Investigating SOcial Competence and Isolation in children with Autism taking part in LEGO®-based therapy clubs In School Environments

I-SOCIALISE

This protocol has regard for the HRA guidance and order of content

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Trial Summary

Trial Title	Investigating SOcial Competence and Isolation in children with Autism taking part in LEGO®-based therapy clubs In School Environments	
Internal ref. no. (or short title)	I-SOCIALISE	
Trial Design	Pragmatic, cluster randomised controlled trial with internal pilot	
Trial Participants	Children diagnosed with autism spectrum disorder (ASD)	
Planned Sample Size	240	
Intervention duration	12 weeks	
Follow-up duration	12 months after randomisation	
Planned Trial Period	4 years	
	Objectives	**Outcome Measures**
Primary (20 weeks)	To examine the clinical effectiveness of LEGO®-based therapy groups on the social and emotional competence (specifically the perceived social skills) of children with ASD within the school setting, when compared with usual support provided for children with ASD.	The social skills subscale of the Social Skills Improvement System (SSIS) – completed by the associated teacher at 20 weeks..(NB: The Social Skills Improvement System (SSIS) is also completed by the associated teacher at baseline and 52 weeks and by the parent at baseline, 20 and 52 weeks. This is a secondary outcome.)
Secondary (20 and 52 weeks)	1. Examine the clinical effectiveness of LEGO®-based therapy groups on the perceived social isolation of children with ASD within the school setting, when compared with usual support provided.	Multidimensional Scale of Perceived Social Support – completed by the child at baseline, 20 and 52 weeks. Asher loneliness scale – completed by the child at baseline, 20 and 52 weeks.

	2. Examine the cost-effectiveness of LEGO®-based therapy groups in terms of health-related quality of life and cost utility at 20 and 52 weeks.	EQ-5D-Y proxy – completed by the parent at 20 and 52 weeks. Child Health Utility 9D (CHU-9D) – completed by the child at 20 and 52 weeks. Bespoke resource use questionnaire – completed by the parent and associated teacher at 20 and 52 weeks.
	3. Determine if the impact of LEGO-®-based therapy is sustainable into the next academic year by comparing effectiveness on social and emotional competence (specifically perceived social skills) at 20 and 52 weeks after randomisation.	The social skills subscale of the Social Skills Improvement System (SSIS) – completed by the associated teacher at 20 and 52 weeks and compared between these time-points.
	4. Examine the acceptability of the intervention at follow-up points using a purpose designed questionnaire and telephone interviews.	Bespoke acceptability questionnaire – completed by the parent and interventionist at 20 weeks (intervention group only).
	5. Examine treatment fidelity through independent observation of treatment sessions across schools.	Fidelity checklist – completed by the interventionist after each session.
	6. To examine the clinical effectiveness of LEGO®-based therapy groups on the academic competence of children with ASD within the school setting, when compared with usual support provided for children with ASD.	The academic competence subscale of the Social Skills Improvement System (SSIS) – completed by the associated teacher at baseline, 20 and 52 weeks.
	7. Examine the emotional and behavioural symptoms in those receiving LEGO®-based therapy compared to usual care provided	Strengths and Difficulties Questionnaire (SDQ) – completed by the parent and associated teacher at baseline, 20 and 52 weeks. The problem behaviours

		subscale of the Social Skills Improvement System (SSIS) – completed by the parent and associated teacher at baseline, 20 and 52 weeks.
	8. Examine the clinical effectiveness of LEGO®-based therapy groups on assertion, social control, externalising and internalising of children with ASD within the school setting, when compared with usual support provided for children with ASD.	Assertion and self control items from the social skills subscale of SSIS and Externalising and Internalising items from the problem behaviours subscale of SSiS – completed by the parent and associated teacher at 20 and 52 weeks.
Intervention	LEGO®-based therapy and usual care vs usual care	
Method of delivery	Teachers and teaching assistants based at the participating children's schools	

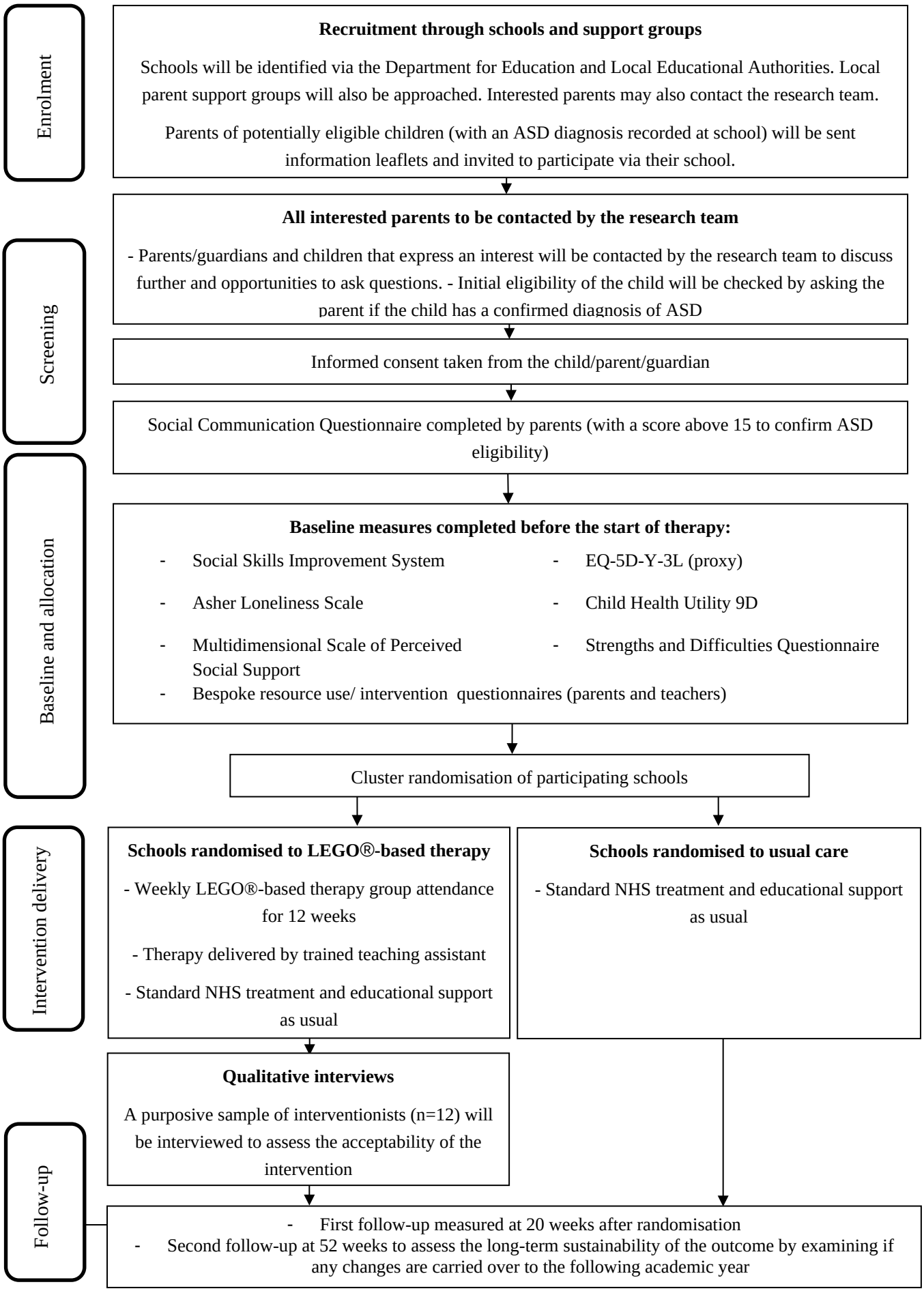
Key words: Autism; Randomised Controlled Trial; LEGO®-based therapy; Child; Adolescent; Therapy; Social skills

Abbreviation List and Glossary

ABA:	Applied Behaviour Analysis
ADHD:	Attention deficit hyperactivity disorder
ASCEND:	Autism Spectrum Conditions - Enhancing Nurture and Development
ASD:	Autism Spectrum Disorder
ASSSIST:	Autism Spectrum Social Stories In Schools Trial
Brick Builder:	The child who puts the pieces together
Brick Engineer:	The child who describes the instructions
Brick Supplier:	The child finds the correct bricks
CAMHS:	Child and Adolescent Mental Health Services
CiCS:	Corporate Information and Computing Services
CTRU:	Clinical Trials Research Unit
DfES:	Department for Education and Skills
DMEC:	Data Monitoring and Ethics Committee
DSM-IV:	Diagnostic and Statistical Manual of Mental Disorders
EQ-5D:	European Quality of Life-5 Dimension
GP:	General Practitioner
HRA:	Health Research Authority
I-SOCIALISE:	Investigating SOcial Competence and Isolation in children with Autism taking part in LEGO®-based therapy clubs In School Environments
IAPT:	Improving Access to Psychological Therapies
ICC:	Intraclass correlation
ICD-10:	International Classification of Diseases
IEP:	Individual education plan
ITT:	Intention to treat analysis
Interventionist:	A member of school staff who will deliver the intervention
NAS:	National Autistic Society
NHS:	National Health Service
NICE:	National Institute for Health and Care Excellence
NIHR:	National Institute for Health Research
NPT:	Normalisation Process Theory
PECS:	Picture Exchange Communication System
PIS:	Participant information sheet

PPI:	Patient and public involvement
QALY:	Quality-adjusted life years
QoL:	Quality of life
RA:	Research assistant
RCT:	Randomised controlled trial
REC:	Research Ethics Committee
SAE:	Serious adverse events
SCQ:	Social Communication Questionnaire
SD:	Standard deviation
SDQ:	Strengths and Difficulties Questionnaire
SEN:	Special educational needs
SENCO:	Special Educational Needs Co-ordinator
SOP:	Standard Operating Procedure
SSIS:	Social Skills Improvement System
SULP:	Social Use of Language Programme
TA:	Teaching assistant
TD:	Typically developing
TMG:	Trial Management Group
TSC:	Trial Steering Committee
UK:	United Kingdom

Trial Flow Chart



Study Protocol

Investigating SOcial Competence and Isolation in children with Autism taking part in LEGO®-based therapy clubs In School Environments

1. Background

1.1. Autism Spectrum Disorder

Autism Spectrum Disorder (ASD) is a lifelong neurodevelopmental disorder that affects up to 1.6% of children in the UK and has an adverse impact on overall adult outcome (Baron-Cohen *et al.,* 2009; Howlin & Moss, 2012). Children with ASD are characterised by qualitative impairments in social communication, rigidity of thought, restricted interests and stereotyped behaviours (American Psychiatric Association, 2013). Consequently, they are less able to intuitively understand societal norms and social rules compared to typically developing (TD) peers (Travis, Sigman, & Ruskin, 2001). These symptoms result in considerable difficulties in many aspects of development which translate into poor long term outcomes in terms of educational attainment, independent living, employment, meaningful friendships and overall social competence (Howlin *et al.,* 2004; Whitehouse *et al.,* 2009) and mental health (Eaves & Ho, 2008). It has become common practice to include children with ASD in regular classrooms to aid with their social and academic development (Chamberlain, Kasari, & Rotheram-Fuller, 2007; DfES, 2002). Despite this, some evidence suggests such placements can increase the risk of isolation and rejection (Ochs *et al.,* 2001).

Peer friendships are a significant beneficial social learning experience for children (McClelland, Morrison, & Holmes, 2000). Friendships require and help children to develop social, cognitive and language ability, as well as provide the child with a sense of belonging and self-worth (Bagwell, Newcomb, & Bukowski, 1998). Unsurprisingly, children with ASD often struggle to initiate flexible cooperative play, preferring structured self-directed activities with clear and explicit rules and limited emotional exchange (Bauminger & Shulman, 2003). This limits the child's experiences and opportunities to develop their social and emotional competence, and over time continues to widen the gap between them and their peers. It is often hypothesised that this failure to engage in social interaction is because social stimuli lacks salience for the child with ASD (Dawson *et al.,* 2004; Grandgeorge *et al.,* 2015). Indeed, social interactions have been shown to be anxiety-provoking for children with ASD (Carrington & Graham, 2001). However, it also has been demonstrated that children with ASD identify feeling lonely significantly more frequently than their peers (Bauminger & Kasari, 2000) and that it may be that social interactions are rewarding for them but they take a different form than for TD children (Ochs & Solomon, 2010). This suggests that children with ASD have an awareness of when they are not included in interactions with their peers. Additionally, there is substantial evidence to suggest they are at increased risk of victimisation and bullying (Rowley *et al.,* 2012). This is a considerable problem for the provision of education and health services for these children as there is strong evidence for both TD children and those with special needs including those with ASD, that the impact of perceived exclusion from friendship groups impacts adversely on mental health, quality of life (QoL), academic achievements and long term outcomes into adult

life including the ability to develop meaningful friendships (Killen, Mulvey, & Hitti, 2013; Sansoni *et al.,* 2010).

1.2. Current Treatment Approaches for the development of social skills

To date, social skills training groups for children with ASD have primarily been used as a means of facilitating their social and emotional competence within the school environment. A recent Cochrane review concluded that there was evidence that social skills training groups improved social competence but there were significant limitations in the published research (Reichow, Steiner, & Volkmar, 2012). Only five studies (Frankel *et al.,* 2010; Koenig *et al.,* 2010; Laugeson, Frankel, Mogil, & Dillon, 2009; Lopata *et al.,* 2010; Solomon, Goodlin-Jones, & Anders, 2004) met the inclusion criteria and one did not report an outcome measure appropriate for meta-analysis (Solomon *et al.,* 2004). Social competence was measured using different instruments across studies. The authors recommended further research focussing on defined outcomes that can better inform reliable recommendations for practice and policy. A recent meta-analysis looking at effect sizes of group-based social skills interventions from different sources found moderate overall improvements in social competence when assessed by self-report, parent/guardian reports, observers and task based exercises, but not when reported by teachers (Gates *et al.,* 2017).

However, current social skills training interventions are limited by their focus on a skills deficit model (based on the difficulties exhibited by children with ASD) rather than on encouraging the child to seek their own solutions. Additionally, the training focuses on how children typically learn complex social rules but relies on the child's intuitive knowledge about how to apply the new skills across different social settings. As a consequence, a well replicated finding is that although children with ASD can learn to demonstrate appropriate responses and social skills within the specific setting of the intervention, applying these new skills to their everyday life is often less successful (Howlin *et al.,* 2004; Licciardello, Harchik, & Luiselli, 2008). Teaching a child the skills to participate and engage in social groups has been shown to be beneficial but does not address the problem that many children with ASD cannot generalise this knowledge into a wider social context.

There are a number of other interventions that are used in some schools for improving social interactions and communication. These include Social Stories (Wright *et al.,* 2016; Marshall *et al.,* 2016), Picture Exchange Communication System (Bondy & Frost, 1994), Applied Behaviour Analysis ((ABA) Baer *et al.,* 1968), Social Use of Language Programme ((SULP) Rinaldi, 2004) and others (Bellini *et al.,* 2007).

1.3. LEGO®-Based Therapy

LEGO®-based therapy (LeGoff *et al.,* 2014) is a group intervention that has gained considerable attention in the UK. Local education authorities are now recommending the use of it in UK schools. The potential benefits of this therapy are that it was designed for school-age children with ASD as opposed to being an adapted form of a more generic social skills training intervention. Using collaborative LEGO®-based play the intention is to harness the child's own interests and so motivate learning and change a focus recommended by international researchers in this area (LeGoff *et al.,* 2014). LEGO® is a predictable, systematic multi-level construction toy that provides intrinsically structured tasks that children with ASD are highly motivated to complete (Owens *et al.,* 2008). LEGO®-based therapy is specifically designed to

make social interactions interesting to the child with ASD so that they learn how to play co-operatively with a toy that they enjoy which in turn increases the likelihood that they can continue to use these skills in their daily functioning. This use of a naturalistic approach to treatment has previously been shown to improve the effectiveness of an intervention by increasing the likelihood that the newly acquired skills will be used beyond the therapy setting (Delprato, 2001). There is some preliminary evidence from the original authors that at follow up social interactions in the school playground were significantly improved (LeGoff *et al.,* 2014).

To date only one small randomised controlled trial (RCT) of 47 children with ASD aged between six and 11 years, has been conducted to investigate the effect on the social and emotional wellbeing of children with ASD (Owens *et al.,* 2008). In this trial LEGO®-based therapy was compared with Social Use of Language Programme (SULP) (a group-based social skills training intervention). These findings were then compared with a separately recruited control group. The findings indicated that ASD specific social difficulties reduced following LEGO®-based therapy, but not in either the SULP or control groups. However, there are several limitations to this trial. The sample was small, full random allocation was not used with the potential impact of selection bias, the researcher organised the delivery of the therapy and no treatment fidelity measures were taken. Furthermore an intention to treat analysis (ITT) was not employed as is best practice for RCTs (Torgerson & Torgerson, 2008).

Therefore, despite the reported potential benefits of LEGO®-based therapy and its adoption by many schools across the UK, the evidence to support its effectiveness on the social and emotional wellbeing of children with ASD is limited and there has been no assessment of cost-effectiveness.

1.4. Trial Summary

This study is a cluster RCT to investigate the effectiveness of LEGO®-based therapy for children with ASD. There will be an internal pilot study which will run for 10 months to examine the feasibility of recruitment. The pilot period will run for 10 months, at which point we expect to have recruited n=120 of which one third (n=40) will have reached the primary endpoint. Stop/Go criteria based on 75% of the recruitment target (n=90) and 70% of the primary outcome measures (n=28) will be used to assess feasibility of continuing the trial. There will be a nested economic evaluation, qualitative component and assessment of fidelity and acceptability.

2. Rationale

A comprehensive set of public health guidelines were published by the National Institute for Health and Care Excellence (NICE, 2008) which indicated that the social and emotional wellbeing of children is a critical determinant of their academic success and physical and mental health. Despite the benefits of a full inclusion policy, there is evidence that children with ASD may be at increased risk of rejection and social isolation and that this may impact on their health and wellbeing. However, the idiosyncratic nature of their symptomatology and the difficulty they have with generalising skills across settings makes it difficult for social skills training groups to have a lasting, transferable effect.

Further NICE recommendations specifically examining interventions for children with ASD were published in 2013. They suggest specific social-communication interventions for the core features of autism using play-based strategies with parents, carers and teachers (NICE, 2013).

The reported potential benefits of LEGO®-based therapy and its adoption by many schools across the UK suggest it could be a key strategy to helping children overcome many of their social difficulties. However, the evidence to support its effectiveness on the social and emotional wellbeing and perceived social isolation of children with ASD is limited. There has also been no assessment of the cost effectiveness of the intervention. Thus, this is a critical period in which we can systematically examine its clinical and cost-effectiveness before it becomes a common feature of the school curriculum.

2.1. Assessment and Management of Risk

We do not anticipate that trial participants will be subject to any substantial risks during this study. LEGO®-based therapy focuses on helping children gain positive social and situational strategies using intrinsically rewarding and varied types of collaborative LEGO®-based play, therefore it is unlikely to cause participants direct harm. There is a potential however, due to the nature of ASD, for the participants to experience some distress associated with the novel social situation and the social roles the child is taking on during the therapy. As with all toys there is a risk of children injuring themselves or each other. To minimise these potential constraints, sessions will be closely supervised by familiar members of school staff (interventionists) with a high degree of experience of using play equipment with children within the school environment. They will follow usual school safety policies. These staff members will receive training in autism awareness as part of the LEGO®-based therapy training. Also, within the first session, and at the start of each subsequent session, the participants will be asked to follow some 'Brick Club rules'. These include procedures for dealing with disagreements, taking turns within the session and being helpful to other participants.

The intervention may intrude on some children's existing routines - this might cause distress for some children with ASD. The design of this study ensures that the intervention will take place within the school day i.e. as part of their existing scheduled activities, minimising this potential disruption.

There is also the risk that LEGO®-based therapy will not be effective leading to a misuse of time and resources in schools. However, given the extensive and growing interest in this therapy in the UK, this risk is counterbalanced by the likelihood that by not undertaking an evaluation at this time a treatment with limited evidence of clinical and cost-effectiveness will be rolled out nationally.

3. Objectives

3.1. Primary Objective

The primary objective of this trial is to examine the clinical effectiveness of LEGO®-based therapy groups on the social and emotional competence (specifically the perceived social skills) of children with ASD within a mainstream school setting, when compared with usual support provided for children with ASD.

This is measured using the social skills subscale of the SSIS, completed by the associated teacher at 20 weeks. (NB: the SSIS is also completed as a secondary outcome by the associated teacher at baseline and 52 weeks and by the parent at baseline, 20 and 52 weeks).

3.2. Secondary Objectives

The secondary objectives of this trial are to:

1. Examine the clinical effectiveness of LEGO®-based therapy groups on the perceived social isolation of children with ASD within the school setting when compared with usual support provided. This is measured using the Multidimensional Scale of Perceived Social Support and the Asher Loneliness scale completed by the child at baseline, 20 and 52 weeks.
2. Examine the cost-effectiveness of LEGO®-based therapy in terms of health-related quality of life and cost utility at 20 and 52 weeks. This is measured using the parent completed EQ-5D-Y proxy and bespoke resource use questionnaire, and the child completed Child Health Utility 9D (CHU-9D) at 20 and 52 weeks.
3. Determine if the impact of LEGO®-based therapy is sustainable into the next academic year by comparing effectiveness on social and emotional competence (specifically perceived social skills) at 20 and 52 weeks. This is measured using the social skills subscale of the SSIS completed by the associated teacher at 20 and 52 weeks and a comparison between them.
4. Examine the acceptability of the intervention at follow-up points using a bespoke purpose designed questionnaire and telephone interviews. This is measured with the parent and interventionist completed bespoke acceptability questionnaire at 20 week (intervention group only).
5. Examine treatment fidelity through independent observation of treatment sessions across schools. This is measured using the fidelity checklist completed by the interventionist after each LEGO®-based therapy session.
6. Examine the clinical effectiveness of LEGO®-based therapy groups on the academic competence of children with ASD within the school setting, when compared with usual support provided for children with ASD. This is measured with the academic competence subscale of the SSIS completed by the associated teacher at baseline, 20 and 52 weeks.
7. Examine the emotional and behavioural symptoms in those receiving LEGO®-based therapy compared to usual care. This is measured using the Strengths and Difficulties Questionnaire (SDQ) and the problem behaviours subscale of the SSIS completed by the parent and associated teacher at baseline, 20 and 52 weeks.
8. Examine the clinical effectiveness of LEGO®-based therapy groups on assertion, social control, externalising and internalising, as measured by individual items in the Social Skills Improvement System (SSIS), of children with ASD within the school setting, when compared with usual support provided for children with ASD. This follows the approach of Frankel et al., (2010) which focused on these items and found 3 of them (excluding externalising) to be sensitive to change resulting from interventions in children with ASD. This is measured using assertion and self-control items from the social skills subscale of the SSIS and externalising and internalising items from the problem behaviours subscale of the SSIS completed by the parent and associated teacher at 20 and 52 weeks.

4. Outcome Measures

A range of measures will be used throughout the I-SOCIALISE trial in order to investigate the primary and secondary objectives (see Tables 1-4 for an overview of the outcome measures and time-points). Follow up booklets can be completed by participants either via post, online or during a face to face visit with a research assistant.

Table 1: Outcome measures to be completed by child participants throughout the I-SOCIALISE trial

Measure	Time points completed	Administered by
Multidimensional Scale of Perceived Social Support (8 items relating to support from friends)	Baseline	Research assistant
	20 weeks after randomisation	Research assistant /post/ online form
	52 weeks after randomisation	Research assistant/post/ online form
Asher Loneliness Scale	Baseline	Research assistant
	20 weeks after randomisation	Research assistant/post/ online form
	52 weeks after randomisation	Research assistant/post/ online form
Child Health Utility 9D	Baseline	Research assistant
	20 weeks after randomisation	Research assistant/post/ online form
	52 weeks after randomisation	Research assistant/post/ online form

Table 2: Outcome measures to be completed by parents throughout the I-SOCIALISE trial

Measure	Time points completed	Administered by
Demographics	Consent	Research assistant
Social Communication Questionnaire	Consent	Research assistant
Social Skills Improvement System	Baseline	Research assistant
	20 weeks after randomisation	Research assistant/post/ online form
	52 weeks after randomisation	Research assistant/post/ online form
Strengths and Difficulties Questionnaire	Baseline	Research assistant
	20 weeks after randomisation	Research assistant/post/ online form
	52 weeks after randomisation	Research assistant/post/ online form
Bespoke resource use questionnaire	Baseline	Research assistant
	20 weeks after randomisation	Research assistant/post/ online form
	52 weeks after randomisation	Research assistant/post/ online form
Bespoke adverse events questionnaire	20 weeks after randomisation	Research assistant
EQ-5D-Y (3L proxy)	Baseline	Research assistant
	20 weeks after randomisation	Research assistant/post/ online form
	52 weeks after randomisation	Research assistant/post/ online form
Bespoke acceptability questionnaire (intervention group only)	20 weeks after randomisation	Research assistant/post/ online form

Table 3: Outcome measures to be completed by associated teacher/teaching assistant throughout the I-SOCIALISE trial

Measure	Time points completed	Administered by
Social Skills Improvement System	Baseline	Research assistant
	20 weeks after randomisation*	Research assistant/post/ online form
	52 weeks after randomisation	Research assistant/post/ online form
Strengths and Difficulties Questionnaire	Baseline	Research assistant
	20 weeks after randomisation	Research assistant/post/ online form
	52 weeks after randomisation	Research assistant/post/ online form
Bespoke resource use questionnaire	Baseline	Research assistant
	20 weeks after randomisation	Research assistant/post/ online form
	52 weeks after randomisation	Research assistant/post/ online form
Bespoke adverse events questionnaire	20 weeks after randomisation	Research assistant/post/ online form

**Primary Outcome*

Table 4: Outcome measures to be completed by interventionist teacher/teaching assistant throughout the I-SOCIALISE trial

Measure	Time points completed	Administered by
Demographics	Baseline	Research assistant
Bespoke acceptability questionnaire	20 weeks after randomisation	Research assistant

Table 5: Recording details of the intervention

Measure	Time points completed	Administered by
Bespoke resource use questionnaire	After each therapy session	Interventionist
Bespoke adverse events questionnaire	After each therapy session	Interventionist
Fidelity checklist	After each therapy session	Interventionist

4.1. Primary endpoint/ outcome

The primary outcome measure for I-SOCIALISE is the social skills subscale of the Social Skills Improvement System (SSIS) (Gresham & Elliott, 2008) completed by the associated teacher/ TA at 20 weeks post randomisation. The SSIS is a behaviour rating scale that can be completed by parents, teaching staff and appropriate students. It is widely used in national portfolio studies and has been shown to be sensitive to change resulting from interventions in children with ASD. It provides a measurement of social skills (particularly empathy, self-control and communication) as well as internalising and externalising problem behaviours. It also rates academic confidence including motivation to learn. It has good reliability and validity and is validated for use by teachers. The social skills subscale of the SSIS maps on to the primary objective of the trial (examining the clinical effectiveness of LEGO®-based therapy groups on the social and emotional competence of children with ASD in a mainstream school setting). The problem behaviours and academic competence subscales of the SSIS will be measured and reported as secondary outcomes. The associated teacher/ TA will be asked to complete the SSIS at baseline, 20 and 52 weeks after randomisation. The primary endpoint is 20 weeks after randomisation. The 20 week follow up point was chosen to be an approximation of the average expected duration of the intervention while allowing for slippage due to potential delay in training, school holidays and absences. When the follow up falls duing the summer holiday period, we will adopt a more pragmatic approach to collect follow up data in term time before the teachers and children break up for the holidays.The primary outcome measurement is unblinded as blinding is not feasible. This is due to the associated teacher completing the SSIS, who will be aware of which arm the school has been randomised to.

4.2. Secondary endpoints/ outcomes

The secondary outcomes of the study are outlined by respondent below. All measures will be collected at baseline, 20 weeks and 52 weeks after randomisation unless otherwise stated. The secondary endpoint is 52 weeks after randomisation.

4.2.1. Child questionnaires

1. The Multidimensional Scale of Perceived Social Support (Zimet, Dahlem, Zimet, & Farley, 1988). Friendship and significant other subscales will be used to assess the child's perceived social support. The full questionnaire is a short 12 item social support scale that assesses the adequacy of a person's perceived social support from family, friends and significant others. For the purposes of this study, we will assess the 8 items relating to support from friends and a significant other (within the school setting).
2. The Asher Loneliness Scale (Asher, Hymel, & Renshaw, 1984) is a friendship subscale that will be used to measure perceived social isolation. This self-report scale consists of 24 items. Respondents mark a 1-to-5 scale indicating the degree to which they feel the statements are 'true', ranging from 'not true at all' to 'always true'.
3. Child Health Utility 9D (CHU-9D) (Stevens, 2011) is a sensitive nine item child health-related quality of life assessment developed specifically with children in mind, rather than being an adjusted version of an adult measure (as for the EQ-5D-Y). The EQ-5D-Y has satisfactory validity and reliability, though we expect the CHU-9D to be a more valid and reliable measure with younger children (Furber & Segal, 2015).

4.2.2. Parent questionnaires

1. The Social Communication Questionnaire (SCQ) (Rutter, Bailey, & Lord, 2003) is a parent completed questionnaire derived from the Autism Diagnostic Interview–Revised (Lord, Rutter, & Le Couteur, 1994). The recommended cut-off to suggest it is likely an individual has ASD is 15. The SCQ has excellent sensitivity and reliability (Chandler et al., 2007). It will only be completed as an eligibility check prior to baseline – *baseline only*.
2. The Social Skills Improvement System (SSIS) (Gresham & Elliott, 2008) (further details in section 4.1).
3. Demographic information pertaining to the child and the parent will be collected. This will be done using a novel demographic information form – *baseline only*.
4. The Strengths and Difficulties Questionnaire (SDQ) (Goodman, 1997), consisting of 25 items, will be used to measure the participating child's emotional and behavioural difficulties, distress and social impairment. Participating parents will mark a 3 point scale indicating if each statement is true, somewhat true, or certainly true (e.g. considerate of other people's feelings). This is an internationally recognised reliable and valid measure used in studies of children & adolescents including those with ASD.
5. The EQ-5D-Y (3L proxy version) (The EuroQol Group, 1990) is a five item generic preference-based measure of health-related quality of life that allows a proxy person to complete the measure for the participant. The use of this measure allows for the comparison between groups across a wide range of comparable dimensions and can therefore be used to perform a cost-utility analysis.
6. Bespoke resource use questionnaires, as described above, to capture the healthcare and non-health resource implications (including costs in the education sector, and costs of productivity loss and out-of-pocket expenditures for parents) attributable to the child's difficulties due to their condition.
7. Bespoke questionnaire to assess acceptability of the intervention – *20 weeks only*.
8. Custom designed questions (included in resource use form at 20 weeks) to assess any adverse events that may have been attributable to the trial intervention or usual care interventions. This will be developed in conjunction with our PPI representatives and the local authorities - *20 weeks only*.

4.2.3. Associated teacher/TA questionnaires

1. The Social Skills Improvement System (SSIS) (Gresham & Elliott, 2008) (further details in section 4.1).
2. The Strengths and Difficulties Questionnaire (SDQ) (Goodman, 1997), consisting of 25 items will be used to measure the participating child's emotional and behavioural difficulties, distress and social impairment. The TA will mark a three point scale indicating if each statement is true, somewhat true, or certainly true (e.g. considerate of other people's feelings). This is an internationally recognised reliable and valid measure used in studies of children & adolescents including those with ASD.
3. Bespoke resource use questionnaires have been developed by the research team to capture the resource implications of a child's behaviour at school and as a way of recording care and interventions as usual received in both arms.

4. Custom designed questions (included in resource use form at 20 weeks) to assess any adverse events that may have been attributable to the intervention. This will be developed in conjunction with our PPI representatives and the local authorities – *20 weeks only*.

4.2.4. Interventionist Teacher/ TA

1. Demographic information will be collected from the interventionist teachers using a novel demographic information form and relating to training and experience – *baseline only*.
2. A bespoke resource use questionnaire has been developed by the research team to capture the resource implications of running the LEGO®-based therapy sessions at school. This will include details on the make-up of the group and basic information on the non-ASD children such as relevant clinical diagnoses or behavioural issues – *after each LEGO®-based therapy session*.
3. Custom designed questions (included in session resource use form) to assess any adverse events that may have been attributable to the intervention - *after each LEGO®-based therapy session*.
4. A fidelity checklist based on the existing treatment manual (LeGoff *et al.,* 2014) - *after each LEGO®-based therapy session*.
5. A bespoke questionnaire to assess acceptability of the intervention. This questionnaire will be completed at the 20 weeks follow-up point. In addition to this, acceptability will be further assessed through qualitative interviews, conducted by telephone with a purposive sample of 20% of the interventionists across school types (primary/secondary and sociodemographic variables) post-intervention (n=12).

5. Study Design and Setting

We will conduct a multi-site (using three recruiting sites) pragmatic cluster RCT comparing LEGO®-based therapy and usual support with a control group receiving usual support alone. Usual support is defined as the existing support routinely provided for a child with ASD from educational services. This will be documented regularly in a systematic way for the duration of the study using a standardised recording tool that has been used successfully by our team in previous school based intervention studies. A pragmatic approach was selected as opposed to a more explanatory design to maximise the external validity of the trial and to allow us to examine the clinical effectiveness, sustainability and cost effectiveness of the intervention (Torgerson & Torgerson, 2008). This design will include a 10 month internal pilot study, a nested qualitative component, an examination of treatment fidelity and an economic evaluation.

Participants will be recruited via their school and treatment will take place in the child's school. Baseline and follow-up visits may take place in schools or participants' homes.

5.1. Internal Pilot

The RCT will contain a ten month internal pilot. At the end of this period, the trial team will report to the NIHR on whether criteria for stopping have been met and whether the trial should continue. Sheffield CTRU will aggregate study data to assess feasibility of the research. Stop/Go criteria (see section 10.1) will be based on the feasibility of recruitment, retention and safety outcomes. We anticipate a recruitment rate of 12 children (six schools) per month. At ten months, we would have expected to recruit 120 children, and we will include a stopping criterion

of 75% of the recruitment target n=90. At this point, one third of the recruited participants would have reached the primary endpoint (n=40) and we would expect that 70% of the outcome measures will have been completed (n=28). As the trial exposes children with autism to a novel social situation, a Data Monitoring and Ethics Committee (DMEC) will review the data at the end of the pilot and throughout the trial for safety (see section 9.1). If there is evidence of harm due to the interventions or measures the trial may be stopped.

6. Eligibility Criteria

A number of inclusion and exclusion criteria must be met before a participant can be included in the trial. As I-SOCIALISE is a pragmatic trial, very few exclusion criteria will be applied. A detailed overview of the inclusion and exclusion criteria for the I-SOCIALISE trial is below.

6.1. Inclusion criteria

A participant will be included if the child:

- Is aged between 7 and 15 years at the time of randomisation of the school (based on previous research and extensive PPI recommendations).
- Attends a mainstream school in years 2-10.
- The child and parent/ guardian have a sufficient understanding of English to be able to provide informed consent and read the LEGO®-based therapy instructions.
- Has an ASD clinical diagnosis from a qualified assessing clinician or team [based on best-practice guidance leading to an ICD-10 (World Health Organization, 1993) or DSM-IV diagnosis (American Psychiatric Association, 2000) as reported by the child's parent/ guardian and in the child's school records (this may include the school's special educational needs (SEN) register, an individual education plan (IEP), individual health care plan, my support plan (MSPs), education health care plans (EHCPs), individual learning plans (ILP's) or equivalent).
- Scores 15 or higher on the Social Communication Questionnaire.
- Has the ability to follow and understand simple instructions (as determined by the associated teacher/ TA or parent/ guardian).

A school will be included if:

- It is a mainstream school located in Leeds, York, Sheffield or surrounding areas in the North of England.
- It has not used LEGO®-based therapy with the child in the current or preceding school term. For research purposes, LEGO®-based therapy is defined as meeting all of the main fidelity checklist criteria.
- They have at least one child diagnosed with ASD (in line with child inclusion criteria above)

6.2. Exclusion criteria

A participant would not be included in the study if:

- They have physical impairments which would prevent them participating in the activities (assessed by the associated teacher/TA).

7. Trial Procedures

7.1. Recruitment

I-SOCIALISE will use four methods of participant recruitment:

1. Contacting mainstream primary and secondary schools.
2. Local parent support groups.
3. Liaising with Local Authority professionals.
4. Local parents contacting the research team.

These methods are outlined in more detail below.

7.1.1. Recruitment from schools

The main recruitment approach for this trial will be achieved by contacting schools directly. The I-SOCIALISE research team has experience recruiting from schools and has established links to education services throughout Yorkshire (Wright et al., 2014; Wright et al., 2016). Potential schools have already been identified through the Department for Education and local council websites, and a database of all schools in each area has been compiled by the I-SOCIALISE research team. Information about the research will be sent to all schools on this database inviting them to participate with instructions to contact the research team if they would like further information, have any questions or would like to express interest, which will be followed up by a phone call to discuss the study with an appropriate member of the school (e.g. a head teacher or a Special Educational Needs Co-ordinator (SENCO)). When an eligible child is identified the researcher will provide the school with child, parent and TA information sheets and consent forms and ask the school staff to forward the appropriate sheets and forms to the child's parents and TA. Once the parents contact the study team or the parent gives verbal permission for the school to pass on their contact details to the study team, a researcher will arrange to meet them to explain the study, answer questions and collect consent from them and consent or assent from their child.

7.1.2. Recruitment from parent support groups

In addition to recruiting through schools, we will recruit through a number of local parent support groups such as the Autism Spectrum Conditions - Enhancing Nurture and Development (ASCEND) parent group (Pillay *et al.,* 2011) in York. The research team will offer to give presentations and share leaflets about the research with autism support groups. Recruitment packs will be given to interested parents and researchers will collect their contact details. It will be made clear that participation is dependant on the school taking part in the research. For interested parents, the school will then be contacted to inform them about the study and to identify the LEGO®-based therapy status of the school and the child. Once contact has been established with the school, the research team will follow the same recruitment procedure outlined above.

7.1.3. Recruitment from liaising with Local Authority professionals

Each recruiting site (Leeds, York, Sheffield or surrounding areas in the North of England) has an educational specialist in ASD within the local authority (also involved in training) as part of the study team, who is responsible for service delivery to children with ASD in that area. This individual will contact the parents of potential participating children with details of the study to assess participant eligibility and interest. Once contact has been established with the school, the research team will follow the same recruitment procedure outlined above. These specialists will also be able to inform the research team when new diagnoses are given to children at schools previously found to be ineligible due to having no children with ASD on their register at the time of contact.

7.1.4. Recruitment from local parents contacting the research team

We are aware that some local eligible families may hear about the trial and contact the research team to express their interest. If a local family contacts the research team, a researcher will confirm the child's age and diagnosis and send them further information regarding the study and will contact the school. It will be made clear that participation is dependent on the school taking part in the research. Once contact has been established with the school, the research team will follow the same recruitment procedure outlined above.

7.2. Screening and Eligibility Checks

Research assistants will contact all families who have expressed an interest in taking part in the trial by telephone to screen participants for eligibility for the I-SOCIALISE trial. Firstly, we will ascertain that child meets the following criteria:

- Is aged between 7 and 15 years at the time of randomisation of the school (based on previous research and extensive PPI recommendations)
- Attends a mainstream school in years 2-10.
- Has an ASD clinical diagnosis from a qualified assessing clinician or team [based on best-practice guidance leading to an ICD-10 (World Health Organization, 1993) or DSM-IV diagnosis (American Psychiatric Association, 2000)] as reported by the parent/guardian.
- Scores 15 or higher on the Social Communication Questionnaire (this will be completed at the first visit).
- Has the ability to follow and understand simple instructions (as determined by the associated teacher/ TA or parent/ guardian).

If a child appears eligible for inclusion after confirming a diagnosis of ASD with parents / guardian over the phone, the research assistant will arrange a face-to-face visit in order to take full informed consent, confirm eligibility and take baseline measures. The parent will be asked to complete the Social Communication Questionnaire on behalf of the child; those who score 15 or higher on the SCQ will be included in the trial. Any child or young person who does not meet the eligibility criteria for study participation and/or do not consent to the trial will be signposted to alternative sources of help relevant to their local area.

7.3. Informed Consent

Participation in the study will be entirely voluntary and written consent (and assent where applicable) from participants will be obtained before baseline data is collected and randomisation is conducted. Potential participants will be sent information leaflets by post. Information sheets will be provided for the parents of the children and age appropriate information sheets will be provided for the children. Each potential participant will have sufficient time (at least 24 hours) to read through the participant information sheet (PIS) and ask questions, either to the school contact or research team, before deciding whether to take part and providing consent.

If either parent or child do not wish to take part in the study then this will be considered as a lack of consent.

Initial consent from parents can be provided over the telephone following a full discussion of the trial and consent forms may be left at the school or posted if the participant is happy to complete them. Written consent will be confirmed at the baseline data collection visits.

All information leaflets and consent forms will be co-developed by the research team and external PPI representatives to ensure acceptability. Written consent will be obtained from teachers/TAs, interventionists and parents. consent or assent from children will be obtained.This consent will be completed either face-to-face, via post, via email, or by leaving the forms at schools for later collection.

If a participant wishes to withdraw from the intervention we will ask the participant if they are happy to continue being followed up so that their results can be included using an Intention to Treat (ITT) analysis.

7.4. Randomisation and Allocation

7.4.1. Randomisation scheme

We will use a cluster randomisation process by participating school. The rationale for this design is due to the group based nature of the therapeutic intervention and to control for contamination within schools. Randomisation will occur after eligibility has been established, consent has been obtained and baseline measures collected from teaching assistants (TAs)/teachers or education professionals. We will stratify randomisation by school level (primary or secondary school). The school will be further stratified if there are more than 6 eligible children.

7.4.2 Method of implementing the allocation sequence

Randomisation and allocation to arms will be conducted remotely by a statistician from the Sheffield Clinical Trials Research Unit (CTRU). Once allocation is made, the trial managers will inform the schools of their group status by phone or email. We will request that the school schedules the 12 weekly intervention sessions as soon as the interventionist TA is trained to deliver LEGO®-based therapy to ensure that they will be delivered before the 20 week follow-up point. A letter with this information and details on what their particular allocation involves will

also be sent to the school after randomisation. This process has been examined and proved effective in a previous school based study on children with ASD (Wright *et al.,* 2016).

7.5. Data Collection

Data collection will be completed by a trained research assistant, after informed consent has been given, at a convenient location for each participant. However, if informed consent is obtained within three months of the end of the summer term the baseline measures will be completed at the beginning of the autumn term to allow the children to receive the therapy without a substantial break inbetween sessions caused by the summer holidays. We will collect baseline measures from children and young people, their parents/guardians and their associated TA. The specific measures to be completed by children and young people and their parents/guardians are outlined in section 4; we estimate that baseline data collection will last approximately 60 minutes (including a break if needed).

Follow-up from parents/guardians and teachers/TAs may be completed via an online survey and text reminders may be sent (where we have consent to do so). A prize draw for parents/guardians will be implemented at the 20 and 52-week follow-up points to help with follow-up retention. There will be two prize draws for parents who completed their follow-up prior to the introduction of the prize-draw (one each for the 20 and 52 week follow-ups) and two prize draws for parents who completed their follow-up after the introduction of the prize-draw (one each for the 20 and 52 week follow-ups). Each prize draw will be for £50 of Love2shop vouchers to make a total prize draw value of £200.

Baseline is defined as the point at which baseline measures are completed by participants. Randomisation is the point at which a school is randomised to a treatment allocation in the study.

7.5.1. Outcome measures completed by children and young people

The child participants will complete a small series of self-report questionnaires at all time points during the study. Although the main focus will be on the child or young person completing these measures, a research assistant (RA) and parent/guardian will be on hand to assist if the child is having difficulties completing questionnaires (e.g. not understanding a question). Two of the three questionnaires the child participants will be asked to complete are pertinent to understand their perceived social isolation. The Asher Loneliness Scale (Asher, Hymel, & Renshaw, 1984) and the 8 items relating to support from friends and a significant other (within the school setting) in The Multidimensional Scale of Perceived Social Support (Zimet, Dahlem, Zimet, & Farley, 1988)will be used to assess perceived social isolation. Lastly, the child participants will be asked to complete the Child Health Utility 9D (CHU-9D) (Stevens, 2011) to assess the child's health-related quality of life.

7.5.2. Outcome measures completed by parents/ guardians

The parents/guardians will complete a range of questionnaires aiming to measure parental perspectives of their child with autism. Before completing baseline measures, the parents/ guardians will be asked to complete the Social Communication Questionnaire (SCQ) to

establish the child's eligibility for the trial; if the SCQ score is 15 or above the child will be eligible for the trial. The parent/ guardian will then be asked to complete a demographic questionnaire pertaining to the child and the parent. Demographic information will be collected using a novel demographic information form and will include questions focusing on the child's clinical ASD diagnosis (such as: name and profession of the person who made the ASD diagnosis, date of diagnosis, assessment type, and whether there is an official diagnosis letter).

Parents/ guardians will also be asked to complete the Social Skills Improvement System, Strengths and Difficulties Questionnaire (SDQ) (Goodman, 1997) to measure the participating child's emotional and behavioural difficulties. Lastly, the EQ-5D (3L proxy version) (The EuroQol Group, 1990) and a bespoke resource use questionnaire will be completed to assess the child's health-related quality of life and to capture the healthcare and non-health resource implications (including costs in the education sector, costs of productivity loss and out-of-pocket expenditures for parents) attributable to the child's difficulties due to their condition. Parents/guardians will also be asked to complete a bespoke questionnaire to assess the acceptability of the intervention to their children (in the intervention group only).

7.5.3. Outcome measures completed by the associated teacher/ TA

At baseline, the associated teacher/ TA to the participating child will be asked to complete the Social Skills Improvement System, the SDQ, and a bespoke resource use questionnaire. The SDQ and the resource use questionnaires will pertain to the participating child and will capture any emotional and behavioural difficulties and the resource implications of the child's behaviour at school. The associated teacher/ TA will also be asked to complete some questions to assess any adverse events that may have been attributable to the intervention.

7.5.4. Outcome measures completed by the interventionist teacher/ TA

At baseline, the interventionist teacher/ TA will be asked to complete a small demographic questionnaire including information such as their role in the school, how long they have worked in an educational setting, and whether they have run LEGO®-based therapy groups previously. After each LEGO®-based therapy session the interventionist teacher/ TA will be asked to complete a fidelity checklist, a bespoke resource use questionnaire to capture the resource implications of running the LEGO®-based therapy groups at school, a custom designed questionnaire to assess any adverse events that may have been attributable to the intervention, and an acceptability questionnaire. In addition to this, acceptability will be further assessed through qualitative interviews, conducted by telephone with a purposive sample of 20% of the interventionists across school types (primary/secondary and sociodemographic variables) post-intervention (n=12).

7.6. Blinding

The trial statisticians will remain blind throughout the duration of the study period. The DMEC will have access to the unblinded data at their request during the trial, for example if they are concerned of potential harm caused by the intervention; this data will be prepared by the data management team in the CTRU, aided by another CTRU statistician when required. Both trial statisticians will be blind to group allocation at each phase of the trial.

Research assistants collecting outcome data will be blinded to the trial treatment. Instances of unblinding will be recorded using a bespoke unblinding form (which will include information on who was unblinded, the source of unblinding, and the reason for unblinding). All measures are self report and children, parents and teachers will be aware of the treatment allocation for the trial.

7.7. Withdrawal criteria

Withdrawal can occur at any point during the study at the request of the participants or schools.

Where a parent wishes to withdraw from the study, withdrawal will be clarified by establishing whether they wish for their child to be withdrawn or if they themselves wish to withdraw. Where withdrawal is only for the participating parent, the child may continue to take part in all aspects of the trial.

Where an interventionist wishes to withdraw, withdrawal will be clarified as whether the school wishes to withdraw or they themselves wish to withdraw. Where withdrawal is only for the interventionist, attempts will be made to replace them for the intervention period.

If a child or their associated teacher/TA or school indicates that they wish to withdraw from the study or the parent wishes to withdraw their child from the study, withdrawal will be clarified by establishing whether the withdrawal is from the intervention, from follow-up or from all aspects of the study. Where withdrawal is only from the intervention then follow-up data will continue to be collected. Data will be retained for all participants up to the date of withdrawal, unless they specifically request for their data to be removed. We will provide an opportunity for all those who withdraw or indeed who choose not to give informed consent to have a chance to explain why they have decided to not continue participation.

Where a teacher withdraws consent we will consent another associated teacher if appropriate. If another teacher completes the questionnaires at follow-up points without the consented teacher formally withdrawing, this will be taken as implied consent to use that data and we will not collect further data from this teacher (e.g. contact details).

In the event that a child is found to be ineligible when basline data is taken, i.e. they do not have a confirmed diagnosis of Autism and/or they score >15 on the SCQ, they will be withdrawn from the study and will not be included in the ITT analysis.

7.8. Acceptability Study

Acceptability of the intervention to children will be assessed by the number of sessions attended and data collected from the interventionist and parent as we do not want to overburden the participants at each session. We will design a survey to assess acceptability of the intervention to the parents and the interventionists at the 20 week time point. In addition to this, acceptability will be further assessed through qualitative interviews, conducted by telephone with a purposive sample of 20% of the interventionists across school types (primary/secondary and sociodemographic variables) post-intervention (n=12).

These interviews will explore experiences of the implementation and delivery of LEGO®-based therapy, using Normalisation Process Theory (NPT) (May *et al.,* 2007) as the underpinning theoretical framework. Interventionists will also be asked to feedback on the perceived acceptability to children, parents and the school. We will use the interviews to investigate arising topics from the parent and interventionist surveys in more depth.

7.9. Qualitative Analysis

A nested qualitative analysis will be conducted near the end of the study. We will interview 12 interventionist teachers/ TAs to explore the arising topics from the parent and interventionist acceptability questionnaires. For the interviews we will use Normalisation Process Theory (NPT) (May *et al.,* 2007) to guide data collection and to frame the analysis to understand how easy it is to implement these interventions into routine practice. NPT conceives making changes in established routines as a complex and dynamic enterprise, and proposes a model which explains the way in which new practices are adopted and absorbed by individuals into existing behavioural conventions and routines. It has been proposed that this can help identify whether interventions are likely to become embedded and integrated as part of routine practice or not (Murray *et al.,* 2010). All interviews will be recorded and transcribed verbatim.

The Framework analysis approach (Spencer *et al.,* 2003) will be used to structure and explore the interview data, and NVivo software will be used to support this process.

7.10. Fidelity Analysis

We will develop a protocol for ensuring and monitoring intervention fidelity and sustainability. This will be composed of the following mechanisms:

1. An abridged training manual will be developed based on the existing LEGO®-based therapy manual (LeGoff *et al.,* 2014).
2. The training manual will be used to inform a programme of training developed and delivered by Gina Gomez de la Cuesta (co-applicant and co-author of the LEGO®-based therapy manual).
3. Supervision teleconferences will be arranged between the trainers and Gina Gomez de la Cuesta on a monthly basis.
4. The content of the treatment sessions will be monitored by video recording a purposively sampled number of schools with full written consent from all group participants.
    a. We will record 72 (10%) of the sessions across the study and sample according to school level (primary/secondary) and sociodemographic variables.
    b. 72 sessions across 24 schools, with three sessions per school recorded (one of the first four sessions, one of the second four sessions and one of the last four sessions).
    c. To assess the fidelity of the intervention, the video sessions will be reviewed by two independent observers and the inter-rater reliability calculated.
    d. The content of the recorded therapy sessions will be monitored using a recording form (fidelity checklist) based on work by Gina Gomez de la Cuesta.
    e. This checklist will also be completed by the interventionist at the end of each session providing data on the content of the sessions. This self-reported data will be compared to the recorded sessions where available.

7.11. Economic Evaluation

Information about the cost of all aspects of the treatment will be collected including training costs. We will undertake an analysis of cost-effectiveness at the end of the trial by comparing the cost of the intervention with any treatment benefit. We will collect data from the participant's associated parent about their resource use, such as visits to their GP and visits to other health

and other social care providers and data from the associated TA about service use in school. We will collect data on these carer costs through our resource use questionnaire. These will include cost of productivity loss and out-of-pocket expenditures.

8. Study Intervention

8.1. LEGO®-Based Therapy

LEGO®-based therapy (LeGoff, Gomez De La Cuesta, Krauss, & Baron-Cohen, 2014) is a group intervention that has gained considerable attention in the UK. The potential benefits of this therapy are that it was designed for school-age children with ASD as opposed to being an adapted form of a more generic social skills training intervention. Using collaborative LEGO®-based play the intention is to harness the child's own interests and so motivate learning and change, a focus recommended by international researchers in this area (LeGoff et al., 2014). LEGO® is a predictable, systematic multi-level construction toy that provides intrinsically structured tasks that children with ASD are highly motivated to complete (Owens, Granader, Humphrey, & Baron-Cohen, 2008). LEGO®-based therapy is specifically designed to make social interactions interesting to the child with ASD so that they learn how to play co-operatively with a toy that they enjoy which in turn increases the likelihood that they can continue to use these skills in their daily functioning.

Participating children allocated to the intervention group will be invited to attend a weekly group by a teacher or TA professionally trained in LEGO®-based therapy for a period of approximately 12 weeks. There may be breaks in the 12 weekly sessions due to illness and school holidays, though a break over the longer summer holiday will be avoided. In LEGO®-based therapy, the task of constructing a LEGO® set is divided into different roles, such that social interaction is necessary to participate. Rather than building alone, children build in pairs or threes. One child acts as the 'Engineer' (describes the instructions), one is the 'Supplier' (finds the correct bricks) and the other is the 'Builder' (puts the pieces together). Children play their role for a certain length of time, or a certain number of steps in the instructions and then swap around. This division of labour with a common purpose requires children to practice many social communication skills such as joint attention, turn taking, sharing, joint problem solving and compromise. More structured play is followed by 'Freestyle' LEGO® activities in which children work in pairs or small groups to create a model from general LEGO® pieces without instructions. This provides opportunities for children to practice creativity, compromise, expressing their ideas and taking other people's ideas into account.

The therapist's role is to assist social learning. Instead of providing children with solutions to social difficulties, they are required to highlight the presence of a problem as and when it occurs. Children then have to identify the problem, and come up with their own solutions (with prompting from the adult if necessary) which are practiced before continuing with LEGO® building. Solutions that children suggest are practiced until they can do it, and the adult reminds children of strategies if similar difficulties arise in future. Adults take the usual role of enabling safe play.

For this study the sessions will follow the guidelines detailed in the abridged manual developed as part of the study setup (see fidelity analysis section 7.10) and based on (LeGoff *et al.,* 2014). Sessions will be run by an interventionist recruited from each school who will be trained by a professional from the local authority or from the research team. Gina Gomez de la Cuesta and colleagues trained by her will provide training to these trainers who will then train all interventionists in the schools.

Groups will be made up of three to six children from a participating school, though they can go ahead with fewer numbers if children are absent on the day of a planned session. In the event that there are siblings within a school allocated to the intervention, schools will be requested to have them in separate groups to avoid bringing any dynamics from home into the groups. In schools where there are not enough children with ASD to make a complete group other children can join the group. This may include children who experience social difficulties that teachers believe may benefit from the intervention. This is the current policy of the local authorities and is the recommended method outlined by (LeGoff *et al.,* 2014). No identifiable data will be collected from these children, however they will be consented for being involved in the filming where applicable.

8.2. Care as usual

Participants allocated to 'usual support' will receive support as usual from their GPs, mental health and education professionals. Usual care is defined as normal practice for the school in question in addition to the usual support from the specialist teaching teams for autism in the area. This may include interventions such as the Picture Exchange Communication System (PECS), workstations, visual supports and schedules, and Social Stories. Services provided by the specialist teams include meeting and observing the child or young person in their setting, meeting their parents/carers and teachers/teaching assistants; liaising closely with colleagues in early years, transition team, health and social care; making recommendations to the setting about ways of supporting the child or young person; training in the use of different interventions, 1 to 1 working for specific interventions and attending reviews and meetings. They will also continue to provide reports and visual resources for home use and conduct monthly Drop In groups for parents. They will not receive the intervention or any extra support services from the research team.

8.3. Intervention Delivery

8.3.1. Treatment Protocol

As LEGO®-based therapy has only recently been established in the UK, it may be a new concept to the education professionals delivering the therapy. Therefore, we will follow a treatment protocol based on the work of Dr Daniel LeGoff and co-applicant Gina Gomez de la Cuesta. Co-applicant Gina Gomez de la Cuesta and colleagues trained by her will provide training to key professionals at each Local Authority and in the research team on how to deliver LEGO®-based therapy sessions successfully, who will in turn provide the training to the education professionals allocated to deliver the therapy. As usual care can differ greatly for

each child, this arm will not follow a treatment protocol devised by the research team. Fidelity and acceptability of LEGO®-based therapy will be assessed using bespoke questionnaires which will be completed by the interventionist and associated teachers/ TAs.

8.3.2. Facilitator Training

The LEGO®-based therapy sessions will be delivered by an educational professional who is employed by each school allocated to the intervention arm. The educational professional may vary between the schools (such as a teacher, TA, SENCO etc). All professionals delivering the therapy will be trained in the study's LEGO®-based therapy protocols. To ensure the therapy sessions are being run correctly, schools will be selected at random to have their session's video recorded. These recordings will be observed by the research team for fidelity checks.

In order to deliver the LEGO®-based therapy for the I-SOCIALISE trial, the interventionists must:

- Have completed training in using the study's protocols for LEGO®-based therapy and be willing to use this protocol to deliver LEGO®-based therapy.
- Be aware of the possibility that a number of their sessions may be recorded, for research fidelity checks.
- Complete a fidelity checklist after each session.

8.4. Modifications or Variations in Delivery

The delivery of the LEGO®-based therapy may require modifications to account for differences in the children's demographic characteristics.

8.4.1. The child's age

Younger children may require a slower pace throughout the sessions. Additionally, we will group children together of appropriate ages to ensure that the sessions run smoothly and are straightforward for the children to follow.

8.4.2. Presence of Comorbid Mental Health Problems

The proposed research will not exclude explicitly on the basis of comorbidities. However, there may be occasions when the teacher/TA or parent/ guardian feels that a comorbid mental health condition may be made worse through trial participation. At these points the child may be withdrawn from the trial but we will continue to collect data from these children if appropriate. Those with comorbidities who are able to continue in the trial will receive the LEGO®-based therapy or usual care as planned. If the child/young person has a care coordinator, we will liaise with them about any specific needs or symptoms that we should consider and/or monitor throughout the intervention delivery.

8.4.3. Presence of Intellectual or Developmental Disabilities, Behavioural or Attention Problems

Some intellectual and developmental disabilities may mean we have to adapt intervention delivery. Where this is likely (e.g. children with ADHD), sessions will be adapted to help the

child complete the sessions. For example, this may involve more frequent breaks, or to have a trusted adult or other items present (e.g. a favourite toy) to comfort the child. Materials designed for younger children (e.g. with pictures and cartoons) may be used with adolescents who have intellectual disabilities.

8.4.4. Peer involvement

If there are not enough children meeting the eligibility criteria in the school allocated to the intervention arm, other children who may benefit from the therapy (e.g. those with social isolation issues) will be approached to attend the LEGO®-based therapy group. We will obtain informed consent from the parents of all children participating in the LEGO®-based therapy groups.

8.4.5. English as an additional language

We do not have funding for translators or to develop the study materials in other languages and so we will not be able to recruit where parents/guardians cannot understand written English, as they will not be able to provide fully informed consent or complete the study measures. Existing school services will be used for children with language and comprehension difficulties where appropriate.

9. Monitoring of Adverse Events

Possible harm as a result of the study is expected to be minimal but will be monitored according the Sheffield CTRU SOPs.

1. Questions relating to Adverse Events (AEs) will be used to record any untoward occurrence affecting the participant after each LEGO®-based therapy session by the interventionist and at the 20 week follow-up conducted by the research assistant.
2. Teachers and parents will be asked if they believe there have been any untoward events (above the child's usual behaviour) at the 20 week time point.
3. All AEs will be assessed for seriousness, and will be recorded as a Serious Adverse Event (SAE) if it;
    - Results in death
    - Is life-threatening
    - Requires hospitalisation or prolongation of existing inpatients hospitalisation
    - Results in persistent or significant disability or incapacity
4. The occurrence of adverse events during the trial will be monitored by the DMEC and the TSC.

9.1. Possible Expected Adverse Events

Minimal adverse events can be expected during or after the LEGO®-based therapy sessions, and these will be reduced by 'club rules' (e.g. no LEGO® in the mouth) and monitoring by the interventionist who will be trained to deal with the child's distress. These adverse events may include:

- Choking on or swallowing LEGO®;

- Emotional distress or social anxiety that could lead to behaviours such as:
  - destruction of property (children may smash LEGO® models, throw furniture or break other items);
  - verbal abuse;
  - physical violence (children with ASD may express frustration/sadness/anxiety through hitting/biting/aggression);
  - running away to escape the situation.

SAEs considered related (to the intervention) and unexpected (i.e. not listed above) will be reported to the sponsor, the DMEC and the TSC within 15 working days of the CTRU being informed of the event and the TSC and DMEC will review all other SAEs at the next scheduled meeting.

10. Statistics and Data Analysis

10.1. Sample size calculation

The sample size calculation is based on the (Reichow *et al.,* 2012) Cochrane review which reported on five studies that examined the effects of social skills groups on social competence. This context was selected as the best indicator of realistic clinical effectiveness on the basis that if the proposed intervention was to be viable it needs to be at least as effective as running a social skills group in school. Of the five studies included in this review, four were RCTs and reported standardised measures of social competence which could be synthesised through meta-analysis techniques. The weighted mean standardised difference in social competence between group treatment and services as usual was 0.47 (95% confidence interval from 0.16 to 0.78). Reichow, *et al.,* (2012) argued that this average effect size of almost 0.5 of an SD corresponds to a clinically significant change, 'to put these gains in more concrete terms, if measuring everyday socials skills using the Vineland (Sparrow 2005) for example an average participant from these studies would increase their repertoire of social skills from 123 to 147 after participating in the social skills group which is a clinically significant increase'. Calculations using this standardised effect size of 0.47, 90% power and 5% two sided significance results in a sample size of 97 participants per condition or 194 participants in total. Attrition rates varied between 0% and 16% for the studies included in the (Reichow *et al.,* 2012) Cochrane review. As such, a conservative estimate of 16% inflates the sample to a final size of 116 participants per condition or 232 in total. To account for trainer/school effects and a cluster size of approximately 4 (2 participants per therapy group and 2 therapy groups per school) (ICC=0.01), based on the findings of the ASSSIST feasibility study conducted in the York area (Wright *et al.,* 2016) this figure was further inflated and rounded up to 120 participants per condition or 240 in total. We anticipate recruitment of 12 per month across all sites and have a retention rate of 84% at 20 week follow-up. The pilot period will run for 10 months, at which point we expect to have recruited n=120 of which one third (n=40) will have reached the primary endpoint. Stop/Go criteria based on 75% of recruitment target (n=90) and 70% of the primary outcome measures (n=28) will be used to assess feasibility of continuing the trial.

10.2. General Approach to Data Analysis

As this trial is a pragmatic cluster RCT, data will be analysed and reported according to both RCT and cluster RCT CONSORT guidelines (Schulz, Altman, & Moher, 2010; Campbell,

Piaggio, Elbourne & Altman, 2012). Baseline demographic (e.g. age, gender) and outcome measures (e.g. SDQ) will be assessed for comparability between groups.

We will use ITT analysis for all outcome measures, including those who withdraw from the treatment but complete outcome measures. This is the most appropriate form of analysis for a pragmatic trial as it maximises the external validity of the data despite the danger of dilution bias (Torgerson & Torgerson, 2008). Hence we can evaluate the evidence that the intervention has an effect on the social competence and perceived social isolation of children with ASD within a school setting. Per protocol analysis will include participants who have received 6 or more sessions of LEGO®-based therapy.

10.3. Primary and secondary outcomes analysis

The primary outcome will be the associated teacher reported social skills subscale of the SSIS measured at 20 weeks after randomisation. The SSIS will also be completed at 52 weeks post randomisation. The social skills subscale of the SSIS is a summated score which we will treat as a continuous variable. All measures will be compared between the two treatment groups using a generalised linear mixed model to account for clustering. We will include the following variables as covariates: age, sex, baseline social skills subscale of the SSIS, participant group (random effect), school (random effect), number of eligible children (stratification variable: less than or equal to 6 or more than 6) and school level (stratification variable: primary or secondary school). An unadjusted analysis (difference between group means and 95% confidence intervals) will be reported alongside the adjusted analysis. The significance level will be set at 5% for testing the primary outcome.

The secondary outcome variables will also be treated as continuous variables and analysed (adjusting for baseline score, age, sex, school level (stratification variable), number of eligible children (stratification variable), participant group (random effect), and school (random effect)) using the generalised linear mixed model framework.

10.4. Missing or spurious data

We anticipate some attrition so missing data may be an issue. Case and item missing data will be examined and multiple imputation methods will be used to reduce bias due to any missing responses in the analyses. Where appropriate, modelling methods that generate robust standard errors in the presence of missing data will be considered.

10.5. Fidelity Analysis

The fidelity evaluation will examine the extent to which the components of the intervention (LEGO®-based therapy) are delivered as planned, and the accommodations required by the host service/system to ensure this. Facilitators' adherence to core components will be assessed using standard, weekly completed checklists developed by the research team to assess implementation fidelity, which comprises indices for adherence, dose/exposure, quality of delivery and participant responsiveness. This will correspond with the components set out in the respective manual.

Adherence to an average of 80% of the content will be considered acceptable fidelity. We will produce descriptive statistics on all completed fidelity checklists.

We will also record 72 (10%) of the LEGO®-based therapy sessions across the study and sample according to school level (primary/secondary) and sociodemographic variables. We will aim to involve 24 schools with three sessions per school recorded (one of the first four sessions, one of the second four sessions and one of the last four sessions). However in the event that there are fewer schools consenting to be video recorded,(recordings are done only if there is consent from each member of the group) we may need to increase the number of sessions recorded per school to achieve our target of 72 (10%) of the sessions. To assess the fidelity of the intervention, the video sessions will be reviewed by two independent observers and the inter-rater reliability calculated.

10.6. Economic Analysis

Using a UK NHS and education perspective, the economic evaluation will take the form of a within-trial cost-effectiveness analysis that will determine the incremental cost per unit of outcome measure for LEGO®-based therapy compared with usual support in children with ASD. Health outcomes will be measured in terms of quality-adjusted life years (QALYs) using EQ-5D-Y proxy as a health descriptor measure [the preferred instrument in the NICE reference case]. The domains of EQ-5D proxy (3L version) will then be valued using UK population tariff to provide utility scores at multiple time points. A secondary analysis will be conducted using the Child Health Utility 9D (CHU-9D) measure to estimate QALYs based on the UK population tariff (Stevens, 2011).

Resource use data will be collected using a bespoke questionnaire that will capture data on the following: (1) use of community health services, including appointments with general practitioner, nurse, child development centre, walk-in-centre, social worker, family support worker, educational psychologist, educational welfare officer and school and college nurse; (2) mental health services, including psychiatrist, psychologist, CAMHS therapist, mental health nurse, family therapist, GP counselling, school counsellor and any privately paid mental health services; (3) hospital visits, including outpatient visits, inpatient admissions, accidents and emergency visits and urgent care centre visits; (4) school-based interventions/support provided by teachers; (5) cost of the LEGO-based therapy sessions; and (6) cost of travel for therapy sessions. Finally, data on costs and outcomes will be analysed together using an incremental cost-effectiveness analysis which evaluates differences in costs and effects against a range of willingness-pay thresholds of the decision maker for a one unit gain in QALY.

10.7. Qualitative Analysis

In addition to the planned quantitative analysis, the proposed research will conduct a qualitative investigation to examine the acceptability of LEGO®-based therapy.

We will invite a sub-sample of the interventionist teachers/ TAs to participate in interviews and use a purposive sample of 20% of the interventionists across school types (primary/secondary and sociodemographic variables) post-intervention (n=12). The interviews will be undertaken by a member of the research team and will be unblinded to trial allocation. Normalisation Process Theory (NPT) (May et al., 2007) will be used throughout the interviews to guide data collection and to frame the analysis to understand how easy it is to implement LEGO®-based therapy into routine practice. All interviews will be recorded and transcribed verbatim. The framework

analysis approach (Spencer et al., 2003) will be used to structure and explore the interview data, and NVivo software will be used to support this process.

Data coding will be undertaken independently by two trained researchers. We will additionally train a PPI representative coder to work alongside these researchers, and to ensure coding takes account of potential differences in perspective. Coders will meet regularly to develop a shared coding manual and to ensure that all emerging codes remain grounded in original data. An Excel spread sheet will be developed which will incorporate preliminary framework themes as column headings and the demographic information related to participants who provided data under each theme. As the constant comparison of new data occurs and the coding team's understandings of the themes under consideration develop, the framework will be amended and re-shaped to enable the introduction of new codes and/or the deletion of redundant, similar or otherwise compromised codes. In this way, a final framework will be achieved that is considered representative of the entire dataset. The final coding manuals, with example entries, will be presented to the TMG and TSC to confirm its validity, coherence and conceptual relevance. Co-applicant Dr Lizzie Coates from the University of Sheffield will supervise the qualitative study and analysis.

The key ethical issues for the qualitative aspect of the study include confidentiality, participant anonymity, and informed consent to participate in research. Whilst the risk is small, there is a small possibility that participants might become distressed by disclosures about their own experiences during interviews and there may be disclosures relating to professional practice. A distress policy will be developed in consultation with the advisory team and a clinical lead will be identified from whom advice and guidance may be sought should the need arise. The information sheets will provide potential participants with information about the study, including the potential benefits and risks of taking part and information on anonymity and confidentiality.

11. Data Handling

11.1. Data collection tools and source document identification

The content of all validated measures used in this trial will not change; however, the Clinical Trials Research Unit (CTRU) will reformat the outcome measures in order to standardise their appearance and layout where possible, and include a participant identification number rather than identifiable details. All measures are self-reported and will form the basis of all source data during this trial.

11.2. Data handling and record keeping

Trial data will be extracted from source documents and entered onto the CTRU's in-house data management system (Prospect). Prospect stores data in a PostgreSQL database on virtual servers hosted by Corporate Information and Computing Services (CiCS) at the University of Sheffield. The system uses industry standard techniques to provide security; all data transmissions are encrypted using SSL/TLS, and access is controlled by usernames and (encrypted) passwords. A comprehensive privilege management feature ensures only the minimum amount of data required is available to each individual to complete their tasks. The system has a full electronic audit trail and is regularly backed up.

Participant names and contact details will be collected and entered on the Prospect database but access to these personal details will be restricted to users with appropriate privileges only. A unique participant ID number will be assigned to all participants, and no patient identifiable data will be transferred from the database to the statistician. Output for analysis will be generated in a format, and at intervals, to be agreed between Sheffield CTRU and the Chief Investigator.

All data will be collected and retained in accordance with the Data Protection Act 2018, the General Data Protection Regulation, and CTRU standard operating procedures (SOPs). Copies of consent forms will be sent to the CTRU for monitoring purposes; this is detailed in the participant information sheets. The study consent form will include a statement affirming agreement with sharing anonymised data and an optional statement affirming agreement to being contacted about future research, thus there is potential for the data from this study to be made available to other researchers.

To assess the fidelity of LEGO®-based therapy, a sample of sessions will be video-recorded. These video recordings will only be completed with informed consent from both the participant and their parent/guardian. With consent, all interviews that are conducted as part of this trial will be audio recorded using an encrypted digital recorder. During the transcription of all interviews pseudonyms will be employed to maintain confidentiality. All video and audio-recordings will be stored in a locked filing cabinet within a locked office to which only members of the research team have access, and digital copies will be stored on access-restricted folders. Any transfer of electronic data to other research sites will be encrypted.

The sponsor will permit monitoring and audits by the relevant authorities, including the HRA. The Chief Investigator will also allow monitoring and audits by these bodies and the sponsor, providing direct access to source data and documents, including the database. The CTRU data management system incorporates quality control to validate study data. Validation reports will be run regularly to check the study data for completeness, accuracy and consistency. Discrepancies will be generated and managed to resolution. The central study team will work with research assistants to ensure the quality of data provided. Data monitoring and audits will be conducted in accordance with the CTRU SOPs.

11.3. Archiving

Study documentation and data will be archived at a suitable time following database lock. All essential study documents will be retained as part of the trial master file and individual site files. After notification of study completion, all documentation and study data will be stored securely for five years and will be accessible for inspections and audits.

12. Monitoring, Audit and Inspection

Trial monitoring procedures and site monitoring will be undertaken at a level appropriate to a risk assessment performed by the Sponsor and the CTRU according to CTRU SOPs, and significant findings will be presented to the appropriate oversight committee.

Three committees will be established to govern the conduct of this study:

- A Trial Steering Committee (TSC).
- An independent Data Monitoring and Ethics Committee (DMEC).

- A Trial Management Group (TMG).

These committees will function in accordance with Sheffield CTRU SOPs. The TSC will consist of an independent chair, an independent subject specialist, an independent clinical academic, an independent statistician and a PPI representative. The DMEC will consist of an independent chair, an independent statistician, and another independent member experienced in research with children and families. The TSC and DMEC will meet approximately every 6 months from the start of the trial. The TMG will comprise the co-applicants, members of the trial team (including the data manager), PPI representatives, and the two trial managers who will be jointly supervised by the CI, and the director of the Sheffield CTRU. Meeting attendance of the co-applicants and trial team will depend on the agenda and relevance to their role.

13 Ethical and Regulatory Considerations

13.1 Research Ethics Committee (REC) review & reports

We will seek ethical approval in line with the University of York's ethics policy, the Research Governance Framework and HRA guidance. No pharmaceutical compounds or medical devices are used in this trial, therefore Clinical Trials Authorisation is not required. NHS ethical approval is not required as we are not recruiting from or undertaking the trial within the NHS, or involving participants identified from, or because of their past or present use of NHS services. Separate research governance approval will be required from each of the areas in which participants are to be recruited. Changes to study documents will be reviewed and approved in line with HRA requirements and annual reports will be sent to the HRA.

13.2 Peer review

The proposed trial has been previously peer reviewed in line with National Institute for Health Research (NIHR) Public Health Research (PHR) funding process.

13.3 Public and Patient Involvement

We are committed to the involvement of patient and public representatives at all stages of the proposed research. The original research proposal was developed in consultation with a representative from the National Autistic Society (NAS), a parent of a child with ASD, and the Young Dynamos, a young person's PPI group based in West Yorkshire. We will continue to work with these groups throughout the trial and will endeavour to incorporate suggestions and feedback where appropriate and possible. Finally, we recognise the need for independent qualitative data analysis, and will train a PPI representative to assist with the qualitative data analysis. The PPI representative will be reimbursed for their time, commensurate with current INVOLVE guidelines.

13.4 Protocol, GCP and Regulatory Compliance

Non-compliance with Good Clinical Practice and the protocol will be monitored and recorded by the I-SOCIALISE study team in accordance with CTRU's SOPs.

13.5 Financial and Competing Interests

Co-applicant Gina Gomez de la Cuesta co-authored the LEGO®-based therapy manual which will form the basis of the LEGO®-based therapy delivered in the trial (LeGoff *et al.,* 2014). The co-authors of the manual have given us full permission to use the manual without license and to develop an abridged version. They have also stated their support for us in writing our own version, and will become co-authors on any future publications. Co-applicant Gomez has also agreed for the team to adapt the fidelity checklist used in her previous study.

The research team are also aware that the LEGO® name is a registered trademark and will follow their fair use policy in regard to the LEGO® brand throughout the duration of the trial.

We have provisional agreement with Jessica Kingsley Publishers who have expressed interest in publishing the abridged manual. However, we are not tied to them as a publisher. There are no other financial and/ or competing interests to declare.

13.6 Indemnity

To meet the potential legal liability for harm to participants arising from the design, conduct and management of the research, NHS employees will be covered by NHS indemnity and university employees will be covered by their institution's insurance. Group sessions will be held on school premises, therefore trial participants and all involved education professionals will be covered by the school's indemnity insurance.

13.7 Amendments

All amendments will be approved by the Chief Investigator and all substantial amendments will be approved by the Chief Investigator, the Sponsor and the TMG and submitted for approval by the ethics committee and the HRA prior to implementation. Amendment history will be tracked by adopting version control and by the use of an amendment log.

13.8 Post trial care

All children on the autism spectrum will continue to have individualised support plans (for example, an individual education plan (IEP), individual health care plan, my support plan (MSPs), education health care plans (EHCPs), individual learning plans (ILP's) or equivalent) and these will be tailored to the needs of each child through usual school/ local authority processes. Where any child has been identified with additional needs then an information leaflet that gives further information about where children and families may obtain additional services will be provided. This would include voluntary agencies, parent support groups, local authority specialist teacher provision for autism, health and disability teams within social care, and CAMHS. Child mental health services in Leeds and York both include school based support and provision, and have a single point of access to engage in an early assessment. All of these services will be available to any child with additional needs.

14 Dissemination Policy

The research team has a strong track record of successful dissemination of work funded by the NIHR and other funding bodies. We will begin to consider our dissemination strategy at an early stage of the project. We will publish the results of each phase of our study in high profile mainstream and specialist science journals, such as the British Journal of Psychiatry, the Journal of Child Psychology and Psychiatry, Clinical Child Psychology and Psychiatry and Journal of Autism and Developmental Disorders.

Presentations of study findings will be taken to relevant research conferences, local research symposia and seminars for CAMHS, child health and educational professionals. In addition, the National Autistic Society and members of service user groups such as ASCEND will be consulted in the development of methods and dissemination which will be effective in reaching families of children with ASD. Additionally, we will produce a short summary of the results that can be distributed to all trial participants as well as relevant interest groups, including patient groups. We will publish findings on relevant websites such as the National Autistic Society, university and child mental health websites. Finally, we will aim to ensure coverage of our findings in the wider media by issuing a press release.

Towards the end of the trial, our PPI representatives will organise a meeting with stakeholders including parents and professionals working with young people with ASD to specifically discuss the dissemination of the study findings and put together a dissemination plan. This will be present at the trial management group and any additional dissemination plans will be added. We will hold a research dissemination event for national and local clinicians and policy makers. Depending on findings, we will make suggestions to NICE about treatment evidence

15 References

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders: DSM-IV-TR* (4th ed., text revision). Washington, DC.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed). Washington, DC.

Asher, SR., Hymel, S., & Renshaw, PD. (1984). Loneliness in children. *Child Development*. 1456-1464.

Baer, D.M., Wolf, M.M., & Risley, T.R. (1968). Some current dimensions of applied behavior analysis. *Journal of Applied Behavior Analysis*. 1(1), 91–97.

Bagwell, CL., Newcomb, AF., & Bukowski, WM. (1998). Preadolescent Friendship and Peer Rejection as Predictors of Adult Adjustment. *Child Development.* 69(1), 140-153.

Baron-Cohen, S., Scott, F., Allison, C., Williams, J., Bolton, P., Mathews, F., & Brayne, C. (2009). Prevalence of autism spectrum condition: UK school-based population study. *British Journal of Psychology.* (194), 500-509.

Bauminger, N., & Kasari, C. (2000). Loneliness and friendship in high-functioning children with autism. *Child Development.* 71(2), 447-456.

Bauminger, N., & Shulman, C. (2003). The Development and Maintenance of Friendship in High-Functioning Children with Autism: Maternal Perceptions. *Autism.* 7(1), 81-97. doi:10.1177/1362361303007001007

Bellini, S., Peters, JK., Benner, L., Hopf, A. (2007). A meta-analysis of school-based social skills interventions for children with autism spectrum disorders. *Remedial and Special Education*. 28(3), 153–162.

Bondy, A., & Frost, L. (1994). The picture exchange communication system. *Focus on Autistic Behavior*. 9, 1–19.

Campbell, MK., Piaggio, G., Elbourne, DR., Altman, DG. (2012). For the CONSORT Group. Consort 2010 statement: extension to cluster randomised trials. *BMJ*. 345:e5661.

Carrington, S., & Graham, L. (2001). Perceptions of school by two teenage boys with Asperger syndrome and their mothers: A qualitative study. *Autism.* 5, 37-48. doi:10.1177/1362361301005001004

Chamberlain, B., Kasari, C., & Rotheram-Fuller, E. (2007). Involvement or Isolation? The Social Networks of Children with Autism in Regular Classrooms. *Journal of Autism and Developmental Disorders.* 37(2), 230-242. doi:10.1007/s10803-006-0164-4

Chandler, S., Charman, T., Baird, G., Simonoff, E., Loucas, T., Meldrum, D., Pickles, A. et al. (2007). Validation of the Social Communication Questionnaire in a Population Cohort of Children with Autism Spectrum Disorders. *Journal of the American Academy of Child and Adolescent Psychiatry.* 46(10), 1324-1332.

Dawson, G., Toth, K., Abbott, R., Osterling, J., Munson, J., Estes, A., & Liaw, J. (2004). Early social attention impairments in autism: social orienting, joint attention, and attention to distress. *Developmental Psychology.* 40(2), 271-283.

Delprato, D. (2001). Comparisons of Discrete-Trial and Normalized Behavioral Language Intervention for Young Children with Autism. *Journal of Autism and Developmental Disorders.* 31(3), 315-325.

Department for Education and Skills. (2002). *Department for Education and Skills: Autistic Spectrum Disorders: Good practice guidance*.

Eaves, L., & Ho, H. (2008). Young Adult Outcome of Autism Spectrum Disorders. *Journal of Autism and Developmental Disorders.* 38(4), 739-747.

Frankel, F., Myatt, R., Sugar, C., Whitham, C., Gorospe, C. M., & Laugeson, E. (2010). A randomized controlled study of parent-assisted Children's Friendship Training with children having autism spectrum disorders. *Journal of Autism and Developmental Disorders.* 40(7), 827-842.

Furber, G., & Segal, L. (2015). The validity of the Child Health Utility instrument (CHU9D) as a routine outcome measure for use in child and adolescent mental health services. *Health and Quality of Life Outcomes.* 13, 22.

Gates, JA., Kang, E., & Lerner, MD. (2017). Efficacy of group social skills interventions for youth with autism spectrum disorder: A systematic review and meta-analysis. *Clin Psychol Rev.* 52, 164-181.

Goodman, R. (1997). The Strengths and Difficulties Questionnaire: a research note. *Journal of Child Psychology and Psychiatry.* 38(5), 581-586.

Grandgeorge, M., Bourreau, Y., Alavi, Z., Lemonnier, E., Tordjman, S., Deleau, M., & Hausberger, M. (2015). Interest towards human, animal and object in children with autism spectrum disorders: an ethological approach at home. *European Child and Adolescent Psychiatry.* 24(1), 83-93.

Gresham, F., & Elliott, SN. (2008). *Social skills improvement system (SSIS) rating scales*. Bloomington, MN: Pearson Assessments.

Howlin, P., Goode, S., Hutton, J., & Rutter, M. (2004). Adult outcome for children with autism. *Journal of Child Psychology and Psychiatry.* 45(2), 212-229.

Howlin, P., & Moss, P. (2012). Adults with autism spectrum disorders. *Canadian Journal of Psychiatry. Revue Canadienne de Psychiatrie.* 57(5), 275-283.

Killen, M., Mulvey, KL., & Hitti, A. (2013). Social Exclusion in Childhood: A Developmental Intergroup Perspective. *Child Development.* 84(3), 772-790.

Koenig, K., White, SW., Pachler, M., Lau, M., Lewis, M., Klin, A., & Scahill, L. (2010). Promoting social skill development in children with pervasive developmental disorders: a feasibility and efficacy study. *Journal of Autism and Developmental Disorders.* 40(10), 1209-1218.

Laugeson, EA., Frankel, F., Mogil, C., & Dillon, AR. (2009). Parent-assisted social skills training to improve friendships in teens with autism spectrum disorders. J*ournal of Autism and Developmental Disorders.* 39(4), 596-606.

LeGoff, D., Gomez De La Cuesta, G., Krauss, GW., & Baron-Cohen, S. (2014). *LEGO® - Based Therapy: How to Build Social Competence Through Lego®-Based Clubs for Children with Autism and Related Conditions*: Jessica Kingsley Pub.

Licciardello, CC., Harchik, AE., & Luiselli, JK. (2008). Social skills intervention for children with autism during interactive play at a public elementary school. *Education and Treatment of Children.* 31(1), 27-37.

Lopata, C., Thomeer, ML., Volker, MA., Toomey, JA., Nida, RE., Lee, GK., et al. (2010). RCT of a manualized social treatment for high-functioning autism spectrum disorders. *Journal of Autism and Developmental Disorders.* 40(11), 1297-1310.

Lord, C., Rutter, M., & Lecouteur, A. (1994). Autism Diagnostic Interview- Revised: A revised version of a diagnostic interview for caregivers of individuals with possible Pervasive Developmental Disorders. *Journal of Autism and Developmental Disorders.* 24(5), 659-685.

Marshall, D., Wright, B., Allgar, V., Adamson, J., Williams, C., Ainsworth, H., Cook, L., Varley, D., Hackney, L., Dempster, P., Ali, S. (2016). Social Stories in mainstream schools for children with autism spectrum disorder: a feasibility randomised controlled trial. *BMJ open*. 6(8), e011748.

May, C., Finch, T., Mair, F., Ballini, L., Dowrick, C., Eccles, M., Heaven, B. et al,. (2007). Understanding the implementation of complex interventions in health care: the normalization process model. *BMC Health Services Research.* 7, 148.

McClelland, MM., Morrison, FJ., & Holmes, DL. (2000). Children at risk for early academic problems: the role of learning-related social skills. *Early Childhood Research Quarterly.* 15(3), 307-329.

Murray, E., Treweek, S., Pope, C., MacFarlane, A., Ballini, L., Dowrick, C., et al. (2010). Normalisation process theory: a framework for developing, evaluating and implementing complex interventions. *BMC Medicine.* 8, 63.

National Institute for Health and Clinical Excellence (2008). *Social and emotional wellbeing in primary education*. London; NICE. .

National Institute for Health and Care Excellence (2013). *Autism in under 19s: support and management*. London; NICE.

Ochs, E., Kremer-Sadik, T., Solomon, O., & Sirota, K. (2001). Inclusion as Social Practice: Views of Children with Autism. *Social Development.* 10, 399-419.

Ochs, E., and Solomon, O. (2010). Autistic sociality. *Ethos*. 38, 69-92.

Owens, G., Granader, Y., Humphrey, A., & Baron-Cohen, S. (2008). LEGO® Therapy and the Social Use of Language Programme: An Evaluation of Two Social Skills Interventions for Children with High Functioning Autism and Asperger Syndrome. *Journal of Autism and developmental Disorders.* 38(10), 1944-1957.

Pillay, M., Alderson-Day, B., Wright, B., Williams, C., & Urwin, B. (2011). Autism Spectrum Conditions - Enhancing Nurture and Development (ASCEND): An evaluation of intervention support groups for parents. *Clinical Child Psychology and Psychiatry.* 16(1), 5-20.

Reichow, B., Steiner, AM., & Volkmar, F. (2012). Social skills groups for people aged 6 to 21 with autism spectrum disorders (ASD). *Cochrane Database Syst Rev.* 7, Cd008511.

Rinaldi, W. (2004). Social Use of Language Programme. Infant and primary school teaching pack. Cranleigh: Wendy Rinaldi.

Rowley, E., Chandler, S., Baird, G., Simonoff, E., Pickles, A., Loucas, T., & Charman, T. (2012). The experience of friendship, victimization and bullying in children with an autism spectrum disorder: Associations with child characteristics and school placement. *Research in Autism Spectrum Disorders.* 6(3), 1126-1134.

Rutter, M., Bailey, A., & Lord, C. (2003). *The social communication questionnaire: Manual*. Western Psychological Services.

Sansoni, J., Marosszeky, N., Sansoni, E., et al. (2010). *Effective Assessment of Social Isolation*. Centre for Health Service Development, Wollongong.

Schulz, KF., Altman, DG., & Moher, D. (2010). CONSORT 2010: statement: Updated guidelines for reporting parallel group randomised trials. *J Pharmacol Pharmacother.* 1(2): 100-7.

Solomon, M., Goodlin-Jones, BL., & Anders, TF. (2004). A social adjustment enhancement intervention for high functioning autism, Asperger's syndrome, and pervasive developmental disorder NOS. *Journal of Autism and Developmental Disorders.* 34(6), 649- 668.

Sparrow, SS., Cicchetti, DV., Balla, DA. (2005). *Vineland Adaptive Behavior Scales*. 2nd Edition. Upper Saddle River, NJ: Pearson.

Spencer, L., Ritchie, J., & O'Connor, W. (2003) Analysis: practices, principles and processes. *In Qualitative Research Practice: A Guide for Social Science Students and Researchers* (Ritchie J. & Lewis J., eds), Sage, London, pp. 199–218.

Stevens, K. (2011). Assessing the performance of a new generic measure of health-related quality of life for children and refining it for use in health state valuation. *Appl Health Econ Health Policy.* 9(3), 157-169.

The EuroQol Group. (1990). EuroQol- A new facility for the measurement of health related quality of life. *Health Policy.* 16(3), 199-208.

Torgerson, DJ., & Torgerson, C. (2008). *Designing randomised trials in health, education and the social sciences : an introduction*. Basingstoke: Palgrave Macmillan.

Travis, L., Sigman, M., & Ruskin, E. (2001). Links between social understanding and social behavior in verbally able children with autism. *Journal of Autism Developmental Disorders.* 31(2), 119-130.

Whitehouse, AJ., Watt, HJ., Line, E., & Bishop, DV. (2009). Adult psychosocial outcomes of children with specific language impairment, pragmatic language impairment and autism. *International Journal of Language and Communication Disorders.* 44(4), 511-528.

World Health Organization. (1993). *The ICD-10 classification of mental and behavioural disorders: Diagnostic criteria for research*. Geneva: World Health Organization.

Wright, B., Marshall, D., Collingridge Moore, D., Ainsworth, H., Hackney, L., Adamson, J., Ali, S., et al. (2014). Autism Spectrum Social Stories In Schools Trial (ASSSIST): study protocol for a feasibility randomised controlled trial analysing clinical and cost-effectiveness of Social Stories in mainstream schools. *BMJ Open.* 4**:**e005952.

Wright, B., Marshall, D., Adamson, J., Ainsworth, H., Ali, S., Allgar, V., Collingridge Moore, D., et al. (2016). Social Stories to alleviate challenging behaviour and social difficulties exhibited by children with autism spectrum disorder in mainstream schools: design of a manualised training toolkit and feasibility study for a cluster randomised controlled trial with nested qualitative and cost-effectiveness components. *Health Technol Assess*. 20(6).

Zimet, GD., Dahlem, NW., Zimet, SG., & Farley, GK. (1988). The Multidimensional Scale of Perceived Social Support. *Journal of Personality Assessment.* 52(1), 30-41.

16. Appendices

16. 1 Appendix 1 – Amendment History

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made
1	2	14/09/2017	DV	Section 4.2.4 of the protocol has been updated to reflect changes to the parent consent form for children without autism (non-ASD) participating in groups, to inform the parents that we will be asking their child's school for basic information relating to the child's involvement in the group sessions.
2	3	19/12/2017	DV	The protocol in light of the comments made by the TSC and the TMG. An extra objective has been added to the study at the TSC's request (section 3.2). In addition, the inclusion criteria (section 6.1), informed consent procedure (section 7.3), reasons for blinding (sections 4.1 and 7.6), and time of baseline (section 7.5) sections have been further clarified.
3	4.0	27/03/2018	SJE	As recommended by the DMEC and TSC (held on 08/02/2018 and 26/02/2018) the time point for the first follow-up has been amended to 20 weeks throughout the protocol (this was previously 16 weeks). In addition, in section 4 clarification has been provided on the various methods that outcome data may be collected. In section 4.1 clarification is provided regarding the pragmatic approach to collect follow up data which fall during the summer holidays. In sections 6.1 & 7.2 clarification regarding inclusion age of partcipants provided (as decided on TMG held on

				21.03.2018). In section 8.1 clarification has been provided on the inclusion of siblings in the study. Sections 8.3.2 & 10.5 have been updated to provide clarification on fidelity video recordings.
4	5	25.09.2018	EK, DV	Trial contacts have been updated. The primary outcome measure has been clarified as being the social skills subscale of the SSIS. The problem behaviour and academic competence subscales have been listed as secondary outcome measures. Expansion of recruiting areas to include Leeds, York, Sheffield AND surrounding areas in the North of England. Children will be withdrawn from the study where it is found the child does not have a clinical disgnosis of autism. Data will not be included in the ITT analysis. Clarification added to delivery of training in LEGO®-based therapy Clarification added to the wording of the statistical power calculations. Per protocol analysis has been specified to include children who completed at least 6 sessions of LEGO®-based therapy. Clarification added to fidelity analysis, descriptive statistics will be produced on all completed fidelity checklists DPA and GDPR have been updated.It has been specified that follow-up points will be completed X number of weeks after *randomisation* as opposed to baseline. The timepoints at which each outcome measure is administered and each study objective is measured have been specified wherever these are discussed. Baseline and randomisation definitions have been clarified. The economic analysis perspective has been changed to UK NHS and education to match the HEAP

				Specification added to who will provide trainer training to local authorities and research staff if Gina Gomez de la Cuesta is not available. We have removed the paragraph in section 8.2 which stated that we would not offer LEGO®-based therapy training to control schools until we had established any risk of harm and cost effectiveness. This follows the decision to offer the training after completion of the last follow-up point for the study as schools would be able to access the training externally through regardless. Specification has been added to say that interested parents can either contact the study team directly or can give verbal permission to the school to pass on their contact details to the study team.
5	6	13.01.2020	EK	Section 7.5 Data Collection has been updated to include a description of the prize draw used to help with parent/guardian follow-up retention.