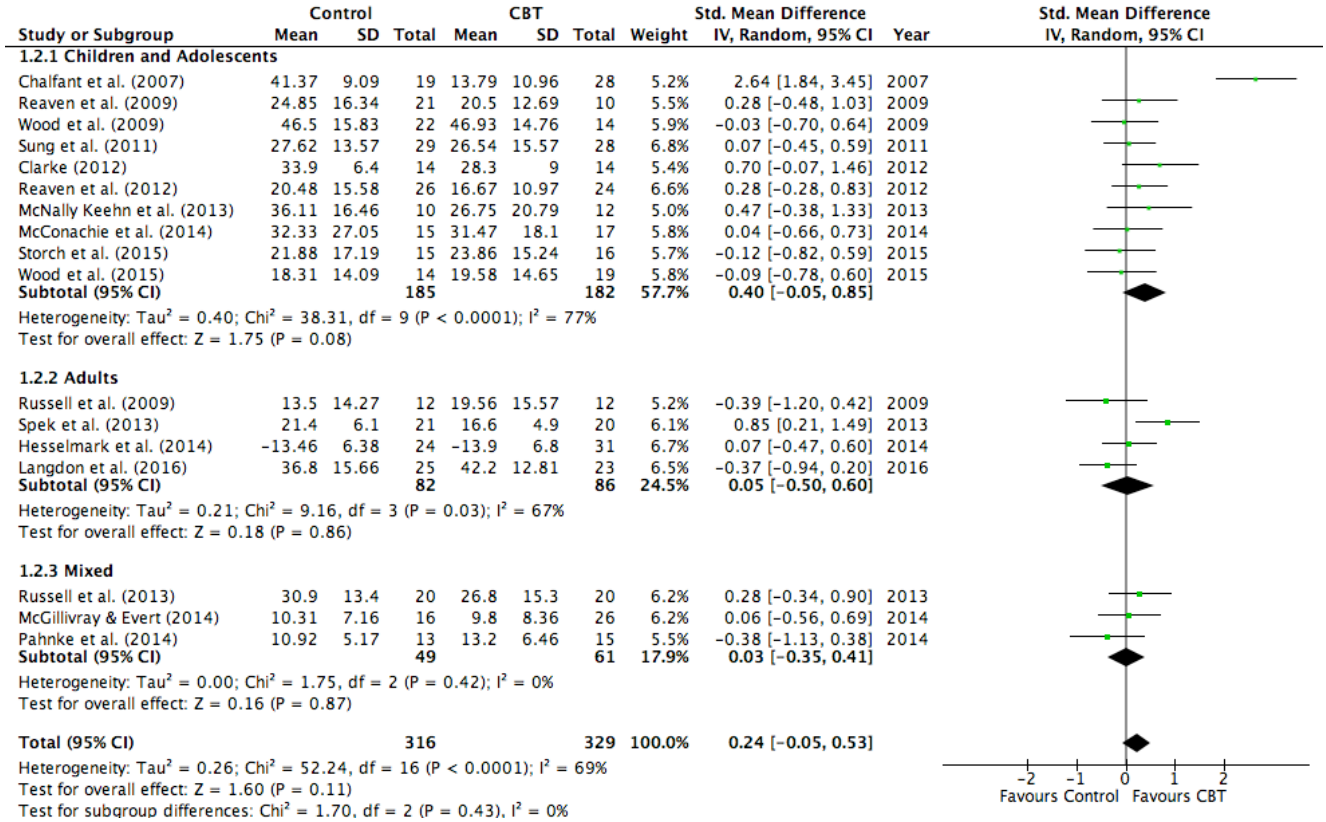

Figure 9. Forest plot showing estimated treatment effect of CBT for co-occurring mental disorders based on self-rated outcomes: age subgroup analysis

3.5.3.1.2 Studies investigating CBT targeting core features of ASD

Subgroup meta-analysis of studies investigating CBT targeting core features of ASD again indicated no significant difference between age groups on self-reported outcomes, with I^2 indicating that 0% of the variability in effect estimates was due to genuine subgroup differences rather than sampling error (p = .84). A "small" combined effect size favouring CBT was found in both child and adolescent (g = 0.25; 95% CI [-0.07, 0.56], z = 1.52, p = .13) and adult (g = 0.33; 95% CI [-0.43, 1.09], z = 0.85, p = .39) studies, although these were non-significant (see Figure 10).

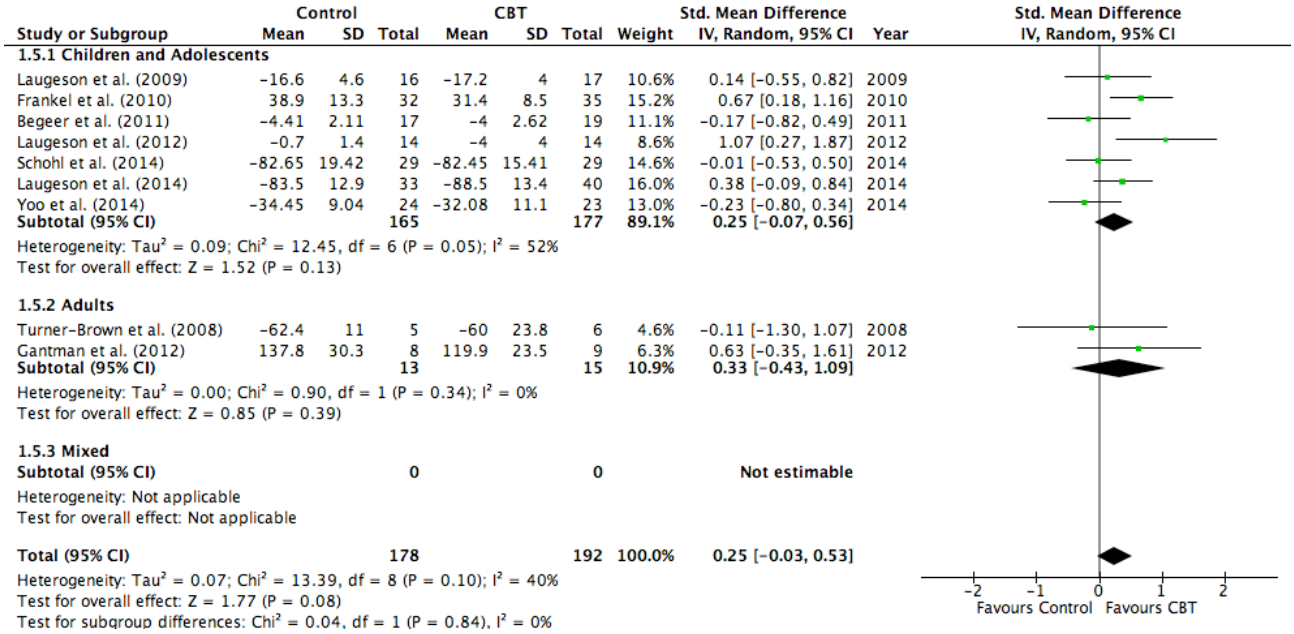

Figure 10. Forest plot showing estimated treatment effect of CBT for core features of ASD based on self-rated outcomes: age subgroup analysis

3.5.3.2 Informant-reported outcomes.

Of the 16 studies that included appropriate informant-reported outcome measures in the investigation of the effectiveness of CBT in reducing symptoms of mental disorder, 15 involved children and adolescents. One study included both adolescents and adults, whilst none included adults only. Similarly, of the 18 studies that included appropriate informant-reported outcome measures in the investigation of the effectiveness of CBT for core features of ASD, 17 involved children and adolescents, whilst one included adults only. Planned subgroup analysis of age group across informant-report type was therefore not possible.

3.5.3.3 Clinician-rated outcomes.

3.5.3.3.1 Studies investigating CBT targeting symptoms of mental disorder in individuals with ASD

Subgroup meta-analysis of studies investigating CBT targeting symptoms of mental disorder in individuals with ASD indicated a significant difference between age groups on clinician-rated outcomes, with I^2 indicating that 80.2% of the variability in effect estimates was due to genuine subgroup differences rather than sampling error (p = .006). Analysis indicated a "large" combined effect size favouring CBT in child and adolescent studies (g = 0.95; 95% CI [0.55, 1.35], z = 4.64, p < .001), whilst no significant effect of CBT was found in adult studies (g = -0.04; 95% CI [-0.50, 0.43], z = 0.15, p = .88) on clinician-rated outcomes (see Figure 11). Exclusion of outliers (Chalfant et al., 2007; Wood et al., 2009) resulted in a lower treatment effect for child and adolescent studies (g = 0.67; 95% CI [0.42, 0.91], z = 5.28, p < .001), although it remained statistically significant. However, this comparison should be treated with extreme caution since there were only two adult trials available for the analysis involving only N = 72 participants, in contrast to the trials involving N = 402 children and adolescents.

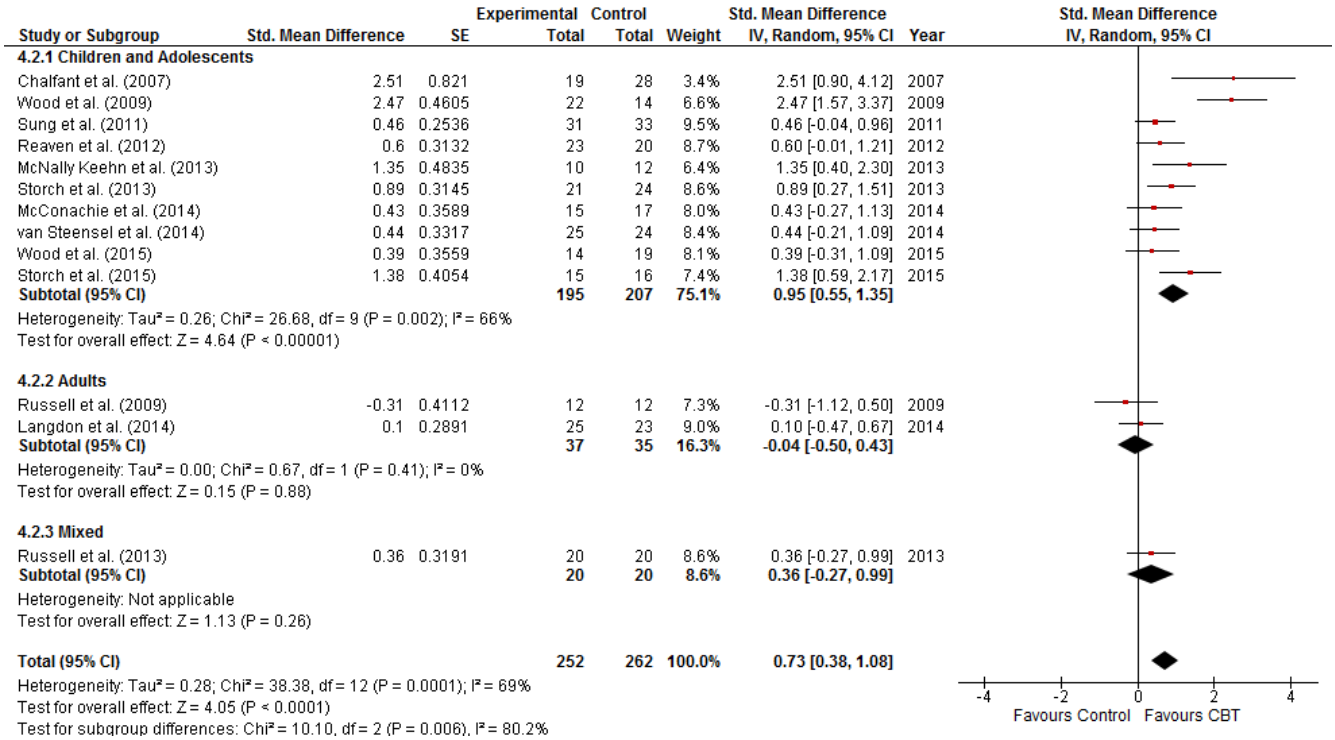

Figure 11. Forest plot showing estimated treatment effect of CBT for co-occurring mental disorders based on clinician-rated outcomes: age subgroup analysis

3.5.3.3.2 Studies investigating CBT targeting core features of ASD

Of the six studies that included appropriate clinician-rated outcome measures in the investigation of the effectiveness of CBT for core features of ASD, five involved children and adolescents, whilst only one included adults. Planned subgroup analysis of age group across clinician-rated outcomes was therefore not possible in studies investigating CBT targeting core features of ASD.

3.5.3.4 Task-based outcomes.

Only one study investigating the effectiveness of CBT for co-occurring symptoms of mental disorder included a task-based measure. All seven of the studies that included an appropriate task-based measure in the investigation of the effectiveness of CBT for core features of ASD involved children and adolescents. Planned subgroup analysis of age group across task-based measures was therefore not possible.

3.5.3.5 Summary.

Planned subgroup analysis to investigate whether the effectiveness of CBT with individuals with ASD is moderated by age was severely limited by the small number of studies involving adult participants. It was not possible to conduct subgroup analysis by age for informant-report or task-based outcomes for this reason.

Subgroup analysis of studies investigating CBT targeting both core features of ASD and co-occurring mental disorder indicated no significant differences between age groups on self-reported outcomes. Subgroup analysis of clinician-rated outcome measures in studies investigating CBT targeting symptoms of mental disorder in individuals with ASD indicated a significantly larger effect for child and adolescent studies than adult studies. However, this

comparison was limited by the fact that only two adult trials were available for the analysis and the outcome should therefore be interpreted with extreme caution.

3.5.4 Research question 4: Is individual CBT more effective than group-based CBT in individuals with ASD?

3.5.4.1 Self-reported outcomes.

As reported in Sections 3.5.1.1 and 3.5.2.1, no significant effect of CBT over control on self-reported outcome measures was found, both in studies investigating the effectiveness of CBT for co-occurring symptoms of mental disorder and studies investigating CBT targeting core features of ASD. However, subgroup analysis was conducted as planned to compare effectiveness across CBT type in order to ensure that a significant effect had not become masked by the inclusion of studies from the opposing group.

3.5.4.1.1 Studies investigating CBT targeting symptoms of mental disorder in individuals with ASD

Subgroup meta-analysis of studies investigating CBT targeting symptoms of mental disorder in individuals with ASD indicated no significant difference between CBT type on self-reported outcomes. I^2 indicated that 59.2% of the variability in effect estimates was due to genuine subgroup differences rather than sampling error, although this was non-significant (p = .12) and the removal of an outlier (Chalfant et al., 2007) reduced I^2 to 2.6%. No significant effect of individual CBT was found (g = -0.03; 95% CI [-0.34, 0.28], z = 0.22, p = .83) on self-rated outcomes (see Figure 12). A "small" combined effect size favouring group-based CBT was found (g = 0.37; 95% CI [-0.03, 0.76], z = 1.82, p = .07), although this was non-significant and exclusion of an outlier (Chalfant et al., 2007) eliminated this effect (g = 0.16; 95% CI [-0.06, 0.38], z = 1.45, p = .15).

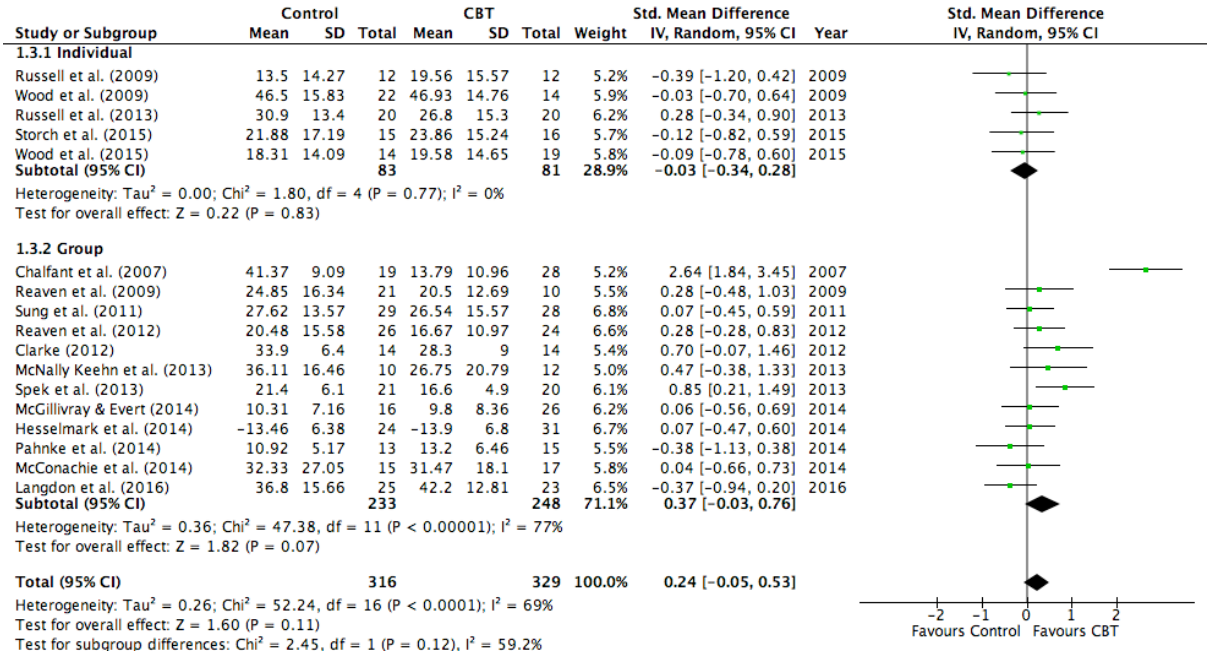

Figure 12. Forest plot showing estimated treatment effect of CBT for co-occurring mental disorders based on self-rated outcomes: CBT type subgroup analysis

3.5.4.1.2 Studies investigating CBT targeting core features of ASD

Of the 9 studies that included appropriate self-reported outcome measures in the investigation of the effectiveness of CBT for core features of ASD, none investigated individual CBT. Planned subgroup analysis of CBT type across informant-report outcomes was therefore not possible in this pool of studies.

3.5.4.2 Informant-reported outcomes.

3.5.4.2.1 Studies investigating CBT targeting symptoms of mental disorder in individuals with ASD

Subgroup meta-analysis of studies investigating CBT targeting symptoms of mental disorder in individuals with ASD indicated no significant difference between CBT type on informant-reported outcomes (see Figure 13), with I^2 indicating that 0% of the variability in effect estimates was due to genuine subgroup differences rather than sampling error (p = .50). Exclusion of one key outlier (Chalfant et al., 2007) indicated that individual-based CBT (g =

0.52; 95% CI [0.04, 1.00], $z = 2.13$, $p = .03$) was slightly more effective than group-based CBT ($g = 0.41$; 95% CI [0.18, 0.64] $z = 3.54$, $p < .001$), although again this difference was not significant ($p = .50$). It should be noted that heterogeneity for studies investigating individual CBT was particularly high ($I^2 = 70\%$).

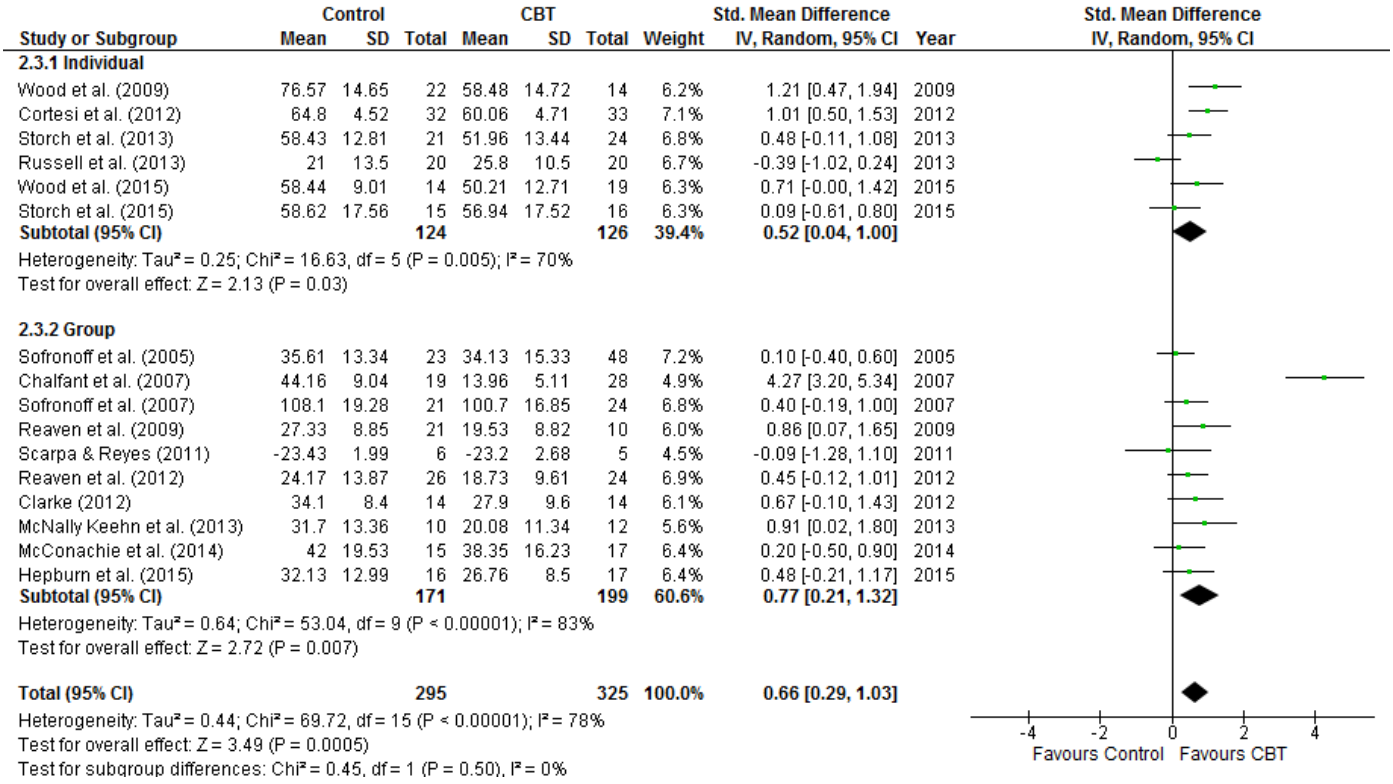

Figure 13. Forest plot showing estimated treatment effect of CBT for co-occurring mental disorders based on informant-reported outcomes: CBT type subgroup analysis

3.5.4.2.2 Studies investigating CBT targeting core features of ASD

Of the 18 studies that included appropriate informant-reported outcome measures in the investigation of the effectiveness of CBT for core features of ASD, none investigated individual CBT. Planned subgroup analysis of CBT type across informant-report outcomes was therefore not possible in this pool of studies.

3.5.4.3 Clinician-rated outcomes.

3.5.4.3.1 Studies investigating CBT targeting symptoms of mental disorder in individuals with ASD

Subgroup meta-analysis of studies investigating CBT targeting symptoms of mental disorder in individuals with ASD indicated no significant difference between CBT type on clinician-rated outcomes (see Figure 14), with I^2 indicating that 0% of the variability in effect estimates was due to genuine subgroup differences rather than sampling error (p = .72). Exclusion of two outliers (Chalfant et al., 2007; Wood et al., 2009) resulted in the same outcome, with no significant difference between individual-based CBT (g = 0.53; 95% CI [0.12, 0.94], z = 2.55, p = .01) and group-based CBT (g = 0.49; 95% CI [0.17, 0.81], z = 2.99, p = .003).

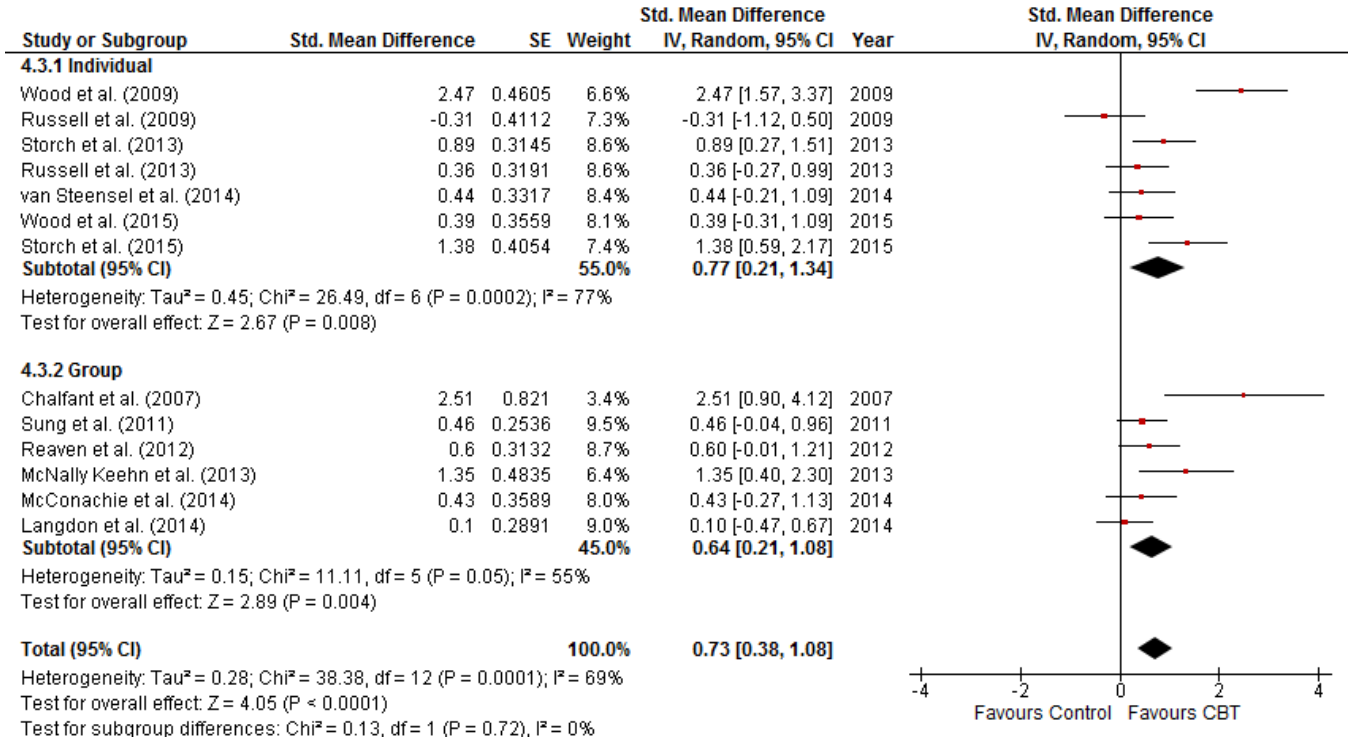

Figure 14. Forest plot showing estimated treatment effect of CBT for co-occurring mental disorders based on clinician-rated outcomes: CBT type subgroup analysis

3.5.4.3.2 Studies investigating CBT targeting core features of ASD

Of the six studies that included appropriate clinician-rated outcome measures in the investigation of the effectiveness of CBT for core features of ASD, four investigated group-based CBT, whilst only one reported on individual CBT. White et al. (2013) utilised both group and individual sessions. Planned subgroup analysis of CBT type across clinician-rated outcomes was therefore not possible in studies investigating CBT targeting core features of ASD.

3.5.4.4 Task-based outcomes.

Only one study investigating the effectiveness of CBT for co-occurring symptoms of mental disorder included a task-based measure. Six of the seven studies that included an appropriate task-based measure in the investigation of the effectiveness of CBT for core features of ASD investigated group-based CBT. One study utilised both group and individual CBT, whilst none investigated individual CBT only. Planned subgroup analysis of age group across informant-report type was therefore not possible.

3.5.4.5 Summary.

Planned subgroup analysis to investigate whether the effectiveness of CBT with individuals with ASD is moderated by CBT type was restricted. For studies investigating CBT for core features of ASD, subgroup analysis by CBT type was not possible for any outcome type due to the lack of studies investigating individual CBT.

In terms of studies investigating CBT for mental disorder, it was not possible to conduct subgroup analysis on task-based outcomes as only one study investigating the effectiveness of CBT for co-occurring symptoms of mental disorder included a task-based measure. Subgroup analysis of self-reported, informant-reported and clinician-rated outcome measures in studies investigating CBT targeting symptoms of mental disorder in individuals with ASD indicated no significant difference in effect between individual and group-based CBT.

3.5.5 Additional analysis: Sub group analysis by age within studies targeting anxiety

Nineteen studies were included within the anxiety subset. A subgroup analysis was conducted to assess potential variations of treatment effects across age groups within this subset of studies, enabling comparison to recent meta-analytic studies which have looked specifically at the effectiveness of CBT for anxiety in children and adolescents with ASD (Kreslins et al., 2015; Sukhodolsky et al., 2013; Ung et al., 2015).

3.5.5.1 Self-reported outcomes.

Fifteen studies, including 558 participants (280 CBT, 278 control), that investigated the effectiveness of CBT in reducing symptoms of anxiety included appropriate self-reported outcome measures. One study (Storch et al., 2013) utilised a relevant self-reported outcome measure but it was not possible to include this in the analysis as an attempt to obtain the data necessary to calculate the effect size was unsuccessful. The outcome measures used varied considerably across studies.

A random-effects meta-analysis indicated no significant difference between age groups on self-reported outcomes, with I^2 indicating that 0% of the variability in effect estimates was due to genuine subgroup differences rather than sampling error ($p = .66$). Analysis indicated a "small" but non-significant combined effect size favouring CBT in child and adolescent studies ($g = .40$; 95% CI [-0.05, 0.85], $z = 1.75$, $p = .08$) on self-reported outcomes. No effect was found when a key outlier (Chalfant et al., 2007) was removed ($g = .15$; 95% CI [-0.07, 0.38], $z = 1.35$, $p = .18$). Similarly, no significant effect of CBT was found in adult studies ($g = .04$; 95% CI [-0.79, 0.86], $z = 0.09$, $p = .93$) or studies involving both adolescents and adults ($g = .16$; 95% CI [-0.30, 0.62], $z = 0.69$, $p = .49$) based on self-reported outcomes (see Figure 15).

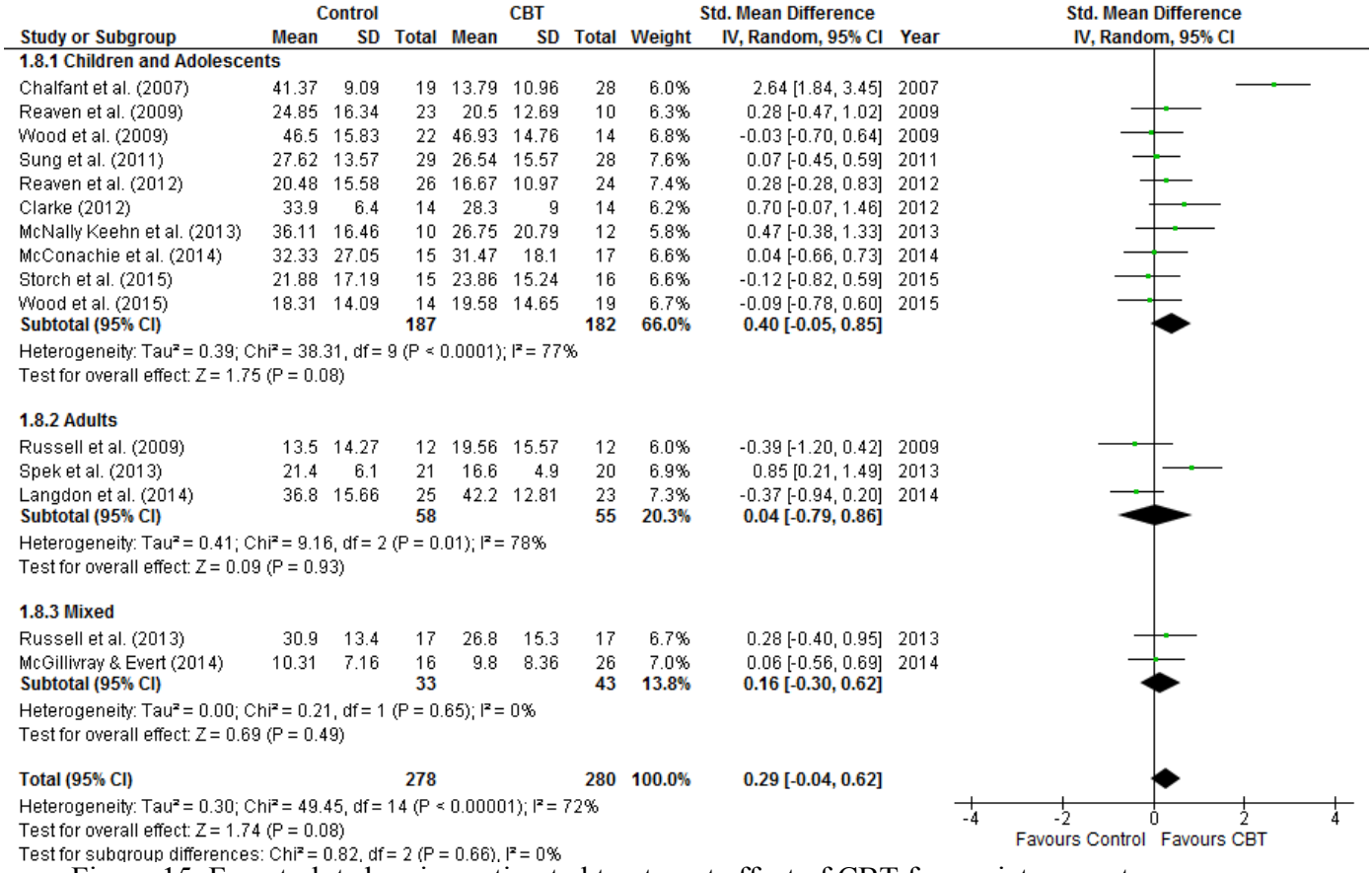

Figure 15. Forest plot showing estimated treatment effect of CBT for anxiety symptoms based on self-reported outcomes: age subgroup analysis

3.5.5.2 Informant-reported outcomes.

Of the 13 studies that included appropriate informant-reported outcome measures in the investigation of the effectiveness of CBT in reducing symptoms of anxiety, 12 involved children and adolescents. One study included both adolescents and adults, whilst none included adults only. Planned subgroup analysis of age group across informant-report type was therefore not possible.

A random-effects meta-analysis of the child and adolescent studies indicated a "large" effect favouring CBT over waiting-list, treatment as usual or active control as reported by informants (g = .80; 95% CI [0.34, 1.25], z = 3.42, p < .001). The analysis indicated a

significant amount of heterogeneity, with I^2 indicating that 80% of the variability in estimated treatment effect was due to heterogeneity rather than chance ($p < .001$).

Chalfant et al., (2007) again had a SMD ($g = 4.27$) considerably higher than the other included studies and a sensitivity analysis was therefore conducted to remove this outlier. Exclusion of this study resulted in a lower treatment effect ($g = 0.49$; 95% CI [0.29, 0.70], $z = 4.74$, $p < .001$), although it remained statistically significant. I^2 reduced to 2% ($p = .42$), indicating the high impact that the inclusion of this study had on the pooled SMD.

3.5.5.3 Clinician-rated outcomes.

Subgroup meta-analysis of studies investigating CBT targeting symptoms of anxiety in individuals with ASD indicated a significant difference between age groups on clinician-rated outcomes, with I^2 indicating that 80.2% of the variability in effect estimates was due to genuine subgroup differences rather than sampling error ($p = .006$). Analysis indicated a "large" combined effect size favouring CBT in child and adolescent studies ($g = 0.95$; 95% CI [0.55, 1.35], $z = 4.64$, $p < .001$), whilst no significant effect of CBT was found in adult studies ($g = -0.04$; 95% CI [-0.50, 0.43], $z = 0.15$, $p = .88$) on clinician-rated outcomes (see Figure 16). Exclusion of outliers (Chalfant et al., 2007; Wood et al., 2009) resulted in a lower treatment effect for child and adolescent studies ($g = 0.67$; 95% CI [0.42, 0.91], $z = 5.28$, $p < .001$), although it remained statistically significant. However, this comparison should be treated with caution since there were only two adult trials available for the analysis, again including only N = 72 participants.

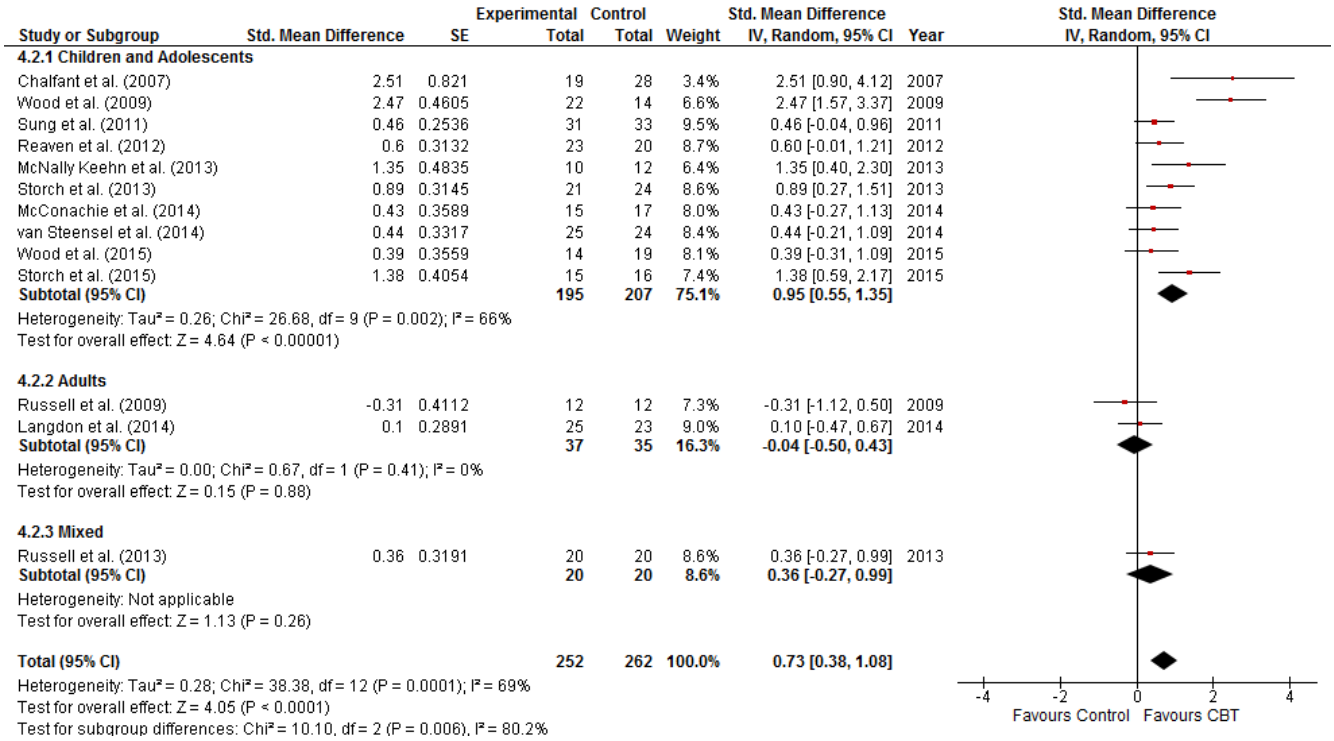

Figure 16. Forest plot showing estimated treatment effect of CBT for anxiety symptoms based on clinician-rated outcomes: age subgroup analysis

3.5.5.4 Task-based outcomes.

None of the 19 studies within the anxiety subset included a task-based outcome measure. It was therefore not possible to calculate a pooled SMD or conduct subgroup analysis in this area.

3.5.5.5 Summary.

Nineteen studies that investigated the effectiveness of CBT in reducing symptoms of anxiety in children, adolescents and adults with ASD were included, and within this subset, no significant difference between age groups was found on self-reported outcomes. In contrast, a significant difference between age groups on clinician-rated outcomes was found, with a "large" combined effect size favouring CBT in child and adolescent studies but no significant effect of CBT in adult studies. It was not possible to conduct subgroup analysis

by age for informant-reported and task-based outcomes due to a lack of adult studies and studies using task-based measures respectively.

The majority of studies investigating CBT for anxiety involved children and adolescents. Within this subgroup, overall effect sizes on informant- reported and clinician-rated outcomes were g= 0.80 and g= 0.95 respectively, both of which may be interpreted as "large" effects. When outlying studies were removed, the magnitude of these effects reduced to g= 0.49 and g= 0.67 respectively, although they remained statistically significant. In contrast, the overall effect size on self-reported outcomes was g= 0.40, which may be interpreted as a "small" but non-significant effect. When an outlying study was removed, the magnitude of the effect reduced to g= 0.15, indicating no superiority of CBT over control on self-reported outcome measures.

3.5.6 Exploration of publication bias.

Publication bias was assessed graphically using funnel plots plotting summary effect size against standard error (Light & Pillemer, 1984). Fail-safe N (Rosenthal, 1979) was used to assess the impact of bias by calculating an estimate of the number of new studies averaging a null result that would be required to bring the overall treatment effect to non-significance.

3.5.6.1 Self-reported outcomes.

Visual inspection of a funnel plot of studies including self-reported outcomes in the investigation of CBT for mental disorder did not indicate significant asymmetry (see Figure 17). As the combined effect size within this outcome type was not found to be significant, Fail-safe N was not calculated.

Exploration of publication bias within studies including self-reported outcomes in the investigation of CBT for core features was not conducted, both because the number of included studies was less than ten (Sterne et al., 2011) and because the combined effect size within this outcome type was found to be non-significant.

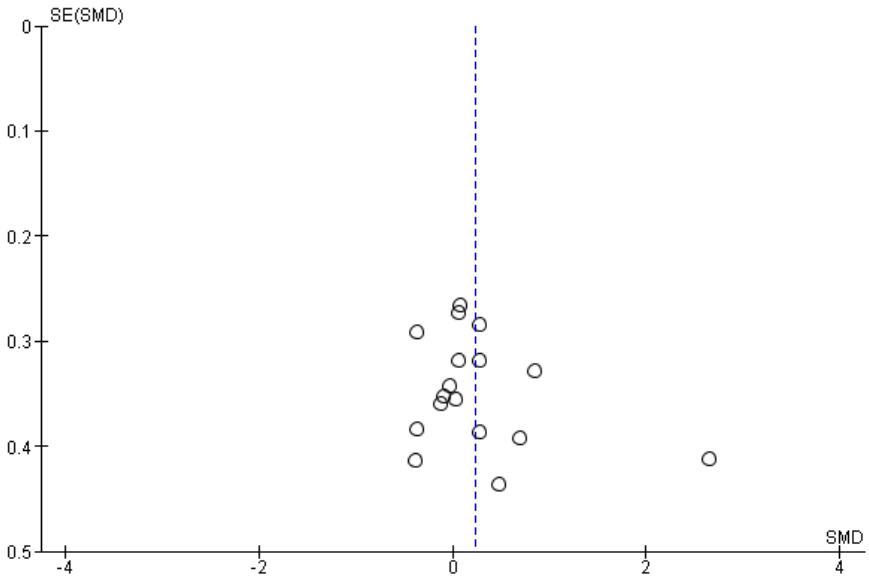

Figure 17. Funnel plot of standard error by Hedge's g: Studies including self-reported outcomes in the investigation of CBT for mental disorder

3.5.6.2 Informant-reported outcomes.

Visual inspection of funnel plots of studies including informant-reported outcomes in the investigation of both CBT for mental disorder and CBT for core features of ASD did not indicate significant asymmetry (see Figures 18 and 19).

The calculation of Fail-safe *N* (Rosenthal, 1979) indicated that 281 new studies averaging a null result would be required to bring the overall treatment effect for studies investigating CBT for mental disorder to non-significance (based on informant-reported outcomes), whilst 287 new studies averaging a null result would be required to bring the overall treatment effect for studies investigating CBT for core features of ASD to non-significance. As these figures exceed 5n+ 10, this indicates that the findings observed in the present study are likely to be robust to the effects of publication bias (Rosenberg, 2005).

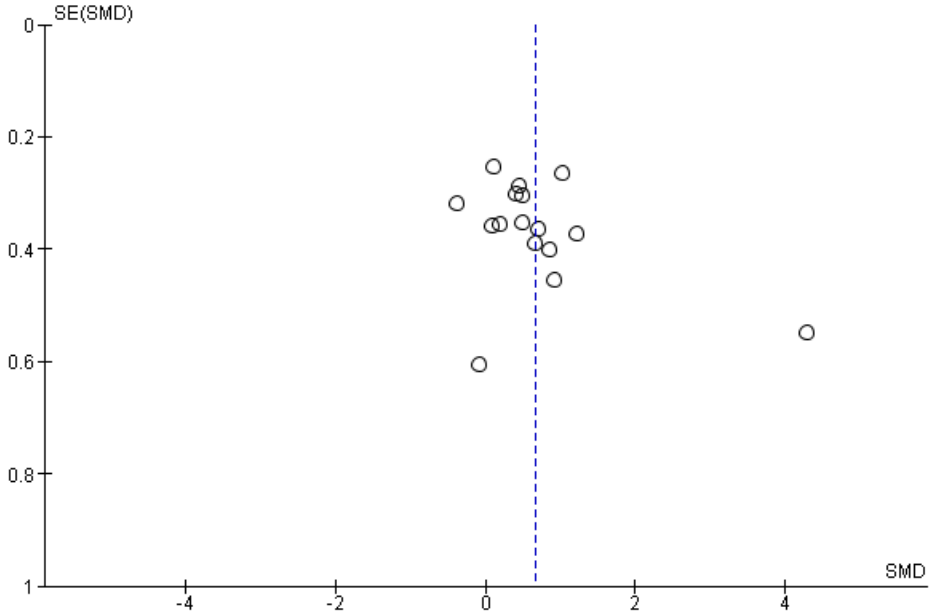

Figure 18. Funnel plot of standard error by Hedge's g: Studies including informant-reported outcomes in the investigation of CBT for mental disorder

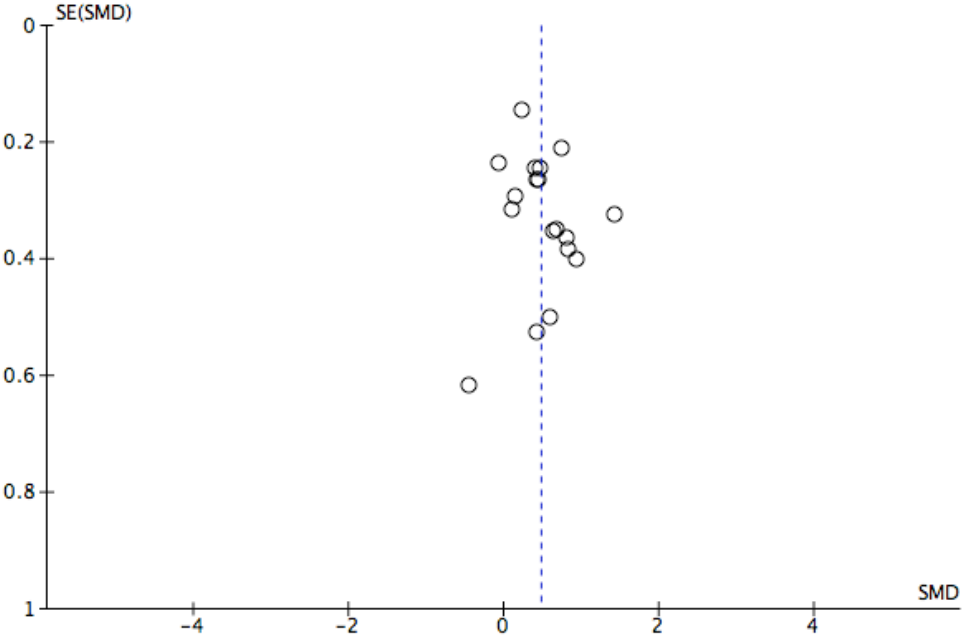

Figure 19. Funnel plot of standard error by Hedge's g: Studies including informant-reported outcomes in the investigation of CBT for core features of ASD

3.5.6.3 Clinician-rated outcomes.

Visual inspection of a funnel plot of studies including clinician-rated outcomes in the investigation of CBT for mental disorder did not indicate significant asymmetry (see Figure 20). A funnel plot of studies including clinician-rated outcomes in the investigation of CBT for core features was not conducted as the number of included studies was less than ten (Sterne et al., 2011).

The calculation of Fail-safe *N* (Rosenthal, 1979) indicated that 227 new studies averaging a null result would be required to bring the overall treatment effect for studies investigating CBT for mental disorder to non-significance (based on clinician-rated outcomes). As this figure exceeds 5n+ 10, this indicates that the findings are likely to be robust to the effects of publication bias (Rosenberg, 2005).

The calculation of Fail-safe *N* (Rosenthal, 1979) for studies investigating CBT for core features of ASD indicated that only 18 new studies averaging a null result would be required to bring the overall treatment effect to non-significance. This may indicate that the findings in this area may be subject to publication bias and the finding is likely to be heavily influenced by the reduced number of studies within this analysis.

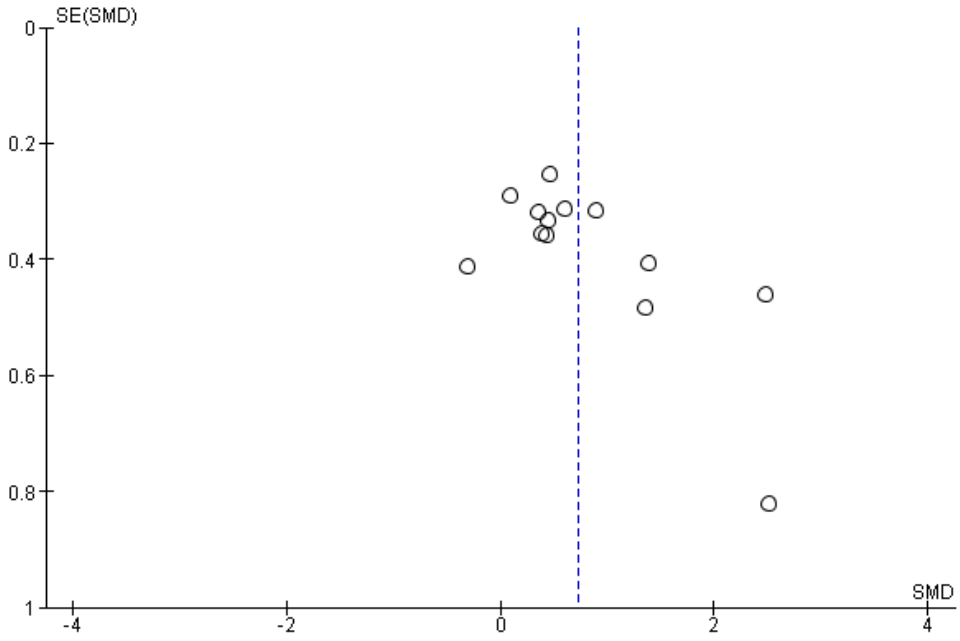

Figure 20. Funnel plot of standard error by Hedge's g: Studies including clinician-rated outcomes in the investigation of CBT for mental disorders

3.5.6.4 Task-based outcomes.

Exploration of publication bias within studies including task-based outcomes in the investigation of CBT for mental disorder was not conducted as it was not possible to calculate a pooled effect size in this area due to a lack of studies.

A funnel plot of studies including task-based outcomes in the investigation of CBT for core features of ASD was not conducted as the number of included studies was less than ten (Sterne et al., 2011). The calculation of Fail-safe *N* (Rosenthal, 1979) for studies investigating CBT for core features of ASD (based on task-based outcome measures) indicated that only 5 new studies averaging a null result would be required to bring the overall treatment effect to non-significance. Again, this may indicate that the findings in this area are subject to publication bias and the finding is likely to be heavily influenced by the reduced number of studies within this analysis.

3.5.6.5 Summary.

A brief exploration of possible publication bias was conducted for outcome types in which the pooled effect size was found to be significant. Based on the visual inspection of funnel plots (Light & Pillemer, 1984) and the calculation of fail-safe *N* (Rosenthal, 1979), results of studies based on informant-report outcomes appear to be robust to the effects of publication bias. A similar conclusion may be drawn from studies investigating CBT for mental disorder based on clinician-rated outcomes. In contrast, the findings for studies including clinician-rated and task-based outcomes in the investigation of CBT for core features of ASD were found to be more vulnerable to the threat of publication bias, i.e. less tolerant to the possible exclusion of null results. However, as discussed in Section 2.7.5, this

approach is not without its limitations and results should therefore be interpreted with caution.

3.6 Chapter Summary

Fifty studies met inclusion criteria for the present research and 48 studies, involving 2099 participants (1081 CBT, 1018 control) were included in the quantitative synthesis. There was very good agreement between the researchers regarding study inclusion. Twenty-four of the included studies assessed the effectiveness of CBT for co-occurring symptoms of mental disorder, whilst 24 studies targeted core features of ASD. The majority of studies involved children and adolescents. There was considerable variation amongst studies in terms of trial design, outcome measures utilised and CBT type, content and intensity.

Regarding quality appraisal, there was 'moderate' agreement between the researchers regarding ratings for internal validity and 'good' agreement regarding ratings for external validity. Key sources of potential bias identified included small sample size, non-randomisation and a lack of blinding. A lack of reporting on compliance to intervention sessions, poor reporting on missing data and minimal information on fidelity checks were also commonly identified issues, as was the lack of specification of a primary outcome measure. However, the exclusion of studies in which a high risk of bias was identified during sensitivity analysis did not have a significant impact on results in most areas.

Quantitative synthesis indicated "small" to "medium" effect sizes for the effectiveness of CBT in reducing symptoms of mental disorder in children, adolescents and adults with ASD, based on informant-reported and clinician-rated outcomes. CBT was not superior to control on self-reported outcome measures. A similar pattern was found in studies specifically investigating the effectiveness of CBT for anxiety, in addition to studies targeting core features of ASD. Planned subgroup analysis to investigate whether the effectiveness of CBT with individuals with ASD is moderated by age was severely limited by the small

number of studies involving adult participants. Planned subgroup analysis to investigate whether the effectiveness of CBT with individuals with ASD is moderated by CBT type was again restricted. However, preliminary analysis of both informant-reported and clinician-rated outcome measures in studies investigating CBT targeting symptoms of mental disorder in individuals with ASD indicated no significant difference in effect between individual and group-based CBT.

Chapter Four: Discussion

4.1 Introduction

There is a growing interest in the development of psychotherapeutic interventions for use with individuals with Autism Spectrum Disorders. Cognitive Behavioural Therapy may be one promising treatment for use with this client group. However, there has been little systematic appraisal of effectiveness research in this area to date, particularly involving studies with adult participants and those investigating CBT targeting core features of ASD. The primary aim of the current study was therefore to systematically appraise the evidence for using CBT in the treatment of either core features of ASD or co-occurring mental disorder in individuals with ASD across the lifespan. This chapter provides an overall discussion of the findings in relation to the research questions and background literature. Clinical and theoretical implications of the study are discussed, in addition to strengths and limitations of the current research. Finally, recommendations regarding how future research can be extended and improved are outlined.

4.2 Summary of Findings in Relation to Research Questions

4.2.1 Research Question 1: How effective is Cognitive Behavioural Therapy in reducing symptoms of mental disorder in individuals with Autism Spectrum Disorders?

To the best of my knowledge there are currently three reviews involving quantitative synthesis of studies investigating CBT for ASD published to date (Kreslins et al., 2015; Sukhodolsky et al., 2013; Ung et al., 2015), all of which focus on the treatment of anxiety symptoms in children. The current study built on these previous meta-analytic reviews by extending search criteria to include studies investigating the treatment of any mental disorder across the lifespan. A total of 24 studies were identified that investigated the effectiveness of CBT in reducing symptoms of mental disorder in children, adolescents or adults with ASD.

Results indicated that CBT is associated with a "small" to "medium" effect size when used to treat co-morbid mental health problems, although this varied according to whether outcome data were taken from self-report, informant-report, clinician-report, or task-based measures.

"Medium" effect sizes of g= 0.66 and g= 0.73 were found on informant- reported and clinician-rated outcomes respectively. However, the removal of outlying studies and studies deemed to be at a high risk of bias resulted in a reduction in the magnitude of these effects to g= 0.45 and g= 0.59. When assessing informant-reported and clinician-rated outcomes, CBT was therefore found to be superior to control conditions in the treatment of mental disorder across the lifespan, with a "small" to "medium" treatment effect. In contrast, a "small" but non-significant effect of g= 0.24 was found for self-reported outcomes. The removal of an outlying study and studies at risk of bias reduced the magnitude of the effect to g= 0.09, indicating no superiority of CBT over control on self-reported outcome measures.

Additional subgroup analysis of the subset of studies investigating the effectiveness of CBT for anxiety in children and adolescents enabled a more direct comparison to the anxiety-specific meta-analytic reviews of Sukhodolsky et al. (2013), Ung et al. (2015) and Kreslins et al. (2015). Consistent with these studies, the present research found overall effect sizes on informant- reported and clinician-rated outcomes of g= 0.80 and g= 0.95 respectively, both of which may be interpreted as "large" effects. When outlying studies were removed, the magnitude of these effects reduced to g= 0.49 and g= 0.67 respectively, although they remained statistically significant. In contrast, the overall effect size on self-reported outcomes was g= 0.40, which may be interpreted as a "small" but non-significant effect. When an outlying study was removed, the magnitude of the effect reduced to g= 0.15, indicating no superiority of CBT over control on self-reported outcome measures.

These findings provide further support to the notion that CBT is effective at reducing anxiety in children and adolescents with ASD when considering informant-reported or

clinician-rated outcomes. However, the effect sizes reported here are lower than those previously reported by Sukhodolsky et al. (2013), Ung et al. (2015) and Kreslins et al. (2015), with all previous meta-analyses in the area having included fewer studies.

4.2.2 Research Question 2: How effective is Cognitive Behavioural Therapy in the treatment of core features of Autism Spectrum Disorders?

Findings from the meta-analysis of studies focused on the treatment of core features of ASD were very similar to those reported for the treatment of co-occurring mental disorder. Twenty-four studies that investigated the effectiveness of CBT in the treatment of core features of ASD in children, adolescents and adults with ASD were included. CBT was again associated with an effect size that ranged from "small" to "medium" and this was again dependent on the type of outcome measure used.

When using data from self-reported outcomes, the difference between CBT and control groups post-treatment failed to reach significance; the overall effect size was g= 0.25, and this was further reduced when a sensitivity analysis was conducted to remove studies deemed to be at a high risk of bias. In contrast, clinician- and informant-reported outcome measures indicated that CBT was superior to control conditions post- treatment. The overall effect size on informant- reported outcomes following sensitivity analysis to remove studies deemed to be at a high risk of bias was g= 0.52, a "medium" treatment effect.

The overall effect size on clinician-rated outcomes was also "medium" (g= 0.65). However, following the exclusion of studies deemed to be at risk of bias to reduce heterogeneity, there was a reduction in effect size (g = .44) and CBT was no longer significantly superior. In a similar pattern, the initial findings from task-based measures were significantly in favour of CBT as an effective treatment, with a "small" effect size (g = .35), although this was no longer statistically significant when studies deemed to be a high risk of bias were removed. It should be noted that there were a very small number of studies within the analysis for

clinician-rated and task-based measures which is likely to have been influential and this hinders our interpretation of the findings.

4.2.3 Research Question 3: Is the effectiveness of Cognitive Behavioural Therapy with individuals with Autism Spectrum Disorders moderated by age?

Subgroup analysis was planned to investigate whether the effectiveness of CBT with individuals with ASD is influenced by age. However, this was severely limited by the small number of studies involving adult participants; it was not possible to conduct sub-group analysis by age for informant-report or task-based outcomes for this reason.

Subgroup analysis of studies investigating CBT targeting both core features of ASD and co-occurring mental disorder indicated no significant differences between age groups on self-reported outcomes. A subgroup analysis based on clinician-rated outcome measures for the treatment of mental disorder was also conducted. The findings indicated a significantly larger effect for child and adolescent studies than for adult studies; CBT was superior than control and was associated with a "large" effect size (g = .95) when used with children and adolescents, while CBT was not superior and was associated with a "small" effect size (g = -.04) in adults. However, this analysis relied on small numbers of studies which hinders interpretation and prevents firm conclusions from being drawn. At present these findings should therefore be regarded as preliminary in nature.

4.2.4 Research Question 4: Is individual Cognitive Behavioural Therapy more effective than group-based Cognitive Behavioural Therapy in individuals with Autism Spectrum Disorders?

The planned subgroup analysis to investigate whether the effectiveness of CBT with individuals with ASD is moderated by CBT type was also restricted. For studies investigating

CBT for core features of ASD, subgroup analysis by CBT type was not possible for any outcome type due to the lack of studies investigating individual CBT.

In terms of studies investigating CBT for mental disorder, it was not possible to conduct subgroup analysis on task-based outcomes as only one study investigating the effectiveness of CBT for co-occurring symptoms of mental disorder included a task-based measure. Subgroup analysis of self-reported, informant-reported and clinician-rated outcome measures in studies investigating CBT targeting symptoms of mental disorder in individuals with ASD indicated no significant difference in effect between individual and group-based CBT. However, this analysis relied on small numbers of studies so, again, it would be unwise to draw firm conclusions in relation to Research Question 4. These findings should be regarded as preliminary in nature.

4.3 Theoretical Implications

The current study provides some support for Gaus's (2007) theoretical rationale for the utility of CBT in individuals with ASD. Gaus (2007) postulates that CBT may be particularly useful in this client group due to the complex nature of ASD and because CBT aims to target behavioural, cognitive and affective skills simultaneously. Individuals with ASD may experience information processing deficits, social skills deficits and difficulties in daily living, all of which are likely to contribute to the development or reinforcement of negative beliefs and affect. In addition, difficulties with social cognition and cognitive rigidity can also make it more difficult for individuals with ASD to make use of contextual information and to modify existing beliefs and affect. CBT may therefore provide a more holistic approach than other psychosocial interventions as its conceptual basis assumes reciprocity between an individual's thoughts, feelings and behaviours in social situations (Beck, 2011) and interventions are thus multifaceted. Social skills training programmes that are not specific to ASD have reported increased effectiveness in interventions incorporating

CBT techniques, in contrast to those that focus on either social, cognitive or behavioural techniques independently (Bauminger, 2007). Whilst the current study has not compared the effectiveness of CBT to that of other interventions, it is the first study to demonstrate that CBT can be beneficial in the treatment of both core features of ASD and symptoms of co-occurring mental disorder, supporting the theoretical rationale outlined above.

The present study may also provide support against the argument that CBT may not be suitable for use with individuals with ASD given the fact that ASD has been shown to be associated with difficulties identifying emotions and cognitions. Although the content of CBT interventions utilised in included studies was not directly investigated in the present research, all included studies incorporated both cognitive and behavioural components based on well-established and theoretically driven principles and techniques. The fact that CBT was shown to be superior to control groups may therefore suggest that individuals with ASD were in fact able to utilise this model in order to make improvements noticeable by informants and clinicians. This is in line with recent evidence which suggests that individuals with ASD are able to accurately report their anxious and depressed cognitions (Ozsivadjian et al., 2014), in addition to performing comparably to typically developing individuals on tasks requiring discrimination among thoughts, feelings and behaviours and cognitive mediation (Lickel et al., 2012).

The fact that many of the included studies involved increased emphasis on teaching practical skills, particularly those targeting the treatment of core features of ASD, also raises important theoretical questions. As discussed in Chapter One, a key component of CBT interventions is the identification and modification of cognitive structures, i.e. thoughts, beliefs and schemas, to facilitate clinical improvement (Beck, 1976). It is therefore interesting to note that CBT was superior to control groups based on informant- and clinician-rated outcomes in the current study, despite a de-emphasis on introspection and increased

emphasis on behavioural techniques across many of the included studies. It was beyond the scope of the current project to directly assess content of intervention; modifications and adaptations varied considerably across studies and it is therefore difficult to make conclusions in this area. However, it is fair to say that a lesser focus on cognitive aspects of CBT was noted across the included studies. More systematic and experimental investigation of intervention content would enable clearer discussion regarding whether the mechanism of action for clinical improvement is robust to more behaviourally focused treatment. This would be a useful addition to literature arguing that there is little evidence that specific cognitive interventions significantly increase the effectiveness of CBT (Longmore & Worrell, 2007). Further exploration in this area would also be important in terms of increasing the efficacy of CBT with this client group.

4.4 Clinical Implications

This is the first study to demonstrate that CBT can be beneficial in the treatment of both core features of ASD and symptoms of co-occurring mental disorder, making it a potentially unique and desirable intervention for use with this client group. However, the fact that CBT was not shown to be effective when based on self-report measures is an important finding which should be addressed. Substantial difference in treatment efficacy dependent on the outcome measure type has been reported, both in the present study and in three meta-analytic studies focused on the treatment of anxiety in children and adolescents with ASD (Kreslins et al., 2015; Sukhodolsky et al., 2013; Ung et al., 2015). In the current study, self-report measures were not associated with significant change following CBT treatment across all age groups, in addition to studies investigating the treatment of both core features of ASD and co-occurring mental disorder. As previously discussed, this may be due to a difficulty in reliably reporting symptoms due to developmental challenges associated with ASD (Kreslins et al., 2015; Sukhodolsky et al., 2013; Ung et al., 2015). The fact that this pattern is consistent

across the lifespan and across symptom type provides further support for this notion, highlighting the need for further research to develop valid and reliable measures for use with individuals with ASD. However, it is also important to consider the fact that the self-reported outcomes may in fact be accurate, i.e. CBT may not be an effective treatment for individuals with ASD. It is possible that informant- and clinician- reported outcomes are biased by an observer-expectancy effect, particularly as the level of blinding across studies was poor and data management was not usually independent. It is therefore important that future studies use masked assessors and improve blinding procedures in order to increase our understanding in this area.

Related to the above, it is also important to acknowledge the fact that even when CBT was shown to be superior to control conditions, all effect sizes reported in the current study are "small" to "medium". This is interesting, given the fact that CBT has been associated with much larger effects in other populations (Hofmann et al., 2012). It is likely that methodological issues across studies are playing a role here, although consideration should be given to the possibility that clinical adaptations currently being utilised in the treatment of individuals with ASD may not be appropriate or could be greatly improved. Thus, it is again argued that further systematic research into the content of CBT being utilised with individuals with ASD would be beneficial. NICE guidelines for the diagnosis and management of autism in children and adults (NICE, 2012a, 2013) state that the method of delivery of cognitive and behavioural interventions for individuals with ASD should include adaptations such as the use of a more concrete and structured approach, greater use of written and visual information, placing greater emphasis on behavioural rather than cognitive interventions and involving family members. Indeed, clinicians and researchers have begun to adapt or modify CBT in order to take into account the specific needs of children and adults with ASD to increase its accessibility and effectiveness (e.g. Moree & Davis, 2010).

However, these adaptations and modifications have not yet been reviewed systematically, or tested experimentally. Whilst the heterogeneity in content of treatment and the modification of CBT techniques for individuals with ASD was noted in the present study, it was beyond the scope of the current research to conduct a thorough review of this area. Such a review would enable an assessment of whether adaptations are in line with theoretical frameworks for conceptualising difficulties experienced by individuals with ASD (e.g. Gaus, 2007), in addition to providing clarity on the actual content and processes used, thus informing clinical practice.

4.5 Strengths and Weaknesses

A notable strength of the current research is that, to the best of my knowledge, this is the first quantitative review investigating the effectiveness of CBT in individuals with ASD to include studies involving adult participants. Whilst it is acknowledged that the number of adult studies in this area is limited, and the research base is certainly less developed than in child and adolescent populations, the inclusion of such studies has enabled preliminary analysis of the effectiveness of CBT for ASD at a later life stage. This has extended findings of previous meta-analytic reviews which have focused specifically on children and adolescents (Kreslins et al., 2015; Sukhodolsky et al., 2013; Ung et al., 2015), in addition to highlighting a clear need for further research involving adult participants in this area.

To the best of my knowledge, this study is also the first to systematically evaluate studies investigating the effectiveness of CBT in individuals with ASD for both co-occurring symptoms of mental disorder and core features of ASD. As previously reported, the use of CBT in the treatment of core features of ASD is receiving an increasing amount of attention, both clinically and in the research field. This study has provided an important contribution by highlighting the comparable effectiveness of CBT targeting core features to CBT targeting co-occurring mental disorder within this client group.

A final strength that should be acknowledged is the fact that the current research considered the effectiveness of CBT based on a variety of outcome report types. As will be discussed below this method was not without its complications, but it allowed comparison of combined effect sizes across different informants and likely contributed to a reduction in heterogeneity given the very wide variation in outcome measures used across report types. Furthermore, by including clinician-rated and task-based measures, the present research provided an additional angle from which to consider previously reported incongruence between self- and informant-reported measures.

Despite these strengths, alongside the promising results reported, the study should be interpreted in the context of its limitations. Whilst in the majority of analyses the level of heterogeneity reduced significantly following the removal of outliers, in some cases considerable heterogeneity in treatment effect sizes remained that could not be explained by the potential moderating factors explored. Planned subgroup analysis was restricted considerably by the limited number of studies within some groups, whilst other potentially moderating variables were not considered. For example, it may have been useful to consider the impact of the involvement of parents in CBT sessions or parallel parent sessions since many, but not all, of the child and adolescent studies included these features. It may also have been useful to consider the intensity of the intervention and the effect of this on CBT efficacy since there was a high level of variability in this area across studies.

A further limitation is that the present research did not address longer term effectiveness of CBT within this client group. Whilst a general limitation of the included studies was the limited length of follow-up, approximately half of the studies included in quantitative synthesis did follow up participants at least six weeks after the end of the intervention. It would have been useful for the current study to have conducted further

analysis using follow-up data in order to investigate whether the treatment effects observed were maintained over time.

Finally, the present research excluded studies which were not published in English which may have introduced a systematic bias and this may limit the conclusions drawn.

4.6 Future Research

In addition to the aforementioned limitations, as with any meta-analysis the validity of the conclusions drawn is highly dependent on the quality of the studies included. As discussed in Section 3.4, the research base on CBT for individuals with ASD has considerable methodological limitations that caused some difficulty in the current review. In order to make recommendations regarding future meta-analytic research it is therefore primarily necessary to discuss such difficulties and to make recommendations regarding future trials in the area.

One key difficulty encountered was the heterogeneity in outcome measures used across studies. One possible reason for this is the lack of assessment tools specifically designed or adapted for individuals with ASD. Development and validation of measures for use with this client group, to assess both core features of ASD and co-occurring symptoms of mental disorder, would improve the specificity of findings in future trials. However, it is acknowledged that this is a time-consuming and ongoing process and it is argued that in the interim more consistent usage of pre-existing outcome measures across studies would also be beneficial. More recent studies targeting social skills in individuals with CBT have taken this approach, with several research groups using the Social Responsiveness Scale as a primary outcome measure (Constantino & Gruber, 2005), which has improved comparability across studies.

The fact that the majority of included studies did not specify a primary outcome measure was also problematic. This complicated the quantitative synthesis process,

particularly in studies in which a high number of outcome measures were utilised and/ or in studies using different measures to assess a range of constructs. Whilst a system was devised in order to provide consistency in the selection of which measure/s to include in the analysis (see Section 2.5.3.1), some element of subjectivity inevitably remained, threatening the validity of the results. Furthermore, the lack of specified primary outcome measures meant that it was not possible to fairly calculate a combined effect size across all studies and analysis was instead segregated across report types. It would therefore be particularly beneficial for researchers conducting future trials to identify primary outcome measures a priori.

Another difficulty across many studies was the fact that outcome measures were predominantly self- or informant-rated. Due to the nature of the intervention, it was not possible to blind or mask raters, leaving trials vulnerable to performance and detection bias. This appears to be something which is improving, with more recently published studies being more likely to include clinician-rated measures, although even on these occasions clinicians were not always adequately blinded to treatment group. In order to make more valid conclusions regarding meaningful changes following treatment, future studies should include measures rated by independent clinicians blinded to treatment group. Improved randomisation, allocation concealment procedures and independent management of data would also be beneficial.

In addition to the aforementioned difficulties relating to outcome measures, a number of other methodological limitations of included studies were identified during quality appraisal. Small sample size is a persistent problem across studies in this area, with a high number of trials being more accurately described as pilot or feasibility studies. This makes it difficult to draw firm conclusions from the research to date. As discussed in Chapter 1, the spectrum of features of ASD means that it is not surprising that heterogeneity exists within

the literature. Larger-scale studies would enable the examination of subgroups based on clinical characteristics. It is clear that further larger-scale and robust clinical trials are needed in the area in order to increase generalisability and to enhance our understanding of the use of CBT with individuals with ASD.

Furthermore, many studies did not report sufficient information regarding participant engagement and fidelity. Information regarding therapist competence and description of interventions was also poor in many cases. It would perhaps be advantageous for researchers to make their intervention protocols available publicly, in order to increase transparency and to enable further investigation of the content and adaptation of CBT across studies.

In summary, the difficulties encountered during the current study have led to the following recommendations which should be considered by groups conducting future clinical trials of CBT with individuals with ASD:

- Small-scale studies should be clearly described as feasibility or pilot trials. Larger-scale definitive trials are essential for the development of the current knowledge base in this area
- Methods and interventions should be described fully, in line with CONSORT recommendations. Standardised reporting and a more uniform approach to study design would help to minimise heterogeneity across studies
- Allocation concealment, randomisation and blinding procedures should be considered a priority and should be described fully
- Where possible, more consistent usage of pre-existing outcome measures across studies would be beneficial in order to increase comparability across trials
- Researchers should specify a primary outcome measure a priori
- Participant engagement and fidelity should be clearly reported

It is suggested that the implementation of such recommendations in future clinical trials would subsequently improve the validity of future meta-analytic studies in the area. Further meta-analytic research incorporating higher quality and larger-scale trials could potentially strengthen the findings of the current research, whilst enabling a more thorough investigation of potentially moderating factors.

4.7 Conclusion

The primary aim of the current research was to systematically appraise the evidence for using CBT in the treatment of either core features of ASD or co-occurring mental disorder in individuals with ASD across the lifespan. Fifty eligible studies involving children, adolescents and adults with ASD were located, 48 of which were included in quantitative synthesis. Following the exclusion of outliers and studies deemed to be at a high risk of bias, results indicated that CBT has a "small" to "medium" treatment effect in the treatment of both core features of ASD or co-occurring mental disorder in individuals with ASD, when based on informant- and clinician-rated outcomes. In contrast, CBT was not found to be superior to control when self-reported outcome measures were utilised. Preliminary evidence indicated that CBT may be more effective for the treatment of children and adolescents with ASD than adults whilst individual and group CBT appeared to be equally effective. However, subgroup analysis was severely limited by a lack of studies, threatening the validity of the findings, and these conclusions should therefore remain tentative until further research is conducted. Future larger-scale clinical trials are needed to further explore the effectiveness of CBT in this client group, with well characterised samples, clearly defined primary outcome measures and adequate randomisation, allocation concealment and blinding.

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Appendices

Appendix A- Manuscript submitted for publication

Effectiveness of cognitive behavioural therapy with people who have autistic spectrum disorders: A systematic review and meta-analysis

Lisa Weston

University of East Anglia

Joanne Hodgekins

University of East Anglia

Peter E Langdon

University of Kent & Hertfordshire Partnership University NHS Foundation Trust

Author Note

Lisa Weston, Department of Clinical Psychology, Norwich Medical School, University of East Anglia, Norwich; Joanne Hodgekins, Department of Clinical Psychology, Norwich Medical School, University of East Anglia, Norwich; Peter E Langdon, Tizard Centre, University of Kent, Canterbury & Broadland Clinic, Hertfordshire Partnership University NHS Foundation Trust in Norfolk.

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LW and PL initially conceived the design of this study, and JH helped refine the earlier design. LW conducted the searches and analysis. Both PL and LW wrote the initial draft and all authors contributed and approved the final manuscript.

All authors declare they have no conflict of interest.

Correspondence concerning this article should be addressed to Dr Peter Langdon, Tizard Centre, University of Kent, Canterbury, CT2 7LR. Email: P.E.Langdon@kent.ac.uk

Abstract

The aims of this study were to undertake a meta-analytic and systematic appraisal of the literature investigating the effectiveness of cognitive behavioural therapy (CBT) when used with individuals who have autistic spectrum disorders (ASDs) for either a) affective disorders, or b) the symptoms of ASDs. Following a systematic search, 48 studies were included. CBT, used for affective disorders, was associated with a non-significant small effect size, *g* = .24, for self-report measures, a significant medium effect size, *g* = .66, for informant-report measures, and a significant medium effect size, *g* = .73, for clinician-report measures. CBT, used as a treatment for symptoms of ASDs, was associated with a small non-significant effect size, *g* = .25, for self-report measures, a significant small effect size, *g* = .48, for informant-report measures, a significant medium effect size, *g* = .65, for clinician-report measures, and a significant small effect size, *g* = .35, for task-based measures. Sensitivity analyses reduced effect size magnitude, with the exception of that based on informant-report measures for the symptoms of ASDs, which increased, *g* = .52. Definitive trials are needed to demonstrate that CBT is an empirically validated treatment for use with people who have ASDs.

KEYWORDS: Autism, Asperger syndrome, Pervasive Developmental Disorder, Cognitive Behaviour Therapy, Effectiveness, Neurodevelopmental Disorders.

Effectiveness of cognitive behaviour therapy with people who have autistic spectrum disorders: A systematic review and meta-analysis

Autism spectrum disorders (ASDs) are a range of neurodevelopmental disorders characterised by difficulties with social communication and interaction across contexts, as well as restricted and repetitive patterns of behaviour, interests and activities. The phenotype incorporates a range of symptoms across multiple domains, including cognitive, behavioural, affective and sensory symptoms (Volkmar, Paul, Klin, & Cohen, 2005; Wiggins *et al.*, 2015). Sleeping and eating difficulties, synaesthesia, as well as affective dysregulation, and difficulties with initiation, planning and organisation are often present (Baron-Cohen, 2008; Wiggins *et al.*, 2015). The prevalence amongst 4 year olds has been estimated to be approximately 13.4 per 1000 (Christensen *et al.*, 2016), while the adult prevalence has been estimated to be 9.8 per 10000 (Brugha *et al.*, 2011).

There has been a marked increase in psychosocial interventions that aim to treat the symptoms or features of ASDs. In the United Kingdom, the National Institute for Health and Care Excellence (2012a) recommended that people with ASDs should be offered age-appropriate psychosocial interventions for comorbid mental health problems and the core symptoms of ASDs. There are a large number of interventions claiming to treat symptoms of ASDs, even though the evidence base is poor (Matson, Adams, Williams, & Rieske, 2013). However, there is evidence to support the use of applied behaviour analysis in the treatment of symptoms of ASDs, and the authors of a Cochrane review concluded that early and intensive behavioural interventions can lead to improvements in adaptive, and communicative behaviour, as well as social skills (Reichow, Barton, Boyd, & Hume, 2012). Nevertheless, there are few studies examining the effectiveness of these types of interventions with adults, as opposed to children, with ASDs (Wright, Brooks, D'Astous, & Grandin, 2013).

Alongside this, psychiatric comorbidity amongst people with ASDs is elevated (Green, Gilchrist, Burton, & Cox, 2000; Kim, Szatmari, Bryson, Streiner, & Wilson, 2000; Lugnegård, Hallerbäck, & Gillberg, 2011; Rescorla, 1986; Russell & Sofronoff, 2005), prompting many to consider how to adapt and deliver psychological therapies for children, adolescents and adults with ASDs. Several meta-analytic or narrative reviews involving studies that recruited samples of children and adolescents have been completed in this area examining the effectiveness of cognitive behavioural therapy (CBT) for anxiety disorders or social skills training (Ho, Stephenson, & Carter, 2014, 2015; Kreslins, Robertson, & Melville, 2015; Spain & Blainey, 2015; Sukhodolsky, Bloch, Panza, & Reichow, 2013; Ung, Selles, Small, & Storch, 2015). While all of the aforementioned studies have concluded that CBT and associated interventions for anxiety amongst children with ASDs appear to be

promising, none have considered CBT across the lifespan, which is clearly relevant because individuals with ASDs experience atypical development. Further none of the previously completed meta-analyses have: (a) considered CBT, as opposed to applied behavioural analysis, when used as a treatment for the actual symptoms or features of ASDs, rather than the treatment of anxiety disorders, (b) included studies involving adult participants, and (c) included other affective disorders, such as depression, alongside anxiety disorders. In order to address these weaknesses, we completed a comprehensive meta-analysis and systematic review of the literature which aimed to investigate the effectiveness of cognitive behavioural therapy across the lifespan for either (a) affective disorders more broadly, or (b) the symptoms and features associated with ASDs. A supplementary aim was to investigate whether there are differences in outcome for children, adolescents and adults.

Method

Relevant studies were identified by systematic searches of the following electronic databases: PsycINFO; MEDLINE; CINAHL Plus, Web of Science, as well as Google Scholar. The Cochrane Library was searched to identify any existing systematic reviews. The key search terms and how they were combined are found in Table 1. Terms were searched using English and American terminology, spelling, and truncation to ensure that all variant word endings were identified. Alongside this, the ancestry method was used to identify any further papers that may have met eligibility criteria. The grey or fugitive literature was also searched in an attempt to minimise publication bias. An initial search was completed via http://www.opengrey.eu which includes research reports, dissertations and conference papers. Dissertation Abstracts – International and the Comprehensive Dissertation Index were also searched, as well as trial registers. The final search for studies was completed on 29 January 2016. The review was registered with PROSPERO, an international database of systematic reviews in health and social care, in order to provide transparency to the review process and to avoid duplication of research effort (Registration Number: CRD42015017766).

Insert Table 1 about here.

Initially, titles and abstracts were screened for eligibility, and studies were included if all of the following criteria were met: (a) participants had a diagnosis of Autism Spectrum Disorder (or autistic disorder, Asperger disorder, childhood disintegrative disorder or pervasive developmental disorder not specified prior to the publication of DSM-V), and diagnosis was made by a qualified clinician and/or using a standardised diagnostic assessment; (b) studies used a control or comparison group design, e.g. waiting list or treatment as usual (TAU), with or without

randomisation; (c) a clinician-led CBT intervention, either individual or group-based, incorporating both cognitive and behavioural components was used. Interventions in which CBT theory and principles were utilised to teach or improve behavioural patterns, e.g. social skills, were included, provided that this was explicitly stated; (d) use of at least one validated and standardised outcome measure of either core features of ASDs, i.e. difficulties in social interaction, impaired social communication or restricted or repetitive patterns of behaviour and interests, or co-occurring symptoms of mental disorder, e.g. anxiety, depression,; and (e) written in English.

Studies that aimed to treat affective disorders or symptoms of ASDs were analysed separately for two reasons: (a) the "target" of the intervention was separate in these studies, with one group focusing on trying to treat symptoms of affective disorders, while the other attempted to reduce difficulties or symptoms associated with having an ASD, and (b) CBT for either incorporated psychoeducation, skills teaching, skills practice, behavioural experiments, and cognitive restructuring. However, the description of the interventions across studies was at times sparse, and it was at times difficult to ascertain the degree to which cognitive restructuring was used within some of the interventions. As a consequence, it was clear that the intervention incorporated both cognitive and behavioural components for some studies, while for others, this was less clear, although in all instances, the interventions were described as using methods drawn from cognitive behavioural therapy. However, it is important to bear in mind that CBT incorporates both cognitive and behavioural components, although for some disorders there is a clear focus on behavioural interventions (e.g. exposure and response prevention) when delivering CBT. As mentioned in the paragraph below, we excluded any studies that solely made use of behavioural methods alone.

Studies were excluded if any of the following criteria were met: (a) the methodology used was a single case, case series, qualitative, meta-analysis or review articles; (b) the design of the study was such that the effect of the CBT intervention could not be isolated from other treatment methods, e.g. psychotropic medication; (c), the primary intervention was applied behavioural analysis or behaviour modification, or behavioural activation as a stand-alone treatment; and (d) the dataset had been used within a previously included study to avoid double counting of data (Senn, 2009). No limits were applied to the date of publication, age of participants or whether the study has been published in a peer review journal.

Studies that were non-randomised were not excluded. While this represents an inherent weakness by increasing the risk of bias, the decision was made to include non-randomised studies at this stage considering the likelihood that few definitive (Phase III) trials within this area have been completed.

Following the removal of duplicate studies, the systematic search of the electronic databases returned 2332 potentially eligible studies. Following an initial screen of the titles and abstracts, 2263 were excluded. In addition to the remaining 69 studies, a further 102 were identified using the ancestry method, and two were located from searching the grey literature. The resulting total number of papers retrieved were 173, six of which were protocols. The authors of protocols were contacted directly to try to source outcome data.; two of these research groups provided data, while the remaining four did not respond and were excluded. A further 107 papers were excluded because they did not include a comparison or control group, five were excluded because they had made use of a pre-existing dataset that had been previously included, four were excluded because they did not include cognitive-behavioural components within the intervention, one was excluded due to a lack of validated or standardised outcome measures, one was excluded because the effects of CBT could not be isolated and one was excluded because we were unable to trace the paper.

The remaining 50 studies met the eligibility criteria, although two studies were excluded at this stage because the published data were insufficient and we could not calculate effect sizes; the authors did not respond to our request for further data (DeRosier, Swick, Davis, McMillen, & Matthews, 2011; Provencal, 2003). Forty-eight studies, involving 2099 participants (1081 CBT, 1018 control) were therefore included in the quantitative synthesis. Figure 1 depicts a PRISMA flow diagram (Moher, Liberati, Tetzlaff, & Altman, 2009), outlining the identification, screening and inclusion or exclusion of articles throughout the process. Reasons for article rejection are clearly indicated. The eligibility criteria were applied by two authors (LW & PL) independently, and inter-rater reliability was excellent, 96.5%, k = .92, 95% *CI* [.85, .98].

Insert Figure 1 about here.

The standardised mean difference (SMD) was calculated to estimate the difference between the treatment and control conditions. Cohen's d was transformed into Hedge's g (Hedges, 1981) using correction factor J to correct for possible positive bias due to small sample sizes. The magnitude of Hedge's g was interpreted using Cohen's convention as small (0.2), medium (0.5), and large (0.8). The variance and standard error of g for each study was calculated. As outcome measures may take the form of self-, clinician- or informant-reports, and there is evidence to suggest that people with ASD may have difficulties with judging their own social or communicative behaviour, (Baron-Cohen, Jolliffe, Mortimore, & Robertson, 1997) effect sizes were calculated individually for each type of outcome measure where possible (i.e. outcome measures were grouped

as either self-report, informant-report, clinician-report, or task-based, where participants were invited to complete a task, such as an emotion recognition task using faces).

The analysis was undertaken using RevMan Version 5.3. A random effects model was used for the following reasons: (a) heterogeneity was anticipated as data came from a variety of sources and we could not assume a common effect size; and (b) inferences made from random effects models are unconditional and can be applied to a population of studies larger than the sample.

Heterogeneity was thought to be associated with whether CBT was delivered as a group or individually, the age range of participants, and symptom severity. This was explored using the I^2 statistic, which describes the percentage of variation across studies due to heterogeneity, rather than chance (Higgins & Thompson, 2002). The I^2 statistic has been chosen rather than Cochran's *Q* since it enables quantification of the effect of heterogeneity, providing a measure of the degree of inconsistency in results (Higgins & Thompson, 2002), and it does not inherently depend on the number of studies included in the meta-analysis (Higgins, Thompson, Deeks, & Altman, 2003). The degree and impact of heterogeneity was assessed using the categorisation of low (25%), medium (50%) and high (75%), in addition to a quality assessment of the methodology (Higgins *et al.*, 2003). A sensitivity analysis was also undertaken. Outliers were removed and the weighted mean effect size was recalculated. Publication bias was assessed graphically using funnel plots, plotting summary effect size against standard error (Light & Pillemer, 1984); a skewed and asymmetrical plot may indicate a publication bias (Iyengar & Greenhouse, 2009). Fail-safe N (Rosenthal, 1991) was used to assess the impact of bias by calculating an estimate of the number of new studies averaging a null result that would be required to bring the overall treatment effect to non-significance. A figure exceeding 5n+ 10 would indicate that the results could be considered robust to the effects of publication bias (Rosenthal, 1991).

Quality appraisal of included studies was undertaken by two authors (LW & PL) independently using the National Institute for Health and Care Excellence Quality Appraisal Checklist for Quantitative Intervention Studies (National Institute for Health and Care Excellence, 2012b), bearing in mind that the use of such scales has been criticised in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidance (Liberati *et al.*, 2009). There was 'moderate' agreement between the two authors for internal validity, 72.0%; k = .48; 95% *CI* [.26, .71], and 'good' agreement for external validity, 84.0%; k = .66; 95% *CI* [.45, .86).

Results

Quality Appraisal

The key characteristics of the 50 included studies are found in Appendix A, while the summary quality appraisal ratings for each study are found in Appendix B. A persistent problem across all studies was small sample size, contributing to reduced power. Freitag et al. (2015) included the highest number of participants (101 CBT, 108 control), whilst eight of the studies included in the quantitative synthesis involved less than ten participants per group. Several of these studies were defined by the authors as pilot or feasibility trials. However, a number of studies that were not called pilot or feasibility trials, were in fact lower in quality and had smaller sample sizes than many clearly defined pilot or feasibility trials. Quality appraisal and risk of bias were therefore considered on a study by study basis and sensitivity analysis was conducted by removing studies deemed to be at high risk of bias, rather than those labelled as pilot or feasibility trials.

Other common problems included the lack of reporting on participant engagement within intervention sessions, poor reporting on missing data, and minimal information on fidelity checks. Very few studies reported adequate allocation concealment and ten of the studies included in meta-analysis were non-randomised, contributing to a high risk of allocation bias. Due to the nature of the interventions involved, it is not possible for investigators to blind participants (and often informants) to intervention allocation. However, blinding of outcome assessors was possible but was not conducted in the majority of studies, contributing to detection bias.

A final common difficulty across studies was failure to specify a primary outcome measure. This complicated the meta-analysis, particularly in studies where a high number of outcome measures were utilised or different measures were used to assess a range of constructs. The lack of measures validated for use with individuals with ASD was noted, although this is clearly a wider issue that needs attention.

Cognitive Behavioural Therapy for Affective disorders. Twenty-four of the included studies aimed to examine the effectiveness of CBT for affective disorders, with the bulk attempting to treat anxiety disorders, with others targeting depression or emotion regulation difficulties. Seventeen of these studies involved children and adolescents, whilst four included adult participants. Three studies included both adolescent and adult participants and were therefore assigned to a 'Mixed Age' subgroup for analysis (McGillivray & Evert, 2014; Pahnke, Lundgren, Hursti, & Hirvikoski, 2014; Russell *et al.*, 2013). Fifteen of the 24 studies examined group-based CBT, whilst eight reported on individual CBT. The remaining study involved 21 group sessions, as well as three individual sessions (Langdon *et al.*, 2016; Langdon *et al.*, 2013). Since this study was predominantly group-based, the decision was made to include it in the 'group-based' subgroup when analysing mode of CBT delivery.

The majority of studies targeted anxiety (15 of the 24 studies). As this was such a large group, a subgroup analysis was conducted to assess potential variations of treatment effects across age groups within this subset of studies. This included studies investigating the treatment of anxiety disorders that had been included in earlier meta-analytic work (Sukhodolsky *et al.*, 2013; Ung *et al.*, 2015), but also included additional studies; two studies targeted symptoms of obsessive compulsive disorder (Russell *et al.*, 2013; Russell, Mataix-Cols, Anson, & Murphy, 2009) were also included within this subset, as was a study investigating depression, anxiety and rumination (Spek, van Ham, & Nyklíček, 2013) and a study investigating depression, anxiety and stress (McGillivray & Evert, 2014). In the latter two studies, only outcomes pertaining specifically to anxiety were used to reduce heterogeneity within the quantitative synthesis as much as possible. In total, 19 studies were included within the anxiety subset. Of the remaining five studies, one targeted anger (Sofronoff, Attwood, Hinton, & Levin, 2007), one targeted general emotional regulation skills (Scarpa & Reyes, 2011), one targeted insomnia (Cortesi, Giannotti, Sebastiani, Panunzi, & Valente, 2012), one targeted self-esteem, quality of life and sense of coherence (Hesselmark, Plenty, & Bejerot, 2014) and one targeted stress and emotional distress (Pahnke *et al.*, 2014).

Fourteen studies were defined as randomised controlled trials, seven of which compared a CBT intervention with a waitlist control group, and three compared CBT to treatment as usual. Three randomised controlled trials compared CBT to a non-CBT group-based treatment: either a social recreational program (Hesselmark *et al.*, 2014; Sung *et al.*, 2011) or an anxiety management group (Russell *et al.*, 2013). The final randomised controlled trial (Cortesi *et al.*, 2012) compared a CBT group to a group which received a placebo drug. This study also included a condition in which participants received melatonin and a condition in which participants received both melatonin and CBT. Participants from these intervention arms were not included as the use of a drug-based comparison group was not utilised in any other included study.

Three of the 24 studies investigating CBT for the treatment of affective disorders were quasi-experimental or non-randomised (Clarke, 2012; McGillivray & Evert, 2014; van Steensel, Dirksen, & Bögels, 2014), whilst seven were called pilot studies. Three of the seven pilot studies within this group were randomised, whilst four were not, and six compared a CBT intervention to a waitlist control group, whilst one compared CBT to treatment as usual.

As anticipated, there was extensive variation in the outcome measures used across studies. Many studies included outcome measures from various sources, with the most common report type being self-report within studies targeting co-occurring symptoms of affective disorder, followed closely by informant-report (usually parent) outcomes and clinician-rated outcomes. Only one study

within this group used a task-based outcome measure (Cortesi *et al.*, 2012). There was also considerable variation in the intensity and content of intervention. The number of sessions ranged from four to 50, whilst the length of each session ranged from 40 to 180 minutes. The majority of studies used a structured protocol (22 out of 24), with 21 of the studies utilised "traditional" CBT methods, with common components including role play, exposure and teaching/ rehearsal of emotional regulation skills. Common adaptations to CBT included an increased emphasis on behavioural rather than cognitive components, the use of social stories and vignettes and increased involvement of family members. One of the studies (Hepburn, Blakeley-Smith, Wolff, & Reaven, 2015) piloted a videoconferencing CBT intervention designed for delivery in a small, multi-family group format, whilst another study (Spek *et al.*, 2013) used a modified version of Mindfulness Based Therapy with cognitive elements omitted. Another used a modified Acceptance and Commitment Therapy protocol and participants in the CBT group engaged in daily mindfulness exercises in addition to structured intervention sessions.

Cognitive Behavioural Therapy for ASD. There were 24 included studies that examined the effectiveness of CBT for symptoms or features of ASD. One study investigated both the effect of CBT on social skills and anxiety (White *et al.*, 2013) and the outcomes pertaining to social skills were included in the meta-analysis. Another intervention study focused upon both social communication and anxiety, but the findings were reported in two separate papers (Fujii *et al.*, 2013; Wood, Fujii, Renno, & Van Dyke, 2014); the decision was made to exclude Fujii et al. (2013) as inclusion would have led to the double counting of data. Provencal (2003) and DeRosier *et al*. (2011) were excluded as attempts to obtain data required to calculate effect sizes were unsuccessful.

The majority of studies targeted social skills (18 of the 24 studies included in quantitative synthesis), while of the remaining six studies, four targeted Theory of Mind (Begeer *et al.*, 2011; Begeer *et al.*, 2015; Ozonoff & Miller, 1995; Solomon, Goodlin-Jones, & Anders, 2004), one targeted affectionate communication (Andrews, Attwood, & Sofronoff, 2013) and one targeted the perception of facial emotions (Baghdadli *et al.*, 2013). A number of studies targeted both social skills and aspects of social cognition. In these circumstances, the primary outcome measure was included, but there was extensive variation in outcome measures across studies. In situations in which the primary outcome measure was not specified, only outcome measures pertaining to social skills were included to avoid comparisons of different constructs across report types. The most common type of outcome measure was informant-report, followed by self-report. In contrast to studies investigating the effectiveness of CBT for affective disorders, seven studies within this group utilised a task-based measures, for example Theory of Mind tasks.

Fourteen of the studies were randomised controlled trials, one of which is the only Phase III trial in this area to date (Freitag et al., 2015). This study compared CBT to treatment as usual, whilst thirteen of the RCT's compared a CBT intervention with a waitlist control group. The final RCT (Soorya *et al.*, 2015) compared CBT to a facilitated play active control group. Three of the remaining ten studies were quasi-experimental or non-randomised, and seven were labelled pilot studies. These studies were included in initial analysis but the quasi-experimental studies involved a variety of control groups: Ozonoff & Miller (1995) compared CBT to no treatment, Laugeson *et al*. (2012) used a waitlist control group and Laugeson *et al.* (2014; Laugeson & Park, 2014) reported the use of an active control group based on a non-CBT social skills curriculum ("Superskills", Coucouvanis, 2004). Three pilot studies used a waitlist control group, two compared CBT to treatment as usual and one compared CBT to "no intervention" (Koning, Magill-Evans, Volden, & Dick, 2013). The remaining study reported the use of an active control group with sessions consisting predominantly of leisure activities (Baghdadli *et al.*, 2013). Six of the seven pilot studies within this group were randomised, whilst the remaining study was quasi-experimental (Turner-Brown, Perry, Dichter, Bodfish, & Penn, 2008).

There was considerable variation in the intensity and content of intervention. The number of sessions ranged from five (Andrews *et al.*, 2013) to 70, with Laugeson *et al.* (2014) reporting on an intervention in which children received 30 minute sessions five days per week over a period of 14 weeks. The length of each session ranged from 30 minutes to whole day sessions. The majority of studies investigating the effectiveness of CBT for core features of ASD used a structured protocol (22 out of 24). In terms of treatment content, studies within this group less commonly reported "traditional" CBT methods. Some studies did not directly refer to cognitive behavioural therapy *per se*, but they explicitly mentioned the inclusion of both cognitive and behavioural techniques in the intervention, and therefore met inclusion criteria for the current study. Content commonly included direct social skills teaching and role play, emotional identification work and problem-solving exercises or discussions. Common adaptations included increased use of social stories and vignettes, increased use of role play and the involvement of family members in intervention sessions and homework activities.

Effectiveness of CBT for reducing symptoms of affective disorders

Self-report outcome measures. Seventeen studies, including 645 participants (329 CBT, 316 control), included self-reported outcome measures. One study utilised a relevant self-reported outcome measure but it was not possible to include this in the analysis as an attempt to obtain the data necessary to calculate the effect size was unsuccessful (Storch *et al.*, 2013). The outcome

measures used varied considerably across studies. A random-effects meta-analysis of these trials indicated a small but non-significant effect favouring CBT over waiting-list, treatment as usual or active control as reported by participants, g = .24; 95% *CI* [-.05, .53], z = .11, p = .11, (Figure 2). The analysis revealed a significant amount of heterogeneity, with I^2 indicating that 69% of the variability in estimated treatment effect was due to heterogeneity rather than chance, p < .001.

As one study, had a SMD (g = 2.64) considerably higher than the other included studies, g ranged from -.39 to .85, a sensitivity analysis was conducted and this outlier was removed (Chalfant, Rapee, & Carroll, 2007). Exclusion of this study resulted in no significant treatment effect, g = .10; 95% *CI* [-.06, .27], z = 1.21, p = .23, and I^2 reduced markedly to 4%, p = .41, indicating the considerable impact that the inclusion of this study had on the pooled SMD. A further sensitivity analysis to remove studies deemed to be at a high risk of bias (Clarke, 2012; Hesselmark *et al.*, 2014; McGillivray & Evert, 2014; Reaven *et al.*, 2009; Russell *et al.*, 2009) resulted in a very similar effect, g = .09; 95% *CI* [-.12, .30], z = .84, p = .40.

Informant-report outcome measures. Sixteen studies, including 620 participants (325 CBT, 295 control), made use of informant-reported outcome measures. One study utilised a relevant informant-reported outcome measure but was excluded because we did not obtain the data necessary to calculate the effect size (Pahnke *et al.*, 2014). The outcome measures used varied considerably across studies. The meta-analysis of these trials indicated a significant medium effect favouring CBT over waiting-list, treatment as usual or active control as reported by informants, g = .66; 95% *CI* [.29, 1.03], z = 3.49, p < .001, (Figure 3). The analysis indicated a significant amount of heterogeneity, with I^2 indicating that 78% of the variability in estimated treatment effect was due to heterogeneity rather than chance, p < .001.

Again, Chalfant et al. (2007) had a SMD, g = 4.27, considerably higher than the other included studies, g ranged from -.39 to 1.21, and a sensitivity analysis was therefore conducted to remove this outlier. Exclusion of this study resulted in a lower treatment effect, g = .47; 95% *CI* [.25, .69], z = 4.17, p < .001, although it remained statistically significant. I^2 reduced to 38%, p = .07, again indicating the impact that the inclusion of this study had on the pooled SMD. A further sensitivity analysis to remove studies deemed to be at a high risk of bias (Clarke, 2012; Hepburn *et al.*, 2015; Reaven *et al.*, 2009; Scarpa & Reyes, 2011) resulted in a very similar effect, g = .45; 95% *CI*, .18 to .72, z = 3.24, p = .001.

Clinician-rated outcome measures. Thirteen studies, including 514 participants (262 CBT, 252 control), made use of clinician-rated outcome measures, but there was substantial variation in the type of choice of measure. Two of these studies presented dichotomous data (Chalfant *et al.*,

2007; van Steensel *et al.*, 2014). In order to include these studies in a random-effects meta-analysis, the odds ratio was calculated and re-expressed as a SMD (Chinn, 2000). A random-effects meta-analysis using the Generic Inverse Variance method was conducted as estimates of effect were calculated for the two aforementioned studies. The analysis indicated a significant medium effect favouring CBT over waiting-list, treatment as usual or active control as rated by clinicians, g = .73; 95% *CI* [.38, 1.08], z = 4.05, p < .001, (Figure 4). The analysis again indicated a significant amount of heterogeneity, with I^2 indicating that 69% of the variability in estimated treatment effect was due to heterogeneity rather than chance, p < .001.

Two studies (Chalfant *et al.*, 2007; Wood *et al.*, 2009) had a SMD, g = 2.51 and g = 2.47 respectively, considerably higher than the other included studies, g ranged from -.31 to 1.38, and a sensitivity analysis was conducted to remove these outliers. Exclusion of these studies resulted in a lower treatment effect, g = .52; 95% *CI* [.27, .77], z = 4.06, p < .001, although it remained statistically significant. I^2 reduced to 36%, p = .11, again indicating the impact that the inclusion of these studies had on the pooled SMD. A further sensitivity analysis to remove studies deemed to be at a high risk of bias (Russell *et al.*, 2009; van Steensel *et al.*, 2014) resulted in a very similar effect, g = .59; 95% *CI* [.33, .85], z = 4.48, p = <.001.

Task-based outcome measures. As only one study made use of this type of outcome measure, if was not possible to calculate the pooled SMD.

Effectiveness of CBT for symptoms associated with autism

Self-report outcome measures. Nine studies (370 participants; 192 CBT, 178 control), investigated the effectiveness of CBT in treating symptoms associated with ASD and included appropriate self-reported outcome measures. As indicated in Figure 5, a random-effects meta-analysis of these trials indicated a small, but non-significant effect favouring CBT over waiting-list, treatment as usual or active control, as reported by participants, g = .25; 95% *CI*, [-.03, .53], z = 1.77, p = .08. Heterogeneity was not significant, although I^2 indicated that 40% of the variability in estimated treatment effect was due to heterogeneity rather than chance, p = .10. A sensitivity analysis to remove studies deemed to be at a high risk of bias (Gantman, Kapp, Orenski, & Laugeson, 2012; Laugeson *et al.*, 2012; Turner-Brown *et al.*, 2008) resulted in no significant treatment effect, g = .10; 95% *CI* [-.24, .45], z = 0.58, p = .56.

Informant-report outcome measures. Eighteen studies (950 participants; 480 CBT, 470 control) were included in this analysis revealing a significant small effect favouring CBT over waiting-list, treatment as usual or active control as reported by informants, g = .48; 95% *CI* [.30, .65], z =

5.39, $p < .001$. Heterogeneity was not significant, although I^2 indicated that 36% of the variability in estimated treatment effect was due to heterogeneity rather than chance, $p = .06$. A sensitivity analysis to remove studies deemed to be at a high risk of bias (Gantman *et al.*, 2012; Ichikawa *et al.*, 2013; Koning *et al.*, 2013; Laugeson *et al.*, 2012) resulted in a slightly larger medium treatment effect, $g = 0.52$; 95% *C*I [0.34, 0.70], $z = 5.63$, $p < .001$, with a small reduction in heterogeneity, $I^2 = 33\%$, $p = .12$.

Clinician-rated outcome measures. Six studies, including 153 participants (79 CBT, 74 control) were included. One of these studies presented the outcome as dichotomous data, and therefore the odds ratio was calculated and expressed as a SMD (Koenig *et al.*, 2010); the generic inverse variance method the estimate of effect was calculated. The analysis indicated a significant "medium" effect favouring CBT over waiting-list, treatment as usual or active control as rated by clinicians, $g = .65$; 95% *CI* [.10, 1.21], $z = 2.30$, $p = .02$), (Figure 7). Heterogeneity was non-significant, although I^2 indicated that 47% of the variability in estimated treatment effect was due to heterogeneity rather than chance, $p = .10$.

One study had a SMD, $g = 2.43$ (Koenig *et al.*, 2010), considerably higher than the other included studies, *g* ranged from .08 to 1.51. Removing this outlier resulted in a lower treatment effect, $g = 0.47$; 95% *CI* [0.09, 0.85], $z = 2.40$, $p = .02$, although it remained statistically significant. I^2 reduced to 1%, p = .40, indicating the considerable impact that the inclusion of this study had on the pooled SMD. A further sensitivity analysis to remove studies deemed to be at a high risk of bias (Ichikawa *et al.*, 2013; Turner-Brown *et al.*, 2008; Wood *et al.*, 2014) resulted in a very similar but lower and non-significant treatment effect, $g = 0.44$; 95% *CI* [-.01, .89], $z = 1.90$, $p = .06$). It is highly likely that this is related to the fact that the exclusion of the above studies left only two studies in the analysis, and as such, this analysis should be interpreted with marked caution.

Task-based outcome measures. Seven studies, incorporating 237 participants (117 CBT, 120 control), were included in this analysis, which revealed a significant small effect in favour of CBT over waiting-list, treatment as usual or active control on task-based measures, $g = 0.35$; 95% *CI* [0.09, 0.61], $z = 2.67$, $p = .008$. Heterogeneity was not an issue, $I^2 = 0\%$, $p = .58$. Removing studies deemed to be at a high risk of bias (Baghdadli *et al.*, 2013; Koning *et al.*, 2013; Ozonoff & Miller, 1995; Solomon *et al.*, 2004) resulted in a very similar non-significant effect size, $g = 0.30$; 95% *CI* [-.12, .72], $z = 1.42$, $p = .16$). Again, it is highly likely that this is related to the fact that the exclusion of the above studies left only three studies in the analysis should therefore be interpreted with marked caution.

The effectiveness of CBT across differing age groups

Further subgroup analysis using self-report outcome measures was not completed because our initial analysis indicated that CBT was not superior to control conditions when used to treat either affective disorders of symptoms associated with autism. While there were 16 studies that made use of informant-report outcome measures when treating affective disorders, none of these included adult participants, and only one study looking at the treatment of symptoms related to autism included adult participants. As such, a subgroup analysis based on informant-report outcome measures was not completed.

Subgroup analysis using clinician-rated outcome measures across different age groups was possible, but only for studies that aimed to treat affective disorders. There was substantial variability that appeared due to genuine subgroup differences, rather than sampling error, I^2 = 80.2%, p = .006, and a large combined effect size in favour of CBT for studies involving children and adolescents, g = .95; 95% *CI* [.55, 1.35], z = 4.64, p < .001, but not for studies involving adults, g = -.04; 95% *CI* [-.50, .43], z = 0.15, p = .88. Exclusion of two outliers (Chalfant *et al.*, 2007; Wood *et al.*, 2009) from the studies involving children and adolescents resulted in a lower but significant effect size, g = .67; 95% *CI* [.42, .91], z = 5.28, p < .001. The comparison between studies involving children, adolescents and adults is inherently problematic and should be interpreted cautiously because only two studies involving adults were included (Figure 9).

Publication Bias

Visual inspection of Funnel plots did not reveal significant asymmetry for self-reported outcome measures used within studies that aimed to treat affective disorders. Fail-safe N was not calculated because CBT was not superior to control conditions. A similar analysis could not be completed for studies that focused on symptoms related to autism because there were less than ten.

Turning to informant-based outcome measures, used for both studies that focused on affective disorders and symptoms associated with autism, no significant asymmetry was found. For studies involving affective disorders, 281 new studies averaging a null result would be required to bring the overall treatment effect to non-significance. For studies targeting symptoms related to autism, 287 new studies averaging a null result would be needed to again bring the overall treatment effect to non-significance. These figures exceed 5n + 10, and the conclusion that these findings are robust to publication bias is valid.

Considering clinician-rated outcome measures, there was no significant asymmetry for studies that treated affective disorders, while a Funnel plot was not created for studies that treated

symptoms of autism because there were fewer than ten. Fail-safe *N* revealed that 227 new studies averaging a null result would be needed to bring the treatment effect to non-significance calculated using clinician-rated outcome measures taken from studies that treated affective disorders. The effect calculated using clinician-rated outcome measures taken from studies treating symptoms associated with autism would become non-significant if only 18 papers averaging a null effect were published suggesting that this finding may be subject to publication bias and influenced by the fewer papers in this area.

Whilst it was not possible to examine task-based outcome measures for studies that treated mental disorder, for studies that focused on symptoms related to autism, because the number of papers was less than ten, a Funnel plot could not be created. However, Fail-safe *N* revealed that only 5 new studies averaging a null effect size would bring the overall treatment effect to non-significance. This means that publication bias may feature, and the conclusions are heavily influenced by there being relatively few papers.

Discussion

The results of the meta-analysis indicated that cognitive behavioural therapy (CBT) is associated with a small to medium effect size when used to treat co-morbid affective disorders with children, adolescents, or adults who have ASDs, but this varied according to whether the outcome data was taken from self-report, informant-report, clinician-report, or task-based measures. CBT was associated with a small and non-significant effect size, g = .24, when the analysis was completed using self-report measures, and associated with significant heterogeneity; when studies at risk of bias were excluded, resulting in low heterogeneity, treatment was associated with a small non-significant effect size, g = .09. CBT was superior to control conditions when the analysis was completed with either informant- and clinician-report measures, both being associated with a medium effect size, but there was significant heterogeneity; a sensitivity analyses reduced heterogeneity, and revealed that CBT remained superior, and was associated with a medium effect size of, *g* = .45, and, *g* = .59, respectively.

Turning to consider CBT for symptoms associated with ASDs, the findings from the meta-analysis were very similar to that found for CBT when used to treat co-morbid affective disorders. CBT, when used as a treatment for the symptoms of ASDs, rather than affective disorders, was associated with an effect size that ranged from small to medium, again, dependent upon the type of outcome measure used. Using data from self-report measures, CBT was associated with a small non-significant effect size, *g* = .25, and while heterogeneity was not significant, excluding studies at risk of bias to reduce heterogeneity reduced the effect size; it remained small and non-significant, *g*

= .1. There was evidence that CBT was significantly beneficial when the analysis was based on informant-report measures, and resulted in a small effect size, *g* = .48, which increased to medium following our sensitivity analysis to account for heterogeneity, g = .52. Considering clinician-report measures, CBT was found to be significantly superior, and associated with a medium effect size, *g* = .65. Following the exclusion of studies thought to be at risk of bias to reduce heterogeneity, CBT was no longer superior, and associated with a non-significant medium effect size, g = .44. Task-based measures, which are both less subjective and completed by the participant, were also evaluated to determine whether CBT is an effective treatment for symptoms of ASDs. The initial findings were significantly in favour of CBT as an effective treatment, and associated with a small effect size, g = .35, but the exclusion of studies thought to be at higher risk of bias, led to a non-significant treatment effect, falling in the small range, *g* = .3.

Sub-group analysis based on the age of the participants was not completed for self-report measures as there was no evidence that CBT was superior to control conditions, nor was this possible for informant-based measures, as few studies involving adults also included an informant-based measure. It was only possible to undertake a sub-group analysis for the treatment of affective disorders based on clinician-report measures, and the findings indicated that CBT was superior and associated with a large effect size, *g* = .95, when used with children and adolescents, while following our sensitivity analysis, this reduced to a medium effect size, *g* = .67. These effect sizes are lower than that previously reported by Sukhodolsky *et al*. (2013) and Kreslins *et al.* (2015), with both previous meta-analyses having included fewer studies. Turning to consider adults, the results indicated that CBT was not superior to control conditions, and was associated with a small effect size, *g* = .04; interpreting this result is problematic because it is only based on two published studies.

Within the current meta-analysis, and those completed previously which focused on the treatment of anxiety amongst children and adolescents (Kreslins *et al.*, 2015; Sukhodolsky *et al.*, 2013; Ung *et al.*, 2015), there are substantial differences in treatment efficacy dependent upon the type of outcome measure included within the analysis. Self-report measures, in contrast to informant- and clinician-report measures, are not reliably associated with significant change following treatment. Within the current meta-analysis, this was the case for studies involving children, adolescents or adults who received treatment for affective disorders more broadly. This was also the case for studies where CBT was used to treat the symptoms of ASDs. As discussed previously by both Sukhodolsky *et al*. (2013) and Kreslins *et al.* (2015) it may be the case that individuals with ASDs have difficulties with reporting symptoms because of associated

developmental challenges (e.g. communication problems) faced by this population leading to difficulties with reliably reporting symptoms. Interestingly, Kreslins *et al.* (2015) suggested that children with ASDs may confuse symptoms of anxiety and ASDs, which may lead to difficulties with completing self-report measures of anxiety. However, it is apparent that adults with ASDs also have these difficulties, as while there are few trials involving adults, those that have been completed had similar difficulties with the use of self-report measures. Alongside this, trials of CBT used to treat symptoms of ASDs, rather than affective disorders, have also encountered similar difficulties with self-report measures. It is perhaps probable that individuals with ASDs may find self-report measures difficult because of their associated developmental problems (e.g. perspective-taking, communication problems) and further work regarding the development of valid and reliable measures for use with this population is needed. However, it must also be mentioned that perhaps CBT does not bring about change for individuals with ASD, and the results using both informant- and clinician-report measures have been subjected to an observer-expectancy effect, considering that is very difficult to mask informants, and not all studies made use of masked assessors, introducing significant bias. While this may not explain all the variability within the data, it has a role to play, and as such, it is vitally important that future trials ensure that they make use of masked assessors and have satisfactory arrangements for independent data management.

Related to these difficulties, there were a variety of issues associated with the included studies, highlighted by the quality appraisal, which need to be considered further. First, the majority of the studies included involved small samples, and trials labelled as feasibility or pilot trials often had larger sample sizes than studies that were not identified as either a feasibility or pilot trial. Eight of the studies included in this meta-analysis had less than ten participants per group. This is problematic, as there are no large scale definitive trials in this area making use of robust methodologies. As such, the conclusions reached within this meta-analysis, and previous meta-analyses are potentially limited. This does not mean that the conclusions are entirely invalid, but it does allow some questions to be raised about validity, which could be addressed in the future with the completion of several large scale definitive trials by different research groups around the world. Related to these issues, the study by Chalfant et al. (2007) tended to have a relatively higher standardised mean difference. While this was a randomised trial, the accessors were not masked, and in fact were the actual therapists who carried out the intervention. Considering the lack of blinding and independent data management within this study, there is an inherent increased risk of bias. Several other studies included within this meta-analysis also had a relatively higher standardised mean difference (e.g. Wood *et al.*, 2009), and the majority of them did not make use of

independent data management and analysis, something we would strongly recommend for future trials in this area.

Second, studies often did not report sufficient information regarding participant engagement and fidelity, while third, there were issues with adequate allocation concealment that must be addressed within future studies. Fourth, it is important to note that ten studies were not randomised, and few reported that data were managed and analysed independently. Fifth, and again looking forward to the future, researchers in this area need to specify a primary outcome measure within their trials, and further work to develop valid and reliable measures of outcome for use with participants who have ASDs is needed. Sixth, it would be advantageous for researchers to describe their interventions more thoroughly or ensure that they are available for scrutiny, perhaps within public databases. Finally, it is recommended that future trials make use of and adhere to the CONSORT recommendations for reporting randomised control trials to help increase the quality of the evidence that is available.

There are a number of strengths associated with the current meta-analysis. Considering strengths, within the current meta-analysis, we attempted to include studies that aimed to treat affective disorders more broadly, rather than just anxiety, and included studies that were designed to evaluate CBT as a treatment for the actual symptoms or core features of ASDs. As such, our work is comprehensive, capturing studies that have attempted to make use of CBT with individuals with ASDs for a variety of problems and this is a marked strength over and above previously completed meta-analytic work. Alongside this, we have included studies with samples of children, adolescents, and adults, or mixed samples, while at the same time, undertaking a subgroup analysis to compare differences between children/adolescents and adults, considering the developmental differences between these populations which may have an impact upon the process of engaging in and completing therapy. We have also made use of an appropriate analytic strategy, and made use of independent reviewers for both screening and the quality appraisal. As such, the current meta-analysis is the most comprehensive to date, covering CBT used to treat either affective disorders or symptoms of autism.

Turning to consider weaknesses, there are a variety of problems with many of the included studies which have been mentioned in the preceding paragraph, and these problems need to be considered when interpreting the results of this meta-analysis. While this does not necessarily invalidate our conclusions, it must be considered when interpreting the findings and considering future research.

We would suggest that future studies in this area adhere to following recommendations, (a) small-scale studies should be clearly described as feasibility or pilot trials, (b) methods and interventions should be described fully, in line with CONSORT recommendations. Standardised reporting and a more uniform approach to study design would help to minimise heterogeneity across studies, (c) appropriate allocation concealment, randomisation, blinding procedures and independent data management should be considered a priority and should be described fully, (d) where possible, consistent usage of pre-existing outcome measures across studies would be beneficial in order to increase comparability across trials, (e) researchers should specify a primary outcome measure a priori, and (f) participant engagement and fidelity should be clearly reported. Looking forward to the future, considering the marked number of small trials, well-designed definitive trials from different research groups around the world are needed in order to demonstrate that CBT is an empirically validated treatment use with people who have ASDs. To date, there has only been a single definitive trial within this area (Freitag *et al.*, 2015).

Bearing the aforementioned recommendations for future studies in mind, and considering the conclusions from both the current and previous meta-analyses, CBT is at least associated with a small non-significant effect size, and at best, associated with a medium effect size, depending on whether you ask those receiving the treatment, those supporting the treatment, or those delivering the treatment. There are three further comments we would like to add to help in the design of future studies, including the interventions. First, there have been a variety of modelling and pilot studies across different countries, but very few researchers have developed interventions within the spirit of co-production with people with autism and their families. Co-production means working together with those who will receive the intervention when developing and running a clinical trial to ensure that those who are likely to receive the intervention have also genuinely helped design the intervention. While some studies employed this, if used more commonly, such a strategy would lead to improved engagement and outcomes, especially from the point of view of children and adults with autism.

Second, many of the reviewed studies focused on delivering group-based interventions for a variety of different problems. While delivering interventions in a group may be more cost effective, this may not be associated with greater effectiveness. The reason for this is that co-morbidity is high amongst people with autism, and within a group there may be participants who have obsessive-compulsive disorder, social phobia, generalised anxiety disorder, depression, or many other psychiatric problems, in addition to the difficulties associated with autism itself. While there are marked similarities, cognitive behavioural therapy for depression is different than cognitive

behavioural therapy for obsessive compulsive disorder, and delivering interventions within a group may have prevented therapists form being able to tailor the intervention to address the needs of each individual within the group adequately. Related to this, there are some individuals with ASDs who may be unable or unwilling to access group-based interventions. As such, we recommend that researchers begin to focus more heavily on formulation-driven and trans-diagnostic interventions delivered with individuals, rather than within a group, bearing in mind that there is evidence that individually delivered CBT is associated with stronger effect sizes than group-based CBT for people with intellectual disabilities, another group which tends to have marked co-morbidity (Vereenooghe & Langdon, 2013).

Finally, there has been little attention paid to the accreditation of cognitive behavioural therapists within the literature. While behavioural therapists are certified through the Behaviour Analyst Certification Board®, those offering cognitive behavioural therapy are not certified in a similar manner in many jurisdictions. In some countries, such as the United Kingdom, there are organisations which accredit cognitive behaviour therapists, namely the British Association for Behavioural and Cognitive Psychotherapies (BABCP), but this does not mean that therapists have appropriate clinical expertise and experience of working with people who have ASDs in order to ensure that they are able to adapt therapy. Related to this, while CBT should be adapted to meet the needs of those with ASDs, we still know relatively little about the effectiveness of many of these adaptations, as they have not been investigated using experimental designs to determine whether they lead to substantial improvements in treatment engagement and outcome. While future definitive trials are certainly needed within this area, alongside this, we also need greater experimental work examining the effectiveness of various adaptations to CBT for use with people who have ASDs.

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Appendix B- Output summaries from initial database search

1) PsycINFO

Tuesday, December 09, 2014 8:53:10 AM

#	Query	Limiters/Expanders	Last Run Via	Results
S16	S15 NOT S6	Limiters - English; Population Group: Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,443
S15	S14 NOT S5	Limiters - English; Population Group: Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,627
S14	S13 NOT S4	Limiters - English; Population Group: Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,633
S13	S12 NOT S3	Limiters - English; Population Group: Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	2,522
S12	S11 NOT S2	Limiters - English; Population Group: Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search	2,768

			Database - PsycINFO	
S11	S10 NOT S1	Limiters - English; Population Group: Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	3,667
S10	S9	Limiters - English; Population Group: Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	4,089
S9	S7 AND S8	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	5,025
S8	"cognitive behavio* therapy" OR "cognitive behavio* treatment" OR "cognitive behavio* intervention" OR "cognitive therapy" OR "cognitive treatment" OR "cognitive intervention" OR "behavio* therapy" OR "behavio* treatment" OR "behavio* intervention" OR "CBT" OR "psychotherap*" OR "problem solving"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	302,494

S7	"autism spectrum disorder" OR "ASD" OR "autis*" OR "asperger*" OR "kanner*" OR "pervasive developmental disorder"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	51,537
S6	ADHD	Limiters - English Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	17,629
S5	epilepsy	Limiters - English Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	25,685
S4	education OR classroom* OR school*	Limiters - English Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,082,816
S3	applied behavio* analysis OR ABA	Limiters - English Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	5,039
S2	gene*	Limiters - English Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	710,799
S1	drug* OR medication* OR	Limiters - English Search modes -	Interface - EBSCOhost Research Databases	369,765

	vitamin* OR hormon* OR pharmacotherap*	Boolean/Phrase	Search Screen - Advanced Search Database - PsycINFO	

2) MEDLINE

Tuesday, December 09, 2014 10:42:48 AM

#	Query	Limiters/Expanders	Last Run Via	Results
S16	S15 NOT S6	Limiters - English Language; Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	627
S15	S14 NOT S5	Limiters - English Language; Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	647
S14	S13 NOT S4	Limiters - English Language; Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	651
S13	S12 NOT S3	Limiters - English Language; Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	1,025
S12	S11 NOT S2	Limiters - English Language;	Interface - EBSCOhost Research Databases Search Screen - Advanced	1,069

		Human Search modes - Boolean/Phrase	Search Database - MEDLINE Complete	
S11	S10 NOT S1	Limiters - English Language; Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	1,417
S10	S9	Limiters - English Language; Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	1,576
S9	S7 AND S8	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	2,001
S8	"cognitive behavio* therapy" OR "cognitive behavio* treatment" OR "cognitive behavio* intervention" OR "cognitive therapy" OR "cognitive treatment" OR "cognitive intervention" OR "behavio* therapy" OR "behavio* treatment" OR "behavio*	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	152,190

	intervention" OR "CBT" OR "psychotherap*" OR "problem solving"			
S7	"autism spectrum disorder" OR "ASD" OR "autis*" OR "asperger*" OR "kanner*" OR "pervasive developmental disorder"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	34,669
S6	ADHD	Limiters - English Language Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	14,579
S5	epilepsy	Limiters - English Language Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	86,943
S4	education OR classroom* OR school*	Limiters - English Language Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	2,825,199
S3	applied behavio* analysis OR ABA	Limiters - English Language Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	7,969

S2	gene*	Limiters - English Language Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	4,775,943
S1	drug* OR medication* OR vitamin* OR hormon* OR pharmacotherap*	Limiters - English Language Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	4,522,498

3) CINAHL Plus

Tuesday, December 09, 2014 7:47:38 AM

#	Query	Limiters/Expanders	Last Run Via	Results
S16	S15 NOT S6	Limiters - English Language; Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	225
S15	S14 NOT S5	Limiters - English Language; Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	230
S14	S13 NOT S4	Limiters - English Language; Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	231
S13	S12 NOT S3	Limiters - English Language; Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	297
S12	S11 NOT S2	Limiters - English Language; Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	318

S11	S10 NOT S1	Limiters - English Language; Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	386
S10	S9	Limiters - English Language; Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	405
S9	S7 AND S8	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	856
S8	"cognitive behavio* therapy" OR "cognitive behavio* treatment" OR "cognitive behavio* intervention" OR "cognitive therapy" OR "cognitive treatment" OR "cognitive intervention" OR "behavio* therapy" OR "behavio* treatment" OR "behavio* intervention" OR "CBT" OR "psychotherap*" OR "problem solving"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	51,747

S7	"autism spectrum disorder" OR "ASD" OR "autis*" OR "asperger*" OR "kanner*" OR "pervasive developmental disorder"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	15,936
S6	ADHD	Limiters - English Language Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	5,221
S5	epilepsy	Limiters - English Language Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	11,244
S4	education OR classroom* OR school*	Limiters - English Language Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	490,337
S3	applied behavio* analysis OR ABA	Limiters - English Language Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	422
S2	gene*	Limiters - English Language Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	303,362
S1	drug* OR medication* OR	Limiters - English Language	Interface - EBSCOhost Research Databases	625,483

	vitamin* OR hormon* OR pharmacotherap*	Search modes - Boolean/Phrase	Search Screen - Advanced Search Database - CINAHL Complete	

4) Web of Science

Web of Science: 09/12/14 17.30

Search History:

Set	Results	Save History / Create Alert | Open Saved History	Edit Sets	Combine Sets AND OR Combine	Delete Sets Select All Delete
# 18	502	#17 NOT #7 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*	Edit	Select to combine sets.	Select to delete this set.
# 17	598	#16 NOT #6 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*	Edit	Select to combine sets.	Select to delete this set.
# 16	608	#15 NOT #5 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*	Edit	Select to combine sets.	Select to delete this set.
# 15	613	#14 NOT #4 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*	Edit	Select to combine sets.	Select to delete this set.
# 14	755	#13 NOT #3 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*	Edit	Select to combine sets.	Select to delete this set.
# 13	830	#12 NOT #2 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*	Edit	Select to combine sets.	Select to delete this set.
# 12	1,049	#11 NOT #1 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*	Edit	Select to combine sets.	Select to delete this set.
# 11	1,158	#9 AND #8 **Refined by:LANGUAGES:** (ENGLISH) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*		Select to combine sets.	Select to delete this set.
# 10	1,247	#9 AND #8 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*	Edit	Select to combine sets.	Select to delete this set.
# 9	119,057	**TOPIC:** ("cognitive behavio* therapy") *OR* **TOPIC:** ("cognitive behavio* treatment") *OR* **TOPIC:**	Edit	Select to combine	Select to delete this

		("cognitive behavio* intervention") *OR* **TOPIC:** ("cognitive therapy") *OR* **TOPIC:** ("cognitive treatment") *OR* **TOPIC:** ("cognitive intervention") *OR* **TOPIC:** ("behavio* therapy") *OR* **TOPIC:** ("behavio* treatment") *OR* **TOPIC:** ("behavio* intervention") *OR* **TOPIC:** ("CBT") *OR* **TOPIC:** ("psychotherap*") *OR* **TOPIC:** ("problem solving") *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*		sets. ☐	set. ☐
# 8	**44,534**	TS=("autism spectrum disorder") OR TS=("ASD") OR TS=("autis*") OR TS=("asperger*") OR TS=("kanner*") OR TS=("pervasive developmental disorder") *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*	Edit	Select to combine sets. ☐	Select to delete this set. ☐
# 7	**7,940,807**	**TOPIC:** (animal) *OR* **TOPIC:** (mice) *OR* **TOPIC:** (mouse) *OR* **TOPIC:** (rat*) *OR* **TOPIC:** (monkey*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*	Edit	Select to combine sets. ☐	Select to delete this set. ☐
# 6	**19,522**	TS=(ADHD) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*	Edit	Select to combine sets. ☐	Select to delete this set. ☐
# 5	**99,311**	TS=(epilepsy) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*	Edit	Select to combine sets. ☐	Select to delete this set. ☐
# 4	**818,067**	**TOPIC:** (education) *OR* **TOPIC:** (classroom*) *OR* **TOPIC:** (school*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*	Edit	Select to combine sets. ☐	Select to delete this set. ☐
# 3	**70,733**	TS=(applied behavio* analysis) OR TS=(ABA) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*	Edit	Select to combine sets. ☐	Select to delete this set. ☐
# 2	**6,461,473**	**TOPIC:** (gene*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*	Edit	Select to combine sets. ☐	Select to delete this set. ☐
# 1	**1,939,217**	**TOPIC:** (drug*) *OR* **TOPIC:** (medication*) *OR* **TOPIC:** (vitamin*) *OR* **TOPIC:** (hormon*) *OR* **TOPIC:** (pharmacotherap*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*	Edit	Select to combine sets. ☐	Select to delete this set. ☐
				○ AND ○ OR Combine	Select All

Appendix C- Email sent to corresponding authors of included studies to request support in identifying unpublished or ongoing research

Dear *[author name]*

I am a Trainee Clinical Psychologist at the University of East Anglia, UK, and I am currently conducting my doctoral thesis on the use of Cognitive Behavioural Therapy in individuals with Autism Spectrum Disorder. I am being supervised by Dr Peter Langdon (University of Kent) and Dr Jo Hodgekins (University of East Anglia). I am planning to include your *[year of study]* trial in a meta-analysis that I am conducting on the effectiveness of CBT in individuals with ASD.

I am keen to include any relevant 'grey' literature which I may not have been able to access via literature searches so I am asking all authors of included studies if they can think of any studies which are less accessible that I may have missed? If you know of any ongoing or unpublished trials investigating the effectiveness of CBT in individuals with ASD I'd be very grateful if you could let me know. There is no restriction on age range of participants and I am including studies investigating the use of CBT for either core features of ASD or co-occurring symptoms of mental disorder.

Thank you very much in advance for any help you can give.

Lisa Weston
Trainee Clinical Psychologist

Appendix D- Data extraction form

Code items with missing data as 99. Code items deemed not applicable as 11.

General

1. **Study ID:** Assign a unique identification number

   _____
2. **Reference:** Text; Document full reference in APA format

   _____
   _____
   _____
3. **Year of Publication:** Four digits

   _____
4. **Country of Origin:** Text

   _____
5. **Type of Report:** Circle
   1. Journal article
   2. Book chapter
   3. Thesis or doctoral dissertation
   4. Conference paper
   5. Other (+ specify) _____

Group Descriptors

6. **CBT Format:** Circle
   1. Individual
   2. Group-based
7. **Number of Control Groups**

   _____
8. **Format of Control Group/s:** If more than one control group, code separately in additional columns
   1. Treatment as usual
   2. Waiting list
   3. Attention placebo

Control Group	1	2	3
Code			

9. **Length of Each Treatment Session**: In minutes

   _____
10. **Number of Treatment Sessions Offered**

    _____
11. **Mean Number of Treatment Sessions Attended**

    _____
12. **Total Length of Treatment Offered:** In minutes

    _____
13. **Mean Total Length of Treatment Received:** In minutes

    _____
14. **Baseline Group Differences**: Circle
    1. Not assessed
    2. Assessed, Negligible Differences
    3. Assessed, Some Difference, Judged Unimportant
    4. Assessed, Some Difference, Judged Important (significant differences across several variables/ significant difference on a major variable, e.g. age)

Sample Descriptors

15. **Total Sample Size (at baseline)**

    _____

16. **Sample Size of Intervention Group (at baseline)**

    _____

17. **Sample Size of Control Group (at baseline):** If more than one control group, code separately in additional columns, ensuring that the columns correspond to those used in Item 7

Control Group	1	2	3
Sample Size			

18. **Mean Age of Total Sample:** An average may be used if only an age range is documented

    _____

19. **Age Range of Total Sample**

    _____

20. **Mean Age of Intervention Group:** An average may be used if only an age range is documented

    _____

21. **Age Range of Intervention Group**

    _____

22. **Mean Age of Control Group:** An average may be used if only an age range is documented. If more than one control group, code separately in additional columns, ensuring that the column numbers correspond to those used in Items 7 and 14

Control Group	1	2	3
Mean Age			

23. **Age Range of Control Group:** If more than one control group, code separately in additional columns, ensuring that the column numbers correspond to those used in Items 7, 14 and 19

Control Group	1	2	3
Age Range			

<u>Design Descriptors</u>

24. **Randomisation**: Circle
    1. Randomised
    2. Non-randomised
25. **CBT Target**: Circle
    1. Core ASD feature/s (+ specify) _____
    2. Co-occurring mental disorder (+ specify) _____
    3. Both core ASD feature/s and co-occurring mental disorder (+ specify) _____
26. **Relevant Features/ Symptoms Quantitatively Measured**; : Circle all that apply
    1. Social interaction difficulties
    2. Social communication difficulties
    3. Restricted or repetitive patterns of behaviour and interests
    4. Other ASD features (+ specify) _____
    5. Anxiety symptomatology
    6. Depressive symptomatology
    7. Psychotic symptomatology
    8. Other symptoms of mental disorder (+ specify) _____
27. **Relevant Outcome Measures Used;** Text

    _____
    _____
    _____

28. **Length of Follow Up**

    _____

Effect Size (ES) Data

If more than one relevant outcome variable is used, code effect size data separately for each outcome variable. All of the following items should be coded for each individual effect size using additional columns in the table below

29. **Effect Size Type**
    1. Immediately post intervention
    2. Follow up
30. **Outcome Descriptor:** Text; Description of outcome variable
31. **Outcome Report Type**
    1. Self Report
    2. Clinician Report
    3. Informant Report
32. **Intervention Group Mean**
33. **Control Group Mean:** If more than one control group, code separately in different rows, ensuring that the row number corresponds to the column numbers used in Items 7, 14, 19 and 20
34. **Intervention Group Standard Deviation**
35. **Control Group Standard Deviation:** If more than one control group, code separately in different rows, ensuring that the row number corresponds to the column numbers used in Items 7, 14, 19 and 20
36. **Direction of Effect**
    1. Favours treatment
    2. Favours control
    3. Neither

	ES 1	ES 2	ES 3	ES 4	ES 5
ES Type					
Outcome Descriptor					
Outcome Report Type					
Intervention Group Mean					
Control Group Mean (1)					
Control Group Mean (2)					
Control Group Mean (3)					
Intervention Group SD					
Control Group SD (1)					
Control Group SD (2)					

Appendix E- Details of individual requests for data

In the event of missing or unclear information needed to calculate effect sizes, corresponding authors of included studies were contacted via email in an attempt to obtain or clarify the data.

Email Template

Dear *[author name]*

I am a Trainee Clinical Psychologist at the University of East Anglia, UK, and I am currently conducting my doctoral thesis on the use of Cognitive Behavioural Therapy in individuals with Autism Spectrum Disorder. I am being supervised by Dr Peter Langdon (University of Kent) and Dr Jo Hodgekins (University of East Anglia). I would like to include your *[year of study]* trial *([title of study]*) in a meta-analysis that I am conducting on the effectiveness of CBT in individuals with ASD.

In order to include your study in the meta-analysis, I would require some additional information and I was wondering if you could help me with this please? I require *[details of missing data]*. I would be very grateful if you would be able to share this data to enable me to include your paper in my study.

Thanks very much in advance for your help

Lisa Weston
Trainee Clinical Psychologist

Details of Correspondence (listed in order of date contacted)

Study	Author Contacted	Data Received (Y/N)
Reaven et al. (2012)	Judy Reaven	Y
Langdon et al. (2016)	Peter Langdon	Y
Sofronoff et al. (2007)	Kate Sofronoff	Y
Storch et al. (2013)	Eric Storch	Y
Chalfant et al. (2007)	Anne Chalfant	Y
DeRosier et al. (2011)	Melissa DeRosier	**N**
Laugeson et al. (2012)	Elizabeth Laugeson	Y
Soorya et al. (2015)	Latha Soorya	Y
Baghdadli et al. (2013)	Amaria Baghdadli	Y
Pahnke et al. (2014)	Tatja Hirvikoski	Y
Gantman et al. (2012)	Elizabeth Laugeson	Y
Yoo et al. (2014)	Elizabeth Laugeson	Y
Laugeson et al. (2014)	Elizabeth Laugeson	Y
Provencal (2003)	Sherri Provencal	**N**
Freitag et al. (2015)	Christine Freitag	Y

Appendix F- NICE Quality Appraisal Checklist for Quantitative Intervention Studies (NICE, 2012)

Checklist items are worded so that 1 of 5 responses is possible:

++	Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias.
+	Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.
−	Should be reserved for those aspects of the study design in which significant sources of bias may persist.
Not reported (NR)	Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.
Not applicable (NA)	Should be reserved for those study design aspects that are not applicable given the study design under review (for example, allocation concealment would not be applicable for case control studies).

In addition, the reviewer is requested to complete in detail the comments section of the quality appraisal form so that the grade awarded for each study aspect is as transparent as possible.

Each study is then awarded an overall study quality grading for internal validity (IV) and a separate one for external validity (EV):

++ All or most of the checklist criteria have been fulfilled, where they have not been fulfilled the conclusions are very unlikely to alter.
+ Some of the checklist criteria have been fulfilled, where they have not been fulfilled, or not adequately described, the conclusions are unlikely to alter.
− Few or no checklist criteria have been fulfilled and the conclusions are likely or very likely to alter.

Checklist

Study identification: (Include full citation details)		
Study design: Refer to the glossary of study designs and the algorithm for classifying experimental and observational study designs to best describe the paper's underpinning study design		
Guidance topic:		
Assessed by:		
Section 1: Population		
1.1 Is the source population or source area well described? Was the country (e.g. developed or non-developed, type of healthcare system), setting (primary schools, community centres etc.), location (urban, rural), population demographics etc. adequately described?	++ + – NR NA	Comments:
1.2 Is the eligible population or area representative of the source population or area? Was the recruitment of individuals, clusters or areas well defined (e.g. advertisement, birth register)? Was the eligible population representative of the source? Were important groups under-represented?	++ + – NR NA	Comments:
1.3 Do the selected participants or areas represent the eligible population or area? Was the method of selection of participants from the eligible population well described? What % of selected individuals or clusters agreed to participate? Were there any sources of bias? Were the inclusion or exclusion criteria explicit and appropriate?	++ + – NR NA	Comments:

Section 2: Method of allocation to intervention (or comparison)		
2.1 Allocation to intervention (or comparison). How was selection bias minimised? Was allocation to exposure and comparison randomised? Was it truly random ++ or pseudo-randomised + (e.g. consecutive admissions)? If not randomised, was significant confounding likely (−) or not (+)? If a cross-over, was order of intervention randomised?	++ + − NR NA	Comments:
2.2 Were interventions (and comparisons) well described and appropriate? Were interventions and comparisons described in sufficient detail (i.e. enough for study to be replicated)? Was comparisons appropriate (e.g. usual practice rather than no intervention)?	++ + -− NR NA	Comments:
2.3 Was the allocation concealed? Could the person(s) determining allocation of participants or clusters to intervention or comparison groups have influenced the allocation? Adequate allocation concealment (++) would include centralised allocation or computerised allocation systems.	++ + − NR NA	Comments:
2.4 Were participants or investigators blind to exposure and comparison? Were participants **and** investigators – those delivering or assessing the intervention kept blind to intervention allocation? (Triple or double blinding score ++) If lack of blinding is likely to cause important bias, score −.	++ + − NR NA	Comments:
2.5 Was the exposure to the intervention and comparison adequate? Is reduced exposure to intervention or control related to the intervention (e.g. adverse effects leading to reduced compliance) or fidelity of implementation (e.g. reduced adherence to protocol)?	++ + −	Comments:

Was lack of exposure sufficient to cause important bias?	NR NA	
2.6 Was contamination acceptably low? Did any in the comparison group receive the intervention or vice versa? If so, was it sufficient to cause important bias? If a cross-over trial, was there a sufficient wash-out period between interventions?	++ + – NR NA	Comments:
2.7 Were other interventions similar in both groups? Did either group receive additional interventions or have services provided in a different manner? Were the groups treated equally by researchers or other professionals? Was this sufficient to cause important bias?	++ + – NR NA	Comments:
2.8 Were all participants accounted for at study conclusion? Were those lost-to-follow-up (i.e. dropped or lost pre-,during or post-intervention) acceptably low (i.e. typically <20%)? Did the proportion dropped differ by group? For example, were drop-outs related to the adverse effects of the intervention?	++ + – NR NA	Comments:
2.9 Did the setting reflect usual UK practice? Did the setting in which the intervention or comparison was delivered differ significantly from usual practice in the UK? For example, did participants receive intervention (or comparison) condition in a hospital rather than a community-based setting?	++ + – NR NA	Comments:
2.10 Did the intervention or control comparison reflect usual UK practice? Did the intervention or comparison differ significantly from usual practice in the UK? For example, did participants receive intervention (or comparison)	++ + –	Comments:

delivered by specialists rather than GPs? Were participants monitored more closely?	NR NA	
Section 3: Outcomes		
3.1 Were outcome measures reliable? Were outcome measures subjective or objective (e.g. biochemically validated nicotine levels ++ vs self-reported smoking −)? How reliable were outcome measures (e.g. inter- or intra-rater reliability scores)? Was there any indication that measures had been validated (e.g. validated against a gold standard measure or assessed for content validity)?	++ + − NR NA	Comments:
3.2 Were all outcome measurements complete? Were all or most study participants who met the defined study outcome definitions likely to have been identified?	++ + − NR NA	Comments:
3.3 Were all important outcomes assessed? Were all important benefits and harms assessed? Was it possible to determine the overall balance of benefits and harms of the intervention versus comparison?	++ + − NR NA	Comments:
3.4 Were outcomes relevant? Where surrogate outcome measures were used, did they measure what they set out to measure? (e.g. a study to assess impact on physical activity assesses gym membership – a potentially objective outcome measure – but is it a reliable predictor of physical activity?)	++ + NR NA	Comments:
3.5 Were there similar follow-up times in exposure and comparison groups?	++ +	Comments:

If groups are followed for different lengths of time, then more events are likely to occur in the group followed-up for longer distorting the comparison. Analyses can be adjusted to allow for differences in length of follow-up (e.g. using person-years).	NR NA	
3.6 Was follow-up time meaningful? Was follow-up long enough to assess long-term benefits or harms? Was it too long, e.g. participants lost to follow-up?	++ + – NR NA	Comments:
Section 4: Analyses		
4.1 Were exposure and comparison groups similar at baseline? If not, were these adjusted? Were there any differences between groups in important confounders at baseline? If so, were these adjusted for in the analyses (e.g. multivariate analyses or stratification). Were there likely to be any residual differences of relevance?	++ + – NR NA	Comments:
4.2 Was intention to treat (ITT) analysis conducted? Were all participants (including those that dropped out or did not fully complete the intervention course) analysed in the groups (i.e. intervention or comparison) to which they were originally allocated?	++ + – NR NA	Comments:
4.3 Was the study sufficiently powered to detect an intervention effect (if one exists)? A power of 0.8 (that is, it is likely to see an effect of a given size if one exists, 80% of the time) is the conventionally accepted standard. Is a power calculation presented? If not, what is the expected effect size? Is	++ + – NR	Comments:

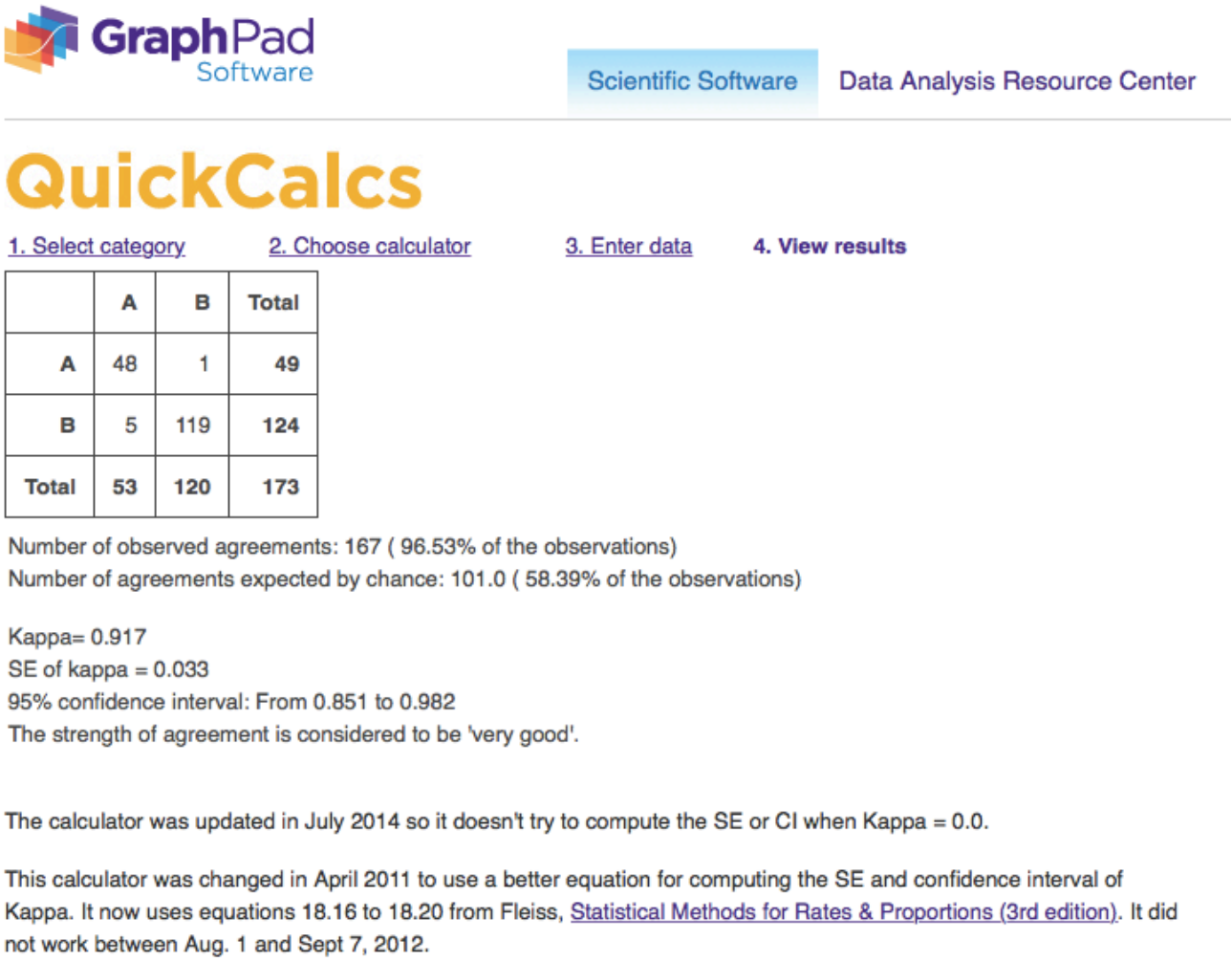
the sample size adequate?	NA	
4.4 Were the estimates of effect size given or calculable? Were effect estimates (e.g. relative risks, absolute risks) given or possible to calculate?	++ + – NR NA	Comments:
4.5 Were the analytical methods appropriate? Were important differences in follow-up time and likely confounders adjusted for? If a cluster design, were analyses of sample size (and power), and effect size performed on clusters (and not individuals)? Were subgroup analyses pre-specified?	++ + – NR NA	Comments:
4.6 Was the precision of intervention effects given or calculable? Were they meaningful? Were confidence intervals or p values for effect estimates given or possible to calculate? Were CI's wide or were they sufficiently precise to aid decision-making? If precision is lacking, is this because the study is under-powered?	++ + – NR NA	Comments:
Section 5: Summary		
5.1 Are the study results internally valid (i.e. unbiased)? How well did the study minimise sources of bias (i.e. adjusting for potential confounders)? Were there significant flaws in the study design?	++ + –	Comments:
5.2 Are the findings generalisable to the source population (i.e. externally valid)? Are there sufficient details given about the study to determine if the findings are generalisable to the source population? Consider: participants, interventions and comparisons, outcomes, resource and policy implications.	++ + –	Comments:

Appendix G- Kappa Calculations

All Kappa calculations were completed using an online calculator:

http://graphpad.com/quickcalcs/kappa1.cfm

1) Kappa calculation for study inclusion



GraphPad Software

Scientific Software | Data Analysis Resource Center

QuickCalcs

1. Select category | 2. Choose calculator | 3. Enter data | **4. View results**

	A	B	Total
A	48	1	**49**
B	5	119	**124**
Total	**53**	**120**	**173**

Number of observed agreements: 167 (96.53% of the observations)
Number of agreements expected by chance: 101.0 (58.39% of the observations)

Kappa= 0.917
SE of kappa = 0.033
95% confidence interval: From 0.851 to 0.982
The strength of agreement is considered to be 'very good'.

The calculator was updated in July 2014 so it doesn't try to compute the SE or CI when Kappa = 0.0.

This calculator was changed in April 2011 to use a better equation for computing the SE and confidence interval of Kappa. It now uses equations 18.16 to 18.20 from Fleiss, Statistical Methods for Rates & Proportions (3rd edition). It did not work between Aug. 1 and Sept 7, 2012.

2) Kappa calculation for internal validity of included studies

GraphPad Software

Scientific Software Data Analysis Resource Center

QuickCalcs

1. Select category 2. Choose calculator 3. Enter data **4. View results**

	A	B	C	Total
A	2	2	0	**4**
B	1	22	3	**26**
C	0	8	12	**20**
Total	**3**	**32**	**15**	**50**

Number of observed agreements: 36 (72.00% of the observations)
Number of agreements expected by chance: 22.9 (45.76% of the observations)

Kappa= 0.484
SE of kappa = 0.115
95% confidence interval: From 0.259 to 0.709
The strength of agreement is considered to be 'moderate'.

The calculations above only consider exact matches between observers. If the categories (A, B, C...) are ordered, you may also wish to consider close matches. In other words, if one observer classifies a subject into group B and the other into group C, this is closer than if one classifies into A and the other into D. The calculation of weighted kappa, below, assumes the categories are ordered and accounts for how far apart the two raters are. This calculation uses linear weights.

Weighted Kappa= 0.526

Assessed this way, the strength of agreement is considered to be 'moderate'.

The calculator was updated in July 2014 so it doesn't try to compute the SE or CI when Kappa = 0.0.

This calculator was changed in April 2011 to use a better equation for computing the SE and confidence interval of Kappa. It now uses equations 18.16 to 18.20 from Fleiss, Statistical Methods for Rates & Proportions (3rd edition). It did not work between Aug. 1 and Sept 7, 2012.

3) Kappa calculation for external validity of included studies

GraphPad Software

Scientific Software Data Analysis Resource Center

QuickCalcs

1. Select category 2. Choose calculator 3. Enter data **4. View results**

	A	B	C	Total
A	1	1	0	**2**
B	1	30	0	**31**
C	0	6	11	**17**
Total	**2**	**37**	**11**	**50**

Number of observed agreements: 42 (84.00% of the observations)
Number of agreements expected by chance: 26.8 (53.52% of the observations)

Kappa= 0.656
SE of kappa = 0.106
95% confidence interval: From 0.447 to 0.864
The strength of agreement is considered to be 'good'.

The calculations above only consider exact matches between observers. If the categories (A, B, C...) are ordered, you may also wish to consider close matches. In other words, if one observer classifies a subject into group B and the other into group C, this is closer than if one classifies into A and the other into D. The calculation of weighted kappa, below, assumes the categories are ordered and accounts for how far apart the two raters are. This calculation uses linear weights.

Weighted Kappa= 0.672

Assessed this way, the strength of agreement is considered to be 'good'.

The calculator was updated in July 2014 so it doesn't try to compute the SE or CI when Kappa = 0.0.

This calculator was changed in April 2011 to use a better equation for computing the SE and confidence interval of Kappa. It now uses equations 18.16 to 18.20 from Fleiss, Statistical Methods for Rates & Proportions (3rd edition). It did not work between Aug. 1 and Sept 7, 2012.