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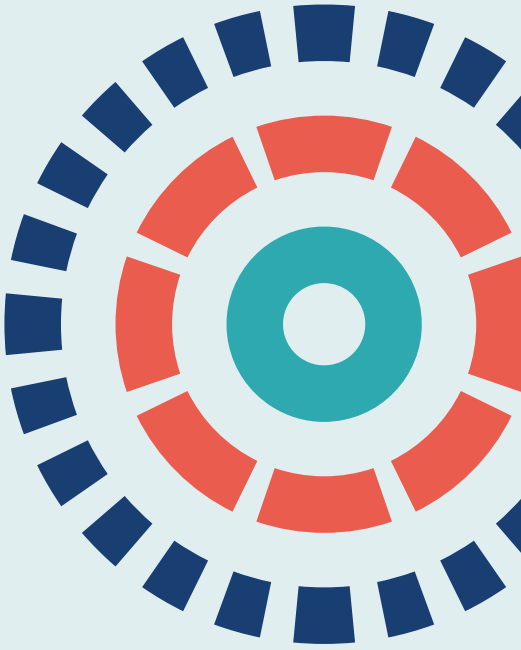

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An adapted social communication intervention at home and education to promote social communication change in children with severe autism: the PACT-G RCT

Jonathan Green,[1,2,3*] Kathy Leadbitter,[1] Ceri Ellis,[1] Lauren Taylor,[4] Heather L Moore,[5,6] Sophie Carruthers,[4] Kirsty James,[7] Carol Taylor,[1] Matea Balabanovska,[1] Sophie Langhorne,[1] Catherine Aldred,[1] Vicky Slonims,[8] Victoria Grahame,[9,10] Jeremy Parr,[5,9,11] Neil Humphrey,[12] Patricia Howlin,[4] Helen McConachie,[6,7] Ann Le Couteur,[5,6] Tony Charman,[4] Richard Emsley[7] and Andrew Pickles[7]

[1]Division of Neuroscience & Experimental Psychology, University of Manchester, Manchester, UK
[2]Royal Manchester Children's Hospital, Manchester, UK
[3]Manchester Academic Health Science Centre, Manchester, UK
[4]Department of Psychology, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
[5]Population Health Sciences Institute, Newcastle University, Newcastle upon Tyne, UK
[6]Sir James Spence Institute, Royal Victoria Infirmary, Newcastle upon Tyne, UK
[7]Department of Biostatistics and Health Informatics, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
[8]Evelina London Children's Hospital, Guy's and St Thomas' NHS Foundation Trust, London, UK
[9]Complex Neurodevelopmental Disorders Service, Cumbria, Northumberland, Tyne and Wear NHS Foundation Trust, Newcastle upon Tyne, UK
[10]Walkergate Park, Centre for Neurorehabilitation and Neuropsychiatry, Newcastle upon Tyne, UK
[11]Great North Children's Hospital, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK
[12]Manchester Institute of Education, University of Manchester, Manchester, UK

*Corresponding author

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Abstract

An adapted social communication intervention at home and education to promote social communication change in children with severe autism: the PACT-G RCT

Jonathan Green,[1,2,3*] Kathy Leadbitter,[1] Ceri Ellis,[1] Lauren Taylor,[4] Heather L Moore,[5,6] Sophie Carruthers,[4] Kirsty James,[7] Carol Taylor,[1] Matea Balabanovska,[1] Sophie Langhorne,[1] Catherine Aldred,[1] Vicky Slonims,[8] Victoria Grahame,[9,10] Jeremy Parr,[5,9,11] Neil Humphrey,[12] Patricia Howlin,[4] Helen McConachie,[6,7] Ann Le Couteur,[5,6] Tony Charman,[4] Richard Emsley[7] and Andrew Pickles[7]

[1]Division of Neuroscience & Experimental Psychology, University of Manchester, Manchester, UK
[2]Royal Manchester Children's Hospital, Manchester, UK
[3]Manchester Academic Health Science Centre, Manchester, UK
[4]Department of Psychology, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
[5]Population Health Sciences Institute, Newcastle University, Newcastle upon Tyne, UK
[6]Sir James Spence Institute, Royal Victoria Infirmary, Newcastle upon Tyne, UK
[7]Department of Biostatistics and Health Informatics, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
[8]Evelina London Children's Hospital, Guy's and St Thomas' NHS Foundation Trust, London, UK
[9]Complex Neurodevelopmental Disorders Service, Cumbria, Northumberland, Tyne and Wear NHS Foundation Trust, Newcastle upon Tyne, UK
[10]Walkergate Park, Centre for Neurorehabilitation and Neuropsychiatry, Newcastle upon Tyne, UK
[11]Great North Children's Hospital, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK
[12]Manchester Institute of Education, University of Manchester, Manchester, UK

*Corresponding author jonathan.green@manchester.ac.uk

Background: Prior evidence suggests that behaviours closely related to the intervention delivered for autism are amenable to change, but it becomes more difficult when generalising treatment effects beyond that immediate context.

Objectives: The objectives were (1) to test an early autism social communication intervention designed to promote child social communication change in the naturalistic contexts of both home and education, with an additive effect on overall child symptom outcomes, and (2) to conduct a mechanistic study investigating the transmission of treatment effects within and across contexts to an overall treatment effect.

Design: The trial was a three-site, parallel-group, randomised controlled trial of the experimental treatment plus treatment as usual and treatment as usual alone. The primary intention-to-treat analysis used analysis of covariance. The mechanism analysis used regression models to test mediation of the primary outcome by parent–child and education staff (learning support assistant)–child social interactions.

Setting: The study took place in three urban/semiurban regions in Manchester, Newcastle upon Tyne and London.

Participants: Children aged 2–11 years who met the criteria for severe autism.

Interventions: The Preschool Autism Communication Trial was adapted to parallel components within home and educational settings using in-person and remote delivery. Treatment as usual was the control condition.

Main outcome measures: The primary outcome was autism symptoms on the Autism Diagnostic Observation schedule-2. The secondary outcomes were Brief Observation of Social Communication Change, dyadic social interaction between child and parent or learning support assistant, reported language, functional outcome and reduction in child disruptive behaviour. Outcomes were measured at baseline and at the 12-month end point in all settings; interim mechanism measurements were taken at 7 months.

Results: Participants ($n = 249$; 122 in the PACT-G group and 127 in the treatment-as-usual group; 51 were female and 197 were male) received a median of 10 (interquartile range 8–12) sessions at home and 8 (interquartile range 5–10) sessions in an educational setting. We found no significant treatment effects on the end-point Autism Diagnostic Observation Schedule-2 primary outcome (–0.04, 95% confidence interval –0.26 to 0.18; $p = 0.734$), on the end-point Brief Observation of Social Communication Change secondary outcome (–0.03, 95% confidence interval –0.31 to 0.25; $p = 0.85$) or on language, repetitive behaviour, adaptive behaviour and child well-being. We did find significant treatment effects on dyadic interactions (increased parent synchronous response 0.54, 95% confidence interval 0.39 to 0.69; $p = 0.001$); child initiations with a parent (0.27, 95% confidence interval 0.12 to 0.41; $p = 0.001$); learning support assistant synchronous response (0.32, 95% confidence interval 0.14 to 0.49; $p = 0.001$); child initiations with a learning support assistant (0.21, 95% confidence interval 0.06 to 0.36; $p = 0.005$); and unblinded measures of improved parental well-being and child disruptive behaviour across home and educational settings. Adult (parent/learning support assistant) synchronous responsiveness in a home/education setting improved child dyadic social initiation. The child dyadic social initiation was also associated with child symptoms on researcher Brief Observation of Social Communication Change.

Limitations: The delivered sessional dosage was 83% of that planned in the home setting and 67% in the educational setting, with 5.5% of home sessions and 5% of educational sessions deemed 'unacceptable', particularly for remote delivery. A change of therapy learning support assistant was experienced by over one-third of children by the mid-point of the trial, by another third by the end point, and by one-fifth at both points.

Conclusions: The multicomponent Paediatric Autism Communication Trial – Generalised (PACT-G) treatment for a child in a home or educational setting did not produce the hypothesised improvement in child autism symptomatology or adaptive behaviour, but did produce significant improvements in proximal adult–child reciprocal dyadic communication.

Future work: Future work will involve building on these results towards a further understanding of delivery options, dosage and multicomponent extension of social communication interventions for young children with autism in naturalistic settings.

Trial registration: Current Controlled Trials ISRCTN25378536.

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List of abbreviations

ABA	applied behaviour analysis
ADOS-2	Autism Diagnostic Observation Schedule, Second Edition
AE	adverse event
BOSCC	Brief Observation of Social Communication Change
CACE	complier-average causal effect
CASUS	Child and Adolescent Service Use Schedule
CFI	comparative fit index
CHU9D	Child Health Utility 9D
CI	confidence interval
CONSORT	Consolidated Standards of Reporting Trials
CSS	Calibrated Severity Score
CTM	comprehensive treatment model
DBC	Developmental Behaviour Checklist
DCMA	Dyadic Communication Measure For Autism
DQ	developmental quotient
DS1-EI	individually delivered social communication and educational attainment-focused intervention
ES	effect size
HSC	home–school conversation
ICC	intraclass correlation
IQR	interquartile range
ITT	intention to treat
LSA	learning support assistant
MCDI	MacArthur Communicative Development Inventory
MoA	Memorandum of Agreement
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health and Care Research
PACT	Preschool Autism Communication Trial
PACT-G	Paediatric Autism Communication Trial – Generalised
PECS	Picture Exchange Communication System
PIS	participant information sheet
PLS	Preschool Language Scale
PPI	patient and public involvement
RA	research assistant
RBQ	Repetitive Behaviour Questionnaire
RCT	randomised controlled trial
RMSEA	root-mean-square error of approximation
RRB	restricted and repetitive behaviour
SA	social affect
SCERTS	Social Communication, Emotional Regulation, and Transactional Support
SCQ	Social Communication Questionnaire (lifetime version)
SD	standard deviation
SDQ	Strengths and Difficulties Questionnaire
SEM	structural equation modelling
SEN	special education needs
SOP	standard operating procedure
TAU	treatment as usual
TEACCH	Treatment and Education of Autistic and related Communication-Handicapped Children
TOPSE	Tool tO measure Parental Self-Efficacy

TSC	Trial Steering Committee	VEPS	Very Early Processing Skills
VABS	Vineland Adaptive Behavior Scales	WEMWBS	Warwick–Edinburgh Mental-Wellbeing Scale

Plain English summary

Our previous trial, the Preschool Autism Communication Trial, showed how video-feedback discussions with a therapist in a clinic helped parents to adapt their interaction style, resulting in improved child communication and long-term reductions in autism symptom severity. The Paediatric Autism Communication Trial – Generalised project hypothesised that offering parallel therapy at home and in the child's educational setting might have even greater effects on overall symptom outcome than those seen in the Preschool Autism Communication Trial.

We randomly allocated 249 children who were aged 2–11 years with severe autism to receive Paediatric Autism Communication Trial – Generalised therapy in addition to normal care (i.e. treatment as usual) or to receive normal care alone. The intervention lasted 7 months, with about two-thirds of the sessions taking place face to face with the therapist and the rest taking place online. At home, the therapist worked with one parent. In educational settings, the therapist worked with a staff member, usually a learning support assistant. The therapist and parent/learning support assistant reviewed and set targets for the communication strategies that they observed together in video-recorded interactive play with the child. Analysis looked at the direct treatment effect on children's outcomes, and also tested whether or not a change in adult–child interaction led to a change in the child's autism symptoms.

The main analysis showed that Paediatric Autism Communication Trial – Generalised therapy did not produce a greater effect than normal care on child autism symptoms, language, social adaptation or well-being. Paediatric Autism Communication Trial – Generalised therapy did produce a greater improvement in parent–child and learning support assistant–child social communication skills, parents' rating of their own well-being, and parent/learning support assistant ratings of children's disruptive behaviour. Improved child social communication in home and educational settings was linked to the improvements in interaction style made by parents and learning support assistants.

The Paediatric Autism Communication Trial – Generalised therapy did not change autism symptoms in the way that we saw in the original Preschool Autism Communication Trial; however, we did find the effects seen in the Preschool Autism Communication Trial on parent–child interaction, although not as strongly. We consider possible reasons why the Paediatric Autism Communication Trial – Generalised did not show original symptom effects, including a reduced number and different delivery of therapy sessions, and challenges from intervention settings in the context of other research.

Scientific summary

Background

Prior evidence suggests that behaviours closely related to the intervention delivered for autism are amenable to change. However, it can be more difficult for many interventions to generalise treatment effects beyond the intervention's immediate context into other naturalistic contexts of the child's life or symptom reduction. We tested an early autism social communication intervention that was an adaptation of our original Preschool Autism Communication Trial (PACT) [Green J, Charman T, McConachie H, Aldred C, Slonims V, Howlin P, *et al.* Parent-mediated communication-focused treatment in children with autism (PACT): a randomised controlled trial. *Lancet* 2010;**375**:2152–60]. The original PACT intervention was delivered by a therapist alongside the child's parents in a clinic-based setting over 18 sessions. Trial work had shown that PACT produced a reduction in severity of autism symptoms (including social communication and restricted, repetitive and sensory behaviours) that was sustained over 6 years after the end of therapy, as well as an improvement in parent–child reciprocal social communication, parental well-being and parent-report child social outcomes. The adapted intervention – Paediatric Autism Communication Trial – Generalised (PACT-G) – consisted of simultaneous, parallel intervention delivery in the child's home and an educational setting, using a mixture of in-person and online delivery and extending the age of intervention up to 11 years (the age range for the PACT was 2–5 years). This method was designed to (1) make delivery easier for families, (2) focus more on child functioning in the educational setting (a key context for their development) than the PACT had, (3) extend the PACT intervention to some autistic children of school age and (4) facilitate maximal intervention effects within these different naturalistic settings (home and education) for the child beyond the clinic setting, on the basis that this might result in enhanced additive effects compared with the PACT on the overall child symptom outcomes measured in a research setting. An associated detailed mechanism study within the trial investigated the process by which there might be transmission of treatment effects within and across settings to an overall research-assessed effect.

Methods/design

The trial was a three-site, parallel-group, randomised controlled trial of the experimental treatment plus treatment as usual and treatment as usual alone as the control condition. The primary outcome was researcher-assessed severity of autism symptoms [using the Autism Diagnostic Observation Schedule, Second Edition (ADOS-2)] at the 12-month trial end point. Secondary outcomes were (1) child autism symptoms rated using the Brief Observation of Social Communication Change (BOSCC) in home, educational and research outcome settings; (2) child reciprocal dyadic social interaction with a parent in the home setting and an education staff member (usually learning support assistant) in the educational setting; (3) child language, well-being and reported functional outcome; (4) reported child disruptive behaviour across home and educational settings; and (5) parental self-efficacy and well-being. Outcomes were measured at baseline and the 12-month end point in all settings, with interim measurements (7 months) in the home and educational settings that were designed to test treatment effect mechanisms. The primary analysis estimated between-group difference in the primary outcome using an analysis of covariance, with a test of homogeneity of effect across preschool- and school-aged groups. The mechanism analysis used regression models to test for mediation on the ADOS-2 and BOSCC outcomes by the observed parent–child and education staff–child social interactions.

Interventions

The PACT-G is a caregiver-mediated intervention for enhancing social communication skills in children with autism. The intervention is designed to be delivered by a trained speech and language therapist to a nominated caregiver in the child's home setting or by a trained specialist professional in the child's educational setting. The intervention utilises video-feedback analysis of child interactions with the caregiver or adult to support implementation of individualised adult strategies with the child. These strategies have been previously evidenced, from our previous PACT and other studies, to be ones that enhance communication skills in children with autism. The intervention has parallel components within home and educational settings, and uses a combination of in-person and remote (teleconference) delivery. The control condition is treatment as usual.

Results

Children aged 2–11 years, who met the criteria for severe autism (a ADOS-2 total score of > 12), were randomised ($n = 249$; 122 in the PACT-G group and 127 in the treatment-as-usual group; 51 were female and 197 were male) and analysed by intention to treat, with just one participant lost to follow-up by the end point. Children received a median of 10 (interquartile range 8–12 sessions) out of 12 possible sessions at home (interquartile range 2–12 sessions) and 8 (interquartile range 5–10 sessions) out of 12 possible sessions in an educational setting (interquartile range 0–12 sessions). A total of 36% of sessions in the home setting and 34% of sessions in the educational setting were delivered remotely, usually by video conferencing, and the rest were delivered in person. Issues related to remote delivery or therapy environment led 5.5% of sessions in the home setting and 5% of sessions in the educational setting to be rated as 'unacceptable' in quality by therapists.

The treatment effect on the end-point ADOS-2 primary outcome was 0.04 (95% confidence interval −0.26 to 0.18; $p = 0.734$). The effect on the end-point BOSCC secondary outcome was −0.03 (95% confidence interval −0.31 to 0.25; $p = 0.85$). No treatment effect was seen on secondary child outcomes of language composite, repetitive behaviour, adaptive behaviour and child well-being. However, a significant treatment effect was found on proximal dyadic interactions [i.e. increased parent synchronous response with child (0.54, 95% confidence interval 0.39 to 0.69; $p = 0.001$), increased child initiations with a parent (0.27, 95% confidence interval 0.12 to 0.41; $p = 0.001$), increased learning support assistant synchronous response with child (0.32, 95% confidence interval 0.14 to 0.49; $p = 0.001$), and increased child initiations with a learning support assistant (0.21, 95% confidence interval 0.06 to 0.36; $p = 0.005$)]. Significant treatment effect was also seen on unblinded measures of increased parental well-being and decreased child disruptive behaviour across home and educational settings.

The mechanism study showed that the significant treatment effects found on child social communication initiation with dyadic partners in both the home setting (with a parent) and educational setting (with a learning support assistant) were mediated by an increase in the respective adult partner's synchronous responsiveness. There was no evidence of a mediation effect on end-point ADOS-2 symptoms, but there was evidence of an association between child social initiations with adults in both home and educational settings and, later, a BOSCC symptom outcome.

Discussion

In this trial, we have, to the best of our knowledge, carried out the largest mechanistic study yet undertaken within an autism intervention trial and one of the largest intervention studies of objectively assessed autism symptoms. Providing multicomponent PACT-G treatment for the child in home and educational settings in parallel did not produce the hypothesised improvement in the outcomes researcher-rated child autism symptomatology or adaptive behaviour. It did show significant planned

treatment effects on the more 'proximal' outcomes of adult–child reciprocal dyadic communication in both home and educational contexts, but at approximately half the ES found in the original clinic-delivered PACT. Our mechanism study replicated the same proximal effects of adult synchronous social response on child social communication, as found in the PACT, in both home and educational settings. Although in the PACT such proximal treatment effects with a parent had mediated significant and sustained subsequent child symptom change, in this study they did not transmit in the same way to child symptom effects on ADOS-2, but there was evidence of some effect on BOSCC.

We explore possible reasons why this PACT-G model of parallel treatment did not produce the full mediated treatment pathway that we found in the previous PACT. We consider factors such as reduced session dosage, the increased multicomponent complexity, impact of remote intervention delivery and impact of characteristics of therapy settings. We discuss the results in the context of other research on implementation of early home, education-based and multicomponent intervention for children with severe autism. We recommend future research areas to build on these results, including further work on remote delivery of complex intervention, dosage thresholds in psychosocial interventions, and multicomponent therapies in an educational setting, with the aim of extending social communication interventions for young children with autism in naturalistic settings.

Trial registration

This trial is registered as ISRCTN25378536.

Funding

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Chapter 1 Introduction

Scientific background

Intervention evaluation research in autism spectrum disorder (hereafter 'autism') has recently accelerated, with studies across a range of interventions considered in recent National Institute for Health and Care Excellence (NICE) guidance,[2] Cochrane Library reviews[3] and other reviews.[4–6] The pattern of findings across a number of early childhood interventions is for reproducible moderate-to-good effects on targeted 'proximal' or intermediate outcomes, such as improvement in social interaction and communication in the local treatment context.[7–9] However, for an intervention to demonstrate a tangible impact on a child's life and overall development, the challenge is to show effects beyond the immediate intervention context, for instance that changes are also seen in non-direct treatment contexts, such as in interactions with other people inside or outside the classroom or in the family home setting, or an impact identified on other developmental function or symptom outcomes over time and in a variety of settings. In this regard, there is much less evidence,[4,6] despite the fact that without such changes the claim that autism interventions are truly effective is harder to substantiate.

Reinforcing the transmission of targeted 'proximal' intervention effects into functional change seen in the wider context pervading the child's life is, thus, a key current challenge for autism treatment research,[6,10] and raises the question why does this appear to be so difficult in autism? The capacity to generalise acquired skills flexibly across different situations, people and environmental contexts – a central feature of skill acquisition in neurotypical development – has often been suggested to be a core difficulty for individuals with autism. In this context, one can consider two different forms or concepts of generalisation, which will be referenced throughout this report. First, the concept of generalisation of specific behaviours (for instance the observation of a specific newly acquired skill or behaviour in one setting that then occurs in another) has been commonly investigated in behavioural learning theory and could be termed 'homotypic' generalisation. Second, the concept of a 'developmental cascade' from precursor skills through to developmentally related but different subsequent skills (e.g. specific vowel sounds in infant development through to evolved language) is the subject of much study in general developmental science, and might be characterised as 'heterotypic' ('homotypic' and 'heterotypic' being terms originating in the longitudinal epidemiology literature). Although a recent systematic review concludes that the empirical evidence for difficulty in generalisation in the first sense is inconsistent,[11] many single-subject design studies using behavioural learning methods have described difficulties that autistic children have in transferring newly taught skills to different settings, people or materials/activities, and it has been an assumption in developmental science, as well as from clinical experience, that there is additional difficulty in generalisation in both senses for autistic children. However, these are assumptions that have not been fully evaluated.

Possible explanations, particularly for the second, heterotypic, form of generalisation, include the autistic child's well-documented lack of internal symbolic representation, which is likely to interfere with the consolidation and thus transfer of procedural aspects of skill across contexts into different forms of behaviour, independent of the specific context in which the skill was acquired. Another related barrier may be weaknesses in autistic cognitive central coherence, associated with an over-reliance on concrete behavioural prompts or reinforcers, which can lead to fragmented learning dissociated from the social pragmatic context as a whole rather than a more diverse integration of

learning with connected understanding in context. There may be further factors related to a general lack of behavioural flexibility in applying new skills across different environments. Plausible approaches to helping overcome some of these generalisation difficulties in autism include embedding the intervention into the social environment through parent mediated and education staff-mediated learning, which may optimise the interpersonal cues and continuity of learning across contexts.[12] This method supports opportunities for incidental or naturalistic learning, by weaving functional social and communication learning into the child's daily experiences, where skills are acquired. Working with children in naturalistic environments is now often highlighted as best practice for early intervention.[13]

Early social communication intervention, delivered through parents, therapists or teachers, is the only early autism intervention with a 'consider' recommendation by NICE.[2] The Preschool Autism Communication Trial (PACT)[7] tested a clinic-delivered, parent-mediated social communication intervention against regular care in what was, to the best of our knowledge, one of the largest randomised controlled trials (RCTs) in the field.[14] The therapy showed a substantial impact on the targeted immediate outcome of parental communicative synchrony with the child [effect size (ES) 1.22, 95% confidence interval (CI) 0.85 to 1.59)] and also on the child's communication initiations with the parent (ES 0.41, 95% CI 0.08 to 0.74). The original publication[7] demonstrated that PACT was associated with non-significant effects on the Autism Diagnostic Observation Schedule, Second Edition (ADOS-2) social communication domain when considered alone, but subsequent analysis of outcome on the full autism symptom phenotype [measured across both social communication and repetitive behaviour and sensory symptom domains in the ADOS-2 Calibrated Severity Score (CSS)] found a significant intervention effect at the end point, with a log-proportional odds ratio of 0.64.[14] Subsequent follow-up of the PACT[7] cohort 6 years after treatment end, when participant mean age was 10.5 years, with blinded assessment of the original randomly allocated groups (80% follow-up completeness on the primary outcome) found evidence suggesting further sustained effect on reduced autism symptom severity on the ADOS-2 (log-odds ES 0.70, 95% CI −0.05 to 1.47), and a significant overall treatment effect when calculated over the treatment and follow-up time period (log-odds ES 0.55, 95% CI 0.14 to 0.91). Non-blind, parent-rated autism symptoms on the Social Communication Questionnaire (lifetime version) (SCQ) (ES 0.40, 95% CI 0.05 to 0.77) and repetitive and sensory behaviours on the Repetitive Behaviour Questionnaire (RBQ) (ES 0.87, 95% CI 0.47 to 1.35) also showed comparable improvement at follow-up.[14]

To our knowledge, the PACT intervention was the first study in the field to show that a preschool autism intervention could have downstream developmental effects to reduce child autism symptom severity for a substantial period after treatment end. This PACT treatment[7] was 93% clinic delivered and the key outcomes were measured in a research context; there was little measurement of effects within educational or home environments. Consequently, in the Paediatric Autism Communication Trial – Generalised (PACT-G), we aimed to extend the work of the original PACT,[7] with the aim of (1) reinforcing the extension of treatment effects within the different naturalistic environments of the child's early life, in home and educational settings, and (2) responding to moves towards home-based therapy delivery. The intervention was taken into the child's daily naturalistic home and nursery/school setting, incorporating parent- and education staff-mediated interventions, and embedding individualised strategies within these naturalistic learning contexts.

A further development was the extension of the intervention into the primary school years, up to the age of 11 years. Autism intervention studies to date have been largely limited to preschool (< 5 years) interventions; however, early communication development continues into the school years,[15] and social communication skills in the early school-age period are strong predictors for later development.[16] The persisting and significant impairments in social interaction and communication among children with autism argue for a developmentally sustained intervention into middle childhood, utilising the child's naturalistic learning environments. However, because of the focus of the intervention on early social communication skill development, the cohort of autistic children of school age (> 5 years) receiving the treatment was restricted to those who had no more than a 4 years' language-equivalent level.

In addition, a mechanism study within PACT-G built on the understanding gained from the mediation analysis in the original PACT.[17] This previous analysis had tested for mediation of primary treatment effects on child autism symptoms (ADOS-G) through the proximal intervention target of improvement in parental synchronous response to child communication, and an increase in child communication initiations with the parent within dyadic communication (both of which were researcher assessed by video-coding blind to intervention group). In this analysis, increases in child initiations with a parent were shown to be strongly (mediated 80%) by the change in parental synchronous response produced by the treatment. These changes in child initiation with a parent then, in turn, were shown to strongly mediate (97%) the change in child autism symptoms. This mediation analysis had supported the theoretical logic model of the PACT[7] intervention by showing a causal-effect chain from parent response to child, to child communication with a parent, and from child communication with a parent to a generalised social communication change in child symptoms. A similar mediation effect had been shown previously in the smaller PACT.[18] In the PACT-G mechanism design, we aimed to test whether or not a similar chain of mediation effect would be maintained when measured in the home and educational settings, and whether or not such changes in two parallel naturalistic settings simultaneously might be further additive in mediating an enhanced effect on symptom outcomes in the research context. In addition, the assessment of mediators and outcomes in different simultaneous naturalistic contexts might provide an innovative opportunity to study key mechanisms of child developmental learning across contexts and whether or not different contextual learning might generalise in an additive way to related downstream symptom outcomes.

Background literature on autism intervention

A significant evidence base from RCTs of early interventions for young children with autism has accumulated over the past 15 years.[4,6,19] Many of these interventions aim to ameliorate the impact of core social communication impairments on early social interactions, particularly with parents, who often find their child's behaviour perplexing and challenging. The tested interventions have varied in design, duration and intensity, and include developmental and behavioural approaches[20] that are mediated through parents and delivered directly by therapists, and there is significant study-to-study variation in the effects found. However, robust evidence now exists that some aspects of social communication can be improved for many young children with autism.[4]

The most consistent findings are improvements in dyadic interaction between children and their parents or another adult.[7,9,21–25] Although many studies report improvements in language and communication on unblinded parent-report measures,[7,14,25–27] findings on observational or standardised measures of communication and language ability are more variable. Thus, some studies report improvements[7,14,23,26–28] whereas others do not.[7,21,24] Only a few studies have demonstrated treatment reductions in autism symptom severity,[14,27] whereas most have not.[25,26,28] A recent review[4] contains a thorough review of this literature in the context of study design and reporting quality.

Despite this promising evidence base, there is wide recognition that the early autism intervention research field faces challenges.[29–31] Even trials demonstrating group-level improvements report modest ESs,[4] reflecting, in part, that a significant proportion of participants in many studies do not benefit. There are sparse examples of designs that would better inform 'personalised medicine' approaches (i.e. '*who* benefits from *which* treatments?'), including comparative or equivalence trials, and rigorous examination of which children benefit from these interventions (moderating effects) and how (mediating effects). Only two long-term follow-ups have been conducted to assess maintenance of effects,[14,21] and there has generally been a lack of independent replication of substantial findings. In addition, reporting standards have been variable and there has been inadequate measurement of and attention to the critical importance of testing if and how interventions have an impact on everyday functional abilities that extend beyond the proximal intervention context.[11]

In an earlier study, we found that a therapist-directed, parent-mediated intervention that uses video-guided feedback to and coaching for parents, following a transactional developmental model,[32] resulted in improvements in parental synchrony and child initiations when interacting with each other. We also found moderate ES reductions in overall autism symptom severity on a blinded observational measure at treatment end point (log-proportional odds ES 0.64, 95% CI 0.07 to 1.20), which was sustained at the 6-year follow-up (log-proportional odds ES 0.70, 95% CI −0.05 to 1.47), with an overall log-proportional odds ES of 0.55 (95% CI 0.14 to 0.91; $p = 0.004$), as was the improvement in child initiations.[14]

A qualitative interview study with parents who had received PACT therapy within the previous PACT[7] confirmed the largely positive evaluation of the core effects of the therapy on communication, interaction and child progress, as well as emphasising valued improvements in the parents' sense of the relationship with their child and enhanced parental and family well-being. However, the study revealed practical difficulties for some families in attending therapy sessions within a clinic environment,[33] including the inconvenience (travel, child care), unfamiliarity with and lack of preparedness for autism in therapy venues, and challenges with occupying the child during video-feedback sessions and discussion. Delivery of the intervention within the home and educational settings and the use of video telecommunication software aimed to address some of these practical challenges, while also, importantly, in theory, providing a method of enhancing the adoption and generalisation of therapeutic strategies within the child's family and everyday naturalistic environments. The use of teleconferencing technology was also thought to have the potential to remove practical barriers, as video material of adult–child interactions could be made in either the home or educational setting prior to the session, and then shared and discussed between the therapist and parent/member of education staff through teleconferencing at a later time without the child present. The advantages and disadvantages of these adjustments found in practice are discussed further below.

Interventions for autism in the educational setting

There are a number of programmes delivered within UK educational contexts to support children with autism.[34] The focus of many of these is on enhancing cognition and learning and reducing challenging behaviours. The majority of interventions fall into two broad categories: comprehensive treatment models (CTMs) and focused interventions. CTMs tend to be developmentally focused, multicomponent educational programmes, aiming to improve functioning across cognition, emotional and social development. They are often embedded within the classroom setting itself and delivered by members of staff.[35] A common UK example of a CTM is the Treatment and Education of Autistic and related Communication-Handicapped Children (TEACCH) programme, which incorporates the use of classroom-based visual schedules and prompts.[36] In the USA, Social Communication, Emotional Regulation, and Transactional Support (SCERTS)[37] and the Learning Experiences and Alternative Program for Preschoolers and their Parents[38] have also been used; these are also occasionally available in UK specialist autism schools. Although these approaches may be based on different conceptual models,[39] they share similar general goals of embedding group, class-based support for children with autism within the educational setting.

Focused interventions tend to target specific skills;[40] for example, the Picture Exchange Communication System (PECS) is used to support picture exchange as an alternative form of making a child's needs known.[41] Alternative and augmentative language systems (e.g. Makaton)[42] and the use of technology, such as voice output communication aids, are also sometimes available in the UK. A teacher-delivered interactive communication intervention for specific language impairments [the Social Communication Intervention Project (SCIP)][43] is also applicable to high-functioning autistic children in middle childhood. Peer-mediated interventions promote naturalistic peer socialisation and support in the school environment[44,45] and have face validity.[46] In contrast to CTMs, the model by which many of these interventions are delivered is through consultation with schools by specialist health professionals (e.g. psychologists, speech and language therapists or trained teachers), but with the aim of collaborating with 'non-specialists' in their

implementation [e.g. peers and learning support assistants (LSAs)].[47] Funded LSAs are often allocated for differentiated support and learning in the classroom for individual children. There is a relative lack of high-quality implementation trials of such interventions in educational settings.[34,48]

Education provision for children with autism in the UK

In the UK, 71% of children with a diagnosis of autism attend a mainstream educational setting.[49] Despite the benefits of inclusion in mainstream schools (notably the, potentially, wider participation in the educational experience, peer role models, acceptance and opportunities to develop academic, social and emotional skills[50]) access to specialist professional support and guidance is often very limited. Depending on the level of special educational needs (SEN), pupils receive non-specialist LSA support, but this is highly variable between schools.[51,52] LSA roles are wide-ranging and include supporting children with complex health, medical, behavioural and learning needs.[53] LSAs in special schools are more likely to work in a team with the teacher and support the whole class of children than they are to work one to one with an individual child.

Chapter 2 Study aims

PACT-G had two aims. The first aim was to test whether or not the multicomponent PACT-G social communication intervention protocol, extended from the original PACT[7] intervention and implemented in both home and educational settings simultaneously, would show treatment effects on (1) autism symptom outcomes, as measured in an independent research setting (primary outcome), and (2) dyadic social communication, functional adaptation and autism symptoms in the separate home and educational settings (secondary outcomes). These objectives were tested using blinded measures, maximising the ability to detect meaningful change (see *Chapter 5*, *Measures*), and were evaluated by analysis at the 12-month trial end point.

The second aim was a mechanism analysis using the experimental trial to investigate aspects of the developmental and cross-context generalisation of specific acquired competencies in autism. We built on the mediation analysis from our previous PACT[7] (see Pickles *et al.*[14]) to test the mediation of the generalised treatment effect in the home and educational settings. We tested how effects in naturalistic contexts might combine to enhance transmission of treatment effect to research-assessed symptoms in a standardised test setting. In doing this, we used prespecified measures of mediation that were identified in our previous PACT.[7]

Chapter 3 Organisation

Trial organogram

The organisation of the three-site trial is shown in *Figure 1*, with the trial principal investigators named and their roles given. The full trial team is named and acknowledged in *Acknowledgements*. The study progress Gantt chart is shown in *Table 1*.

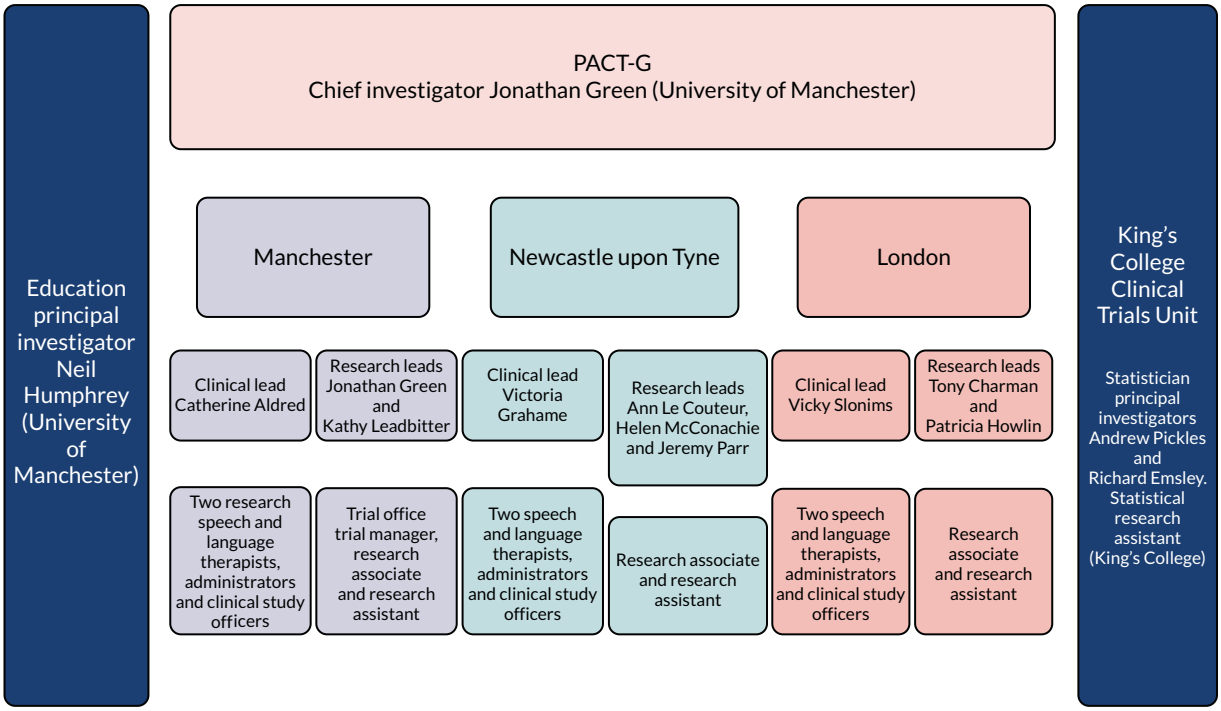

FIGURE 1 Trial organogram.

TABLE 1 Trial Gantt chart

	Month											
PACT-G timeline task	**January**	**February**	**March**	**April**	**May**	**June**	**July**	**August**	**September**	**October**	**November**	**December**
2016												
Start of grant												
Recruit research associates												
Research associates in post (36 months)												
Recruit SALTs												
SALTs in post (33 months)												
Recruit research assistants												
Research assistants in post (26 months)												
Pilot study												
2017												
Research associates in post (36 months)												
SALTs in post (33 months)												
Research assistants in post (26 months)												
Main trial												
2018												
Research associates in post (36 months)												
SALTs in post (33 months)												
Research assistants in post (26 months)												
Main trial												
Video scoring, data checking and entry												
2019												
Research associates in post (36 months)								N/A	N/A	N/A	N/A	N/A
SALTs in post (33 months)								N/A	N/A	N/A	N/A	N/A
Research assistants in post (26 months)								N/A	N/A	N/A	N/A	N/A
Main trial								N/A	N/A	N/A	N/A	N/A
Video scoring, data checking and entry								N/A	N/A	N/A	N/A	N/A
Analysis								N/A	N/A	N/A	N/A	N/A

N/A, not applicable; SALT, speech and language therapist.

Chapter 4 Pilot feasibility study

PACT-G formally started on 1 February 2016. As per the deliverability project plan from January 2016 (see *Appendix 3*), the management team was contracted to demonstrate by month 12 that the following success criteria had been met in relation to two stop–go decision points to allow progression to the main trial:

- Stop–go 1: at the end of the pilot phase of the trial, a minimum of 27 educational settings have been engaged with the educational setting buy-in protocol, with a written Memorandum of Agreement (MoA) from at least 11.
- Stop–go 2: by the end of the 6-month pilot phase (month 12 of the study), the team will have identified, assessed for eligibility and consented a sufficient number of patients to proceed to treatment in 24 patients (eight in each site).

Stop–go 1: educational engagement

Contact with educational settings

The process for contacting educational settings varied between the sites (Manchester, Newcastle upon Tyne, London), depending on the size and type of provision. Sites mainly approached specialist schools and schools with significant specialist provision with which they were familiar. For most of the younger children recruited to the pilot phase, who had been referred through clinical services, we contacted their nursery or preschool at the point of the family's consent to seek their engagement in the project.

Table 2 shows each educational setting that was contacted, as well as those where further discussions took place and the outcome of the engagement. A small number of educational settings that were contacted did not want further information. For those educational settings that wanted to learn more about the study, we sent the study information sheet and produced a standard presentation that was given at most educational setting visits. We also collected standardised information from the educational settings, including information about their provision of specialist education, the educational setting size and key staff involved in this service.

Numbers of educational settings contacted, engaged and agreeing to participate

Table 2 shows the number of educational settings at each site that were contacted, the number that received further information and engaged with the study team, and the number that signed the MoA. The results clearly demonstrate our achievement in meeting the success criteria for stop–go 1; we engaged 31 educational settings against a target of 27, and had signed MoAs from 18 educational settings against a target of 11.

TABLE 2 Educational settings contacted in the feasibility study

Site	Number initially contacted	Number engaged	Number that signed the MoA
Manchester	17	14	10
Newcastle upon Tyne	10	10	6
London	7	7	2
Total	34	31	18

Stop–go 2: pilot phase recruitment

Identified families

In total, we contacted 34 families during the pilot phase of the study. We consented and then assessed the children against the prespecified eligibility criteria on three assessments:

1. observed autism symptom severity on the ADOS-2
2. reported autism symptom severity in the parental autism diagnostic interview (preschool-aged children) or parent-rated SCQ (school-aged children)
3. necessary developmental level (i.e. 12 months) on the Mullen Scales of Early Learning (preschool-aged children) or British Ability Scales (school-aged children).

Three families dropped out after consent: one family worried about the impact of participating in an autism study and the potential stigma in the community, one family dropped out because of family pressures and one family could not be contacted to arrange eligibility assessments following initial consent.

Number of families approached, consented and assessed as eligible

Table 3 sets out the number of families contacted at each site, those that consented and the number of participants assessed as eligible and ready to proceed to treatment. A full anonymised recruitment log showing dates of birth and dates of consent is available from the authors.

The results indicate our success against the criteria in stop–go 2; we assessed eight patients as eligible in each site.

In November 2016, the team reviewed progress in the pilot feasibility study, with the results being signed off on 3 November in a meeting with the Trial Steering Committee (TSC), that supported trial progression.

TABLE 3 Families contacted in the feasibility study

Site	Number approached	Number consented	Number assessed as eligible
Manchester	9	8	8
Newcastle upon Tyne	12	9	8
London	13	10	8
Total	34	27	24

Chapter 5 The PACT-G randomised controlled trial

Design

The trial was a three-site, two-group, RCT of the experimental treatment plus treatment as usual (TAU) compared with TAU alone. Children aged 2–10 years with autism were recruited to the trial in the local areas following referral by clinical specialists and education professionals. Consented families were then randomised to three sites around the UK to receive either the PACT-G social communication intervention in addition to TAU (referred to as the PACT-G group) or TAU alone (referred to as the TAU group). Assessments were administered on entry (baseline) to the trial, at the 7-month mid-point and at the 12-month end point. An embedded mechanism study aimed to test specific mediation hypotheses in the trial and to, potentially, use the experimental intervention design with repeated measures to contribute to a general understanding of the generalisation of acquired skills in autism development across both time and setting, and also in terms of downstream predicted developmental cascades to symptom and adaptive outcomes for the child.

Settings

The settings for the trial were family homes, mainstream nurseries and preschools, specialist nurseries, mainstream schools with specialist autism units and specialist SEN/autism school settings, all of which were in Greater Manchester, London or Newcastle upon Tyne.

Study population

The inclusion criteria were as follows:

- Participants aged 2–10 years.
- Diagnosis of autism given by referral services.
- Meeting criteria for autism on the ADOS-2.
- Scoring $\geq$ 15 (school aged) or $\geq$ 12 (preschool aged) on the SCQ – the accepted clinical cut-off points for children at these ages.
- Children aged $\geq$ 5 years between P3 and P8 for the English curriculum. (In England, at the time of the study, P scales described targets for children aged 5–16 years with special educational needs. P3 communication skills indicate that a child is beginning to use 'intentional communication'. P8 was taken to represent an expressive language age-equivalent of approximately 4 years in a typically developing child.)
- Parents with sufficient English to potentially participate in the intervention and who speak English to their child at least some of the time.

The exclusion criteria were as follows:

- having a sibling with autism already in the trial
- participation in the PACT-G pilot phase
- children aged $\leq$ 12 months with a non-verbal age-equivalent level
- epilepsy not controlled by medication
- children with an identified genetic disorder that would impact on their ability to participate or affect the validity of data
- severe hearing or visual impairment in parent or child

- current severe learning disability in the parent or current severe parental psychiatric disorder
- current safeguarding concerns or other family situation that would affect child/family participation in the trial
- no agreement to participate from child's educational setting.

Sample size

The PACT[7] showed an ES of 1.22 (95% CI 0.85 to 1.59) on parental synchrony [Dyadic Communication Measure for Autism (DCMA)], which mediated 70% of the ES of 0.41 (95% CI 0.08 to 0.74) on child communication, which in turn mediated 72% of the ES of 0.24 (95% CI 0.59 to 0.11) on symptom outcome (ADOS-2). The intervention strategies in PACT-G were specifically targeted to enhance generalisation of the child communication to increase primary outcome effects in home, educational and research settings. Therefore, we expected the ES for the symptom outcome to be substantially above 0.24 and clinically meaningful.

For PACT-G, power was calculated using the sampsi command in Stata® (StataCorp LP, College Station, TX, USA), for an analysis using analysis of covariance with $\alpha = 05$, with pre- and post-measures correlated 0.67 (from PACT[7]). With 110 patients followed up in each group (70/70 preschool-aged and 40/40 school-aged children), 80% power was retained for an ES of 0.28 and 90% power for an ES of 0.33. Allowing for 10% attrition (compared with 4% in PACT[7]), we proposed to recruit 244 families (rounding up to 82 per site: 52 with preschool-aged children and 30 with school-aged children).

Interventions

The PACT-G intervention is an adaptation and extension of the original, largely clinic-delivered, PACT[7] intervention into home and educational settings (93% of original PACT[7] sessions were delivered in a clinic setting, whereas all of the PACT-G sessions were delivered in a home setting, in an educational setting or by teleconferencing). PACT[7] is a 'caregiver-mediated' intervention; in this context, the carers are the parents and education professionals who are the primary recipients of the individualised intervention sessions. PACT-G utilises videos of caregiver–child interaction to provide feedback and guide caregivers to adapt their communication with the child. Therapists support caregivers to adopt evidence-based strategies in their communication so as to enhance child communication development,[7,54] and to practise these strategies initially during the 30-minute home practice sessions and eventually throughout the day. Recent research indicates that optimal interaction with a sensitive and responsive communication partner can be effective in increasing communication and social interaction skills in children with autism.[4] In the original PACT,[7] this caregiver-mediated approach was found to be effective in increasing the quality of parental communicative responses to the child, which in turn led to increased child-initiated communications with the parent and generalised effects on reduced child autism symptom severity.[7]

The PACT-G intervention retains these effective elements, but encourages generalisation of the child's newly acquired skills into other settings. For instance, the design of PACT-G includes more integration of PACT[7] techniques into daily routines and play, and the addition of an adult from the child's educational setting supports skill development in school.[55,56] The intervention is intended to begin with the caregiver at home and then extend into the child's educational setting. However, sometimes the contingencies of school term times meant that sessions were coincident in timing. Furthermore, the PACT-G intervention incorporated more recent advances in research[17] since the publication of the original PACT.[7] These included focusing on specific strategies to enhance the child's response to shared attention with objects and play as precursors to the early stages of language development.[57,58] These modifications allow more differentiation of the starting point of the intervention to ensure that it is appropriate for the individual child's initial level of object play and social engagement.

In common with the original PACT[7] therapy, PACT-G therapy takes a staged approach that is based on theoretically informed precursor skills for typical communication development, as well as on addressing atypical communication and language development in autism.[15,59,60] Caregivers are initially encouraged to adopt strategies for establishing essential foundation skills for the child's communication and language development, including shared attention[57] and initiating social communication skills,[37] before moving on to strategies that support and enhance the child's receptive and expressive language development[8,58] and reciprocal conversation.[43]

In contrast to many manualised intervention programmes, PACT[7] and PACT-G do not provide a curriculum or prescribed topic guide for sessions. The manual instead outlines six stages, each with a 'toolbox' of strategies that could be used to facilitate development. Therapists are trained to minutely analyse videos of caregiver–child interactions to assess the areas for further development and the potential strengths.[61] Based on these observations, therapists then establish which of the manualised therapy targets are most appropriate for that dyad at that stage of development, and agree these as targets for intervention with the caregiver. Therefore, targets and strategies are individualised for each child, depending on their interactive style. Progress is evaluated and subsequent targets for each dyad are based on that pair's progress, allowing for a highly individualised intervention approach that accommodates each individual, but can remain within a well-defined framework. This is described further below.

The PACT-G method of video feedback facilitates a collaborative partnership, empowering caregivers.[22,33] A new caregiver–child interaction video is recorded at each session, and the therapist guides the caregiver in observing and analysing the most successful moments of dyadic interaction on video, thereby helping the caregiver to see how their use of strategies promotes and enhances the development of the child's communication. Insights from this discussion are then used to set individual step-by-step caregiver goals (i.e. strategies they will adopt) within the stages of the manual that are appropriate to the identified individual needs of the child. Between sessions, caregivers are encouraged to practise using these strategies with the child, initially in protected time and later at opportune moments throughout the day. The PACT-G intervention is designed for preschool- and primary school-aged children, from those with little communication or no language to children who use spoken sentences. Progression through the stages of PACT-G is individually differentiated so it is related to both the caregiver and the child's readiness to progress. Many dyads may remain at the early stages focusing on shared attention, caregiver-adapted responding and child communication initiation; others may progress to later PACT-G stages of language expansion and reciprocal conversation.

The PACT-G intervention manual provides clearly defined stage aims, child outcomes, therapy targets and a range of caregiver strategies. Each of the six stages includes a list of objective measures to determine a dyad's readiness to progress to the next stage.

Stage 1

'Establishing shared attention' helps the caregiver to establish and maintain extended periods of mutual shared attention with the child.[8,57] All dyads complete at least one session at stage 1. For dyads already showing extended periods of mutual shared attention, the focus of the single stage 1 session ensures caregiver understanding of the concept of shared attention and highlights successful strategies that are applied. For dyads at the very earliest stages of development, with fleeting or no shared attention, further sessions at stage 1 are needed and include play with or without toys and caregiver modelling. In stage 1, the caregiver learns to sensitively observe the child's focus, as well as non-verbal and verbal signals, and thereby to identify opportunities for shared attention.

Stage 2

'Synchronicity and sensitivity' emphasises caregiver sensitivity in responding, with a focus on the child's perspective and experiences.[54] Caregivers are encouraged to closely observe the child to identify opportunities to respond, thereby reducing asynchronous communication (mistimed responses that

place a demand on the child) and increasing adult synchronous communication. Caregiver observations from video help them identify and reduce demands, instructions and directive responses, and replace them with synchronous responses to the child's communicative behaviours and social initiations, commenting on or acknowledging intentions.

Stage 3

'Focusing on language input' helps the caregiver to model language that accurately matches the child's interests and communication competencies.[8,13,58] Caregiver language and non-verbal gestures are carefully monitored and modified to be contingent on the child's focus and comprehension. The caregiver is assisted to respond to the child's non-verbal communication and to model complementary verbal responses that express the child's inferred communication intent.

Stage 4

'Establishing routines and anticipation' is a consolidation phase that aims to develop child verbal understanding, anticipation and participation using repetitive rhymes, predictable routine phrases and familiar interactive play.[54]

Stage 5

'Increasing communication functions' is carried out by eliciting communication acts through the sensitive use of communication 'teasers' to provide opportunities for child initiation. For example, the caregiver may make use of pauses and gaps within familiar, predictable play situations that the child fills with social and verbal responses. Communicative teasers entice the child to initiate intentional communication.[17,37] These are gradually extended to pose deliberate problems and/or to introduce 'sabotage' in situations where the caregiver makes obvious mistakes (e.g. offering an empty cup or unopened snack, or a puzzle/game with pieces missing). A range of pragmatic communication acts can be elicited in this way, including requesting, negating, directing and commenting.

Stage 6

'Expanding language and conversations' involves expanding on the child's understanding and use of language.[8,58] This enhances the child's language repertoire, including extending vocabulary, phrases, sentences[15] and the social use of language, and develops to-and-fro conversation.[43]

Intervention delivery

Parent sessions

Parents were offered 12 intervention sessions at home over 6 months. This was a reduction from the original PACT,[7] in which 18 sessions were offered over 12 months. In the previous trial, the best proximal effect of intervention on parent–child dyadic interaction was achieved by 12 sessions (6–8 months), and this proximal dyadic effect strongly mediated the reduction in 13-month end-point autism symptom severity. Pragmatically, we needed to adopt this reduced session number for each setting in this trial so as to make the treatment in the parallel home and educational settings feasible within a fixed time frame.

Prior to starting the PACT-G programme, a home visit was conducted to introduce the intervention to the parents, understand the family context and set expectations. The PACT-G approach to parent sessions differed from that of the original PACT[7] in setting, number of sessions and nature of delivery. The therapy sessions were delivered in the home and, instead of the solely in-person sessions in PACT,[7] the therapy sessions alternated between home-based in-person sessions and video conferencing or telephone-delivered consultations, with the delivery style being flexible in accordance with the needs of the family. This approach aimed to promote generalisation of new skills development in the home setting. Other clinical and research experience has indicated that video conferencing session formats were popular with parents.[62]

Each parent session began with a discussion and review of the progress made since the last session. The parent and child were then filmed while playing for 10 minutes. Immediately after this, the therapist and parent watched the video, or, during video conferencing sessions, the therapist and parent watched a 1- to 2-minute parent-filmed video of a home-based practice session. The therapist facilitated parents to identify child communications and to adopt PACT-G strategies in their interactions with the child. Parents were assisted to set goals for themselves based on the interaction strategies discussed. The parent and therapist discussed the opportunities to practise these strategies each day at home for half an hour, as in the original PACT.[7]

Educational setting sessions

In most cases, therapy in the educational setting began after the parent had commenced therapy at home. The start times and duration of educational setting-based therapy were aimed to fit in two education terms, where possible. In the educational setting, PACT-G sessions were delivered by a LSA or equivalent, nominated by the senior management team. LSAs and other education staff received an initial training session to introduce them to PACT-G therapy. The education-based intervention then consisted of therapist–LSA sessions that mirrored the therapist–parent sessions in the home. Videos recordings of the LSA and the child were used to coach the LSA in the use of PACT-G strategies in a similar procedure to the parent. The LSA was then asked to implement these with the child daily – inside or outside class. There was a maximum of 12 therapist–LSA sessions over 6 months, alternating educational setting visits and video conference or telephone consultations. PACT-G strategies were expected to be integrated in a complementary way with other communication strategies that may already have been in use in the educational setting. This combination of therapist–parent and therapist–LSA sessions resulted in a maximal offer of 24 sessions for PACT-G across home and educational settings.

Collaboration between parent and education staff

The separate therapeutic work with parents and LSAs described above was designed to be supplemented with a schedule of joint parent–LSA meetings [i.e. home–school conversations (HSC)] to support communication and complementary use of strategies across the home and education settings. These meetings used the manualised and validated technique of HSC.[63,64] Meetings were structured around 'explore', 'focus', 'plan' and 'review' stages, which allowed the LSA and parent to share experiences to promote generalisation of techniques across settings. HSCs have been shown to be highly effective in motivating parents and education staff.[63,64] HSC sessions were designed to take place in the educational setting and were planned to occur as regularly as possible during the intervention period, in association with therapist's visits to the educational setting. This allowed for up to six HSC sessions, with the minimum acceptable number set at three per child. *Table 4* summarises the intervention procedure over time.

Training and fidelity of treatment

Training in the PACT-G therapy was conducted centrally by the lead speech and language therapists, who undertook overall co-ordination of the therapy in the trial and organised quarterly across-site therapist meetings. Therapists were regularly supervised by the clinical lead in each site. All therapy sessions were videotaped, and randomly selected tapes of one home and one education in-person session per therapist were independently rated using the PACT-G fidelity rating scale (see *Appendix 4*) at regular intervals across the trial period. Therapists and research staff were trained in practices that minimise non-compliance and dropout. Arrangements were also made at each site to ensure that PACT-G therapists had no contact with TAU only (control intervention) families. Therapy compliance and receipt of other interventions outside the protocol were monitored.

TABLE 4 Sequence of the PACT-G intervention and outcome assessment

	Month											
Session type	**0 (baseline)**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12 (end point)**
Researcher assessment	ADOS-2												ADOS-2
	BOSCC												BOSCC
Parent assessment	BOSCC							BOSCC					BOSCC
	DCMA							DCMA					DCMA
Intervention with parent			Initial home visit 12 intervention sessions (home-based sessions and telephone/ video conference support sessions) HSC sessions in educational setting						HSC sessions continue for the period of the educational setting-based intervention. The number will vary depending on term times, but with a minimum number of three sessions				
School assessment	BOSCC							BOSCC					BOSCC
	DCMA							DCMA					DCMA
Intervention in educational setting					Initial LSA in educational setting training visit[a] Up to 12 intervention sessions (educational setting alternating with video conference/telephone support) incorporating HSC meetings with parents						HSC sessions continue until final assessment		

BOSCC, Brief Observation of Social Communication Change.
a Start of education element accommodates education terms.

Treatment as usual

The control intervention was TAU only. We had detailed information on TAU in the preschool population from the group's previous work on the original PACT and in older children from the PACT 7–11 follow-up study.[65] Data on the services received by all families recruited to PACT-G were collected by the research team.

Avoidance of contamination

There were separate clinical and research leads at each site and separate training and supervision structures. Researchers were housed separately from the staff involved in the delivery of the PACT-G intervention. Mid- and end-point research interviews and assessments were conducted so as to avoid inadvertent divulging of information that could reveal treatment status. The assessment suite and materials used were different in type and location to those used for the therapy intervention in home or educational settings to avoid any familiarity effect for children in the treatment group.

Measures

Primary outcome: ADOS-2

The ADOS-2[66,67] is a standard autism diagnostic symptom measure with good external validity for long-term outcomes in autism development. The assessment was undertaken during researcher–child

interaction using a standardised set of social presses and was video-recorded for later coding to preserve blindness in follow-up assessments. The scoring metrics of ADOS-2 have been modified in line with the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition,[68] with social communication and repetitive behaviour symptom domains combined into a unitary total symptom score [social affect (SA) and restricted and repetitive behaviour (RRB) overall total raw score]. ADOS-2 modules are available for different stages of child development and were assigned at baseline accordingly. The same module was used at the end point as the baseline for each child. Recent studies[14,69] have demonstrated the ability of the ADOS-2 to measure treatment effects; for instance, in the PACT follow-up study,[14] effects were sustained for 6 years after treatment end.

Other measures

Diagnostic inclusion

The Mullen Scales of Early Learning[70] or British Ability Scales[71] were used depending on the child's age and ability level. These are standard measures of early development that enable a developmental level of non-verbal abilities to be ascertained for inclusion criteria and allow characterisation of the cohort in relation to other autism treatment trials.

The SCQ[72] is a brief (40-item) parent-report screening measure that identifies characteristics associated with autism. Items cover three subdomains: reciprocal social interaction; communication; and restricted, repetitive and stereotyped patterns of behaviour. The 'lifetime' version refers to the entire developmental history of the child.

Secondary outcomes

The Brief Observation of Social Communication Change (BOSCC) with a researcher[73–75] involved the researcher coding the autism symptoms from videotaped child–adult interactions. It addresses the same autism symptom constructs as the ADOS-2, but is designed to detect clinically meaningful symptom change in treatment studies. Codings combine symptom frequency, severity and atypicality on a 16-item, 0–5 scale (overall range 0–80). The BOSCC is designed to be a standard treatment outcome measure for the autism field and is currently used in large, funded trials in the USA and the European Union. The BOSCC has high-to-excellent inter-rater and test–retest reliability and has convergent validity with measures of communication and language skills. It demonstrated increased sensitivity to change over time compared with the ADOS-2 CSS in an observational study.[75] Three moderate-sized RCTs applying the standard naturalistic BOSCC as an outcome measure reported small and non-significant ESs.[76–78] When applying the standard BOSCC coding scheme to a non-standard, structured parent–child interaction, one study[27] found a large, significant intervention effect.

For module 1 BOSCC (non-verbal or minimally verbal children), the recommended protocol consists of 4 minutes of free play followed by 2 minutes of bubble play, which is then repeated with a new set of toys. From this, 4 minutes of free play and 1 minute of bubble play were coded for each of the two segments. For module 2 BOSCC (phrase speech), as there was no recommended administration procedure developed at the start of PACT-G, a play and conversation administration was agreed with the developers in which the children had 4 minutes of free play followed by 2 minutes of conversation, which was then repeated with a new set of toys, before 2 minutes of bubble play.

The BOSCC with a parent and LSA[73–75] was a measure of the intervention effect in the naturalistic settings in which the intervention took place. It involved the coding of video-recordings of child–parent play sessions in the home setting (at baseline, 7-month mid-point and 12-month end point) and child–LSA play sessions in the educational setting (baseline, 7-month interim and 12-month end point). BOSCC

ratings were made from the same video-capture as for the DCMA (see below) and, to allow this, its administration deviated slightly from the recommended BOSCC protocol. For module 1 BOSCC, each child had 8 minutes of free play with the adult with the same box of toys, followed by 2 minutes of bubble play. From this, 4 minutes of free play and 1 minute of bubble play were coded for each BOSCC segment. For module 2 BOSCC, parent and teacher BOSCCs had 8 minutes of free play with the same set of toys, 4 minutes of conversation, and then 2 minutes of bubble play, based on a prototype 'verbal' BOSCC administration using module 1 toys. It became apparent during the trial that the conversation element was too challenging for the majority of module 2 children and it was decided, in discussion with the BOSCC developers, to code the module 2 items from 4 minutes of free play and 1 minute of bubble play in each segment.

The DCMA with parent and with LSA[14] was coded from the same videos as for the BOSCC. This measure includes independent codes of adult communication (synchronous response) and child communication (child initiations). The DCMA synchronous response variable is defined as the proportion of the adult's total communication acts that are synchronous with the child, where a synchronous communication act is a comment or acknowledgement that follows the child's focus of play, actions, thoughts or intentions. Requests, directions, commands, questions and negations are not considered synchronous, even if related to the child's focus of attention. The DCMA child initiations variable is defined as the proportion of the child's total communication acts that are initiations, where initiations are verbal or non-verbal communication acts that serve to start an episode of interaction. This measure had proved sensitive in the original PACT mediation analysis and is used in PACT-G to test treatment effect and mediation in home and educational settings.

The Vineland Adaptive Behavior Scales (VABS) (parent and teacher versions)[79] includes domains of communication, daily living skills and socialisation; it has been used widely and measures child functional ability in the home and educational settings.

The MacArthur Communicative Development Inventories (MCDIs) (word and gestures, sentences and grammar),[80] the Receptive and Expressive One-word Picture Vocabulary Test (EOWPVT)[81] and the Preschool Language Scale-5 (PLS-5)[82] are standardised assessments used to measure children's overall language level to supplement the measures of autism-specific communication included in the BOSCC and ADOS-2.

The Very Early Processing Skills (VEPS)[59,60] assesses children's sociocognitive skills (social responsiveness, joint attention and symbolic comprehension).

The RBQ[83] is a 26-item parent questionnaire for assessing repetitive behaviours in children with autism.

The Developmental Behaviour Checklist (DBC) – Parent (2nd edition)[84] is a 96-item instrument used for the assessment of behavioural and emotional problems in young people aged 4–18 years with developmental and intellectual disabilities. It includes two subscales, the Disruptive/Anti-social Subscale and the Anxiety Subscales (36 items), and is completed by a parent or carer.

The Strengths and Difficulties Questionnaire (SDQ) – parent and teacher versions[85] – is a 25-item brief measure of psychological well-being in 2- to 17-year-olds and is completed by parents and teachers.

The Child Health Utility 9D (CHU9D)[86] is a paediatric measure of health-related quality of life. It consists of nine items, rated on five levels (ranging from no problems to severe problems). It is designed to be completed by children aged 7–17 years. Proxy completion by parents on behalf of their child is also possible for younger or children with developmental disabilities.

The Warwick–Edinburgh Mental-Wellbeing Scale (WEMWBS)[87] is a self-rated parental well-being questionnaire recommended by the UK Department of Health and Social Care as the preferred measure of mental well-being to incorporate in studies of this kind.

The Tool tO measure Parenting Self-Efficacy (TOPSE)[88] is a 48-item, self-reported measure of parenting competence. It is a measure of possible change in parents' confidence in their ability to make a difference to their child's development. It was completed at baseline and end-point assessments.

The Child and Adolescent Service Use Schedule (CASUS) and the School Service Use Schedule[65] were developed to record therapies and service use accessed throughout the study. Forms were adapted to young populations with autism in PACT[7] and PACT 7–11.[6]

The Working Alliance Inventory-Short Revised (WAI-SR)[89] is a measure of engagement with therapy for parents and LSAs in group only. For parents and LSAs, there is a simple rewording of the client and therapist versions of the Working Alliance Inventory, which has been validated and is now frequently used. It was completed at the 2- and 5-month stages of the intervention.

Demographic, clinical and family language information comprised relevant demographic and clinical information and details of home language(s) spoken with the child. The intervention schedule is summarised in *Table 5*.

TABLE 5 Schedule of assessments

Time point	Measure
Eligibility	ADOS-2
	SCQ
	Mullen Scales of Early Learning (preschool-aged children)
	British Ability Scales (school-aged children)
Baseline	BOSCC – researcher
	BOSCC/DCMA – parent
	BOSCC/DCMA – LSA
	VABS – parent interview
	VABS – teacher survey
	VEPS
	EOWPVT
	RBQ
	WEMWBS
	MCDIs (word and gestures; sentences and grammar)
	SDQ – parent
	SDQ – teacher
	TOPSE
	CHU9D
	Key information and demographics
	Clinical information and service use
	School Service Use Schedule
	Family language interview

continued

TABLE 5 Schedule of assessments (*continued*)

Time point	Measure
Mid-point home/parent	BOSCC/DCMA – parent
	Status form
Mid-point LSA/school	BOSCC/DCMA – LSA
End point	ADOS-2
	RBQ
	BOSCC – researcher
	BOSCC/DCMA – parent
	BOSCC/DCMA – LSA
	PLS-5
	EOWPVT
	VABS – parent interview
	VABS – teacher survey
	WEMWBS
	MCDIs (word and gestures)
	DBC – parent (disruptive/antisocial and anxiety subscales)
	SDQ – parent
	SDQ – teacher
	TOPSE
	Changes to key information and demographics
	School Service Use Schedule
	CASUS
	CHU9D

Procedures

Data collection

Research staff confirmed eligibility and obtained consent. Baseline assessments were undertaken prior to treatment assignment.

Randomisation

Randomisation took place using a web-based service hosted at the King's Clinical Trial Unit.[90] This system was accessed only by trained trial staff who had previously been allocated a username and password. Requests for passwords were sent through the trial manager to the King's Clinical Trial Unit. Randomisation was at the level of the individual participant, 1 : 1, stratified for site, age group (2–4 years and 5–11 years) and gender imbalance using random block sizes. Once randomised, the system automatically generated and sent an unblinded e-mail confirmation to the therapy lead (for records, blinded copy was sent to the local researcher who made the request and to the Manchester trial manager).

Blinding/concealment

Researchers who administered assessments were blind to participants' group allocation and every effort was made to maintain blindness throughout the trial: research staff were located separately from therapists, parents were reminded at every meeting with the researchers not to divulge allocation

information, staff in the educational settings were given photographs to distinguish therapists from research staff, and, where possible, different school staff signed in therapists and researchers.

To preserve blinding in follow-up visits, the primary outcome and putative mechanisms at the end points were cross-coded from videos by researchers at the other sites who had been trained to high levels of reliability and blinded to intervention allocation. A randomly selected proportion of assessments were double rated for reliability. All other researcher assessments were also blinded; however, parent and teacher questionnaires and interview measures were unblinded. Participant families could not be blinded to allocation. All therapy sessions were video-recorded. Variability due to therapist effects was minimised by frequent clinical supervision and checks of continuing therapist fidelity against the treatment manual; randomly selected sessions for each therapist were formally coded for fidelity over the course of the study by independent clinicians using the model successfully used in the PACT.

Engagement with referrers, schools and families

Extensive information-sharing and engagement activities with clinical teams and local mainstream and specialist educational settings were undertaken to promote clinical referrals and engagement with both home and educational aspects of the intervention. Regular trial newsletters to participating families, schools and nurseries and clinical teams, along with voucher payments to educational settings (schools and nurseries), acted to maintain involvement and adherence. Families received an individualised feedback report on the assessments conducted with their child, copied to school and clinical teams with parental consent, if desired. Parents received a small voucher payment at the end of their participation to thank them for their time and efforts. A local referring clinician for each participant was informed of the study progress and findings, with procedures for clinical support and aftercare beyond the study, should this be necessary.

Memorandum of Agreement with participating educational settings

There has been a recent emphasis on the need for collaborative research partnerships between educational settings and evidence-focused partners.[91,92] To address this call,[46] more research teams are utilising MoAs or similar to formalise partnerships with the educational settings that participate in their large-scale trials.[93] Although traditionally used in school–school partnerships to share best practice, there is a clear benefit to developing mutually beneficial links between educational settings and evidence-focused partners. There is a great need for collaboration in these contexts and stakeholders to understand how effective interventions for children with autism can be developed.[54,55,94]

A MoA was developed for PACT-G to develop working relationships with participating educational settings. The MoA and accompanying information sheet contained information about the PACT-G intervention, explaining the requirements of the randomised control design of the trial and the need for an appropriate member of staff to be available to attend intervention sessions and participate in research assessments, and providing information on how the educational setting would benefit for taking part.

The decision on who to nominate as the intervention partner was made by the educational setting; however, we theorised that the LSA would best fit this role because of the likelihood that they would spend the most contact time with children out of all education staff and because they had more time in the school day than teachers.

The MoA itself required a signature from a senior member of management and a member of the governing body, when applicable, which meant that 'buy-in' was formalised for the educational setting. Evidence shows that the drive for improvement and demonstration of good practice from senior leadership has a downstream positive effect on school culture.[95] Moreover, Goodrich and Cornwell[96] suggest that the influence of organisational culture, routines and training plays a substantial role in the quality of care and outcomes.

Data management

All data in the trial were anonymised. Site files were held at each site and a trial master file was held centrally by the trial manager at the University of Manchester. This contained the key linking the anonymised trial name to personal details. The main trial data were entered into the web-based data entry service of King's Clinical Trials Unit, which has a full audit trail. Appropriate quality control was carried out during the trial and before the database lock, and recorded in a standard operating procedure (SOP). This included data entry checking of:

- all measures of the first two cases entered by each individual carrying out data entry
- 10% source data verification on data entry for all measures
- all the primary and secondary outcome data entries, including ADOS-2 and researcher BOSCC data.

Primary analysis of the data was undertaken by the trial statisticians, with senior statisticians masked to treatment allocation. Analyses involving therapy data were not masked and were undertaken in part by the chief investigator's administrative team. Full data sets were also shared with each site in the collaboration.

Adverse events

Adverse events (AEs) were enquired about systematically by researchers at each meeting with the family. AEs were also collected in parallel by trial therapists, as and when a situation became known to them, and documented separately in a therapy log. As well as recording AEs in a predefined standard format, we included AEs relating to child health, well-being and behaviour; significant issues in the educational setting; and family events such as separation or significant parental ill health. AEs were monitored using a bespoke semistructured interview and documented by the research team post intervention and as they arose during intervention sessions, regardless of the relationship to the study intervention or research procedures. Hospitalisation and bereavement in a family member residing in the home were considered severe AEs. We reported on all serious AEs (any AE which results in death, is life-threatening, requires hospitalisation or prolongs hospitalisation, causes persistent or significant disability, or results in birth defects) and all suspected unexpected serious adverse reactions (serious AEs that are believed to have a causal relationship with the PACT-G treatment). We also recorded events particularly relevant to this trial, such as significant changes in family or school situation. The clinical principal investigators (JG, TC, JP, ALC, HMc, VS, CA, VG) reviewed and agreed all AEs at the end of the study. An unblinded list of AEs by group was prepared by the statistical team and reviewed by the study Data Monitoring and Ethics Committee.

Adherence to allocated treatment, session validity and manual fidelity

Any departures from intended treatment assignment were described. The total numbers of sessions with parents, LSAs and in HSCs were reported, as well as the number of sessions that met the criterion for satisfactory quality. The service use form was used to identify any TAU families who had made use of the PACT treatment outside the trial. Therapists were regularly supervised by the clinical lead at each site.

Intervention manual fidelity

All therapy sessions were video-recorded at regular intervals across the trial period; one in-person session in the home setting and one in the educational setting were randomly selected per therapist for rating (CT, JG and PH), independent of therapy delivery and supervision, using the PACT fidelity rating scale (see *Appendix 4*). The scale has 16 items, rated 0 or 1, and was used to assess adherence to the PACT-G protocol. The proportion of tapes above the 80% fidelity threshold was reported.

Remote sessions and HSCs were not formally rated because of anticipated difficulties in recording these adequately, but they were informally monitored by the therapy supervisors during therapy supervision. The independent fidelity raters did, however, review a selection of remotely delivered sessions in the home and educational settings, chosen to reflect the range of remote sessions delivered, to assess the acceptability of remote intervention in the different settings.

Session validity from therapist logs

A key component of the PACT-G therapy is the use of video-mediated feedback. However, as the PACT-G therapy was being delivered in both home and educational settings, and often in challenging circumstances, a set of criteria was developed against which therapists could judge the 'acceptability' of each session. Detailed therapist logs were maintained through the course of the trial. Information from these was used to collate (1) the number of sessions delivered in each category, (2) the acceptability of these sessions against quality criteria and (3) qualitative notes on treatment setting, barriers to delivery, feasibility and acceptability. A number of 'exclusion deviations' were prespecified which, if present, resulted in the session being rated as falling below an acceptability threshold. Criteria for a number of 'acceptable deviations' were also prespecified. These were deviations from the content of an 'ideal' session that, despite the deviation, the therapist rated as a good enough therapy session to be valid.

The home–school conversation sessions

Home–school conversation sessions were not video-recorded or rated for acceptability or fidelity purposes. However, the number of sessions and session length were recorded. HSCs lasting < 30 minutes were deemed unacceptable as a valid session.

Chapter 6 Patient and public involvement

Patient and public involvement input into original intervention development

Ongoing sequential development of the PACT intervention has been carried out in close collaboration with families and service users. At an early stage, the team co-developed with service users the first user-nominated measure of treatment outcome in autism,[97] which helped focus on key parent-nominated priorities. Parent reports on the experience of receiving PACT therapy in the initial stages were evaluated through independently conducted interviews and the results were fed back into the design of the next iteration of the therapy within PACT-G.[33] This feedback, including around clinic visits and home-based practice, informed the design of the home-based aspects in PACT-G.

Patient and public involvement review following the pilot phase

This planned review included input into research design and adaptation of the intervention prior to finalisation of the trial protocol.

Aim

We aimed to involve parents and education staff as service users in the design and piloting of novel aspects of the intervention, including generalisation of the parent training sessions into the home and educational settings and joint working with educational settings.

Methods

At the end of the pilot phase, we carried out a feedback exercise with pilot families and education staff. We interviewed seven parents, five members of nursery/school management and two LSAs to obtain feedback on the participant information sheet (PIS) provided about the study, trial documentation, baseline assessment burden and intervention process. We asked about their experiences of taking part in the intervention and how intervention sessions could be delivered in a way that minimised any additional burden to families or educational settings. Additional feedback from therapists and research staff was also incorporated. This feedback was summarised and fed back to the PACT-G trial team.

Results and subsequent actions

Generally speaking, interviewees spoke positively about their experience of the study. They reported that the research burden was acceptable. A summary of the main points from their feedback is given below. This feedback was shared with the PACT-G trial team and led to multiple changes in our procedures that are also detailed below.

Participant information sheet

The PIS could be easily understood by most; however, one parent commented that she found the PIS to be too long and complicated:

- We obtained an ethics committee amendment agreement for a short and easy-read version of the PIS. This was offered to parents alongside the full PIS.

Running the research in educational settings

The combination of written and verbal information sources provided to educational settings was appropriate in quantity and accessibility. The research team were advised to make sure that LSAs had all the practical information that they required for intervention delivery, as they did not always attend the initial orientation session. Education staff suggested that the time commitment involved in the study

needed to be presented much more clearly from the outset and that it was important for appointments to be booked as far in advance as possible. This was fed back to all trial staff working with educational settings. Education staff also commented that they needed clearer guidance on aspects of research design, such as the inclusion criteria, avoiding group contamination and researcher unblinding:

- Members of education management teams were encouraged to attend the orientation session, as this provided them with the practical details of the study. A copy of the information sheet was also available for reference and to share with other staff members. We adjusted procedures to ensure that education staff fully understood the time commitment to the study from the earliest stages.
- Steps were taken to ensure that parents and staff in educational settings understood the different roles of researchers/therapists. A handout was produced for education staff, summarising research design issues and how educational settings can help with these. Posters with photographs of research/therapy personnel were made available so that all staff in educational settings knew who was who to prevent unblinding.

Burden of baseline assessments on parents

The burden of baseline assessments was acceptable to parents. Some thought that the child assessment session was tiring and one parent felt awkward in the play assessment:

- Research staff recognised that child assessment sessions mean a long day for the child and did what they could to reduce burden (offer breaks, etc.). They also reassured parents that the researchers recognised that some aspects of the play assessments might not seem as natural as usual.

Organising research assessments/therapy sessions

No parents reported problems with organising appointments, but flexibility of therapists in accommodating them was appreciated by a number of parents. Staff in educational settings found this more challenging because of practical and logistical reasons:

- Therapists booked therapy sessions and research assessments well in advance/at regular times to allow educational settings to organise rooms/staff cover.

Video-conferencing/telephone sessions

Problems were described by parents and LSAs/education management (and by therapists) in terms of making videos (if no other adult was present or if the child did not like being video-recorded), and sending videos [problems with system, parent has limited internet capacity, handing over universal serial buses (USBs) instead of using video-sharing software/education information technology (IT) set-up/difficulty if only one device for looking at video and Skyping (Skype™; Microsoft Corporation, Redmond, WA, USA) simultaneously]:

- Written information on using technology (Skype/video-sharing) was produced for parents/LSAs.

Home–school conversations

All parents reported HSCs to be easy or fairly easy to arrange and found these to be helpful or very helpful – they liked hearing how their child was getting on in an educational setting and sharing their experiences. Both LSAs who were interviewed had a HSC and found these easy to organise. One LSA found these HSCs to be very informal and was unclear on the objective of the session:

- LSAs were given an initial explanation about the purpose and format of HSCs and how they are different from the more usual type of education planning meetings they might have been involved in.

Critical reflections on this process

This feedback was very informative and ensured that parents and particularly education staff were fully informed about the commitment required for the research and key aspects of trial design. It also meant that members of the trial therapy team understood how best to support allocated education staff to access and benefit from the therapy sessions.

Patient and public involvement input to the Trial Steering Committee and Local Steering Groups

Two parent representatives were members of the TSC. Both were parents of children with autism and one was a qualified teacher with experience of working in both mainstream and specialist schools. At all meetings, the parent representatives contributed to discussions and provided valuable input on aspects of the trial design and the therapy process. Some specific areas of feedback from the parent service user TSC members that led to changes to procedures included:

- Discussion around how researchers could sensitively introduce some of the research assessments, which led to SOP researcher guidelines on how to introduce research measures.
- Ways to keep parents engaged with the trial team to maximise participant retention, especially in the TAU group. This led to the purchase of trial-branded merchandise (coffee cups, magnets, pens, etc.), which kept particpants aware of the trial and acted as a small token of appreciation.
- Discussion about borderline eligibility issues, such as significant parent mental ill health, child epilepsy and child genetic conditions. This led to a tightening of the eligibility criteria, ensuring that referring clinicians and trial personnel understood the clear and consistent eligibility criteria for participation.
- Reflections on potential parental experiences of the HSC and some of the parent–education staff dynamics that might affect the delivery and success of these sessions. This resulted in greater awareness among the trial team and increased sensitivity to some of these issues.

Critical reflection

The two patient and public involvement (PPI) representatives contributed in a positive and constructive way that led to increased understanding of the perceptions and experiences of parents and education staff and to material changes to procedures. One of the PPI representatives has since continued to collaborate with the team by acting as a parent representative co-investigator on another National Institute for Health and Care Research (NIHR)-funded trial (the HTA-funded REACH-ASD trial, HTA 17/80/09).

A local PACT-G steering group took place every 6 months throughout the study at the Newcastle upon Tyne site. The group included a parent representative (who had taken part in the previous PACT), two representatives from special needs schools and two referring clinicians, as well as members of the research and therapy team. These meetings shared local knowledge up-to-date information about the whole study to promote recruitment and retention procedures. Important lessons included feedback on acceptable study merchandise; using text messages and e-mails to contact recruited parents who might not answer unrecognised telephone numbers; the value for parents of the research assessment reports; promoting recruitment opportunities with local parent support groups and at multidisciplinary/multiagency events; and sharing methods of providing regular feedback on research procedures with key co-ordinating professionals in both educational settings and clinical services (e.g. the use of study posters to minimise unblinding and sharing examples of best practice to support recruitment and retention). This information was fed back to the PACT-G trial team.

Chapter 7 Analysis

Aims of formal analysis

Objective 1: testing the efficacy of the PACT-G intervention

To test whether or not the extended PACT-G social communication intervention protocol, using targeted enhancement strategies within home and educational settings, showed a treatment effect on:

- researcher-assessed autism symptom primary outcome
- dyadic social communication and autism symptoms in home and educational settings.

This objective was tested using a variety of measures to maximise the ability to detect meaningful change (see *Chapter 5*, *Measures*) and evaluated by estimation of effects at the trial end point.

Objective 2: mechanism analysis

The mechanism analysis used the experimental trial to illuminate core processes of generalisation of specific, acquired competencies in autism across contexts:

- We built on the mediation analysis from our previous PACT[56] to test mediation of the generalised treatment effect in home and educational setting.
- We tested whether or not and how effects in naturalistic contexts might combine to enhance transmission of effect to research-assessed symptoms in a standardised test setting.

A statistical analysis plan was written by the trial statisticians (AP and RE) and agreed by the trial principal investigators before approval by the TSC and Data Monitoring Committee prior to completion of data entry, data lock and analysis. All statistical analyses were carried out using Stata or M*plus* (Muthén & Muthén, Los Angeles, CA, USA).[98]

In accordance with the Consolidated Standards of Reporting Trials (CONSORT) statement for non-pharmacological interventions,[99] we report all participant flow. Descriptive statistics summarise recruitment, dropout and completeness of interventions. Analysis was undertaken after all 12-month outcome measures were completed. The main efficacy analysis followed intention-to-treat (ITT) principles. For the primary outcome, baseline measurement was completed to confirm eligibility for randomisation. The proposed primary analysis was a regression of end-point ADOS-2 score, stratified by ADOS-2 module, on baseline ADOS-2, and dummy variables for randomisation stratifiers and treatment assignment. Continuously scored secondary outcomes with both baseline and end-point measures were analysed by joint baseline–end-point regression analyses[100] that efficiently recover ITT estimates using data from all participants with any pre- or post-randomisation measurement under the missing at random assumption. When outcomes were unavailable for > 10% of participants, a sensitivity analysis was to be undertaken in which outcome scores were multiply imputed using relevant available auxiliary baseline and follow-up measures and assuming the absence of a treatment effect. There were no planned interim analyses for efficacy or futility. Summary statistics of baseline characteristics are presented by randomised group without formal statistical tests.

Phase 1: objective 1 testing the efficacy of the PACT-G intervention

We tested the primary hypothesis for between-group differences in the outcome ADOS-2 total score using linear regression, stratified by ADOS-2 module, covarying by baseline ADOS-2 total and dummy variables for site, gender and age group. Standard residual diagnostics were applied and, when required, skew-minimising transformations were adopted. An overall ES was calculated pooling stratum-specific estimates for strata defined by the ADOS-2 module, weighted by their precision, and

using a 95% CI estimated from 5000 bootstrap replicates. The secondary outcomes were analysed in a similar way but without stratification by the ADOS-2 module. A forest plot of ESs for primary and secondary outcomes is presented (see *Figure 8*). A test of homogeneity of ES for the ADOS-2 and BOSCC scales is reported. The primary analysis reports a test of homogeneity of effect for the primary outcome in preschool- and school-aged children. Secondary analysis (see *Phase 3: moderation and subgroups*) is to report an optimal moderation index,[101] including bias correction from overfitting to a finite sample.

Phase 2: objective 2 mechanisms evaluation

Mediation analysis[17] gave detailed insight into an attenuated transmission or generalisation in the original PACT across changes in person, task and context (see *Chapter 1*). In PACT-G, we tested for enhanced generalisation into home by keeping parent–child dyadic cues constant but increasing functionally relevant interaction contexts, and into education by introducing education staff (i.e. LSA)–child dyadic interventions and enhancing relevant parent–education staff (i.e. LSA) communication. The mechanism study investigated the mediation process in this model and, through that, aimed to illuminate key basic knowledge about developmental generalisation of acquired skills in autism. Some of the pathways of interest are illustrated in *Figure 2*. If the efficacy analysis showed significant between-group differences in the mediators [DCMA and/or BOSCC at home (path a) and in education contexts (path c); see *Figure 9*], then we used parametric regression models to:

1. test for mediation of the intervention on primary symptom outcome (ADOS-2) through DCMA and/or BOSCC at home (paths a, e and f)
2. test for mediation of the intervention on primary symptom outcome through DCMA and/or BOSCC in educational setting (paths c, d and f)
3. test for mediation of intervention on DCMA and/or BOSCC in educational setting through DCMA and/or BOSCC at home (paths a, b and c)
4. use structural equation modelling to examine multiple pathways through DCMA and/or BOSCC at home and in the educational setting to primary symptom outcome (paths a–f).

We repeated these four steps using researcher BOSCC as the outcome variable in place of the ADOS-2. As all of the measures are continuous, the indirect effects were calculated by multiplying relevant pathways. Bootstrapping was used to produce valid standard errors for the indirect effects. All analyses were adjusted for baseline measures of the mediators (BOSCC/DCMA), primary outcome (ADOS-2) and putative measured confounders. Mediation analyses are potentially biased by measurement error in mediators and hidden confounding between mediators and outcomes; we built on our previous methodological and applied work in this context to include repeated measurement of mediators and outcomes to account for classical measurement error[17] and baseline confounding.[102]

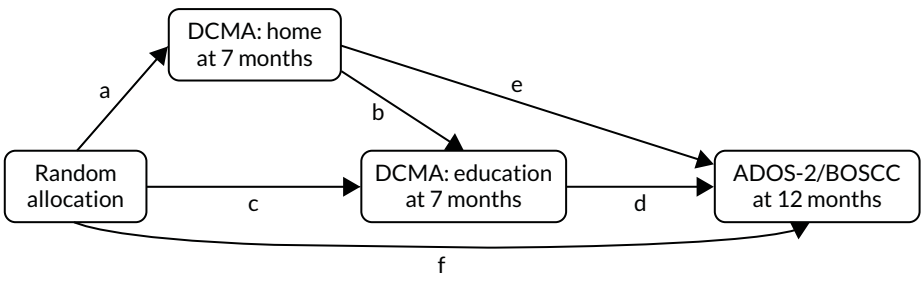

FIGURE 2 Key mediation pathways tested in the PACT-G mechanism study.

Phase 3: moderation and subgroups

We tested whether or not the mediation analysis was consistent across the two age groups by testing for moderation of paths a–f by age group stratifier (including interaction terms or performing a multiple group analysis in the structural equation model). The heterogeneity of autism is well recognised and, therefore, offers numerous potential moderators of treatment effects (e.g. language level, RRB, functional impairment). We planned to examine an extended list of moderators using bias correction/cross-validation methods to identify robust evidence for moderation and a moderation index, both on the overall effect and also along the steps of the mediation.

Primary outcome analysis

The ADOS-2 is a structured researcher-led assessment that maximises ascertainment of both social communicative competency and autism-related atypicality. Both tasks and scoring vary with the child's verbal ability according to the ADOS-2 module completed, and the same module was used at baseline and end point. Stratified by module (and, for module 1, by child's level of language to allow for the three items that differ for children with/without words), a module and language-level stratified regression of the end-point ADOS-2 SA plus RRB raw total score included treatment assignment, randomisation stratifiers (dummy variables for site, age group and gender), baseline ADOS-2 score and any other baseline variables found to predict missingness. Residual plots were used to determine whether or not prior transformation of the ADOS-2 scores was required. Using the within-group end-point standard deviation (SD), an ES was calculated for each module stratum. A single estimate pooled across modules was calculated using a weighted mean, where the weights were the inverse of the variance of each stratum-specific estimate. A CI for this pooled estimate was obtained using 1000 bootstrapped samples. The stratified analysis is illustrated below in *Figure 3*. To be consistent with the treatment main effects analysis, the test of difference in treatment effect by age group was based on the bootstrap *p*-value over 5000 replicates of the pooled within-ADOS-2 stratum estimate of the treatment difference.

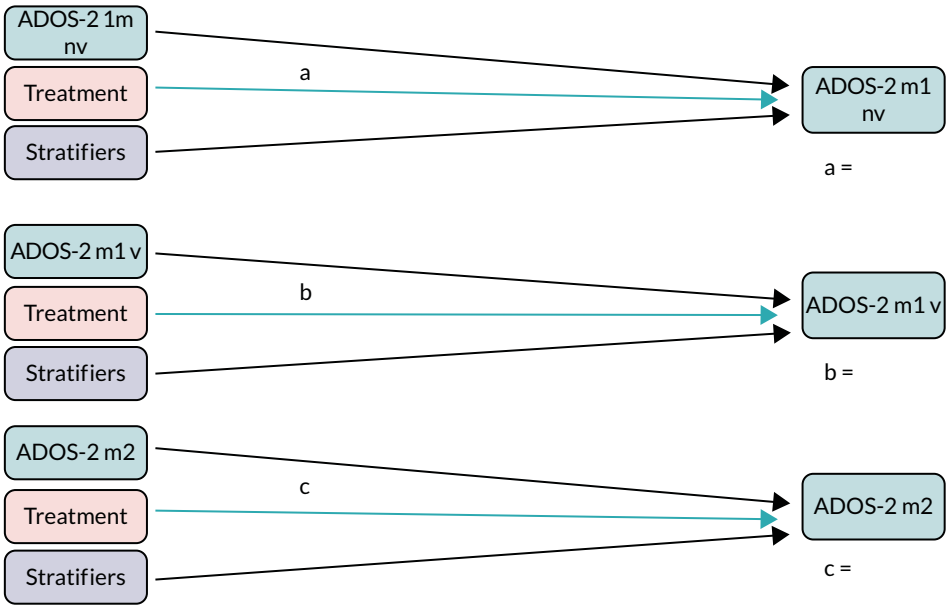

FIGURE 3 Stratified structure of analysis model. Analysis of primary outcomes: weighted sum of a, b and c (each standardised by within-group variance of outcome). 1m nv, module 1 non-verbal; m1 v, module 1 verbal; m2, module 2.

Non-adherence and complier-average causal effect estimator

The total number of therapy sessions meeting the satisfactory quality and fidelity criterion was used to define the dose of PACT-G therapy received (see *Table 13*). We estimated the effect of each satisfactory therapy session using instrumental variable regression (the model being identified by assuming the exclusion restriction that the offer of treatment does not itself influence the outcome) after accounting for receipt of treatment. The model had two correlated equations, the first for the number of satisfactory sessions received and the second predicting outcome, with treatment received replacing treatment assignment. The distributional form for the number of sessions was examined to determine whether or not this could be assumed Gaussian, or overdispersed Poisson with, the model being estimated using Stata sem or gsem, as appropriate. A dose–response model, assuming a linear dose–response relationship, was used to calculate how many sessions would be required to achieve a criterion level of clinical efficacy – defined here as the ES included in the power calculation, that is, an ES of 0.28.

We defined a more approximate variable for TAU families, where significant use of PACT-like treatment was identified. If this exceeded 10% of TAU participants using PACT, then an extended complier-average causal effect (CACE) model was estimated.

Sensitivity analysis

As per the statistical analysis plan, if missingness of the primary outcomes exceeded 10%, sensitivity analyses were to be carried out using multiple imputation; as missingness was very low (4.4%), no such analyses have been performed.

Analysis and presentation of secondary outcomes

Secondary outcomes with baseline, mid-point and end-point data:

- the parent BOSCC total
- the LSA BOSCC total
- the researcher BOSCC total (no mid-point)
- parent synchrony from the DCMA
- LSA synchrony from the DCMA
- child initiations from the parent DCMA
- child initiations from the LSA DCMA.

Secondary outcomes with baseline and/or end-point data:

- Language composite – MCDI receptive and expressive scores, the one-word tests and the PLSs.
- Anxiety composite – DBC anxiety and emotional subscale of the SDQ. DBC anxiety was collected at the end point only.
- SCQ – collected at baseline only.
- Repetitive behaviour composite – parent SCQ and insistence on sameness and sensory motor scores from the RBQ. Parent SCQ was collected at baseline only.
- Adaptive behaviour composite – VABS composite standard scores from parent and teacher and the prosocial subscale of the SDQ parent and teacher.
- Parent well-being composite – WEMWBS and TOPSE.
- Child health-related quality of life – CHU9D.
- Disruptive behaviour composite – SDQ conduct subscale and disruptive/behaviour problems from the DBC. The DBC was collected at the end point only.

Secondary outcomes are presented either as a single-measure estimate from an analysis of covariance or, where multiple measures contributed, formed into composites and analysed using structural

equation modelling (SEM), as illustrated below in *Figure 4* for a composite with three baseline and four end-point components.

Assessing quality of outcome measures

ADOS-2

All ADOS-2 video coding was completed blind to treatment allocation. Baseline ADOS-2 videos were coded by the research assistant (RA) at the local site (London, Manchester or Newcastle upon Tyne). End-point ADOS-2 videos were coded by the RA at a different site. End-point ADOS-2 videos were allocated for coding balancing for treatment group and site. Consensus meetings were held approximately every 5–6 months, with clinical leads chairing rating discussions (six meetings in total) to maintain coder reliability at all three sites across the coding period.

Dyadic interaction

DCMA: coding team

The team comprised five coders, all based in the UK (SL, CP, LK, FM and LD): three psychology graduates student, one psychology postdoctoral researcher, and one speech and language therapy undergraduate student. The coders were trained (by CA and HMc) in a 6-hour workshop, including introduction to the Behavioral Observation Research Interactive Software (BORIS)[103] coding platform and how to export files in Excel (Microsoft Corporation, Redmond, WA, USA). The coders then independently coded two video-recordings to check the level of accuracy of coding against consensus. Coding was completed blind to treatment allocation and time point. Each coder was allocated videos in balanced blocks – each block contained a balance of treatment group (PACT-G plus TAU or TAU only), context (LSA or parent) and time point (baseline, mid-point or end point) for a range of cases. A total of 1396 DCMAs were coded. Consensus meetings were held monthly by telephone conference during the main coding period (six meetings in all), discussing two independently coded videos on each occasion, with written feedback, to maintain reliability. In addition, coding questions were addressed in an ongoing social media group. Thirty-five DCMAs were double-coded for formal reliability.

BOSCC: coding team

There were twenty coders in total: nine module 1 coders based in the UK (SC, LL, NEH, LP, MB, OW, YAK, RR and CH) and 11 coders based in the USA, divided between module 1 (KM, NBu, AJ, GG and AA) and module 2 (AH, KB, RN, MT, AM and NBa). Of the 20 coders, two were psychology/neuroscience undergraduate students and all others were graduates of psychology and/or neuroscience. A UK-based

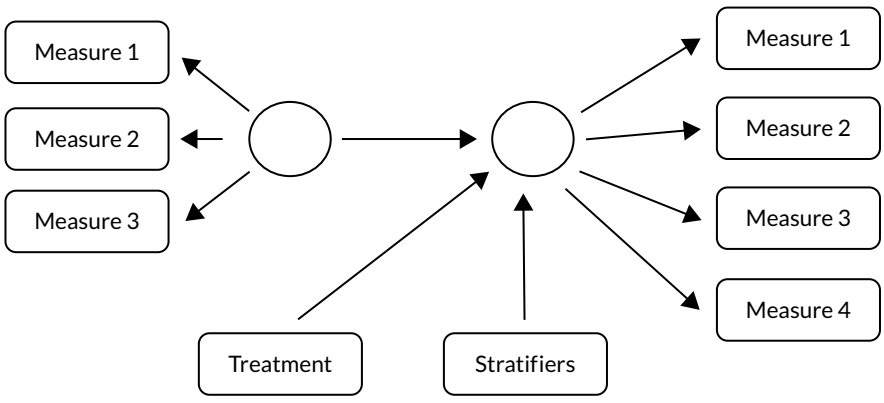

FIGURE 4 Structure of SEM-based models for the analysis of composites.

BOSCC trainer (Sue Fletcher-Watson) provided initial training to a cohort of five UK-based coders. SC was also trained to reliability by the BOSCC developers in the USA. SC oversaw initial and ongoing reliability and trained a further four UK coders. The 11 US-based coders had previously been trained to reliability in BOSCC coding by the BOSCC developers and through training by SC on the PACT-G BOSCC tapes. All coders were required to meet reliability with the UK PACT-G coders before commencing coding; reliability was judged as three consecutive tapes within four points of overall total and 12 out of 15 items per segment within 1 point, as per the manual. Coding was completed blind to treatment allocation and time point. Each coder, once trained to reliability, was allocated videos to rate independently in balanced blocks, each block containing a balance of treatment group (PACT-G plus TAU or TAU only), context (LSA, parent or researcher) and time point (baseline, mid-point or end point) for a range of cases. A total of 1840 BOSCCs were coded (*Table 6*).

The BOSCC videos were coded over a period of 2 years by UK and USA coding teams. During busier coding periods, and following any new coders starting their coding, consensus meetings were held every 2 weeks, in person or online. During times of less intense coding (e.g. two coders coding a few videos per week), consensus meetings were held monthly. These meetings were held to maintain coder reliability across the coding period. BOSCCs were multiple-coded for formal reliability. All coders, in varied pairings and groupings that included combinations of US- and UK-based coders, contributed to this process, with secondary coding being stratified in proportion to the number of videos they had been allocated for primary coding.

For module 1 BOSCC reliability, a total of 63 BOSCCs were coded for formal reliability. Fifty-seven BOSCCs were double-coded by UK-based coders. To check UK–USA consistency, a subset was also allocated for US coding. Thirty BOSCCs were double-coded by US-based coders. Formal reliability was assessed across UK and USA sites and 24 BOSCC videos were quadruple-coded by a UK pair and a USA pair. For module 2 BOSCC, which were all coded in the USA, 48 BOSCCs were double-coded for formal reliability.

TABLE 6 Breakdown of BOSCC videos

	Time point (*n*)			
BOSCC	**Baseline**	**Mid-point**	**End point**	**Total (*n*)**
Researcher	238	N/A	233	471
LSA	237	225	223	685
Parent	236	221	227	684

N/A, not applicable.

Chapter 8 Results

Participant flow

Participant flow is summarised in *Figure 5*. The first randomisation into the trial occurred on 18 January 2017, and last randomisation on 19 April 2018. The follow-up mid-point assessments ran from 15 August 2017 to 7 December 2018 and the end-point assessments ran from 5 January 2018 to 3 May 2019. Study withdrawal rates were very low and, as shown in *Table 7*, were predominantly from the TAU group. Although there were small variations in the numbers of mid-point and end-point assessments completed in the different settings, completion rates were very high. Only one participant did not contribute data to the analysis of the primary outcome.

Baseline comparability of randomised groups

Table 8 summarises baseline characteristics by treatment group. Participants were predominantly white (60.1%) and male (79.4%) and spoke only English at home (79.4%). There was very little missing baseline demographic information. The participant population was ethnically diverse, in keeping with the large urban context of two of the sites and the mixed urban–rural setting of the third.

Tables 9 and *10* present selected baseline measures by age group. With a few exceptions, the children in the older age group scored ≥ 2 SDs below the population mean for the Mullen Scales of Early Learning developmental quotient (DQ) and development of communication. Children in the younger age group showed somewhat lower autism severity than those in the school-aged group, but were nevertheless markedly intellectually and communicatively impaired.

Table 10 shows that, with respect to autism severity, the groups were similar and at a level consistent with the inclusion criteria of severe autism.

Although the same module was used at baseline and at the end point, two items used in the module 1 ADOS-2 algorithm for calculating the ADOS-2 total score for 'no-words' children were replaced by different items when the 'some words' level of language was achieved, and vice versa if language regressed. *Table 11* shows the modules and level of language of participants at baseline and the end point.

Education provision

The educational settings across both groups of the trial, characterised at baseline, are shown in *Table 12*. The majority of preschool-aged children recruited to PACT-G attended a mainstream nursery [for both the PACT-G ($n = 45$) and TAU ($n = 48$) groups]. These settings consisted of privately owned independent day nurseries and local authority day nurseries. A small number of children in this age group attended a specialist nursery (PACT-G $n = 3$; TAU group, $n = 2$). These settings were either charity-led or local authority nurseries. One child attended a child-minding setting (TAU). All of these settings deliver a child-led curriculum within the Early Years Foundation Stage (EYFS).[104]

The majority of school-aged children in the PACT-G ($n = 44$) and TAU ($n = 56$) groups attended a special educational setting. These settings were either for children with a range of disabilities or were

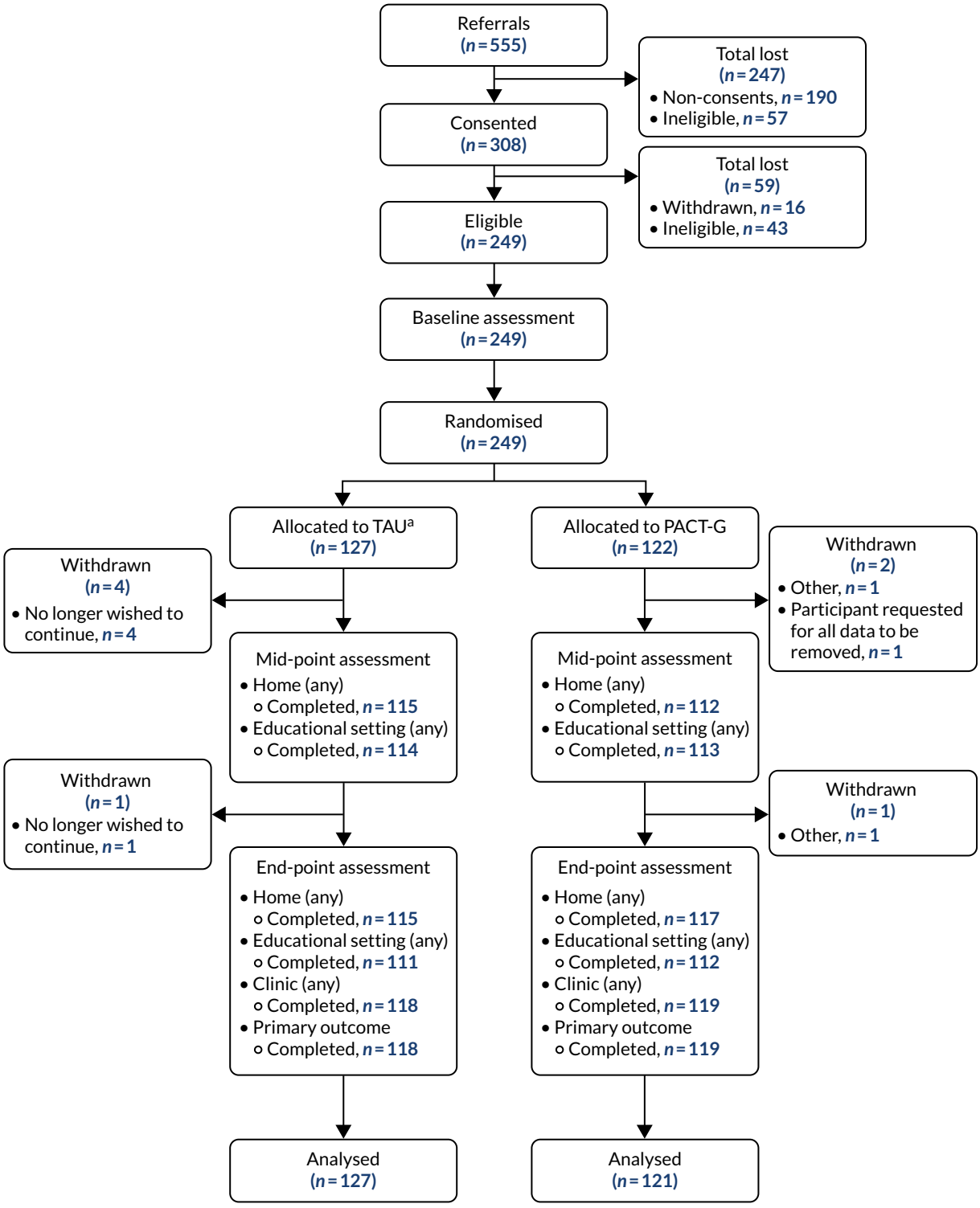

FIGURE 5 The PACT-G CONSORT flow diagram. a, One family inadvertently received PACT-G treatment.

specialist autism schools. Other children in this age group attended a mainstream primary school (PACT-G group, $n = 25$; TAU group, $n = 25$) or a resourced specialist provision within a mainstream primary school (PACT-G group, $n = 4$; TAU group, $n = 4$). These children access the national curriculum (key stage standards) and have SEN support at school or have an education, health and care plan in place.[91]

TABLE 7 Participant withdrawals by treatment group

Withdrawals	Treatment group, *n* (%)		Overall, *n* (%)
	TAU	PACT-G	
Did the participant withdraw from the study?			
No	121 (95.3)	119 (98.3)	240 (96.8)
Yes	5 (3.9)	2 (1.7)	7 (2.8)
Yes, and requested all data to be removed	1 (0.8)	0 (0.0)	1 (0.4)
Reason for withdrawal			
Participant no longer wishes to continue	5 (100.0)	0 (0.0)	5 (71.4)
Participant moved	0 (0.0)	1 (50.0)	1 (14.3)
Participant unhappy with progression of intervention	0 (0.0)	1 (50.0)	1 (14.3)

TABLE 8 Participant baseline descriptive data by treatment group

Characteristic	Treatment group, *n* (%)		Overall, *n* (%)
	TAU	PACT-G	
Age (years)			
Preschool aged, *n* (%)	77 (60.6)	74 (61.2)	151 (60.9)
School aged, *n* (%)	50 (39.4)	47 (38.8)	97 (39.1)
Preschool age, mean (SD)	3.9 (0.7)	4.1 (0.6)	4.0 (0.6)
School age, mean (SD)	6.9 (1.4)	7.4 (1.6)	7.1 (1.5)
Sex, *n* (%)			
Female	27 (21.3)	24 (19.8)	51 (20.6)
Male	100 (78.7)	97 (80.2)	197 (79.4)
Ethnicity, *n* (%)			
White	73 (57.5)	76 (62.8)	149 (60.1)
Black	21 (16.5)	19 (15.7)	40 (16.1)
Asian	16 (12.6)	13 (10.7)	29 (11.7)
Mixed	17 (13.4)	6 (5.0)	23 (9.3)
Other	0 (0.0)	7 (5.8)	7 (2.8)
Second parent in household?, *n* (%)			
No	28 (22.0)	27 (22.3)	55 (22.2)
Yes	99 (78.0)	94 (77.7)	193 (77.8)
Languages spoken to child at home, *n* (%)			
English only	98 (77.2)	99 (81.8)	197 (79.4)
Other only	3 (2.4)	1 (0.8)	4 (1.6)
English and other	26 (20.5)	21 (17.4)	47 (19.0)
Non-verbal IQ, *n*	127	121	248
Mullen – visual standard *t*, mean (SD)	25.2 (11.7)	22.9 (8.0)	24.1 (10.1)
Mullen – visual raw score mean (SD)	28.3 (7.8)	28.5 (7.0)	28.4 (7.4)
Mullen – fine motor standard *t*, mean (SD)	22.8 (8.6)	21.8 (7.3)	22.3 (8.0)
Mullen – fine motor raw score mean (SD)	26.3 (6.9)	27.2 (6.5)	26.7 (6.7)

IQ, intelligence quotient. Mullen, Mullen Scales of Early Learning; SD, standard deviation.

TABLE 9 Baseline ADOS-2 module by age group and VEPS baseline scores and intelligence quotient from the Mullen Scales of Early Learning

Baseline	Age group	
	Preschool aged (*N* = 151)	School aged (*N* = 97)
Module 1 (non-verbal), *n* = 110	63	47
VEPS – social response, median [range] (IQR)	0 [0–12] (0 –1)	1 [0–11] (0–3)
VEPS – joint attention, median [range] (IQR)	2 [0–13] (0–5.5)	2 [0–17] (1–6)
Mullen – visual raw score, median [range] (IQR)	23 [16–34] (20–25)	26 [16–41] (23–29)
> 2 SDs below standard norm, *t*-score	97%	100%
Mullen – fine motor raw score median [range] (IQR)	22 [15–29] (19–24)	23 [15–44] (20–25)
> 2 SDs below standard norm, *t*-score	98%	100%
Module 1 (verbal), *n* = 77	52	25
VEPS – social response, median [range] (IQR)	1.5 [0–12] (0–3)	2 [0–10] (0–3)
VEPS – joint attention, median [range] (IQR)	6 [0–18] (3–9)	8 [0–15] (6–11)
Mullen – visual raw score, median [range] (IQR)	26.5 [17–44] (24–29.5)	31 [22–48] (28–34)
> 2 SDs below standard norm, *t*-score	88%	96%
Mullen – fine motor raw score, median [range] (IQR)	27 [19–44] (25–28)	29 [19–46] (28–35.5)
> 2 SDs below standard norm, *t*-score	92%	96%
Module 2, *n* = 61	36	25
VEPS – social response, median [range] (IQR)	6 [0–12] (2–8)	3 [0–12] (1–8)
VEPS – joint attention, median [range] (IQR)	12 [0– 18] (7–15)	10 [0–18] (8–12)
Mullen – visual raw score, median [range] (IQR)	33 [21–50] (30.5–42)	33 [25–49] (30.5–43)
> 2 SDs below standard norm, *t*-score	56%	92%
Mullen – fine motor raw score, median [range] (IQR)	30 [23–44] (28–36)	33.5 [21–47] (29.5–39.5)
> 2 SDs below standard norm, *t*-score	67%	96%
All modules	151	97
VEPS – social response, median [range] (IQR)	1 [0– 12] (0–3)	2 [0– 12] (0–4.5)
VEPS – joint attention, median [range] (IQR)	6 [0– 18] (1–10)	6 [0– 18] (2–10)
Mullen – visual raw score, median [range] (IQR)	26 [16– 50] (23–31)	29 [16– 49] (25–32)
> 2 SDs below standard norm, *t*-score	84%	97%
Mullen – fine motor raw score, median [range] (IQR)	26 [15– 44] (22–28)	27 [15– 47] (23–32)
> 2 SDs below standard norm, *t*-score	89%	98%

IQR, interquartile range; Mullen, Mullen Scales of Early Learning.

TABLE 10 Baseline ADOS-2 CSS by age group[a]

ADOS-2 CSS baseline	Age group, *n* (%)	
	Preschool aged (*N* = 150)	School aged (*N* = 97)
6	48 (32)	35 (36)
7	53 (35)	26 (27)
8	23 (15)	27 (28)
9	13 (7)	6 (6)
10	13 (7)	3 (3)

a Data missing for two patients: one requested withdrawal of all data and one was outside the CSS algorithm mapping.

TABLE 11 The ADOS-2 data by stratum

	Time point, *n* (%)					
	Baseline			End point		
ADOS-2	TAU	PACT-G	Overall	TAU	PACT-G	Overall
Module 1 (non-verbal)	53 (42)	57 (47)	110 (44)	48 (41)	48 (40)	96 (41)
Module 1 (verbal)	42 (33)	35 (29)	77 (31)	40 (34)	42 (35)	82 (34)
Module 2	32 (25)	29 (24)	61 (25)	30 (25)	29 (24)	59 (25)

TABLE 12 Education provision of children at baseline

	Treatment group (*n*)					
	PACT-G			TAU		
Education setting	London	Manchester	Newcastle upon Tyne	London	Manchester	Newcastle upon Tyne
Mainstream nursery	20	13	12	26	11	11
Specialist nursery	0	3	0	0	1	1
Mainstream primary school	8	10	7	3	15	7
Mainstream school with SEN/autism resource class/base	4	0	0	2	1	1
Special school with mixed disabilities	1	10	12	3	12	17
Specialist autism school	8	3	10	7	12	5
Childminder	0	0	0	0	1	0

Intervention delivery

PACT-G implementation at home

In the PACT-G group, there was a median of 10 [interquartile range (IQR) 8–12; range 2–12] parent sessions per case out of 121 observations. Across the whole trial implementation, 64% of the home sessions were in person and 36% were by video conferencing. Of these sessions, 2% of the in-person sessions and 12% of the online video-conferencing sessions were judged as unacceptable by therapists in their logs, using the set criteria referred to above (see *Chapter 5*, *Session validity from therapist logs*). Of these unacceptable sessions, the majority of the online video-conferencing sessions were unacceptable because of the lack of ability to share a home-filmed video; the reasons for unacceptability in the in-person sessions were more varied (*Table 13*).

PACT-G implementation in educational settings

Professionals delivering PACT-G in educational settings

Initial discussion with each participating educational setting (pre randomisation) allowed them to identify the professional in the education structure who would be best to participate in the trial and deliver the PACT-G therapy as appropriate in their context. The nominated professionals are shown in *Table 14*. The majority of nominated staff across both groups of the trial were in a teaching assistant/LSA role (PACT-G group, $n = 92$; TAU group, $n = 92$). There was also a balance of early years assistants across both arms (PACT-G group, $n = 11$; TAU group, $n = 9$). Other nominated adults in educational settings had more senior roles, including teachers (PACT-G group G, $n = 7$; TAU group, $n = 10$), SEN co-ordinators (PACT-G group, $n = 3$; TAU group, $n = 9$) and nursery managers/deputies (PACT-G group, $n = 2$; TAU group, $n = 1$).

TABLE 13 Details of implemented session in home and educational settings

Session details	Home setting		Educational setting	
	In person	Video conference/ telephone	In person	Video conference/ telephone
Total sessions, *n* (%)	765 (64)	424 (36)	632 (66)	320 (34)
Acceptable sessions, *n* (%)	720 (94)	364 (86)	591 (94)	269 (85)
Reasons for session being unacceptable, %				
No targets set	18	0	17	6
It was not possible for the adult and therapist to watch a video of ACI	27	98	17	86
Child did not take part in ACI	17	0	24	0
Sibling interfered in ACI to the extent that it disrupted the session	17	0	0	0
No therapy feedback	21	0	10	8
Acceptable session deviations, *n* (%)	428 (57)	94 (22)	140 (22)	42 (13)
Additional person in during session, %	13	5	9	5
Technical difficulties experienced, %	2	38	18	46
Therapist and adult both watched video but not simultaneously, %	0	12	0	11
Sibling present during session, %	17	3	0	0
Feedback disrupted by child, %	44	17	16	7
ACI interrupted, %	3	0	7	0
Additional full face-to-face sessions instead of remote (i.e. greater dosage), %	2	0	6	0
Video-conferencing/telephone session carried out in person, %	2	7	5	22
Review carried out after ACI, %	2	0	9	0
Missing data because of technical difficulty (but session fully delivered), %	7	8	16	4
PACT approach required modification (e.g. teaching), %	6	9	5	4
ACI video short, %	2	2	10	0

ACI, adult–child interaction.

Change in education professional within therapy

Eighty-five (34.3%) children across the trial experienced a change in the education professional delivering PACT-G between baseline and the mid-point, and 94 (37.9%) children experienced a change in education professional between the mid-point and end point. Twenty-two (20%) children experienced changes at both time points. When this change occurred, the therapist began the PACT-G therapy again with the new education professional. For the purposes of assessing the adequacy of the delivery of the PACT-G therapy, a pragmatic assumption was made that a notional two sessions would be needed for the replacement education professional to achieve minimum familiarity with the method delivery of the therapy and to establish a consistent interaction with the child.

TABLE 14 Nominated adult role per educational setting type

	Treatment group (*n*)												
	PACT-G						TAU						
Adult role	Mainstream nursery	Specialist nursery	Mainstream primary school	Resourced provision within mainstream	Special school with mixed disabilities	Specialist autism school	Mainstream nursery	Specialist nursery	Mainstream primary school	Resourced provision within mainstream	Special school with mixed disabilities	Specialist autism school	Childminders
Teaching assistant/ LSA	27	3	24	1	20	17	27	1	18	2	31	13	
Teacher	3				3	1	5		4		1		
Special education needs co-ordinator	3						9						
Nursery manager/ deputy manager	2						1						
Inclusion manager							1						
Head of room	1												
Intervention co-ordinator				2						1			
Nursery/early years officer/ nurse/practitioner	9		1	1			5	1	3				
Speech and language therapist										1			
Outreach worker							1						
Childminder													1
Communication champion						3						1	

Therapy implementation in education

From 117 observations, a median of 8 (IQR 5–10; range 0–12) teacher sessions were undertaken during the trial. Of those in-educational setting sessions, 66% were in person and 34% were by online video conferencing; 1% of the in-person sessions and 11% of the online video-conferencing sessions were judged as unacceptable by therapists in their logs using the set criteria referred to above (see *Chapter 5*, *Session validity from therapist logs*). Reasons for unacceptability showed a similar profile to the home-based sessions as above: the main cause of unacceptability in the online video-conferencing educational-setting sessions was a lack of available video-sharing. Acceptable deviations for educational-setting sessions were noted in 22% of in-person and 13% of video-conferencing sessions, with a similar profile across both in-person and online video-conferencing sessions (see *Table 13*).

Implementation by stages of PACT-G therapy across home and educational settings

As noted in *Chapter 5*, *Interventions*, the PACT therapy proceeds on the basis of manualised sequential stages. All dyads begin at stage 1; the progression that they make depends on child characteristics such as cognitive ability, developmental level and autism severity, as well as the characteristics, progress and adaptations of their carer or LSA as the therapy progresses. Not all dyads are expected to achieve stage 6. As the home and education implementations of PACT-G were separate but involved the same child as the interactive dyadic partner, it is possible to compare the stage progress made for an individual child in each context. *Table 15* shows the proportion of children reaching each stage at home and in the educational setting, or at a group level. Although the median stage reached by both parents and LSAs was the same, namely stage 3, a mixed ordinal logistic regression (not prespecified) suggested that parents attained a significantly higher stage than the LSAs ($p = 0.014$).

Intervention manual fidelity

In-person sessions

Ten therapists delivered a total of 1397 in-person intervention sessions during the trial. Fidelity checks were carried out at three time points across the trial: 6, 12 and 18 months from the beginning of the main trial phase. This was to make sure that fidelity was maintained and did not drift during the trial. At each time point, one education session and one in-home session per active therapist was randomly selected to give a representative picture. Of the 45 sessions selected, two could not be rated because of technical difficulties and COVID-19 restrictions, giving 43 sessions (21 in home settings and 22 in educational settings), representing 3.1% of the total in-person sessions delivered in the trial (2.7% in home settings and 3.5% in educational settings). Scores could range from 0 to 16, with a score of 13 (representing > 80% items passed) set as the minimum fidelity threshold. The mean fidelity across all rated sessions was 14.67 (median 15, range 10–16), with the fidelity threshold being met for 37 (86%) sessions and not met for 6 (14%) sessions (*Figure 6*).

TABLE 15 Stage reached in PACT-G implementation

	Children reaching each stage, *n* (%)	
End-point stage	Parents	LSAs
1	12 (10)	24 (20)
2	29 (24)	27 (22)
3	44 (36)	42 (34)
4	17 (14)	15 (12)
5	15 (12)	9 (7)
6	4 (3)	4 (3)
Total	121	121

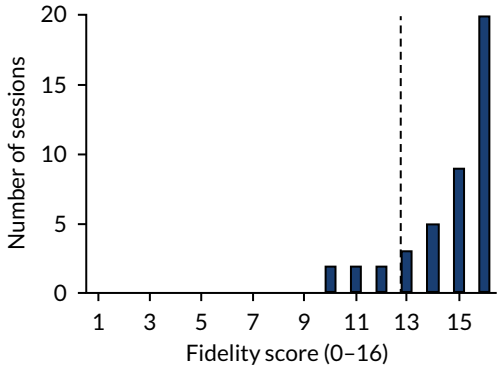

FIGURE 6 Distribution of fidelity ratings ($n = 43$; score > 13 represents acceptable fidelity).

Within the overall total, 17 out of 21 (81%) in-home sessions reached an acceptable mean fidelity score of 14.3 (median 15, range 10–16) and 20 out of 22 (91%) education sessions reached an acceptable mean fidelity score of 14.95 (median 16, range 10–16). *Table 16* shows that this did not vary substantially by therapist.

Remote sessions (video conferencing or telephone)

Informal fidelity monitoring of a small number ($n = 11$; 2%) of the remote sessions indicated that, where parents and LSAs had supplied suitable interactive play videos and there were no technical difficulties, the sessions could be of similar quality to face-to-face sessions. However, given the small sample, we can make no inference as to the overall quality of remote session delivery in this trial.

Home–school conversations

The HSC meetings were arranged between a therapist, parent and LSA to facilitate the generalisation of skills across the home and educational settings. HSC meetings were structured around 'explore', 'focus', 'plan' and 'review' stages, which allowed the LSA and parent to discuss strategies and techniques that worked well in different settings. The trial had planned up to six HSC sessions per case, with the minimum acceptable number set at three per child. These were to be arranged between the parent and LSA, with the therapist in attendance when possible, particularly for the early sessions.

TABLE 16 Fidelity ratings by therapist

Therapist	Mean fidelity (range; median)
1	14.3 (10–16; 15)
2	15.5 (14–16; 16)
3	15.25 (13–16; 16)
4	14.67 (12–16; 15)
5	13.8 (11–15; 15)
6	15 (14–16; 15)
7	15.75 (15–16; 16)
8	13.6 (10–16; 14)
9	14.5 (13–16; 14.5)
10	15.5 (15–16; 15.5)

In the trial period, 281 HSCs were recorded for 125 participants, with an average of 2.2 HSCs per participant. The numbers varied by trial site: London completed 120 HSCs for 42 participants, with an average of 2.9 HSCs per participant; Newcastle upon Tyne completed 42 HSCs for 43 participants, with an average of 1.0 HSC per participant; and Manchester completed 119 HSCs for 40 participants, with an average of 3.0 HSCs per participant.

We have anecdotal information from trial therapists as to the difficulties in arranging HSCs that led to an average below the acceptable minimum planned. Problems included (1) the practical difficulties of organising the sessions in addition to the treatment within school curriculum time, (2) HSCs required further time out of class for the LSAs and (3) the difficulties encountered arranging mutually convenient times between the LSA, the parent and, when necessary, the therapist. The lack of time available for HSCs within the educational setting in the main trial seemed at variance with the results from the feasibility pilot and PPI feedback (see *Chapters 4* and *6*).

Treatment as usual

Home-based therapy

Parent reports of non-PACT-G treatment received across both trial arms in home and clinic settings during the 12-month trial is shown in *Table 17*. Home-based therapy consisted of a programme of at least four home-based sessions that were delivered directly to the child in the home [either by the parent or trained therapist, e.g. applied behaviour analysis (ABA)]. Speech and language therapy provision was recorded for a programme of therapy (i.e. more than general advice-giving) and was administered either directly to the child or with the parent in the home or clinic setting.

TABLE 17 Number of families receiving non-PACT-G treatments during the 12-month trial based on parental report

	Treatment group	
Treatment type	**PACT-G (*N* = 118)**	**TAU (*N* = 117)**
Home-based therapy (at least four sessions)		
ABA	10	10
Number of sessions, mean (range)	65 (5–236)	89 (15–226)
Duration of sessions (minutes), mean (range)	135 (120–300)	153 (45–240)
CAMHS behaviour management	1	0
Number of sessions	6	0
Duration of sessions (minutes)	45	0
Listening therapy[a]	1	0
Number of sessions	500	0
Duration of sessions (minutes)	15	0
Intensive interaction	1	0
Number of sessions	12	0
Duration of sessions (minutes)	240	0
Speech and language provision in home or clinic settings		
PECS	1	5
Number of sessions	3	6 (range 1–12)
Duration of sessions (minutes)	45	47 (range 30–60)
Hanen	0	1
Number of sessions	0	8
Duration of sessions (minutes)	0	150

TABLE 17 Number of families receiving non-PACT-G treatments during the 12-month trial based on parental report (*continued*)

Treatment type	Treatment group	
	PACT-G (*N* = 118)	TAU (*N* = 117)
EIBI/verbal behaviour	1	1
Number of sessions	12	60
Duration of sessions (minutes)	360	3
Colourful semantics	1	0
Number of sessions	2	0
Duration of sessions (minutes)	40	0
Unnamed or eclectic therapy package	30	28
Number of sessions, mean (range)	10 (1–50)	12 (2–40)
Duration of sessions (minutes), mean (range)	50 (15–90)	58 (30–120)
Video feedback involved[b]	1	6
Autism-related parent training courses		
Generic autism awareness/post-diagnostic course	30	34
Number of sessions, mean (range)	6 (1–12)	6 (1–20)
Duration of sessions (minutes), mean (range)	144 (60–180)	134 (60–240)
Communication/interaction	6	11
Number of sessions, mean (range)	2.5 (1–8)	7 (1–12)
Duration of sessions (minutes), mean (range)	170 (60–420)	153 (90–300)
Alternative and augmentative systems (e.g. Makaton)	2	5
Number of sessions, mean	1	3 (range 1–8)
Duration of sessions (minutes), mean (range)	105 (90–120)	126 (60–180)
Behaviour/sensory processing/emotion regulation	5	2
Number of sessions, mean (range)	2.8 (1–8)	7 (1–12)
Duration of sessions (minutes), mean	174 (range 120–240)	180
Non-specific/other parent training	8	5
Number of sessions, mean (range)	4.75 (1–10)	3 (1–7)
Duration of sessions (minutes), mean (range)	197 (120–480)	135 (120–180)

ABA, applied behaviour analysis; CAMHS, Child and Adolescent Mental Health Services; EIBI, early intensive behavioural intervention.

a This therapy consisted of the child listening to electronically modified sounds through headphones at various points of the day at home (e.g. pre and post school).

b This information was collected because of the similarities with and relevance to the video-feedback elements of the PACT-G intervention. Parents typically reported attending group-based programmes that were generic in nature, and that video interactions were a 'one-off' or used as a pre–post record of progress. There was one family from London (in the PACT-G group) who reported that they had received PACT therapy.

Child's educational setting

Non-PACT-G treatments received in educational settings across both trial groups during the trial reported by the child's class teacher are shown in *Table 18*. These treatments were delivered by either professionals external to the education context or staff within the setting. General advice from professionals (e.g. speech and language therapists) or post-assessment feedback sessions were not counted as treatment sessions. The majority of treatment delivered in both arms was an unnamed or eclectic therapy package (PACT-G group, $n = 36$; TAU group, $n = 50$). The interventions characterised here, on the whole, were 'discrete' rather than 'comprehensive'; that is, these were bespoke, pragmatic interventions developed as solutions in the naturalistic context of school using the resources available in the setting, rather than a selected intervention 'package'. Some interventions in this category employed the use of video feedback (PACT-G group, $n = 4$; TAU group, $n = 4$).

TABLE 18 Number of children receiving non-PACT-G treatments in educational settings reported by the class teacher

Treatment type	Treatment group	
	PACT-G ($n = 118$)	TAU ($n = 117$)
SCERTS	1	0
Colourful semantics	3	4
Music therapy	1	1
LEGO® (LEGO System A/S, Billund, Denmark) therapy	2	1
Intensive interaction	3	4
ABA/EIBI/verbal behaviour	0	2
PECS	12	4
Visual supports/TEACCH	1	3
Makaton/sign language	2	0
Unnamed or eclectic therapy package	36	50
Video feedback involved	4	4

EIBI, early intensive behavioural intervention.

Use of PECS was reported more frequently in the PACT-G group ($n = 12$) than in the TAU group ($n = 4$). There may be under-reporting of the use of PECS as an intervention because specialist school settings use PECS and similar communication systems as an integrated system in the classroom. Thus, it is not necessarily viewed as an intervention per se, but more as a mode of communication in the classroom. Other interventions reported in education contexts were colourful semantics (PACT-G group, $n = 3$; TAU group, $n = 4$), intensive interaction (PACT-G group, $n = 3$; TAU group, $n = 4$), ABA, (PACT-G group, $n = 0$; TAU group, $n = 2$), visual supports/TEACCH (PACT-G group, $n = 1$; TAU group, $n = 3$), Makaton (PACT-G group, $n = 2$; TAU group, $n = 0$), LEGO therapy (PACT-G group, $n = 2$; TAU group, $n = 1$) and music therapy (PACT-G group, $n = 1$; TAU group, $n = 1$). One child in the PACT-G group was also reported to be receiving SCERTS. SCERTS and TEACCH are fully integrated approaches to supporting autistic children in their development and education. However, for the purposes of reporting, these have been included as the strategies and principles used specifically in allocated intervention sessions with the child.

Treatment as usual across trial arms

Analysis of non-PACT-G treatment received during the treatment period indicates that home-based therapy programmes were similar across the two trial arms. Ten parents reported home-based intensive ABA; however, the TAU group reported an average of 24 more sessions (PACT-G group, mean 65 sessions; TAU group, mean 89 sessions), with an average duration 18 minutes longer than the PACT-G group (PACT-G group, mean 135 minutes; TAU group, mean 153 minutes). All other types of home-based therapy programmes were received by participants in the PACT-G group, which included intensive interaction ($n = 1$), listening therapy ($n = 1$) and a Child and Adolescent Mental Health Services (CAMHS) behaviour management programme ($n = 1$).

Speech and language provision in the home and other settings was less well defined, with the majority of parents reporting that they accessed an 'unnamed or eclectic' programme of therapy (PACT-G group, $n = 30$; TAU group, $n = 28$). The delivery of speech and language interventions in this category was varied, with some parents reporting that they attended a clinic or the therapist came to their home to provide bespoke strategies that they could use with their child. These intervention sessions also varied between direct implementation of strategies with the child or giving parents strategies to use with their child; in-clinic sessions varied between individual and group sessions for children.

Other named interventions accessed were, on balance, equivalent across arms and included Hanen (PACT-G group, $n = 0$; TAU group, $n = 1$), ABA/early intensive behavioural intervention (EIBI)/verbal

behaviour (PACT-G group, pivotal response therapy, $n = 1$; TAU group, ABA, $n = 1$) and colourful semantics (PACT-G group, $n = 1$). More parents in the TAU group than the PACT-G group accessed PECS sessions, although this number was small overall (PACT-G group, $n = 1$; TAU group, $n = 5$). Autism parent training courses (independent of group deliverer profession) were also similar across trial arms, for example group-based autism post-diagnostic psychoeducation (PACT-G group, 25%; TAU group, 27%) and communication and interaction-focused training (PACT-G group, 5%; TAU group, 9%).

Assessing quality of outcome measures

ADOS-2

A random sample of 24 ADOS-2 videos was sampled to assess coding reliability (16 module 1 and 8 module 2 videos), including a proportionate balance of preschool- and school-aged children. These were triple-coded blind to treatment allocation (i.e. by all three RAs). The intraclass correlations (ICCs) were 0.80 (95% CI 0.61 to 0.91) for module 1, 0.70 (95% CI 0.38 to 0.90) for module 2 and 0.78 (95% CI 0.62 to 0.88) overall.

DCMA

All coders, in varied pairings, contributed to this process, with the double-coding being stratified in proportion to the number of videos raters had been allocated for primary coding. The ICCs were 0.75 (95% CI 0.53 to 0.89) for parent proportions and 0.78 (95% CI 0.57 to 0.90) for child proportions.

Outcome estimation

Table 19 shows the baseline and end-point ADOS-2 total scores for the participants by treatment group. In both the TAU and PACT-G groups, changes in ADOS-2 scores within module 1 (non-verbal) and module 2 (older) were small; there was modest improvement (i.e. decline in scores) in module 1 (verbal) and more marked improvement in module 2 (young). The pattern was similar across both the SA and RRB subscales. Outcome estimation by trial group is reported below.

The language and communication scores from *Table 20* show that, at baseline, > 40% of the sample were at the basal level of the receptive one-word test and almost 50% were at the basal level of the expressive one-word test, with these percentages decreasing by around 8% at the end point in each case. Improvement was also seen in the MCDI measure at the end point. In other secondary outcomes (*Table 21*), except for education reported VABS composite, all cells show changes in the expected direction.

The researcher BOSCCs were collected at baseline and the end point, whereas the BOSCC/DCMAs with the parent and with the LSA were collected at baseline, the 7-month mid-point and the end point.

TABLE 19 Clinical symptom measures

	Baseline			End point		
Scale	TAU	PACT-G	Overall	TAU	PACT-G	Overall
ADOS-2 total score, *n*	127	121	248	118	119	237
Module 1 (non-verbal), mean (SD)	21.4 (2.9)	20.9 (2.5)	21.2 (2.7)	20.9 (3.2)	20.4 (3.4)	20.6 (3.3)
Module 1 (verbal), mean (SD)	17.6 (3.1)	17.3 (2.6)	17.5 (2.9)	16.8 (4.6)	16.0 (4.2)	16.3 (4.4)
Module 2 (young), mean (SD)	15.2 (2.8)	15.5 (4.0)	15.3 (3.4)	11.5 (4.3)	13.7 (3.6)	12.6 (4.1)
Module 2 (old), mean (SD)	15.0 (4.4)	17.7 (3.5)	16.3 (4.1)	15.5 (3.2)	17.3 (3.5)	16.4 (3.4)
ADOS-2 total score, mean (SD)	18.6 (4.0)	18.8 (3.6)	18.7 (3.8)	17.5 (5.0)	17.6 (4.5)	17.6 (4.8)
ADOS-2 SA, mean (SD)						
Module 1 (non-verbal)	16.4 (2.7)	16.1 (2.1)	16.3 (2.4)	16.4 (2.5)	15.7 (2.5)	16.0 (2.5)
Module 1 (verbal)	13.9 (2.6)	13.3 (2.5)	13.7 (2.5)	12.8 (3.7)	12.6 (3.2)	12.7 (3.4)

continued

TABLE 19 Clinical symptom measures (*continued*)

Scale	Baseline			End point		
	TAU	PACT-G	Overall	TAU	PACT-G	Overall
Module 2 (young)	12.4 (3.0)	12.1 (2.9)	12.3 (2.9)	10.1 (4.2)	11.3 (3.1)	10.7 (3.7)
Module 2 (old)	11.8 (3.5)	13.8 (2.5)	12.8 (3.2)	11.8 (2.8)	13.7 (2.6)	12.7 (2.8)
ADOS-2 SA total score	14.5 (3.3)	14.5 (2.8)	14.5 (3.1)	13.8 (4.0)	13.8 (3.3)	13.8 (3.6)
ADOS-2 RRB, mean (SD)						
Module 1 (non-verbal)	5.0 (1.5)	4.8 (1.6)	4.9 (1.6)	4.5 (1.6)	4.8 (1.5)	4.6 (1.6)
Module 1 (verbal)	3.7 (1.5)	3.9 (1.5)	3.8 (1.5)	3.9 (1.8)	3.3 (1.7)	3.6 (1.8)
Module 2 (young)	2.8 (1.2)	3.4 (1.4)	3.1 (1.3)	1.4 (0.9)	2.4 (1.5)	1.9 (1.3)
Module 2 (old)	3.2 (1.7)	3.9 (1.4)	3.5 (1.6)	3.8 (1.6)	3.7 (1.9)	3.7 (1.7)
ADOS-2 RRB total score	4.1 (1.7)	4.3 (1.6)	4.2 (1.7)	3.8 (1.9)	3.8 (1.8)	3.8 (1.9)
RBQ, *n*	119	115	234	100	105	205
RBQ – sensory motor, mean (SD)	10.9 (5.3)	9.4 (4.7)	10.1 (5.1)	10.2 (5.4)	9.1 (5.3)	9.6 (5.4)
RBQ – insistence on sameness, mean (SD)	8.6 (6.4)	8.3 (5.9)	8.5 (6.1)	8.6 (6.2)	7.8 (5.6)	8.2 (5.9)
SCQ, *n*	127	121	248	–	–	–
SCQ total score, mean (SD)	23.4 (5.2)	23.6 (5.4)	23.5 (5.3)	–	–	–

TABLE 20 Language and communication scales

Scale	Baseline			End point		
	TAU	PACT-G	Overall	TAU	PACT-G	Overall
Language scores, *n*	127	120	247	118	116	234
Receptive one word, *n* at basal level	57	46	103	42	39	81
Receptive one word (raw score), mean (SD)	29.4 (22.5)	32.1 (19.3)	30.8 (20.9)	42.2 (21.9)	43.2 (20.0)	42.7 (20.9)
Expressive one word, *n* at basal level	62	58	120	52	49	101
Expressive one word (raw score), mean (SD)	28.2 (19.2)	32.0 (12.9)	30.1 (16.4)	42.0 (21.7)	42.5 (18.5)	42.2 (20.1)
MCDI, *n*	120	119	239	101	107	208
MCDI words understood, mean (SD)	202.4 (128.4)	213.4 (134.7)	207.9 (131.4)	260.6 (130.6)	264.8 (121.9)	262.8 (125.9)
MCDI words understood and said, mean (SD)	139.1 (141.5)	152.1 (144.3)	145.6 (142.8)	188.7 (156.1)	175.7 (159.3)	182.0 (157.5)
VEPS, *n*	124	116	240	–	–	–
VEPS social response, mean (SD)	2.6 (3.4)	2.7 (3.2)	2.7 (3.3)	–	–	–
VEPS joint attention, mean (SD)	6.3 (5.4)	6.1 (5.2)	6.2 (5.3)	–	–	–
VEPS – symbolic total, mean (SD)	4.1 (5.0)	3.8 (4.2)	3.9 (4.6)	–	–	–

TABLE 21 Non-verbal ability, adaptive functioning and behaviour

Scale	Baseline			End point		
	TAU	PACT-G	Overall	TAU	PACT-G	Overall
Non-verbal IQ						
Non-verbal IQ, *n*	127	121	248			
Mullen – visual standard *t*-score, mean (SD)	25.2 (11.7)	22.9 (8.0)	24.1 (10.1)			
Mullen – visual raw score, mean (SD)	28.3 (7.8)	28.5 (7.0)	28.4 (7.4)			
Mullen – fine motor standard *t*-score, mean (SD)	22.8 (8.6)	21.8 (7.3)	22.3 (8.0)			
Mullen – fine motor raw score, mean (SD)	26.3 (6.9)	27.2 (6.5)	26.7 (6.7)			
SNC – standard score, mean (SD)		55.0 (15.6)	55.0 (15.6)			
VABS composite standard score						
VABS – parent, *n*	127	120	247	111	117	228
VABS – parent, mean (SD)	62.2 (10.3)	61.6 (8.9)	61.9 (9.6)	63.9 (12.8)	62.7 (11.5)	63.3 (12.2)
VABS – teacher, *n*	117	110	227	103	105	208
VABS – teacher, mean (SD)	58.9 (15.7)	57.4 (14.1)	58.2 (14.9)	58.1 (16.5)	58.9 (16.5)	58.5 (16.5)
Child Health Utility, *n*	116	114	230	103	104	207
Child Health Utility, mean (SD)	17.4 (5.4)	16.7 (5.3)	17.0 (5.3)	16.4 (5.3)	15.5 (4.6)	15.9 (5.0)
Strength and Difficulties total score						
SDQ – teacher, *n*	123	113	236	104	105	209
SDQ – teacher, mean (SD)	17.4 (4.5)	17.7 (4.8)	17.5 (4.6)	17.2 (5.1)	16.2 (4.7)	16.7 (4.9)
SDQ – parent, *n*	118	118	236	102	107	209
SDQ – parent, mean (SD)	19.1 (4.4)	18.3 (4.6)	18.7 (4.5)	18.5 (5.3)	17.2 (5.1)	17.8 (5.2)
WEMWBS, *n*	117	117	234	103	104	207
WEMWBS – total, mean (SD)	49.6 (9.0)	48.9 (9.9)	49.2 (9.5)	48.8 (9.5)	50.6 (9.9)	49.7 (9.7)
TOPSE, *n*	120	113	233	99	106	205
TOPSE, mean (SD)	368.7 (57.2)	368.5 (53.5)	368.6 (55.3)	370.5 (55.5)	379.8 (53.1)	375.3 (54.3)

Mullen, Mullen Scales of Early Learning; SNC, special non-verbal composite.

All cells in *Table 22* show changes in the expected direction for the BOSCC. On average, the mid-point assessments were completed 7.3 months after randomisation, with a range of 4.7–10.9 months. End-point assessments were completed, on average, 12.2 months after randomisation, with a range of 10.5–15.6 months. Changes in the DCMA were small for the TAU group, but for the PACT-G group there was some improvement for LSAs, and more marked improvement for parents, by the mid-point, with some loss of the gains by the end point.

Primary outcome analysis

Univariate logistic regression was used to detect if any further baseline variables were predictive of missing primary outcome data. No baseline variables were seen to predict missingness beyond those that would already be included in the model (stratifiers and baseline measures of the scale), so no others were included.

TABLE 22 The BOSCC and DCMA interaction-based assessment

	Baseline			Mid-point			End point		
Assessment	TAU	PACT-G	Overall	TAU	PACT-G	Overall	TAU	PACT-G	Overall
BOSCC									
Researcher, *n*	124	114	238				118	115	233
Researcher, mean (SD)	39.9 (9.3)	40.0 (8.3)	40.0 (8.8)				37.0 (10.9)	37.0 (11.2)	37.0 (11.0)
LSA, *n*	119	118	237	114	111	225	111	112	223
LSA, mean (SD)	37.8 (9.8)	38.7 (10.0)	38.2 (9.9)	35.2 (10.1)	36.8 (11.0)	36.0 (10.6)	35.1 (11.5)	36.4 (11.6)	35.7 (11.5)
Parent, *n*	124	112	236	109	112	221	112	115	227
Parent, mean (SD)	36.1 (9.4)	36.7 (8.7)	36.4 (9.1)	33.5 (10.1)	34.9 (10.6)	34.2 (10.4)	33.7 (9.8)	34.4 (11.3)	34.0 (10.6)
DCMA: LSA									
LSA, *n*	125	119	244	109	113	222	110	114	224
LSA synchronous response, mean (SD)	0.32 (0.14)	0.31 (0.13)	0.31 (0.13)	0.34 (0.12)	0.46 (0.18)	0.40 (0.16)	0.32 (0.12)	0.44 (0.17)	0.38 (0.16)
Child, *n*	125	118	243	109	112	221	109	113	222
Child initiations, mean (SD)	0.26 (0.17)	0.24 (0.19)	0.25 (0.18)	0.24 (0.18)	0.32 (0.22)	0.28 (0.20)	0.25 (0.18)	0.32 (0.21)	0.29 (0.20)
DCMA: parent									
Parent, *n*	124	121	245	115	112	227	115	115	230
Parent synchronous response, mean (SD)	0.35 (0.11)	0.33 (0.13)	0.34 (0.12)	0.37 (0.14)	0.47 (0.18)	0.42 (0.17)	0.36 (0.13)	0.43 (0.18)	0.40 (0.16)
Child, *n*	124	121	245	114	110	224	113	115	228
Child initiations, mean (SD)	0.29 (0.21)	0.26 (0.20)	0.28 (0.20)	0.25 (0.21)	0.36 (0.25)	0.30 (0.24)	0.24 (0.20)	0.29 (0.22)	0.27 (0.21)

The end-point ADOS-2 algorithm score was treated as a continuous variable, with the baseline score as a covariate and randomisation factors included. Three regression relationships were estimated, one for each of the strata defined by the ADOS-2 module [module 1 (non-verbal), module 1 (verbal), module 2] at the end point (*Table 23*). Regression residual plots were checked within each strata. These showed no evidence of non-normality (see *Appendix 1*). A single estimate of the treatment effect was obtained by pooling the three stratum-specific ES estimates using the minimum variance estimator. As shown in *Table 19*, the ITT analysis did not detect an effect of the intervention on the primary outcome of ADOS-2 at the end point. To be consistent with the treatment main effects analysis, the test of difference in treatment effect by age group was based on the bootstrap *p*-value of > 5000 replicates of the pooled within-ADOS-2 stratum estimate of the treatment difference.

We mapped the change in the ADOS-2 algorithm scores to the CSS, which allows comparison across ADOS-2 modules. Shown in *Figure 7*, there was little difference between the distributions expected for the study participants undergoing PACT-G treatment and those undergoing TAU, with expected rates in the non-autism 1–3 range of 2.6% and 2.5%, in the autism 4–5 range of 7.3% and 6.9%, in the autism 6–8 range of 78.3% and 75.5%, and in the high-severity cut-off range of 11.8% and 15.1%, respectively.

TABLE 23 Autism Diagnostic Observation Schedule-2 treatment effects by module

ADOS-2	Unstandardised effect	Standard error	Standardised effect (95% CI)
Module 1 (non-verbal), $n = 96$	−0.45	0.59	−0.13 (−0.48 to 0.21)
Module 1 (verbal), $n = 82$	−1.18	0.81	−0.27 (−0.63 to 0.09)
Module 2, $n = 59$	1.48	0.83	0.36 (−0.04 to 0.75)

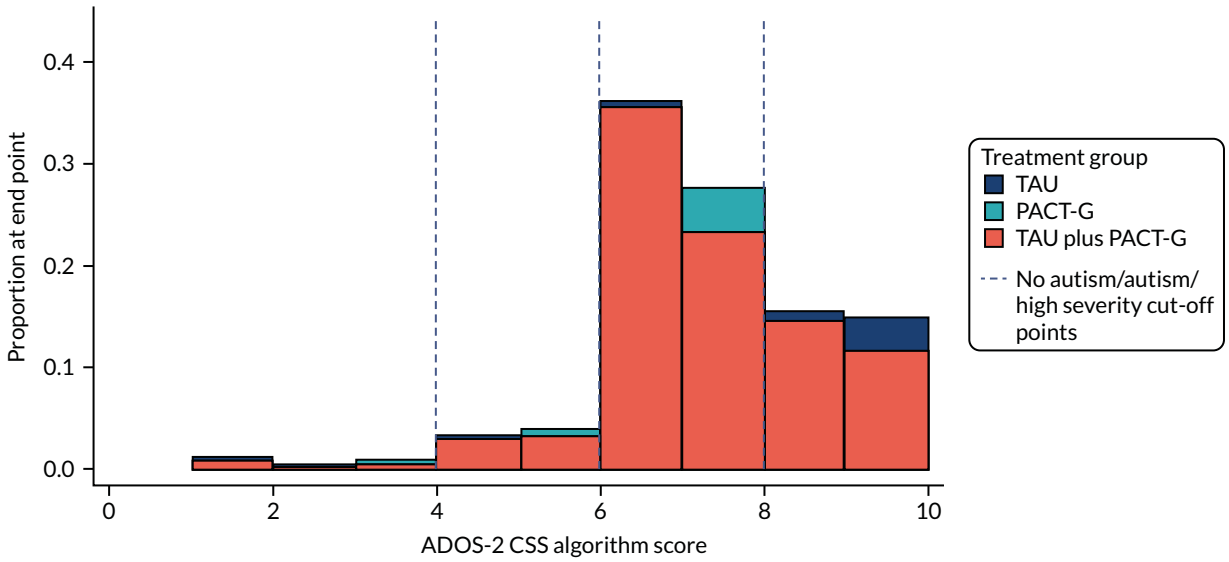

FIGURE 7 Distributions of CSS outcome. Plotted by treatment group at the end point for all participants, as implied by the estimated effect on the ADOS-2 algorithm total score (the mapping of scores was carried out using Stata's multiple imputation command using nearest neighbour matching of predicted scores and the published 18-stratum total score to the CSS algorithm).

Primary outcome complier-average causal effect estimator

In the PACT-G group, out of 121 observations, there was a median of 10 (IQR 8–12) acceptable parent sessions, with an IQR of 2–12 and, from 117 observations, a median of 8 (IQR 5–10) acceptable LSA sessions, with an IQR of 0–12. An instrumental variable estimator of a CACE was calculated. Treatment receipt was measured as the number of acceptable sessions with a parent and LSA. We report the estimated effect of receiving a total of eight sessions across home or educational settings (the TAU group being considered as receiving no sessions), which was the minimum number of sessions therapists and the research team took to constitute a delivered treatment. The across-strata, pooled CACE estimate for a dose of eight sessions was non-significant (–0.02; $p = 0.755$). To reach the minimum clinically significant change of 0.28, 112 sessions would be required.

Secondary outcomes

Table 24 shows the effect estimates for all secondary measures and composites.

Significant changes are seen on the parent and LSA DCMA measures, which are the proximal target behavioural mediators of the therapy (*Table 22*). Similarly, the child initiations, as measured using the DCMA with both parents and LSAs, also show significant effects. The BOSCC measure, an observational measure of autism-specific behaviours, showed no significant change in any of the three settings of interaction with a parent, LSA and researcher. Parent-reported measures of language, anxiety, repetitive and adaptive behaviour, and an overall measure of child health-related quality of life showed no effect. There was significant improvement in parent- and teacher-reported child disruptive behaviour and parental well-being (*Table 25*).

TABLE 24 Effect estimates

Outcome	Estimated treatment effect	95% CI	*p*-value
Primary outcome			
ADOS-2	–0.04	–0.26 to 0.18	0.734
Secondary outcomes			
BOSCC – parent	0.01	–0.19 to 0.21	0.889
BOSCC – teacher	–0.001	–0.18 to 0.18	0.991
BOSCC – researcher	–0.03	–0.31 to 0.25	0.850
DCMA – parent synchrony	0.54	0.39 to 0.69	< 0.001
DCMA – LSA synchrony	0.32	0.14 to 0.49	< 0.001
DCMA – child initiations with a parent	0.27	0.12 to 0.41	< 0.001
DCMA – child initiations with a LSA	0.21	0.06 to 0.36	0.005
Language composite	–0.03	–0.15 to 0.10	0.671
Anxiety composite	–0.01	–0.54 to 0.52	0.978
Repetitive behaviour composite	0.001	–0.35 to 0.35	0.997
Adaptive behaviour composite	0.01	–0.15 to 0.18	0.651
Parent well-being composite	0.44	0.08 to 0.79	0.016
CHU9D	–0.09	–0.34 to 0.15	0.450
Disruptive behaviour composite	–0.29	–0.57 to –0.01	0.046

TABLE 24 Effect estimates (*continued*)

Outcome	Estimated treatment effect	95% CI	*p*-value
ADOS-2 split by age group			
Preschool aged	−0.11	−0.45 to 0.23	0.524
School aged	0.08	−0.27 to 0.43	0.667
Difference[a]	−0.19	−0.67 to 0.30	0.447

a The test of difference in treatment effect by age group was based on the bootstrap *p*-value over 5000 replicates of the pooled, within-ADOS-2 stratum estimate of the treatment difference.

TABLE 25 Secondary outcome composites

	Baseline			End point		
Outcome	TAU	PACT-G	Overall	TAU	PACT-G	Overall
Language composite *MCDI, mean (SD)*						
Words understood	202.4 (128.4)	213.4 (134.7)	207.9 (131.4)	260.6 (130.6)	264.8 (121.9)	262.8 (125.9)
Words understood and said	139.1 (141.5)	152.1 (144.3)	145.6 (142.8)	188.7 (156.1)	175.7 (159.3)	182.0 (157.5)
Language scores						
Receptive one word, *n* at basal	57	46	103	42	39	81
Receptive one word, mean (SD)	29.4 (22.5)	32.1 (19.3)	30.8 (20.9)	42.2 (21.9)	43.2 (20.0)	42.7 (20.9)
Expressive one word, *n* at basal	62	58	120	52	49	101
Expressive one word, mean (SD)	28.2 (19.2)	32.0 (12.9)	30.1 (16.4)	42.0 (21.7)	42.5 (18.5)	42.2 (20.1)
PLS						
Receptive, mean (SD)				59.5 (18.9)	57.7 (13.7)	58.7 (16.6)
Expressive, mean (SD)				59.3 (20.0)	57.5 (14.9)	58.4 (17.7)
Anxiety composite, mean (SD) *SDQ*						
Teacher emotional	2.1 (1.9)	2.2 (2.1)	2.1 (2.0)	2.5 (1.9)	2.2 (1.9)	2.3 (1.9)
Parent emotional	3.1 (2.1)	2.5 (2.2)	2.8 (2.2)	3.0 (2.2)	2.6 (2.1)	2.8 (2.1)
DBC						
Anxiety subscale				5.3 (4.1)	6.2 (4.1)	5.7 (4.1)
Repetitive behaviour composite, mean (SD) *SCQ*						
Parent repetitive	6.5 (1.8)	6.4 (1.7)	6.5 (1.7)			
RBQ						
Insistence on sameness	8.6 (6.4)	8.3 (5.9)	8.5 (6.1)	8.6 (6.2)	7.8 (5.6)	8.2 (5.9)
Sensory motor	10.9 (5.3)	9.4 (4.7)	10.1 (5.1)	10.2 (5.4)	9.1 (5.3)	9.6 (5.4)

continued

TABLE 25 Secondary outcome composites (*continued*)

Outcome	Baseline			End point		
	TAU	PACT-G	Overall	TAU	PACT-G	Overall
Adaptive behaviour composite, mean (SD)						
SDQ						
Teacher prosocial	1.6 (1.9)	1.8 (2.0)	1.7 (1.9)	2.2 (2.5)	2.5 (2.3)	2.3 (2.4)
Parent prosocial	2.4 (2.1)	2.6 (2.2)	2.5 (2.1)	3.2 (2.4)	3.5 (2.3)	3.4 (2.4)
VABS						
Parent	62.2 (10.3)	61.6 (8.9)	61.9 (9.6)	63.9 (12.8)	62.7 (11.5)	63.3 (12.2)
Teacher	58.9 (15.7)	57.4 (14.1)	58.2 (14.9)	58.1 (16.5)	58.9 (16.5)	58.5 (16.5)
Parent well-being, mean (SD)						
WEMWBS total	49.6 (9.0)	48.9 (9.9)	49.2 (9.5)	48.8 (9.5)	50.6 (9.9)	49.7 (9.7)
TOPSE	368.7 (57.2)	368.5 (53.5)	368.6 (55.3)	370.5 (55.5)	379.8 (53.1)	375.3 (54.3)
Child health-related quality of life, mean (SD)						
CHU9D	17.4 (5.4)	16.7 (5.3)	17.0 (5.3)	16.4 (5.3)	15.5 (4.6)	15.9 (5.0)
Disruptive behaviour composite, mean (SD)						
DBC						
Disruptive				12.9 (9.8)	14.7 (9.2)	13.8 (9.5)
SDQ						
Disruptive subscale	2.9 (1.5)	2.8 (1.9)	2.9 (1.7)	3.0 (1.7)	2.4 (1.5)	2.7 (1.7)

Overall outcomes

Figure 8 shows the pattern of treatment effect across all planned outcomes, with directions of effects signed with beneficial effects on the right-hand side of the null.

Adverse events

Table 26 shows AEs collated by treatment group. There were 46 AEs, with six of these classified as serious. Seven events were possibly related to the study, and these were balanced across treatment arms. One serious AE was deemed possibly related to the study: an impact on a parent's mental health because of the autism diagnostic process and collaborative nature of therapy received.

Mechanism study

In this planned analysis of treatment effect mechanism, we examined several putative mechanisms between randomisation and outcomes in a series of mediation analyses. As in the primary outcome analysis, estimates are made for each ADOS-2 or BOSCC module, which are then combined into a total score using an inverse variance-weighted estimator. The findings are presented with no adjustment for measurement error in the mediator, and the results are displayed as unstandardised effect estimates.

For each analysis, the results show the estimated effect of treatment on the mediator, the estimated effect of the mediator on the outcome, the estimated indirect effect (the product of the preceding two estimates), the direct effect that represents any other pathway from treatment to outcome that does not act through the mediator being considered and the total effect (the sum of the direct and indirect effects). In *Tables 27–33*, we present the effect estimates, standard errors, 95% CIs and *p*-values.

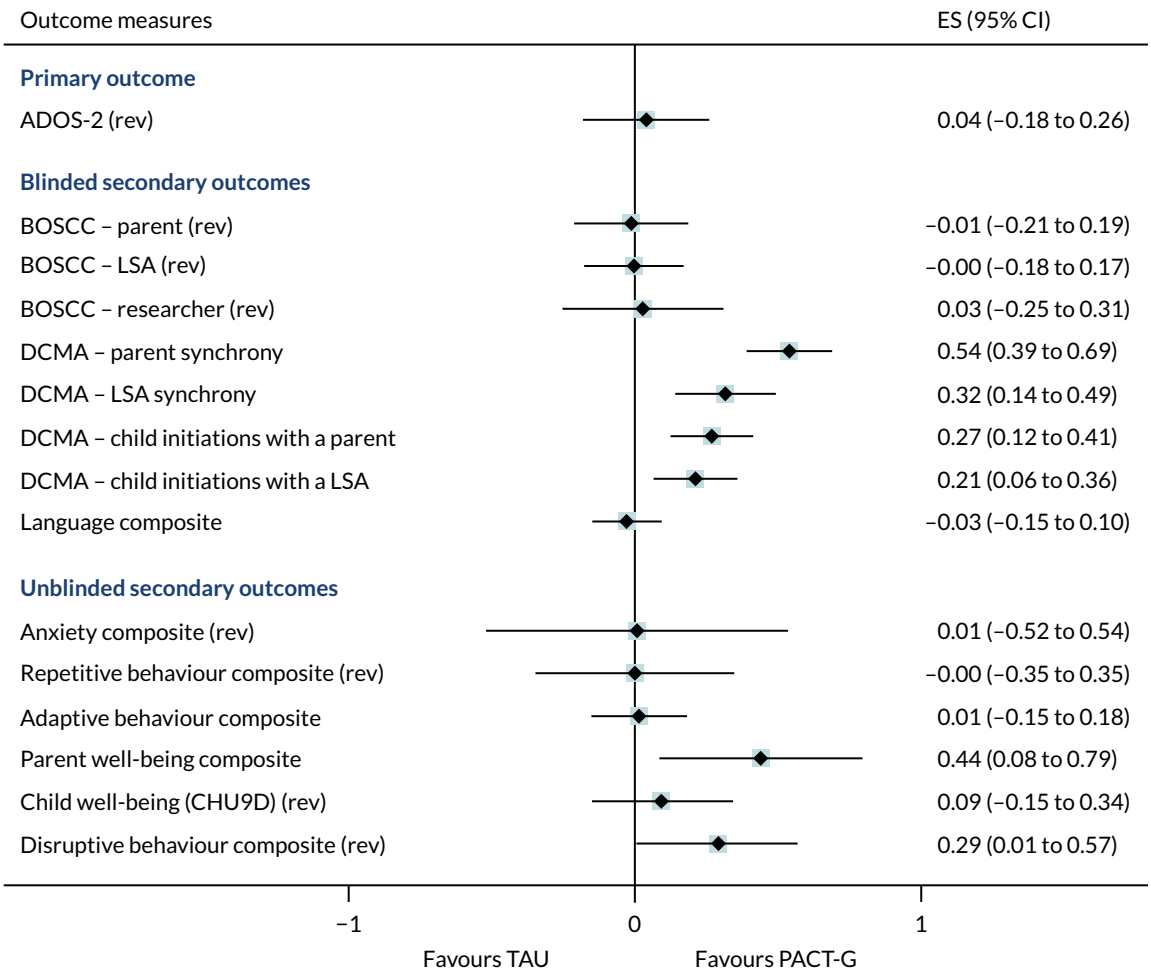

FIGURE 8 The ESs of the primary and secondary outcomes. rev, reversed.

TABLE 26 Adverse events

Event characteristic	Treatment group, *n* (%)		Overall, *n* (%)
	TAU	PACT-G	
Is the event serious?			
No	20 (90.9)	20 (83.3)	40 (87.0)
Yes, requires hospitalisation	2 (9.1)	2 (8.3)	4 (8.7)
Yes, persistent or significant disability	0 (0.0)	2 (8.3)	2 (4.3)
AE-type events (people)			
Reduction in school attendance	1 (4.5)	0 (0)	1 (2.2)
Other issues with school	1 (4.5)	1 (4.2)	2 (4.3)
Relationship breakdown (parent)	0 (0)	5 (20.8)	5 (10.9)
Significant change in child behaviour or well-being	13 (59.1)	11 (45.8)	24 (52.2)
Significant family illness	1 (4.5)	1 (4.2)	2 (4.3)
Death in immediate family	1 (4.5)	1 (4.2)	2 (4.3)
Other personal/family issue	4 (18.2)	3 (12.5)	7 (15.2)
Other	1 (4.5)	2 (8.3)	3 (6.5)
Relationship to study			
Possibly related	4 (18.2)	3 (12.5)	7 (15.2)
Not related	18 (81.8)	21 (87.5)	39 (84.8)

The first model examines mediation of treatment to DCMA parent synchrony at 7 months to ADOS-2 at 12 months (*Figure 9*).

To summarise the findings presented in *Table 27*, there is no total effect to be mediated (as demonstrated in the primary ITT analysis), but there is a significant effect of treatment on parent synchrony at 7 months (A path) in favour of the PACT-G intervention.

We found no association between parent synchrony at 7 months and ADOS-2 at 11 months (B path), and the indirect effect is non-significant, which we concluded was because of the non-significant B paths.

We see the opposite signs for the B path in module 2 than those seen in module 1: an increase in parent synchrony leads to lower ADOS-2 scores in module 2, but to higher ADOS-2 scores in module 1. This leads to the indirect effects having opposite signs between module 2 and module 1, and opposite signs to the direct and total effects, where module 1 showed improvement and module 2 showed worsening.

This direct effect reduced symptom severity in module 1, but increased symptom severity in module 2 [the positive coefficient indicating a worse (higher) score in the PACT-G group]. The negative coefficient for the overall direct effect indicates a reduction in ADOS-2 independent of the mediator, although this effect is non-significant.

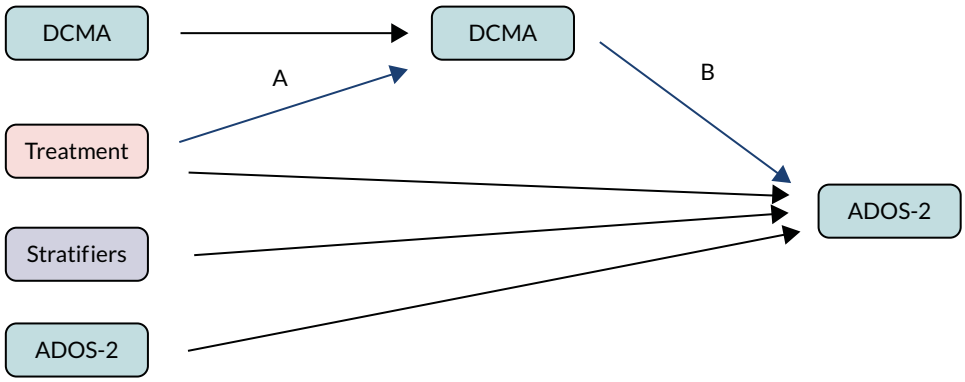

FIGURE 9 Model pathway from treatment to ADOS-2 outcome.

TABLE 27 Mediation of DCMA parental synchrony at 7 months on end-point ADOS-2 outcome at 12 months

ADOS-2	A path (SE); (95% CI); *p*-value	B path (SE); (95% CI); *p*-value	Indirect effect (SE); (95% CI); *p*-value	Direct effect (SE); (95% CI); *p*-value	Total effect (SE); (95% CI); *p*-value
Module 1 (non-verbal), $n = 91$	0.10 (0.03); (0.04 to 0.15); 0.001	0.81 (2.29); (−3.68 to 5.30); 0.724	0.08 (0.22); (−0.36 to 0.51); 0.727	−0.52 (0.63); (−1.76 to 0.71); 0.406	−0.45 (0.59); (−1.60 to 0.71); 0.450
Module 1 (verbal), $n = 82$	0.17 (0.04); (0.10 to 0.24); < 0.001	2.85 (2.76); (−2.55 to 8.26); 0.300	0.49 (0.49); (−0.46 to 1.45); 0.312	−1.65 (0.93); (−3.47 to 0.16); 0.074	−1.18 (0.81); (−2.77 to 0.42); 0.147
Module 2, $n = 58$	0.12 (0.03); (0.06 to 0.18); < 0.001	−0.93 (4.07); (−8.91 to 7.04); 0.819	−0.11 (0.49); (1.06 to 0.84); 0.818	1.60 (0.96); (−0.29 to 3.49); 0.096	1.48 (0.83); (−0.15 to 3.12); 0.075
Overall	0.12 (0.02); (0.09 to 0.16); < 0.001	1.24 (1.62); (−1.93 to 4.40); 0.444	1.33 (1.42); (−1.45 to 4.12); 0.347	−0.32 (0.46); (−1.22 to 0.58); 0.486	−0.16 (0.41); (−0.97 to 0.65); 0.699

SE, standard error.

In the analysis shown in *Table 28*, we consider child initiations at 7 months as the mediator, and find that the A path shows significant treatment effect on child initiations at 7 months in module 1 (verbal) and module 2, but not in module 1 (non-verbal). Overall, there is a significant effect in favour of the PACT-G intervention. As with parent synchrony, there is no association between child initiations at 7 months and ADOS-2 at 12 months. There are no significant mediated effects, and the direct effects have the same pattern as with parent synchrony, described previously.

Table 29 shows that there is a significant effect of treatment on LSA synchrony at 7 months (A path), but there is no association between LSA synchrony at 7 months and ADOS-2 at 12 months (B path). The indirect effect is non-significant because of the non-significant B paths. In this analysis, we see opposite signs for the B path in module 1 (verbal) than in module 1 (non-verbal) and module 2.

The analysis in *Table 30* shows a similar pattern to previous findings, demonstrating significant effects of the treatment on child initiations with a LSA at 7 months (A path). As with parent and LSA synchrony, there is no association between child initiations at 7 months and ADOS-2 at 12 months (B path) and, overall, there are no significant mediated effects.

TABLE 28 Mediation of DCMA child initiations with a parent at 7 months on end-point ADOS-2 at 12 months

ADOS-2	A path (SE); (95% CI); *p*-value	B path (SE); (95% CI); *p*-value	Indirect effect (SE); (95% CI); *p*-value	Direct effect (SE); (95% CI); *p*-value	Total effect (SE); (95% CI); *p*-value
Module 1 (non-verbal), $n = 91$	0.03 (0.03); (−0.03 to 0.09); 0.336	1.11 (2.15); (−3.10 to 5.31); 0.605	0.03 (0.08); (−0.11 to 0.18); 0.654	−0.52 (0.59); (−1.68 to 0.65); 0.386	−0.45 (0.59); (−1.60 to 0.71); 0.450
Module 1 (verbal), $n = 82$	0.14 (0.04); (0.07 to 0.22); < 0.001	2.42 (2.52); (−2.52 to 7.36); 0.337	0.35 (0.38); (−0.39 to 1.09); 0.356	−1.45 (0.89); (−3.18 to 0.29); 0.103	−1.18 (0.81); (−2.77 to 0.42); 0.147
Module 2, $n = 58$	0.10 (0.05); (0.01 to 0.19); 0.033	−4.56 (2.50); (−9.45 to 0.34); 0.68	−0.44 (0.31); (−1.04 to 0.16); 0.151	1.88 (0.83); (0.26 to 3.50); 0.023	1.48 (0.83); (−0.15 to 3.12); 0.075
Overall	0.08 (0.02); (0.04 to 0.12); < 0.001	−0.20 (1.37); (−2.88 to 2.48); 0.882	1.30 (1.42); (1.48 to 4.08); 0.359	−0.10 (0.42); (−0.93 to 0.73); 0.820	−0.16 (0.41); (−0.97 to 0.65); 0.699

TABLE 29 Mediation of DCMA LSA synchrony at 7 months on end-point ADOS-2 at 12 months

ADOS-2	A path (SE); (95% CI); *p*-value	B path (SE); (95% CI); *p*-value	Indirect effect (SE); (95% CI); *p*-value	Direct effect (SE); (95% CI); *p*-value	Total effect (SE); (95% CI); *p*-value
Module 1 (non-verbal), $n = 96$	0.10 (0.04); (0.03 to 0.17); 0.007	−2.82 (1.76); (−6.26 to 0.62); 0.108	−0.28 (0.20); (−0.68 to 0.12), 0.167	−0.15 (0.61); (−1.34 to 1.04); 0.805	−0.45 (0.59); (−1.60 to 0.71), 0.450
Module 1 (verbal), $n = 82$	0.13 (0.03); (0.07 to 0.20); < 0.001	3.67 (2.79); (−1.80 to 9.15); 0.189	0.49 (0.39); (−0.28 to 1.25); 0.210	−1.64 (0.87); (−3.35 to 0.07); 0.061	−1.18 (0.81); (−2.77 to 0.42); 0.147
Module 2, $n = 59$	0.15 (0.03); (0.09 to 0.21); < 0.001	−0.89 (4.13); (−8.98 to 7.20); 0.829	−0.14 (0.63); (−1.37 to 1.10); 0.830	1.63 (1.08); (−0.49 to 3.75); 0.131	1.48 (0.83); (−0.15 to 3.12); 0.075
Overall	0.13 (0.02); (0.09 to 0.17); < 0.001	−0.98 (1.40); (−3.72 to 1.77); 0.485	−0.15 (1.42); (−2.93 to 2.63); 0.915	−0.24 (0.45); (−1.13 to 0.65); 0.600	−0.16 (0.41); (−0.97 to 0.65); 0.699

TABLE 30 Mediation of DCMA child initiations with a LSA at 7 months on end-point ADOS-2 at 12 months

ADOS-2	A path (SE); (95% CI); *p*-value	B path (SE); (95% CI); *p*-value	Indirect effect (SE); (95% CI); *p*-value	Direct effect (SE); (95% CI); *p*-value	Total effect (SE); (95% CI); *p*-value
Module 1 (non-verbal), $n = 96$	0.13 (0.05); (0.03 to 0.22); 0.011	−0.69 (1.31); (−3.26 to 1.89); 0.600	−0.09 (0.17); (−0.42 to 0.25); 0.608	−0.39 (0.61); (−1.58 to 0.79); 0.516	−0.45 (0.59); (−1.60 to 0.71); 0.450
Module 1 (verbal), $n = 82$	0.15 (0.05); (0.05 to 0.24); 0.002	−0.60 (1.99); (−4.51 to 3.30); 0.762	−0.09 (0.30); (−0.67 to 0.49); 0.764	−1.08 (0.87); (−2.78 to 0.62); 0.212	−1.18 (0.81); (−2.77 to 0.42); 0.147
Module 2, $n = 59$	0.09 (0.05); (0.00 to 0.19); 0.042	3.19 (2.64); (−1.98 to 8.36); 0.227	0.30 (0.29); (−0.26 to 0.86); 0.292	1.18 (0.86); (−0.51 to 2.86); 0.171	1.48 (0.83); (−0.15 to 3.12); 0.075
Overall	0.12 (0.03); (0.07 to 0.18); < 0.001	−0.10 (1.01); (−2.08 to 1.89); 0.925	−0.73 (1.42); (−3.51 to 2.04); 0.606	−0.17 (0.43); (−1.01 to 0.67); 0.695	−0.16 (0.41); (−0.97 to 0.65); 0.699

We repeated these analyses using the same modelling approach, replacing the outcome measures as the BOSCC instead of the ADOS-2. An example is shown in *Figure 10*. Estimates are shown for each BOSCC module, and then combined into a total score using an inverse variance-weighted estimator.

Table 31 shows the results for four different mediators. As these mediators are unchanged, we have already demonstrated that there is a significant treatment effect on each of these (the A paths).

We find there are overall effects of child initiations with both the parent and the LSA on the BOSCC score at 12 months. This leads to a statistically significant indirect effect of the treatment through child initiations with the parent ($p = 0.022$) and weak evidence for an indirect effect of child initiations with the LSA ($p = 0.073$). All of the direct effects are not statistically significant and, as noted in the primary analysis, there are no statistically significant total effects on the BOSCC.

We tested if there was a mediation of treatment effects between the DCMA measures of parent/LSA synchrony and child initiations at 12 months. The results are shown in *Table 32*.

This test demonstrates that there is mediation of the effect of treatment on child initiations with a parent at 12 months through parent synchrony at 7 months, and there is mediation of the effect of treatment on child initiations with a LSA at 12 months through LSA synchrony at 7 months.

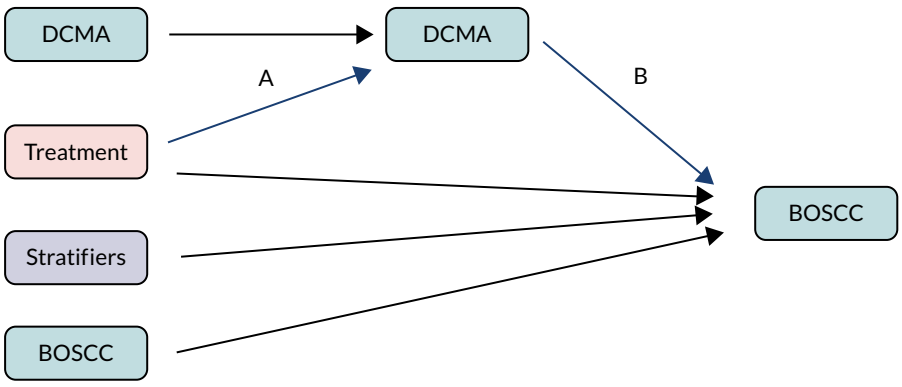

FIGURE 10 Model pathway from treatment to BOSCC outcome.

TABLE 31 Mediation of treatment effects on researcher BOSCC at 12 months

Mediator at 7 months		A path (SE); (95% CI); *p*-value	B path (SE); (95% CI); *p*-value	Indirect effect (SE); (95% CI); *p*-value	Direct effect (SE); (95% CI); *p*-value	Total effect (SE); (95% CI); *p*-value
Parent synchrony	Module 1, *n* = 191	0.12 (0.02); (0.07 to 0.16); < 0.001	0.09 (3.56); (−6.89 to 7.07); 0.980	0.01 (0.42); (−0.81 to 0.84); 0.980	−0.21 (1.12); (−2.39 to 1.98); 0.854	−0.19 (1.02); (−2.19 to 1.81); 0.854
	Module 2, *n* = 57	0.13 (0.03); (0.07 to 0.18); < 0.001	−10.23 (16.27); (−42.12 to 21.66); 0.529	−1.30 (2.08); (−5.38 to 2.77); 0.531	−0.02 (3.86); (−7.60 to 7.55); 0.995	−1.28 (3.33); (−7.81 to 5.25); 0.700
	Overall	0.12 (0.02); (0.09 to 0.16); < 0.001	−0.38 (3.48); (−7.20 to 6.43); 0.912	−0.21 (0.50); (−1.18 to 0.76); 0.671	−0.19 (1.07); (−2.29 to 1.91); 0.858	−0.28 (0.97); (−2.19 to 1.63); 0.773
Child initiations with a parent	Module 1, *n* = 191	0.07 (0.03); (0.02 to 0.12); 0.003	−6.82 (3.16); (−13.01 to −0.63); 0.031	−0.51 (0.29); (−1.08 to 0.07); 0.084	0.27 (1.03); (−1.75 to 2.28); 0.796	−0.20 (1.02); (−2.20 to 1.80); 0.843
	Module 2, *n* = 57	0.11 (0.05); (0.02 to 0.20); 0.023	−18.32 (9.61); (−37.16 to 0.51); 0.057	−1.98 (1.32); (4.57 to 0.61); 0.133	1.19 (3.48); (−5.63 to 8.02); 0.732	−1.01 (3.42); (−7.73 to 5.70); 0.767
	Overall	0.08 (0.02); (0.04 to 0.13); < 0.001	**−7.94 (3.00); (−13.82 to −2.06); 0.008**	**−0.78 (0.34); (−1.44 to −0.11); 0.022**	0.34 (0.99); (−1.59 to 2.28); 0.730	−0.27 (0.98); (−2.18 to 1.65); 0.784
LSA synchrony	Module 1, *n* = 191	0.11 (0.02); (0.06 to 0.16); < 0.001	3.99 (3.22); (−2.33 to 10.30); 0.216	0.43 (0.37); (−0.28 to 1.15); 0.235	−0.62 (1.08); (−2.73 to 1.49); 0.563	−0.18 (1.02); (−2.17 to 1.82); 0.863
	Module 2, *n* = 57	0.17 (0.04); (0.10 to 0.24); < 0.001	−41.82 (13.45); (−68.18 to −15.45); 0.002	−6.92 (2.68); (−12.17 to −1.67); 0.010	7.58 (4.44); (−1.13 to 16.28); 0.088	−0.47 (3.86); (−8.03 to 7.09); 0.903
	Overall	0.13 (0.02); (0.09 to 0.17); < 0.001	1.50 (3.13); (−4.64 to 7.64); 0.633	−0.45 (0.46); (−1.34 to 0.44); 0.324	−0.17 (1.05); (−2.22 to 1.88); 0.873	−0.19 (0.98); (−2.12 to 1.73); 0.843
Child initiations with a LSA	Module 1, *n* = 191	0.12 (0.03); (0.06 to 0.19); < 0.001	−4.23 (2.38); (−8.90 to 0.44); 0.076	−0.52 (0.32); (−1.16 to 0.12); 0.109	0.29 (1.05); (−1.76 to 2.34); 0.784	−0.18 (1.02); (−2.18 to 1.82); 0.857
	Module 2, *n* = 57	0.14 (0.05); (0.04 to 0.24); 0.008	−9.30 (9.23); (−27.38 to 8.78); 0.313	−1.30 (1.39); (−4.02 to 1.42); 0.350	−0.14 (3.66); (−7.32 to 7.05); 0.971	−1.37 (3.41); (−8.05 to 5.31); 0.687
	Overall	0.13 (0.03); (0.07 to 0.18); < 0.001	**−4.55 (2.31); (−9.06 to −0.03); 0.049**	−0.67 (0.37); (−1.40 to 0.06); 0.073	0.26 (1.00); (−1.71 to 2.22); 0.800	−0.28 (0.98); (−2.20 to 1.64); 0.774

Bold indicates significance.

TABLE 32 Mediation of parent/LSA synchrony at 7 months on end-point child initiations at 12 months

Outcome at 12 months	Mediator at 7 months	A path (SE); (95% CI); *p*-value	B path (SE); (95% CI); *p*-value	Indirect effect (SE); (95% CI); *p*-value	Direct effect (SE); (95% CI); *p*-value	Total effect (SE); (95% CI); *p*-value
Child initiations with a parent	Parent synchrony	0.12 (0.02); (0.08 to 0.16); < 0.001	0.46 (0.08); (0.30 to 0.62); < 0.001	0.05 (0.01); (0.03 to 0.08); < 0.001	0.02 (0.02); (−0.02 to 0.07); 0.341	0.08 (0.02); (0.03 to 0.12); 0.001
Child initiations with a LSA	LSA synchrony	0.11 (0.02); (0.07 to 0.15); < 0.001	0.31 (0.09); (0.14 to 0.49); < 0.001	0.03 (0.01); (0.01 to 0.06); 0.003	0.02 (0.03); (−0.04 to 0.07); 0.508	0.05 (0.03); (0.00 to 0.11); 0.048

One of the assumptions underpinning the analysis approach is the absence of measurement error in the mediator. If present, this could cause a bias in the estimation of the B path and the direct effect, and lead to misleading conclusions. To check this assumption, we extended the structural equation models to allow for measurement error in the mediator by using an approach outlined in Pickles *et al.*[17] This involves fitting a latent variable model for the repeated measures of the mediator, constraining the factor loadings and measurement error variance across time and ADOS-2 group. We allowed the variance of the factors to vary across ADOS-2 group. The mediator in this model is the latent measure of DCMA at 7 months, which is taken to be a measurement error-free construct. As previously, estimates are shown for each ADOS-2 module, and then combined into a total score using an inverse-weighted estimator. A schematic of the model is shown in *Figure 11*.

The pattern of results, shown in *Table 33*, is consistent with those seen previously for the effect of treatment on ADOS-2 mediated through parent synchrony at 7 months. There is no evidence of an association between the mediator and outcome, implying that measurement error was not attenuating this association previously. We display this for one mediation analysis for illustrative purposes.

Figure 12 displays a summary of the mediation analysis findings from *Tables 27–33*. These need to be understood in relation to the hypothesised chain of effect (found in our previous studies[7,14,17,18,54]) from the intervention to (1) caregiver adult response to the child in the dyadic context, measured at 7 months; (2) child response to the caregiver adult in that same context, also measured at 7 months; and (3) child response to another adult (researcher) in a generalised research context, measured at 12 months.

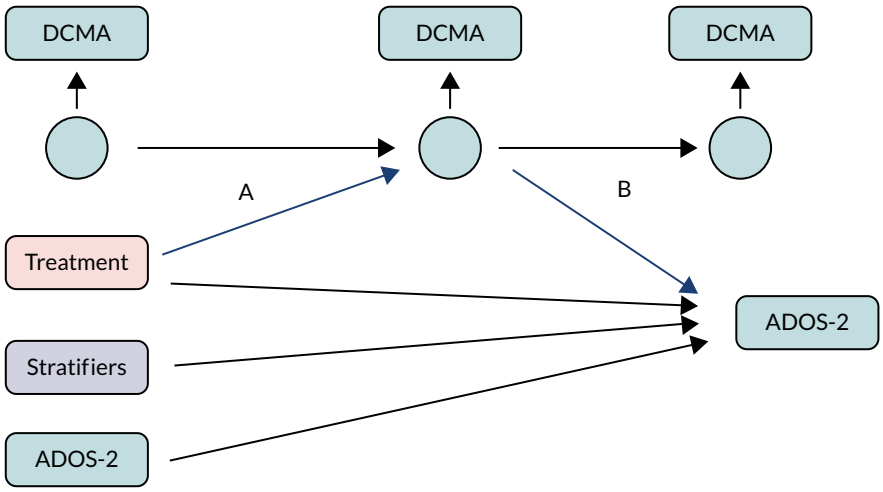

FIGURE 11 Model allowing for measurement error using repeated measures.

TABLE 33 Mediation of treatment to parent synchrony at 7 months to end-point ADOS-2 at 12 months

ADOS-2	A path (SE); (95% CI); *p*-value	B path (SE); (95% CI); *p*-value	Indirect effect (SE); (95% CI); *p*-value	Direct effect (SE); (95% CI); *p*-value	Total effect (SE); (95% CI); *p*-value
Module 1 (non-verbal); *n* = 96	1.48 (0.59); (0.31 to 2.64); 0.013	0.06 (0.51); (−0.95 to 1.06); 0.909	0.09 (0.76); (−1.40 to 1.57); 0.910	−0.53 (1.02); (−2.53 to 1.46); 0.599	−0.45 (0.60); (−1.63 to 0.73); 0.457
Module 1 (verbal); *n* = 82	2.14 (0.63); (0.91 to 3.36); 0.001	3.36 (8.41); (−13.12 to 19.83); 0.690	7.17 (18.95); (−29.97 to 44.31); 0.705	−8.25 (18.87); (−45.23 to 28.73); 0.662	−1.13 (0.85); (−2.79 to 0.53); 0.181
Module 2, *n* = 59	1.84 (0.73); (0.40 to 3.28); 0.012	−2.08 (4.95); (−11.78 to 7.62); 0.674	−3.83 (10.06); (−23.55 to 15.89); 0.704	5.34 (10.18); (−14.62 to 25.30); 0.600	1.51 (0.86); (−0.17 to 3.18); 0.079
Overall	1.80 (0.53); (0.75 to 2.85); 0.001	0.05 (0.51); (−0.94 to 1.04); 0.925	0.23 (1.17); (−2.06 to 2.53); 0.842	−0.50 (1.01); (−2.47 to 1.47); 0.620	−0.16 (0.41); (−0.97 to 0.65); 0.699

In all of these analyses, there was a consistent statistically significant effect of treatment on caregiver synchronous response with the child, indicating that the PACT-G intervention led to a between-group difference effect on the initial target mechanism, as found in our previous studies. The analyses also demonstrated the second hypothesised effect, that is from caregiver synchrony to later child communication initiation, so that the effect on child initiation was mediated through synchrony with the respective partner.

We did not find any evidence of a downstream effect from the mediator to the ADOS-2 outcomes. However, in keeping with our previous work, there was a significant association between child initiation with both the parent and the LSA in home and educational settings, and later symptom change on the BOSCC at 12 months, and a significant indirect effect was estimated through the parent synchrony measure.

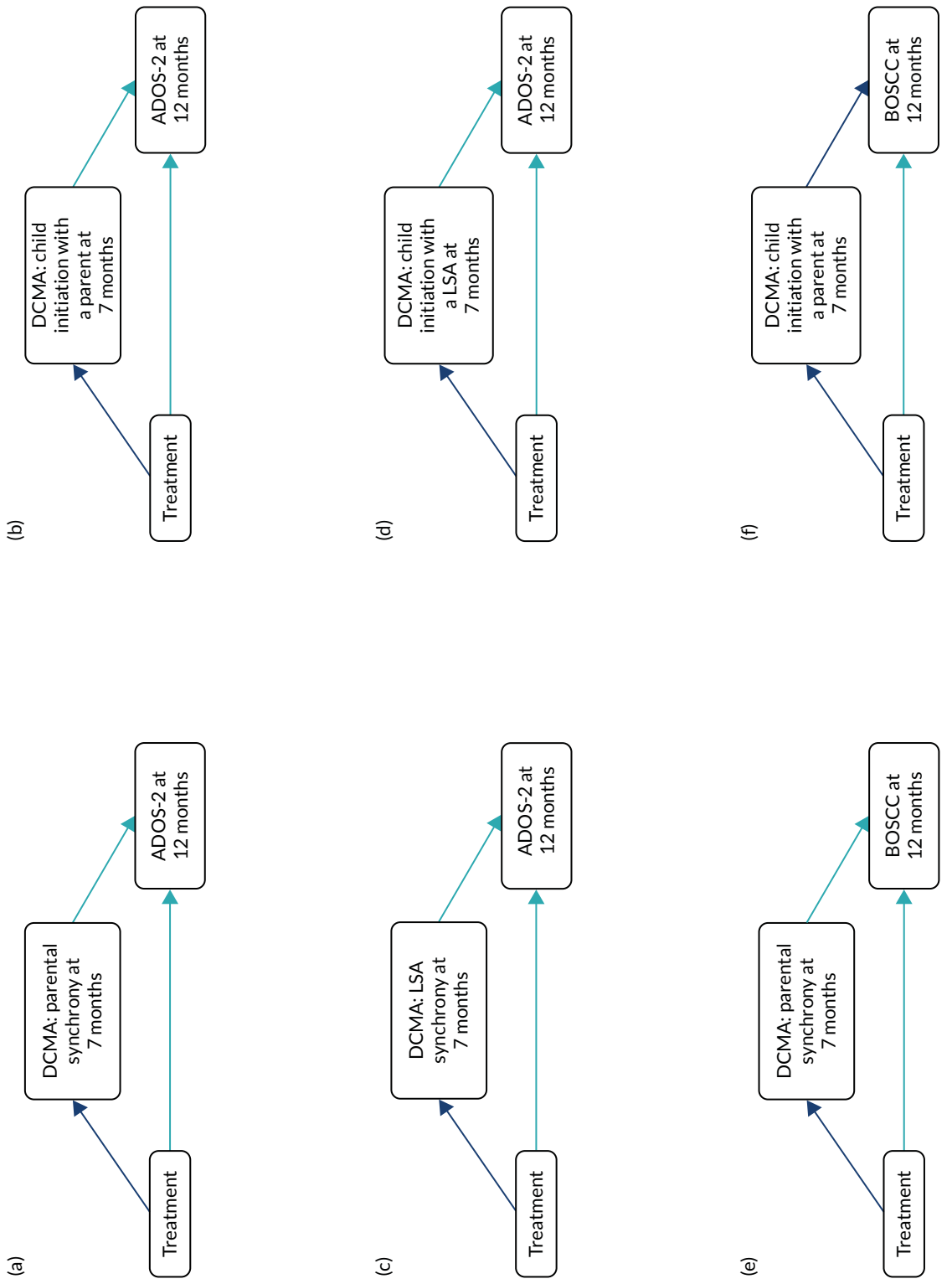

FIGURE 12 Summary of mediation analysis findings from *Tables 27–33*. Statistically significant paths ($p < 0.05$) are shown as dark-blue arrows. *(continued)*

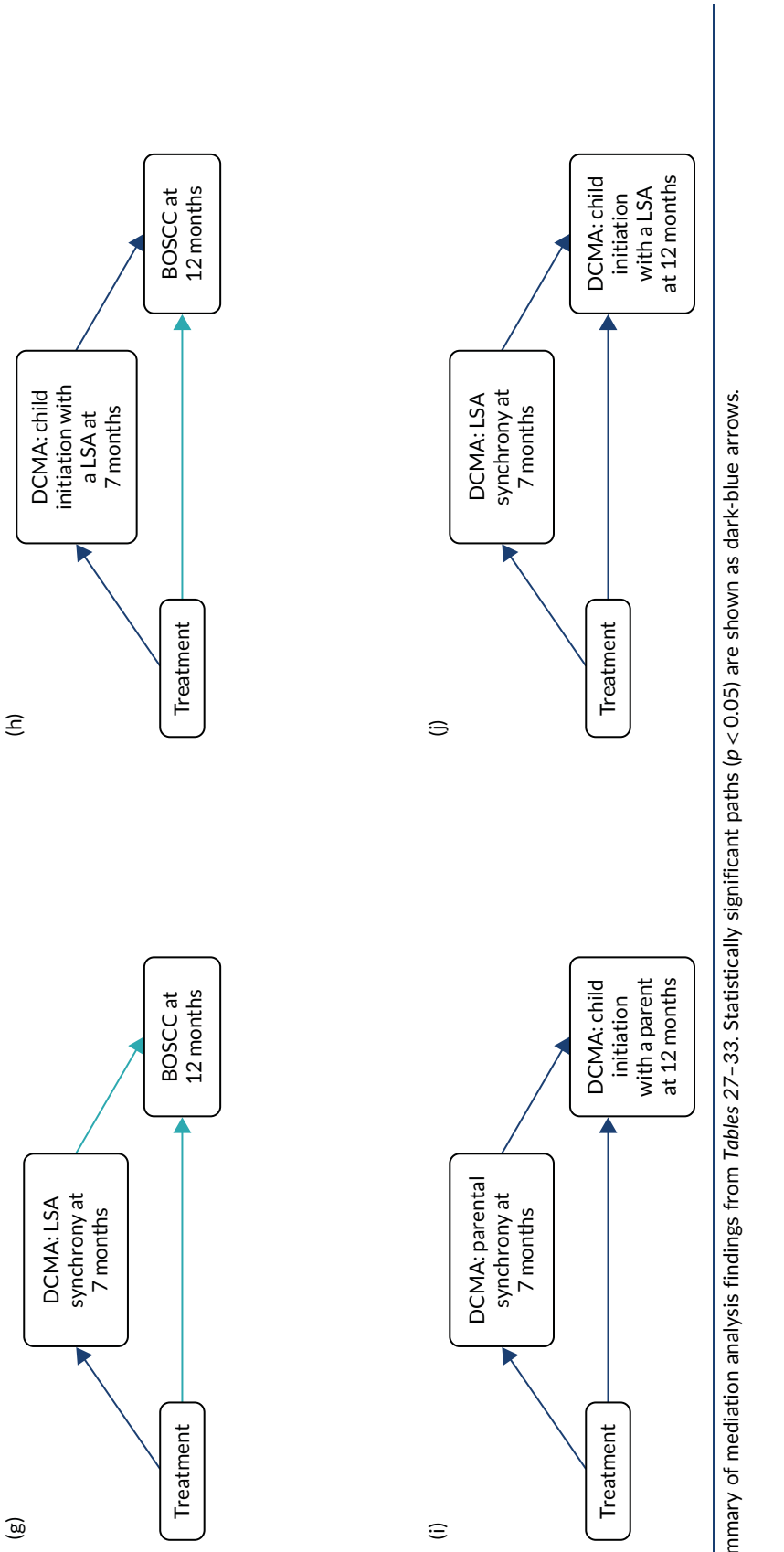

FIGURE 12 Summary of mediation analysis findings from *Tables* 27–33. Statistically significant paths ($p < 0.05$) are shown as dark-blue arrows.

Chapter 9 Discussion

Aims

This trial addressed a number of contemporary challenges in autism intervention research. The first was extending a manualised, largely clinic-based treatment within the naturalistic community settings of home and education, and, for added efficiency, including use of remote video-conferencing sessions, in addition to in-person delivery. Second, we introduced parallel home and education therapy for the child, with the aim of reinforcing the child's developmental learning across contexts and persons. The purpose of this was to address a key difficulty, suggested in many single-subject design studies, that autistic children are thought to have in generalising and implementing acquired skills across contexts[11] – a difficulty assumed to place significant limitations on the functional effectiveness of interventions in development. Third, the study extends the intervention into the early school years for children with intellectual disability and autism, whereas most early psychosocial interventions to date have been implemented in the preschool period. In addition, our large and detailed *Mechanism study*, one that we believe to be by far the most extensive yet in the autism field and perhaps across wider developmental science, provided the opportunity to, for the first time, look in detail at autism symptoms across different contexts and, from our mediation analysis, to investigate processes of generalisation of change through intervention.

This trial addresses current NHS priorities in child development and mental health, for instance the emphasis on therapy delivery within educational contexts in *The NHS Long Term Plan*.[105] The trial's focus on autism symptoms as the primary outcome is consistent with our previous work in addressing the core defining characteristics of autism, and supports the mechanistic approach to analysing both proximal and distal effects of intervention and mediation. The data-rich, repeated-measures design provided enhanced power to account for the measurement error in behavioural studies of this kind and allowed mediation/mechanism modelling of the findings.

Strengths and limitations

Validity and measurement

Data from the CONSORT flow diagram (see *Figure 5*) show highly successful implementation and internal validity in this complex trial. Only one child out of 249 randomised children was lost to end-point analysis under ITT (one participant withdrew from the PACT-G group). Primary outcome analysis was achieved on 118 out of 127 (93%) participants in the TAU group and 119 out of 122 (98%) in the PACT-G group. Overall, attrition was very low, at 8 out of 249 (3.2%) children withdrawing (five in the TAU group and three in the PACT-G group). Data completeness was excellent and did not require imputation strategies. The trial sampling was across three urban/semiurban settings throughout England (i.e. Manchester, London, Newcastle upon Tyne). By using broad inclusion criteria for children with severe autism, we aimed for a broadly representative sampling of autistic children in England.

The intermediate outcome and mechanistic analysis required a very large number of video-interaction captures and structured, blinded video coding. The DCMA coding system of naturalistic social communication between the child and parent or LSA was applied to six captures per participant across the trial, at baseline, mid-point and end point. This resulted in a total of 1610 codings, each taking approximately half an hour of coding time. The BOSCC, a semistructured interactive assessment of child autism symptoms across contexts, was applied to eight captures per participant (home and educational settings at three time points, and the research clinic setting at two time points). This resulted in a total of 2147 codings across the trial, each taking approximately an hour of coding time.

Both sets of codings (i.e. DCMA and BOSCC) achieved excellent internal validity and inter-rater reliability. This total of approximately 3500 detailed manualised codings in a repeated-measures design over 1 year, undertaken by UK and US coders, is, we believe, an unprecedented achievement within a developmental science study. Apart from its utility in the mechanism analysis, it represents a unique resource for data-sharing within international autism developmental science. An add-on study using a cohort analysis from these data, additional to our trial protocol, is noted in *Appendix 1* as an example of a novel analysis of the comparison of acquired skills in autism development across context and person.

A resulting strength from the mechanistic design and high level of reliable data completion is that this trial has allowed us to successfully address aspects of intervention effects and developmental change in autistic children in a way that we think is unprecedented in autism intervention trials to date.

Intervention adherence

The implementation achieved means of 10 out of 12 (83%) and 8 out of 12 (66%) sessions, delivered through in-person and remote sessions against the intended dose in home and educational settings, respectively; 5.5% of these sessions in home and 5% in education were rated as 'unacceptable' (see *Chapter 5*, *Intervention manual fidelity*, and *Table 13*). This compares with a mean 16 out of 18 (89%) session delivery in the original, predominantly clinic-delivered, in-person PACT intervention trial.[7] The figures reflect the challenges of home and, particularly, education environments for delivery of the intervention in PACT-G (for considerations of dosage, see *Overall evidence*); however, independent fidelity checks on a random sampling of 3.1% of sessions across therapists and time points suggested that delivered sessions that were rated had a similar manual fidelity to the PACT[7] fidelity. In addition, six structured collaborative conversations (i.e. HSCs) between parents and LSA were intended per case, with the aim of enhancing the integration of the parallel home and education treatment programmes. However, in practice, the HSC was essentially not achieved, with a mean of 2.2 HSC sessions delivered per case, compared with a prespecified minimum acceptable threshold of three sessions per case.

We have therefore shown that it is possible to deliver an individualised early autism intervention using video feedback in home and educational settings – a finding that is important and relevant in the context of NHS priorities.[105] However, we have also highlighted potential problems with the implementation of and adherence to the intervention, particularly in educational settings. Specific considerations, detailed below in the report, provide important learning for future work of this kind. Feedback from therapists and participants on our online, remotely delivered therapy sessions indicated advantages and disadvantages. Therapists reported that it was often not possible to deliver the full therapy session as planned using the available video-conferencing technology, but also that the video-conferencing sessions were popular with some parents for scheduling reasons. These reflections and experiences are now of greater relevance in the light of the COVID-19 pandemic.[106]

Overall evidence

Outcomes estimation

The outcomes estimation for the PACT-G intervention delivered in home and educational settings did not show an effect on child autism symptom severity in the primary outcome research setting or in the home or educational settings. This finding was also seen in the unblinded parent rated measures, where there was no evidence of group difference on the child's adaptive behaviour, rates of repetitive behaviours or quality of life. Similarly, there was no group difference on the objectively rated language composite.

The more proximal target outcomes of the intervention were, however, achieved in both home and educational settings. These were changes in the quality of adult–child dyadic social communication interaction (adult synchronous response and child communication initiations) with a parent at home and with a LSA (or equivalent) in education. This effect was significant, but at about half the ES on

parent–child communication reported in the original PACT.[7] Two other areas where the PACT-G therapy also showed significant positive group difference were in improving parental well-being and reducing child disruptive behaviour. The latter measure is a composite of unblinded ratings by both parents and the teacher, suggesting that the improvement in child disruptive behaviour occurred across home and educational settings.

Mechanism study

The hypothesis of the PACT-G design was that the delivery of the intervention in both home and school contexts in parallel would produce increased opportunities for the autistic child to make overall developmental progress in communication skills, and promote the generalisation of changes in more distal autistic behaviours and skills measured using independently observed symptom outcomes. The mechanism study was designed to test this hypothesis and illuminate the process of generalisation of acquired skills within development. By 'generalisation' in this context, as discussed in *Chapter 1*, we refer both to (1) the generalisation of a newly acquired behaviour or skill from one context into another context of person or environment and (2) the generalisation of an acquired precursor behaviour or skill into a downstream effect on other abilities through a cascading chain of effect across context and through time (what could be termed a 'homotypic' vs. a 'heterotypic' generalisation).

An example of the heterotypic form of generalisation is intrinsic to the theory behind the PACT-G treatment, and was supported in our mediation analysis from the PACT.[17] Here, a primary targeted enhancement of adult social responsiveness results in an enhancement of child social initiation in a specific dyadic context between them (a chain effect across persons). Then, this child dyadic social initiation generalises into an alteration in child symptoms with another person in another context (generalisation across context, person and developmental skill). To the limited extent that the measure of child symptoms also involves dyadic social initiation from the child, this can be understood as 'homotypic' generalisation in the first sense, but for the majority of social affective skills, sensory sensitivities and repetitive and restricted behaviours impacted by PACT treatment, this represented a 'heterotypic' generalisation into developmentally related ongoing change. To further test this generalisation model in PACT-G, the trial gathered what is, to the best of our knowledge, an unprecedented quantity of detailed, repeated-measures observational data on functional dyadic communication with parents and LSA, and symptom expression in both home and educational settings, as well as in an independent research setting.

Useful background for considering the results of the PACT-G mechanism study comes from a post hoc analysis of the study cohort using the BOSCC measure to consider independently observed child symptom expression across time and context (see *Appendix 1*, analysis not specified in the trial protocol). The analysis tracked the expression of autism symptomatology simultaneously across contexts and investigated how change in one context over time may relate to change in the same symptomatology in another context. The analysis found that developmental change in social communication and autism-related behaviours with the parent during the first 7 months of the study was significantly associated with developmental change in the same domains with the LSA in the educational setting over the same period. In addition, these context-specific changes were both independently associated with change in child symptom behaviours in the research context between baseline and the 12-month end point. When changes in both the home and educational settings were modelled together, the home context proved more salient and the education context was no longer significantly associated with symptom change. The analysis suggests, but does not unequivocally prove, 'generalisation' or 'transmission' from one context to another, as the association could reflect confounding because of intrinsic developmental progression in the child expressed simultaneously in different contexts. The theory of the PACT-G intervention was based on a presumption of the existence of these kinds of generalising developmental effects across contexts in autism, and how they could be enhanced. In this treatment trial, for instance, by introducing an intervention to enhance the rate of change of dyadic developmental skills that are precursors to the symptomatology, we could test the potential causal influences between them.

In the event, the findings of the mechanism analysis in the treatment trial context present a mixed picture. The intervention succeeded in improving the precursor dyadic social interaction in both the parent–home and LSA–education contexts as planned. As in our previous work, this improvement in adult synchronous response mediated the improvement in child dyadic social interaction – with this study thereby extending the results of the previous work in showing the effect both between parent and child at home and between LSA and child in education. However, in contrast to the previous PACT, these improvements in precursor dyadic behaviours did not translate into improvement in child symptom outcomes, in the home or educational settings, or in independent researcher assessment. This lack of generalisation to symptom change is all the more striking given the strong mediation in the original PACT from child communication change to symptom outcome improvement in the researcher context.[17] However, despite the lack of symptom outcome change, the mechanism analysis did provide partial evidence to support the full mediation pathway found in the previous PACT. The improvement in child dyadic social communication with an adult (parent in home and LSA in educational settings) mediated change in 12-month BOSCC symptom outcome (see *Table 31*) – a pattern that was not found in the ADOS-2 outcome. The full mechanism study findings are illustrated in *Figure 12*.

Interpretation

Outcome effects and the health literature

The lack of primary treatment effect on symptom outcome in this trial is in the context of a wider literature on the impact of early interventions on autism symptoms. Some previous RCTs of parent-mediated video-feedback-aided interventions (e.g. used in PACT-G and in the original PACT[7,14]) have found positive symptom outcome effects,[14,54,107] but others have not.[69,76,108] A relatively intensive treatment model of parent training combined with child intervention reportedly had significant effects on symptoms using the BOSCC measure, but measurement was not independent of therapy context;[27] other relatively intensive approaches have not shown symptom change.[25,26,28] On the other hand, the positive effects of the PACT-G intervention in targeted change in adult-child dyadic communication do replicate a number of previous findings on the effectiveness of video-feedback therapy and similar therapies across demographic and cultural contexts. These include studies of children diagnosed with autism;[7,23,25,54,108] infants at familial risk of autism in the USA, the UK[107–110] and South Asia;[76,111] and in non-autistic populations at psychosocial risk.[112–115]

In general terms, the PACT-G result is consistent with the commonly reported finding that autism interventions impact proximal intermediate targets, but rarely achieve change in autism symptoms across context and person.[30] The original PACT was one of the few studies that demonstrated a transmission from proximal effects to wider symptom outcome, and, to the best of our knowledge, the only one to date to do so over a lengthy time period. We discuss possible reasons why PACT-G did not achieve the same result in the subsequent sections.

Outcome effects in the education literature

There have been a number of recent trial reports of interventions within the educational setting that are relevant to PACT-G. The closest in style is a RCT, conducted over 1 year, of an individually delivered social communication and educational attainment-focused intervention (DS1-EI) in specialist autism settings in France (day-care hospitals and medicoeducational institutes).[116] Participants comprised 72 children aged 5–9 years with 'severe' autism and intellectual disability.[116] Children in the intervention group received 10 hours per week of one-to-one instruction with a trained teacher (considerably more than attempted in PACT-G). The trial found no significant differences in main clinical outcomes reflecting autism symptoms, but educational attainment was significantly improved for the DS1-EI group and led to more students in the intervention group being included in mainstream classrooms at the 3-year end point. Two other intervention studies reported on the implementation of a more classroom level (CTM) approach. A recent, good-quality cluster-randomised trial from the USA of a classroom-embedded, curriculum-based SCERTS intervention delivered by teachers over a school year[117] reported a significant small to moderate treatment effect in improving objectively observed social interaction in the classroom. Although this measure does

not constitute an autism symptom outcome, it does reflect aspects of social functioning. There was no treatment effect on an observed 'instructional participation' component involving emotional regulation and academic involvement, nor on formal language progress. Unblinded parent and teacher reports suggested effects on child social functioning, communication and executive skills. Kaale *et al.*[118] had previously reported the 12-month follow-up of a teacher-delivered social communication and joint attention skills (JASPER) intervention in preschool-aged children ($n = 61$), implemented twice daily for 20 minutes over 8 weeks, predominantly in mainstream school settings. The study reported gains in two out of five proximal social communication outcomes, but no improvements in the core autism outcome [measured with the Social Communication Questionnaire – Current (SCQ-C)]. A previous school-based social communication trial for children with language disorder had similar findings.[43] Another systematic review[119] reported some positive effects but was based solely on single case study designs. Overall, this relatively small number of studies shows that RCTs for autism can be conducted in educational settings. Results are mixed, with no effects found on autism symptoms, but improvements in social functioning reported in the curriculum-based SCERTS trial[117] and on academic performance in the DS1-EI trial.[116] A briefer social communication classroom-based intervention[118] achieved results somewhat similar to PACT-G.

In the education context, our PACT-G LSA-delivered intervention was an individually targeted approach that aimed to build synergy with the parallel home-based therapy for an individual child. It was not embedded in the curriculum as a CTM and was delivered with the individual child outside the classroom. Proximal positive change in objectively rated social initiation with a LSA was seen, but this did not translate into autism symptom change. The section below will reflect on possible reasons for this and how they could be further investigated.

We can conclude that this mode of therapy is feasible (albeit with challenges) in educational settings, was acceptable (and, indeed, welcomed by many school teachers and LSAs), and produced communication change between the autistic children and their communication partners. Informal feedback suggested that the education partners often found the method intuitive and appealing as an approach to working with the child and, although the trial did not demonstrate downstream benefits of this dyadic change on adaptation social competency, it did show a significant, albeit modest, effect on reduction in child disruptive behaviour measured across home and educational settings. This is important because emotional and behavioural difficulties are the norm and not the exception in young children with autism and comprehensive approaches to management and care should address these alongside social communication development.[43] We cannot be sure from this current analysis whether or not the reduction in disruptive behaviour was mediated by the identified changes in dyadic interactions, but disruptive behaviours in the classroom are a major issue in practice for educational settings (nurseries and schools) and have an inevitable impact on classroom integration and curriculum access. In this regard, these findings merit further investigation.

Learning points

Lack of generalisation from dyadic effects to autism symptoms

What might explain the lack of generalising transmission to symptom change compared with that found in the original PACT? We consider dosage, therapy environment, treatment fidelity, and the sensitivity and specificity of measures.

Dosage

The original PACT intervention consisted of 18 in-person, parent-mediated therapy sessions, with a median of 16 sessions delivered.[7] In PACT-G, the dosage of comparable parent-mediated sessions differed in three respects: (1) the therapy was delivered at home and not predominantly in the clinic, (2) the maximum number of sessions offered was 12, with a median of 10 delivered and (3) 36% of these were delivered by video conferencing rather than in-person, with 12% of the video-conferencing sessions deemed inadequate, compared with 2% of the in-person sessions. In the educational setting, a median of 8 out of 12 possible sessions were delivered, 34% of which were by video conferencing,

with 11% deemed unacceptable, compared with 1% of the in-person sessions (see *Table 13*). In education, the LSA therapy partner for the child changed in one-third of cases at mid-point, in another third at the end point, and in one-fifth at both time points.

Thus, although the total number of therapy sessions offered overall in PACT-G was greater than in the original PACT, in PACT-G these sessions were divided between parent- and LSA-mediated components, resulting, for instance, in an effective reduction of 40% in the parent-mediated component delivered in PACT-G, compared with what was delivered in PACT (in which there was no comparable educational component). Positive intermediate effects on proximal dyadic outcomes after 12 sessions in the PACT had originally encouraged this design in PACT-G, along with the constraints of mounting parallel delivery across two settings; but, with hindsight, it is possible that this resulted in insufficient therapy dosage in each setting in this trial to achieve the intended result on symptoms. This effect may have been compounded by the inclusion of video-conferencing delivery in one-third of the sessions, and therapists rated video-conferencing delivery to be more commonly compromised than the in-person sessions in both home and education settings. In the educational setting, findings for a classroom-based implementation of a related social communication therapy[43] are somewhat similar to PACT-G (with positive proximal effects not translating to longer-term language and social function measures); insufficient dosage was also postulated as a reason in this trial, which consisted of 80 brief teacher-delivered sessions over 2 months. Dosage of the two comprehensive classroom-embedded interventions discussed above (DS1-EI and SCERTS), which achieved objective educational and social interaction gains, respectively, was in effect all day, every day over a school year[116,117] and thus delivered with a very substantially higher dose equivalent than in PACT-G.

Consistent with a dose explanation is the fact that the PACT-G additional data collection and video-conferencing sessions delivered in PACT-G produced about half the effect on parent–child dyadic interaction compared with the PACT (PACT-G ES: parent synchrony 0.54, child initiation 0.27; PACT ES: parent synchrony 1.22, child initiations 0.41). Against a dose explanation is our CACE analysis, which demonstrated that simply increasing the dose, assuming a linear dose–response relationship, would fail to produce an effect. In addition, the strong mediation found in the PACT from child dyadic interaction to autism symptom change, should have implied at least some effect on symptoms from our dyadic measures, whereas the current analysis showed otherwise. An alternative explanation could involve non-linear dose threshold effects on the transmission from dyadic interaction to independently observed symptoms, with the lesser ES on proximal measures not sufficient to mediate a change in the child autism symptomatology outcome. Such non-linear effects are commonly found in other treatment modalities,[120] but were not tested here.

Multicomponent complexity

Adaptation of the PACT intervention into PACT-G involved a significant increase in multicomponent complexity. The PACT-G intervention was based on a theoretical assumption that a multicomponent therapy delivered in parallel in two contexts could have an additive effect on child learning and outcomes. The rationale for this, as discussed, was that there would be an additive effect between home-based and education-based components of intervention on overall child outcomes. It is possible, however, that the provision of these therapy experiences with two different adults might, in fact, be confusing and contradictory for the autistic child, particularly because the therapeutic process could be at a slightly different stage in each context (see *Table 15*). While typically developing children, like adults, are used to synthesising diverse and contradictory experiences, it is possible that the combination of this disjunction along with the lower relative dosage, as above, may have made learning slower and less effective. In addition, the HSCs initially designed to maximise co-ordination between home and education therapy often proved impracticable (see *Chapter 8*, *Home–school conversations*). In the context of general child development, the hypothesis of additive effects in multicomponent interventions was tested in a significant meta-analysis of 213 universal multicomponent interventions for social and emotional skills development across community and education.[121] Against this starting hypothesis, this study did not find the expected benefit of multicomponent over single-component programmes,

speculating that the former are more challenging to implement and also less likely to ensure that critical components are delivered. In a number of ways, the learning points described above also possibly support this view in the current autism context, which could be a matter of consideration for policy and research planning going forward.

Remotely delivered sessions

PACT-G used remote virtual sessions to complement traditional face-to-face delivery. These sessions constituted 36% of home sessions and 34% of education sessions, usually delivered through video conferencing, but sometimes by telephone. In keeping with NHS guidance that recommends that remote sessions are not used to start treatment, all caregivers in PACT-G had two face-to-face sessions prior to any remote delivery. Online sessions needed to be conducted using a secure and NHS-approved video-call platform. For PACT-G, we needed the additional competency of screen-sharing to allow the caregiver and therapist to watch the therapy video together.

During the period of this trial (2016–19), remote online delivery of interventions was still relatively uncommon and posed some related challenges. The online sessions were more likely to be rated as inadequate by therapists (12% of sessions in the home and 11% in education compared with 1% and 2% respectively for in-person sessions). Given the already reduced dosage in this trial compared with previous work, this suggestion from therapists that remote sessions were not fully productive was a concern. Qualitative feedback from therapists about difficulties often related to technical problems in sharing videos. Therapists also reported that they required more regular and longer supervision to deal with the added aspects of online working, as face-to-face sessions were not the same as remote virtual sessions. This included thinking through therapeutic considerations, such as building a trusted relationship (which is an essential element of effective therapy), more regular summarising of techniques, and thinking through positioning in relation to camera and screen. For future practice, there are also challenges such as unequal access to digital technology; issues about whether or not vulnerable caregivers can and will engage with digital content; and personal preferences, as some caregivers did not find it as supportive to their needs.

However, on the positive side, there are some clear potential advantages for virtual delivery over traditional delivery mechanisms. Online delivery can be more convenient, with sessions arranged flexibly around working schedules and child-care arrangements. The video-recording and therapist sessions can be arranged at different times, enabling parent/caregivers to identify a quiet time to focus on their feedback. Teleconference PACT can be delivered in the comfort of the home/caregiver setting, removing the need for travelling, parking or waiting in waiting rooms. Online remote sessions can be more efficient and reduce stress for both professionals and families, releasing professional time, energy and resources to, for instance, see more children and conduct more sessions from their work or home work base. Remote sessions can feel personal and more representative, with the benefit of observing video footage of the child's daily interaction in their familiar setting. They can remove logistical and geographical barriers. These advantages have been exemplified during the current COVID-19 pandemic when, for much of the period, remote sessions have been the only available resource for many services and it is likely that this will remain as a feature of future service delivery post pandemic.[122,123]

We return to these issues in *Recommendations for research*.

Therapy environment

The therapy environment in both home and educational settings differed considerably from that of the original PACT. Home delivery can be subject to the distractions and interruptions of everyday family life. This was frequently observed in the fidelity ratings, as just 81% of therapy sessions met the fidelity criteria. Although parent feedback in the original PACT[33] showed that some parents would prefer home-based and video-conferencing sessions, in terms of convenience, scheduling and avoiding non-attendance at clinic, such acceptability does not necessarily equate to efficacy. Another evaluation that

included home-based intervention delivery gave some support for its effect.[9] Further assessment of the impact of parent-mediated video interventions delivered both online and in the home will be needed to more fully evaluate treatment efficacy and effectiveness for this form of delivery.

The educational setting proved considerably more challenging than initially hoped for this individualised and focused intervention, which required delivery to the child from a consistent adult (see below). The mobility in LSA roles and activities across classrooms and years in education, with 34.3% of trial children experiencing a change in LSA by mid-point, 37.9% a change between mid-point and end point, and 20% experiencing multiple change between these points, may be typical within an education environment at this time, but provides an obvious difficulty for delivery of an individualised therapy predicated on consistency of adult delivery. The proportion of session dose adherence achieved in the educational setting (67% of planned sessions were delivered) was also smaller than that in the home context. Although the manual fidelity of sessions sampled from those actually delivered was comparable to or even higher than that of home sessions, it is at least likely that the child's experience of those sessions will have been compromised by the changes in therapy partner.

A further consideration is the frequency of opportunities for parents and LSAs to practise the PACT-G intervention strategies. In the original PACT, and in PACT-G, parents were asked to practise the strategies learned in the clinic for 30 minutes per day at home. For PACT-G, the same request was made for parents at home, but in the educational setting this was slightly shorter for pragmatic reasons (30 minutes per day, three times per week). A feature of both PACT and PACT-G was that it was not objectively practicable to test adherence to these requests in either home or education contexts; however, informal feedback in PACT-G indicated that this kind of practice was not easy to achieve for LSAs alongside other curriculum demands and this was sometimes similar for parents at home.

Sample and measurement issues

One of the differences between the original PACT and PACT-G is the inclusion of primary school-aged children. For inclusion in the trial, the children's ability was capped at the minimally verbal level, meaning that this group's overall developmental level [Mullen's developmental quotient (DQ)] was considerably lower than that of the preschool sample (see *Table 9* and *Appendix 2*). About one-quarter of the school-aged sample met the criteria for ADOS-2 module 2, but nearly all these children had a DQ $\geq$ 2 SD below the mean; one-quarter of the preschool sample also met the criteria for module 2, but only half of these children had a DQ > 2 SD below the mean. The proportions in module 1 were relatively balanced for age group, although the school-aged group contained a slightly larger proportion of children in the module 1 (non-verbal) stratum. In sum, at baseline, the preschool subgroup had a wider range of ability, with a proportion ($\approx$ 10%) who were relatively higher functioning and met the criteria for module 2. The school-aged subgroup had lower cognitive functioning (by definition, given the inclusion criteria) and almost all had a low DQ ($\geq$ 2 SD below the standard *t*-score). It is notable that this was a cognitive DQ function effect, not an autism symptom severity effect; autism severity measured by the ADOS-2 CSS showed balance across the age groups (see *Table 10*). The potential impact of a lower DQ combined with age on intervention response may, therefore, be a further consideration, although, as above, there is no simple age cohort effect on the outcome estimates.

The ADOS-2 measurement system had evolved between the original PACT and PACT-G, particularly in relation to the module for minimal verbal development. This necessitated a more complex analysis of the ADOS-2 into three strata for this trial, based on end-point developmental module assignment. Considered by module, the treatment ESs show opposite directions by stratum: module 1 (verbal) showing a moderate positive effect of the PACT-G intervention, module 1 (non-verbal) showing a weak positive effect, and module 2 showing a moderate negative effect of treatment compared with TAU (see *Table 11*). This same diverging pattern by module is seen in the mechanism analysis, where there are opposite signs between ADOS-2 modules for the 'B paths' from mediator to outcome (e.g. see *Tables 27–29* and *Mechanism study*). Although this could have been a chance finding, the consistency of the pattern across the primary outcome and mechanism analyses is striking and suggests a need for

further consideration of the direction of treatment effects from this therapy across ADOS-2 module, age and DQ.

Implementation issues within education

The current *NHS Long Term Plan*[105] promotes the importance of the education context for community delivery of child and adolescent mental health interventions. However, this is an emerging field of practice and recent literature highlights some of the implementation barriers for cross-agency work of this kind.[124] As described in *Chapter 1*, there is a distinction to be made between health interventions delivered in a school context (e.g. PACT-G) and interventions embedded in the classroom curriculum. In a small number of studies (as above), the classroom-based approach seems to produce stronger effects, but the tailored approach to an individual child in school may still be theoretically and practically relevant for targeting individual needs effectively.

However, in a review of the implementation of interventions in education contexts, Lendrum and Humphrey[124] describe how the expectation on staff to implement an ever-increasing number of new interventions has resulted in scepticism about the permanence and practicability of interventions.[125,126] This is cautionary about any assumption that school-based delivery of health interventions is straightforward, and emphasises the need for clinicians and researchers to work collaboratively with schools, develop meaningful relationships with them and take into account the social ecology and organisational culture of the school in intervention planning.[13,94]

Delivering a RCT design in a complex environment, such as educational settings, inevitably places responsibility and pressure on the individuals delivering the intervention. For example, in our study, LSAs were asked not to disclose information about the components of the intervention that they were delivering to the child to maintain the blindness of the research team. Aspects of the trial such as this are contrary to their usual model of practice and support within a school setting.[127] However, rigorous testing of education-based intervention delivery is essential, and LSAs have reported a desire for further training in their roles, which would increase their profile in the school team, their self-efficacy and their job satisfaction.[128,129]

PACT-G does show that delivering a high-quality manualised therapy and rigorous experimental trial design in an educational setting is feasible, although there are real challenges, reflected by a lower sessional adherence of the PACT-G intervention and the HSCs and in the reduced effectiveness shown here in comparison with a clinic-delivered intervention. Practical barriers to implementation include the alteration of the child and staff member's routine in the educational setting, and the need for flexibility and time when working around other daily education priorities and in their delivery of the day-to-day curriculum. Dingfelder and Mandell[130] emphasise that, to be useful to practitioners, such information about training and the resource burden of interventions should be reported alongside outcomes. Some comparative evidence suggests improved outcomes for children receiving an intervention in mainstream preschool settings compared with other types of setting.[130] Our implementation seemed feasible across both settings, and one other study,[131] which randomised the same autism intervention between either mainstream or special school settings, found no evidence that this made a difference.

The dual delivery model (parents/carers and LSAs) included the idea that PACT-G would enhance a collaborative approach between home and school, with the clinical team as intermediaries/mediators providing support for both of these implementation contexts. Such home–school collaboration is commonly espoused as an ideal. Future work could explore, in more detail than was possible in this study, how this may best be achieved. The literature on home–school collaboration indicates that the most effective interventions are those characterised by a two-way exchange of information (e.g. parent–teacher action research teams, daily report cards, school-to-home notes)[132,133] and shared decision-making in the pursuit of mutually determined goals. However, due consideration needs to be given to the range of contextual factors that may facilitate or impede effective collaboration,

including policy/legislation, the relational history between a given family and school, and family and school cultural issues (e.g. congruence of beliefs, values and expectations).[133]

Conclusions

PACT-G tested an adaptation of the original, essentially clinic-delivered PACT intervention,[14,54,63] into a multicomponent parallel home/education intervention. The rationale was that provision of concurrent parallel intervention for the child, embedded in each of these settings, could have an additive effect on overall developmental progress and symptom reduction, thereby enhancing generalisation of treatment effects in a useful way. Therapy sessions were divided across home and educational settings, with the home-based dosage in practice at 60% of the original PACT, and included remote as well as in-person sessions.

The original PACT had demonstrated a mediated effect between the proximal intervention target of change in parent–child dyadic social communication and the child's social communication and symptoms in a generalised independent research context,[17,18] representing a generalisation of treatment effect in both behavioural and developmental senses across person, time and context (see *Chapters 1* and *9*). The mechanism study within PACT-G aimed to test this same mediation pathway within the home and educational settings, as well as testing the potential for additive mediated effects on research outcomes.

The results show that the therapy produced significant proximal dyadic social communication change between child and adults in both settings, at about half the ES seen with parents in the original PACT.[14] However, there was no generalised treatment effect on the primary outcome of autism symptoms in the outcome research assessment setting or either treatment setting, and also no effect on parent report of language and parent-/teacher-reported adaptive behaviour. There were, by contrast, significant positive secondary outcome effects with small to moderate ESs on improving parental self-reported well-being and teacher-/parent-reported child disruptive behaviour across home and educational settings.

The mechanism study demonstrated a replication, in both home and educational settings, of the original mediation found in PACT between the intervention effect on parental social communication and improved child dyadic social communication.[17] In addition, there was potential evidence of an overall 'dose–response' in the intervention on parental synchrony when compared across the PACT and PACT-G studies. In PACT-G, the intervention achieved 60% of overall session dosage compared with PACT, one-third of which were remote video-conferencing sessions, resulting in about half the proximal ES on parent and child dyadic communication compared with PACT. In the original PACT, this treatment effect on child social communication in the dyad, in turn, strongly mediated the overall treatment effect on child autism symptom outcomes. In PACT-G, there was some evidence of this latter mediation pathway, from the improvements found in child dyadic communication in both home and educational settings to change in child end-point BOSCC symptoms. However, this was not sufficient to lead to an overall treatment group effect on symptom outcome. Thus, although we have evidence of the transmission pathway operating as it did in the PACT, the degree of effect seems insufficient to give an overall symptom change. Given that the PACT-G effect on dyadic child–adult interaction is about half the size of that found in the PACT (see above), we have postulated that there may be a dose-threshold effect here on symptom change (albeit, in the light of our CACE analysis, this would need to have been a non-linear effect). We have also postulated explanations for the reduced power of intervention, in terms of environmental factors in home and school, or the impact of the complexity of the multicomponent delivery method.

Implications for health care

The trial has shown that it is feasible to implement a sophisticated video-feedback therapy not only with parents in the home setting (something we and others have demonstrated previously both for autism and other conditions),[76,107,111,120,134] but also in educational settings (something rarely attempted in this way; although see Adams *et al.*[43]). Given that current (i.e. 2021) health-care policy in the UK strongly supports the school-based implementation of mental health interventions, this is important

evidence of feasibility. The intervention was found to be acceptable and welcome in both settings and, although there were no improvements seen in child generalised autism symptoms or adaptation, there were demonstrated improvements in parental well-being and child disruptive behaviour, which are both of potential clinical value.

Although we have shown some effects in the education environment, it is important to note that the education component of PACT-G was designed not as an embedded standalone education intervention per se, but rather to extend and complement home-based practice by providing implementation of this health intervention in an educational setting (as in current health policy). We did not collect systematic measures of curriculum access or learning progress, and so cannot evaluate any change there; however, evidence from the comparator education-based interventions discussed[116,117] suggests that daily classroom-embedded curriculum-based intervention over a longer period than was the case for PACT-G may be needed to achieve noticeable change in school-based performance.

We note other evidence that multicomponent combined education and community interventions similar to PACT-G in other areas of child development have been found to add considerable complexity, and do not seem to confer an additive effect over a single-component intervention;[121,135] indeed, the increased complexity may reduce efficacy. Thus, a judgement on the clinical utility of this implementation in the educational setting will depend on whether or not the improved dyadic social communication and reduced disruptive behaviour, both important goals in their own right, are felt to be of sufficient benefit for the intervention investment. *Implementation issues within education* suggests additional modifications to PACT-G that could be considered in the future to enhance the embeddedness of the intervention within everyday school contexts.

Within the home setting, the flexible home-based and remote online delivery of the intervention was often welcomed by parents and is in line with many recent trends in health-care delivery, particularly accelerated by the COVID-19 pandemic. However, a caveat must be included as to whether or not intervention efficacy and effectiveness are diluted by these modes of delivery. Potential dosage and other contextual effects on intervention effectiveness are critical to consider in generalised implementation. Simple inference from demonstrated efficacy in a clinic-based setting to other modes of delivery cannot be assumed. Therefore, in the future, it will be prudent to advise a reversion to the full 18-session PACT dosage for home-based therapy (for which there was evidence of good efficacy; see *Chapter 1*); and carefully monitor any diluting effects on treatment fidelity or efficacy of online delivery (see *Recommendations for research*).

The mechanism analysis in this trial gives further support to part of the theoretical model of PACT-style video-aided intervention in autism, in that enhancement of parental synchronous responsiveness mediates the improved child dyadic social communication. However, there was no overall treatment effect on the symptom outcome measures. Despite this, we did find evidence for a mediation path from increased child dyadic response to reduced autism symptom severity on the BOSCC measure (although not on ADOS-2), in both home and educational settings. This is partial replication of the mediation model developed from the original PACT for a social communication intervention in autism. The finding supports the premise of early social communication-based intervention in aiming for downstream and generalised developmental effects.

Recommendations for research

Remote intervention

An innovation in this trial was the inclusion of alternate remote video-conferencing therapy delivery of sessions along with in-person delivery. Given the rapid current development towards provision of online therapies of all kinds, in mental health and elsewhere, it will be important to build on this trial in evaluating the efficacy of remote and online delivery. One RCT of fully online PACT delivery is in its early stages, and others are planned, including the blended approach used in PACT-G. These further studies of mode of delivery and dose will be critical going forward. As noted above, it cannot be assumed

that the efficacy of any therapy from a clinic context will be preserved in online implementation, and specific dose-finding and online implementation studies will need to be a priority across all interventions, including this one, to ensure that there is not a dilution of already evidenced effects in psychosocial treatments going forward.

Dosage threshold

In the light of the lack of transmission across contexts in this trial compared with the previous PACT intervention, and potential explanation of non-linear dose–response, it will be important to further investigate potential dose-threshold effects in the context of a complex intervention that involves video-delivered therapy across different contexts/settings. This recommendation goes hand in hand with further mechanistically focused and adaptive trials on the active components of autism treatments more generally – essential for the field to incrementally move towards more efficient and effective forms of intervention. It is also widely recognised for psychosocial interventions, including in the autism field, that 'one size does not fit all'.[136] Building further evidence for individualisation and improving the person-fit of different intervention approaches, and components thereof, will require further large-scale mechanistically informed trials, such as the current one and others that adopt 'new-generation', so-called adaptive trial designs, such as Sequential Multiple Assignment Randomised Trials (SMART).[137]

Multicomponent therapy in the education context

We have seen that there is only a small literature on rigorous trials of therapy for autism in the education context. Given the increasing focus on the education environment as a locus for treatments for improving mental health and well-being in general and in autism in particular, there needs to be more focus on designing and implementing such mechanistic trials in the UK across health and education. For interventions like PACT-G that rely on effective home–school collaboration, research could usefully focus on how this could be optimised.

Fundamental research in autism social development

PACT-G has acquired large-scale data on dyadic communication and autism symptom behaviours of autistic children across different contexts (e.g. at home with a parent, in education with a LSA, in a research environment with a researcher) and across three time points during a 1-year period in trial conditions. This represents, to our knowledge, a unique data resource internationally that could be used to study aspects of the social development of autistic children over time. One of the key perceived areas of difficulty for autistic children has been the generalisation of acquired and related skills across context, person and time – this data set provides an opportunity to study these aspects of skill development, and the potential for follow-up of this cohort into later development. Video-based child interaction data have been a mainstay of the developmental science investigation into early childhood autism and currently there is active interest in sharing such video material across research groups internationally; this large data set will be potentially of great value in that endeavour, the raw data lending themselves to analysis through methods that are the same as or different from those we have used.

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Sponsor and monitor

Manchester University NHS Foundation Trust, Central Research Office, Nowgen Building, Grafton Street M13 9WL. Telephone: 01612764125.

Trial adoption

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Final trial protocol

V6, July 2018; available from corresponding author (see *Appendix 5* for summary of protocol amendments during the trial).

Trial website

http://research.bmh.manchester.ac.uk/pactg/ (accessed June 2021).

Contributions of authors

Jonathan Green (https://orcid.org/0000-0002-0143-181X) (Professor, Child Psychiatry) conceived and led the design of the study and the application for funding, and was chief investigator. He was responsible for the drafting and revision of the report and for the final report submission.

Kathy Leadbitter (https://orcid.org/0000-0002-0744-2800) (Research Fellow, Psychology) conceived and designed the study, and managed and conducted the trials. She contributed to training, supervision and quality assurance of data collection and observational coding; the interpretation of results; and the writing of the report.

Ceri Ellis (https://orcid.org/0000-0002-8735-9993) (Research Associate, Psychology) contributed to the trial design, data collection, coding, data entry, and the writing and editing of the report. She also provided comments on drafts.

Lauren Taylor (https://orcid.org/0000-0002-1821-6163) (Research Assistant, Psychology) was responsible for overseeing the day-to-day running of the research aspects of the study at the London site. This involved participant recruitment and retention, data collection, data entry and data management.

Heather L Moore (https://orcid.org/0000-0002-2999-8332) (Research Assistant, Psychology) contributed to the design of the study and the evaluation of the feasibility and acceptability of the pilot study, and was responsible for data collection and data entry at the Newcastle upon Tyne site.

Sophie Carruthers (https://orcid.org/0000-0003-1616-415X) (Research Assistant, Psychology) contributed to the acquisition, analysis and interpretation of data; and contributed to the drafting of parts of the report.

Kirsty James (https://orcid.org/0000-0002-2657-8148) (Research Assistant, Statistics) co-analysed the quantitative data for the primary and secondary outcomes of the trial.

Carol Taylor (https://orcid.org/0000-0003-3317-2207) (Research Assistant, Speech and Language Therapy) contributed to the design of the study, contributed to the development of the intervention and its adaptation for schools, evaluated the feasibility and acceptability of the pilot study and contributed to the design. She also assessed and monitored the intervention fidelity and the reliability of measures, and contributed to the writing of the report.

Matea Balabanovska (https://orcid.org/0000-0002-3585-1935) (Research Assistant, Psychology) contributed to data acquisition (a substantial part of the BOSCC data, and other data collected during clinic assessments) and the management of BOSCC coding, including main coding processes, video allocations, reliability calculations and also had a minor contribution to the writing of the report (the breakdown of BOSCC videos).

Sophie Langhorne (https://orcid.org/0000-0003-1293-3310) (Research Assistant, Psychology) contributed to observational coding of DCMA data, quality assurance of observational video-coding data and the writing of the report.

Catherine Aldred (https://orcid.org/0000-0002-9686-8685) (Lecturer, Speech and Language Therapy) contributed to the design of the study, the development of the intervention and its adaptation for schools, older children and online use. She was responsible for the training and supervision of the RAs and therapists, the assessment and monitoring of intervention fidelity, liaising with stakeholders, resolving issues and data collection, and contributed to the writing of the report.

Vicky Slonims (https://orcid.org/0000-0003-3339-2365) (Consultant, Speech and Language Therapy) contributed to the original ideas, as well as the design and planning of the study, the development, delivery, measurement and evaluation of the therapy; and contributed to the interpretation and reporting of results, and the plans for implementation and dissemination.

Victoria Grahame (https://orcid.org/0000-0003-4541-7574) (Consultant, Clinical Psychology) was the clinical lead at the Newcastle upon Tyne site, provided weekly supervision to the therapists and also contributed to writing of this report.

Jeremy Parr (https://orcid.org/0000-0002-2507-7878) (Professor, Paediatrics) was the co-investigator and contributed to the funding application, trial design and delivery, attended local and trial co-investigator meetings, co-supervised the Newcastle upon Tyne research team and contributed to drafts of the final report.

Neil Humphrey (https://orcid.org/0000-0002-8148-9500) (Professor, Education) consulted on the adaptation for education/school settings and on the implementation-related aspects of the study.

Patricia Howlin (https://orcid.org/0000-0002-1804-6053) (Professor, Psychology) advised on study design and implementation, assessed treatment fidelity and contributed to the writing of the final report.

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Ann Le Couteur (https://orcid.org/0000-0001-9991-3608) (Professor, Child Psychiatry) contributed to the conception and design of the research and, as research lead for the Newcastle upon Tyne site, was responsible for the training and supervision of the RAs based in Newcastle upon Tyne. She also contributed to the training of RAs across all sites on some of the research measures, contributed to the interpretation of the study findings and to the writing and reviewing of the content of the final report.

Tony Charman (https://orcid.org/0000-0003-1993-6549) (Professor, Psychology) obtained funding, was involved in designing the study and then read, made revisions to and approved the final version of the manuscript.

Richard Emsley (https://orcid.org/0000-0002-1218-675X) (Professor, Methodology and Statistics) contributed to the design of the trial, co-conducted the statistical analysis and also contributed to reading, evaluating and approving the final report.

Andrew Pickles (https://orcid.org/0000-0003-1283-0346) (Professor, Methodology and Statistics) contributed to the design and implementation of the study and led the majority of the analysis and reporting.

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Data-sharing statement

We will make data available to the scientific community with as few restrictions as feasible, while retaining exclusive use until the publication of major outputs. All data request should be submitted to the corresponding author for consideration. Access to anonymised data may be granted following review.

Patient data

This work uses data provided by patients and collected by the NHS as part of their care and support. Using patient data is vital to improve health and care for everyone. There is huge potential to make better use of information from people's patient records, to understand more about disease, develop new treatments, monitor safety, and plan NHS services. Patient data should be kept safe and secure, to protect everyone's privacy, and it's important that there are safeguards to make sure that it is stored and used responsibly. Everyone should be able to find out about how patient data are used. #datasaveslives You can find out more about the background to this citation here: https://understandingpatientdata.org.uk/data-citation.

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Appendix 1 Acquisition of social communication over time and across contexts

As described in the protocol and main report, to examine the extent to which change in behaviour in one context, with one interaction partner, was carried through to change in behaviour in other contexts, with another interaction partner, PACT-G recorded naturalistic interaction with the parent and LSA at baseline, mid-point and end point and with the researcher at baseline and end point. These were coded blind to treatment group and assessment point by UK and US video-coding teams (both trained to reliability and meeting reliability criteria obtained from a random sample of multiply-rated tapes stratified by rater). Summary statistics are shown in *Table 34* and showed high levels of completeness.

Change in teaching assistant

Changes in the school-based interaction partner during the course of the trial occurred more frequently than expected. Eighty-five (34.3%) children experienced a change in LSA between baseline and the mid-point, and 94 (37.9%) children between the mid- and end point. Twenty-two children experienced changes at both time points.

Structural equation model

Generalisation was examined by fitting models of the form shown in *Figure 3*. The model was stratified as a two-group model by the BOSCC module and estimated by maximum likelihood. In the light of changes in interaction partner, the model included dummy variables to allow for a mean difference where a change in partner had occurred. The models were estimated in M*plus* using maximum likelihood estimation with robust standard errors, and standardised estimates are reported. At the mid-point, the path from parent to LSA is included but the reverse reciprocal was not significantly different from zero and, therefore, not included.

The model was run with the social communication subscale of the BOSCC. The length and setting of the interaction was considered to elicit too few RRBs to make their separate analysis reliable.

TABLE 34 Descriptives: mean (SD) BOSCC social communication subscales by time point and rater

	Baseline		Mid-point		End point	
Group	TAU	PACT-G	TAU	PACT-G	TAU	PACT-G
Researcher module 1	30.8 (6.24), *n* = 96	31.0 (4.90), *n* = 90			28.4 (7.30), *n* = 90	28.3 (7.29), *n* = 90
Researcher module 2	35.0 (12.1), *n* = 28	37.9 (9.36), *n* = 23			30.8 (13.2), *n* = 28	32.5 (13.0), *n* = 25
Parent module 1	28.0 (6.60), *n* = 95	27.9 (6.24), *n* = 87	27.1 (7.37), *n* = 79	27.1 (7.21), *n* = 85	26.9 (7.55), *n* = 83	26.1 (7.80), *n* = 89
Parent module 2	30.4 (11.9), *n* = 29	33.0 (10.2), *n* = 25	27.3 (9.54), *n* = 27	30.0 (11.7), *n* = 25	24.9 (9.26), *n* = 29	29.5 (11.6), *n* = 26
LSA module 1	29.3 (6.95), *n* = 91	29.4 (6.95), *n* = 92	27.2 (7.24), *n* = 87	27.5 (7.15), *n* = 85	27.1 (8.46), *n* = 84	27.5 (8.36), *n* = 86
LSA module 2	32.6 (11.2), *n* = 28	33.3 (10.4), *n* = 28	28.2 (12.1), *n* = 27	32.8 (13.3), *n* = 26	29.8 (12.3), *n* = 27	31.3 (13.2), *n* = 25

Results

Social communication subscale

Parent and researcher

First, we ran the model using only BOSCC data from interactions with a parent and a researcher. This model was just-identified with no residual degrees of freedom [root mean square error of approximation (RMSEA) of 0.000 and comparative fit index (CFI) of 1.00]. With both modules constrained to be equal, the path from the parent mid-point to researcher end point was significant ($p < 001$), with a coefficient of 0.67 (95% CI 0.51 to 0.82).

Teacher assistant and researcher

Second, for the LSA and researcher bivariate model, with one residual degree of freedom owing to the additional change of teacher variable, the model fit was good, with a RMSEA of 0.051 and a CFI of 0.958. The path from the LSA mid-point to researcher end point was significant ($p < 0.001$), with a coefficient of 0.49 (95% CI 0.31 to 0.67) for module 1 and a coefficient of 0.48 (95% CI 0.32 to 0.64) for module 2.

Parent, teacher and researcher

For the model combining all three contexts, model fit was good, with a RMSEA of 0.014 and a CFI of 0.997. Direct paths from the parent mid-point to researcher end point, parent mid-point to LSA mid-point, and LSA mid-point to researcher end point are given in *Table 35*. In addition to the direct path between the parent mid-point and researcher end point, there is an indirect path between the two through the LSA mid-point. The total path from the parent mid-point to researcher end point is also provided in *Table 35*, which incorporates the direct and indirect path.

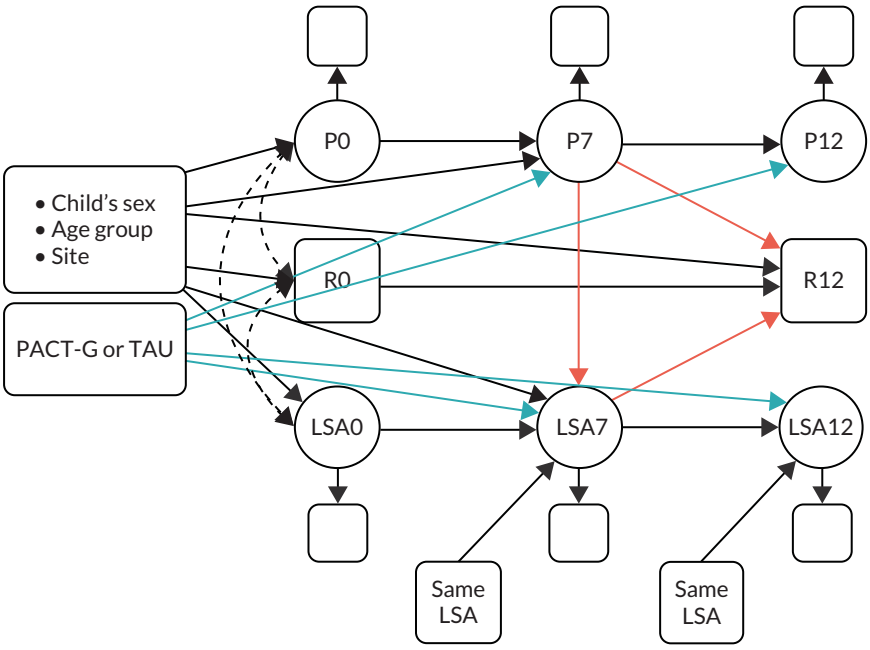

FIGURE 13 Structural equation model fitted to baseline, mid-point and end-point BOSCC data from parent, teacher and researcher. R, researcher; P, parent. Numerical suffix = month from start of therapy. Circles represent latent variables, squares represent observed variables. Light blue arrows represent the paths from intervention to BOSCC assessment, and orange arrows represent the generalisation paths tested. Covariation paths are dashed double-headed curved paths.

TABLE 35 Results of the SEM model for BOSCC social communication subscale across interactions with a parent, teacher and researcher (unstandardised effects constrained across module)

Path	Standardised coefficient	95% CI	*p*-value
Direct paths			
Parent mid-point to researcher end point			
Module 1[a]	0.86	0.47 to 1.26	< 0.001
Module 2[a]	0.82	0.40 to 1.23	< 0.001
Parent mid-point to teaching assistant mid-point			
Module 1[a]	1.01	0.49 to 1.53	< 0.001
Module 2[a]	0.74	0.51 to 0.96	< 0.001
LSA mid-point to researcher end point			
Module 1[a]	−0.20	−0.60 to 0.20	0.338
Module 2[a]	−0.25	−0.76 to 0.25	0.328
Indirect paths			
Parent mid-point to researcher end point (via LSA mid-point)			
Module 1	−0.20	−0.61 to 0.21	0.347
Module 2	−0.19	−0.58 to 0.20	0.349
Total paths			
Parent mid-point to researcher end point			
Module 1	0.67	0.51 to 0.82	< 0.001
Module 2	0.63	0.42 to 0.84	< 0.001

a Standardised estimates are reported.

Summary

These analyses were set out to explore the extent to which children's social communication, as measured by the BOSCC, generalised across contexts from interaction with familiar adults (i.e. parent and LSA) to an unfamiliar setting and unfamiliar adult (i.e. the researcher). This was tested using the social communication subscale of the BOSCC. The initial model, considering only two contexts at a time, showed that social communication with a parent generalised to later interaction with a researcher, such that increased social communication skills in interactions with the parent transferred to improved social skills with the researcher. This appeared also to be true for social communication during interactions with a LSA. In each of these analyses, the generalisation arising from the excluded interaction partner may be considered an omitted confounder. A trivariate analysis with all three raters is required to confirm the effects. When all three contexts were included in the same model, although the generalisation of social communication from parent to researcher remained (both directly and overall including the indirect effect), the effect from LSA to researcher was no longer significant. Generalisation was also shown to be significant for the parent mid-point to LSA mid-point. This analysis provides supportive evidence for cross-context generalisation in behavioural change, particularly from the home setting to educational setting. However, although we account for both measurement error and baseline confounding, our analyses have not yet eliminated the possible confounding effects of context general shared developmental change in autism severity as a source of bias. We hope to further develop our analyses of the mechanisms of cross-context and cross-behavioural (DCMA/ADOS-2) change to address this source of developmental confounding.

Appendix 2 Breakdown of Autism Diagnostic Observation Schedule, Second Edition module by developmental quotient

TABLE 36 Breakdown of ADOS-2 module by DQ

Baseline	Preschool aged (*N* = 151)	School aged (*N* = 97)
Module 1 (non-verbal), *n* = 110	63	47
Visual reception DQ, mean (SD)	44.7 (12.0)	27.4 (8.6)
Fine motor DQ, mean (SD)	44.8 (11.4)	26.5 (8.9)
Module 1 (verbal), *n* = 77	52	25
Visual reception DQ, mean (SD)	54.2 (13.2)	41.0 (16.4)
Fine motor DQ, mean (SD)	56.6 (13.0)	42.4 (16.0)
Module 2, *n* = 61	36	25
Visual reception DQ, mean (SD)	73.9 (21.9)	48.4 (18.2)
Fine motor DQ, mean (SD)	67.3 (14.4)	49.2 (15.7)
All modules	151	97
Visual reception DQ, mean (SD)	54.9 (19.0)	36.2 (16.3)
Fine motor DQ, mean (SD)	54.2 (15.5)	36.3 (16.2)

Appendix 3 Deliverability project plan: January 2016

Chief Investigator	Prof Jonathan Green
Project ref number	Ref: 13/119/18
Project title	The Paediatric Autism Communication Trial - Generalised (PACT-G)

- Stop/Go decision points will form part of your contract with the Department of Health, and will be used by the EME Programme to review whether funding should continue at each identified stage of the project.

- Stop/Go decision points will be applied if there is a realistic expectation (other than failure to deliver) that a project could be discontinued at an appropriate stage.

- This table identifies the stages of the project and the criteria used in deciding whether the project should progress. The criteria should be robust and measurable. You will be expected to provide a report at stop/go points outlining whether the criteria have been met.

Stop/Go Decision Point 1 (S/G 1)
School buy-in

Time from start to S/G 1 (months)	12 months
Expenditure within S/G 1 (£)	£560,118
Estimate of meeting S/G 1 criteria (%)	40%

Milestones for S/G 1 (max 250 words, bulleted)
• At the end of the pilot phase of the trial, a minimum of 27 schools (9/site) will have been engaged with the school buy-in protocol. • Rationale: our sample have severe autism and at therefore least 50% will be in specialist autism schools with most of the others in specialist autism units within mainstream education (data from our previous PACT trial and its follow up study). Such schools and units are well known in our respective areas and can be further identified from organisations such as the National Autistic Society (http://www.autism.org.uk/directory). For instance in the North West site there are 4 specialist schools and up to 20 specialist units in mainstream schools; since placements will be skewed towards the specialist school environment, the majority of our participants are likely to be in a maximum of 18 schools in the area. We will thus be contacting about 50% of these within the pilot period – and the same will be true of the other sites. • The engagement protocol consists of; i) initial contact from senior therapists via the head teacher; ii) initial information pack explaining the study with telephone follow-up to discuss school-specific issues; iii) research team school visit with detailed presentation and Learning Support Assistant (LSA) orientation training; iv) written agreement from schools to take part in the study protocol in principle and/or specific agreement to take part with a recruited child.

Success criteria and target values (max 250 words, bulleted)
• Completion of engagement protocol and written confirmation of agreement to participate from 11/27 (>40%) of the schools approached during the pilot phase. • Rationale: Our agreed deliverability criteria states that, to achieve the recruitment target, less than 15% of the population pool need to be recruited and randomised. Assuming a worst-case scenario of the loss of 60% of patients approached due to lack of school buy-in, we would therefore still only require just 38% of the available patient pool to be recruited in order to achieve our recruitment target - a figure we consider still very achievable and that was exceeded in our PACT trial. Thus we set our minimum necessary criteria for progression at 40% school buy-in.

Reports required during S/G 1	Report of the procedure of contacting engaging schools, the outcome of the engagement and record of agreement letters received

Stop/Go Decision Point 2 (S/G 2)
Progression from identification to treatment

Time from start to S/G 2 (months)	12 months
Expenditure within S/G 2 (£)	£560,118
Estimate of meeting S/G 2 criteria (%)	25%

Milestones for S/G 2 (max 250 words, bulleted)
• By the end of the six-month external pilot phase (month 12 of the study) we will have identified, assessed for eligibility and consented sufficient cases for us to proceed to treatment in 24 cases (eight in each site).

Success criteria and target values (max 250 words, bulleted)
• Criteria for success is that <75% of identified and eligible patients are lost between identification and treatment initiation for reasons unrelated to school buy-in (itself addressed in SG1); or that a maximum of 96 cases have needed to be ascertained to achieve the pilot cohort of N=24. • Rationale: Our agreed deliverability criteria were that, to achieve the recruitment target, less than 15% of the available population pool need to be recruited and randomised. In our previous PACT trial,[6] which had the same recruitment protocol, 90/242 (37%) of cases identified as eligible were excluded before randomisation; and none lost between randomisation and treatment initiation. These exclusions before randomisation mainly related to non-consent, but also included moving out of area, loss of contact and other reasons. This trial over-recruited against target. We have no reason to consider that the exclusion rate would be higher in this current trial, but assume for the purpose of a worst-case scenario that 75% of

	cases are lost between identification and randomisation. Even in this event recruitment to target would remain feasible since we would still need to identify then only 60% of the available patient pool. For the pilot phase we thus set minimum necessary threshold of 25% of ascertained cases progressing through to treatment. Since we achieved 63% to randomisation in the PACT trial, this is very achievable.

Reports required during S/G 2	Report identifying for the pilot phase: i) number of cases identified and ascertained as eligible; ii) number of cases proceeding through to treatment initiation.

Appendix 4 The PACT-G treatment fidelity rating scale

A. General Therapeutic Procedures

1. Review of Home/School Practice

   0 The therapist did not review the home/school programme or the parent/LSA's progress with the communication goals set.

   1 The therapist asked the parent/LSA to recall communication goals set in the last session and written in the home/school programme, and reviewed the parent/LSA's progress with the goals in the home/school practice sessions.

2. Use of Video Excerpts to Illustrate Parent/LSA Achievement of their Goals

   0 The therapist did not show appropriate positive excerpts to illustrate achievement of parent/LSA communication goals, or selected excerpts and made comments on the parent/LSA-child communication that were vague or not related to the communication targets set.

   1 The therapist showed appropriate video excerpts highlighting parent/LSA achievement of the communication targets set and elicited positive parent/LSA comments on change in parent/LSA communication style and child response.

3. Use of Video Excerpts as the Basis of Feedback Discussions

   0 The therapist did not adequately use positive video clips to promote discussion of the parent/LSA-child interaction, the focus of the stage and the strategies, AND/OR focused too much on negative clips rather than positive ones.

   1 The therapist used appropriate positive video clips to facilitate parent/LSA reflection on the parent/LSA-child interaction, leading to the discussion of stage specific strategies and the focus of the stage.

4. Eliciting Parent/LSA Feedback following the Video Playback

   0 Limited therapist use of probes to elicit parent/LSA feedback. Did not use enough cascading probes to encourage the parent/LSA to reflect on the interaction and her/his role in it, or to be sure the parent/LSA understood the communication strategies and concepts being discussed.

   1 The therapist elicited sufficient feedback from the parent/LSA. Cascading probes were effectively used to encourage parent/LSA reflection on the interaction and to determine the parent/LSA's understanding of the communication strategies and concepts under discussion.

5. Response to Parent/LSAs Focus

0 No attempt to recognise or respond to parent/LSA's own observations and descriptions.

1 The therapist recognised and responded appropriately to parent/LSA's own descriptions of the interaction when reviewing the video; the therapist used the parent/LSA's own vocabulary and language to describe observations and strategies.

6. Structuring the Session

7. Pacing

0 Little or no structure to the therapy time and/or there were significant peripheral or unproductive digressions that were not handled well by the therapist.

1 The therapist structured session well, so there was a clear beginning, middle and closing of the session. Peripheral and unproductive digressions were either very uncommon, or handled well by the therapist.

0 The therapist's pacing and timing was either too rushed or not appropriately adapted to the parent/LSAs pace. The therapist may have moved on too quickly to another goal, giving the parent/LSA insufficient time to reflect and describe the changes in observed interaction or parent/LSA-child responses.

1 The therapist's pacing and timing was appropriately adapted to the parent/LSA's pace, giving sufficient time for the parent/LSA to reflect, participate and contribute observations to the discussion about the videoed interaction.

B. Interpersonal Effectiveness

8. ***Sensitivity Skills***

0 The therapist did not sufficiently reflect or rephrase what the parent/LSA explicitly said, or showed problems responding to implicit or subtle parent/LSA communication. The therapist missed opportunities to respond to the parent/LSA's comments or responses during feedback.

1 The therapist generally seemed to grasp the parent/LSA's meaning as reflected by both what the parent/LSA explicitly said and what the parent/LSA communicated more subtly, and re-capped appropriately reflecting the parent/LSA's comments or descriptions.

9. Validation and Positive Feedback

0 The therapist missed opportunities to reinforce or praise parent/LSA achievements and insights throughout the session.

1 The therapist recognised and appropriately reinforced or praised parent/LSA achievements and insights throughout the session.

C. Specific Communication Therapy Techniques (score appropriate stage only)

1. ***10.1 Focus on shared attention (use for PACT-G stage 1)***

The emphasis of this stage is on the development of shared attention between the parent/LSA and child.

0 The therapist did not adequately focus on the concept of shared attention and the stage 1 strategies that promote it, and/or the discussion of stage 1 strategies was not adequately linked to the development of shared attention.

1 There was adequate focus on the concept of shared attention. Appropriate stage 1 strategies were discussed and were adequately linked to the resultant changes in child responses and the development of shared attention.

2. ***10.2 Focus on parent/LSA synchronous communication style (use for PACT-G stage 2)***

The focus of stage 2 is the development of parent/LSA's synchronous communication. The aim is to decrease parent/LSA's verbal demands on the child and replace these with comments aimed at facilitating and sustaining the child's communication responses. The parent/LSA's non-verbal responses and language become synchronous with the actions and intentions of the child.

0 There was not adequate focus on the concept of synchrony and the impact of the parent/LSA's communication style on the child's responses, AND/OR Stage 2 strategies were discussed but not adequately linked to the resultant responses of the child and the concept of synchrony.

1 There was adequate focus on the impact of the parent/LSA's communication style on their child's responses. Types of communication which elicited increased responses in the child were identified and discussed. Stage 2 strategies were appropriately introduced and adequately linked to the concept of parent/LSA synchrony.

10.3 Focus on Language Input (use for PACT-G stage 3)

Stage 3 focuses on ensuring that the language input the parent/LSA is giving the child maximises the child's opportunity to understand what they are hearing and to develop their language comprehension.

0 Lack of adequate focus on the identification of language mapping/ modelling opportunities and/or discussion of the appropriate level of language complexity for the child, AND/OR Stage 3 strategies introduced but not adequately linked to the development of the child's comprehension.

1 Therapist focuses session on the identification of opportunities for language mapping/modelling and/or discussion on the appropriate level of language complexity to use with the child. Stage 3 strategies are appropriately introduced and linked to the child's developing understanding of language.

10.4

Focus on predictable routines (use for PACT-G stage 4)

10.5

Focus on Communication initiation techniques (use for PACT-G stage 5)

Stage 5 focuses on the parent/LSA eliciting child intentional communication acts. The parent/LSA purposely uses pause and openings for the child to fill with a non-verbal or verbal response and includes the use of subtle teasing. This stage extends to the therapist facilitating the parent/LSA in eliciting child initiation for a range of communication functions, seeking/ directing adult attention, requesting, negating, acknowledging.

10.6

Focus on language extension, elaboration and reciprocal conversation (for PACT-G stage 6)

Stage 6 focuses on the therapist assisting the parent/LSA to elaborate on and expand the child's expressive language repertoire i.e. finding opportunities to expand their utterances with semantically contingent information. The aim of this stage is to develop and extend child semantics and syntax. The therapist should also facilitate the parent/LSA in reciprocating in verbal interactions to develop mini-conversations that constitute at least 4 element conversational turns.

0 The therapist does not adequately focus on identifying opportunities for parent/LSAs to extend and elaborate on the child's language and does not adequately discuss techniques for

doing this. The therapist's attempts to identify opportunities for verbal reciprocal interchanges between parent/LSA and child were incomplete or inadequate.

1 Therapist focused the session on identifying opportunities and discussing techniques to extend and elaborate the child's language. An adequate variety of child language extension techniques and opportunities for verbal reciprocal conversations were identified with the parent/LSA.

Stage 4 focuses on the parent/LSA using consistent, repetitive, familiar language routines and social routines commensurate with the child's level of language understanding. This is a phase of consolidation of all the preceding stages covering the use of repetition in play, interaction, language (e.g. repetitive rhymes, play themes, interactive routines). It also acts as a bridge to later stages, setting up predictable language routines in which the child may use their expressive language as it develops.

0. Lack of adequate feedback on the parent/LSA's use of consistent language, routines and play. Lack of adequate linking of the use of repetition to facilitate child verbal understanding and to set up predictable interactions in which the child may begin to use their expressive language in later stages.
1. Therapist focuses the session on identifying and encouraging the parent/LSA's appropriate use of consistent language, familiar routine and play. The therapist identifies opportunities for consolidation and elicits parent/LSA understanding of the way repetition facilitates child comprehension and processing, and may provide opportunities for child expression in later stages.

11. No or very limited discussion of techniques or games parent/LSA can use to create opportunities for child communication initiation, AND/OR No or limited discussion of the range of communication functions the child uses/could develop.

12. Therapist focused the session on identifying opportunities for child communication initiation and on discussion of techniques and games the parent/LSA can use to facilitate this. The therapist adequately discussed the range and function of the child's communication responses and initiations.

Setting of mutually agreed goals for the Home/School Programme (PACT-G all stages)

0 Goals were assigned with limited collaboration or were vague or incomplete, AND/OR goals set did not reflect the discussions in the session.

1 There was adequate setting of mutually agreed goals that included specific communication targets arising from the parent/LSA's observations, and insights achieved during the feedback session.

Written Home Programme (PACT-G all stages)

0 No written goals in the home/school programme, or goals were unclear and/or not written in words the parent/LSA uses or understands AND/OR sections summarising the achievements in the session and giving practical examples of goals were not adequately completed.

1 Goals set in the session were written clearly in the home/school programme, in words the parent/LSA uses/understands. The home/school programme adequately summarised the achievements in the session and gave ideas of how the parent/LSA might practice the goals at home/school.

Deviation from Manual
Were there any ***other*** *deviations from the standard approach measured by this scale?*

If so do you think they were justifiable? (Do not include anything already scored)

0 There were deviations and they were not justifiable (explain below)

1 There were no deviations **OR** any deviations were justifiable (explain below)

13. Details of Deviations:

D. Overall Ratings and Comments

14. Appropriate Use of Materials

0 The therapist's selection of materials did not facilitate interaction.

1 The therapist's selection of materials did facilitate interaction.

15. Room Environment

Did the room setting meet the requirements set out in the Standard Operating Procedures?

0 No

1 Yes

16. Quality Time

Was there adequate opportunity for parent/LSA- therapist discussion?

0 No 1 Yes

PACT-G Fidelity Rating: adapted for use in PACT-G by Dr Catherine Aldred, Prof Jonathan Green from the Cognitive Therapy Scale (Jeffrey Young & Aaron Beck, modified by Leech, Harrington and Dubicka, 2002).

Appendix 5 Trial protocol amendments

A substantive change to the protocol following trial commencement was the alteration of the nominated primary outcome – from BOSCC to ADOS-2 in the final analysis plan. A change to the primary outcome was first proposed in October 2017, following new published data from our group[14] and others, indicating that ADOS-2 measurement could be sensitive to change from the intervention, and in our study showing sustained change for 6 years after intervention end. The initial alteration proposed was to use a combined BOSCC/ADOS-2 outcome metric. Following discussion with the funders, this change was modified to using the ADOS-2 measure alone, with BOSCC as a secondary outcome. This change was agreed with the TSC, reflected in the final version of the trial protocol (version 6, July 2018) and in the subsequently published trial protocol paper,[6] as well as the final statistical analysis plan, finalised and lodged before data-lock and data analysis (see *Chapter 7*, *Aims of formal analysis*).

TABLE 37 Changes made to the trial protocol following trial commencement

Old version	New version	Date	Amendment
1.0	2.0	6 October 2016	Addition of parent questionnaires in sections 8.2 and 8.3
2.0	3.0	18 November 2016	• Finalised list of assessments in section 8.2 and add schedule table in 8.3 • Added safeguarding to exclusion criteria • Updated score on SCQ inclusion • Updated data collection and Clinical Trials Unit information • Added exclusion criterion for non-agreement by schools
3.0	4.0	2 February 2017	• Throughout protocol: change to timing of mid-point and end-point assessments • Section 6.2: addition of exclusion criterion • Section 7.2: clarified a maximum of 12 therapist–LSA sessions • Section 8.2: deletion of Epworth Measure of Daytime Sleepiness • Section 8.2: inclusion of DBC • Section 15: information added about ethics approvals
4.0	5.0	1 September 2017	• Section 6.2: further details added about *p*-value-level inclusion criterion • Section 7.2: updated details of treatment protocol • Section 8.1: updated primary outcome measure • Updated CONSORT flow diagram • Section 9: statistical analyses – changes as a result of proposed change to primary outcome • Section 15 – updated ethics approvals
5.0	6.0		• Updated contact details • Section 8.1: updated primary outcome measure • Section 9: statistical analyses – changes as a result of proposed change to primary outcome

Section numbers refer to sections of the trial protocol.

EME
HSDR
HTA
PGfAR
PHR

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