THE LANCET
Psychiatry

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Creswell C, Taylor L, Giles S, et al. Digitally augmented, parent-led CBT versus treatment as usual for child anxiety problems in child mental health services in England and Northern Ireland: a pragmatic, non-inferiority, clinical effectiveness and cost-effectiveness randomised controlled trial. *Lancet Psychiatry* 2024; published online Feb 6. https://doi.org/10.1016/S2215-0366(23)00429-7.

Supplementary Materials

Table of Contents

Throughout this document the following acronyms are used:

OSI +TS: Online Support and Intervention with Therapist Support
C-TAU=child mental health services treatment as usual.

Supplementary Table S1: Demographic and clinical characteristics of parents/carers who took part in post-treatment qualitative interviews

Variable		OSI+TS (n=12)
Parent gender	Woman	11
	Man	1
Parent age	32-37 years	4
	38-42 years	4
	43-48 years	4
Parent ethnicity	White British	9
	Any other White	3
	Black and ethnic minority	0
Parent education	School completion	2
	Further education	4
	Higher education	0
	Postgraduate	6
Marital status	Married	6
	Single	2
	Separated	3
	Divorced	1
Household Income (net p.c.m)	Benefits or <£900	5
	£901- £2500	0
	>£2500	6
	Prefer not to say	1
Location	London	2
	Southern England	5
	Central England	1
	Northern England	3
	Not known	1
Child age	5-8 years	6
	9-12 years	6
Child gender	Girls	7
	Boys	4
	Non-binary	1
Child ethnicity	White British	8
	Any other White	2
	Black and ethnic minority	1
	Prefer not to say	1

Note. p.c.m. = per calendar month. OSI+TS=Online Support and Intervention for child anxiety plus therapist support.

Supplementary Table S2: Demographic and clinical characteristics of clinicians (n=10) taking part in qualitative interviews

Variable		(n=10)
Clinician gender	Woman	7
	Man	3
Professional background	Educational Mental Health Practitioner	4
	Children's Wellbeing Practitioner	1
	Mental Health Support Worker	2
	Counsellor	1
	Assistant Psychologist	1
	Link worker (in training)	1
Years qualified	0-1 year	5
	1-2 years	0
	2-3 years	1
	4-5 years	0
	5+ years	1
	Not applicable (no professional qualification)	2
	Not known	1
Location	London	1
	Southern England	5
	Central England	1
	Northern England	3
Service	Clinic-based	5
	School-based	5
Number of cases	1	7
	2	2
	3	0
	4	1

Supplementary Table S3: Demographic information provided by therapists who delivered treatment in the study.

	n	%
Professional background		
Educational Mental Health Practitioner (EMHP)	55	29·26
Trainee EMHP	9	4·79
Child Wellbeing Practitioner (CWP)	33	17·55
Trainee CWP	15	7·98
Assistant Psychologist	11	5·85
Psychotherapist	4	2·13
Unspecified Trainee	4	2·13
Social Worker	3	1·60
Psychiatric Nurse	3	1·60
Psychological Wellbeing Practitioner (PWP)	3	1·60
Trainee PWP	2	1·06
Clinical Psychologist	3	1·60
Mental Health Support Worker	2	1·06
Emotional Wellbeing Practitioner	2	1·06
Registered Nurse	2	1·06
Counsellor	2	1·06
CBT Therapist	2	1·06
Emotional Health Worker	1	0·53
Trainee Clinical Psychologist	1	0·53
Trainee Counsellor	1	0·53
Trainee Social Worker	1	0·53
Cognitive Behaviour Psychotherapist	1	0·53
Psychiatric Nurse and Counsellor	2	1·06
Counsellor and Psychotherapist	2	1·06
PWP and CWP	1	0·53
EMHP and Psychologist	1	0·53
EMHP and Counsellor	1	0·53
No information	21	11·17
Mean age (SD)	33·87 (8·76)	
Ethnicity		
White British	115	61·17
Irish	4	2·13
Any other White background	14	7·45
Mixed White and Black Caribbean	5	2·66
White and Black African	1	0·53
White and Asian	1	0·53
Asian or Asian British	7	3·72
Pakistani	4	2·13
Any other Asian background	2	1·06
Black or Black British African	9	4·79
Caribbean	2	1·06
Any other Ethnic group	1	0·53
I do not wish to state my Ethnicity	2	1·06

No information	21	11·17
Years qualified		
Less than a year	32	17·02
1 to 3 years	45	23·94
3 to 5 years	9	4·79
5 or more years	14	7·45
No information	88	46·81
Years in practice		
Less than a year	25	13·30
1 to 3 years	42	22·34
3 to 5 years	9	4·79
5 or more years	17	9·04
No information	95	50·53
Working arrangement		
Full time	149	79·26
Part time	18	9·57
No information	21	11·17
Previously delivered parent-led CBT for child anxiety problems		
Yes	122	64·89
No	45	23·94
No information	21	11·17
Mean no. of families therapists have used this approach with (sd)	12·06 (15·64)	
Undertaken training in psychological treatments		
Yes, within my professional training	107	56·91
Yes - formal qualification beyond any professional training	13	6·91
Yes - informal courses e.g. workshops	22	11·70
No	25	13·30
No information	21	11·17
Preferred way of working with children with anxiety problems		
Cognitive Behaviour Therapy (CBT)	132	70·21
Family Therapy	2	1·06
Child Psychotherapy	1	0·53
Brief Solution Focused Therapy	6	3·19
Other*	25	13·30
No information	22	11·70

*Other: Low Intensity CBT (14), New to role - no preferred treatment currently (2), An integrative approach (1), CBT and solution focused (1), CBT Informed (1), Combination of list of the above (1), Evidence-Based Psychological Interventions for the Education Setting (1), Integrative; informed by CBT, behavioural and systemic approaches (1), Only trained in Low Intensity CBT (1), Psychoeducation and solution focused. (1), Solihull Parenting Approach (1).

Supplementary Materials S4: Unit costs and costs of school absence

Unit costs

Unit costs for healthcare and social service use were obtained from the UK National Cost Collection Data 2020/21 [1] and the Unit Costs of Health and Social Care 2021, produced by the Personal Social Services Research Unit (PSSRU) [2]. Medication unit costs were taken from the Prescription Cost Analysis for England 2020/21 [3], with an out-of-pocket prescription cost of £9.15 used for each medication prescribed to parents [4]. The direct school opportunity cost of child missed school days was estimated by dividing the 2020/21 per pupil cost for children in English schools [5] by the number of school days per year [6]. The indirect lifetime loss of human capital, in terms of future lost earnings, associated with a missed school day was estimated using the model below [7]. The indirect opportunity cost of parent time, to value missed work due to their child's anxiety problems, time spent in the intervention and associated travel time, was obtained from national average wage rates [8]. All costs were expressed in pounds sterling at 2020/21 prices. Where necessary, NHS and PSS prices were adjusted for inflation using the NHS cost inflation index [9], with all other prices adjusted using the retail price index [10]. The specific unit cost applied to each resource used is detailed in Table S5 below.

Cost of School Absence - loss of future earnings

When costing childhood anxiety from a societal perspective, we took the cost of school absence caused by anxiety problems into account. At least two sources of the societal cost related to school absence should be considered: 1) the unrealised pre-paid educational spending and 2) the loss of human capital. The former is usually included in economic evaluations. We obtained the unit price as £33.1 per absent day by dividing the 2020/21 UK national school funding per pupil (£6,280 in 2020/21 price) by the typical school days in the UK (190 days) [11]. The loss of human capital due to school absence was one part of the societal cost that has not been widely accounted for in previous economic evaluations. Labour economics literature has referred to human capital as one's life-cycle earning profile and documented the role of education in human capital formation [12]. In our study, we quantified the daily human capital loss associated with anxiety-related school absence using a model recently proposed by Psacharopoulos[7] et al. (2021).

In their framework, the human capital loss of one year of absence in school, L, is captured by

$$L = PV\ (Y \times a \times r),$$

where PV (·) is the present value function, Y is the average annual earning, a is the fraction of a school year that someone missed, and r is the return of one year of schooling. To obtain the human capital loss in the setting of the UK, we inserted the British values for the parameters in this model. We used the UK median gross annual earnings, £26,055 (2021 price), for Y [13]. To estimate the human capital loss per missed school day, we set a = 1/190. Note that Psacharopoulos[7] et al.'s (2021) original model also included the total number of students and a remote learning alternative. We ignored these two parameters due to the different nature of our research. Consistent with Psacharopoulos[7] et al. (2021), we considered the return rate of education, r, to be 8%. We assumed average British workers receive earnings for 45 years and discounted their future earnings with a 3% discount rate. As a result, the daily human capital loss turned out to be £279.95 per missed day of school.

Supplementary Materials S5: Unit costs (2020/21 prices)

Item	Unit cost	Source	Notes
A&E	£296.87	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Weighted mean of all A&E attendances.
Adult inpatient, long stay	£5,141.31	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Weighted mean of non-Paediatric Elective Inpatients and Non Elective Long Stay.
Adult inpatient, short stay	£1,699.85	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Weighted mean of non-Paediatric Elective Inpatients and Non-Elective Short Stay.
Adult outpatient, face-to-face	£226.23	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Weighted mean of non-Paediatric Consultant Led Non-Admitted Face-to-Face Attendance, First.
Adult outpatient, non-face-to-face	£168.93	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Weighted mean of non-Paediatric Consultant Led Non-Admitted Non-Face-to-Face Attendance, First.
Ambulance	£268.87	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Weighted mean of all ambulance activities.
Audiology, adult, face-to-face	£263.71	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Audiology, Consultant Led Non-Admitted Face-to-Face Attendance, First.
Audiology, adult, non-face-to-face	£122.68	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Audiology, Consultant Led Non-Admitted Non-Face-to-Face Attendance, First.

Item	Unit cost	Source	Notes
Audiology, child, face-to-face	£366.91	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Paediatric Audiological Medicine, Consultant Led Non-Admitted Face-to-Face Attendance, First.
Audiology, child, non-face-to-face	£133.49	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Paediatric Audiological Medicine, Consultant Led Non-Admitted Non-Face-to-Face Attendance, First.
Ophthalmology, face-to-face, adult	£213.13	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Ophthalmology, Consultant Led Non-Admitted Face-to-Face Attendance, First.
Ophthalmology, non-face-to-face, adult	£143.56	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Ophthalmology, Consultant Led Non-Admitted Non-Face-to-Face Attendance, First.
Ophthalmology, face-to-face, paediatric	£225.47	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Paediatric Ophthalmology, Consultant Led Non-Admitted Face-to-Face Attendance, First.
Ophthalmology, non-face-to-face, paediatric	£195.49	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Paediatric Ophthalmology, Consultant Led Non-Admitted Non-Face-to-Face Attendance, First.
Child inpatient, short stay	£1,327.83	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Weighted mean of Paediatric Elective Inpatients and Non-Elective Short Stay.
Child inpatient, long stay	£5,541.72	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Weighted mean of Paediatric Elective Inpatients and Non Elective Long Stay.
Paediatric outpatient, face-to-face	£267.92	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Weighted mean of Paediatric Consultant Led Non-Admitted Face-to-Face Attendance, First.

Item	Unit cost	Source	Notes
Paediatric outpatient, non-face-to-face	£211.79	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Weighted mean of Paediatric Consultant Led Non-Admitted Non-Face-to-Face Attendance, First.
Paediatrician, face-to-face	£385.13	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Paediatrics. Consultant Led Non-Admitted Face-to-Face Attendance, First.
Paediatrician, non-face-to-face	300.90	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Paediatrics. Consultant Led Non-Admitted Non-Face-to-Face Attendance, First.
Community and social care			
Advice lines	£0	Self Help UK. 2023. Self Help Groups & Contacts. https://www.selfhelp.org.uk/directory (Accessed 14 Feb 2023).	There are a variety of free to use self-help charity groups, providing support in a variety of areas.
Children & Adolescent Mental Health Services (CAMHS) nurse	£160.29	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Community Health Services. Nursing Services for Children. CAMHS nurse assumed to have the same unit cost as a Community children's nurse.
Citizens Advice Bureau	£18.47	Creswell, Violato (14)	Appendix. Unit costs. 2013/14 prices (£16.48) inflated to 2020/21 prices using RPI.
Community children's nurse	£160.29	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Community Health Services. Nursing Services for Children.
Community specialist nurse, adult, face-to-face	£90.27	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Community Health Services. Other Specialist Nursing, Adult, Face to face.
Community specialist nurse, adult, non-face-to-face	£88.62	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Community Health Services. Other Specialist Nursing, Adult, Non face to face.

Item	Unit cost	Source	Notes
Community specialist nurse, child, face-to-face	£120.68	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Community Health Services. Other Specialist Nursing, Child, Face to face.
Community specialist nurse, child, non-face-to-face	£70.64	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Community Health Services. Other Specialist Nursing, Child, Non face to face.
Complementary therapist/ alternative medicine e.g. homeopath	£77.50	NHS. Homeopathy. https://www.nhs.uk/conditions/homeopathy/ (Accessed 4 Jan 2023).	The price for a consultation with a homeopath can vary from around £30 to £125. Mean price is considered here.
Dietician	£92.00	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 4 Jan 2023).	7.1 NHS reference costs for hospital services, community services. Community dietician average cost per session.
Education welfare officer	£18.54	National Careers Service. 2023. Education welfare officer. https://nationalcareers.service.gov.uk/job-profiles/education-welfare-officer (Accessed 14 Feb 2023).	Mean annual salary of an education welfare officer. Unit cost calculated using information on employer contribution to pension schemes and National Insurance.
Educational psychologist	£35.19	Prospects. 2022. Educational psychologist. https://www.prospects.ac.uk/job-profiles/educational-psychologist (Accessed 14 Feb 2023).	Mean annual salary of an education psychologist. Unit cost calculated using information on employer contribution to pension schemes and National Insurance.
Family Centre	£58.88	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2017. University of Kent, 2017. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-2017/ (Accessed 4 Jan 2023).	Table 11.8. Cost per hour of client related work. Family centre worker assumed to have the same unit cost as a family support worker. 2016/17 prices (£54.00) inflated to 2020/21 prices using the NHS cost inflation index (NHSCII).
Family liaison officer	£58.88	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2017. University of Kent, 2017. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-2017/ (Accessed 4 Jan 2023).	Table 11.8. Cost per hour of client related work. Family liaison officer worker assumed to have the same unit cost as a family support worker. 2016/17 prices (£54.00) inflated to 2020/2021 prices using the NHS cost inflation index (NHSCII).

Item	Unit cost	Source	Notes
Family planning clinic, face-to-face	£138.86	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Family Planning Clinic. Consultant Led Non-Admitted Face-to-Face Attendance, First.
Family planning clinic, non-face-to-face	£141.19	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Family Planning Clinic. Consultant Led Non-Admitted Non-Face-to-Face Attendance, First.
Family support worker	£58.88	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2017. University of Kent, 2017. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-2017/ (Accessed 4 Jan 2023).	Table 11.8. Cost per hour of client related work. 2016/17 prices (£54.00) inflated to 2020/21 prices using the NHS cost inflation index (NHSCII).
Family therapist	£58.88	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2017. University of Kent, 2017. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-2017/ (Accessed 4 Jan 2023).	Table 11.8. Cost per hour of client related work. Family therapist assumed to have the same unit cost as a family support worker. 2016/17 prices (£54.00) inflated to 2020/21 prices using the NHS cost inflation index (NHSCII).
GP consultation, at home	£34.00	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 4 Jan 2023).	Table 10.3b. With qualification costs, Excluding direct care staff costs. Cost of home consultation not available, using in surgery consultation as proxy.
GP consultation, in surgery	£34.00	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 4 Jan 2023).	Table 10.3b. With qualification costs, Excluding direct care staff costs.
GP consultation, telephone/video	£21.63	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 4 Jan 2023).	10.4 The cost of online consultations, Table 1. Sum of average cost of GP-led triage cost and GP telephone calls.
Home-Start	£117.12	Creswell, Violato (14)	Appendix. Unit costs. 2013/14 prices (£98.30) inflated to 2020/21 prices using RPI.

Item	Unit cost	Source	Notes
Housing department	£26.39	Reed. 2022. Average Housing Officer salary in the UK. https://www.reed.co.uk/average-salary/average-housing-officer-salary (Accessed 4 Jan 2023).	Average housing officer salary in the UK. Unit cost calculated using information on employer contribution to pension schemes and National Insurance.
Occupational therapist, adult	£87	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 4 Jan 2023).	7.1 NHS reference costs for hospital services, community services. Occupational therapy average cost per one-to-one session.
Occupational therapist, child	£160	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 4 Jan 2023).	6.1 NHS reference costs for children's health services, community services. Occupational therapy average cost per one-to-one session.
Physiotherapist, adult	£69.00	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 4 Jan 2023).	7.1 NHS reference costs for hospital services, community services. Community physiotherapy average cost per one-to-one session.
Physiotherapist, child	£114.00	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 4 Jan 2023).	6.1 NHS reference costs for children's health services, community services. Community physiotherapy average cost per one-to-one session.
Play therapist	£27.37	Prospects. 2022. Play therapist. https://www.prospects.ac.uk/job-profiles/play-therapist (Accessed 4 Jan 2023).	Mean annual salary of a play therapist. Unit cost calculated using information on employer contribution to pension schemes and National Insurance.
Practice nurse consultation, at home	£7.13	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 4 Jan 2023).	Cost of home consultation not available, using in surgery consultation as proxy.
Practice nurse consultation, in surgery	£7.13	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 4 Jan 2023).	Table 10.2. Costs including qualification, based on duration of contact of 9.72 minutes as per Hobbs, Bankhead (15)

Item	Unit cost	Source	Notes
Practice nurse consultation, telephone/video	£7.62	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 4 Jan 2023).	10.5 Telephone triage – GP-led and nurse-led. Cost per nurse-led triage intervention excluding other costs.
Primary mental health worker	£231.93	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2020. University of Kent, 2020. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-2020/ (Accessed 4 Jan 2023).	6.1 NHS reference costs for children's health services. CAMHS average cost per patient contact, community contact. Primary mental health worker assumed to have the same unit cost as CAMHS. 2019/20 prices (£225.00) inflated to 2020/21 prices using the NHS cost inflation index (NHSCII).
Psychiatrist, adult, face-to-face	£125.43	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Psychotherapy. Consultant Led Non-Admitted Face-to-Face Attendance, First.
Psychiatrist, adult, non-face-to-face	£111.67	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Psychotherapy. Consultant Led Non-Admitted Face-to-Face Attendance, First.
Psychiatrist, child	£406.75	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Child and Adolescent Psychiatry. Weighted mean of Consultant Led Non-Admitted Face-to-Face Attendance, First and Follow-up.
Psychologist	£155.59	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2014. University of Kent, 2014. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-2014/ (Accessed 2 Feb 2023).	Table 9.5. Cost per hour of client contact. 2013/14 prices (£138.00) inflated to 2020/21 prices using the Hospital & Community Health Services (HCHS) and NHS cost inflation index (NHSCII).
Self-help groups	£0	Self Help UK. 2023. Self Help Groups & Contacts. https://www.selfhelp.org.uk/directory (Accessed 14 Feb 2023).	There are a variety of free to use self-help groups, providing support in a variety of areas.
Social worker, adult services	£52.00	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 4 Jan 2023).	Table 11.1. Cost per hour, including qualifications.

Item	Unit cost	Source	Notes
Social worker, children's services	£52.00	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 4 Jan 2023).	Table 11.2. Cost per hour, including qualifications.
Special Education Needs Co-ordinator (SENCO)	£44.18	Prospects. 2021. Special educational needs coordinator (SENCO). https://www.prospects.ac.uk/job-profiles/special-educational-needs-coordinator-senco (Accessed 4 Jan 2023).	Mean annual additional allowance received by SENCOs added to mean annual salary of qualified teachers in England (excluding London) and Wales used above. Unit cost calculated using information on employer contribution to pension schemes and National Insurance.
Speech and language therapist, adult	£111	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 4 Jan 2023).	7.1 NHS reference costs for hospital services, community services. Speech therapy service average cost per one-to-one session.
Speech and language therapist, child	£114	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 4 Jan 2023).	6.1 NHS reference costs for children's health services, community services. Speech therapy service average cost per one-to-one session.
Teacher (additional contact)	£30.52	Prospects. 2022. How much do teachers get paid? https://www.prospects.ac.uk/jobs-and-work-experience/job-sectors/teacher-training-and-education/how-much-do-teachers-get-paid (Accessed 4 Jan 2023).	Mean annual salary of qualified teachers in England (excluding London) and Wales. Unit cost calculated using information on employer contribution to pension schemes and National Insurance.
Other			
Autism assessment team	£191.46	Authors' calculations.	Mean of (i) paediatrician, (ii) child psychiatrist, (iii) speech and language therapist, (iv) psychologist, (v) community children's nurse and (vi) specialist teacher (SENCO) cost in this table, as per NICE guidance (https://www.nice.org.uk/guidance/cg128/chapter/Recommendations#local-pathway-for-recognition-referral-and-diagnostic-assessment-of-possible-autism).
Breast cancer screening	£190	GenesisCare. 2023. Mammogram for breast screening. https://www.genesiscare.com/uk/diagnostics/imaging-scans/mammography (Accessed 20 Feb 2023).	Cost of a private mammogram starts from £190.

Item	Unit cost	Source	Notes
Cardiology, adult, face-to-face	£257.20	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Cardiology, Consultant Led Non-Admitted Face-to-Face Attendance, First.
Cardiology, child, face-to-face	£311.21	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Paediatric Cardiology, Consultant Led Non-Admitted Face-to-Face Attendance, First.
Charity groups	£0	Self Help UK. 2023. Self Help Groups & Contacts. https://www.selfhelp.org.uk/directory (Accessed 14 Feb 2023).	There are a variety of free to use self-help charity groups, providing support in a variety of areas.
Children & Adolescent Mental Health Services (CAMHS), other	£231.93	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2020. University of Kent, 2020. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-2020/ (Accessed 4 Jan 2023).	6.1 NHS reference costs for children's health services. CAMHS average cost per patient contact, community contact. 2019/20 prices (£225.00) inflated to 2020/21 prices using the NHS cost inflation index (NHSCII).
Children's wellbeing practitioner	£41	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 4 Jan 2023).	9. Scientific and professional staff. Band 5 cost per working hour. CWPs are paid at Agenda for Change Band 5 (https://www.healthcareers.nhs.uk/explore-roles/psychological-therapies/roles-psychological-therapies/childrens-wellbeing-practitioner/childrens-wellbeing-practitioner).
Chiropractor	£55	NHS. Chiropractic. https://www.nhs.uk/conditions/chiropractic/ (Accessed 17 Feb 2023).	The price for a consultation with a chiropractor can vary from around £30 to £80. Mean price is considered here.
Dentist	£133	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 4 Jan 2023).	10.6 NHS dentist – Performer-Only. Cost per hour of patient contact.
Counsellor	£53.33	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 4 Jan 2023).	9. Scientific and professional staff. Mean of Band 5, 6 and 7 cost per working hour. Counsellors are paid at Agenda for Change Band 5, 6 or 7 (https://www.prospects.ac.uk/job-profiles/counsellor).

Item	Unit cost	Source	Notes
Dermatology, adult	£203.99	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Dermatology. Consultant Led Non-Admitted Face-to-Face Attendance, First.
Dermatology, child	£261.57	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Paediatric Dermatology. Consultant Led Non-Admitted Face-to-Face Attendance, First.
Education mental health practitioner	£41	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 4 Jan 2023).	9. Scientific and professional staff. Band 5 cost per working hour. EMHPs are paid at Agenda for Change Band 5 (https://www.healthcareers.nhs.uk/explore-roles/psychological-therapies/roles-psychological-therapies/education-mental-health-practitioner/education-mental-health-practitioner).
Endocrinology, adult, face-to-face	£330.26	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Endocrinology, Consultant Led Non-Admitted Face-to-Face Attendance, First.
Endocrinology, adult, non-face-to-face	£198.65	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Endocrinology, Consultant Led Non-Admitted Non-Face-to-Face Attendance, First.
Endocrinology, child, face-to-face	£439.82	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Paediatric Endocrinology, Consultant Led Non-Admitted Face-to-Face Attendance, First.
Endocrinology, child, non-face-to-face	£249.02	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Paediatric Endocrinology, Consultant Led Non-Admitted Non-Face-to-Face Attendance, First.
Group therapy, adult	£97.31	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Community Health Services. Allied Health Professionals, Other Therapist, Adult, Group.
Group therapy, child	£48.13	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Community Health Services. Allied Health Professionals, Other Therapist, Child, Group.

Item	Unit cost	Source	Notes
Gynaecological oncology	£202.90	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Gynaecological oncology, Consultant Led Non-Admitted Face-to-Face Attendance, First.
Hospital dentist, adult	£445.79	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Restorative Dentistry, Consultant Led Non-Admitted Face-to-Face Attendance, First.
Hospital dentist, child	£444.53	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Paediatric Dentistry, Consultant Led Non-Admitted Face-to-Face Attendance, First.
Improving Access to Psychological Therapies (IAPT)	£132	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 4 Jan 2023).	2.1 NHS national costing data for mental health services. IAPT Contacts.
Learning mentor at school	£19.81	Prospects. 2022. Learning mentor. https://www.prospects.ac.uk/job-profiles/learning-mentor (Accessed 4 Jan 2023).	Mean annual salary of a learning mentor. Unit cost calculated using information on employer contribution to pension schemes and National Insurance.
Neurology, adult, face-to-face	£300.33	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Neurology, Consultant Led Non-Admitted Face-to-Face Attendance, First.
Neurology, adult, non-face-to-face	£207.84	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Neurology, Consultant Led Non-Admitted Non-Face-to-Face Attendance, First.
Neurology, child, face-to-face	£572.97	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Paediatric Neurology, Consultant Led Non-Admitted Face-to-Face Attendance, First.
Neurology, child, non-face-to-face	£337.45	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Paediatric Neurology, Consultant Led Non-Admitted Non-Face-to-Face Attendance, First.

Item	Unit cost	Source	Notes
NVR Practitioners Consortium	£72.75	NVR Practitioners Consortium. Training courses for parents and carers. https://nvrpc.org.uk/for-parents%2Fcarers (Accessed 17 Feb 2023).	8-week courses are £582, equating to £72.75 per session.
Oncology, adult	£355.28	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Medical Oncology, Consultant Led Non-Admitted Face-to-Face Attendance, First.
Oncology, child	£474.25	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Paediatric Medical Oncology, Consultant Led Non-Admitted Face-to-Face Attendance, First.
Orthodontist	£133	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 4 Jan 2023).	10.6 NHS dentist – Performer-Only. Cost per hour of patient contact. Orthodontist assumed to have the same unit cost as a dentist.
Orthopaedics, adult, face-to-face	£225.54	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Trauma & Orthopaedics, Consultant Led Non-Admitted Face-to-Face Attendance, First.
Orthopaedics, adult, non-face-to-face	£150.07	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Trauma & Orthopaedics, Consultant Led Non-Admitted Non-Face-to-Face Attendance, First.
Orthopaedics, child, face-to-face	£256.45	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Paediatric Trauma and Orthopaedics, Consultant Led Non-Admitted Face-to-Face Attendance, First.
Orthopaedics, child, non-face-to-face	£160.56	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Paediatric Trauma and Orthopaedics, Consultant Led Non-Admitted Non-Face-to-Face Attendance, First.
Orthotics	£203.66	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Orthotics, Consultant Led Non-Admitted Face-to-Face Attendance, First.

Item	Unit cost	Source	Notes
Outreach worker	£25	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 4 Jan 2023).	11.7 Support and outreach worker. Unit cost per hour.
Pastoral Support Officer	£17.94	Talent.com. 2023. Pastoral Support Officer average salary in United Kingdom. https://uk.talent.com/salary?job=pastoral+support+officer (Accessed 20 Feb 2023).	Average annual salary of Pastoral Support Worker in UK. Unit cost calculated using information on employer contribution to pension schemes and National Insurance.
Police officer	£24.21	Police Federation. 2023. Constable pay scales. https://www.polfed.org/resources/pay-scales/constable-pay-scales/ (Accessed 20 Feb 2023).	Mean annual salary of pay points 0-7 for constables appointed on or after 1 April 2013. Unit cost calculated using information on employer contribution to pension schemes and National Insurance.
Private counsellor	£40	NHS. Counselling. https://www.nhs.uk/mental-health/talking-therapies-medicine-treatments/talking-therapies-and-counselling/counselling/ (Accessed 20 Feb 2023).	The cost of private counselling can vary from £10 to £70. Mean price is considered here.
School nurse	£97.79	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Community Health Services. Nursing, School Based Children's Health Core Services, One to One.
Urology, adult, face-to-face	£193.52	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Urology, Consultant Led Non-Admitted Face-to-Face Attendance, First.
Urology, adult, non-face-to-face	£141.26	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Urology, Consultant Led Non-Admitted Non-Face-to-Face Attendance, First.
Urology, child, face-to-face	£190.06	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Paediatric Urology, Consultant Led Non-Admitted Face-to-Face Attendance, First.
Urology, child, non-face-to-face	£164.68	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Paediatric Urology, Consultant Led Non-Admitted Non-Face-to-Face Attendance, First.

Item	Unit cost	Source	Notes
VOICE programme	£10	VOICE Programme. https://voicepartnership.com/179-2/ (Accessed 17 Feb 2023).	10 week courses are £100, equating to £10 per session.
Wheelchair services, adult	£200.27	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Community Health Services. Weighted mean of all Adult Wheelchair Services.
Wheelchair services, child	£321.82	2020/21 National Cost Collection Data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ (Accessed 4 Jan 2023).	Community Health Services. Weighted mean of all Child Wheelchair Services.
NHS prescription costs	BNF01: £5.42 BNF02: £4.72 BNF03: £14.63 BNF04: £7.80 BNF05: £6.21 BNF06: £13.04 BNF07: £8.48 BNF08: £39.86 BNF09: £11.36 BNF10:£5.74 BNF11: £10.22 BNF12: £7.07 BNF13: £9.65 BNF14: £9.85 BNF15: £16.52 BNF19: £28.55	Prescription Cost Analysis – England – 2020/21. https://www.nhsbsa.nhs.uk/statistical-collections/prescription-cost-analysis-england/prescription-cost-analysis-england-2020-21 (Accessed 02 Oct 2023)	Totals by BNF Chapters
Out-of-pocket prescription payments	Parents: £9.15 Children: £0	2020 NHS prescription charges. https://www.gov.uk/government/speeches/nhs-prescription-charges-from-1-april-2020 (Accessed 02 Oct 2023)	Children under 16 are exempt from the prescription payments.
Over-the-counter (OTC) medicine	£3.29	PAGB. 2018. Conditions for which over the counter items should not routinely be prescribed in primary care: A Consultation on guidance for CCGs. https://www.pagb.co.uk/content/uploads/2018/03/FINAL-PAGB-response-to-OTC-not-routinely-prescribed-consultation-13-03-18.pdf (Accessed 15 Feb 2022).	Average cost of an OTC medicine. 2017 prices (£2.94) inflated to 2021 prices using RPI inflation indices.

Item	Unit cost	Source	Notes
Therapist hourly rate	Band 4: £35 Band 5: £41 Band 6: £54 Band 7: £65	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 02 Oct 2023).	The therapist hourly rate was obtained from the Excel file "unit-cost-of- health-and-social-care-staff-2020-21.xlsx", Worksheet "Community-based scientific and professional staff", with the same information also reported in the PSSRU Unit Cost Report 2021, Chapter 9, page 111. The hourly rate of a specific therapist depends on the salary band of their profession. We used the actual salary band of the therapists providing the treatment in each case. Around 80% of the therapists were in bands 4 (£35) and 5 (£41).
Supervisor hourly rate	Band 8a: £75	Personal Social Services Research Unit. Unit Costs of Health & Social Care 2021. University of Kent, 2021. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 02 Oct 2023)	Supervisors are typically band 8a staff.
Time off work (parent)	Men: £ 119.12 Women: £ 88.4 Prefer not to say: £ 103.76	Measures of employee earnings based on SOC 2020, UK: 2021. https://www.ons.gov.uk/releases/annualsurveyofhoursandearnings2021basedonsoc2020 (Accessed 02 Oct 2023)	
Daily cost of school absence: school opportunity cost	£33.1	Revenue funding to state-funded schools in England for pupils aged 5-16, in cash and real terms, 2010-11 to 2023-24. https://explore-education-statistics.service.gov.uk/find-statistics/school-funding-statistics (Accessed 02 Oct 2023)	Per pupil funding in 2020/21 school year: £6,280; school days: 190 days. The daily cost is 6280/190=£33.1
Daily cost of school absence: loss of lifetime earning	£279.95	Measures of employee earnings based on SOC 2020, UK: 2021. https://www.ons.gov.uk/releases/annualsurveyofhoursandearnings2021basedonsoc2020 (Accessed 02 Oct 2023)	Calculated based on a model proposed by Psacharopoulos[7] et al. (2021). The calculation method is detailed in Supplementary material S4.

Supplementary Materials S6: Statistical Analysis Plan

Primary Care Clinical Trials Unit

STATISTICAL ANALYSIS PLAN

Child Anxiety Treatment in the context of COVID-19 (Co-CAT):

Enabling Child and Adolescent Mental Health Services (CAMHS) to provide efficient remote treatment for child anxiety problems

Version 4.0 25th October 2022

	NAME	TITLE	Signature	Date
Written by:	Nicola Williams (version 1.1 onwards)	Senior Trial Statistician		25th October 2022
Reviewed by:	Ly-Mee Yu	Lead Trial Statistician		1 Nov 2022
Approved by:	Cathy Creswell	Chief Investigator		30th October 2022

Version History

Version:	Version Date:	Changes:
0.1	30 Sept 2020	Original
0.2	08 October 2020	Responded to reviewer comments by JM
0.3	27 October 2020	Responded to comments by CC
0.4	09 November 2020	Minor updates
0.5	13 November 2020	Updated with comments from CC and JM
0.6	17 November 2020	Updated with comments from CC
0.7	18 November 2020	Updated with comments from JM
0.8	20 November 2020	Clean version
1.0	01 December 2020	Finalised for sign off.

1.1	14 July 2021	Updated to incorporate changes to protocol (now based on v2.0 of protocol) – specifically minimisation variables used in randomisation Add derivation of outcome measures based on questionnaires
1.2	2 November 2021	Updated and removed comments following meeting with Lucy Taylor and Cathy Creswell. • Addition of time windows for inclusion in primary and sensitivity analyses • Removal of t scores 2.1.2.2.1 • Change 2.1.2.5 to 7 itmes, not 9 • Change per protocol to modules 0-4 not 0-3
1.3	10 March 2022	Update to derivation of SCAS-P-8 (section 2.1.2.2.2) following review by Lucy Taylor
2.0	10 March 2022	Finalised for sign off
2.1	1st September 2022	Updated power calculation to be in line with version 2.3 15th July 2022 of protocol (Sample Size Determination updated to reflect sample size requirements from just 90% power to both 80% and 90% power)
3.0	1st September 2022	Finalised for sign off
3.1	25th October 2022	Clarification of per protocol analysis to require completion of modules 0-4 within the 26 weeks.
4.0	25th October 2022	Finalised for sign off

TABLE OF CONTENTS

1 INTRODUCTION

1.1 PREFACE

Chief Investigator: Professor Cathy Creswell

Trial Statisticians: Dr Ly-Mee Yu, Dr Victoria Harris

This SAP supports version 2.3 of the protocol dated 15th July 2022.

1.2 PURPOSE AND SCOPE OF THE PLAN

This document details the proposed analyses of primary and secondary objectives for the Child Anxiety Treatment in the context of COVID-19 (Co-CAT) study. Subsequent analyses of a more exploratory nature will not be bound by this strategy, though they are expected to follow the broad principles laid down here. The principles are not intended to curtail exploratory analysis nor to prohibit accepted practices, but they are intended to establish the rules that will be followed, as closely as possible, when analysing and reporting the trial.

The statistical analysis plan will be available on request when the principal papers are submitted for publication in a journal. Suggestions for subsequent analyses by the journal editors or referees will be considered carefully, and carried out as far as possible in line with the principles of the analysis strategy; if reported, the source of the suggestion will be acknowledged.

Any deviations from the statistical analysis plan will be described and justified in the final report of the trial.

1.3 TRIAL OVERVIEW

More than a quarter of the population have an anxiety disorder at some point during their life and half of these people first experience an anxiety disorder by the age of 11 years (Kessler et al., 2005). Anxiety disorders in childhood often continue into adolescence and adulthood and put these children at increased risk for other serious mental health disorders and impaired quality of life in adulthood (Copeland, Angold, Shanahan, & Costello, 2014).

Cognitive behaviour therapy (CBT) for children with anxiety disorders works well (James, James, Cowdrey, Soler, & Choke, 2013), but only a minority of children with anxiety disorders access treatment (Green, McGinnity, Meltzer, Ford, & Goodman, 2005; Merikangas et al., 2011). Improving treatment efficiency further could enable more families to access effective treatment when they first need it. Online delivery of parent-guided treatment offers a means to do this by substantially reducing the amount of therapist contact time needed. Delivering treatment online also has the potential to increase access to families who may experience barriers to accessing traditional treatment approaches.

We have worked in collaboration with families, NHS clinicians and a tech-company to co-design an online version of our parent-guided treatment for child anxiety disorders called OSI (Online Support and Intervention for child anxiety). OSI comprises a parent website, accompanying therapist case management system, and accompanying child game app (see *OSI Overview and Screenshots* document). Modules are supported by 7 x weekly 20-minute telephone sessions between the parent and a therapist and a review session 4 weeks after the final treatment session).

Importance in the context of COVID-19

The Health Innovation Network (Health Innovation Network South London, 2020) highlighted that children with existing anxiety issues are a high risk population during the COVID-19 pandemic, and our UKRI funded Co-SPACE study (CUREC R69060/RE010) that has been tracking child and adolescent mental health throughout the pandemic has identified high levels of fear and worry about COVID-19 among children.

OSI provides a potential means to address the current challenges that CAMHs face in meeting the needs of children with anxiety problems and their families; it can be delivered as intended despite social distancing measures and is sufficiently flexible to address COVID-19 specific fears/worries. It has not yet been subject to systematic evaluation and we do not know whether outcomes are as good as those CAMHS are currently achieving and whether OSI enables further efficiencies.

Aims

The proposed research will evaluate the clinical and cost-effectiveness of OSI with therapist support for the treatment of child anxiety compared to 'COVID-19 treatment as usual' (C-TAU) in CAMHS throughout the next phases of the COVID-19 pandemic. Further aims are to explore the trajectory of change as reported within the OSI platform, to inform further developments, and to understand therapists' and parents' experiences of treating child anxiety (across both arms) in the current context to maximise learning to (a) enable rapid implementation of remote treatment delivery in CAMHS in any subsequent periods of social distancing, and (b) maintain the use of online platforms (such as OSI) in CAMHS when 'normal service' resumes.

If successful, the research will provide:

1. A solution for efficient psychological treatment for child anxiety disorders while social distancing (for the current context and future pandemics);
2. An efficient means of treatment delivery as 'normal service' resumes to enable CAMHS to cope with the anticipated increase in referrals when social distancing measures are relaxed and schools re-open;
3. A demonstration of rapid, high quality evaluation and application of online interventions within NHS CAMHS to drive forward much-needed further digital innovation and evaluation in CAMHS settings.

The primary beneficiaries will be children with anxiety disorders and their families, NHS CAMHS teams, and commissioners who will access a potentially effective, cost-effective, and efficient treatment for child anxiety problems.

1.4 Objectives

Objectives	**Outcome Measures**	**Timepoint(s) of evaluation of this outcome measure (if applicable)**
Primary Objective To evaluate the parent-reported clinical effectiveness of OSI+therapist support for the treatment of child anxiety compared to 'COVID-19 treatment as usual' (C-TAU) in CAMHS throughout the next phases of the COVID-19 pandemic.	1) The Child Anxiety Impact Scale- parent report (CAIS-P) captures the degree to which anxiety is interfering in the child and family's life.	26 weeks post-randomisation
Secondary Objectives **(1)** Further assessment of the clinical effectiveness of OSI+therapist support for the treatment of child anxiety compared to 'COVID-19 treatment as usual' (C-TAU) in CAMHS throughout the next phases of the COVID-19 pandemic.	Secondary clinical outcomes: Child reported anxiety interference (CAIS-C), child reported anxiety symptoms (RCADS-C) Parent report on child's anxiety symptoms (RCADS-P, SCAS-8P), overall functioning (ORS), COVID-19 specific worries, and common comorbid emotional and behavioural problems (SDQ-P).	14 weeks post-randomisation 26 weeks post-randomisation

(2) Evaluate the cost-effectiveness of OSI+therapist support for the treatment of child anxiety compared to 'COVID-19 treatment as usual' (C-TAU) in CAMHS	Economic outcomes: Parent quality of life (EQ-5D-5L, parent-self report); and child quality of life (CHU-9D proxy version, i.e. parent-report on child). School attendance (actual school attendance as a percentage of expected school attendance) Therapist logs of time spent on treatment delivery	14 weeks post-randomisation 26 weeks post-randomisation
Exploratory Objectives **(1)** Explore the trajectory of change reported within the OSI arm	Measures used to monitor child outcomes built in to OSI (RCADS-P, CAIS-P, SCAS-8P; ORS; SRS; GBOs)	Weeks 1-7 of OSI treatment
(2) Understand therapist and parents' experiences of treating child anxiety in the current context to maximise learning to (a) enable rapid implementation of remote treatment delivery in CAMHS in any subsequent periods of social distancing, and (b) maintain the use of online interventions (such as OSI) in CAMHS when 'normal service' resumes.	Qualitative interviews with parents and therapists. Therapist experience of treatment questionnaire	14-26 weeks post randomisation End of treatment phase

2 TRIAL DESIGN

We will conduct a two arm, multi-site, randomised controlled non-inferiority trial to evaluate the clinical and cost-effectiveness of OSI with therapist support compared to CAMHS 'COVID-19 treatment as usual' (C-TAU) during the COVID-19 outbreak and to explore parent and therapists' experiences. The study procedure is in line with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) statement 2013 (Chan et al, 2013).

2.1 OUTCOMES MEASURES AND THEIR DERIVATIONS

2.1.1 PRIMARY OUTCOME

The Child Anxiety Impact Scale- parent report (CAIS-P). The CAIS-P will be used to determine the extent to which anxiety interferes in the child's life. This measure covers three psychosocial domains (academic, social activities and home/family environments) and consists of 27 items rated on a 4-point scale. In keeping with other trials with pre-adolescent children, we are using a 25 item version of the measure (without two items which ask about boyfriend/girlfriends and dating; e.g. Evans et al (2017) and Thirlwall et al (2013)). An additional 4 'global' items assess overall interference. The CAIS-p will be completed at baseline, and then at 14 and 26 weeks post randomisation by both parent/carer and child. The primary outcome is the CAIS-P at 26 weeks post randomisation.

There are versions for children and parents to complete, both of which have been shown to have good psychometric properties (Langley et al., 2014; Langley, Bergman, McCracken, & Piacentini, 2004). The Child Anxiety Impact Scale- child report (CAIS-C) will be analysed as a secondary outcome.

Derivation

Each item is scored on a 4-point Likert scale ("0" not at all, "1" just a little, "2" pretty much, "3" very much). A total score sums the scores of the first 25 items, giving a possible range of 0 to 75.

Missing data for individual questions can be handled by prorating the remaining items to get a total score. This can be done if at least 75% of items have been completed. If more than 75% are missing the total will be set to missing.

A total score for the 4 global items (questions 28-31) will be obtained, with a possible range of 0-12. As above, if at least 75% of the questions have been answered, the total score can be obtained by prorating the remaining items. If more than 75% are missing the total will be set to missing.

2.1.2 Secondary outcomes and Their Derivations

2.1.2.1 Child Anxiety Impact Scale

The Child Anxiety Impact Scale- child report (CAIS-C) covers the same domains as the CAIS-P and will be completed at the same time points as the CAIS-P.

Derivation

The Child Anxiety Impact Scale – child report score is calculated in the same way as for the parent report.

2.1.2.2 Symptoms of Child Anxiety

2.1.2.2.1 Revised Child Anxiety and Depression Scale-Child and Parent versions (RCADS-c/p).

The RCADS-c/p are routinely used within CAMHS. It is a 47-item questionnaire, with corresponding child-report and parent-report versions that assess symptoms of separation anxiety disorder, social anxiety disorder, generalized anxiety disorder, panic disorder, obsessive compulsive disorder and major depressive disorder. Responders rate how often each item applies on a 0 ('never') to 3 ('always') scale. The RCADS-c/p have been shown to have robust psychometric properties in children from age 7 (Chorpita, Moffitt, & Gray, 2005; Ebesutani, Bernstein, Nakamura, Chorpita, & Weisz, 2010). RCADS-c/p will be completed at baseline, and then at 14 and 26 weeks post randomisation by both parent/carer and child.

Derivation

Each of the 47 items is scored on a 4-point Likert scale ("0" never, "1" sometimes, "2" often, "3" always). Question 48 is required for the SCAS-8P only.

Two scores will be obtained:

- A total score for anxiety, which sums the scores for all except major depression (possible range 0 to 111)
- A total overall score which sums scores of all items, giving a possible range of 0 to 141.

These will be presented as raw scores and will not be converted to t-scores.

Disorder/Syndrome	Related Items
Social Anxiety	4, 7, 8, 12, 20, 30, 32, 38, 43
Panic Disorder	3, 14, 24, 26, 28, 34, 36, 39, 41
Major Depression	2, 6, 11, 15, 19, 21, 25, 29, 40, 47
Separation Anxiety	5, 9, 17, 18, 33, 45, 46

Generalized Anxiety	1, 13, 22, 27, 35, 37
Obsessive-Compulsive	10,16, 23, 31, 42, 44

Missing data for raw scores can be handled by prorating the remaining items. It is recommended that the total anxiety score can have up to 10 missing items, but only if each subscale has no more than 2 missing; and the total anxiety and depression score can have up to 12 missing items, but only if each subscale has no more than 2 missing items. To estimate the scale score, take the sum of the completed items within that scale and divide that by the number of items completed, then multiple by the total number of items in that scale, and then round the result.

2.1.2.2.2 Brief Spence Children's Anxiety Scale-Parent Version (SCAS-P-8).

The SCAS-P-8 is a brief version of the Spence Children's Anxiety Scale (Reardon, Spence, Hesse, Shakir & Creswell, 2018). It is an 8-item questionnaire designed to assess symptoms of anxiety disorders in children. An initial evaluation of the questionnaire indicates it has good psychometric properties in children from age 7 to 11 (Reardon, et al., 2018). Only 1 of the 8 items are required to be collected to score this measure as 7/8 items overlap with those already collected within the RCADS-p. The additional item that enables us to calculate a SCAS-P-8 total score will be completed at baseline, and then at 14 and 26 weeks post randomisation by the parent/carer.

Derivation

Each of the 8 items is scored on a 4-point Likert scale ("0" never, "1" sometimes, "2" often, "3" always). The total score will be calculated as the sum of these 8 items, giving a possible range of 0 to 24. The items of the RCADS which make up this score are 1,9,18,27,32,34,43 and 48.

2.1.2.3 Overall Functioning (ORS)

Outcome Rating Scale (ORS). The ORS (Miller, Duncan, Brown, Sparks & Claud, 2003) will be used to assess functioning across different areas of the child's life. It comprises four simple rating scales in which the parent/carer rates how their child has been feeling over the last week (individually, interpersonally, socially, and overall wellbeing). Each item is rated using a variable length (as it is done online the length of the line is not always 10cm) visual analogue scale, with instructions to place a mark on each line. A higher score indicates better functioning. It has good reliability and validity (Bringhurst, Watson et al. 2006). The ORS will be completed at baseline, and then at 14 and 26 weeks post randomisation by the parent/carer.

Derivation

Each of the four visual analogue scales is approximately 10cm, but this varies due to it being done online. The proportion of the line along which the mark is made will be cacluated and converted to a 0-10 scale, measured to 1 decimal place. The four scores are added together to give an overall score. The total possible score is 40.

2.1.2.4 COMMON COMORBID EMOTIONAL AND BEHAVIOURAL PROBLEMS (SDQ-P)

Strengths and Difficulties Questionnaire (SDQ-P). The SDQ-P (Goodman, Meltzer & Bailey, 1998) is a behavioural screening questionnaire. It comprises of 5 scales assessing: emotional symptoms, conduct problems, hyperactivity/inattention, peer relationship problems, and prosocial behaviour. It has satisfactory reliability (Yao et al., 2009; Goodman, 2001) and good concurrent and discriminant validity (Muris, Meesters & van den Berg, 2003; Lundh, Wangby-Lundh & Bjarehed, 2008). The parent-report version will be completed at baseline, and then at 14 and 26 weeks post randomisation.

Derivation

Each of the 25 questions is rated as "not true", "somewhat true" or "certainly true". These are scored as 0, 1 and 2 respectively, unless they are listed in the 'items to be reverse scored' column in the table below. For these items 'not true' will be scored as 2 and 'certainly true' will be scored as 0. For each of the 5 scales the score can range from 0 to 10 if all items have been completed. These scores can be scaled up pro-rata if at least 3 items have been completed.

The total difficulties score is generated by summing scores from all the scales except the prosocial scale. The resultant score ranges from 0 to 40, and is counted as missing if at least one of the 4 component scores is missing.

The separate scales in the table below will also be analysed separately.

Scale	Related Items	Items to be reverse scored
Emotional symptoms	3, 8, 13, 16, 24	None
Conduct problems	5, 7, 12, 18, 22	7
Hyperactivity/inattention	2, 10, 15, 21, 25	21, 25
Peer relationship problems	6, 11, 14, 19, 23	11, 14
Prosocial behaviour	1 , 4, 9, 17, 20	None

2.1.2.5 COVID-19 SPECIFIC WORRIES (PAS)

Pandemic Anxiety Scale (PAS). The PAS (McElroy et al., 2020) is a 9-item scale designed to capture specific aspects of the COVID-19 pandemic that are provoking anxiety, as well as to explore how these vary by health and demographic factors. An initial evaluation of the scale indicates that the PAS is a reliable and valid measure (McElroy et al., 2020) and based on parent and adolescent self-report comprised two factors (using 7 items): disease anxiety (e.g. catching, transmitting the virus) and consequence anxiety (e.g. impact on economic prospects). The PAS will be completed by the parent/carer at baseline, and then at 14 and 26 weeks post randomisation.

Derivation

The 7 item scale will be used for analysis. Each of the 7 questions is rated as "strongly disagree", "disagree" or "neither disagree/agree", "agree" or "strongly agree". These are scored as 0, 1, 2, 3 and 4 respectively.

The total score will be sum of questions 2, 3, 4, 5, 7, 8 and 9 (not including "My child thinks that COVID-19 is a very serious issue" or "My child is worried we won't have enough food and other essential items during the outbreak" . The total score will range from 0 to 28.

The 2 subscales will be calculated as the sum of the following:

- Disease anxiety – questions 2, 3, 4 and 5 (range 0-16)
- Consequence anxiety – questions 7, 8 and 9 (range 0-12)

2.1.2.6 HEALTH ECONOMIC MEASURES

Health economic outcomes will not be covered in this analysis plan.

2.1.2.7 TREATMENT CREDIBILITY AND EXPERIENCE (CEI)

Credibility and Expectation of Improvement Scale (CEI). Parent/carer will be asked to complete the CEI to assess participant expectations and views regarding treatment credibility, after randomisation and prior to treatment commencing (Borkovec & Nau, 1972). It consists of three items, rated on a scale from 0 "not at all" to 10 "completely", asking about how logical the treatment seems, confidence in its success at reducing their symptoms, and their likelihood to recommend the therapy to a friend with similar symptoms. This measure is administered after randomisation with reference to the treatment arm allocated.

An adapted version of the CEI will also be administered post treatment (14 weeks post randomisation), to give a retrospective account of treatment credibility (i.e. the questions are reworded to be considered in light of having received treatment).

We have also adapted the CEI to evaluate therapists' experiences of treatment within this trial. This comprises items referring to how logical they found the treatment, how comfortable they felt delivering the treatment, how prepared they felt, certainty in the success of the intervention, confidence recommending the treatment to other therapists, and likelihood of administering the treatment again.

Derivation

Each item will be analysed separately and will be a score ranging from 0 to 10.

2.1.2.8 ADVERSE EVENTS REPORTING OPPORTUNITY

CAMHS therapists will be asked to report any adverse events that they become aware of while working with families in either arm over the whole treatment period. We will also provide parents/carers and children an opportunity to describe any negative impacts of participating in the study after completing the questionnaires at 14 and 26 weeks and (for parents) after completing the qualitative interview. So as not to 'lead' answers we will enquire about positive and negative consequences of taking part in the treatment. The research team will regularly review responses to identify any responses that indicate the presence of an adverse event.

2.1.3 EXPLORATORY OUTCOMES

2.1.3.1 MEASURES ROUTINELY USED TO MONITOR OUTCOMES IN OSI

For the OSI+therapist support arm only, the OSI platform collects routine outcome measures and these will be used to help therapists to evaluate progress of participants through treatment and to explore the trajectory of participant improvement across the course of treatment. The OSI platform routinely collects the CAIS-P, RCADS-p, SCAS-P8, and ORS as described above, and session rating scales and goal-based outcomes as described below:

Session Rating Scales (SRS). The SRS (Duncan, Miller, & Sparks, 2003) assesses key dimensions of an effective therapeutic relationship and will be given at the end of each therapy session to get feedback from the parents/carers so that any issues related to therapeutic alliances can be immediately identified and addressed within treatment. The SRS comprises four simple rating scales in which the parent rates their experience of the treatment session (with regard to relationship with the therapist, goals and topics, approach or method and an overall rating). It uses the same visual analogue scale as the ORS. It has well-established reliability and validity (Duncan, Miller et al. 2003, Campbell and Hemsley 2009). The total score will be the sum of the 4 scales and will have a possible range of 0-40.

Goal Based Outcomes (GBOs). This is a simple rating scale in which the parent rates on an 11 point scale (0 – 10) the extent to which their child has made progress towards up to three treatment goals (Law & Jacob, 2015). Although this measure is now widely used in CAMHS (as part of the CYP IAPT initiative), its psychometric properties have not yet been established. This will be presented both separately for each treatment goal, and as a mean across all treatment goals.

Routinely collected sessional measures will be used to explore the trajectory of change within the OSI+therapist support arm only to inform future developments of the programme. We will not be collecting routine outcome measures from the treatment as usual arm for comparative purposes as these will vary according to site specific practice and treatment specific requirements.

2.1.3.2 QUALITATIVE INTERVIEWS WITH PARENTS/CARERS AND THERAPISTS.

Qualitive outcomes will not be covered in this analysis plan.

2.2 TARGET POPULATION

Children aged 5-12 with anxiety as the primary presenting problem, and their parents/carers.

Therapists who deliver psychological treatments within Child and Adolescent Mental Health Services in England.

2.2.1 INCLUSION CRITERIA

Child

1. is aged 5-12 years at intake
2. primary problem is anxiety
3. willing and able to assent

Parent/Carer

1. has sufficient English language to complete measures/ access interventions
2. family has access to the internet
3. is willing and able to provide consent.

Therapists

1. provides psychological treatment to children in participating services
2. willing and able to provide informed consent

2.2.2 EXCLUSION CRITERIA

Participants are not eligible if ANY of the following apply:

Child

1. has co-morbid conditions that are likely to interfere with treatment delivery, (established autism spectrum condition/ learning disability, suicidal intent/ recurrent or potentially life limiting self-harm)
2. is identified by social services due to child protection concerns.

Parent/Carer

1. has a significant intellectual impairment or severe mental health problem that is likely to interfere with treatment delivery.

2. is unable to access or understand the written English language materials necessary for the interventions.

Therapist

There are no exclusion criteria for Therapists.

2.3 SAMPLE SIZE

Between 418 and 560 children (209 - 280 per group) with an anxiety disorder and their parent/carer will be randomised across the two treatment arms. This sample size is considered to be sufficient to provide a standardised noninferiority margin=0.33 and between 80% - 90% power (allowing for 30% attrition).

2.4 RANDOMISATION AND BLINDING IN THE ANALYSIS STAGE

Participants will be randomised in a 1:1 ratio to (i) OSI+therapist support or (ii) CAMHS Treatment as Usual for child anxiety problems within the COVID-19 context (C-TAU; typically 'face to face' treatment delivered over phone/video). Randomisation will be minimised by child age (<=8; >=9), gender, service type (school based or not school based), and baseline anxiety-associated interference. Participants will be randomised using a fully validated and secured web-based randomisation system called Sortition using blocked randomisation (with varying permuted block size) that will automatically occur after the participating parent/carer completes the consent and baseline measures, and the child completes assent (online). The treatment allocation will be communicated to the participants (child and parent/carer) in a follow-up email. The online system will also send an email to the clinical team providing information about treatment allocation for each participating family. Due to the nature of the trial, blinding is not possible to the trial participants of the allocated psychological therapy nor to the research team. The statistician conducting the analysis will be blinded to treatment allocation whilst analysing the primary and secondary outcomes. The exploratory analysis will be carried out after unblinding the statistician and either after version 1.0 of the Statistical Analysis Report is signed off or by a separate statistician. In order to minimise the risk of bias the statistical analysis plan will be finalised prior to analysis.

3 Analysis – General considerations

3.1 Descriptive statistics

Summary descriptions for continuous measurements will be means and standard deviations. Medians and interquartile ranges will be presented if more appropriate. Counts and percentages will be presented for categorical variables. Summary statistics will be provided by randomised group and overall.

3.2 Characteristics of participants

Baseline characteristics of the patients (demographics and baseline of all outcome variables where available) will be reported by randomised group as well as overall.

There will be no tests of statistical significance nor confidence intervals for differences between randomised groups on any baseline variables.

3.3 Definition of population for analysis

The primary analysis population is defined as all participants for whom data are available, analysed according to the groups they were randomly allocated to, regardless of treatment compliance. They must have completed their assessment within 4 weeks of the 14 week and 26 week time points.

Two sensitivity analyses will be carried out based on altering the time frame allowed for the assessments. These are detailed in section 6.

A per-protocol analysis will be carried out excluding those who have deviation from the protocol. Compliance with protocol to be included in the per protocol analysis will be defined as completing a minimum of the first 5 treatment sessions (sessions 0, 1, 2, 3 and 4) within the 26 weeks for participants in either arm.

3.4 Pooling of investigational sites

Service type (school vs clinic) is used as a minimisation variable in the randomisation model and so will be included in the primary analysis model. No other clustering by site is assumed.

3.5 Data Monitoring Committee And Interim Analyses

A Trial Steering Committee (TSC) will be convened and will meet approximately every 4 months throughout the study. Recruitment to the trial will be rapid and no interim analyses are planned so a separate Data Monitoring and Ethics Committee will not be formed, however we reserve the option to form one if the TSC deem it necessary at any point during the trial.

Due to the rapid nature of the trial there is not an internal pilot and there are no formal stopping criteria. There is no planned interim analysis.

4 PRIMARY ANALYSIS

4.1 PRIMARY OUTCOME

Analysis of the primary outcome will be performed using a generalised linear mixed effects model adjusting for minimisation variables, will be used to determine the difference in means between the 2 groups and it's 95% confidence interval. The mixed effect models will include the outcome as the response variable, time point, randomised group, and baseline score as fixed effects and a participant specific random intercept. An interaction between time and randomised group will be fitted as a fixed effect to allow estimation of treatment effect at all time points. Additionally the following minimisation variables will be included as fixed in the model: child age,gender, baseline anxiety associated interference and service type (school vs clinic). . The primary endpoint of interest is 26 weeks, although measures at 14 weeks will also be included in the model to assist with estimation in the presence of missing data. Non-inferiority is claimed if the lower limit of the 95% confidence interval around the standardized effect size is less than -0.33. A P-value for the null hypothesis of inferiority of the OSI intervention compared to usual care will also be calculated.

4.2 HANDLING MISSING DATA

The availability of the outcome data for the primary outcome will be summarised by randomised group. Missing primary outcome data will be reported overall and by randomised group. The primary analysis model is valid under a missing at random (MAR) assumption, that is, it is valid if variables predictive of missingness are included in the model.

Additionally baseline characteristics will be summarised by availability of the primary outcome and logistic regression models will explore any association between baseline characteristics and availability of the primary outcome. Covariates found to be predictive of missingness ($P< 0.05$) will be included in the analysis model in a sensitivity analysis of the primary outcome.

4.3 HANDLING OUTLIERS

Any outliers will be checked and verified to ensure that they are true values. Outliers will be identified as those observations more than four standard deviations from the mean. Once they have been confirmed, a sensitivity analysis will be carried out to assess the impact of these values on the results by excluding these participants.

4.4 HANDLING MULTI-CENTRE/CLUSTERED DATA

Randomisation was minimised byservice type (school vs clinic) and this will be included in all models. No other clustering by site is assumed.

4.5 Multiple comparisons and multiplicity

A single primary outcome is specified in the protocol and the secondary outcomes are considered exploratory, so no adjustment for multiple comparisons will be carried out.

4.6 Model assumptions

The primary analysis model assumes normality of the residuals. The distribution of the primary outcome will be assessed and the assumptions of the model will be checked. If any of the assumptions are violated, then p-values and confidence intervals for the model coefficients will be obtained by means of bootstrapping.

5 SECONDARY ANALYSIS

5.1 Secondary outcomes

Secondary outcomes will be analysed in the same way as the primary outcome using a generalised linear mixed effects model adjusting for minimisation variables.

5.2 Exploratory outcomes

5.2.1 Treatment credibility

Treatment credibility, acceptability and experience scores will be calculated and compared for both treatment groups, using simple mean comparisons. Comparisons of means will be carried out using a t-test or suitable non-parametric equivalent (Mann-Whitney-U) if the distributions are non-normal.

5.2.2 Trajectory Of Change Reported Within The Osi Arm

Measures collected only in the OSI arm will be summarised at each time point. Change in child symptoms and functioning on a sessional basis will be plotted to explore the trajectory of change in the OSI arm.

6 SENSITIVITY ANALYSIS

If outliers are identified, a sensitivity analysis excluding these outliers will be carried out to determine the impact of these observations on the treatment effect of the primary outcome.

As a sensitivity analysis of the primary outcome, baseline covariates found to be predictive of missingness will be included as main effects in the linear mixed effects model.

The primary analysis will be repeated in the per-protocol population excluding those who have deviation from the protocol. Compliance with protocol to be included in the per protocol analysis will be defined as completing a minimum of the first 5 treatment sessions for participants in either arm (modules 0-4) within the 26 weeks.

Two sensitivity analyses of the primary outcome will be carried out based on altering the window in which the assessments must have been made. They are as follows:

1. Include all outcomes, regardless of the length of time elapsed from either 14 or 26 weeks.
2. As above, but if the 26 week outcome is missing and the 14 week outcome has been collected within ±4 weeks of 26 weeks, treat this as the 26 week outcome.

7 SUBGROUP ANALYSES

There is no planned subgroup analysis.

8 SAFETY ANALYSIS

Adverse events (AEs) and serious adverse events (SAEs) will be summarised according to severity and relatedness by treatment arm.

A Serious Adverse Events (SAE) is any untoward medical occurrence that:

- results in death
- is life-threatening
- requires inpatient hospitalisation or prolongation of existing hospitalisation
- results in persistent or significant disability/incapacity
- consists of a congenital anomaly or birth defect.

Other 'important medical events' may also be considered a serious adverse event when, based upon appropriate medical judgement, the event may jeopardise the participant and may require medical or surgical intervention to prevent one of the outcomes listed above.

NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.

There is a very low risk of SAEs in the current trial, however the following details a non-exhaustive list of potential SAEs and Adverse Events (AE):

Potential Serious Adverse Events (SAEs) (to parent/child):

1. Admission to psychiatric hospital (parent/child);
2. Sectioned under the Mental Health Act;
3. Significant and sustained deterioration of pre-existing mental health condition that requires immediate intervention that cannot be accommodated within the treatment protocol (as determined in clinical supervision);
4. Diagnosis of new mental health condition;

5. Suicidal behaviour;
6. A serious safeguarding issue is revealed.

Potential Serious Adverse Events (SAEs) not directly related to the trial and Adverse Events (AEs):

1. Children's schooling or parent/guardians work is adversely affected (e.g. due to time spent in therapy or assessments encroaching on school or homework time).
2. One or more aspect of the therapy or assessment procedure induces unacceptable levels of distress for either the participant, their parent/guardian, or the therapist.
3. It becomes apparent that one of more of the exclusion criteria is met (or inclusion criteria not met) by the participant. [NB. This will be logged but the participant remains in treatment as long as clinically appropriate and retained in the intent to treat sample].
4. A sustained and significant increase in detrimental behaviours (e.g. safety seeking behaviours) as determined by any of the outcome measures collected throughout the study.
5. The emergence of new detrimental behaviours (e.g. self-harm).
6. Drop-out of treatment / request to change therapist.
7. Any actual or potential breach of confidentiality.
8. A complaint is received from a participant, their parent/guardian, or the therapist referring to an actual or perceived adverse event as defined above.

The window for reporting SAEs and AEs will be:

(i) During the treatment phase based on therapist report

(ii) Up to the end of study based on parent/carer report (i.e. up to the 26 week assessment or qualitative interview, whichever is later).

The 14 week and 26 week assessments within this trial will include questionnaires monitoring participants' functioning and quality of life, therefore, some of the potential adverse events identified in this document will be monitored routinely. Therapists will also be asked to indicate the presence of an SAE or AE that arises during the course of treatment.

9 VALIDATION

A second Trial Statistician will validate the primary outcome and safety data analyses and review the statistical analysis report.

10 CHANGES TO THE PROTOCOL OR PREVIOUS VERSIONS OF SAP

None to report.

Dolan, P., Gudex, C., Kind, P., & Williams, A. (1995). A social tariff for EuroQol: results from a UK general population survey. *Working Papers.*

Ebesutani, C., Bernstein, A., Nakamura, B. J., Chorpita, B. F., & Weisz, J. R. (2010). A psychometric analysis of the revised child anxiety and depression scale-parent version in a clinical sample. *Journal of Abnormal Child Psychology, 38(2),* 249–260. https://doi.org/10.1007/s10802-009-9363-8

EuroQuol. (2020). European Quality of Life-5 Dimension 5-level: EQ-5D-5L. https://euroqol.org/eq-5d-instruments/eq-5d-5l-about/ (accessed 30.07.2020).

Evans, R., Thirlwall, K., Cooper, P., & Creswell, C. (2017). Using symptom and interference questionnaires to identify recovery among children with anxiety disorders. *Psychological Assessment*, *29*(7), 835.

Fenwick, E., Marshall, D.A., Levy, A.R., & Nichol, G. (2006). Using and interpreting cost-effectiveness acceptability curves: An example using data from a trial of management

strategies for atrial fibrillation. *BMC Health Services Research, 6,* 1.

Goodman R, Meltzer H, Bailey V (1998) The Strengths and Difficulties Questionnaire: A pilot study on the validity of the self-report version. *European Child and Adolescent Psychiatry, 7,* 125-130.

Goodman. R. (2001). Psychometric properties of the strengths and difficulties questionnaire. *Journal of the American Academy of Child and Adolescent Psychiatry, 40 (11),* 1337-1345.

Green, H., McGinnity, A., Meltzer, H., Ford, T., & Goodman, R. (2005). Mental Health of Children and Young People in Great Britain, 2004. National Statistics. https://doi.org/10.1037/e557702010-001

Health Innovation Network South. (2020). Needs of Children & Young People <13 Years During the Covid19 Crisis in Contact with Mental Health or Community Services.

Husereau, D., Drummond, M., Petrou, S., Carswell, C., Moher, D., Greenberg, D., Augustovski, F., Briggs, A.H., Mauskopf, J., &. Loder, E. (2013). Consolidated health economic evaluation reporting standards (CHEERS) statement. *Cost Effectiveness and Resource Allocation, 11(1)*, 6.

James, A. C., James, G., Cowdrey, F. A., Soler, A., & Choke, A. (2013). Cognitive behavioural therapy for anxiety disorders in children and adolescents. *The Cochrane Database of Systematic Reviews, 6(2),* CD004690. https://doi.org/10.1002/14651858.CD004690.pub3

Kessler, R., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in National Comorbidity Survey Replication. *Archives of General Psychiatry, 62(6),* 593–602. https://doi.org/10.1001/archpsyc.62.6.593

Langley, A. K., Bergman, R. L., McCracken, J., & Piacentini, J. C. (2004). Impairment in Childhood Anxiety Disorders: Preliminary Examination of the Child Anxiety Impact Scale–Parent Version. *Journal of Child and Adolescent Psychopharmacology, 14(1),* 105–114. https://doi.org/10.1089/104454604773840544

Langley, A. K., Falk, A., Peris, T., Wiley, J. F., Kendall, P. C., Ginsburg, G., … Piacentini, J. (2014). The Child Anxiety Impact Scale: Examining Parent- and Child-Reported Impairment in Child Anxiety Disorders. *Journal of Clinical Child and Adolescent Psychology, 43(4),* 579–591. https://doi.org/10.1080/15374416.2013.817311

Lundh, L.G., Wangby-Lundh, M., & Bjarehed, J. (2008). Self reported emotional and behavioral problems in Swedish 14 to 15-year-old adolescents: A study with the self-report version of the Strengths and Difficulties Questionnaire. *Scandinavian Journal of Psychology, 49,* 523–532.

Muris, P., Meesters, C., & van den Berg, F. (2003). The Strengths and Difficulties Questionnaire (SDQ): Further evidence for its reliability and validity in a community sample of Dutch children and adolescents. *European Child and Adolescent Psychiatry, 12* (1), 1–8.

McCrone, P., Dhanasiri, S., Patel, A., Knapp, M., & Lawton-Smith, S. (2008). Paying the price: the cost of mental health care in England to 2026. King's Fund. https://doi.org/10.1192/bjp.184.5.386

McElroy, E., Patalay, P., Moltrecht, B., Shevlin, M., Shum, A., Creswell, C., & Waite, P., Dr. (2020, May 8). Demographic and health factors associated with pandemic anxiety in the context of COVID-19. https://doi.org/10.31234/osf.io/2eksd

Merikangas, K. R., He, J., Burstein, M., Swendsen, J., Avenevoli, S., Case, B., ... Olfson, M. (2011). Service utilization for lifetime mental disorders in U.S. adolescents: results of the National Comorbidity Survey-Adolescent Supplement (NCS-A). *Journal of the American Academy of Child and Adolescent Psychiatry, 50(1),* 32–45. https://doi.org/10.1016/j.jaac.2010.10.006

Miller, S. D., Duncan, B. L., & Claud, D. A. (2003). The Outcome Rating Scale : *Journal of Brief Therapy, 2(2),* 91–100.

National Institute for Health and Care Excellence (NICE). 2019. Position statement on use of the EQ-5D-5L value set for England (updated October 2019)

https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/technology-appraisal-guidance/eq-5d-5l (accessed 30.07.2020)

National Institute for Health and Clinical Excellence (NICE). Guide to the Methods of Technology Appraisal, 2013.

https://www.nice.org.uk/process/pmg9/resources/guide-to-the-methods-of-technology-appraisal-2013-pdf-2007975843781 (accessed 30.07.20).

National Institute for Health and Care Excellence (NICE). 2019. Position statement on use of the EQ-5D-5L value set for England (updated October 2019)

https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/technology-appraisal-guidance/eq-5d-5l (accessed 30.07.2020)

O'Brien, D., Harvey, K., Young, B., Reardon, T., & Creswell, C. (2017). GPs' Experiences of Children with Anxiety Disorders in Primary Care: a Qualitative Study. *British Journal of General Practice, 67(665),* e888–e898.

Pennant, M. E., Loucas, C. E., Whittington, C., Creswell, C., Fonagy, P., Fuggle, P., ... & Group, E. A. (2015). Computerised therapies for anxiety and depression in children and young people: a systematic review and meta-analysis. *Behaviour research and therapy, 67,* 1-18. doi:10.1016/j.brat.2015.01.009

Personal Social Services Research Unit (PSSRU) Unit costs of health and social care, various years, University of Kent and the London School of Economics and Political Science https://www.pssru.ac.uk/project-pages/unit-costs/ (accessed 03.08.2020)

Reardon, T., Harvey, K., & Creswell, C. (2019). Seeking and accessing professional support for child anxiety in a community sample. *European child & adolescent psychiatry*, 1-16, https://doi.org/10.1007/s00787-019-01388-4

Reardon, T., Harvey, K., Young, B., O'Brien, D., & Creswell, C. (2018). Barriers and facilitators to parents seeking and accessing professional support for anxiety disorders in children: qualitative interview study. *European child & adolescent psychiatry, 27(8),* 1023-1031. Retrieved from https://doi.org/10.1007/s0078

Reardon, T., Hill, C., O'Brien, D., & Creswell, C. (2018). Online treatments for child anxiety: a survey of parent and GP attitudes. Manuscript in Preparation.

Reardon, T., Spence, S. H., Hesse, J., Shakir, A., & Creswell, C. (2018). Identifying children with anxiety disorders using brief versions of the Spence Children's Anxiety Scale for children, parents, and teachers. *Psychological assessment, 30(10),* 1342.

Stevens, K (2012). Valuation of the Child Health Utility 9D Index., *Pharmacoeconomics 30(8)*, 729-747.

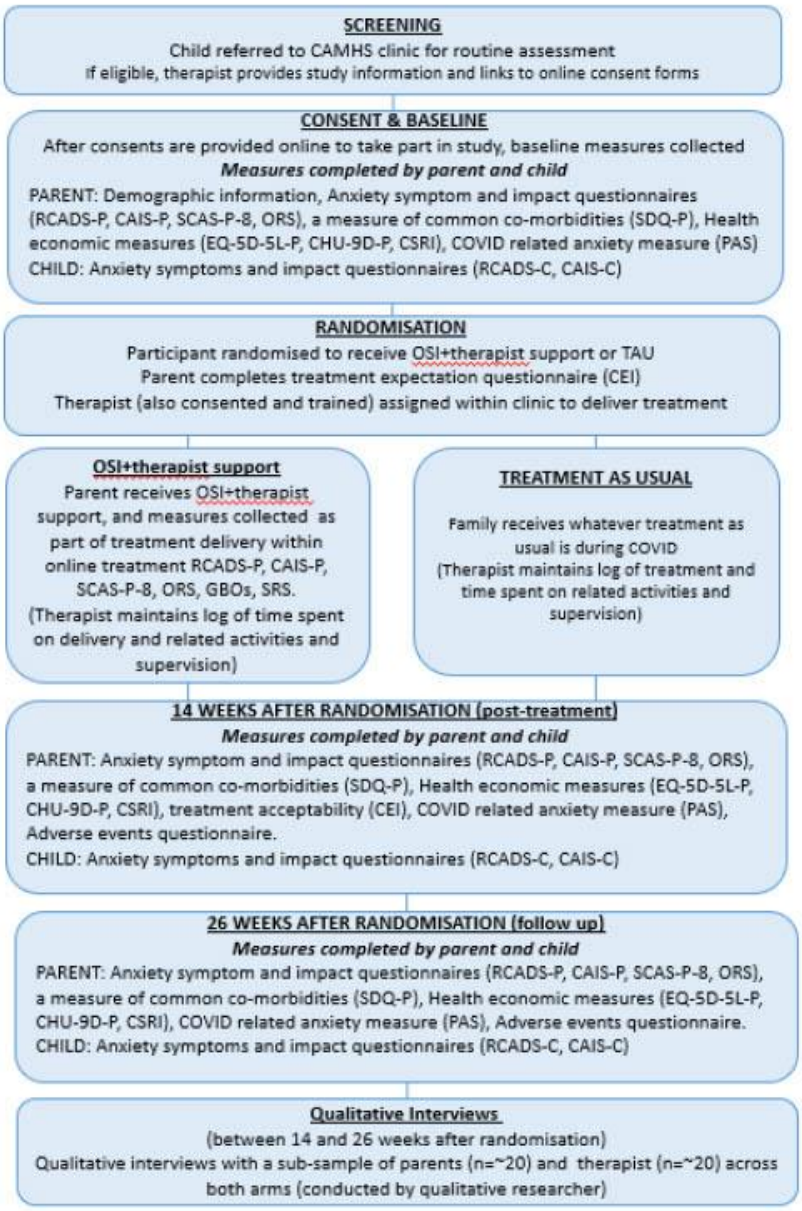
Thirlwall, K., Cooper, P. J., Karalus, J., Voysey, M., Willetts, L., & Creswell, C. (2013). Treatment of child anxiety disorders via guided parent-delivered cognitive-behavioural therapy: randomised controlled trial. *The British Journal of Psychiatry 203(6),* 436–44. https://doi.org/10.1192/bjp.bp.113.126698

Van Hout B, Janssen M, Feng Y et al. (2012) Interim scoring for the EQ 5D 5L: Mapping the EQ 5D 5L to EQ 5D 3L value sets. *Value in Health, 15:* 708-15.

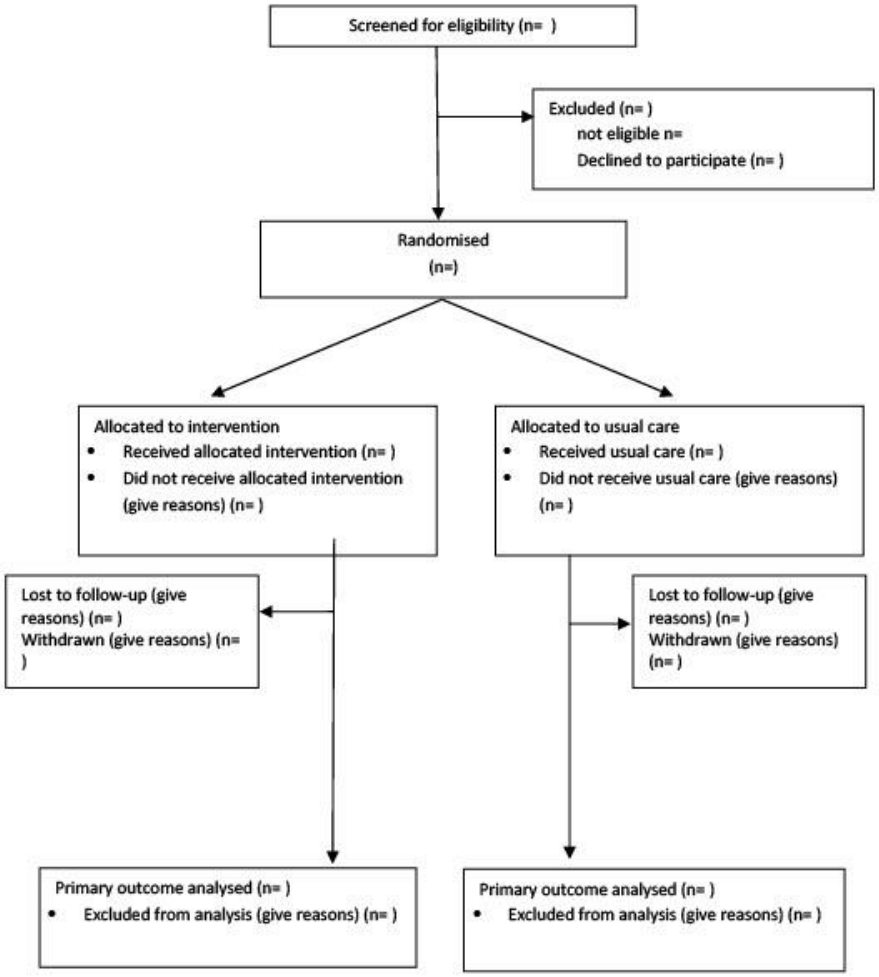
Yao, S., Zhang, C., Zhu, X., Jing, X., McWhinnie, C. M., & Abela, J. R. Z. (2009). Measuring Adolescent Psychopathology: Psychometric Properties of the Self-Report Strengths and Difficulties Questionnaire in a sample of Chinese adolescents. *Journal of Adolescent Health, 45,* 55–62.

12 Appendices

12.1 Appendix A: Flowchart of Trial Procedures



12.2 APPENDIX B: FLOW DIAGRAM OF TRIAL PARTICIPANTS



Child Anxiety Treatment in the context of COVID-19 (Co-CAT):

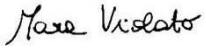
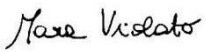
Enabling Child and Adolescent Mental Health Services (CAMHS) to provide efficient remote treatment for child anxiety problems

Health Economics Analysis Plan

Health Economics Analysis Plan (HEAP) – Child Anxiety Treatment in the context of COVID-19 (Co-CAT)

Essential items

		Description	Study-specific description
Section 1: Administrative information			
1.1	Title	Title that matches protocol and which includes the phrase 'Health Economics Analysis Plan'	Health economics analysis plan for the Child Anxiety Treatment in the context of COVID-19 (Co-CAT): Enabling Child and Adolescent Mental Health Services (CAMHS) to provide efficient remote treatment for child anxiety problems
1.2	Trial registration number	Trial registration number and name of registry that uniquely identifies the clinical trial on a publicly-accessible registry (and other relevant trial study numbers)	ISRCTN12890382 (registered 23/10/2020) https://doi.org/10.1186/ISRCTN12890382
1.3	Source of funding	Name of funders for trial and economic evaluation and funder(s)' reference number(s)	Department of Health and Social Care (DHSC)/UK Research and Innovation (UKRI) COVID-19 Rapid Response Initiative (managed by the Medical Research Council) and National Institute for Health Research (NIHR) Policy Research Programme (PRP).
1.4	Purpose of HEAP	Brief statement of the purpose of the HEAP	The purpose of this HEAP is to describe the analysis and reporting procedure intended for the economic analyses to be undertaken. The analysis plan is designed to ensure that there is no conflict with the protocol and associated statistical analysis plan and it should be read in conjunction with them.
1.5	Trial protocol version	Trial protocol version number associated with this HEAP	This document has been written based on information contained in the trial protocol version 2.5, dated 21 October 2022.
1.6	Trial Statistical Analysis Plan (SAP) version	SAP version number associated with this HEAP	SAP Version: 4.0, Date: 25 October 2022
1.7	Trial HEAP version	Sequential number and date of this version	HEAP Version: 1.0, Date: 1st November 2022

1.8	HEAP revisions	Date, justification for revision and summary of changes to the HEAP. Specify the individual making any revisions/changes to the HEAP.	N/A
1.9	Roles and responsibilities	Names, affiliations and roles of individuals who have significantly contributed to the HEAP	This HEAP was prepared by Assoc Prof Mara Violato (senior health economist), Health Economics Research Centre, Nuffield Department of Population Health, University of Oxford. The trial junior (Jack Pollard) and senior (Mara Violato) health economists are responsible for conducting and reporting the economic evaluation in accordance with the HEAP.
1.10a	Signature(s) of person(s) writing HEAP	Signature(s) of the person(s) writing the HEAP (and date)	 Date: 01/11/2022
1.10b	Signature of senior health economist	Signature of senior health economist who is guarantor of the economic evaluation (and date)	 Date: 01/11/2022
1.10c	Signature of Chief Investigator	Signature of the Chief Investigator for the trial (and date)	 Date: 02/11/2022
Section 2: Trial introduction & background			

2.1	Trial background and rationale	Synopsis of trial background and rationale including a brief description of research question and brief justification for undertaking the trial	More than a quarter of the population have an anxiety disorder at some point during their life and half of these people first experience an anxiety disorder by the age of 11 years (1). Anxiety disorders in childhood often continue into adolescence and adulthood and put these children at increased risk for other serious mental health disorders and impaired quality of life in adulthood (2). As a result, societal costs for anxiety disorders are substantial (3). Anxiety problems are a common reason for referral to the NHS Child and Adolescent Mental Health Services (CAMHS). Children with pre-existing anxiety problems are particularly vulnerable in the context of COVID-19, and there are concerns about likely increases in childhood anxiety as schools reopen and the pandemic unfolds. Co-CAT is a multi-site randomised non-inferiority trial to establish whether a novel online, parent-led cognitive behaviour therapy program (OSI; Online Support and Intervention for child anxiety) is as effective as what CAMHS have been delivering in the COVID-19 context, and whether it brings health-economic benefits. This research has the potential to create a step change in the digital delivery of treatments in CAMHS, bringing benefits in the COVID-19 context and beyond.

2.2	Aim(s) of the trial	Clearly and briefly state the main aim(s) of the trial	Briefly, the Co-CAT trial aims to evaluate the clinical and cost-effectiveness of OSI with therapist support for the treatment of child anxiety compared to 'COVID-19 treatment as usual' (C-TAU) in CAMHS throughout the next phases of the COVID-19 pandemic. Further aims are to explore the trajectory of change as reported within the OSI platform, to inform further developments, and to understand therapists' and parents' experiences of treating child anxiety (across both arms) in the current context to maximise learning to (a) enable rapid implementation of remote treatment delivery in CAMHS in any subsequent periods of social distancing, and (b) maintain the use of online platforms (such as OSI) in CAMHS when 'normal service' resumes.

2.3	Objectives and/or research hypotheses of the trial	Describe specific trial objectives (primary and secondary) or trial hypotheses	Primary objective: To evaluate the parent-reported clinical effectiveness (primary clinical outcome: the Child Anxiety Impact Scale- Parent report (CAIS-P)) of a brief parent-led cognitive behavioural treatment (CBT) delivered by the OSI platform with therapist support (OSI+therapist support) for the treatment of child anxiety compared to 'COVID-19 treatment as usual' (C-TAU) in CAMHS throughout the next phases of the COVID-19 pandemic. Secondary objective: (i) Further assessment of the clinical effectiveness (secondary clinical outcomes: CAIS-C, RCADS-C, RCADS-P, SCAS-8P,ORS, COVID-19 specific worries, and SDQ-P) of OSI+therapist support for the treatment of child anxiety compared to 'COVID-19 treatment as usual' (C-TAU) in CAMHS throughout the next phases of the COVID-19 pandemic. (ii) to evaluate the cost-effectiveness of OSI+therapist support for the treatment of child anxiety compared to 'COVID-19 treatment as usual' (C-TAU) in CAMHS. Explorative objectives: (i) Explore the trajectory of change reported within the OSI arm. (ii) Understand therapist' and parents' experiences of treating child anxiety in the current context to maximise learning to (a) enable rapid implementation of remote treatment delivery in CAMHS in any subsequent periods of social distancing, and (b) maintain the use of online interventions (such as OSI) in CAMHS when 'normal service' resumes.

2.4	Trial population	Describe the trial inclusion and exclusion criteria	Target population: (i) Children aged 5-12 with anxiety as the primary presenting problem, and their parents/carers. (ii) Therapists who deliver psychological treatments within Child and Adolescent Mental Health Services in England. Inclusion criteria: *Child*: is aged 5-12 years at intake; primary problem is anxiety; willing and able to assent. *Parent*: has sufficient English language to complete measures/ access interventions; family has access to the internet; is willing and able to provide consent. *Therapist*: provides psychological treatment to children in participating services, i.e. child and adolescent mental health services (CAMHS) across the NHS and Local Authorities in the UK, including Third Sector organisations that provide child mental health care on behalf of the NHS/Local Authorities; willing and able to provide informed consent (for qualitative interviews only). Exclusion criteria: Participants are not eligible if ANY of the following apply: *Child*: has co-morbid conditions that are likely to interfere with treatment delivery (established autism spectrum condition/ learning disability, suicidal intent/ recurrent or potentially life limiting self-harm); is identified by social services due to child protection concerns. *Parent*: has a significant intellectual impairment or severe mental health problem that is likely to interfere with treatment delivery; is unable to access

			or understand the written English language materials necessary for the interventions. *Therapist*: There are no exclusion criteria for Therapists.
2.5	Intervention(s) and comparator(s)	Describe the intervention(s) and comparator(s)	Intervention: OSI (Online Support and Intervention for child anxiety) is an online adaptation of an evidence-based brief parent-guided CBT program for the treatment of anxiety problems in preadolescent children. OSI comprises a parent website, accompanying therapist case management system, and accompanying child game app. Modules are supported by 7 x weekly 20 minute telephone sessions between the parent/carer and a therapist, and a review session 4 weeks after the final treatment session. Therapists will receive a video-based training programme (1 hour) and a treatment manual. All teams will be offered regular Q&A sessions throughout the treatment delivery phase to support set-up and delivery. Clinical supervision will be provided within CAMHS teams following their usual procedures. Comparator: 'COVID-19 Treatment as Usual' (C-TAU), i.e. whatever treatment the participating services are delivering to treat child anxiety problems in the COVID-19 context.

2.6	Trial design	Briefly describe the trial design including type of trial such as cluster, crossover, etc. Can also include details of power calculation, sample size (including any separate calculations for economic endpoints), randomisation and blinding.	This is a two arm, multi-site, randomised controlled non-inferiority trial to evaluate the clinical and cost-effectiveness of OSI with therapist support compared to CAMHS 'COVID-19 treatment as usual' (C-TAU) during the COVID-19 outbreak and to explore parent's and therapists' experiences. The study procedure is in line with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) statement 2013 (4). Between 418 and 560 children (209 - 280 per group) with a primary anxiety disorder and their parents will be randomised across the two treatment arms. This sample size is considered to be sufficient to provide a standardised noninferiority margin=0.33 and between 80 - 90% power (allowing for 30% attrition). Participants will be randomised in a 1:1 ratio to (i) OSI+therapist support or (ii) CAMHS Treatment as Usual for child anxiety problems within the COVID-19 context (C-TAU). Randomisation will be carried out via minimisation by child age (<=8; >=9), gender, service type (school based or not school based), and baseline anxiety-associated interference. Due to the nature of the trial, blinding is not possible to the trial participants of the allocated psychological therapy nor to the research team.
2.7	Trial start and end dates	Trial recruitment start and end dates and the follow-up period	Recruitment started in December 2020 and finished in July 2022. The follow-up period will be assessed at 26 weeks post-randomisation ending in March 2023.
Section 3: Economic approach/overview			

3.1	Aim(s) of economic evaluation	Describe the aim(s) of the economic evaluation	The aim of the economic evaluation is to address the question “What is the cost-effectiveness of ‘OSI with therapist support’ (OSI) for the treatment of child anxiety compared to ‘COVID-19 Treatment as usual’ (C-TAU)?”
3.2	Objective(s) of economic evaluation	Describe the objectives (primary and secondary) of the economic evaluation	The primary objective of the health economic evaluation is to estimate the cost-effectiveness of ‘OSI with therapist support’ (OSI) for the treatment of child anxiety compared to ‘COVID-19 Treatment as usual’ (C-TAU), 26 weeks post-randomisation, in a within-trial economic evaluation.

3.3	Overview of economic analysis	Briefly outline and justify the type of economic evaluation to be undertaken, identifying the primary economic analysis and outlining the analysis plan and the methods that will be used	The within-trial economic analysis will be performed using individual participant (child) level data from the Co-CAT trial. The analytical approaches will take the form of a cost-utility analysis (CUA- outcome: child health-related quality of life) in the primary economic evaluation, and cost-effectiveness analyses (CEA – two outcomes considered: CAIS-P, the primary clinical outcome; and school absence) in the secondary economic evaluations. For both primary and secondary economic analyses, the treatment cost for the OSI intervention will be estimated in two ways. First, we will base the cost on the actual time spent by the OSI therapist to train for and deliver the OSI treatment for each child treated; second, we will use the average time for training and delivery as reported by the OSI therapists who delivered the OSI treatment to more than two children within the trial and/or times based on expected OSI caseload if it were rolled out. This is to avoid overestimating the cost of OSI should a large proportion of OSI therapists end up delivering the OSI treatment to only one child, with the consequences that 1) the initial training would look like it applies per case; and 2) we would not properly capture the efficiency benefits that clinicians in other similar trials report as deriving with familiarity with the treatment, reached after the latter is delivered to several children. Based on trial evidence, incremental cost-utility and cost-effectiveness ratios will be calculated by taking a ratio of the difference in the mean costs (numerator) and mean utility /effect (denominator) in the CUA and CEA, respectively.

3.4	Jurisdiction(s)	Specify the jurisdiction(s) in which the analysis will be conducted including details of the country(s) and health system(s)	The trial is conducted in the UK, which has a national health service (NHS), providing publicly funded healthcare, primarily free of charge at the point of use.
3.5	Perspective(s)	State the perspective(s) from which the economic analysis is being conducted, such as societal perspective and/or healthcare payer perspective	Both the primary and secondary economic analyses will be from the NHS and personal social services (PSS) perspective in the base-case analyses. A sensitivity analysis for both will include a societal perspective.
3.6	Time horizon(s)	State the time horizon(s) over which costs and consequences are being evaluated	The economic analyses will compare the costs and consequences of each trial arm at 26 weeks post-randomisation.
Section 4: Economic data collection & management			
4.1	Statistical software	Specify the statistical software that will be used to carry out the health economic analysis	Stata version 17.0 or higher (StataCorp LP; College Station, TX) will be used for conducting the economic analysis.

4.2	Identification of resources	Justify and describe items of resource use that will be measured as part of the trial	The following items of health care resource use and broader resources that may differ between trial arms will be measured during the study period, with primary analyses including only those that refer to the child, and sensitivity analyses including both child's and parent's resources: primary and secondary health care and social care resource use for the child and the parent/carer; medication for the child and the parent/carer; travel time/cost associated with accessing those resources, whenever applicable; time off school for the child; time off work and associated productivity losses for the parent/carer; opportunity cost for the parent/carer associated with them using OSI (i.e. time spent online on OSI and time spent on support calls from therapists) or attending some sessions/part of sessions in the C-TAU arm (e.g. whenever C-TAU involved different combinations of family members at different parts of the sessions). In addition, OSI therapist's time spent in training, supervision, administrative tasks, and delivery of the intervention, and supervisor's time spent training/supervising the CWPs (as derived by the therapists' forms) will be measured to assess the amount of resources and cost of the intervention. For the C-TAU arm, time spent by therapists in supervision and delivering the treatment, as well as sessions preparation time, sessions administration time, travelling time/cost (e.g. travel time to home visits, if applicable) and other costs (e.g. printing, materials) related to the treatment will be measured. Supervisors' time will be derived by the therapists' forms and/or from published literature as

			will training time for both C-TAU therapists and supervisors, as applicable.
4.3	Measurement of resource-use data	Describe the resource-use data collection method(s) (including external routine datasets) and the time points at which they will be used.	Child and parent/carer resource use data will be collected online and measured using a modified version of the Client Services Receipt Inventory (CSRI) (5) which will be completed by the parent/carer at baseline, 14 weeks and 26 weeks post-randomisation. At baseline and 14 weeks assessments, parents will also be provided with a diary to keep a record of time off school/work and use of services throughout the study duration so to facilitate completing subsequent CSRIs. During the treatment phase, to identify and measure resources used in the OSI intervention arm and in the C-TAU control arm, we will use 'ad hoc' designed therapist' logs. As for C-TAU there is not a set number of sessions, we will continue to collect this information until the 26-week follow-up, as applicable.

4.4	Valuation of resource-use data	For each resource item measured, describe how the unit cost will be derived and from which specific price year. Outline how adjustments will be made for sources from different price years and which inflation index will be used.	All resource use will be valued in monetary terms using appropriate UK unit costs derived from local and national sources and/or participant's valuations estimated at the time of the study (2020-2023). Costs will be expressed in pounds sterling at 2022/2023 prices, as available. Adjustments will be made for inflation, when necessary, using the NHS cost inflation index (NHSCII) for health professionals / health care services and the ONS Retail Price Index for other resources (6). Unit costs for primary and social care and other community services will be obtained from the PSSRU publications (6). Unit NHS reference costs will be employed to value hospital resource use, e.g. A&E visits, outpatient and inpatient attendances (7). Medication costs will be taken from the British National Formulary (BNF) (8) and the Prescription Cost Analysis (PCA) for England (9). Time off school for children will be costed as a minimum as 'opportunity cost' for the educational sector (10, 11) using values from relevant governmental sources (e.g. department of education school spent per pupil), and acknowledging the limitations of the approach. If new published literature emerges, which reports on valuations of the cost of school absence for the child's future prospects, those valuations will be used to capture more comprehensively the cost of school absence for the child. Time off work for parent/carer will be costed using the Annual Survey of Hours and Earnings (ASHE) (12).

4.5	Identification of outcome(s)	Specify and justify the outcome(s) that will be measured	The primary economic outcome measures will be child's Quality-Adjusted Life Years (QALYs) derived from utility scores, obtained using the CHU-9D (parent-report on child) quality of life instrument (13-15), in the CUA. The secondary economic outcomes will be the CAIS-P (primary clinical outcome) and the child's percentage of school attendance, respectively in the CEAs. There is evidence that child anxiety may be associated with absence from school (16), which in turn may impact educational achievements (17) with potential impacts on later labour market engagement. However, if we observe no important difference in this outcome by trial arm, or if parent-report on this variable is poor, we may decide that is not appropriate/informative to conduct such an analysis. Parent/carer Quality-Adjusted Life Years (QALYs) derived from utility scores, obtained using the EQ-5D-5L quality of life instrument(18, 19) will be calculated for both trial arms. Parent–child dyad QALYs will be obtained by additively combining individual parent and child QALYs (20) and used as the outcome in a cost-utility sensitivity analysis from the societal perspective. Potential limitation of this approach will be discussed (21).
4.6	Measurement of outcome(s)	Describe the outcome data collection method(s) and the time points at which they will be used	Outcome data will be collected online at baseline, and at 14 weeks and 26 weeks post randomisation.

4.7	Valuation of outcome(s)	For each outcome measured, describe how it will be valued and the source of these valuations	Utility scores for the child will be derived from responses to the CHU-9D parent-report on child, using both the preference weights obtained from a sample of the UK adult general population (primary valuation) (14) and preferences weights obtained from Australian adolescents aged 11 to 17 years (secondary valuation) (22), as no established guideline exists as to which value set is more appropriate. Parent utility scores will be derived from responses to the EQ-5D-5L. UK utility values will be derived using the approach recommended by NICE, which currently is to use a validated mapping function from the existing EQ-5D-3L (19, 23, 24). Utility score will be used to generate child and parent QALYS over the duration of the trial (from baseline to 26 weeks follow-up).
Section 5: Economic data analysis			
5.1	Analysis population	Outline the analysis population that will be used in the economic base-case analysis (such as intention to treat, per protocol)	Both an intention-to-treat and per-protocol approach will be adopted for primary and secondary analyses, as it is common in inferiority trials (25-27).
5.2	Timing of analyses	Describe the timing of all planned analyses (e.g. interim and final analyses)	The final analysis (within-trial analysis) will be conducted once all participants have been followed for 26 weeks post-randomisation.
5.3	Discount rates for costs and benefits	Detail the source of, and justification for, discount rates used for costs and benefits	Given the short time-frame of the treatment and follow-up, discounting will not be applied to costs or effects.

5.4	Cost-effectiveness threshold(s)	Detail the cost-effectiveness threshold(s) to be used in analysis/interpretation	In the CUA, a cost-effectiveness threshold of £20,000-£30,000 per QALY will be used, as per NICE guidelines (19). For the CEA, the maximum threshold value that society is willing to pay for an additional child free from anxiety and for increased school attendance is unknown.
5.5	Statistical decision rule(s)	Describe how inference will be drawn (e.g. significance level, confidence intervals or mean net benefit)	Mean differences in costs and effects (QALYs, CAIS-P, and percentage of school attendance) will be estimated with associated 95% confidence intervals.
5.6	Analysis of resource use	Describe how differences in the use of resources/services between randomised groups will be compared	Mean differences in the use of services between randomised groups will be described and compared statistically, stratified by type of resource use.
5.7	Analysis of costs	Describe analyses of the cost data, specifying any covariates for statistical adjustment, assumptions, and alternative methods	Unadjusted and adjusted (for baseline costs) differences in overall mean costs between the arms will be analysed initially using Ordinary Least Squares (OLS) regression. The distribution of residuals from the regression model will then be examined and a decision will be made as to whether OLS is appropriate or another type of regression model should be considered (e.g. Generalised Linear Models (GLM)). Other covariates may also be considered in discussion with the statisticians in order to align the statistical and economic analyses as much as possible. These may include minimisation variables, i.e. child age, gender and site type (school versus clinic).

5.8	Analysis of outcomes	For each outcome used in the economic analysis, describe how the outcome will be analysed, specifying any covariates for statistical adjustment, assumptions, and alternative methods	Unadjusted and adjusted (for baseline utility in the CUA, and baseline CAIS-P and percentage of school attendance in the CEAs) mean differences in outcomes will be analysed using an appropriate regression model (e.g. OLS, LPM, GLM). Other covariates for adjustment will also be considered in discussion with the statisticians in order to align the statistical and economic analyses as much as possible. These may include minimisation variables, i.e. child age, gender and site type (school vs clinic).
5.9	Data cleaning for analysis	Outline how data will be cleaned before analysis	Descriptive statistics will be used to identify potential mistakes (e.g. typos at the data entry level). Suspected mistakes will be reported to the trial manager who will check the data against the source documents/master data. Reporting errors may occur too, which may require some decision rules to be taken. Corrections of identified typos as well as decision rules adopted to deal with reporting errors will be documented in the Stata code.

5.10	Missing data	Specify the procedure for dealing with missing data	Trial data will be examined for any missing data. Missing data will be imputed by use of conditional mean imputation for missing values deemed highly deterministic (e.g. online/ face-to-face therapist contacts), and multiple imputation for other missing items (e.g. GP consultations) and/or missing cases, under the assumption of missing at random (28). Most likely, for missing cases, the most aggregated measure will be imputed (e.g. total cost, rather than each component of cost), although in some cases it may be decided that disaggregated measures may be more appropriate. The primary analyses will be conducted on the imputed datasets, with analyses on complete cases being conducted as a sensitivity analysis. The specification of the imputation model will be considered in discussion with the statisticians in order to align the statistical and economic analyses as much as possible.
5.11	Analysis of cost-effectiveness	Describe the methods that will be used to summarise cost-effectiveness.	Cost and QALY data will be combined to calculate an incremental cost-effectiveness ratio (ICER) from both the NHS & PSS perspective and a societal perspective. Seemingly Unrelated Regression (SUR) will be used, if appropriate, to account for the correlation between the costs and the effects.

5.12	Sampling uncertainty	Describe how uncertainty around the costs and effectiveness estimates and summary cost-effectiveness measures will be explored	Uncertainty in the cost-effectiveness results will be analysed by use of cost-effectiveness acceptability curves (29) over a range of potential threshold values that the health system might be willing to pay for an additional QALY gained, in the CUA. Cost-effectiveness acceptability curves will be used also in the CEAs, although the maximum threshold value that society is willing to pay for an additional child free from anxiety and for increased school attendance is unknown.
5.13	Subgroup analyses or analysis of heterogeneity	Describe any analyses of subgroups or heterogeneity in cost-effectiveness and the analysis methods used	N/A

5.14	Sensitivity analyses	Describe any sensitivity analyses and their form	Several sensitivity analyses will be undertaken to explore uncertainties surrounding key parameters in the economic evaluation. These will include: using the most likely OSI treatment cost, should the treatment be rolled out in the NHS, which will be proxied by the lower costs incurred by the trial OSI therapists after treating multiple cases and/or cost based on expected OSI caseload if it were rolled out (please see point 3.3 above) and, if appropriate/possible, also using training and delivery costs from other trials using the OSI treatment (e.g. the iCATS trial: https://osiresearch.org.uk/icats/; or the MY-CAT trial https://osiresearch.org.uk/my-cats/; or the OSI GROWS study https://osiresearch.org.uk/osi-grows/); using each of the two available preference weights to value CHU-9D in the CUA; taking a societal perspective for both the CUA and the CEA where the outcomes refer to the child only; NHS and societal perspectives in the CUA, where the outcomes are parent–child dyad QALYs; conducting base-case analyses on complete cases only. Other sensitivity analyses may be required once the data have been made available.
Section 6: Modelling			
6.1	Extrapolation or decision analytic modelling	Outline whether decision analytic modelling or any other extrapolation will be used to estimate cost-effectiveness results beyond the period of the trial or to introduce an additional comparator or other evidence.	N/A
6.2	Model type	Describe the modelling approach that will be used and duration of extrapolation	N/A

6.3	Model structure	Detail the model structure (where possible, include diagram of model states and transitions between them)	N/A
6.4	Treatment effect beyond the end of the trial	Describe the duration and size of treatment effect in the period beyond the end of the trial	N/A
6.5	Other key assumptions	List the key structural assumptions of the model	N/A
6.6	Methods for identifying and estimating parameters	For each model parameter, describe the methods and data sources that will be used to estimate the parameter (e.g. from the RCT, systematic review, meta-analysis, other published data or expert opinion)	N/A
6.7	Model uncertainty	Describe the methods that will be used to assess parameter uncertainty in the results. Describe sensitivity analyses for the impact of other types of uncertainty on results.	N/A
6.8	Model validation	Describe the methods and data that will be used to check the face, internal and external validity of the model	N/A
6.9	Subgroup analyses/heterogeneity	Describe subgroup or heterogeneity analyses that will be executed and reported within the extrapolation or decision analytic modelling	N/A
Section 7: Reporting/publishing			
7.1	Reporting standards	Describe any guidelines that will be followed when publishing results	CHEERS guidelines (30) will be followed when reporting the health economic evaluation.
7.2	Deviations from the HEAP	Describe the procedure for reporting any deviations from the HEAP	Any deviation from HEAP will be described and justified in the final published report.
Section 8: Appendices			
8.1	Health economic collection tools	Include template examples of the resource-use data collection sheets and resource-use questionnaires	Data collection questionnares used throughout the trial will be included in an Appendix of the final report.

Optional items

		Description	Example
Section 1: Administrative information			
O1.1	Table of contents	List of HEAP contents with page numbers	N/A
O1.2	Abbreviations/glossary of terms/definitions	List of abbreviations and/or acronyms used within the HEAP alongside their meanings/definitions	CEA: cost-utility analysis. CHU-9D: Child Health Utility 9 Dimension instrument CSRI: Client Service Receipt Inventory CUA: cost-effectiveness analysis EQ-5D-5L: EuroQol 5 Dimension 5 Level instrument NHS: National Health Service PSS: personal and social services QALY: quality-adjusted life year
Section 4: Economic data collection & management			
O4.1	Monitoring collection of health economic data	Outline how the health economic data collected will be monitored	The health economics questionnaires will be administered online using REDCap (Research Electronic Data Capture) databases, therapist logs will be collected using excel files, and OSI usage data will be collected within the OSI online platform, and exported as excel files. The trial health economist(s) will work closely with the trial team throughout the data collection period. Data collection forms will be assessed throughout the trial period to monitor quality of the data and amend any forms or procedures if necessary.
O4.2	Database management	Outline how the economic data will be stored and managed and by whom	Economic data will be securely stored on the trial database and managed by the trial database manager, Lucy Taylor. Specifically, parent-reported data will be stored in RedCap and Treatment logs excel files will be stored on Microsoft Teams.

O4.3	Data entry	Outline how data will be entered/handled and outline any checking systems in place	All the health economics questionnaire data will be captured online. The database will use controls to limit data entry to plausible values. Individual therapist logs will be completed using excel files. The study team will manually check logs for potential errors and merge data from individual logs into a single database. OSI usage data exports will be regularly checked by the team to identify potential errors.
O4.4	Data archiving	State whether datasets, interim datasets and final analysis will be archived, and if so, how	A copy of health economic analysis files, derived datasets, interim datasets and final analysis will be locked and archived. Archived datasets will be held by the University of Oxford and will conform to the University data security policy and data compliance and Data Protection Act policies. The study team will develop plans to make a version of the de-identified dataset (together with detailed procedure documents, data dictionaries and analysis files) that is available for sharing via a suitable repository, and the original final de-identified datasets will be retained on the University server.
Section 6: Modelling			
O6.1	Value of information analysis	Describe whether value of information analysis is planned and the type and methods that will be used to calculate value of information	N/A
Section 8: Appendices			

O8.1	Cross-referencing to other trial documents	Reference to other relevant trial documents that are adhered to and followed when writing the HEAP and any other references used when writing the HEAP	N/A
O8.2	Illustrations	Illustrations such as annotated questionnaires detailing the database fieldnames, flow charts outlining the flow of data for the economic evaluation, or template tables	N/A

References

1. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry. 2005;62(6):593-602.
2. Copeland WE, Angold A, Shanahan L, Costello EJ. Longitudinal patterns of anxiety from childhood to adulthood: the Great Smoky Mountains Study. J Am Acad Child Adolesc Psychiatry. 2014;53(1):21-33.
3. McCrone P, Dhanasiri S, Patel A, Knapp M, Lawton-Smith S. Paying the price: the cost of mental health care in England to 2026. King's Fund; 2008.
4. Chan AW, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-7.
5. Beecham J. Client Service Receipt Inventory (CSRI) – Children's Version.1999 22/03/2022. Available from: http://www.dirum.org/instruments/details/45.
6. Unit Costs of Health and Social Care 2021 [Internet]. 2022 [cited 22/03/2022]. Available from: https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/.
7. National Cost Collection for the NHS – 2019/20 [Internet]. 2022 [cited 22/03/2022]. Available from: https://www.england.nhs.uk/national-cost-collection/.
8. British National Formulary (BNF) [Internet]. 2022 [cited 22/03/2022]. Available from: https://bnf.nice.org.uk/.
9. Prescription Cost Analysis (PCA) data [Internet]. 2022 [cited 22/03/2022]. Available from: https://www.nhsbsa.nhs.uk/prescription-data/dispensing-data/prescription-cost-analysis-pca-data.
10. Creswell C, Violato M, Fairbanks H, White E, Parkinson M, Abitabile G, et al. Clinical outcomes and cost-effectiveness of brief guided parent-delivered cognitive behavioural therapy and solution-focused brief therapy for treatment of childhood anxiety disorders: a randomised controlled trial. Lancet Psychiatry. 2017;4(7):529-39.
11. Bodden DH, Dirksen CD, Bögels SM, Nauta MH, De Haan E, Ringrose J, et al. Costs and cost-effectiveness of family CBT versus individual CBT in clinically anxious children. Clin Child Psychol Psychiatry. 2008;13(4):543-64.
12. Annual Survey of Hours and Earnings (ASHE) [Internet]. 2022 [cited 22/03/2022]. Available from: https://www.ons.gov.uk/surveys/informationforbusinesses/businesssurveys/annualsurveyofhoursandearningsashe.
13. Stevens K. Developing a descriptive system for a new preference-based measure of health-related quality of life for children. Qual Life Res. 2009;18(8):1105-13.
14. Stevens K. Valuation of the Child Health Utility 9D Index. Pharmacoeconomics. 2012;30(8):729-47.
15. Stevens KJ. Working with children to develop dimensions for a preference-based, generic, pediatric, health-related quality-of-life measure. Qual Health Res. 2010;20(3):340-51.
16. Finning K, Ukoumunne OC, Ford T, Danielson-Waters E, Shaw L, Romero De Jager I, et al. Review: The association between anxiety and poor attendance at school - a systematic review. Child Adolesc Ment Health. 2019;24(3):205-16.

17. Dalsgaard S, McGrath J, Østergaard SD, Wray NR, Pedersen CB, Mortensen PB, et al. Association of Mental Disorder in Childhood and Adolescence With Subsequent Educational Achievement. JAMA Psychiatry. 2020;77(8):797-805.
18. Herdman M, Gudex C, Lloyd A, Janssen MF, Kind P, Parkin D, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ- 5D-5L). Quality of Life Research. 2011;20(10):1727-36.
19. National Institute for Health and Care Excellence (NICE). NICE health technology evaluations: the manual - Process and Methods [PMG36] 2022 31 January 2022.
20. Weinstein MC, Torrance G, McGuire A. QALYs: the basics. Value Health. 2009;12 Suppl 1:S5-9.
21. Devlin N, Norman R, Ratcliffe J, Mulhern B, Dalziel K, Chen G, et al. Do child QALYs = adult QALYs? Five reasons why they might not2020 22/03/2022. Available from: https://www.ohe.org/news/do-child-qalys-adult-qalys-five-reasons-why-they-might-not.
22. Ratcliffe J, Huynh E, Stevens K, Brazier J, Sawyer M, Flynn T. Nothing About Us Without Us? A Comparison of Adolescent and Adult Health-State Values for the Child Health Utility-9D Using Profile Case Best-Worst Scaling. Health Econ. 2016;25(4):486-96.
23. Hernandez Alava M, Pudney S, Wailoo A. The EQ-5D-5L Value Set for England: Findings of a Quality Assurance Program. Value Health. 2020;23(5):642-8.
24. Hernandez Alava M, Wailoo A, Pudney S. Methods for mapping between the EQ 5D 5L and the 3L. 2017.
25. Bosmans JE, de Bruijne MC, van Hout HPJ, Hermens MLM, Adèr HJ, van Tulder MW. Practical Guidelines for Economic Evaluations Alongside Equivalence Trials. Value in Health. 2008;11(2):251-8.
26. Rhodes S, Richards DA, Ekers D, McMillan D, Byford S, Farrand PA, et al. Cost and outcome of behavioural activation versus cognitive behaviour therapy for depression (COBRA): study protocol for a randomised controlled trial. Trials. 2014;15(1):29.
27. (CHMP) EMACFMPFHU. Guideline on the Choice of the Non-Inferiority Margin. London: European Medicines Agency; 2005.
28. Faria R, Gomes M, Epstein D, White IR. A guide to handling missing data in cost-effectiveness analysis conducted within randomised controlled trials. Pharmacoeconomics. 2014;32(12):1157-70.
29. Fenwick E, Marshall DA, Levy AR, Nichol G. Using and interpreting cost-effectiveness acceptability curves: an example using data from a trial of management strategies for atrial fibrillation. BMC Health Services Research. 2006;6(1):52.
30. Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, et al. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) Statement: Updated Reporting Guidance for Health Economic Evaluations. Value in Health. 2022;25(1):3-9.

Supplementary Materials S8

Further detail on the health economic analyses

Mean (standard deviation (SD)) treatment resource use was reported by trial arm, stratified by each component (e.g. time spent on delivery, preparation, supervision). Other resource use was reported by trial arm, separately for the child and the parent, as the mean, SD, range and the percentage who reported at least one use per resource category. Differences in the use of services between trial arms were reported descriptively but not compared statistically, to avoid problems of multiple testing and ensure the focus of the economic analysis remained on cost and cost-effectiveness, rather than the individual resource use components [16].

Current best-practice methods for conducting and reporting economic evaluation alongside randomised controlled trials were adhered to [17]. Health economics analyses were pre-specified in the Health Economics Analysis Plan (Supplementary Material S7) [18] finalised before the end of the trial and before accessing any data. Mean (standard error (SE)) and mean differences (95% confidence interval (CI)) in outcomes and costs were estimated and presented in tabular form (Tables S15.9 and S15.10, respectively), including adjusted mean differences controlling for baseline values where possible, using linear regression.

Both an intention-to-treat (ITT) and per-protocol (PP) approach was adopted for primary and secondary analyses, as is common in non-inferiority trials [19-21]. Similarly to the statistical analyses, the per-protocol population included participants who had (i) received five or more treatment sessions, (ii) received the treatment they were originally assigned to, (iii) submitted their final questionnaire within 30 weeks of randomisation, and (iv) started treatment within 12 weeks of being randomised. Missing data were imputed using mean imputation conditional on treament arm for missing items and, when appropriate, also conditional on other characteristiscs (e.g. items relating to online/phone therapist's contact time were conditional on both treatment arm and session number). Multiple imputation using chained equations was utilised for missing responses (e.g. supervision time) and missing cases, under the assumption of missing at random [22]. Estimates derived from each imputed dataset were combined using Rubin's rules [23].

Uncertainty in the cost-effectiveness results was analysed by bootstrapping costs and effects 500 times from each of the 40 imputed datasets (i.e. 20,000 bootstraps in total), running the incremental analysis on each

bootstrapped dataset, and extracting the treatment effect [24]. The 20,000 bootstrapped results were presented graphically using the cost-effectiveness plane (CE-plane), while the probability of OSI-TS being cost-effective over a range of willingness-to-pay (WTP) values for an additional QALY gained was presented using a cost-effectiveness acceptability curve (CEAC) [25]. A WTP threshold of £20,000-£30,000 per QALY gained was used to evaluate whether OSI-TS was cost-effective compared to C-TAU, as per NICE guidelines [26]. Net Health Benefits (NHB) and Net Monetary Benefit (NMB) were also reported for all our cost-utility analyses (CUAs) (Table S17.3) for the willingness to pay of £20,000 and £30,000 per QALY (Quality-Adjusted Life Year), as recommended by the same NICE guidelines [26]. The NHB is a summary statistics that captures the impact on the health of the population of adopting a new intervention, in our case OSI+TS. NHB is generally measured using QALYs and is calculated using the following formula: "incremental gain in QALYs – (incremental cost / opportunity cost threshold)". A positive NHB in Table S17.3, indicates that that overall population health would improve if OSI+TS is adopted, while a negative NHB indicates that the health benefits of OSI+TS may not be enough to offset the health losses that may be generated if some healthcare ends to be funded in order to free resources for OS+TS [27]. The NMB is a summary statistics that captures the value of OSI+TS in monetary terms for WTP thresholds of £20,000 and £30,000 per QALY gained in our study. It is calculated according to the formula: "incremental benefit x threshold) – incremental cost". A positive NMB means that OSI+TS is cost-effective compared with C-TAU at the given willingness-to-pay threshold [28].

A similar approach (i.e. CE-plans and CEACs) was used in the cost-effectiveness analyses CEA, although the maximum threshold value that the decision maker is willing to pay for an improvement in the CAIS-P is unknown. We nevertheless presented a range of possible maximum values that a decision maker might be willing to pay for a unit improvement in outcome.

Various pre-specified sensitivity analyses (SA) were undertaken to explore uncertainties around assumptions made in the base-case analyses and test the robustness of the results. For both of the CHU9D value sets, the following ITT CUA sensitivity analyses were undertaken: (1) assuming the optimum delivery time for the OSI-TS arm was achieved for all participants (SA1 for UK value set and SA2 for Australia value set) where the optimum delivery of OSI has 8 modules at most (i.e., modules 0-7): Module 0, an initial meeting, takes 15 minutes, while each of Modules 1-7 takes 20 minutes. In addition, a therapist spends 7.5 minutes on preparation and 10 minutes on administration.; (2) taking a societal perspective for costs, excluding missed school human

capital costs (SA3 and SA4); (3) taking a societal perspective for costs, including missed school human capital costs (SA5 and SA6); (4) using the parent-child dyad QALYs as the outcome and societal costs, excluding missed school human capital costs (SA7 and SA8); (5) conducting the CUA for complete cases (SA9 and SA10). The same CUA sensitivity analyses (1) to (4) were undertaken on the per-protocol sample (SA11 to SA18 in Supplementary Table S17.2).

Sensitivity analyses (1) to (3) were also undertaken on the ITT (SA19 to SA21 in Supplementary Table S17.4) and per-protocol (SA22 to SA24 in Supplementary Table S17.4). All analyses were undertaken in Stata (MP) version 17.1 (StataCorp LP; College Station, TX).

Preliminary health economic results were presented to PPI representatives to get feedback on interpretation and presentation.

Supplementary Materials S9

Primary child anxiety subtype as determined by treating clinicians

Anxiety Type	Overall	OSI+TS	C-TAU
Separation anxiety disorder	130	66	64
Generalised anxiety disorder	107	53	54
Social anxiety disorder	40	22	18
Specific phobia	13	9	4
Panic disorder	11	11	0
Selective mutism	1	1	0
Separation/Social Anxiety	1	0	1
Other	7	3	4
Primary anxiety problem not specified	26	12	14
No treatment log	107	43	64
Grand Total	**443**	**220**	**223**

OSI+TS=Online Support and Intervention for child anxiety plus therapist support; C-TAU=child mental health services treatment as usual.

Supplementary Materials S10: Statistical Analysis Report

Primary Care Clinical Trials Unit

STATISTICAL ANALYSIS REPORT

Child Anxiety Treatment in the context of COVID-19 (Co-CAT)

Enabling Child and Adolescent Mental Health Services (CAMHS) to provide efficient remote treatment for child anxiety problems

CONFIDENTIAL

Version 2.0

11 December 2023

	NAME	TITLE	SIGNATURE	DATE
Written by:	Sam Mort	Statistician		11 December 2023
Reviewed by:	Nicola Williams	Senior Statistician		11 December 2023
Approved by:	Prof. Cathy Creswell	Chief Investigator		11 December 2023

VERSION HISTORY

Version	Version Date	Changes
0.1	14 February 2023	First draft of the statistical analysis report.
0.2	23 February 2023	Corrected several typos. Included treatment received in CONSORT diagram. Included table of treatment completion. Updated requirement to be included in the per-protocol analysis.
0.3	28 February 2023	Removed the analysis of the individual components of the RCADS-P/C. Updated the safety analysis based on what intervention the participants actually received instead of what the participant was randomised to receive.
0.4	7 March 2023	Updated results based on the 6 March 2023 data download. Updated per protocol analysis. Formatted forest plots.
0.5	17 March 2023	Corrected several typos. Updated results based on the 17 March 2023 data download. Updated per protocol analysis. Included statement from CI regarding ongoing adverse events.
0.6	27 March 2023	Changed the wording on the CONSORT diagram, tables and text from "Screened" to "Referred to Study Information by Clinical Teams" as screening was not done. Included more decimal points in table 1. Included range of treatment sessions received in table 4. Included an overall column in table 5. Changed the number of decimal points of the P-values for the primary and secondary analysis in table 7 due to how small they are. Included the analysis of the CEI from the therapists in table 8. Included seven missing adverse events into the safety analysis.
0.7	31 March 2023	Clarified that the cost effectiveness and exploratory objectives are not covered in this report. Updated forest plots with P-values to 2 significant figures.
0.8	4 May 2023	Updated other reason on CONSORT diagram. Updated P-values in tables and figures to Lancet style. Included a post hoc analysis for the within-group treatment effects for the primary and secondary outcomes. Included a post hoc sensitivity analysis for a less restrictive per protocol population. Included range to the CEI.
0.9	9 May 2023	Corrected typos. Updated other reasons on CONSORT diagram
0.10	16 May 2023	Updated other reasons on CONSORT diagram. Explained why the trajectory of changes within the OSI + therapist support arm were not conducted.
1.0	16 May 2023	Signed off
1.1	11 December 2023	Corrected typo
2.0	11 December 2023	Signed off

CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

1 INTRODUCTION

Trial Title: Enabling Child and Adolescent Mental Health Services (CAMHS) to provide efficient remote treatment for child anxiety problems

Short Title: Child Anxiety Treatment in the context of COVID-19 (Co-CAT)

Ethics Ref: 20/HRA/4431

IRAS Project ID: 288074

Sponsor: University of Oxford

Funder: Department of Health and Social Care (DHSC)/UK Research and Innovation (UKRI) COVID-19 Rapid Response Initiative (managed by the Medical Research Council), and the NIHR Policy Research Programme

Protocol Date and Version No.: 02 September 2022, version 2.4

Statistical Analysis Plan Date and Version No.: 25 October 2022, version 4.0

1.1 PREFACE

Chief Investigator: Professor Cathy Creswell – cathy.creswell@psych.ox.ac.uk

Clinical Trial Manager: Lucy Taylor – lucy.taylor@psych.ox.ac.uk

Trial Statistician: Sam Mort – sam.mort@phc.ox.ac.uk

Validating Statistician: Nicola Williams – nicola.williams@phc.ox.ac.uk

Data Manager: James Van Santen – james.vansanten@phc.ox.ac.uk

This document details the main analysis for the main paper reporting results for the Department of Health and Social Care (DHSC), and UK Research and Innovation (UKRI) COVID-19 Rapid Response Initiative (managed by the Medical Research Council), and the NIHR Policy Research Programme funded randomised controlled trial to evaluate the parent-reported clinical effectiveness of a brief parent-led cognitive behavioural treatment (CBT) delivered by the OSI platform with therapist support (OSI + therapist support) for the treatment of child anxiety problems compared to 'COVID-19 treatment as usual' (C-TAU) in CAMHS. The results reported here follow the strategy set out in the statistical analysis plan (SAP). Subsequent analyses of a more exploratory nature will not be bound by this strategy though they are expected to follow the broad principles laid down in the SAP.

The analysis strategy will be available on request when the principal papers are submitted for publication in a journal. Suggestions for subsequent analysis by journal editors or referees, will be considered carefully, and carried out as far as possible in line with the principles of the analysis strategy; if reported the source of the suggestion will be acknowledged.

This report contains the main results from the main analysis based on the statistical analysis plan "ST101-A_Statistical_Analysis_Plan_SAP_Co-CAT 4.0 25Oct2022.pdf" dated 25 October 2022. The results of the analysis contained in this report were conducted after the hard datalock on 27 March 2023. Any deviations from the statistical analysis plan will be described and justified in this report of the trial.

1.2 VALIDATION

This report was reviewed by Nicola Williams (Senior Trial Statistician).

1.3 SOFTWARE EMPLOYED

All datasets, programs, and output are saved on the PC-CTU restricted drive, in the folder "\\phc.imsu.ox.ac.uk\PHC\clinical_trials\HB_O\Co-CAT\STATS\5. Analysis". The data was exported from the clinical database by the data manager as a DTA file which is stored in the subfolder "1.Data Received (read only)". Stata (SE) version 16.1 was used for all data management/manipulation and the statistical analysis. The datasets that were generated and used in the analysis are stored in the subfolder "2.Data for Analysis (e.g. dta or sas)". All programs used in the data management and analysis are saved in the folder "3.Programs – Sam Mort". All output that was generated from the analysis is saved in the folder "4.Output".

2 METHODS

2.1 BACKGROUND INFORMATION

More than a quarter of the population have an anxiety disorder at some point during their life and half of these people first experience an anxiety disorder by the age of 11 years (Kessler at al., 2005). Anxiety disorders in childhood often continue into adolescence and adulthood and put these children at increased risk for other serious mental health disorders and impaired quality of life in adulthood (Copeland, Angold, Shanhan, & Costello, 2014). As a result, societal costs for anxiety disorders are substantial, with estimated total cost in England of £8.9 billion, expected to rise to £14.2 billion by 2026 (McCrone, Dehanasiri, Patel, Knapp, & Lawton-Smith, 2008).

Cognitive behaviour therapy (CBT) for children with anxiety disorders works well (James, James, Cowdrey, Soler, & Choke, 2013), but only a minority of children with anxiety disorders access treatment (Green, McGinnity, Meltzer, Ford, & Goodman, 2005; Merikangas et al., 2011). A recent UK survey found that more than 60% of children with anxiety disorders had not received any professional support, and only 2% had received CBT (Reardon, Harvey, & Creswell, 2018). Families face extensive barriers accessing professional support for child anxiety disorders including high demands on services, limited available support, and long waiting lists (O'Brien, Harvey, Young, Reardon, & Creswell, 2017; Reardon, Harvey, Young, O'Brien, & Creswell, 2018).

Traditional CBT for child anxiety disorders is typically lengthy and involves specialists working directly with the child. We have developed a briefer version of the traditional treatment that involves working directly with parents, and supporting them in helping their child overcome their difficulties with anxiety. This brief parent-guided treatment has similar outcomes to the traditional approach, and can be delivered by non-specialists (Creswell et al., 2017; Thirlwall et al., 2013). However, improving treatment efficiency further could enable more families to access effective treatment when they first need it. Online delivery of parent-guided treatment offers a means to do this by substantially reducing the amount of therapist contact time needed. Delivering treatment online also has the potential to increase access to families who may experience barriers to accessing traditional treatment approaches. In a recent survey of parents of children with elevated anxiety, all parents had some form of internet access, and more than 85% of parents reported that online treatment delivery would reduce stigma for families and allow families to use it at any time, and from home (Reardon, Hill, O'Brien, & Creswell, 2018).

We have worked in collaboration with families, NHS clinicians and a tech-company to co-design an online version of our parent-guided treatment for child anxiety disorders called OSI (Online Support and Intervention for child anxiety). OSI comprises a parent website, accompanying therapist case management system, and accompanying child game app (see *OSI Overview and Screenshots* document). Modules are supported by 7 x weekly 20-minute telephone sessions between the parent and a therapist and a review session 4 weeks after the final treatment session).

Importance in the context of COVID-19

The Health Innovation Network (Health Innovation Network South London, 2020) highlighted that children with existing anxiety issues are a high risk population during the COVID-19 pandemic, and our UKRI funded Co-SPACE study (CUREC R69060/RE010) that tracked child and adolescent mental health throughout the pandemic identified high levels of fear and worry about COVID-19 among children, including fears about leaving the house, and a significant increase in emotional symptoms in primary school aged children during lockdown (Co-SPACE Report 3, 2020). CAMHS and parents were concerned that child anxiety would increase as we approached the post-lockdown phase and schools re-opened (Health Innovation Network South London, 2020).

In our Co-SPACE study, parents reported that they wanted help via online materials and personalised support from a professional, however there are currently no evidence-based platforms available to CAMHS to do this (Pennant et al., 2015). From extensive contact with CAMHS therapists, we understood that they were typically delivering 'face to face' therapy via phone/videocall, but had little evidence about how to do this most effectively and efficiently. OSI provides a potential means to address the current challenges that CAMHS face in meeting the needs of children with anxiety problems and their families; it could be delivered as intended despite social distancing measures and is sufficiently flexible to address COVID-19 specific fears/worries. The OSI platform was recently introduced into the Anxiety and Depression in Young People (AnDY) Research Clinic at the University of Reading following a codesign and usability testing phase (Hill et al. 2022) with good engagement from families (Hill et al. 2021). However, it has not yet been subject to systematic evaluation and we do not know whether outcomes are as good as those CAMHS are currently achieving and whether OSI enables further efficiencies.

Aims

The proposed research evaluated the clinical and cost-effective of OSI with therapist support for the treatment of child anxiety compared to 'COVID-19 treatment as usual' (C-TAU) in CAMHS and other children's mental health services throughout the latter phases of the COVID-19 pandemic. Further aims were to explore the trajectory of change as reported within the OSI platform to inform further developments, and to understand therapist and parents' experiences of treating child anxiety problems (across both arms) in the current context to maximise learning to (a) enable rapid implementation of remote treatment delivery in CAMHS in any subsequent periods of social distancing, and (b) maintain the implementation of online platforms (such as OSI) in CAMHS when 'normal service' resumes.

2.2 Trial/Study Design

This is a two arm, multi-site, randomised controlled non-inferiority trial to evaluate the clinical cost-effectiveness of OSI with therapist support compared to CAMHS and other child mental health services 'COVID-19 treatment as usual' (C-TAU) during and beyond the COVID-19 outbreak and to explore parent and therapists' experiences. The study procedure is in line with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) statement 2013 (Chan et al., 2013)

See Appendix I for SPIRIT schedule of enrolment, intervention, and assessments.

See Appendix II for the trial procedures flowchart.

2.3 Objectives

All study objectives are described below.

2.3.1 Primary Objective

The primary objective is to evaluate the parent-reported clinical effectiveness of a brief parent-led cognitive behavioural treatment (CBT) delivered by the OSI platform with therapist support (OSI + therapist support) for the treatment of child anxiety problems compared to 'COVID-19 treatment as usual' (C-TAU) in CAMHS throughout the next phases of the COVID-19 pandemic.

2.3.2 Secondary Objectives

The secondary objectives are as follows:

1) Further assessment of the clinical effectiveness of OSI + therapist support for the treatment of child anxiety problems compared to 'COVID-19 treatment as usual' (C-TAU) in CAMHS throughout the next phase of the COVID-19 pandemic,
2) Evaluate the cost-effectiveness of OSI + therapist support for the treatment of child anxiety problems compared to 'COVID-19 treatment as usual' (C-TAU) in CAMHS.

2.3.3 Exploratory Objectives

The exploratory objectives are as follows:

1) Explore the trajectory of change reported within the OSI arm,
2) Understand therapist and parents' experiences of treating child anxiety in the current context to maximum learning to:
    a. Enable rapid implementation of remote treatment delivery in CAMHS in any subsequent periods of social distancing, and
    b. Maintain the usual online interventions (such as OSI) in CAMHS when 'normal services' resumes.

The cost effectiveness and exploratory objectives are not covered in this report.

See Appendix III for a full summary of the study objectives and outcome measures.

2.4 TARGET POPULATION

Children aged 5-12 years with anxiety as the primary presenting problem, and their parents/carers.

2.4.1 Inclusion Criteria

Child

- is aged 5-12 years at intake,
- primary problem is anxiety,
- and willing and able to assent.

Parent/Carer

- has sufficient English language to complete measures/access interventions,
- family has access to the internet,
- and is willing and able to provide consent.

2.4.2 Exclusion Criteria

Participants were not eligible if ANY of the following applied:

Child

- has co-morbid conditions that are likely to interfere with treatment delivery (established autism spectrum conditions/learning disability, suicidal intent/recurrent or potential life limiting self-harm),
- is identified by social services due to child protection concerns,
- is identified via a Schools Team and is in Reception year, year 1, or year 2 in a school that is taking part in the MyCATS (ISRCTN Registration Number 82398107) study (another study where the child may receive the OSI intervention.

Parent/Carer

- has a significant intellectual impairment or severe mental health problem that is likely to interfere with treatment delivery,
- is unable to access or understand the written English language materials necessary for the intervention.

2.5 INTERVENTIONS

2.5.1 Intervention

OSI (Online Support and Intervention for child anxiety) is an online adaptation of an evidence-based brief therapist-guided, parent-led CBT program for the treatment of anxiety problems in preadolescent children. OSI comprises a parent website, accompanying therapist case management system, and accompanying child game app. Modules were supported by 7 x weekly 20-minute telephone/video call sessions between the parent/carer and a therapist and a review session 4 weeks after the final treatment session. Therapists received a video-based training programme (45 minutes) and a treatment manual. All teams were offered regular Q&A sessions throughout the treatment delivery phase to support set-up and delivery. Clinical supervision was provided within teams following their usual procedures.

2.5.2 Comparator

'COVID-19 Treatment as Usual' (C-TAU), i.e., whatever treatment the participating services are delivering to treat child anxiety problems in clinical Child and Adolescent Mental Health Services (CAMHS) in the COVID-19 context and beyond.

2.6 OUTCOME MEASURES

2.6.1 Child Anxiety Impact Scale – Parent Version (CAIS-P)

The primary objective is to evaluate the parent-reported clinical effectiveness of OSI + therapist support for the treatment of child anxiety compared to 'COVID-19 treatment as usual' (C-TAU) in CAMHS throughout the next phases of the COVID-19 pandemic.

The primary outcome was assessed using the Child Anxiety Impact Scale – parent version (CAIS-P). The CAIS-P was used to determine the extent to which anxiety interferes in the child's life. This measure covers three psychosocial domains (academic, social activities, and home/family environments) and consists of 27 items rated on a 4-point scale. In keeping with other trials with pre-adolescent children, we used the 25-item version of the

measure (without two items which ask about boyfriend/girlfriends, and dating; e.g. Evans et al (2017) and Thirlwall et al (2013)). An additional 4 'global' items assess overall interference. The CAIS-P was completed at baseline, and then at 14 and 26 weeks post-randomisation by both the parent/carer and the child. The primary outcome is the CAIS-P at 26 weeks post randomisation.

Both the child and parent versions of the CAIS have been shown to have good psychometric properties (Langley et al., 2014; Langley, Bergman, McCracken, & Piacentini, 2004). The Child Anxiety Impact Scale – child version (CAIS-C) was analysed as a secondary outcome.

Derivation

Each item is scored on a 4-point Likert scale (0 = "Not at all", 1 = "Just a little", 2 = "Pretty much", 3 = "Very much"). A total score sums the scores of the first 25 items, giving a possible range of 0 to 75. Missing data for individual questions was handled by prorating the remaining items to get a total score. This was done if at least 75% of items had been completed. If more than 25% were missing the total was set to missing. A total score for the 4 global items was also obtained, with a possible range of 0-12. As above, if at least 75% of the questions had been answered, the total score was obtained by prorating the remaining items. If more than 25% are missing the total was set to missing.

2.6.2 Child Anxiety Impact Scale – Child Version (CAIS-C)

The Child Anxiety Impact Scale – child version (CAIS-C) covers the same domains as the CAIS-P and was completed at the same time points as the CAIS-P.

Derivation

The CAIS-C score was calculated in the same way as for the parent version (see section 2.6.1).

2.6.3 Revised Child Anxiety & Depression Scale – Parent & Child Versions (RCADS-P/C)

The Revised Child Anxiety and Depression scale – parent & child versions (RCADS-P/C) are routinely used within CAMHS. It is a 47-item questionnaire, with corresponding parent-report and child-report versions that assess symptoms of anxiety disorders and major depressive disorder. Responders rate how often each item applies on a 0 ("never") to 3 ("always") scale. The RCADS-P/C has been shown to have robust psychometric properties in children from age 7 (Chorpita, Moffitt, & Gray, 2005; Ebesutani, Bernstein, Nakamura, Chorpita, & Weisz, 2010). RCADS-P/C was completed at baseline, and then at 14 and 26 weeks post randomisation by both parent/carer and child.

Derivation

Each of the 47 items is scored on a 4-point Likert scale (0 = "never", 1 = "sometimes", 2 = "often", 3 = "always").

Two scores were obtained:

1) A total score for anxiety, which sums the scores for all except major depression, with a possible range of 0 to 111, and
2) A total score for anxiety and depression (overall score) which sums scores of all items (excluding 48), with a possible range of 0 to 141.

Missing data for raw scores were handled by prorating the remaining items. It is recommended that the total anxiety score can have up to 10 missing items, but only if each subscale has no more than 2 missing; and the total anxiety and depression score can have up to 12 missing items, but only if each subscale has no more than 2 missing items. To estimate the scale score, the sum of the completed items within each scale was divided by the number of items completed, then multiplied by the total number of items in that scale, and then rounded.

2.6.4 Brief Spence Children's Anxiety Scale – Parents Version (SCAS-P-8)

The SCAS-P-8 is a brief version of the Spence Children's Anxiety Scale (Reardon, Spence, Hesse, Shakir & Creswell, 2018). It is an 8-item questionnaire designed to assess symptoms of anxiety disorders in children. An initial evaluation of the questionnaire indicates it has good psychometric properties in children from age 7 to 11 (Reardon et al., 2018). Only 1 of the 8 items are required to be collected to score this measure as 7/8 items overlap with those already collected within the RCADS-P. The additional item that enables us to calculate a SCAS-P-8 total score was completed at baseline, and then at 14 and 26 weeks post randomisation by the parent/carer.

Derivation

Each of the 8 items is scored on a 4-point Likert scale (0 = "never", 1 = "sometimes", 2 = "often", 3 = "always"). The total score was calculated as a sum of these 8 items, giving a possible range of 0 to 24. The items of the RCADS which make up this score are 1, 9, 18, 27, 32, 34, 43, and 48.

2.6.5 Overall Functioning (ORS)

The Outcome Rating Scale (ORS) (Miller, Duncan, Brown, Sparks & Claud, 2003) was used to assess functioning across different areas of the child's life. It comprises four simple rating scales in which the parent/carer rates how their child has been feeling over the last week (individually, interpersonally, socially, and overall wellbeing). Each item is rated using a variable length (as it is done online the length of the line is not always 10cm) visual analogue scale, with instructions to place a mark on each line. A higher score indicates better functioning. It has good reliability and validity (Bringhurst, Watson et al. 2006). The ORS was completed at baseline, and then at 14 and 26 weeks post randomisation by the parent/carer.

Derivation

Each of the four visual analogue scales are approximately 10cm, but this varied due to it being done online. The proportion of the line along which the mark was made was calculated and converted to a 0-10 scale, measured to 1 decimal place. The four scores are added together to give an overall score with a possible range of 0-40.

2.6.6 Common Comorbid Emotional and Behavioural Problems (SDQ-P)

The Strengths and Difficulties Questionnaire (SDQ-P) (Goodman, Meltzer & Bailey, 1998) comprises of 5 scales assessing: emotional symptoms, conduct problems, hyperactivity/inattention, peer relationship problems, and prosocial behaviour. It has satisfactory reliability (Yao et al, 2009; Goodman, 2001) and good concurrent and discriminant validity (Muris, Meesters & van den Berg, 2003; Lundh, Wangby-Lundh & Bjarehed, 2008). The parent-report version was completed at baseline, and then at 14 and 26 weeks post randomisation.

Derivation

Each of the 25 questions is rated as 0 = "not true", 1 = "somewhat true", or 2 = "certainly true".

Emotional symptoms is measured by items 3, 8, 13, 16, and 24. Conduct problems is measured by items 5, 7, 12, 18, 22. Hyperactivity/inattention is measured by items 2, 10, 15, 21, and 25. Peer relationship problems is measured by items 6, 11, 14, 19, and 23. Prosocial behaviour is measured by items 1, 4, 9, 17, and 20. Items 7, 11, 14, 21, and 25 were reserve scored (i.e., for these items "not true" was scored as 2, and "certainly true" was scored as 0). For each of the 5 scale the score can range from 0 to 10 if all items have been completed. These scores were scaled up pro-rata if at least 3 items had been completed.

The total difficulties score was generated by summing scores from all the scales except the prosocial scale, with a possible range between 0 and 40, and was set to missing if at least one of the 4 component scores is missing.

2.6.7 COVID-19 Specific Worries (PAS)

The Pandemic Anxiety Scale (PAS) (McElroy et al., 2020) is a 9-item scale designed to capture specific aspects of the COVID-19 pandemic that are provoking anxiety, as well as to explore how these vary by health and demographic factors. An initial evaluation of the scale indicates that the PAS is a reliable and valid measure (McElroy et al., 2020) and based on parent and adolescent self-report comprised two factor (using 7 items): disease anxiety (e.g. catching, transmitting the virus) and consequence anxiety (e.g. impact on economic prospects). The PAS was completed by the parent/carer at baseline, and then at 14 and 26 weeks post randomisation.

Derivation

The 7-item scale was used for the analysis. Each of the 7 questions is rated as "strongly disagree", "disagree", "neither disagree/agree", "agree", or "strongly agree". These are scored as 0, 1, 2, 3, and 4 respectively.

The total score was calculated as the sum of questions 2, 3, 4, 5, 7, 8, and 9 (not including "My child thinks that COVID-19 is a very serious issue", or "My child is worried we won't have enough food and other essential items during the outbreak"). The total score ranges from 0 to 28.

The 2 subscales were calculated as the sum of the following:

i) Disease anxiety – questions 2, 3, 4, and 5 (range 0-16)
ii) Consequence anxiety – question 7, 8, and 9 (range 0-12)

2.6.8 Treatment Credibility and Experience (CEI)

Parents/carers were asked to complete the Credibility and Expectation of Improvement Scale (CEI) to assess participant expectations and views regarding treatment credibility, after randomisation and prior to treatment commencing (Borkovec & Nau, 1972). It consists of three items, rated on a scale for 0 "not at all" to 10 "completely", asking about how logical the treatment seems, confidence in its success at reducing their symptoms, and their likelihood to recommend the therapy to a friend with similar symptoms. This measure was administered after randomisation with reference to the treatment arm allocation.

An adapted version of the CEI was also administered post randomisation (14 weeks post randomisation), to give a retrospective account of treatment credibility (i.e., the questions were reworded to be considered in light of having received treatment).

The CEI was also adapted to evaluate therapists' experiences of treatment within this trial. This comprises items referring to how logical they found the treatment, how comfortable they felt delivering the treatment, how prepared they felt, certainty in the success of the intervention, confidence recommending the treatment to other therapists, and likelihood of administering the treatment again.

Derivation

Each item of the CEI was analysed separately and was a score ranging from 0 to 10.

2.7 SAMPLE SIZE

It was planned that between 418 and 560 children (209 - 280 per group) with an anxiety disorder and their parents/carers were to be randomised across the two treatment arms. This sample size was considered to be sufficient to provide a standardised noninferiority margin of -0·33 and 80% - 90% power (allowing for 30% attrition).

2.8 RANDOMISATION AND BLINDING IN THE ANALYSIS STAGE

Participants were randomised on a 1:1 ratio to (i) OSI + therapist support or (ii) CAMHS Treatment as Usual for child anxiety problems within the COVID-19 context (C-TAU; typically, 'face to face' treatment delivered over phone/video). Randomisation was minimised by child age (≤8, ≥9), gender, service type (school based, or not school based), and baseline anxiety-associated interference. Participants were randomised using a fully validated and secured web-based randomisation system called Sortition using block randomisation (with varying permuted block sizes) that automatically occurred after the participating patent/carer completed the consent and baseline measures, and the child completed assent (online). The treatment allocation was communicated to the participants (child and parent/carer) in a follow-up email. The online system also sent an email to the clinical team providing information about treatment allocation for each participating family.

Due to the nature of the trial, blinding was not possible to the trial participants of the allocated psychological therapy nor to the research team.

2.9 DATA CLEANING

In general, data underwent statistical data checking by means of distribution analysis and range estimates to ensure values and dates were valid. Data points identified as out of range were flagged and these were sent to the data manager to be checked. These were performed before the final data lock.

2.10 ANALYSIS FOR DATA MONITORING COMMITTEE MEETINGS

Recruitment to the trial was expected to be rapid, so no interim analyses were planned, and a Data Monitoring and Ethics Committee (DMEC) was not formed, however the option to form one if the Trial Steering Committee (TSC) deemed it necessary at any point during the trial was reserved, however this did not occur.

Due to the rapid nature of the trial, there was no internal pilot, and there were no formal stopping criteria.

2.11 DEFINITION OF POPULATION FOR ANALYSIS

The primary analysis population was defined as all participants for whom data are available analysed according to the groups they were randomly allocated to, regardless of treatment compliance. Participants must have completed their follow-up assessments within 4 weeks of the 14 week and 26 week time points, if the participant completed their follow-up assessment outside of this window their outcomes at these time points have been set as missing. Two sensitivity analyses were carried out based on altering the time frame allowed for the assessments. A sensitivity analysis was carried out based on a per-protocol population, excluding those who had deviated from the protocol. Compliance with the protocol to be included in the per-protocol population was defined as: i) participants needed to have received five or more treatment sessions, ii) participants needed to have received the treatment that they were originally randomised to, iii) participants needed to have submitted their final questionnaire within 30 weeks post-randomisation, and iv) participants needed to have started treatment within 12 weeks of being randomised.

2.12 DEVIATION FROM STATISTICAL ANALYSIS PLAN

The per-protocol population in the SAP was defined as those participants who completed a minimum of the first 5 treatment sessions (sessions 0, 1, 2, 3, and 4) within 26 weeks. The information to determine if a participant should be included in the per-protocol population came from the participant's treatment log, this information was not uploaded to the clinical database or provided to the statistician. The per-protocol population was determined by the trial team, the criteria used to categorised the participants to be included in the per-protocol population were that participants needed to have: i) received five or more treatment sessions, ii) received the treatment that they were originally randomised to, iii) submitted their final questionnaire within 30 weeks of randomisation, and iv) started treatment within 12 weeks of being randomised.

It was planned for in the protocol to explore the trajectory of change within the OSI + therapist support arm to inform future developments of the programme by summarising and plotting graphically the measures routinely used to monitor outcomes in the OSI platform. These include the Child Anxiety Impact Scale – parent version (CAIS-P), the Revised Child Anxiety and Depression Scale – parent version (RCADS-P), the Brief Spence Children's Anxiety Scale – parent version (SCAS-P-8), the Outcome Rating Scale (ORS), the Session Rating Scales (SRS) and the Gold based Outcomes (GBOs). This data is collected and stored on the OSI platform. As this data was stored outside of the clinical database, and the analysis of these outcomes were not described in the SAP, this data was not sent to the statistician and thus was not analysed as part of the statistical analysis.

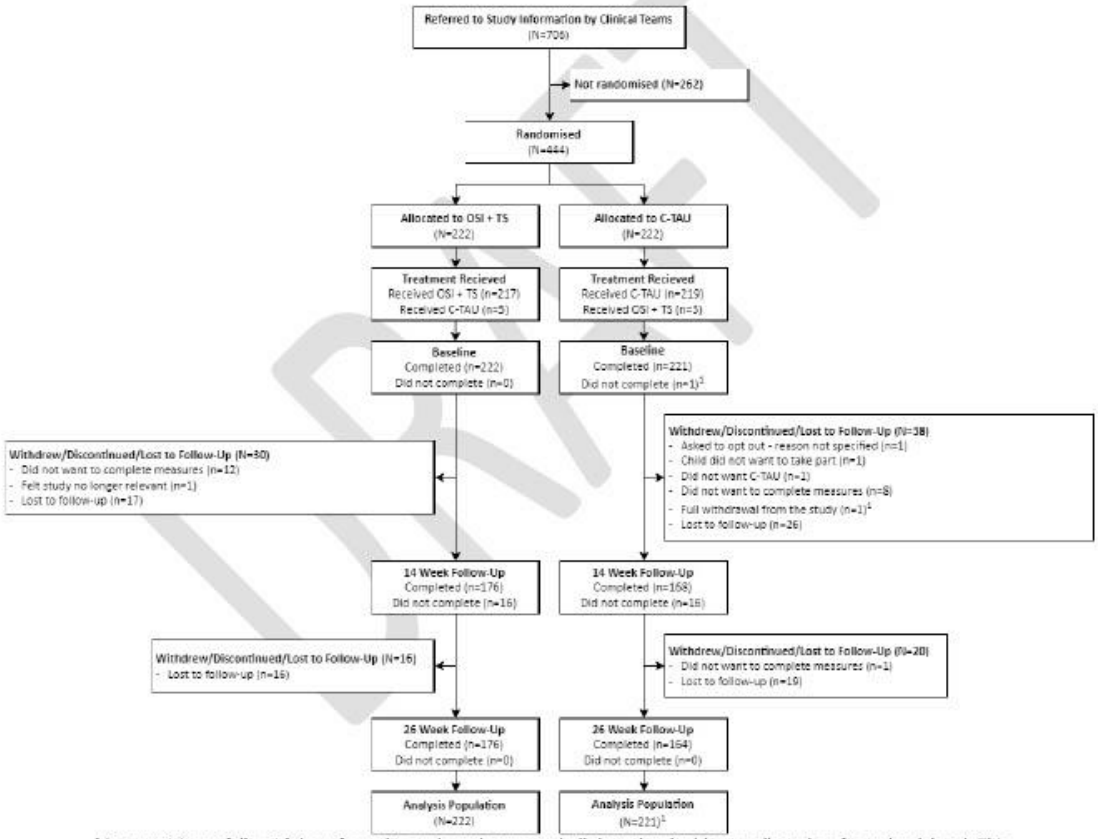
Two post hoc analyses were conducted after the initial unblinded results in this report were presented to the chief investigator. One is presenting the within-group treatment effects from the primary analysis and all the secondary analyses, and the second is an additional per protocol analysis using a less restrictive population definition. These were not described or detailed in the SAP; however, they follow the broad principles laid down there. The suggestions for these analyses were carefully considered, discussed, and agreed upon between the trial statistician, a senior trial statistician, and the chief investigator. The results from these analyses should be considered exploratory.

The Brief Spence Children's Anxiety Scale – parent version (SCAS-P-8) was misspecified in the trial protocol, the statistical analysis plan, and previous versions of this report as the SCAS-8P. This has been corrected in this current version of the report.

3 RESULTS

3.1 REPRESENTATIVENESS OF STUDY SAMPLE AND PATIENT THROUGHPUT

A CONSORT flow diagram of the participants throughout the study period is presented in Figure 1. 706 children with an anxiety disorder and their parent/carers were referred to study information by the clinical teams of whom 262 (37%) did not go on to consent to the study. A total of 444 children and their parent/carers were randomised to the trial; 222 (50%) were allocated to the OSI + therapist support arm, and 222 (50%) were allocated to the COVID-19 treatment as usual arm. One participant fully withdrew from the study and requested all data that had been collected so far to be deleted. This participant has been excluded from the analysis population. All randomised and eligible participants were included in the analysis population.



[1]One participant fully withdrew from the study and requested all data that had been collected so far to be deleted. This participant has been excluded from the analysis population.

FIGURE 1 CONSORT FLOW DIAGRAM

3.2 BASELINE CHARACTERISTICS OF PARTICIPANTS

Table 1 provides the baseline characteristics of the participants by randomised arm, as well as overall.

TABLE 1 BASELINE CHARACTERISTICS

	OSI + TS (N=222)	C-TAU (N=221)	Overall (N=443)
CHILD BASELINE CHARACTERISTICS			
Age, mean (SD) [n]	9·31 (1·83) [222]	9·08 (1·74) [221]	9·20 (1·79) [443]
Gender, n/N (%)			
Male	92/222 (41·44)	92/221 (41·63)	184/443 (41·53)
Female	127/222 (57·21)	128/221 (57·92)	255/443 (57·56)
Other	2/222 (0·90)	1/221 (0·45)	3/443 (0·68)
Prefer not to say	1/222 (0·45)	0/221 (0·00)	1/443 (0·23)
Ethnicity, n/N (%)			
White[1]	194/222 (87·39)	206/221 (93·21)	400/443 (90·29)
Mixed[2]	19/222 (8·56)	14/221 (6·33)	33/443 (7·45)
Asian or Asian British[3]	3/222 (1·35)	0/221 (0·00)	3/443 (0·68)
Black or Black British[4]	1/222 (0·45)	1/221 (0·45)	2/443 (0·45)
Other Ethnic groups[5]	2/222 (0·90)	0/221 (0·00)	2/443 (0·45)
Not stated	3/222 (1·35)	0/221 (0·00)	3/443 (0·68)
Previous treatment for anxiety or other psychological difficulties, n/N (%)	46/222 (20·72)	30/221 (13·57)	76/443 (17·16)
Prescribed medication for anxiety or other psychological difficulties, n/N (%)	2/222 (0·90)	6/221 (2·71)	8/443 (1·81)
Education, n/N (%)			
State school	214/222 (96·40)	209/221 (94·57)	423/443 (95·49)
Independent school	4/222 (1·80)	7/221 (3·17)	11/443 (2·48)
Special provision school	2/222 (0·90)	2/221 (0·90)	4/443 (0·90)
Home educated	2/222 (0·90)	3/221 (1·36)	5/443 (1·13)
Special educational needs, n/N (%)	33/222 (14·86)	32/221 (14·48)	65/443 (14·67)
Type of special educational needs, n/N (%)[6]			
Communicating and interacting	15/33 (45·45)	11/32 (34·38)	26/65 (40·00)
Cognition and learning	16/33 (48·48)	15/32 (46·88)	31/65 (47·69)
Social, emotional, and mental health difficulties	24/33 (72·73)	20/32 (62·50)	44/65 (67·69)
Sensory and/or physical needs	13/33 (39·39)	12/32 (37·50)	25/65 (38·46)
CAIS-P: Total Score, mean (SD) [n]	26·87 (15·26) [222]	25·96 (14·63) [221]	26·42 (14·94) [443]
CAIS-P: Global Items, mean (SD) [n]	6·20 (3·00) [222]	5·86 (2·95) [221]	6·03 (2·98) [443]
CAIS-C: Total Score, mean (SD) [n]	26·13 (14·44) [210]	25·75 (15·06) [212]	25·94 (14·74) [422]
CAIS-C: Global Items, mean (SD) [n]	5·30 (2·85) [210]	5·17 (3·18) [212]	5·24 (3·02) [422]
RCADS-P: Total Anxiety Score, mean (SD) [n]	46·35 (19·83) [222]	45·91 (19·93) [221]	46·13 (19·86) [443]
RCADS-P: Total Anxiety and Depression Score, mean (SD) [n]	56·18 (23·79) [222]	55·40 (24·17) [221]	55·79 (23·96) [443]
RCADS-C: Total Anxiety Score, mean (SD) [n]	47·14 (19·68) [204]	46·26 (19·96) [209]	46·69 (19·81) [413]

	OSI + TS (N=222)	C-TAU (N=221)	Overall (N=443)
RCADS-C: Total Anxiety and Depression Score, mean (SD) [n]	56·98 (23·54) [204]	55·84 (24·14) [209]	56·40 (23·82) [413]
SCAS-P-8, mean (SD) [n]	11·85 (4·78) [222]	11·69 (4·89) [221]	11·77 (4·83) [443]
Overall Rating Scale (ORS), mean (SD) [n]	26·25 (8·15) [222]	27·19 (7·78) [221]	26·72 (7·97) [443]
SDQ-P: Total Problems Score, mean (SD) [n]	17·95 (7·05) [222]	17·26 (6·53) [221]	17·61 (6·80) [443]
Pandemic Anxiety Scale (PAS), mean (SD) [n]	9·65 (5·14) [222]	9·63 (5·71) [221]	9·64 (5·42) [443]
PARENT BASELINE CHARACTERISTICS			
Age, mean (SD) [n]	39·00 (5·93) [222]	38·28 (5·67) [221]	38·64 (5·80) [443]
Gender, n/N (%)			
Male	9/222 (4·05)	8/221 (3·62)	17/443 (3·84)
Female	212/222 (95·50)	213/221 (96·38)	425/443 (95·94)
Other	0/222 (0·00)	0/221 (0·00)	0/443 (0·00)
Prefer not to say	1/222 (0·45)	0/221 (0·00)	1/443 (0·23)
Ethnicity, n/N (%)			
White[1]	203/222 (91·44)	215/221 (97·29)	418/443 (94·36)
Mixed[2]	11/222 (4·95)	2/221 (0·90)	13/443 (2·93)
Asian or Asian British[3]	3/222 (1·35)	1/221 (0·45)	4/443 (0·90)
Black or Black British[4]	1/222 (0·45)	2/221 (0·90)	3/443 (0·68)
Other Ethnic groups[5]	2/222 (0·90)	1/221 (0·45)	3/443 (0·68)
Not stated	2/222 (0·90)	0/221 (0·00)	2/443 (0·45)
Household circumstances, n/N (%)			
Mortgaged/Owned	137/222 (61·71)	122/221 (55·20)	259/443 (58·47)
Council rented	29/222 (13·06)	22/221 (9·95)	51/443 (11·51)
Housing association	19/222 (8·56)	30/221 (13·57)	49/443 (11·06)
Privately rented	32/222 (14·41)	44/221 (19·91)	76/443 (17·16)
Other	5/222 (2·25)	3/221 (1·36)	8/443 (1·81)
Is child fostered?, n/N (%)	0/222 (0·00)	0/221 (0·00)	0/443 (0·00)
Is child adopted?, n/N (%)	1/222 (0·45)	1/221 (0·45)	2/443 (0·45)
Education, n/N (%)			
School completion	35/222 (15·77)	33/221 (14·93)	68/443 (15·35)
Further education	103/222 (46·40)	101/221 (45·70)	204/443 (46·05)
Higher education	39/222 (17·57)	53/221 (23·98)	92/443 (20·77)
Postgraduate qualification	45/222 (20·27)	34/221 (15·38)	79/443 (17·83)
Partnered, n/N (%)	177/222 (79·73)	176/221 (79·64)	353/443 (79·68)
Co-habiting (living together), n/N (%)[7]	165/177 (93·22)	163/176 (92·61)	328/353 (92·92)
Partner's education, n/N (%)[7]			
School completion	50/177 (28·25)	38/176 (21·59)	88/353 (24·93)
Further education	65/177 (36·72)	76/176 (43·18)	141/353 (39·94)
Higher education	30/177 (16·95)	27/176 (15·34)	57/353 (16·15)
Postgraduate qualification	20/177 (11·30)	22/176 (12·50)	42/353 (11·90)
Not stated	12/177 (6·78)	13/176 (7·39)	25/353 (7·08)

	OSI + TS (N=222)	C-TAU (N=221)	Overall (N=443)
Employment, n/N (%)			
Full time	84/222 (37·84)	82/221 (37·10)	166/443 (37·47)
Part time	87/222 (39·19)	73/221 (33·03)	160/443 (36·12)
Sheltered/supported employment	1/222 (0·45)	0/221 (0·00)	1/443 (0·23)
Unemployed	7/222 (3·15)	20/221 (9·05)	27/443 (6·09)
Student	3/222 (1·35)	2/221 (0·90)	5/443 (1·13)
Homemaker	26/222 (11·71)	28/221 (12·67)	54/443 (12·19)
Retired	0/222 (0·00)	0/221 (0·00)	0/443 (0·00)
Other	14/222 (6·31)	16/221 (7·24)	30/443 (6·77)
Total household income, n/N (%)			
Under £16,000 per year	17/141 (12·06)	18/136 (13·24)	35/277 (12·64)
£16,001 - £30,000 per year	27/141 (19·15)	25/136 (18·38)	52/277 (18·77)
£30,001 - £40,000 per year	14/141 (9·93)	18/136 (13·24)	32/277 (11·55)
£40,001 - £50,000 per year	11/141 (7·80)	12/136 (8·82)	23/277 (8·30)
£50,001 - £60,000 per year	12/141 (8·51)	17/136 (12·50)	29/277 (10·47)
£60,001 - £70,000 per year	11/141 (7·80)	7/136 (5·15)	18/277 (6·50)
£70,001 - £80,000 per year	8/141 (5·67)	10/136 (7·35)	18/277 (6·50)
£80,001 - £90,000 per year	6/141 (4·26)	5/136 (3·68)	11/277 (3·97)
£90,001 - £120,000 per year	8/141 (5·67)	4/136 (2·94)	12/277 (4·33)
More than £120,000 per year	3/141 (2·13)	6/136 (4·41)	9/277 (3·25)
Prefer not to say	24/141 (17·02)	14/136 (10·29)	38/277 (13·72)

NB Percentages have been computed with the number of participants with the response available as the denominator. [1]Including British, Irish, and any other White background. [2]Including White and Black Caribbean, White and Black British, White and Asian, and any other mixed background. [3]Including Indian, Pakistani, Bangladeshi, and any other Asian background. [4]Including African, Caribbean, and any other Black background. [5]Including Chinese, and any other Ethnic group. [6]Only includes those with special educational needs. [7]Only includes those who are partnered.

3.3 NUMBER ANALYSED

The frequency and percentage of the number of participants completing follow-up assessments, withdrawing, and lost to follow-up is presented in Table 2 by randomised arm and by overall. Summaries of treatment completion are presented in Table 3. The number and percentage with available primary, secondary, and exploratory outcome data is presented in Table 4 by randomised arm and overall. A comparison between the two randomised arms is presented in Table 5 with those who completed the primary outcome and those who have missing data. A breakdown of the participants who were lost to follow-up is presented in Table 6 in relation to randomised arm and baseline covariates, as well as a test of statistical significance for the baseline characteristics association of missingness of the primary outcome. Individual logistic regressions were performed for each baseline covariate to obtain the P-value for the association of missingness.

TABLE 2 COMPLETION OF FOLLOW-UP ASSESSMENTS, WITHDRAWALS, AND LOST TO FOLLOW-UP

	OSI + TS	C-TAU	Overall
Referred to Study Information by Clinical Teams	-	-	706
Excluded (not randomised)	-	-	262
Randomised	222	222	444
Study assessment completed, n/N (%)			
Baseline	222/222 (100·0)	221/222 (99·5)	443/444 (99·8)
14 weeks follow-up	176/192 (91·7)	168/184 (91·3)	344/376 (91·5)
26 weeks follow-up	176/176 (100·0)	164/164 (100·0)	340/340 (100·0)
Withdrew/Discontinued/Loss to follow-up after randomisation, n/N (%)			
Non-adherence to study procedures	0/46 (0·0)	1/58 (1·7)	1/104 (1·0)
Participant withdrew consent	0/46 (0·0)	2/58 (3·4)	2/104 (1·9)
Other reason	13/46 (28·3)	11/58 (19·0)[1]	24/104 (23·1)[1]
Lost to follow-up	33/46 (71·7)	44/58 (75·9)	77/104 (74·0)
Included in analysis population	222/222 (100·0)	221/222 (99·5)	443/444 (99·8)

NB Percentages for the study assessment completed has been computed with the number of participants remaining in the study at each time point, and the percentages for the withdrew/discontinued/lost to follow-up has been computed with the number of participants that either withdrew, discontinued, or were lost to follow-up. [1]One participant fully withdrew from the study and requested all data that had been collected so far to be deleted. This participant has been excluded from the analysis population.

TABLE 3 TREATMENT COMPLETION SUMMARY

	OSI + TS (N=222)	C-TAU (N=221)	Overall (N=443)
Treatment sessions received, median (IQR) [n] and [range]	8·0 (6·0 to 8·0) [186] [0·0 to 12·0]	6·0 (4·0 to 8·0) [173] [0·0 to 33·0]	7·0 (5·0 to 8·0) [359] [0·0 to 33·0]
≤4 sessions	32/186 (17·2)	54/174 (31·0)	86/360 (23·9)
≥5 sessions	154/186 (82·8)	120/174 (69·0)	274/360 (76·1)
Received allocated treatment	217/222 (97·7)	218/221 (98·6)	435/443 (98·2)
Completed 26 week follow-up within 30 weeks post-randomisation	166/222 (74·8)	150/221 (67·9)	316/443 (71·3)
Started treatment within 12 weeks of randomisation	172/222 (77·5)	151/221 (68·3)	323/443 (72·9)
Included in per-protocol population[1]	111/222 (50·0)	84/221 (38·0)	195/443 (44·0)

[1]Participants needed to fulfil all 4 criteria above to be included in the per-protocol analysis population.

TABLE 4 AVAILABILITY OF OUTCOME DATA AT EACH ASSESSMENT TIMEPOINT

	OSI + TS (N=222)	C-TAU (N=221)	Overall (N=443)
PRIMARY OUTCOME			
Child Anxiety Impact Scale – Parent Version (CAIS-P), n (%)			
Baseline	222 (100·0)	221 (100·0)	443 (100·0)
14 weeks	163 (73·4)	145 (65·6)	308 (69·5)
26 weeks	159 (71·6)	130 (58·8)	289 (65·2)
SECONDARY OUTCOMES			
Child Anxiety Impact Scale – Child Version (CAIS-C), n (%)			
Baseline	210 (94·6)	212 (95·9)	422 (95·3)
14 weeks	127 (57·2)	114 (51·6)	241 (54·4)
26 weeks	124 (55·9)	111 (50·2)	235 (53·0)
Revised Child Anxiety and Depression Scale – Parent Version (RCADS-P), n (%)			
Baseline	222 (100·0)	221 (100·0)	443 (100·0)
14 weeks	161 (72·5)	143 (64·7)	304 (68·6)
26 weeks	157 (70·7)	129 (58·4)	286 (64·6)
Revised Child Anxiety and Depression Scale – Child Version (RCADS-C), n (%)			
Baseline	204 (91·9)	209 (94·6)	413 (93·2)
14 weeks	127 (57·2)	112 (50·7)	239 (54·0)
26 weeks	122 (55·0)	111 (50·2)	233 (52·6)
Brief Spence Children's Anxiety Scale – Parent Version (SCAS-P-8), n (%)			
Baseline	222 (100·0)	221 (100·0)	443 (100·0)
14 weeks	161 (72·5)	143 (64·7)	304 (68·6)
26 weeks	157 (70·7)	129 (58·4)	286 (64·6)
Overall Functioning (Outcome Rating Scale (ORS)), n (%)			
Baseline	222 (100·0)	221 (100·0)	443 (100·0)
14 weeks	161 (72·5)	143 (64·7)	304 (68·6)
26 weeks	154 (69·4)	127 (57·5)	281 (63·4)
Common Comorbid Emotional and Behavioural Problems (Strengths & Difficulties Questionnaire (SDQ-P))			
Baseline	222 (100·0)	221 (100·0)	443 (100·0)
14 weeks	161 (72·5)	143 (64·7)	304 (68·6)
26 weeks	154 (69·4)	128 (57·9)	282 (63·7)
COVID-19 Specific Worries (Pandemic Anxiety Scale (PAS)), n (%)			
Baseline	222 (100·0)	221 (100·0)	443 (100·0)
14 weeks	161 (72·5)	143 (64·7)	304 (68·6)
26 weeks	154 (69·4)	129 (58·4)	283 (63·9)
EXPLORATORY OUTCOMES			
Treatment Credibility and Experience – Parent Version (CEI-P), n (%)			
Post-randomisation	218 (98·2)	209 (94·6)	427 (96·4)
14 weeks	160 (72·1)	143 (64·7)	303 (68·4)
Treatment Credibility and Experience – Therapist Version (CEI-T), n (%)			
End of treatment	155 (69·8)	128 (57·9)	283 (63·9)

TABLE 5 ASSOCIATION BETWEEN RANDOMISED GROUP AND AVAILABILITY OF PRIMARY OUTCOME

	OSI + TS (N=222)	C-TAU (N=221)	Odds ratio [95% CI][1]	P-value[2]
Primary outcome, n/N (%)			0·57 [0·38 to 0·84]	0·0049
Available	159/222 (71·6)	130/221 (58·8)		
Missing	63/222 (28·4)	91/221 (41·2)		

[1]OSI + Therapist Support versus C-TAU. Logistic regression of the availability of the primary outcome modelled against intervention group. [2]Level of significance = 0·05

63 participants are missing the primary outcome in the OSI + TS arm due to: 46 participants did not complete their 26 week follow-up, 3 participants completed their 26 week follow-up but did not complete the CAIS-P, and 14 participants completed their 26 week follow-up outside of the 26±4 week window.

91 participants are missing the primary outcome in the C-TAU arm due to: 57 participants did not complete their 26 week follow-up, 1 participant completed their 26 week follow-up but did not complete the CAIS-P, and 33 participants completed their 26 week follow-up outside of the 26±4 week window.

TABLE 6 BASELINE CHARACTERISTICS OF THOSE PARTICIPANTS WHO HAVE THE PRIMARY OUTCOME OF CAIS-P SCORE AT 26 WEEKS FOLLOW-UP AVAILABLE OR MISSING, AND THE PROBABILITY OF EACH CHARACTERISTIC PREDICTING MISSINGNESS OF THE PRIMARY OUTCOME

	P-value[1]	OSI + Therapist Support (N=222)		COVID-19 Treatment as Usual (N=221)		Overall (N=443)	
		Available (N=159)	Missing (N=63)	Available (N=130)	Missing (N=91)	Available (N=289)	Missing (N=154)
CHILD BASELINE CHARACTERISTICS							
Age, mean (SD) [n]	0·96	9·3 (1·8) [159]	9·4 (1·8) [63]	9·1 (1·7) [130]	9·0 (1·8) [91]	9·2 (1·8) [289]	9·2 (1·8) [154]
Gender, n/N (%)	0·12						
Male		71/159 (44·7)	21/63 (33·3)	58/130 (44·6)	34/91 (37·4)	129/289 (44·6)	55/154 (35·7)
Female		86/159 (54·1)	41/63 (65·1)	72/130 (55·4)	56/91 (61·5)	158/289 (54·7)	97/154 (63·0)
Other		1/159 (0·6)	0/63 (0·0)	0/130 (0·0)	0/91 (0·0)	1/289 (0·3)	0/154 (0·0)
Prefer not to say		1/159 (0·6)	1/63 (1·6)	0/130 (0·0)	1/91 (1·1)	1/289 (0·3)	2/154 (1·3)
Ethnicity, n/N (%)	0·97						
White[2]		137/159 (86·2)	57/63 (90·5)	122/130 (93·8)	84/91 (92·3)	259/289 (89·6)	141/154 (91·6)
Mixed[3]		15/159 (9·4)	4/63 (6·3)	7/130 (5·4)	7/91 (7·7)	22/289 (7·6)	11/154 (7·1)
Asian or Asian British[4]		3/159 (1·9)	0/63 (0·0)	0/130 (0·0)	0/91 (0·0)	3/289 (1·0)	0/154 (0·0)
Black or Black British[5]		0/159 (0·0)	1/63 (1·6)	1/130 (0·8)	0/91 (0·0)	1/289 (0·3)	1/154 (0·6)
Other Ethnic groups[6]		2/159 (1·3)	0/63 (0·0)	0/130 (0·0)	0/91 (0·0)	2/289 (0·7)	0/154 (0·0)
Not stated		2/159 (1·3)	1/63 (1·6)	0/130 (0·0)	0/91 (0·0)	2/289 (0·7)	1/154 (0·6)
Previous treatment for anxiety or other psychological difficulties, n/N (%)	0·71	31/159 (19·5)	15/63 (23·8)	20/130 (15·4)	10/91 (11·0)	51/289 (17·6)	25/154 (16·2)
Prescribed medication for anxiety or other psychological difficulties, n/N (%)	0·87	1/159 (0·6)	1/63 (1·6)	4/130 (3·1)	2/91 (2·2)	5/289 (1·7)	3/154 (1·9)
Education, n/N (%)	0·15						
State school		154/159 (96·9)	60/63 (95·2)	124/130 (95·4)	85/91 (93·4)	278/289 (96·2)	145/154 (94·2)
Independent school		2/159 (1·3)	2/63 (3·2)	4/130 (3·1)	3/91 (3·3)	6/289 (2·1)	5/154 (3·2)
Special provision school		2/159 (1·3)	0/63 (0·0)	2/130 (1·5)	0/91 (0·0)	4/289 (1·4)	0/154 (0·0)
Home educated		1/159 (0·6)	1/63 (1·6)	0/130 (0·0)	3/91 (3·3)	1/289 (0·3)	4/154 (2·6)

Primary Care Clinical Trials Unit

UNIVERSITY OF OXFORD

Co-CAT Statistical Analysis Report Version 2.0 11 December 2023

	P-value[1]	OSI + Therapist Support (N=222)		COVID-19 Treatment as Usual (N=221)		Overall (N=443)	
		Available (N=159)	Missing (N=63)	Available (N=130)	Missing (N=91)	Available (N=289)	Missing (N=154)
Special educational needs, n/N (%)	0·87	24/159 (15·1)	9/63 (14·3)	19/130 (14·6)	13/91 (14·3)	43/289 (14·9)	22/154 (14·3)
Type of special educational needs, n/N (%)[7]							
Communicating and interacting	0·39	13/24 (54·2)	2/9 (22·2)	6/19 (31·6)	5/13 (38·5)	19/43 (44·2)	7/22 (31·8)
Cognition and learning	0·39	11/24 (45·8)	5/9 (55·6)	7/19 (36·8)	8/13 (61·5)	18/43 (41·9)	13/22 (59·1)
Social, emotional, and mental health difficulties	0·44	19/24 (79·2)	5/9 (55·6)	12/19 (63·2)	8/13 (61·5)	31/43 (72·1)	13/22 (59·1)
Sensory and/or physical needs	0·47	11/24 (45·8)	2/9 (22·2)	7/19 (36·8)	5/13 (38·5)	18/43 (41·9)	7/22 (31·8)
CAIS-P: Total Score, mean (SD) [n]	0·68	26·4 (15·1) [159]	28·0 (15·7) [63]	26·0 (14·8) [130]	26·0 (14·5) [91]	26·2 (14·9) [289]	26·8 (15·0) [154]
CAIS-P: Global Items, mean (SD) [n]	0·93	6·1 (3·1) [159]	6·4 (2·9) [63]	5·9 (3·0) [130]	5·8 (2·8) [91]	6·0 (3·0) [289]	6·1 (2·8) [154]
CAIS-C: Total Score, mean (SD) [n]	0·68	25·6 (13·9) [151]	27·5 (15·9) [59]	25·9 (14·9) [130]	25·6 (15·4) [82]	25·7 (14·3) [281]	26·4 (15·6) [141]
CAIS-C: Global Items, mean (SD) [n]	0·88	5·1 (2·8) [151]	5·9 (3·0) [59]	5·5 (3·4) [130]	4·7 (2·8) [82]	5·3 (3·0) [281]	5·2 (3·0) [141]
RCADS-P: Total Anxiety Score, mean (SD) [n]	0·47	45·5 (19·5) [159]	48·4 (20·6) [63]	45·8 (19·1) [130]	46·1 (21·1) [91]	45·6 (19·3) [289]	47·1 (20·9) [154]
RCADS-P: Total Anxiety and Depression Score, mean (SD) [n]	0·40	55·2 (23·5) [159]	58·7 (24·4) [63]	55·0 (23·3) [130]	56·0 (25·4) [91]	55·1 (23·4) [289]	57·1 (25·0) [154]
RCADS-C: Total Anxiety Score, mean (SD) [n]	0·30	46·2 (19·5) [147]	49·6 (20·0) [57]	45·8 (19·1) [130]	47·1 (21·4) [79]	46·0 (19·3) [277]	48·1 (20·8) [136]
RCADS-C: Total Anxiety and Depression Score, mean (SD) [n]	0·22	55·7 (23·6) [147]	60·1 (23·4) [57]	55·0 (23·3) [130]	57·3 (25·5) [79]	55·4 (23·4) [277]	58·5 (24·6) [136]
SCAS-P-8, mean (SD) [n]	0·77	11·7 (4·6) [159]	12·1 (5·2) [63]	11·7 (4·8) [130]	11·7 (5·1) [91]	11·7 (4·7) [289]	11·9 (5·1) [154]
Overall Rating Scale (ORS), mean (SD) [n]	0·98	26·0 (8·2) [159]	26·8 (8·2) [63]	27·6 (7·9) [130]	26·6 (7·6) [91]	26·7 (8·1) [289]	26·7 (7·8) [154]
SDQ-P, mean (SD) [n]	0·67	18·4 (7·4) [159]	16·9 (6·0) [63]	16·9 (6·8) [130]	17·8 (6·1) [91]	17·7 (7·2) [289]	17·4 (6·0) [154]
Pandemic Anxiety Scale (PAS), mean (SD) [n]	0·31	9·7 (5·2) [159]	9·6 (5·0) [63]	10·0 (5·6) [130]	9·1 (5·8) [91]	9·8 (5·4) [289]	9·3 (5·5) [154]

	P-value[1]	OSI + Therapist Support (N=222)		COVID-19 Treatment as Usual (N=221)		Overall (N=443)	
		Available (N=159)	Missing (N=63)	Available (N=130)	Missing (N=91)	Available (N=289)	Missing (N=154)
PARENT BASELINE CHARACTERISTICS							
Age, mean (SD) [n]	0·33	38·7 (5·6) [159]	39·9 (6·6) [63]	39·0 (5·9) [130]	37·2 (5·1) [91]	38·8 (5·8) [289]	38·3 (5·9) [154]
Gender, n/N (%)	0·97						
Male		5/159 (3·1)	4/63 (6·3)	6/130 (4·6)	2/91 (2·2)	11/289 (3·8)	6/154 (3·9)
Female		153/159 (96·2)	59/63 (93·7)	124/130 (95·4)	89/91 (97·8)	277/289 (95·8)	148/154 (96·1)
Other		1/159 (0·6)	0/63 (0·0)	0/130 (0·0)	0/91 (0·0)	1/289 (0·3)	0/154 (0·0)
Prefer not to say		0/159 (0·0)	0/63 (0·0)	0/130 (0·0)	0/91 (0·0)	0/289 (0·0)	0/154 (0·0)
Ethnicity, n/N (%)	0·81						
White[2]		144/159 (90·6)	59/63 (93·7)	128/130 (98·5)	87/91 (95·6)	272/289 (94·1)	146/154 (94·8)
Mixed[3]		9/159 (5·7)	2/63 (3·2)	1/130 (0·8)	1/91 (1·1)	10/289 (3·5)	3/154 (1·9)
Asian or Asian British[4]		3/159 (1·9)	0/63 (0·0)	0/130 (0·0)	1/91 (1·1)	3/289 (1·0)	1/154 (0·6)
Black or Black British[5]		0/159 (0·0)	1/63 (1·6)	1/130 (0·8)	1/91 (1·1)	1/289 (0·3)	2/154 (1·3)
Other Ethnic groups[6]		2/159 (1·3)	0/63 (0·0)	0/130 (0·0)	1/91 (1·1)	2/289 (0·7)	1/154 (0·6)
Not stated		1/159 (0·6)	1/63 (1·6)	0/130 (0·0)	0/91 (0·0)	1/289 (0·3)	1/154 (0·6)
Household circumstances, n/N (%)	0·086						
Mortgaged/Owned		98/159 (61·6)	39/63 (61·9)	81/130 (62·3)	41/91 (45·1)	179/289 (61·9)	80/154 (51·9)
Council rented		21/159 (13·2)	8/63 (12·7)	8/130 (6·2)	14/91 (15·4)	29/289 (10·0)	22/154 (14·3)
Housing association		15/159 (9·4)	4/63 (6·3)	19/130 (14·6)	11/91 (12·1)	34/289 (11·8)	15/154 (9·7)
Privately rented		21/159 (13·2)	11/63 (17·5)	20/130 (15·4)	24/91 (26·4)	41/289 (14·2)	35/154 (22·7)
Other		4/159 (2·5)	1/63 (1·6)	2/130 (1·5)	1/91 (1·1)	6/289 (2·1)	2/154 (1·3)
Is child fostered?, n/N (%)	-	0/159 (0·0)	0/63 (0·0)	0/130 (0·0)	0/91 (0·0)	0/289 (0·0)	0/154 (0·0)
Is child adopted?, n/N (%)	-	1/159 (0·6)	0/63 (0·0)	1/130 (0·8)	0/91 (0·0)	2/289 (0·7)	0/154 (0·0)

Primary Care Clinical Trials Unit

UNIVERSITY OF OXFORD

Co-CAT Statistical Analysis Report Version 2.0 11 December 2023

	P-value[1]	OSI + Therapist Support (N=222)		COVID-19 Treatment as Usual (N=221)		Overall (N=443)	
		Available (N=159)	Missing (N=63)	Available (N=130)	Missing (N=91)	Available (N=289)	Missing (N=154)
Education, n/N (%)	0·08						
School completion		29/159 (18·2)	6/63 (9·5)	16/130 (12·3)	17/91 (18·7)	45/289 (15·6)	23/154 (14·9)
Further education		66/159 (41·5)	37/63 (58·7)	56/130 (43·1)	45/91 (49·5)	122/289 (42·2)	82/154 (53·2)
Higher education		30/159 (18·9)	9/63 (14·3)	32/130 (24·6)	21/91 (23·1)	62/289 (21·5)	30/154 (19·5)
Postgraduate qualification		34/159 (21·4)	11/63 (17·5)	26/130 (20·0)	8/91 (8·8)	60/289 (20·8)	19/154 (12·3)
Partnered, n/N (%)	0·0018	132/159 (83·0)	45/63 (71·4)	111/130 (85·4)	65/91 (71·4)	243/289 (84·1)	110/154 (71·4)
Co-habiting (living together), n/N (%)[8]	0·023	124/132 (93·9)	41/45 (91·1)	107/111 (96·4)	56/65 (86·2)	231/243 (95·1)	97/110 (88·2)
Partner's education, n/N (%)[8]	0·79						
School completion		38/159 (23·9)	12/63 (19·0)	24/130 (18·5)	14/91 (15·4)	62/289 (21·5)	26/154 (16·9)
Further education		49/159 (30·8)	16/63 (25·4)	50/130 (38·5)	26/91 (28·6)	99/289 (34·3)	42/154 (27·3)
Higher education		21/159 (13·2)	9/63 (14·3)	17/130 (13·1)	10/91 (11·0)	38/289 (13·1)	19/154 (12·3)
Postgraduate qualification		16/159 (10·1)	4/63 (6·3)	16/130 (12·3)	6/91 (6·6)	32/289 (11·1)	10/154 (6·5)
Not stated		35/159 (22·0)	22/63 (34·9)	23/130 (17·7)	35/91 (38·5)	58/289 (20·1)	57/154 (37·0)
Employment, n/N (%)	0·23						
Full time		55/159 (34·6)	29/63 (46·0)	47/130 (36·2)	35/91 (38·5)	102/289 (35·3)	64/154 (41·6)
Part time		68/159 (42·8)	19/63 (30·2)	43/130 (33·1)	30/91 (33·0)	111/289 (38·4)	49/154 (31·8)
Sheltered/supported employment		1/159 (0·6)	0/63 (0·0)	0/130 (0·0)	0/91 (0·0)	1/289 (0·3)	0/154 (0·0)
Unemployed		4/159 (2·5)	3/63 (4·8)	12/130 (9·2)	8/91 (8·8)	16/289 (5·5)	11/154 (7·1)
Student		0/159 (0·0)	3/63 (4·8)	1/130 (0·8)	1/91 (1·1)	1/289 (0·3)	4/154 (2·6)
Homemaker		20/159 (12·6)	6/63 (9·5)	16/130 (12·3)	12/91 (13·2)	36/289 (12·5)	18/154 (11·7)
Retired		0/159 (0·0)	0/63 (0·0)	0/130 (0·0)	0/91 (0·0)	0/289 (0·0)	0/154 (0·0)
Other		11/159 (6·9)	3/63 (4·8)	11/130 (8·5)	5/91 (5·5)	22/289 (7·6)	8/154 (5·2)

	P-value[1]	OSI + Therapist Support (N=222)		COVID-19 Treatment as Usual (N=221)		Overall (N=443)	
		Available (N=159)	Missing (N=63)	Available (N=130)	Missing (N=91)	Available (N=289)	Missing (N=154)
Total household income, n/N (%)	0·38						
Under £16,000 per year		10/102 (9·8)	7/39 (17·9)	8/84 (9·5)	10/52 (19·2)	18/186 (9·7)	17/91 (18·7)
£16,001 - £30,000 per year		19/102 (18·6)	8/39 (20·5)	16/84 (19·0)	9/52 (17·3)	35/186 (18·8)	17/91 (18·7)
£30,001 - £40,000 per year		12/102 (11·8)	2/39 (5·1)	8/84 (9·5)	10/52 (19·2)	20/186 (10·8)	12/91 (13·2)
£40,001 - £50,000 per year		6/102 (5·9)	5/39 (12·8)	8/84 (9·5)	4/52 (7·7)	14/186 (7·5)	9/91 (9·9)
£50,001 - £60,000 per year		8/102 (7·8)	4/39 (10·3)	12/84 (14·3)	5/52 (9·6)	20/186 (10·8)	9/91 (9·9)
£60,001 - £70,000 per year		8/102 (7·8)	3/39 (7·7)	5/84 (6·0)	2/52 (3·8)	13/186 (7·0)	5/91 (5·5)
£70,001 - £80,000 per year		6/102 (5·9)	2/39 (5·1)	9/84 (10·7)	1/52 (1·9)	15/186 (8·1)	3/91 (3·3)
£80,001 - £90,000 per year		5/102 (4·9)	1/39 (2·6)	2/84 (2·4)	3/52 (5·8)	7/186 (3·8)	4/91 (4·4)
£90,001 - £120,000 per year		5/102 (4·9)	3/39 (7·7)	3/84 (3·6)	1/52 (1·9)	8/186 (4·3)	4/91 (4·4)
More than £120,000 per year		1/102 (1·0)	2/39 (5·1)	4/84 (4·8)	2/52 (3·8)	5/186 (2·7)	4/91 (4·4)
Prefer not to say		22/102 (21·6)	2/39 (5·1)	9/84 (10·7)	5/52 (9·6)	31/186 (16·7)	7/91 (7·7)

NB Percentages have been computed with the number of participants with the response available as the denominator. [1]Logistic regression of the availability of the primary outcome of the child anxiety impact scale – parent version (CAIS-P) at 26 weeks follow-up modelled against baseline characteristics. Level of significance = 0·05. [2]Including British, Irish, and any other White background. [3]Including White and Black Caribbean, White and Black British, White and Asian, and any other mixed background. [4]Including Indian, Pakistani, Bangladeshi, and any other Asian background. [5]Including African, Caribbean, and any other Black background. [6]Including Chinese, and any other Ethnic group. [7]Only includes those with special educational needs. [8]Only includes those who are partnered.

3.4 PRIMARY AND SECONDARY ANALYSES

Primary outcome

The primary objective is to evaluate the parent-reported clinical effectiveness of a brief parent-led cognitive behavioural treatment (CBT) delivered by the OSI platform with therapist support (OSI + therapist support) for the treatment of child anxiety problems compared to 'COVID-19 treatment as usual' (C-TAU) in CAMHS throughout the latter phases of the COVID-19 pandemic. The primary outcome was measured using the Child Anxiety Impact Scale – parent version (CAIS-P), which captures the degree to which anxiety is interfering in the child and family's life, which was evaluated at baseline, 14 weeks, and 26 weeks post randomised. The primary outcome is the 26 week time point. The primary outcome is presented in a dot plot at each assessment time point and split by randomised group in Figure 2.

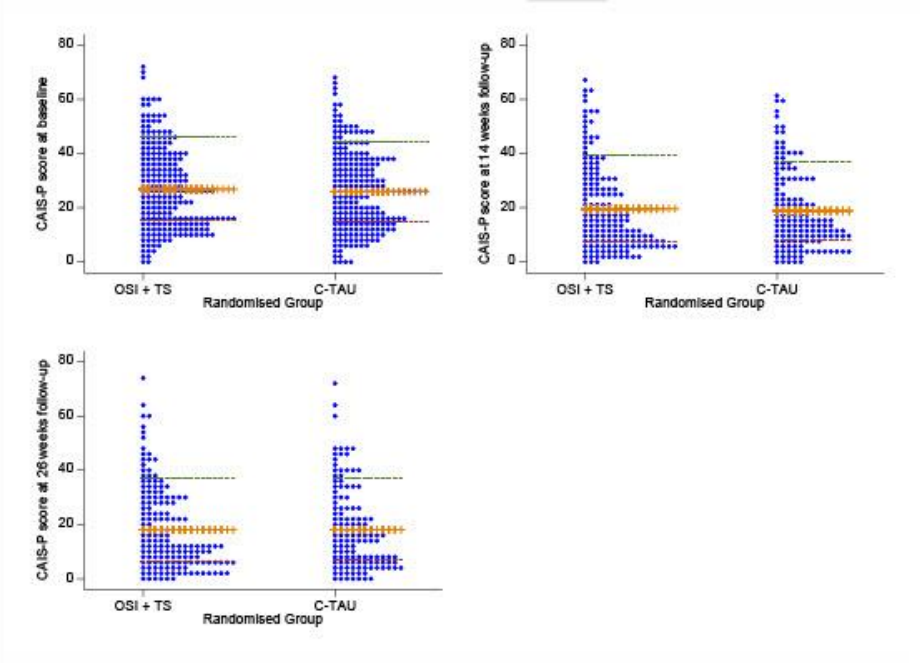


FIGURE 2 DOT PLOT OF THE CHILD ANXIETY IMPACT SCALE – PARENT VERSION (CAIS-P)

Hypothesis and Primary Analysis

$$H_0: \frac{Adjusted(\mu_t - \mu_c)}{Baseline\ \sigma} \geq \Delta \qquad H_1: \frac{Adjusted(\mu_t - \mu_c)}{Baseline\ \sigma} < \Delta$$

The null hypothesis is that the standardised mean difference of the CAIS-P score at 26 weeks is greater than or equal to the non-inferiority margin (Δ) of 0·33. Therefore, the alternative hypothesis is that the standardised mean difference between the intervention arm and the control arm is less than 0·33. The standardised mean difference is defined as the adjusted mean difference between the intervention arm and the control arm divided by the baseline standard deviation.

The non-inferiority margin stated in the protocol and the SAP of -0·33, is based on the difference between the control and the intervention arm. The analysis was conducted based on the difference between the intervention and the control arm, which is convention for clinical trials. For the primary outcome of CAIS-P score, a lower score indices lower levels of anxiety, as such a non-inferiority margin of 0·33 is used in the interpretation of the results. Non-inferiority will be claimed if the upper limit of the 95% confidence interval around the standardised mean difference is less than the non-inferiority margin of 0·33.

The primary outcome is presented descriptively using means and standard deviations and was analysed by a generalised linear mixed effects model, fitted to the data with the outcome at 14 weeks, and 26 weeks follow-up as the dependent variable. Included in the model were fixed effects for randomised group, assessment time point, minimisation variables; child's age, child's gender, baseline anxiety associated interference, and service type (school/clinic), and an interaction term between randomised group and assessment time point to allow the treatment effect to be estimated at each time point. The model also included a random intercept for each participant to account for the repeated measures on the same participants. The adjusted mean differences with 95% confidence intervals were obtained from the model using a linear contrast statement at each assessment time point, in addition, the standardised mean differences with 95% confidence intervals were calculated and are presented alongside the associated one-sided P-value for non-inferiority in Table 7. The results from the analysis are also presented graphically in a forest plot in Figure 3.

The normality assumptions of the generalised linear mixed effects model was assessed by plotting a histogram of the outcomes at each time point split by randomised group, a histogram of the model residuals, an inverse normal plot of the standardised model residuals, and a scatter plot of the fitted values versus the model residuals, this is presented in Appendix V in Figure 9.

Secondary outcomes

The secondary outcomes of interest are: the total of the global items component of the Child Anxiety Impact Scale – parent version (CAIS-P). The total score and the total score of the global items component of the Child Anxiety Impact Scale – child version (CAIS-C). The total anxiety score and the total anxiety and depression score for both the parent version and the child version of the Revised Child Anxiety and Depression Scale (RCADS-P and RCADS-C). The total score of the Brief Spence Children's Anxiety Scale – parent version (SCAS-P-8). Overall functioning which is measured by the Outcome Rating Scale (ORS), this scale is made up of the individually, interpersonally, socially, and overall components, as well as a total score. Common comorbid emotional and behavioural problems which is measured by the Strengths and Difficulties Questionnaire (SDQ-P) which is made up of the emotional symptoms, conduct problems, hyperactivity/inattention, peer relationship problems, prosocial behaviour sections, as well as a total score. COVID-19 specific worries which is measured by the Pandemic Anxiety Scale (PAS), this scale is made up of a disease anxiety and a consequence anxiety subscale, as well as a total score.

For all secondary outcomes except for each component and total score of the outcome rating scale and the prosocial behaviour component of the strengths and difficulties questionnaire, a lower score indicates lower levels of anxiety, as such a non-inferiority margin of 0·33 is used in the interpretation of the results. For each component and total score of the outcome rating scale and the prosocial behaviour component of the strengths and difficulties questionnaire, a higher score indicates lower levels of anxiety, as such a non-inferiority margin of -0·33 is used in the interpretation of the results. In these cases, non-inferiority will be claimed if the lower limit of the 95% confidence interval around the standardised mean difference is greater than the non-inferiority margin of -0·33.

All secondary outcomes are presented descriptively using means and standard deviations and were analysed by a generalised linear mixed effects model, fitted to the data was the outcome at 14 weeks, and 26 weeks post-randomisation as the dependent variable. Included in the models were fixed effects for randomised group, assessment time point, baseline outcome measure, minimisation variables; child's age, child's gender, baseline anxiety associated interference, and service type (school/clinic), and an interaction term between randomised group and assessment time point to allow the treatment affect to be estimated at each time point. The models also included a random intercept for each participant to account for the repeated measures on the same participants. The adjusted mean differences with 95% confidence intervals were obtained from the model using a linear contrast statement at each assessment time point, in addition, the standardised mean differences with 95% confidence intervals were calculated and are presented alongside the associated one-sided P-value for non-inferiority in Table 7. The results from the analyses are also presented graphically in forest plot in Figure 3 to Figure 7.

The normality assumptions of the generalised linear mixed effects models were assessed by plotting a histogram of the outcomes at each time point split by randomised group, a histogram of the model residuals, an inverse normal plot of the standardised model residuals, and a scatter plot of the fitted values versus the model residuals, these are presented in Appendix V in Figure 9 to Figure 31.

Post hoc analysis

An additional analysis was conducted to obtain the within-group treatment effects for the primary outcome and for each secondary outcomes at 14 weeks and 26 weeks follow-up. This was conducted after the initial unblinded results in this report were presented to the chief investigator. This analysis was not described or detailed in the SAP, however it follows the broad principles laid down there. It is considered bad practice to present within-group treatment effects in a randomised control trial as it is prone to regression to the mean, however the suggestion for this analysis was carefully considered, discussed, and agreed upon between the trial statistician, a senior trial statistician, and the chief investigator to facilitate comparisons with other trials. The results from this analysis should be considered exploratory as the true treatment effect will likely be overestimated due to the within-group standard error being underestimated since the within-group variability is likely to be smaller than the between-group variability. The results from this post hoc analysis are presented in Appendix IV in Table 12.

TABLE 7 SUMMARY STATISTICS, ADJUSTED MEAN DIFFERENCES, STANDARDISED MEAN DIFFERENCES, AND THE P-VALUE FOR NON-INFERIORITY FOR THE PRIMARY AND SECONDARY ANALYSES

	OSI + TS (N=222)	C-TAU (N=221)	Adjusted Mean Difference [95% CI][1]	Standardised Mean Difference [95% CI]	P-value for non-inferiority[3]
PRIMARY ANALYSIS					
Child Anxiety Impact Scale – Parent Version (CAIS-P)					
CAIS-P: Total Score, mean (SD) [n]					
Baseline	26·87 (15·26) [222]	25·96 (14·63) [221]	-	-	-
14 weeks	19·64 (16·00) [163]	18·89 (14·52) [145]	0·00 [-2·34 to 2·34]	0·00 [-0·16 to 0·16]	<0·0001
26 weeks[2]	**17·99 (15·39) [159]**	**18·08 (15·08) [130]**	**0·14 [-2·26 to 2·53]**	**0·01 [-0·15 to 0·17]**	**<0·0001**
SECONDARY ANALYSES					
CAIS-P: Global Items, mean (SD) [n]					
Baseline	6·20 (3·00) [222]	5·86 (2·95) [221]	-	-	-
14 weeks	4·07 (3·12) [163]	3·97 (2·88) [145]	-0·13 [-0·63 to 0·37]	-0·04 [-0·21 to 0·12]	<0·0001
26 weeks	3·60 (3·06) [159]	3·62 (2·84) [130]	0·08 [-0·42 to 0·59]	0·03 [-0·14 to 0·20]	0·00026
Child Anxiety Impact Scale – Child Version (CAIS-C)					
CAIS-C: Total Score, mean (SD) [n]					
Baseline	26·13 (14·44) [210]	25·75 (15·06) [212]	-	-	-
14 weeks	19·27 (15·13) [127]	20·73 (14·50) [114]	-1·61 [-4·55 to 1·33]	-0·11 [-0·31 to 0·09]	<0·0001
26 weeks	17·03 (15·83) [124]	19·89 (16·64) [111]	-2·67 [-5·64 to 0·30]	-0·18 [-0·38 to 0·02]	<0·0001
CAIS-C: Global Items, mean (SD) [n]					
Baseline	5·30 (2·85) [210]	5·17 (3·18) [212]	-	-	-
14 weeks	3·63 (3·05) [127]	4·03 (2·62) [114]	-0·30 [-0·90 to 0·30]	-0·10 [-0·30 to 0·10]	<0·0001
26 weeks	3·61 (3·28) [123]	3·40 (3·18) [111]	0·30 [-0·31 to 0·90]	0·10 [-0·10 to 0·30]	0·012
Revised Child Anxiety and Depression Scale – Parent Version (RCADS-P)					
RCADS-P: Total Anxiety Score, mean (SD) [n]					
Baseline	46·35 (19·83) [222]	45·91 (19·93) [221]	-	-	-
14 weeks	34·09 (23·01) [161]	34·84 (19·92) [143]	-2·22 [-5·49 to 1·04]	-0·11 [-0·28 to 0·05]	<0·0001
26 weeks	30·57 (23·29) [157]	32·03 (20·98) [129]	-0·96 [-4·27 to 2·36]	-0·05 [-0·22 to 0·12]	<0·0001

Primary Care Clinical Trials Unit

UNIVERSITY OF OXFORD

Co-CAT Statistical Analysis Report Version 2.0 11 December 2023

	OSI + TS (N=222)	C-TAU (N=221)	Adjusted Mean Difference [95% CI][1]	Standardised Mean Difference [95% CI]	P-value for non-inferiority[3]
RCADS-P: Total Anxiety and Depression Score, mean (SD) [n]					
Baseline	56·18 (23·79) [222]	55·40 (24·17) [221]	-	-	-
14 weeks	41·25 (28·26) [161]	41·55 (23·89) [143]	-2·22 [-6·16 to 1·73]	-0·09 [-0·26 to 0·07]	<0·0001
26 weeks	37·45 (28·77) [157]	38·22 (25·39) [129]	-0·54 [-4·54 to 3·46]	-0·02 [-0·19 to 0·14]	<0·0001
Revised Child Anxiety and Depression Scale – Child Version (RCADS-C)					
RCADS-C: Total Anxiety Score, mean (SD) [n]					
Baseline	47·14 (19·68) [204]	46·26 (19·96) [209]	-	-	-
14 weeks	31·40 (23·18) [127]	32·10 (21·26) [112]	-1·29 [-5·58 to 3·00]	-0·07 [-0·28 to 0·15]	0·00017
26 weeks	29·96 (24·91) [122]	29·53 (22·75) [111]	1·41 [-2·89 to 5·71]	0·07 [-0·15 to 0·29]	0·0098
RCADS-C: Total Anxiety and Depression Score, mean (SD) [n]					
Baseline	56·98 (23·54) [204]	55·84 (24·14) [209]	-	-	-
14 weeks	37·91 (28·37) [127]	38·11 (25·38) [112]	-0·99 [-6·15 to 4·17]	-0·04 [-0·26 to 0·18]	0·00039
26 weeks	36·30 (30·86) [122]	35·04 (27·27) [111]	2·31 [-2·86 to 7·49]	0·10 [-0·12 to 0·31]	0·018
Brief Spence Children's Anxiety Scale – Parent Version (SCAS-P-8)					
SCAS-P-8: Total Score, mean (SD) [n]					
Baseline	11·85 (4·78) [222]	11·69 (4·89) [221]	-	-	-
14 weeks	8·86 (5·46) [161]	8·82 (4·94) [143]	-0·38 [-1·22 to 0·46]	-0·08 [-0·25 to 0·09]	<0·0001
26 weeks	7·97 (5·52) [157]	8·15 (5·33) [129]	-0·19 [-1·04 to 0·66]	-0·04 [-0·22 to 0·14]	<0·0001
Overall Functioning (Outcome Rating Scale (ORS))					
ORS: Individually (Personal well-being), mean (SD) [n]					
Baseline	6·45 (2·39) [222]	6·66 (2·28) [221]	-	-	-
14 weeks	7·52 (2·06) [161]	7·59 (1·98) [143]	-0·03 [-0·41 to 0·35]	-0·01 [-0·17 to 0·15]	<0·0001
26 weeks	7·65 (2·10) [154]	7·82 (1·78) [127]	-0·18 [-0·57 to 0·21]	-0·08 [-0·24 to 0·09]	0·0016
ORS: Interpersonally (Family, close relationships), mean (SD) [n]					
Baseline	7·55 (2·27) [222]	7·59 (2·14) [221]	-	-	-
14 weeks	7·89 (2·08) [161]	8·28 (1·67) [143]	-0·29 [-0·65 to 0·07]	-0·13 [-0·30 to 0·03]	0·0092
26 weeks	8·02 (2·05) [154]	8·07 (1·99) [127]	0·00 [-0·38 to 0·38]	0·00 [-0·17 to 0·17]	<0·0001

	OSI + TS (N=222)	C-TAU (N=221)	Adjusted Mean Difference [95% CI][1]	Standardised Mean Difference [95% CI]	P-value for non-inferiority[3]
ORS: Socially (Work, school, friendships), mean (SD) [n]					
Baseline	5·91 (2·64) [222]	6·25 (2·56) [221]	-	-	-
14 weeks	6·98 (2·57) [161]	7·37 (2·35) [143]	-0·20 [-0·64 to 0·25]	-0·08 [-0·25 to 0·10]	0·0018
26 weeks	7·27 (2·54) [154]	7·49 (2·28) [127]	-0·08 [-0·54 to 0·38]	-0·03 [-0·21 to 0·15]	0·00045
ORS: Overall (General sense of well-being), mean (SD) [n]					
Baseline	6·34 (2·32) [222]	6·69 (2·25) [221]	-	-	-
14 weeks	7·41 (2·10) [161]	7·70 (2·00) [143]	-0·14 [-0·51 to 0·22]	-0·06 [-0·22 to 0·10]	0·00051
26 weeks	7·73 (2·06) [154]	7·83 (1·80) [127]	-0·04 [-0·42 to 0·34]	-0·02 [-0·18 to 0·15]	0·00010
ORS: Total Score, mean (SD) [n]					
Baseline	26·25 (8·15) [222]	27·19 (7·78) [221]	-	-	-
14 weeks	29·80 (7·97) [161]	30·94 (7·00) [143]	-0·58 [-1·90 to 0·74]	-0·07 [-0·24 to 0·09]	0·0011
26 weeks	30·68 (8·11) [154]	31·21 (6·77) [127]	-0·21 [-1·58 to 1·15]	-0·03 [-0·20 to 0·14]	0·00025
Common Comorbid Emotional and Behavioural Problems (Strengths and Difficulties Questionnaire (SDQ-P))					
SDQ-P: Emotional Symptoms, mean (SD) [n]					
Baseline	6·41 (2·29) [222]	6·21 (2·40) [221]	-	-	-
14 weeks	4·99 (2·89) [161]	4·62 (2·61) [143]	0·03 [-0·45 to 0·51]	0·01 [-0·19 to 0·22]	0·0011
26 weeks	4·40 (2·76) [154]	4·51 (2·82) [128]	-0·24 [-0·73 to 0·25]	-0·10 [-0·31 to 0·11]	<0·0001
SDQ-P: Conduct Problems, mean (SD) [n]					
Baseline	2·84 (2·08) [222]	2·72 (2·02) [221]	-	-	-
14 weeks	2·48 (2·12) [161]	2·44 (2·07) [143]	-0·01 [-0·30 to 0·29]	0·00 [-0·15 to 0·14]	<0·0001
26 weeks	2·55 (2·16) [154]	2·39 (2·14) [128]	-0·05 [-0·36 to 0·25]	-0·03 [-0·17 to 0·12]	<0·0001
SDQ-P: Hyperactivity/Inattention, mean (SD) [n]					
Baseline	5·94 (2·89) [222]	5·66 (2·75) [221]	-	-	-
14 weeks	5·19 (3·01) [161]	4·85 (3·06) [143]	-0·04 [-0·46 to 0·37]	-0·02 [-0·16 to 0·13]	<0·0001
26 weeks	5·44 (3·13) [154]	4·85 (2·74) [128]	0·01 [-0·41 to 0·44]	0·00 [-0·15 to 0·16]	<0·0001

	OSI + TS (N=222)	C-TAU (N=221)	Adjusted Mean Difference [95% CI][1]	Standardised Mean Difference [95% CI]	P-value for non-inferiority[3]
SDQ-P: Peer Relationship Problems, mean (SD) [n]					
Baseline	2·77 (2·34) [222]	2·67 (2·14) [221]	-	-	-
14 weeks	2·57 (2·33) [161]	2·22 (2·16) [143]	0·19 [-0·12 to 0·49]	0·08 [-0·05 to 022]	0·0002
26 weeks	2·55 (2·27) [154]	2·27 (2·03) [128]	0·09 [-0·22 to 0·41]	0·04 [-0·10 to 0·18]	<0·0001
SDQ-P: Prosocial Behaviour, mean (SD) [n]					
Baseline	7·42 (2·33) [222]	7·48 (2·24) [221]	-	-	-
14 weeks	7·47 (2·31) [161]	7·50 (2·20) [143]	-0·03 [-0·34 to 0·29]	-0·01 [-0·15 to 0·13]	<0·0001
26 weeks	7·27 (2·35) [154]	7·61 (2·34) [128]	-0·15 [-0·48 to 0·17]	-0·07 [-0·21 to 0·08]	0·00016
SDQ-P: Total Score, mean (SD) [n]					
Baseline	17·95 (7·05) [222]	17·26 (6·53) [221]	-	-	-
14 weeks	15·24 (8·37) [161]	14·13 (7·58) [143]	-0·05 [-1·07 to 0·97]	-0·01 [-0·16 to 0·14]	<0·0001
26 weeks	14·93 (8·35) [154]	14·02 (7·49) [128]	-0·41 [-1·46 to 0·64]	-0·06 [-0·21 to 0·09]	<0·0001
COVID-19 Specific Worries (Pandemic Anxiety Scale (PAS))					
PAS: Disease Anxiety, mean (SD) [n]					
Baseline	6·94 (3·95) [222]	6·88 (4·02) [221]	-	-	-
14 weeks	5·94 (4·11) [161]	5·64 (3·83) [143]	0·04 [-0·60 to 0·69]	0·01 [-0·15 to 0·17]	<0·0001
26 weeks	5·47 (3·82) [154]	5·52 (3·92) [129]	-0·07 [-0·74 to 0·59]	-0·02 [-0·19 to 0·15]	<0·0001
PAS: Consequence Anxiety, mean (SD) [n]					
Baseline	2·71 (2·37) [222]	2·76 (2·76) [221]	-	-	-
14 weeks	2·48 (2·43) [161]	2·45 (2·59) [143]	0·03 [-0·47 to 0·52]	0·01 [-0·18 to 0·20]	0·00052
26 weeks	2·24 (2·41) [154]	2·59 (2·54) [129]	-0·23 [-0·73 to 0·28]	-0·09 [-0·29 to 0·11]	<0·0001
PAS: Total Score, mean (SD) [n]					
Baseline	9·65 (5·14) [222]	9·63 (5·71) [221]	-	-	-
14 weeks	8·42 (5·69) [161]	8·10 (5·58) [143]	0·11 [-0·86 to 1·08]	0·02 [-0·16 to 0·20]	0·00035
26 weeks	7·71 (5·44) [154]	8·11 (5·62) [129]	-0·24 [-1·24 to 0·76]	-0·04 [-0·23 to 0·14]	<0·0001

[1]OSI + Therapist Support versus C-TAU. Generalised linear mixed effects model adjusted for randomised arm, assessment time point, baseline score, minimisation variables (child's age, gender, baseline anxiety associated interference, service type), an interaction between randomised arm and assessment timepoint as fixed effects, and a random intercept for each participant. [2]Primary outcome. [3]Wald test. One-sided. Level of statistical significance = 0·025

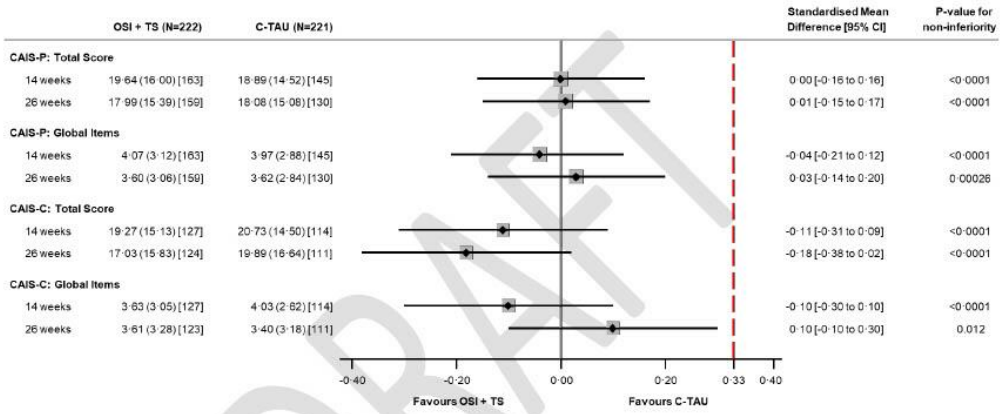


FIGURE 3 FOREST PLOT FOR THE RESULTS OF THE ANALYSIS OF THE CHILD ANXIETY IMPACT SCALE (CAIS)

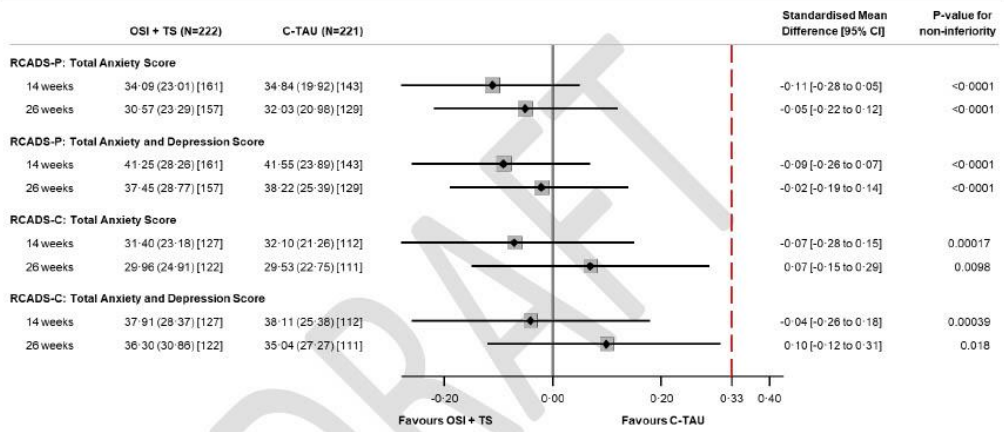


FIGURE 4 FOREST PLOT FOR THE RESULTS OF THE ANALYSIS OF THE REVISED CHILD ANXIETY AND DEPRESSION SCALE (RCADS)

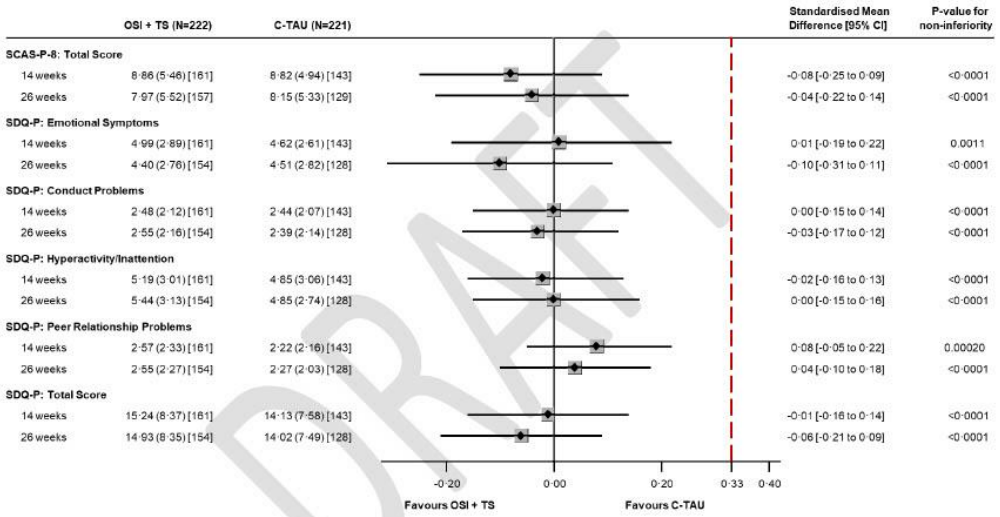


FIGURE 5 FOREST PLOT FOR THE RESULTS OF THE ANALYSIS OF THE BRIEF SPENCE CHILDREN'S ANXIETY SCALE – PARENT VERSION (SCAS-P-8) AND THE COMMON COMORBID EMOTIONAL AND BEHAVIOURAL PROBLEMS (STRENGTHS AND DIFFICULTIES QUESTIONNAIRE (SDQ-P)) (MINUS THE PROSOCIAL BEHAVIOUR SECTION)

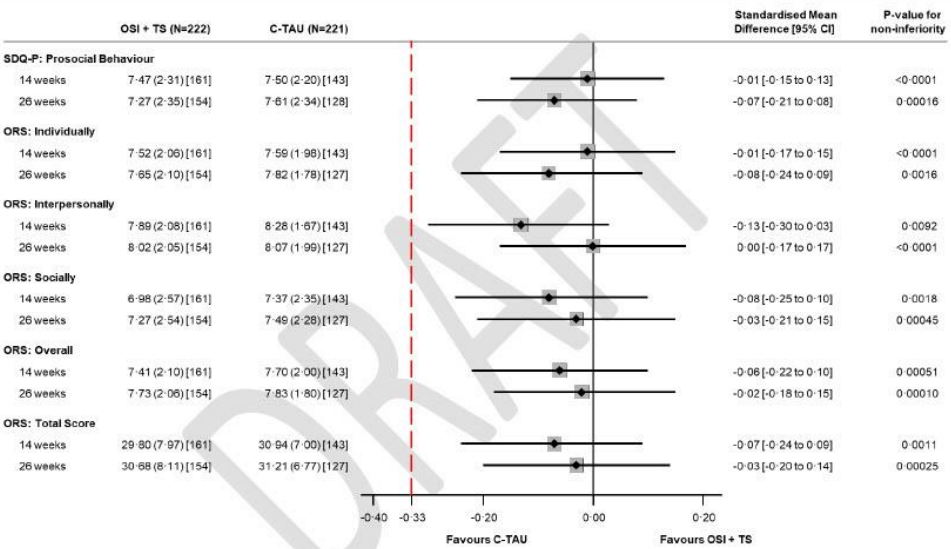


FIGURE 6 FOREST PLOT FOR THE RESULTS OF THE ANALYSIS OF THE PROSOCIAL BEHAVIOUR SECTION OF THE COMMON COMORBID EMOTIONAL AND BEHAVIOURAL PROBLEMS (STRENGTHS AND DIFFICULTIES QUESTIONNAIRE (SDQ-P)) AND THE OVERALL FUNCTIONING (OUTCOME RATING SCALE (ORS))

	OSI + TS (N=222)	C-TAU (N=221)	Standardised Mean Difference [95% CI]	P-value for non-inferiority
PAS: Disease Anxiety				
14 weeks	5·94 (4·11) [161]	5·64 (3·83) [143]	0·01 [-0·15 to 0·17]	<0·0001
26 weeks	5·47 (3·62) [154]	5·52 (3·92) [129]	-0·02 [-0·19 to 0·15]	<0·0001
PAS: Consequence Anxiety				
14 weeks	2·48 (2·43) [161]	2·45 (2·59) [143]	0·01 [-0·18 to 0·20]	0.00052
26 weeks	2·24 (2·41) [154]	2·59 (2·54) [129]	-0·09 [-0·29 to 0·11]	<0·0001
PAS: Total Score				
14 weeks	8·42 (5·69) [161]	8·10 (5·58) [143]	0·02 [-0·16 to 0·20]	0.00035
26 weeks	7·71 (5·44) [154]	8·11 (5·62) [129]	-0·04 [-0·23 to 0·14]	<0·0001

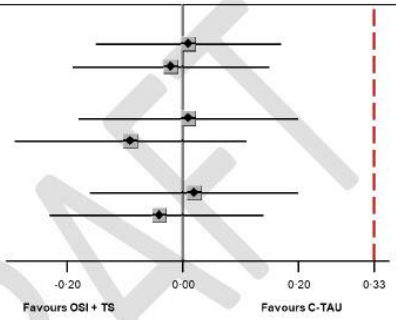


FIGURE 7 FOREST PLOT FOR THE RESULTS OF THE ANALYSIS OF THE COVID-19 SPECIFIC WORRIES (PANDEMIC ANXIETY SCALE (PAS))

3.5 EXPLORATORY ANALYSIS

Parents were asked to complete the Credibility and Expectations of Improvement scale (CEI) post-randomisation and at 14 weeks follow-up. The CEI-P asked the parents how logical they consider the type of treatment to be, how certain they are that this method will be successful in the treatment of their child's anxiety problems, and with what degree of confidence would they recommend this treatment to another family with a child with the same type of anxiety problems as their child has. The therapists were also asked to complete the CEI at the end of the study. The CEI-T comprised of items referring to how logical they found the treatment, how comfortable they felt delivering the treatment, how prepared they felt, certainty in the success of the intervention, confidence recommending the treatment to other therapists, and likelihood of administering the treatment again. An exploratory analysis was conducted on the CEI-P and the CEI-T to explore the treatment credibility.

The data for the CEI scales were highly skewed (see Figure 32 and Figure 33 in Appendix VI), as such medians and interquartile ranges are presented for each item of the CEI scale by randomised arm and at each timepoint, and the exploratory analysis was conducted using a Mann-Whitney U test. The results of the tests of significance are presented in Table 8.

TABLE 8 SUMMARY STATISTICS AND THE TEST OF SIGNIFICANCE FOR THE EXPLORATORY ANALYSES

	OSI + TS (N=222)	C-TAU (N=221)	P-value[1]
EXPLORATORY ANALYSES			
Credibility and Expectation of Improvement Scale – Parent Version (CEI-P)			
CEI-P: How logical do you consider this type of treatment to be?, median (IQR) [n] and [range]			
Post-randomisation	7·0 (6·0 to 9·0) [218] [3·0 to 10·0]	7·0 (5·0 to 9·0) [209] [0·0 to 10·0]	0·17
14 weeks	8·5 (7·0 to 10·0) [160] [2·0 to 10·0]	8·0 (7·0 to 10·0) [143] [0·0 to 10·0]	0·36
CEI-P: How certain are you that this method will be successful in the treatment of your child's anxiety?, median (IQR) [n] and [range]			
Post-randomisation	6·0 (5·0 to 7·0) [218] [0·0 to 10·0]	5·0 (5·0 to 7·0) [209] [0·0 to 10·0]	0·0059
14 weeks	7·0 (5·0 to 9·0) [160] [0·0 to 10·0]	7·0 (5·0 to 9·0) [143] [0·0 to 10·0]	0·39
CEI-P: With that degree of confidence would you recommend this treatment to another family with a child with the same type of anxiety problems as your child has?, median (IQR) [n] and [range]			
Post-randomisation	6·0 (5·0 to 8·0) [218] [0·0 to 10·0]	5·0 (5·0 to 7·0) [209] [0·0 to 10·0]	0·15
14 weeks	8·0 (6·0 to 10·0) [160] [0·0 to 10·0]	8·0 (5·0 to 10·0) [143] [0·0 to 10·0]	0·19

	OSI + TS (N=222)	C-TAU (N=221)	P-value[1]
Credibility and Expectation of Improvement Scale – Therapist Version (CEI-T)			
CEI-T: How logical did you consider the treatment to be?, median (IQR) [n] and [range]			
End of treatment	9·0 (7·0 to 10·0) [155] [0·0 to 10·0]	8·0 (7·0 to 10·0) [128] [4·0 to 10·0]	0·42
CEI-T: How comfortable did you feel in your therapist role in delivering the treatment?, median (IQR) [n] and [range]			
End of treatment	7·0 (6·0 to 9·0) [154] [2·0 to 10·0]	8·0 (7·0 to 10·0) [127] [3·0 to 10·0]	0·012
CEI-T: How well prepared did you feel to deliver the treatment?, median (IQR) [n] and [range]			
End of treatment	8·0 (6·0 to 9·0) [154] [2·0 to 10·0]	8·0 (7·0 to 10·0) [127] [3·0 to 10·0]	0·072
CEI-T: How certain are you that this method was successful in the treatment of children's anxiety problems?, median (IQR) [n] and [range]			
End of treatment	7·0 (5·0 to 9·0) [155] [0·0 to 10·0]	7·0 (5·0 to 9·0) [126] [0·0 to 10·0]	0·60
CEI-T: With what degree of confidence would you recommend this treatment to another therapist to treat child anxiety problems?, median (IQR) [n] and [range]			
End of treatment	8·0 (7·0 to 10·0) [155] [1·0 to 10·0]	8·0 (7·0 to 10·0) [127] [2·0 to 10·0]	0·29
CEI-T: How likely are you to use this method in the future to treat children's anxiety problems?, median (IQR) [n] and [range]			
End of treatment	8·0 (7·0 to 10·0) [155] [0·0 to 10·0]	9·0 (7·0 to 10·0) [127] [2·0 to 10·0]	0·0033

[1]OSI + TS versus C-TAU. Mann-Whitney U test. Exact P-values. Level of statistical significance = 0·05

3.6 SENSITIVITY ANALYSES

Five sensitivity analyses were pre-specified in the statistical analysis plan to examine the robustness of the results of the primary analysis. All sensitivity analyses were conducted on the primary outcome of the CAIS-P score, which a lower score indices lower levels of anxiety, as such a non-inferiority margin of 0·33 is used in the interpretation of the results. Non-inferiority will be claimed if the upper limit of the 95% confidence interval around the standardised mean difference is less than the non-inferiority margin of 0·33. The results of the sensitivity analyses are presented in Table 9 and also graphically in a forest plot in Figure 8.

Any outliers that were identified were to be excluded from the analysis to determine the impact of these observations on the treatment effect of the primary outcome. An outlier was defined as an observation more than four standard deviations from the mean. However, no values for the primary outcome were more than four standard deviations from the mean and no outliers were identified, therefore this sensitivity analysis was not conducted.

The availability of the outcome data for the primary outcome is summarised by randomised group, logistic regression models were used to explore any association between baseline characteristics and the availability of the primary outcome (see Table 6). The covariates that were found to be statistically significant of predicting the missingness of the primary outcome are: partnered (P=0·0018), and co-habiting (P=0·023). A sensitivity analysis was conducted re-running the model used in the primary analysis with these factors as additional covariates in the model as fixed effects.

A sensitivity analyses was conducted based on a per-protocol population excluding those participants who had deviated from the protocol. To be included in the per-protocol population participants needed to have: i) received five or more treatment sessions, ii) received the treatment that they were originally randomised too, iii) submitted their final questionnaire within 30 weeks of randomisation, and iv) started treatment within 12 weeks of being randomised.

Two sensitivity analyses of the primary outcome were carried out based on altering the window in which the assessment must have been made, the first one includes all outcomes, regardless of the length of time that has elapsed from either 14 or 26 week. And a second one, similar to the first, including all outcomes, but if the 26 week outcome is missing and the 14 week outcome had been collected within ±4 weeks of the 26 week follow up, then this is treated as the 26 week outcome.

An additional per-protocol analysis was conducted after the initial unblinded results in this report were presented to the chief investigator. This was not described in the SAP; however, it follows the broad principles laid down there. The Trial Steering Committee questioned whether the 4 criteria for the per-protocol were too restrictive and resulted in a small sample size and suggested to look at using 2 criteria (received five or more treatment sessions, and received the treatment that they were originally randomised to) instead. This suggestion was carefully considered, discussed, and agreed upon between the trial statistician, a senior trial statistician, and the chief investigator. The result from this additional analysis should be considered exploratory.

The normality assumptions of the generalised linear mixed effects models for the sensitivity analyses were assessed by plotting a histogram of the outcomes at each time point split by randomised group, a histogram of the model residuals, an inverse normal plot of the standardised model residuals, and a scatter plot of the fitted values versus the model residuals, these are presented in Appendix VII in Figure 34 to Figure 38.

TABLE 9 SUMMARY STATISTICS, ADJUSTED MEAN DIFFERENCES, STANDARDISED MEAN DIFFERENCES, AND THE P-VALUE FOR NON-INFERIORITY FOR THE SENSITIVITY ANALYSES

	OSI + TS (N=222)	C-TAU (N=221)	Adjusted Mean Difference [95% CI][1]	Standardised Mean Difference [95% CI]	P-value for non-inferiority[3]
SENSITIVITY ANALYSES					
CAIS-P: Total Score – Including Factors Found to be Predictive of Missingness in the Model (see Table 6)[2], mean (SD) [n]					
Baseline	26·87 (15·26) [222]	25·96 (14·63) [221]	-	-	-
14 weeks	19·64 (16·00) [163]	18·89 (14·52) [145]	-0·42 [-2·85 to 2·01]	-0·03 [-0·19 to 0·13]	<0·0001
26 weeks	17·99 (15·39) [159]	18·08 (15·08) [130]	-0·70 [-3·16 to 1·76]	-0·05 [-0·21 to 0·12]	<0·0001
CAIS-P: Total Score – Per-Protocol Population, mean (SD) [n]					
Baseline	25·29 (15·46) [111]	24·71 (14·08) [84]	-	-	-
14 weeks	17·52 (14·69) [101]	15·93 (12·38) [71]	1·35 [-1·77 to 4·47]	0·09 [-0·12 to 0·30]	0·013
26 weeks	15·68 (13·89) [106]	15·64 (13·26) [77]	0·36 [-2·69 to 3·41]	0·02 [-0·18 to 0·23]	0·0018
CAIS-P: Total Score – Additional Per-Protocol Population, mean (SD) [n]					
Baseline	25·84 (15·23) [150]	24·35 (13·24) [118]	-	-	-
14 weeks	19·01 (16·03) [128]	16·26 (12·42) [90]	1·50 [-1·33 to 4·33]	0·10 [-0·09 to 0·30]	0·012
26 weeks	16·31 (14·39) [118]	15·12 (12·97) [84]	0·84 [-2·05 to 3·74]	0·06 [-0·14 to 0·26]	0·0041
CAIS-P: Total Score – Including All Outcomes (regardless of the length of time elapsed from either 14 or 26 weeks), mean (SD) [n]					
Baseline	26·87 (15·26) [222]	25·96 (14·63) [221]	-	-	-
14 weeks	20·16 (16·31) [174]	20·06 (14·83) [165]	-1·02 [-3·40 to 1·36]	-0·07 [-0·23 to 0·09]	<0·0001
26 weeks	18·08 (15·77) [173]	18·13 (15·10) [163]	-0·78 [-3·17 to 1·60]	-0·05 [-0·21 to 0·11]	<0·0001
CAIS-P: Total Score – Including All Outcomes (substituting missing 26 week outcome with 14 week outcome if collected within 26±4 weeks), mean (SD) [n]					
Baseline	26·87 (15·26) [222]	25·96 (14·63) [221]	-	-	-
14 weeks	20·16 (16·31) [174]	19·98 (14·84) [164]	-1·02 [-3·40 to 1·37]	-0·07 [-0·23 to 0·09]	<0·0001
26 weeks	18·08 (15·77) [173]	18·23 (15·10) [164]	-0·81 [-3·19 to 1·58]	-0·05 [-0·21 to 0·11]	<0·0001

[1]OSI + TS versus C-TAU. Generalised linear mixed effects model adjusted for randomised arm, assessment time point, baseline score, minimisation variables (child's age, gender, baseline anxiety associated interference, service type), an interaction between randomised arm and assessment timepoint as fixed effects, and a random intercept for each participant. [2]Also includes factors found to the predictive of missingness as fixed effects (partnered, and co-habiting). [3]Wald test. One-sided. Level of statistical significance = 0·025

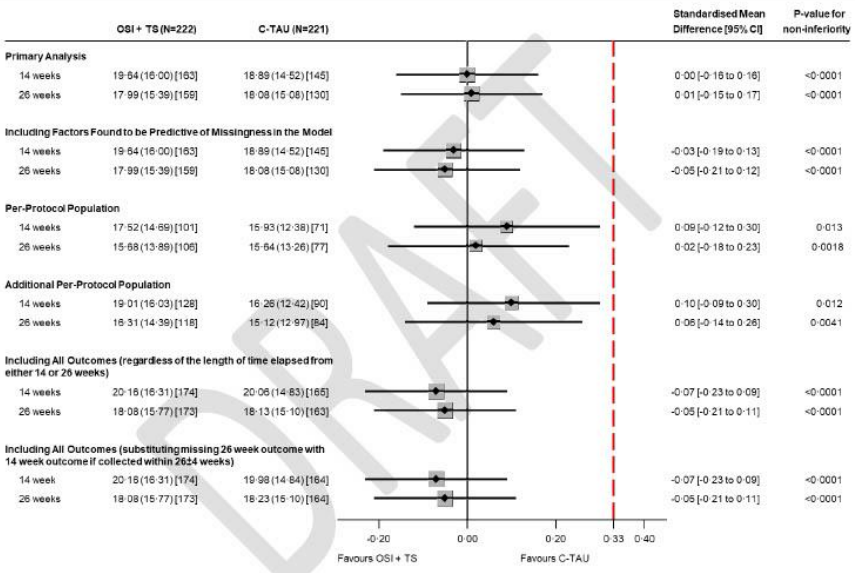


FIGURE 8 FOREST PLOT FOR THE RESULTS OF THE SENSITIVITY ANALYSIS OF THE CHILD ANXIETY IMPACT SCALE – PARENT VERSION (CAIS-P)

3.7 SUBGROUP ANALYSIS

No subgroup analysis was planned.

3.8 SAFETY ANALYSIS

All participants are included in the safety analysis and are analysed based on which intervention they received, instead of which intervention they were randomised to.

An adverse event (AE) is defined as any untoward medical occurrence in a participant to whom a medical product (or study intervention) has been administered, including occurrences which are not necessarily caused by or related to that product.

A Serious Adverse Event (SAE) is any untoward medical occurrence that:

- results in death,
- is life-threatening,
- requires inpatient hospitalisation or prolongation of existing hospital,
- results in persistent or significant disability/incapacity,
- consists of a congenital anomaly or birth defect.

Other 'important medical events' were also considered to be serious adverse events when, based upon appropriate medical judgment, the event may have jeopardised the participant and may have required medical or surgical intervention to prevent one of the outcomes listed above.

NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.

The windows for reporting AEs and SAEs were:

i) During the treatment phase based on therapist report
ii) Up to the end of study based on parent/carer report (i.e. up to the 26 week assessment or qualitative interview, whichever is later).

The 14 week and 26 week assessment within this trial included questionnaires monitoring participants' functioning and quality of life, therefore some of the potential adverse events identified in the protocol were monitored routinely. Therapists were asked to indicate the presence of an AE or SAE that arise during the course of treatment.

The number of adverse events and serious adverse events are presented in Table 10 by which intervention the participant received, and a full detailed list of the adverse events which were reported during the trial can be found in Table 11. No serious adverse events were reported during the trial.

TABLE 10 FREQUENCY AND PERCENTAGE OF ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

	Received OSI + TS (N=220)	Received C-TAU (N=223)	P-value[1]
SAFETY ANALYSIS			
Experienced an adverse event, n/N (%)	9/220 (4·1)	8/223 (3·6)	0·81
None	211/220 (95·9)	215/223 (96·4)	
1	8/220 (3·6)	6/223 (2·7)	
2	1/220 (0·5)	2/223 (0·9)	
Intensity of adverse event, n/N (%)			
N (Number of AEs)	10	10	0·087
Mild	6/10 (60·0)	9/10 (90·0)	
Moderate	4/10 (40·0)	0/10 (0·0)	
Severe	0/10 (0·0)	1/10 (10·0)	
Causality of adverse event, n/N (%)			
N (Number of AEs)	10	10	0·32
Definitely not related	3/10 (30·0)	1/10 (10·0)	
Unlikely to be related	1/10 (10·0)	1/10 (10·0)	
Possibly related	4/10 (40·0)	7/10 (70·0)	
Likely to be related	2/10 (20·0)	0/10 (0·0)	
Definitely related	0/10 (0·0)	1/10 (10·0)	
Experienced a serious adverse event, n/N (%)	0/220 (0·0)	0/223 (0·0)	-

[1]Fisher's exact test. Level of significance = 0·05

NOTE: The outcome of three adverse events below are classed as 'ongoing'. The trial team has attempted to contact the families of the child who experienced these adverse events to determine the outcome, however they were unable to, and due to time constraints of the trial these three AEs have been left as ongoing on the database and the database was hard locked (see TM112-D: File Note 3, dated 17 March 2023). AE 027 consisted of the parent writing in their self-report AE from during the 26 week questionnaire "My son did think a lot more about his anxieties which heightened them at first. And he now believes that having anxieties are a bad thing that only he is dealing with. We are talking this through with him to assume him otherwise." In AE 028 the child wrote "makes me feel sad" in their self-report AE form at 26 weeks. These were the 11th and 12th instances of the child reporting feelings of distress/upset due to an aspect of the study or the questionnaires. The TSC were made aware in October 2022 about the similar number of events. It was decided by the TSC that AEs of this nature did not require any further action as the events were not considered to be specific to the trial (but reflected procedures that are routine in clinical practice, e.g. administration of the anxiety measures). It was also noted that the study participant information sheets mention that "Some of the questions will involve discussing thoughts and feelings that may be upsetting". In AE 029 the parent wrote "My daughter picked up another habit as part of her bedtime rituals" in the self-report AE form, this was raised with the chair of the TSC who confirmed that they were happy with the actions taken (though noting the need for separate follow-up as and when the trial team are able to make contact with the parent to assess as a potential adverse event) as the clinician has had direct contact with the family, and confirms the parent is happy with the intervention. The TSC chair did not see this has having any implications for the trial data.

TABLE 11 LIST OF ADVERSE EVENTS

Who is the Event in Relation to?	Adverse Event	Date of Onset	Date of Resolution	Was the Event Unexpected[2]?	Outcome	Action	Intensity	Frequency *(if known)*	Causality	Intervention Received
Participant (child)	Had a Zoom call with Parent, and during the conversation, the parent spoke about the participant breaking her arm approximately 3 weeks ago whilst playing out on her scooter. She lost her balance and put her hands down to steady herself, breaking her arm. The participants parent took the participant to the hospital, she had the injury x-rayed and they determined that she had broken her arm. She had a temporary cast put on the time and was released on the same day. Participant was distressed as a result of this for a few days afterwards. Parent reported no further issues. Due to have cast removed 19/03/2021.	19/02/2021	15/03/2021	Yes	Resolved	Continued with study	Moderate	N/A	Definitely not related	OSI + TS
Participant (Parent / Carer)	Family completed 14 week questionnaires and added that 'When trying a technique out on a school morning, things went very wrong to the point the family as a whole are now receiving help'. Form completed 30/05/21 (OSI treatment finished 16/06/21 so potentially during treatment). 18/03/2022 LR sent following email to nominated Co-CAT admin in the service: [EMAIL REMOVED]. Discussed at TSC 01/04/2022: decided not a serious adverse event.	30/05/2021	07/04/2022	Yes	Resolved	Continued with study	Moderate		Possibly related to the treatment	OSI + TS
Participant (child)	Concerns surrounding co-cat participant. Increasingly difficult to keep the conversation in the OSI call on track and boundaried. Mum has shared [risk information]. No one from early help/ social care is currently involved. Strongly believe anxiety management is not what is needed at this point in time, and feel her input with CO-CAT should end so that I can offer a CAMHS review and sign-post to the correct service/ refer to a more appropriate treatment pathway. OUTCOME - [Clinician] to offer review, to consider attachment pathway with clinical supervisor.	16/12/2021	17/12/2021	Yes	Resolved with sequelae	Discontinued study	Moderate	Last week (once for this participant and 1st occurrence ins study)	Definitely not related	OSI + TS
Participant (child)	'Parent reported in W14 AE self-report form (completed 03/06/2022): "The last questionnaire seemed to trigger her anxiety from last year along with class moving seats, unfortunate timing and resulted in significant absence from school over past 3 months after a 6 month period being almost 100% attendance. Obviously I don't know for sure, but after the	21/02/2022	06/06/2022	Yes	Resolved	Continued with study	Mild	2nd occurence in the study	Possibly related to the assessments	C-TAU

Who is the Event in Relation to?	Adverse Event	Date of Onset	Date of Resolution	Was the Event Unexpected[2]?	Outcome	Action	Intensity	Frequency *(if known)*	Causality	Intervention Received
	questionnaire on the Monday, Tuesday brought major anxiety and no school attendance. The teacher was also rearranging seating in the class, perhaps overwhelmed by both and only past two weeks have we had 90% attendance. Also with change of practitioners due to initial one moving jobs and second one also moving jobs has been a little unsettling, although my daughter appears to handle that ok.""									
Participant (child)	Parent reported in W14 AE self-report form (completed 04/03/2022): 'Anxiety is still very much there and we are still desperate for some help.' From our records it is looks like the family haven't started treatment yet. Contacted clinical team 18/03/22 to ask if family were due to start treatment yet. Admin confirmed that clinician had spoken to family and booked treatment in on 23/03/22. Updated retrospectively 20/03/2023 - seems that team decided was not an AE at the time.	04/03/2022	23/03/2022	Yes	Resolved	Continued with study	Mild	1st occurrence in study	Definitely not related	OSI + TS
Participant (child)	Clinician let us know that participant had been hospitalised due to a horse riding accident. Asked to complete form, then signed off by team lead. Treatment to be postponed until recovered.	16/05/2022	17/05/2022	Yes	Resolved	Continued with study	Severe	1st occurrence in study	Definitely not related	C-TAU
Participant (child)	Research team carried out welcome call 17/5 and spoke to the parent who explained that they were going to withdraw from treatment due to changes at school. They were dissapointed to not receive OSI, as this was the reason they enrolled on the trial. When encourage to complete FU, parent explained that child got very angry and upset completing baseline questionnaires, and the whole experience was distressing so did not want to proceed with the study.	17/05/2022	17/05/2022	No	Resolved	Discontinued study	Mild	1st occurrence in study	Definitely related to the treatment	C-TAU
Participant (child)	Parent reported in 14-week self-report form (completed 03/10/2022) under 'Did anything bad happen because of taking part?' that 'Son struggled to answer such personal questions, he became upset and distressed after the first set of questions'. (Baseline child questionnaires completed 19/06/2022.) Phone contact made with parent, happy to continue in study. Keen to try the 14 week child questionnaire but will stop at the first sign of any distress.	19/06/2022	10/10/2022	No	Resolved	Continued with study	Mild	5th occurrence	Possibly related to other	C-TAU

Who is the Event in Relation to?	Adverse Event	Date of Onset	Date of Resolution	Was the Event Unexpected[F]?	Outcome	Action	Intensity	Frequency *(if known)*	Causality	Intervention Received
Participant (child)	Parent reported in 14-week self-report form (completed 23/08/2022) under 'Did anything bad happen because of taking part?' that their child is 'now on medication to help during the day and at night'. Research team called parent on 26/08/2022: parent explained that as a result of being part of the study, their child was seen by a paediatrician and is now on medication. Parent did not think this was related to completing the questionnaires or as a direct result of the study. Co-CAT PI made aware on 26/08/2022, local PI informed 30/08/2022.	23/08/2022	30/08/2022	Yes	Resolved	Continued with study	Mild	1st occurrence	Unlikely to be related	C-TAU
Participant (child)	Parent reported in 14-week self-report form (completed 05/09/2022) under 'Did anything bad happen because of taking part?' that 'the only negative was the upset it caused my daughter, it heightened her anxiety at times'. Research team phoned parent 06/09/2022: parent stated that the upset and heightened anxiety was not caused by the questionnaires or treatment directly, more than any kind of demand causes the child to become upset.	05/09/2022	09/09/2022	No	Resolved	Continued with study	Mild	3rd occurrence	Possibly related to other	C-TAU
Participant (child)	Parent reported in 14-week self-report form (completed 05/09/2022) under 'Did anything bad happen because of taking part?' that 'I feel it mentally drained my child more'. Research team attempted to call parent 06/09/2022. Parent did not pick up so voicemail was left asking them to call us back. No phone call was received by the end of the day so email was sent to parent. As of 09/09/2022, no response received via email or phone from the parent. As attempts to contact have been made and the event is mild, decision made to not take any further action and consider the AE resolved.	05/09/2022	09/09/2022	No	Resolved	Continued with study	Mild	4th occurrence	Possibly related to other	OSI + TS
Participant (child)	Parent reported in 26-week self-report form (completed 28/11/2022) under 'Did anything bad happen because of taking part?' that 'The bad is that [child] is so against it and just shuts down or cries at the mention of anything to do with it'. Also wrote that she found the study 'very frustrating as my daughter just doesn't want to open up about the study, she gets upset filling in the forms, talking about the step plan,	28/11/2022	01/12/2022	No	Resolved	Continued with study	Mild	6th occurrence in study	Possibly related to the assessments	C-TAU

Primary Care Clinical Trials Unit

UNIVERSITY OF OXFORD

Co-CAT Statistical Analysis Report Version 2.0 11 December 2023

Who is the Event in Relation to?	Adverse Event	Date of Onset	Date of Resolution	Was the Event Unexpected[F]?	Outcome	Action	Intensity	Frequency *(if known)*	Causality	Intervention Received
	so it's been hard'. Parent emailed Co-CAT team after completed the 26-week questionnaire to inform us that the will broach doing the child questionnaire with her daughter but she refused last time. Research team responded to reassure the parent that the child questionnaire is optional and it's fine not to ask child to do it. Later that day child form was completed - child commented in their AE form that they don't like talking about feelings and that the study was 'annoying'.									
Participant (child)	'Parent reported in 26-week self-report form (completed 21/12/2022) under "Did anything bad happen because of taking part?" that "My child did not cope with the questionnaires he got very upset with the questions and would not answer them with a true reflection of himself. He did not and still does not like talking about how he is feeling etc. We stopped completing the child questionnaires after the second one." (Baseline child questionnaires completed 19/06/2022.) Parent had written similar in their 14-week self-report form. Research team had previously phoned parent on 04/10/2022 regarding the same AE reported in their 14-week form: phone contact made with parent, they were happy to continue in study. Parent was reassured that the child questionnaires are optional and it's fine not to do them. No further child questionnaires were completed so distressed reported in the current AE is likely to referring to the baseline questionnaires. Parent has now finished the study so no further action taken. '	21/12/2022	06/01/2023	No	Resolved	Continued with study	Mild	7th occurrence in study	Possibly related to the assessments	C-TAU
Participant (child)	'Child reported in 26-week self-report form (completed 05/01/2023) under "Did anything bad happen because of taking part?" that " Yes because it makes my anxiety worse'. They also rated taking part in the study as 'very negative' because it 'makes my anxiety worse thinking or talking about it'. Previously the parent had written in their 14-week self-report form that the study 'mentally drained their child'. Attempts were made to contact the parent but did not hear back. The parent did not write any comments in	05/01/2023	16/01/2023	Yes	Resolved	Continued with study	Moderate	8th occurrence in study	Likely to be related to the treatment	OSI + TS

Who is the Event in Relation to?	Adverse Event	Date of Onset	Date of Resolution	Was the Event Unexpected[F]?	Outcome	Action	Intensity	Frequency *(if known)*	Causality	Intervention Received
	the 26-week form. Research team attempted to call parent 09/01/2023. Parent did not pick up so voicemail was left and an email sent. Parent responded to email the same day, indicating that they are happy to talk to us. No phone call returned however so research team will continue to follow up. EW tried phoning again 13/01/2023, left another VM and mentioned we will try contacting their service. Research team also contacted clinician Clinician16/01 to gain some insight. No concerns raised from the clinician about family's involvement in Co-CAT. Clinician reported some 'difficulties with step-plan' but clinician reported other contextual factors such as transition from primary/secondary made this harder. Clinician mentioned that parent had reported that they had seen progress in areas unrelated to school. Clinician mentioned 'high sensory needs' and suspected underlying neurodevelopmental difficulties made 'tackling anxiety' harder. '									
Participant (child)	Parent wrote in 26 week questionnaires on 12/01/2023 'My daughter picked up another habit as part of her bedtime rituals'. Research team attempted to call parent 02/03/2023. Parent did not pick up so voicemail was left asking them to call us back and email was also sent. 10/03/2023 - no response from parent and event is classified on the basis of the information provided. The research team will continue to contact the parent and will contact the clinical team if needed.	12/01/2023		No	Ongoing	Continued with study	Mild	No other reports from parent. 1st occurrence in study	Possibly related to the treatment	OSI + TS
Participant (child)	In 26 week questionnaires completed on 23/01/2023 child reported: 'Makes me feel sad' Research team attempted to call parent 02/03/2023. Parent did not pick up so voicemail was left asking them to call us back and email was also sent. 10/03/23 still no response from parent so event was classified based on information provided and based on similar classified events in the study. The research team will continue to contact the parent and will contact clinical team if needed.	23/01/2023		No	Ongoing	Continued with study	Mild	No other reports from parent. 12th occurrence.	Possibly related to other	C-TAU

Primary Care Clinical Trials Unit

UNIVERSITY OF OXFORD

Co-CAT Statistical Analysis Report Version 2.0 11 December 2023

Who is the Event in Relation to?	Adverse Event	Date of Onset	Date of Resolution	Was the Event Unexpected[F]?	Outcome	Action	Intensity	Frequency *(if known)*	Causality	Intervention Received
Participant (child)	Parent wrote in 26 week questionnaire on 27/01/2023 'It hasn't helped my child at all he seems to be getting worse'. Research team spoken to parent on the phone 02/03/2023 - parent felt that main issue for child was ASC which they've now been referred for an assessment for. Was very grateful to have received OSI as they felt it was the first time they'd been listened to and offered support - thanked the project for helping in that way and very happy that they have the support they need now. Parent expressed that the child getting worse was not due to treatment or taking part in the study. Still under care of clinician and clinician aware, but parent was happy for us to speak to them if needed.	27/01/2023	03/03/2023	Yes	Resolved	Continued with study	Mild	9th occurrence in study	Unlikely to be related	OSI + TS
Participant (child)	Parent wrote in W26 self report AE form 08/02/23: 'When trying to get [child] to do more of the things he was anxious about it caused more of a meltdown but this is probably due to him potentially having autism'. Research team tried calling parent 02/03/2023 but got VM - left VM and sent parent email asking them to get in touch with us. Parent phoned 07/03/2023 spoke to LR. They were offered treatment before autism assessment, to rule out anxiety. Step plan related exposure made the child worse rather than better but mum recognises this was due to the child's needs not necessarily being anxiety at that point in time. Currently on waiting list for ASC assessment, felt there was a gap in care - went from having treatment to nothing while waiting but aware that was just how the system worked. Didn't feel we needed to contact the clinician. Glad they took part - ruled out anxiety. Said thanks for the opportunity and that we'd explained everything really well etc.	08/02/2023	07/03/2023	No	Resolved	Continued with study	Mild	No other known occurrences for this participant, 10th occurrence in study.	Possibly related to the treatment	OSI + TS
Participant (child)	Parent wrote in 26 week questionnaire on 16/02/23 that '[Child] didn't your stand why she wasn't getting to speak to the councillor herself therefore behaviours started to show.' Research team contacted parent 02/03/2023 and spoke on the phone. Parent explained that the child was mainly exhibiting frustration as they had expected that they'd speak to the therapist	16/02/2023	03/03/2023	No	Resolved	Continued with study	Mild	1	Likely to be related to the treatment	OSI + TS

Who is the Event in Relation to?	Adverse Event	Date of Onset	Date of Resolution	Was the Event Unexpected[1]?	Outcome	Action	Intensity	Frequency *(if known)*	Causality	Intervention Received
	themselves and didn't understand why it went through the parent. Parent felt that it was due to the nature of the treatment being parent-led but nothing specific within the treatment causing further upset. Therapist aware - Still being supported by them and will have a face to face appointment this month. Happy for us to discuss with therapist if necessary.									
Participant (child)	Parent wrote in W26 self report 19/02/23 AE form: 'My son did think a lot more about his anxieties which heightened them at first. And he now believes that having anxieties are a bad thing that only he is dealing with. We are talking this through with him to assure him otherwise.' Research team tried calling parent 02/03/2023 but got VM - left VM and sent parent email asking them to get in touch with us. 10/03/23 - still no response from parent so AE classified on basis of information provided and similar previous events in study. The research team are continuing to contact the family and will contact clinical team if needed.	19/02/2023		No	Ongoing	Continued with study	Mild	No other reports from parent. 11th occurrence.	Possibly related to other	C-TAU

[1]*Unexpected is defined as an event that was not previously outlined by the information leaflet, protocol, or consent.*

4 REFERENCES

Beecham, J. (1999). CSRI - children's version. http://www.dirum.org/instruments/details/45 accessed 03.08.2020

Bringhurst, D. L., Watson, C. W., Miller, S. D., & Duncan, B. L. (2006). The Reliability and Validity of the Outcome Rating Scale: A Replication Study of a Brief Clinical Measure. *Journal of brief Therapy, 5(1),* 23-30.

Chorpita, B., Moffitt, C. E., & Gray, J. (2005). Psychometric properties of the Revised Child Anxiety and Depression Scale in a clinical sample. *Behaviour Research and Therapy, 43,* 309–322. https://doi.org/10.1016/j.brat.2004.02.004

Copeland, W. E., Angold, A., Shanahan, L., & Costello, E. J. (2014). Longitudinal patterns of anxiety from childhood to adulthood: The great smoky mountains study. *Journal of the American Academy of Child and Adolescent Psychiatry.* https://doi.org/10.1016/j.jaac.2013.09.017

Co-Space Study: Supporting Parents, Adolescents and Children during Epidemics. https://www.psy.ox.ac.uk/research/topic-researchgroup/supporting-parents-adolescents-and-children-during-epidemics (accessed 06.05.2020)

Co-Space Study: Report 03. Pearcey, Shum, Waite & Creswell (2020). Parents/carers report on their own and their children's concerns about children attending school. Retrieved from: https://emergingminds.org.uk/wp-content/uploads/2020/05/Co-SPACE-report03_School-concerns_23-05-20.pdf

Creswell, C., Violato, M., Fairbanks, H., White, E., Parkinson, M., Abitabile, G., … Cooper, P. J. (2017). Clinical outcomes and cost-effectiveness of brief guided parent-delivered cognitive behavioural therapy and solution-focused brief therapy for treatment of childhood anxiety disorders: a randomised controlled trial. *The Lancet Psychiatry, 4(7),* 529–539. https://doi.org/10.1016/S2215-0366(17)30149-9

Dolan, P., Gudex, C., Kind, P., & Williams, A. (1995). A social tariff for EuroQol: results from a UK general population survey. *Working Papers.*

Ebesutani, C., Bernstein, A., Nakamura, B. J., Chorpita, B. F., & Weisz, J. R. (2010). A psychometric analysis of the revised child anxiety and depression scale-parent version in a clinical sample. *Journal of Abnormal Child Psychology, 38(2),* 249–260. https://doi.org/10.1007/s10802-009-9363-8

EuroQuol. (2020). European Quality of Life-5 Dimension 5-level: EQ-5D-5L. https://euroqol.org/eq-5d-instruments/eq-5d-5l-about/ (accessed 30.07.2020).

Evans, R., Thirlwall, K., Cooper, P., & Creswell, C. (2017). Using symptom and interference questionnaires to identify recovery among children with anxiety disorders. *Psychological Assessment*, *29*(7), 835.

Fenwick, E., Marshall, D.A., Levy, A.R., & Nichol, G. (2006). Using and interpreting cost-effectiveness acceptability curves: An example using data from a trial of management strategies for atrial fibrillation. *BMC Health Services Research, 6,* 1.

Goodman R, Meltzer H, Bailey V (1998) The Strengths and Difficulties Questionnaire: A pilot study on the validity of the self-report version. *European Child and Adolescent Psychiatry, 7,* 125-130.

Goodman. R. (2001). Psychometric properties of the strengths and difficulties questionnaire. *Journal of the American Academy of Child and Adolescent Psychiatry, 40 (11),* 1337-1345.

Green, H., McGinnity, A., Meltzer, H., Ford, T., & Goodman, R. (2005). Mental Health of Children and Young People in Great Britain, 2004. National Statistics. https://doi.org/10.1037/e557702010-001

Health Innovation Network South. (2020). Needs of Children & Young People <13 Years During the Covid19 Crisis in Contact with Mental Health or Community Services.

Hill, C., Chessell, C., Percy, R., & Creswell, C. (2021). Online Support and Intervention (OSI) for child anxiety: a case series within routine clinical practice. *Behavioural and Cognitive Psychotherapy, 50, 429-445*. https://doi.org/10.1017/S1352465822000157

Hill, C., Reardon, T., Taylor, L., Creswell, C. (2022). Online Support and Intervention for Child Anxiety (OSI): Development and Usability Testing. *JMIR Form Res, 6(4):e29846*. https://doi.org/10.2196/29846

Husereau, D., Drummond, M., Petrou, S., Carswell, C., Moher, D., Greenberg, D., Augustovski, F., Briggs, A.H., Mauskopf, J., &. Loder, E. (2013). Consolidated health economic evaluation reporting standards (CHEERS) statement. *Cost Effectiveness and Resource Allocation, 11(1)*, 6.

James, A. C., James, G., Cowdrey, F. A., Soler, A., & Choke, A. (2013). Cognitive behavioural therapy for anxiety disorders in children and adolescents. *The Cochrane Database of Systematic Reviews, 6(2),* CD004690. https://doi.org/10.1002/14651858.CD004690.pub3

Kessler, R., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in National Comorbidity Survey Replication. *Archives of General Psychiatry, 62(6),* 593–602. https://doi.org/10.1001/archpsyc.62.6.593

Langley, A. K., Bergman, R. L., McCracken, J., & Piacentini, J. C. (2004). Impairment in Childhood Anxiety Disorders: Preliminary Examination of the Child Anxiety Impact Scale–Parent Version. *Journal of Child and Adolescent Psychopharmacology, 14(1),* 105–114. https://doi.org/10.1089/104454604773840544

Langley, A. K., Falk, A., Peris, T., Wiley, J. F., Kendall, P. C., Ginsburg, G., … Piacentini, J. (2014). The Child Anxiety Impact Scale: Examining Parent- and Child-Reported Impairment in Child Anxiety Disorders. *Journal of Clinical Child and Adolescent Psychology, 43(4),* 579–591. https://doi.org/10.1080/15374416.2013.817311

Lundh, L.G., Wangby-Lundh, M., & Bjarehed, J. (2008). Self reported emotional and behavioral problems in Swedish 14 to 15-year-old adolescents: A study with the self-report version of the Strengths and Difficulties Questionnaire. *Scandinavian Journal of Psychology, 49,* 523–532.

Muris, P., Meesters, C., & van den Berg, F. (2003). The Strengths and Difficulties Questionnaire (SDQ): Further evidence for its reliability and validity in a community sample of Dutch children and adolescents. *European Child and Adolescent Psychiatry, 12* (1), 1–8.

McCrone, P., Dhanasiri, S., Patel, A., Knapp, M., & Lawton-Smith, S. (2008). Paying the price: the cost of mental health care in England to 2026. King's Fund. https://doi.org/10.1192/bjp.184.5.386

McElroy, E., Patalay, P., Moltrecht, B., Shevlin, M., Shum, A., Creswell, C., & Waite, P., Dr. (2020, May 8). Demographic and health factors associated with pandemic anxiety in the context of COVID-19. https://doi.org/10.31234/osf.io/2eksd

Merikangas, K. R., He, J., Burstein, M., Swendsen, J., Avenevoli, S., Case, B., … Olfson, M. (2011). Service utilization for lifetime mental disorders in U.S. adolescents: results of the National Comorbidity Survey-Adolescent Supplement (NCS-A). *Journal of the American Academy of Child and Adolescent Psychiatry, 50(1),* 32–45. https://doi.org/10.1016/j.jaac.2010.10.006

Miller, S. D., Duncan, B. L., & Claud, D. A. (2003). The Outcome Rating Scale : *Journal of Brief Therapy, 2(2),* 91–100.

National Institute for Health and Care Excellence (NICE). 2019. Position statement on use of the EQ-5D-5L value set for England (updated October 2019) https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/technology-appraisal-guidance/eq-5d-5l (accessed 30.07.2020)

National Institute for Health and Clinical Excellence (NICE). Guide to the Methods of Technology Appraisal, 2013. https://www.nice.org.uk/process/pmg9/resources/guide-to-the-methods-of-technology-appraisal-2013-pdf-2007975843781 (accessed 30.07.20).

National Institute for Health and Care Excellence (NICE). 2019. Position statement on use of the EQ-5D-5L value set for England (updated October 2019) https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/technology-appraisal-guidance/eq-5d-5l (accessed 30.07.2020)

O'Brien, D., Harvey, K., Young, B., Reardon, T., & Creswell, C. (2017). GPs' Experiences of Children with Anxiety Disorders in Primary Care: a Qualitative Study. *British Journal of General Practice, 67(665),* e888–e898.

Pennant, M. E., Loucas, C. E., Whittington, C., Creswell, C., Fonagy, P., Fuggle, P., ... & Group, E. A. (2015). Computerised therapies for anxiety and depression in children and young people: a systematic review and meta-analysis. *Behaviour research and therapy, 67,* 1-18. doi:10.1016/j.brat.2015.01.009

Personal Social Services Research Unit (PSSRU) Unit costs of health and social care, various years, University of Kent and the London School of Economics and Political Science https://www.pssru.ac.uk/project-pages/unit-costs/ (accessed 03.08.2020)

Reardon, T., Harvey, K., & Creswell, C. (2019). Seeking and accessing professional support for child anxiety in a community sample. *European child & adolescent psychiatry*, 1-16, https://doi.org/10.1007/s00787-019-01388-4

Reardon, T., Harvey, K., Young, B., O'Brien, D., & Creswell, C. (2018). Barriers and facilitators to parents seeking and accessing professional support for anxiety disorders in children: qualitative interview study. *European child & adolescent psychiatry, 27(8),* 1023-1031. Retrieved from https://doi.org/10.1007/s0078

Reardon, T., Hill, C., O'Brien, D., & Creswell, C. (2018). Online treatments for child anxiety: a survey of parent and GP attitudes. Manuscript in Preparation.

Reardon, T., Spence, S. H., Hesse, J., Shakir, A., & Creswell, C. (2018). Identifying children with anxiety disorders using brief versions of the Spence Children's Anxiety Scale for children, parents, and teachers. *Psychological assessment, 30(10),* 1342.

Stevens, K (2012). Valuation of the Child Health Utility 9D Index., *Pharmacoeconomics 30(8),* 729-747.

Thirlwall, K., Cooper, P. J., Karalus, J., Voysey, M., Willetts, L., & Creswell, C. (2013). Treatment of child anxiety disorders via guided parent-delivered cognitive-behavioural therapy: randomised controlled trial. *The British Journal of Psychiatry 203(6),* 436–44. https://doi.org/10.1192/bjp.bp.113.126698

Van Hout B, Janssen M, Feng Y et al. (2012) Interim scoring for the EQ 5D 5L: Mapping the EQ 5D 5L to EQ 5D 3L value sets. *Value in Health, 15:* 708-15.

Yao, S., Zhang, C., Zhu, X., Jing, X., McWhinnie, C. M., & Abela, J. R. Z. (2009). Measuring Adolescent Psychopathology: Psychometric Properties of the Self-Report Strengths and Difficulties Questionnaire in a sample of Chinese adolescents. *Journal of Adolescent Health, 45,* 55–62.

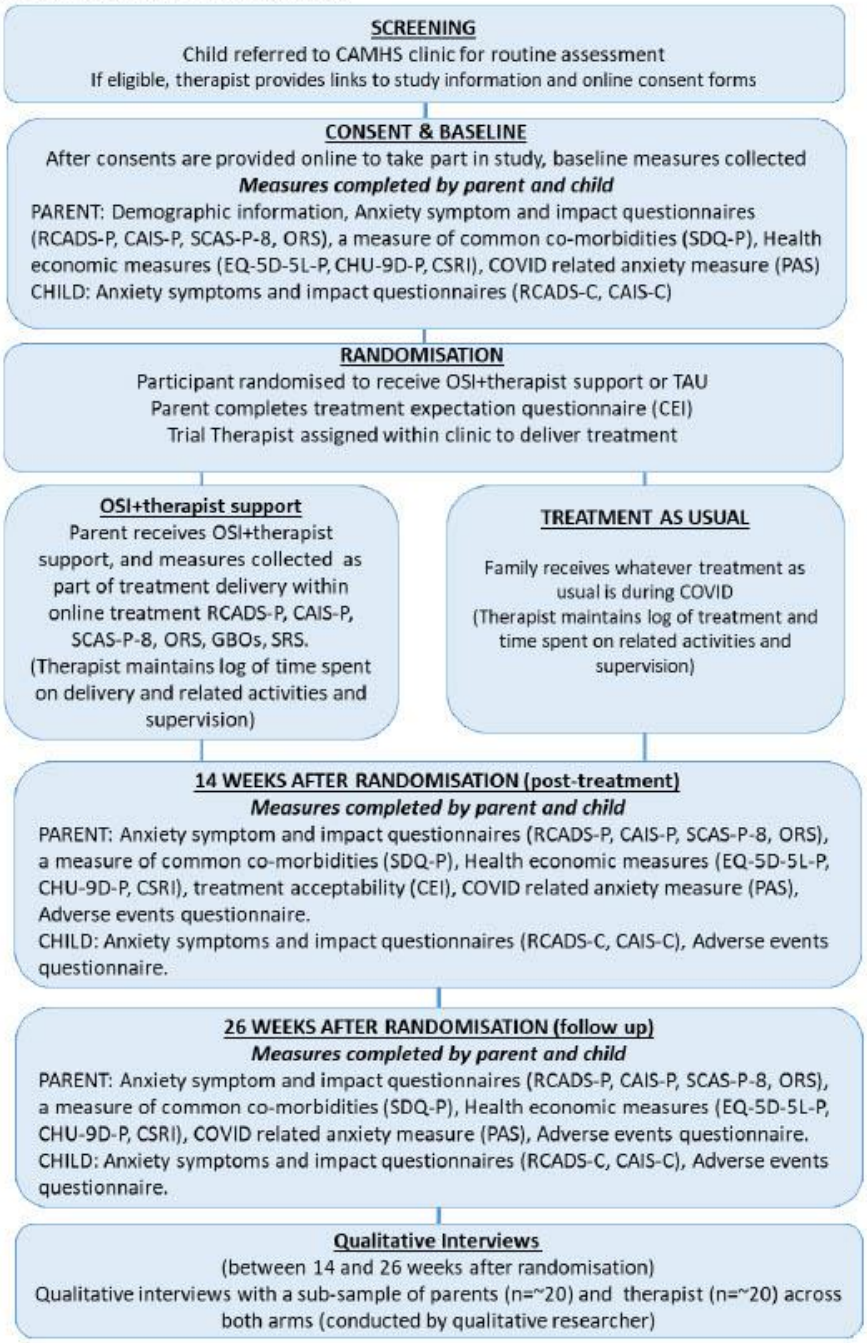
5 APPENDICES

APPENDIX I SPIRIT SCHEDULE OF ENROLMENT, INTERVENTIONS, AND ASSESSMENTS

		Enrolment			Post-allocation		Close-out
			After consent	After randomisation	Treatment	14 weeks after randomisation	26 weeks after randomisation
Timepoint:			**Baseline**			**Post-treatment**	**Follow-up**
ENROLMENT	Eligibility screen	X					
	Informed consent	X					
	Allocation			X			
	Demographic information		X				
INTERVENTIONS	OSI				X		
	C-TAU				X		
ASSESSMENTS							
CHILD REPORT							
Symptom measure	RCADS-C		X			X	X
	CAIS-C		X			X	X
PARENT REPORT							
Symptom measures	RCADS-P		X			X	X
	SCAS-P-8		X			X	X
Functional impairment	CAIS-P		X			X	X
	ORS		X			X	X
Co-morbid problem	SDQ-P		X			X	X
Pandemic Anxiety Scale	PAS		X			X	X
Treatment acceptability	Credibility and Expectation of Improvement scale			X		X	
Health economics	CSRI		X			X	X
	EQ-5D-5L-P		X			X	X
	CHU-9D (YP proxy)		X			X	X

		Enrolment			Post-allocation		Close-out
			After consent	After randomisation	Treatment	14 weeks after randomisation	26 weeks after randomisation
Timepoint:			**Baseline**			**Post-treatment**	**Follow-up**
OSI + therapist support arm only Measures collected during treatment (parent only)	RCADS-P				X		
	SCAS-P-8				X		
	CAIS-P				X		
	ORS				X		
	SRS				X		
	GBOs				X		
Qualitative interviews						X (subgroup of participants interviewed once each between 14 and 26 weeks)	X (subgroup of participants interviewed once each between 14 and 26 weeks)
Therapist Logs					X	X	X

APPENDIX II FLOWCHART OF TRIAL PROCEDURES



APPENDIX III OBJECTIVES AND OUTCOME MEASURES

Objectives	Outcome Measures	Timepoint(s) of evaluation of this outcome measure (if applicable)
Primary Objective To evaluate the parent-reported clinical effectiveness of a brief parent-led cognitive behavioural treatment (CBT) delivered by the OSI platform with therapist support (OSI + therapist support) for the treatment of child anxiety compared to 'COVID-19 treatment as usual' (C-TAU) in CAMHS throughout the next phases of the COVID-19 pandemic.	The Child Anxiety Impact Scale-parent report (CAIS-P) captures the degree to which anxiety interfering in the child and family's life.	26 weeks post-randomisation
Secondary Objectives **(1)** Further assessment of the clinical effectiveness of OSI + therapist support for the treatment of child anxiety compared to 'COVID-19 treatment as usual' (C-TAU) in CAMHS throughout the next phases of the COVID-19 pandemic.	Secondary clinical outcomes: Child reported anxiety interference (CAIS-C) Child reported anxiety symptoms (RCADS-C) Parent report on child's anxiety symptoms (RCADS-P, SCAS-P-8), overall functioning (ORS), COVID-19 specific worries, and common comorbid emotional and behavioural problems (SDQ-P).	 14 weeks post-randomisation 26 weeks post-randomisation
(2) Evaluate the cost-effectiveness of OSI + therapist support for the treatment of child anxiety compared to 'COVID-19 treatment as usual' (C-TAU) in CAMHS	Economic outcomes: Parent quality of life (EQ-5D-5L, parent-self report); and child quality of life (CHU-9D proxy version, i.e. parent-report on child). School attendance (actual school attendance as a percentage of expected school attendance) Therapist logs of time spend on treatment delivery	 14 weeks post-randomisation 26 weeks post-randomisation

Objectives	Outcome Measures	Timepoint(s) of evaluation of this outcome measure (if applicable)
Exploratory Objectives **(1)** Explore the trajectory of change reported within the OSI arm	Measures used to monitor child outcomes built in to OSI (RCADS-P, CAIS-P, SCAS-P-8; ORS; SRS; GBOs)	Weeks 1-7 of OSI treatment
(2) Understand therapist and parents' experiences of treating child anxiety in the current context to maximise learning to (a) enable rapid implementation of remote treatment delivery in CAMHS in any subsequent periods of social distancing, and (b) maintain the use of online interventions (such as OSI) in CAMHS when 'normal services' resumes.	Qualitative interviews with parents and therapists Therapist experience of treatment questionnaire	14-26 weeks post randomisation End of treatment phase

APPENDIX IV POST-HOC WITHIN-GROUP EFFECT SIZES FOR THE PRIMARY AND SECONDARY ANALYSES

TABLE 12 ADJUSTED AND STANDARDISED WITHIN-GROUP MEAN DIFFERENCES, AND THE P-VALUES FOR THE PRIMARY AND SECONDARY ANALYSES

	OSI + Therapist Support (N=222)			COVID-19 Treatment as Usual (N=221)		
	Adjusted Within-Group Mean Difference [95% CI]	Standardised Within-Group Mean Difference [95% CI]	P-value	Adjusted Within-Group Mean Difference [95% CI]	Standardised Within-Group Mean Difference [95% CI]	P-value
PRIMARY ANALYSIS						
Child Anxiety Impact Scale – Parent Version (CAIS-P)						
CAIS-P: Total Score						
14 weeks	-6·42 [-8·06 to -4·77]	-0·42 [-0·53 to -0·31]	<0·0001	-6·13 [-7·86 to -4·40]	-0·42 [-0·54 to -0·30]	<0·0001
26 weeks*	-8·30 [-9·95 to -6·64]	-0·54 [-0·65 to -0·43]	<0·0001	-7·98 [-9·78 to -6·17]	-0·55 [-0·67 to -0·42]	<0·0001
SECONDARY ANALYSES						
CAIS-P: Global Items						
14 weeks	-1·99 [-2·35 to -1·62]	-0·66 [-0·78 to -0·54]	<0·0001	-1·70 [-2·08 to -1·32]	-0·58 [-0·71 to -0·45]	<0·0001
26 weeks	-2·50 [-2·87 to -2·13]	-0·83 [-0·96 to -0·71]	<0·0001	-2·30 [-2·70 to -1·91]	-0·78 [-0·91 to -0·65]	<0·0001
Child Anxiety Impact Scale – Child Version (CAIS-C)						
CAIS-C: Total Score						
14 weeks	-5·79 [-7·90 to -3·68]	-0·40 [-0·55 to -0·25]	<0·0001	-4·37 [-6·57 to -2·17]	-0·29 [-0·44 to -0·14]	<0·0001
26 weeks	-8·20 [-10·33 to -6·07]	-0·57 [-0·72 to -0·42]	<0·0001	-5·80 [-8·02 to -3·58]	-0·39 [-0·53 to -0·24]	<0·0001
CAIS-C: Global Items						
14 weeks	-1·43 [-1·89 to -0·98]	-0·50 [-0·66 to -0·34]	<0·0001	-1·09 [-1·56 to -0·62]	-0·34 [-0·49 to -0·19]	<0·0001
26 weeks	-1·45 [-1·91 to -0·99]	-0·51 [-0·67 to -0·35]	<0·0001	-1·77 [-2·25 to -1·30]	-0·56 [-0·71 to -0·41]	<0·0001
Revised Child Anxiety and Depression Scale – Parent Version (RCADS-P)						
RCADS-P: Total Anxiety Score						
14 weeks	-11·38 [-13·55 to -9·20]	-0·57 [-0·68 to -0·46]	<0·0001	-9·24 [-11·53 to -6·95]	-0·46 [-0·58 to -0·35]	<0·0001
26 weeks	-15·23 [-17·42 to -13·03]	-0·77 [-0·88 to -0·66]	<0·0001	-14·01 [-16·39 to -11·63]	-0·70 [-0·82 to -0·58]	<0·0001

	OSI + Therapist Support (N=222)			COVID-19 Treatment as Usual (N=221)		
	Adjusted Within-Group Mean Difference [95% CI]	Standardised Within-Group Mean Difference [95% CI]	P-value	Adjusted Within-Group Mean Difference [95% CI]	Standardised Within-Group Mean Difference [95% CI]	P-value
RCADS-P: Total Anxiety and Depression Score						
14 weeks	-13·78 [-16·38 to -11·18]	-0·58 [-0·69 to -0·47]	<0·0001	-11·56 [-14·30 to -8·82]	-0·48 [-0·59 to -0·37]	<0·0001
26 weeks	-18·06 [-20·69 to -15·44]	-0·76 [-0·87 to -0·65]	<0·0001	-17·18 [-20·03 to -14·34]	-0·71 [-0·83 to -0·59]	<0·0001
Revised Child Anxiety and Depression Scale – Child Version (RCADS-C)						
RCADS-C: Total Anxiety Score						
14 weeks	-14·67 [-17·56 to -11·78]	-0·75 [-0·89 to -0·60]	<0·0001	-13·14 [-16·17 to -10·11]	-0·66 [-0·81 to -0·51]	<0·0001
26 weeks	-16·15 [-19·08 to -13·23]	-0·82 [-0·97 to -0·67]	<0·0001	-17·00 [-20·03 to -13·96]	-0·85 [-1·00 to -0·70]	<0·0001
RCADS-C: Total Anxiety and Depression Score						
14 weeks	-17·68 [-21·13 to -14·22]	-0·75 [-0·90 to -0·60]	<0·0001	-16·33 [-19·95 to -12·72]	-0·68 [-0·83 to -0·53]	<0·0001
26 weeks	-19·34 [-22·84 to -15·84]	-0·82 [-0·97 to -0·67]	<0·0001	-20·95 [-24·58 to -17·32]	-0·87 [-1·02 to -0·72]	<0·0001
Brief Spence Children's Anxiety Scale – Parent Version (SCAS-P-8)						
SCAS-P-8: Total Score						
14 weeks	-2·81 [-3·38 to -2·24]	-0·59 [-0·71 to -0·47]	<0·0001	-2·42 [-3·02 to -1·82]	-0·50 [-0·62 to -0·37]	<0·0001
26 weeks	-3·80 [-4·37 to -3·22]	-0·79 [-0·91 to -0·67]	<0·0001	-3·55 [-4·17 to -2·92]	-0·73 [-0·85 to -0·60]	<0·0001
Overall Functioning (Outcome Rating Scale (ORS))						
ORS: Individually (Personal well-being)						
14 weeks	0·97 [0·65 to 1·29]	0·40 [0·27 to 0·54]	<0·0001	0·83 [0·49 to 1·16]	0·36 [0·22 to 0·51]	<0·0001
26 weeks	1·15 [0·82 to 1·48]	0·48 [0·34 to 0·62]	<0·0001	1·16 [0·81 to 1·51]	0·51 [0·35 to 0·66]	<0·0001
ORS: Interpersonally (Family, close relationships)						
14 weeks	0·30 [-0·00 to 0·59]	0·13 [-0·00 to 0·26]	0·051	0·54 [0·23 to 0·85]	0·25 [0·11 to 0·40]	0·00071
26 weeks	0·54 [0·23 to 0·84]	0·24 [0·10 to 0·37]	0·00049	0·49 [0·17 to 0·81]	0·23 [0·08 to 0·38]	0·0031
ORS: Socially (Work, school, friendships)						
14 weeks	1·03 [0·67 to 1·38]	0·39 [0·25 to 0·53]	<0·0001	1·00 [0·63 to 1·37]	0·39 [0·24 to 0·54]	<0·0001
26 weeks	1·38 [1·02 to 1·74]	0·52 [0·39 to 0·66]	<0·0001	1·21 [0·82 to 1·60]	0·47 [0·32 to 0·62]	<0·0001

	OSI + Therapist Support (N=222)			COVID-19 Treatment as Usual (N=221)		
	Adjusted Within-Group Mean Difference [95% CI]	Standardised Within-Group Mean Difference [95% CI]	P-value	Adjusted Within-Group Mean Difference [95% CI]	Standardised Within-Group Mean Difference [95% CI]	P-value
ORS: Overall (General sense of well-being)						
14 weeks	1·00 [0·70 to 1·30]	0·43 [0·30 to 0·56]	<0·0001	0·88 [0·57 to 1·20]	0·39 [0·25 to 0·53]	<0·0001
26 weeks	1·37 [1·07 to 1·67]	0·59 [0·46 to 0·72]	<0·0001	1·14 [0·82 to 1·47]	0·51 [0·36 to 0·65]	<0·0001
ORS: Total Score						
14 weeks	3·30 [2·28 to 4·31]	0·40 [0·28 to 0·53]	<0·0001	3·23 [2·17 to 4·29]	0·42 [0·28 to 0·55]	<0·0001
26 weeks	4·44 [3·41 to 5·47]	0·55 [0·42 to 0·67]	<0·0001	3·98 [2·87 to 5·08]	0·51 [0·37 to 0·65]	<0·0001
Common Comorbid Emotional and Behavioural Problems (Strengths and Difficulties Questionnaire (SDQ-P)						
SDQ-P: Emotional Symptoms						
14 weeks	-1·35 [-1·68 to -1·01]	-0·59 [-0·73 to -0·44]	<0·0001	-1·35 [-1·70 to -1·00]	-0·56 [-0·71 to -0·42]	<0·0001
26 weeks	-2·01 [-2·35 to -1·68]	-0·88 [-1·02 to -0·73]	<0·0001	-1·68 [-2·05 to -1·32]	-0·70 [-0·85 to -0·55]	<0·0001
SDQ-P: Conduct Problems						
14 weeks	-0·29 [-0·50 to -0·09]	-0·14 [-0·24 to -0·04]	0·0051	-0·26 [-0·48 to -0·04]	-0·13 [-0·24 to -0·02]	0·019
26 weeks	-0·42 [-0·63 to -0·21]	-0·20 [-0·30 to -0·10]	<0·0001	-0·36 [-0·59 to -0·13]	-0·18 [-0·29 to -0·07]	0·0018
SDQ-P: Hyperactivity/Inattention						
14 weeks	-0·67 [-0·95 to -0·39]	-0·23 [-0·33 to -0·14]	<0·0001	-0·62 [-0·92 to -0·33]	-0·23 [-0·33 to -0·12]	<0·0001
26 weeks	-0·67 [-0·96 to -0·39]	-0·23 [-0·33 to -0·13]	<0·0001	-0·69 [-1·00 to -0·38]	-0·25 [-0·36 to -0·14]	<0·0001
SDQ-P: Peer Relationship Problems						
14 weeks	-0·19 [-0·41 to 0·03]	-0·08 [-0·18 to 0·01]	0·093	-0·36 [-0·60 to -0·13]	-0·17 [-0·28 to -0·06]	0·0023
26 weeks	-0·25 [-0·48 to -0·02]	-0·11 [-0·20 to -0·01]	0·03	-0·31 [-0·56 to -0·07]	-0·15 [-0·26 to -0·03]	0·012
SDQ-P: Prosocial Behavioural						
14 weeks	0·05 [-0·18 to 0·27]	0·02 [-0·08 to 0·12]	0·70	0·08 [-0·16 to 0·32]	0·03 [-0·07 to 0·14]	0·53
26 weeks	0·04 [-0·19 to 0·27]	0·02 [-0·08 to 0·12]	0·75	0·19 [-0·06 to 0·44]	0·09 [-0·03 to 0·20]	0·13
SDQ-P: Total Score						
14 weeks	-2·52 [-3·18 to -1·86]	-0·36 [-0·45 to -0·26]	<0·0001	-2·55 [-3·25 to -1·85]	-0·39 [-0·50 to -0·28]	<0·0001
26 weeks	-3·38 [-4·05 to -2·70]	-0·48 [-0·57 to -0·38]	<0·0001	-3·03 [-3·76 to -2·30]	-0·46 [-0·58 to -0·35]	<0·0001

	OSI + Therapist Support (N=222)			COVID-19 Treatment as Usual (N=221)		
	Adjusted Within-Group Mean Difference [95% CI]	Standardised Within-Group Mean Difference [95% CI]	P-value	Adjusted Within-Group Mean Difference [95% CI]	Standardised Within-Group Mean Difference [95% CI]	P-value
COVID-19 Specific Worries (Pandemic Anxiety Scale (PAS))						
PAS: Disease Anxiety						
14 weeks	-1·10 [-1·57 to -0·63]	-0·28 [-0·40 to -0·16]	<0·0001	-1·17 [-1·66 to -0·67]	-0·29 [-0·41 to -0·17]	<0·0001
26 weeks	-1·57 [-2·05 to -1·09]	-0·40 [-0·52 to -0·28]	<0·0001	-1·49 [-2·00 to -0·97]	-0·37 [-0·50 to -0·24]	<0·0001
PAS: Consequence Anxiety						
14 weeks	-0·17 [-0·55 to 0·21]	-0·07 [-0·23 to 0·09]	0·39	-0·27 [-0·67 to 0·12]	-0·10 [-0·24 to 0·04]	0·18
26 weeks	-0·38 [-0·77 to 0·00]	-0·16 [-0·32 to 0·00]	0·05	-0·23 [-0·64 to 0·18]	-0·08 [-0·23 to 0·07]	0·28
PAS: Total Score						
14 weeks	-0·17 [-0·55 to 0·21]	-0·01 [-0·04 to 0·01]	0·39	-0·27 [-0·67 to 0·12]	-0·02 [-0·05 to 0·01]	0·18
26 weeks	-0·38 [-0·77 to 0·00]	-0·03 [-0·05 to 0·00]	0·05	-0·23 [-0·64 to 0·18]	-0·02 [-0·04 to 0·01]	0·28

Generalised linear mixed effects model adjusted for randomised arm, assessment time point, minimisation variables (child's age, gender, baseline anxiety associated interference, service type), an interaction between randomised arm and assessment timepoint as fixed effects, and a random intercept for each participant. ²Primary outcome. Level of statistical significance = 0·05

APPENDIX V HISTOGRAMS OF THE PRIMARY AND SECONDARY OUTCOMES BY RANDOMISED ARM AT EACH ASSESSMENT TIME POINT AND POST ESTIMATE PLOTS OF THE MODEL RESIDUALS FROM THE MIXED GENERALISED LINEAR MODELS

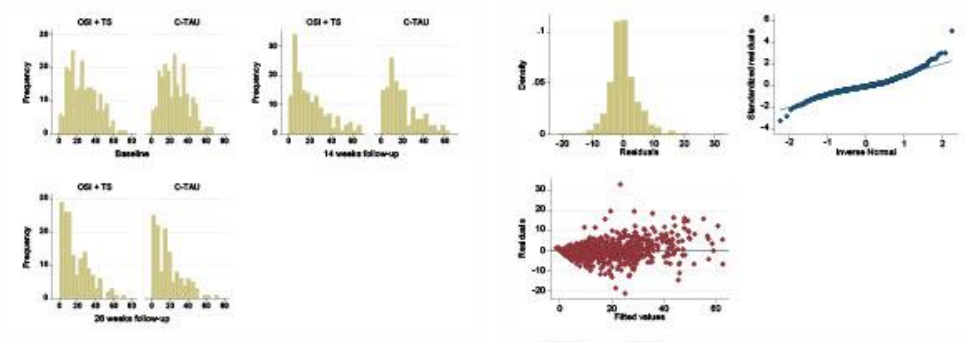


FIGURE 9 HISTOGRAMS AND MODEL RESIDUALS FOR THE TOTAL SCORE OF THE CHILD ANXIETY IMPACT SCALE – PARENT VERSION (CAIS-P)

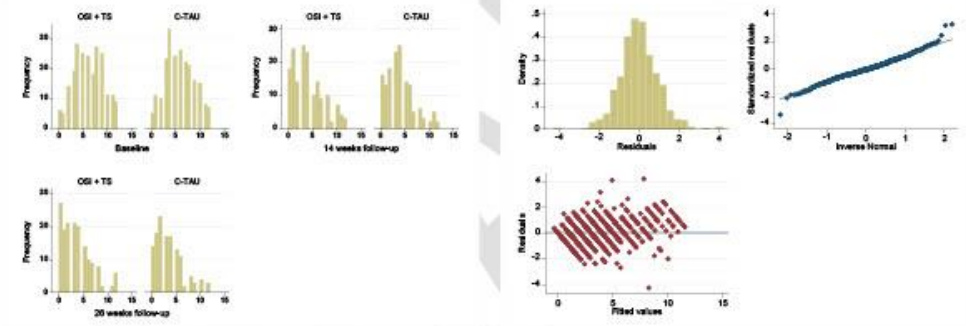


FIGURE 10 HISTOGRAMS AND MODEL RESIDUALS FOR THE GLOBAL ITEMS OF THE CHILD ANXIETY IMPACE SCALE – PARENT VERSION (CAIS-P)

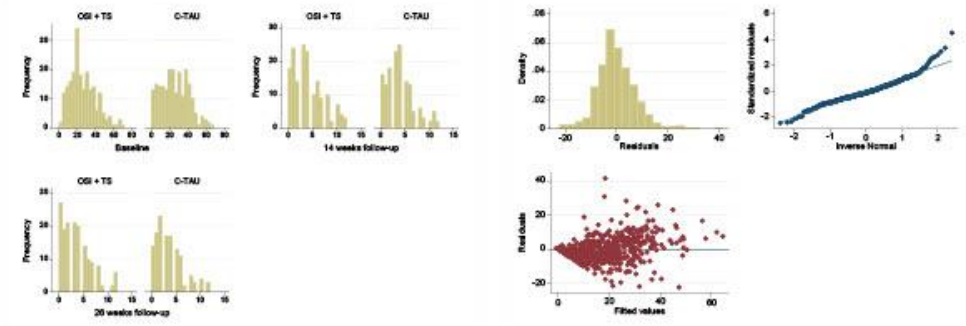


FIGURE 11 HISTOGRAMS AND MODEL RESIDUALS FOR THE TOTAL SCORE OF THE CHILD ANXIETY IMPACT SCALE – CHILD VERSION (CAIS-C)

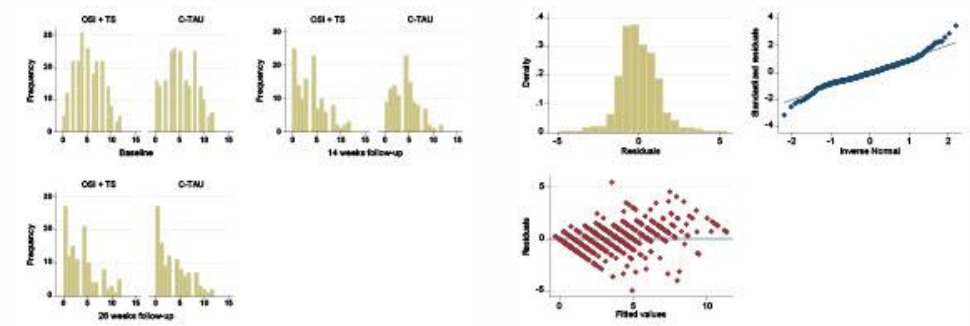


FIGURE 12 HISTOGRAMS AND MODEL RESIDUALS FOR THE GLOBAL ITEMS OF THE CHILD ANXIETY IMPACT SCALE – CHILD VERSION (CAIS-C)

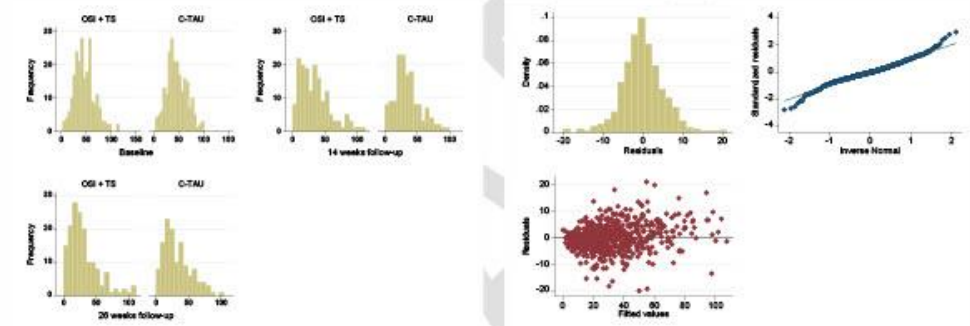


FIGURE 13 HISTOGRAMS AND MODEL RESIDUALS FOR THE TOTAL ANXIETY SCORE OF THE REVISED CHILD ANXIETY AND DEPRESSION SCALE – PARENT VERSION (RCADS-P)

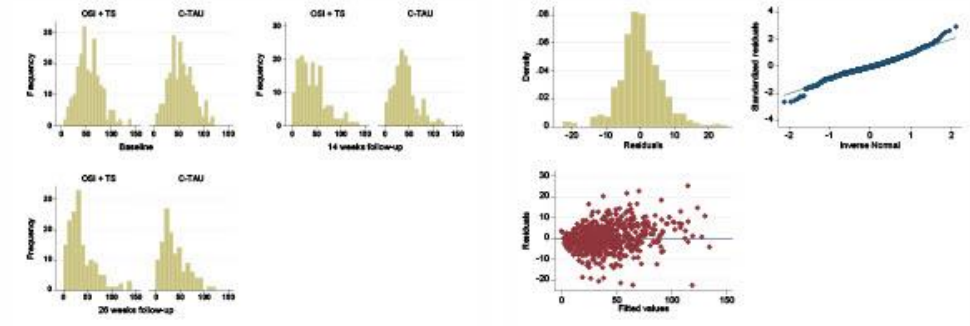


FIGURE 14 HISTOGRAMS AND MODEL RESIDUALS FOR THE TOTAL ANXIETY AND DEPRESSION SCORE OF THE REVISED CHILD ANXIETY AND DEPRESSION SCALE – PARENT VERSION (RCADS-P)

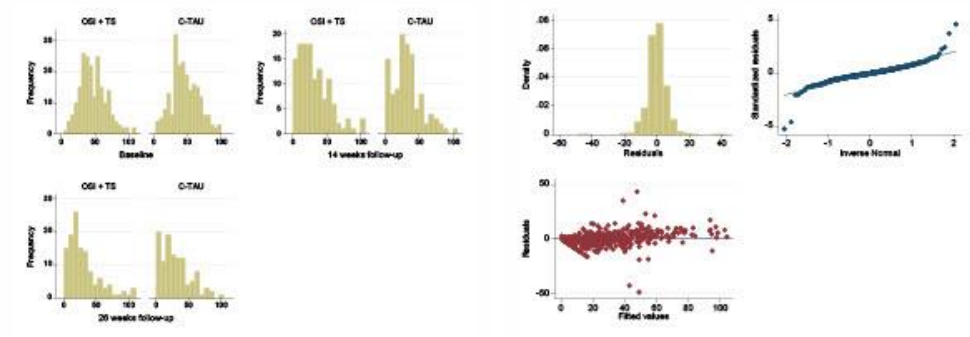


FIGURE 15 HISTOGRAMS AND MODEL RESIDUALS FOR THE TOTAL ANXIETY SCORE OF THE REVISED CHILD ANXIETY AND DEPRESSION SCALE – CHILD VERSION (RCADS-C)

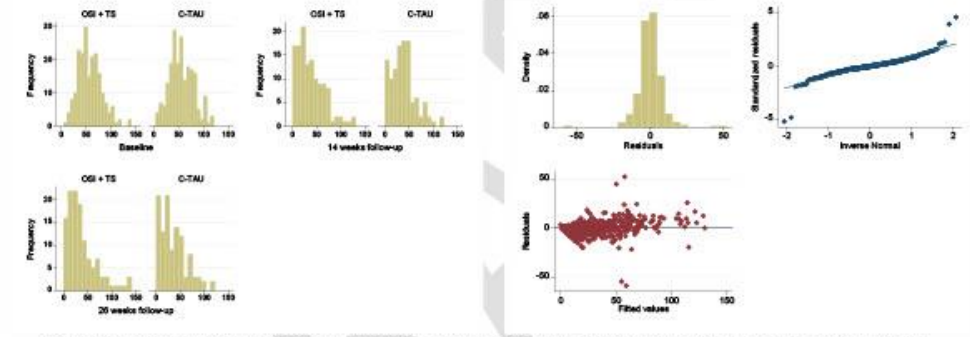


FIGURE 16 HISTOGRAMS AND MODEL RESIDUALS FOR THE TOTAL ANXIETY AND DEPRESSION SCORE OF THE REVISED CHILD ANXIETY AND DEPRESSION SCALE – CHILD VERSION (RCADS-C)

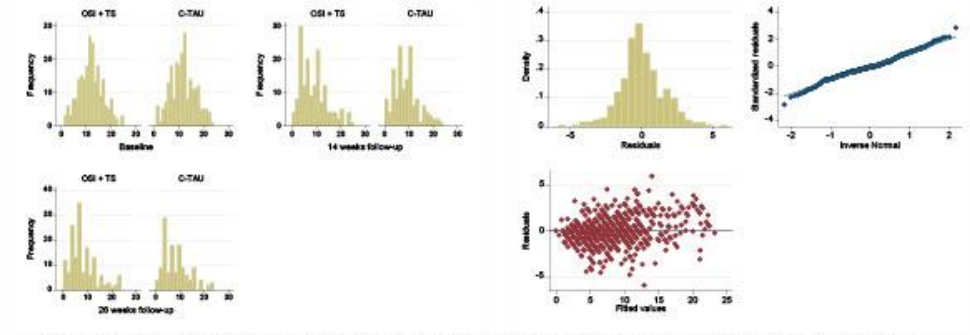


FIGURE 17 HISTOGRAMS AND MODEL RESIDUALS FOR THE TOTAL SCORE OF THE BRIEF SPENCE CHILDREN'S ANXIETY SCALE – PARENT VERSION (SCAS-P-8)

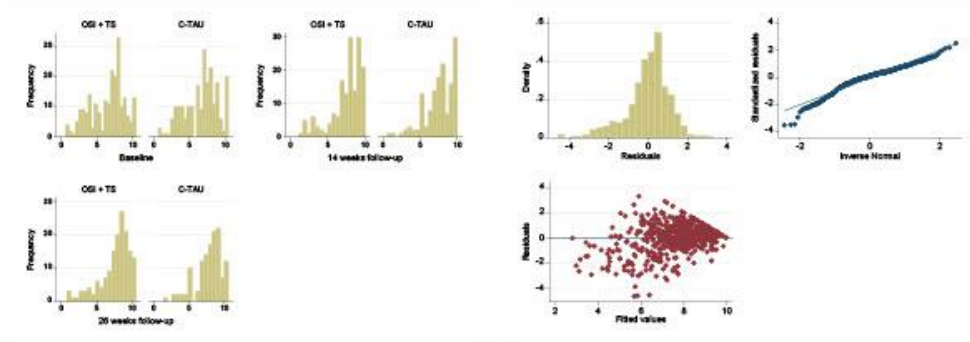


FIGURE 18 HISTOGRAMS AND MODEL RESIDUALS FOR THE INDIVIDUALLY SECTION OF THE OUTCOME RATING SCALE (ORS)

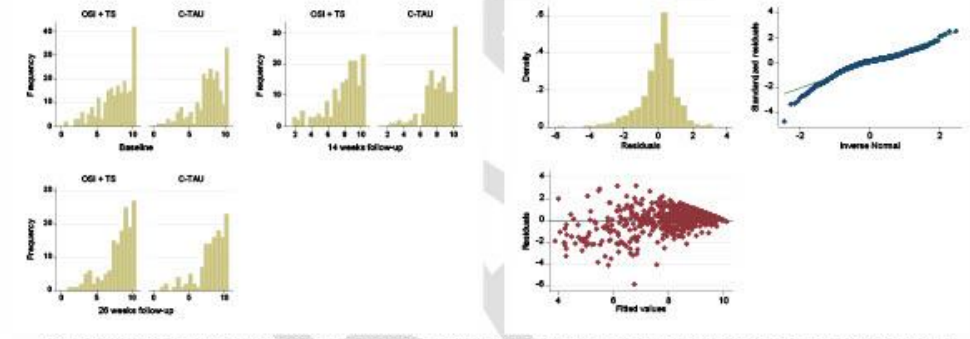


FIGURE 19 HISTOGRAMS AND MODEL RESIDUALS FOR THE INTERPERSONALLY SECTION OF THE OUTCOME RATING SCALE (ORS)

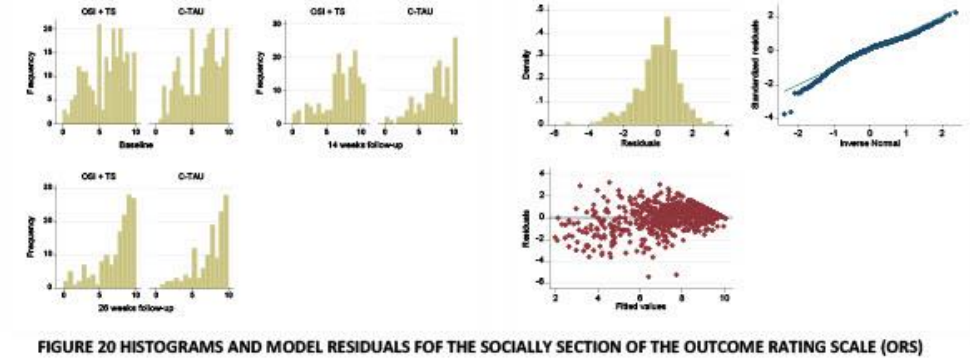


FIGURE 20 HISTOGRAMS AND MODEL RESIDUALS FOF THE SOCIALLY SECTION OF THE OUTCOME RATING SCALE (ORS)

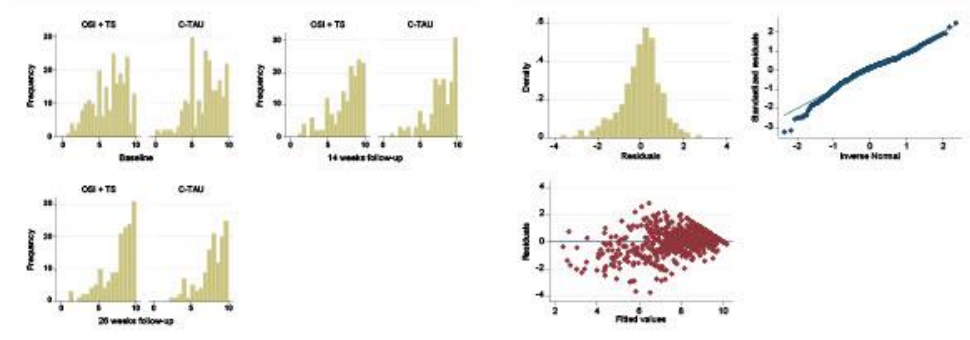


FIGURE 21 HISTOGRAMS AND MODEL RESIDUALS FOR THE OVERALL SECTION OF THE OUTCOME RATING SCALE (ORS)

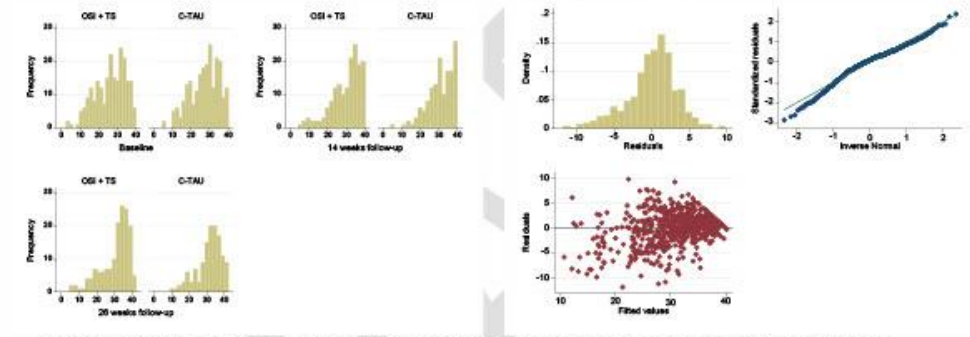


FIGURE 22 HISTOGRAMS AND MODEL RESIDUALS FOR THE TOTAL SCORE OF THE OUTCOME RATING SCALE (ORS)

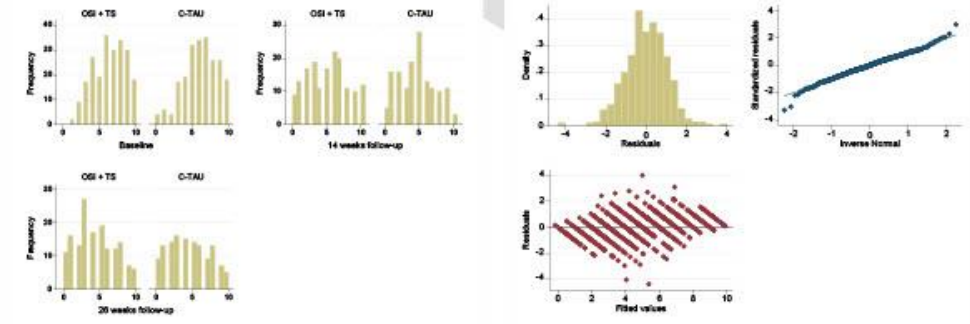


FIGURE 23 HISTOGRAMS AND MODEL RESIDUALS FOR THE EMOTIONAL SYMPTOMS SECTION OF THE STRENGTHS AND DIFFICULTIES QUESTIONNAIRE (SDQ-P)

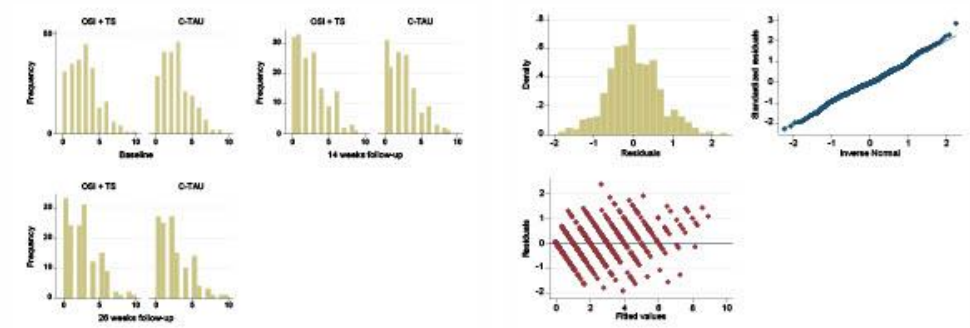


FIGURE 24 HISTOGRAMS AND MODEL RESIDUALS FOR THE CONDUCT PROBLEMS SECTION OF THE STRENGTHS AND DIFFICULTIES QUESTIONNAIRE (SDQ-P)

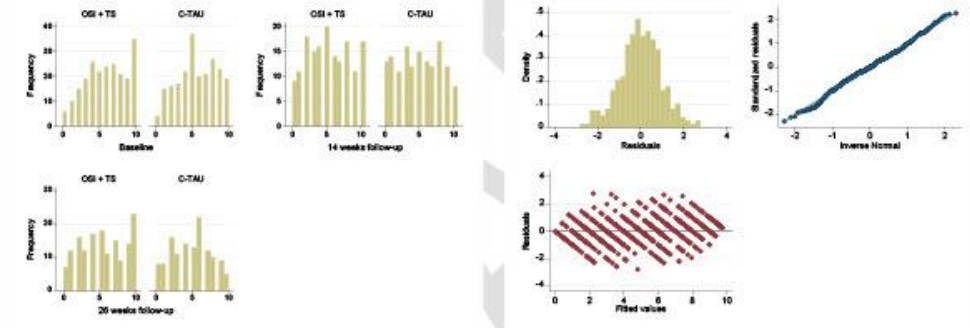


FIGURE 25 HISTOGRAMS AND MODEL RESIDUALS FOR THE HYPERACTIVITY/INATTENTION SECTION OF THE STRENGTHS AND DIFFICULTIES QUESTIONNAIRE (SDQ-P)

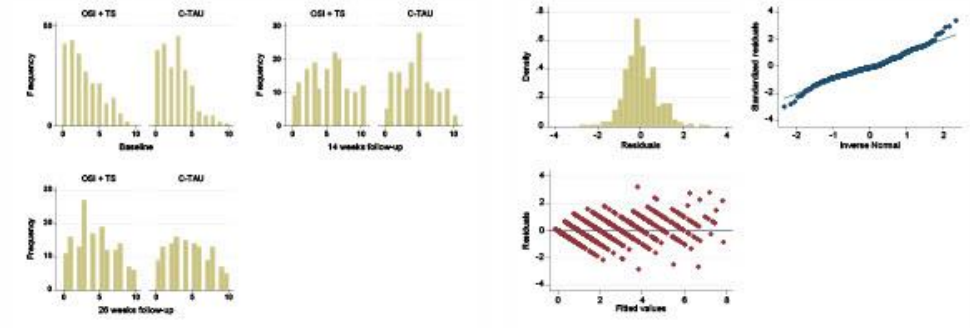


FIGURE 26 HISTOGRAMS AND MODEL RESIDUALS FOR THE PEER RELATIONSHIP PROBLEMS SECTION OF THE STRENGTHS AND DIFFICULTIES QUESTIONNAIRE (SDQ-P)

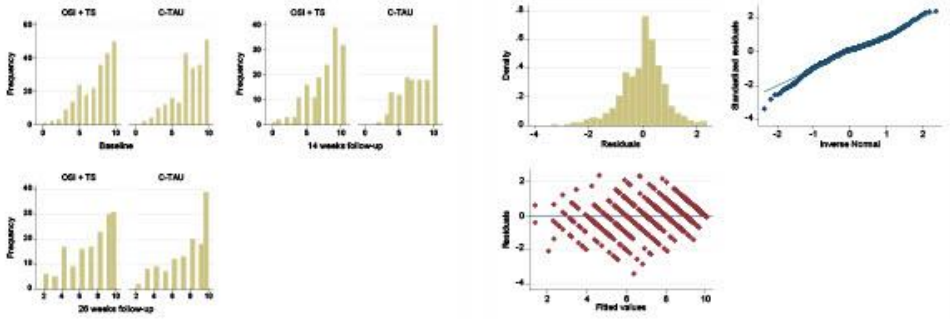


FIGURE 27 HISTOGRAMS AND MODEL RESIDUALS FOR THE PROSOCIAL BEHAVIOUR SECTION OF THE STRENGTHS AND DIFFICULTIES QUESTIONNAIRE (SDQ-P)

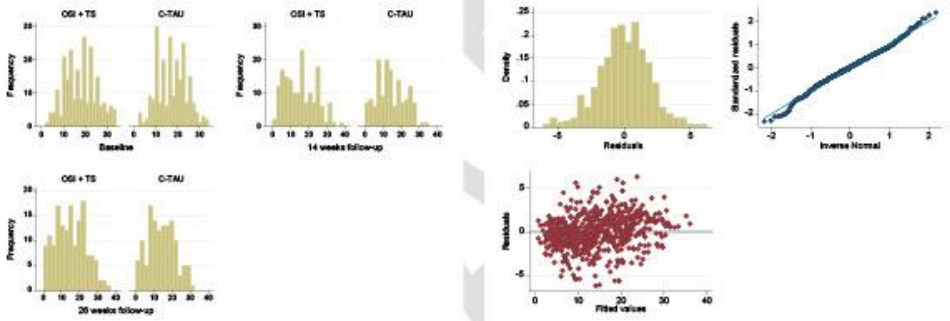


FIGURE 28 HISTOGRAMS AND MODEL RESIDUALS FOR THE TOTAL SCORE OF THE STRENGTHS AND DIFFICULTIES QUESTIONNAIRE (SDQ-P)

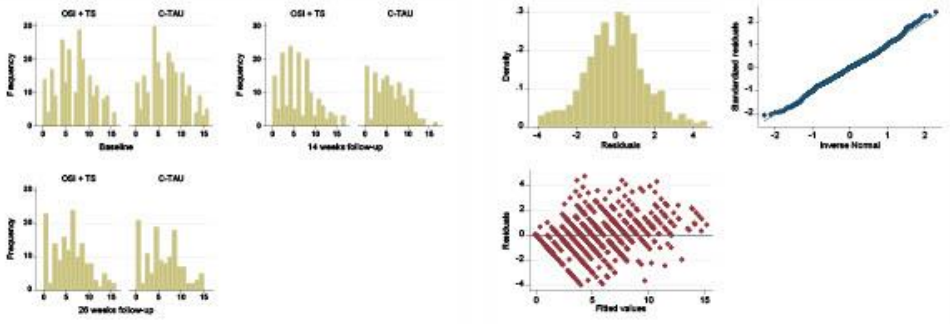


FIGURE 29 HISTOGRAMS AND MODEL RESIDUALS FOR THE DISEASE ANXIETY SECTION OF THE PANDEMIC ANXIETY SCALE (PAS)

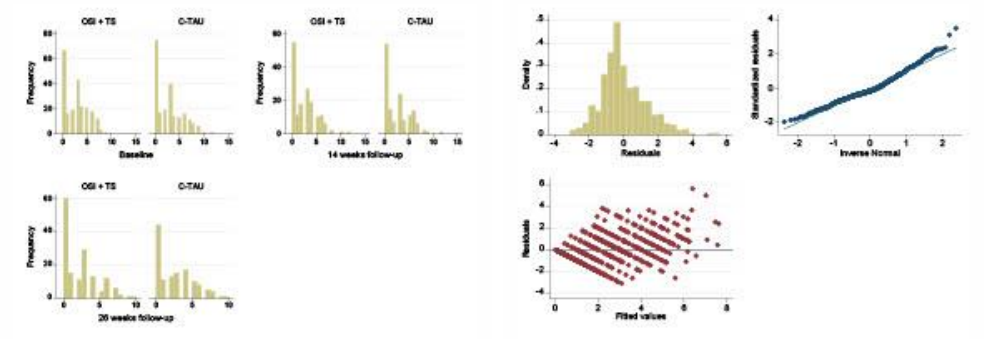


FIGURE 30 HISTOGRAMS AND MODEL RESIDUALS FOR THE CONSEQUENCE ANXIETY SECTION OF THE PANDEMIC ANXIETY SCALE (PAS)

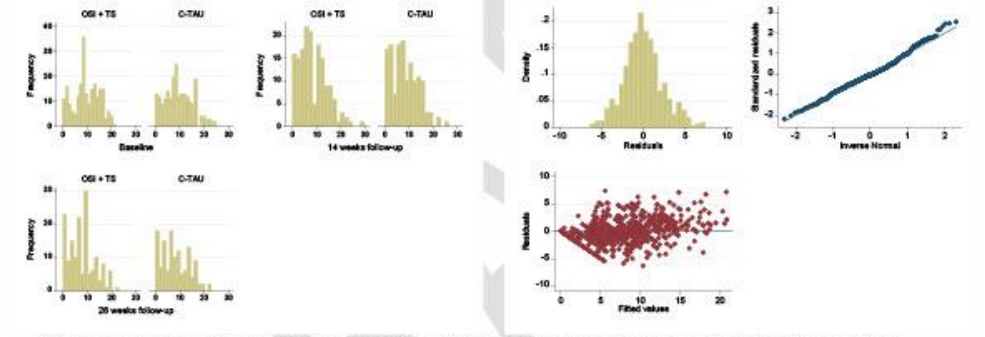


FIGURE 31 HISTOGRAMS AND MODEL RESIDUALS FOR THE TOTAL SCORE OF THE PANDEMIC ANXIETY SCALE (PAS)

APPENDIX VI HISTOGRAMS OF THE EXPLORATORY OUTCOMES

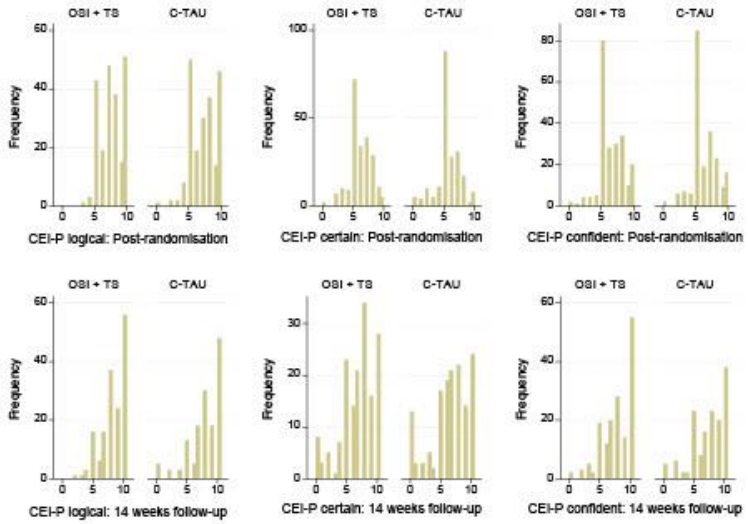


FIGURE 32 HISTOGRAMS FOR THE CREDIBILITY AND EXPECTATION OF IMPROVEMENT SCALE – PARENT VERSION (CEI-P) BY ITEM

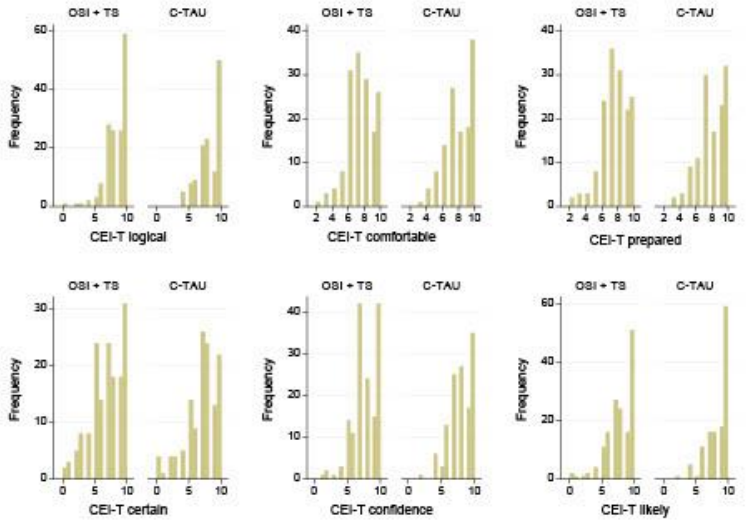


FIGURE 33 HISTOGRAMS FOR THE CREDIBILITY AND EXPECTATION OF IMPORVEMENT SCALE – THERAPIST VERSION (CEI-T) BY ITEM

APPENDIX VII HISTOGRAMS BY RANDOMISED ARM AT EACH ASSESSMENT TIME POINT AND POST ESTIMATE PLOTS OF THE MODEL RESIDUALS FROM THE MIXED GENERALISED LINEAR MODELS FOR THE SENSITIVITY ANALYSES

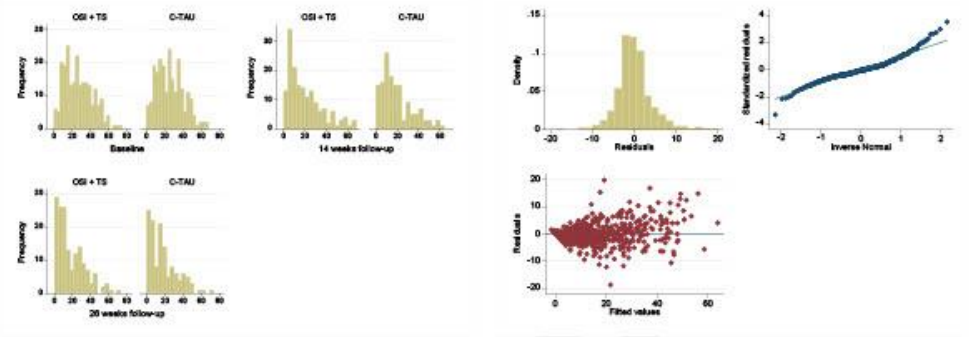


FIGURE 34 HISTOGRAMS AND MODEL RESIDUALS FOR THE SENSITIVITY ANALYSIS INCLUDING FACTORS FOUND TO BE PREDICTIVE OF MISSINGNESS IN THE MODEL

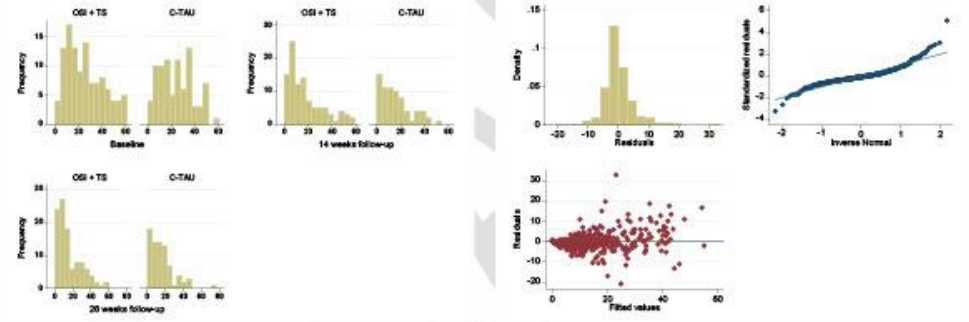


FIGURE 35 HISTOGRAMS AND MODEL RESIDUALS FOR THE SENSITIVITY ANALYSIS BASED ON THE PER-PROTOCOL POPULATION

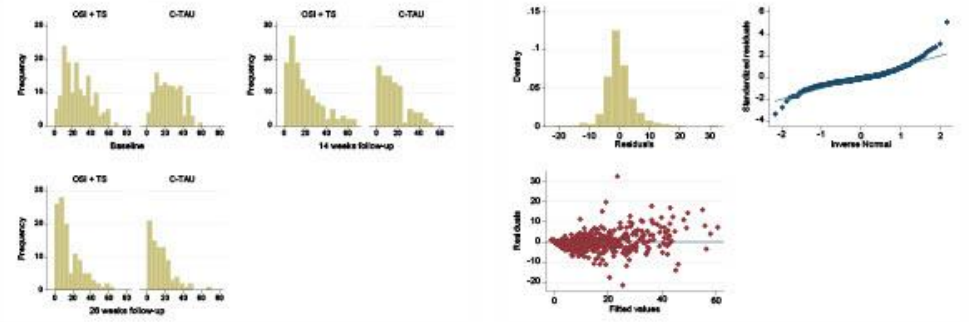


FIGURE 36 HISTOGRAMS AND MODEL RESIDUALS FOR THE SENSITIVITY ANALYSIS BASED ON THE ADDITIONAL PER-PROTOCOL POPULATION

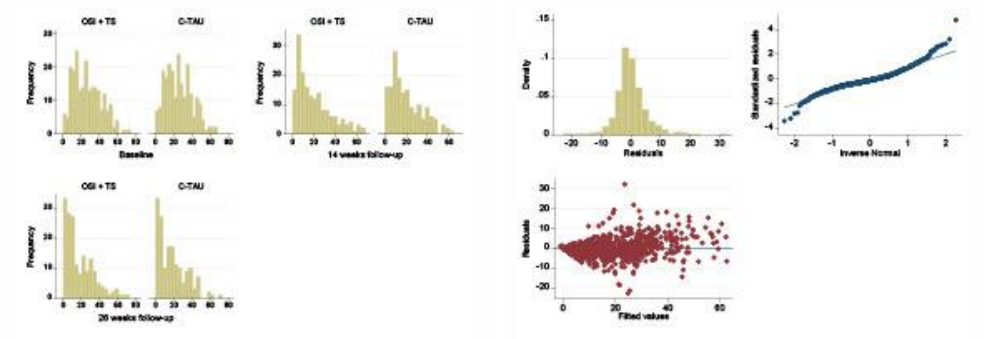


FIGURE 37 HISTOGRAMS AND MODEL RESIDUALS FOR THE SENSITIVITY ANALYSIS INCLUDING ALL OUCOMES REGARDLESS OF THE LENGTH OF TIME ELAPSED FROM EITHER 14- OR 26 WEEKS

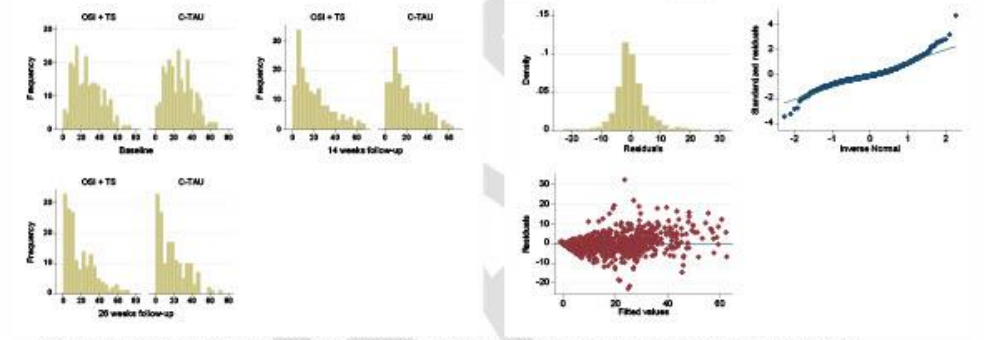


FIGURE 38 HISTOGRAMS AND MODEL RESIDUALS FOR THE SENSITIVITY ANALYSIS INCLUDING ALL OUTCOMES SUBSTITUTING MISSING 26 WEEK OUTCOME WITH 14 WEEK OUTCOME IF IT HAS BEEN COLLECTED WITHIN 26±4 WEEKS

END OF REPORT

Supplementary Materials S11

Summary of primary and sensitivity clinical analyses

	OSI + TS (N=222)	C-TAU (N=221)	Adjusted Mean Difference [95% CI]	Standardised Mean Difference [95% CI]	P-value for non-inferiority
Primary Analysis					
Baseline	26·87 (15·26) [222]	25·96 (14·63) [221]	-	-	-
14 weeks	19·64 (16·00) [163]	18·89 (14·52) [145]	0·00 [-2·34 to 2·34]	0·00 [-0·16 to 0·16]	<0·0001
26 weeks	**17·99 (15·39) [159]**	**18·08 (15·08) [130]**	**0·14 [-2·26 to 2·53]**	**0·01 [-0·15 to 0·17]**	**<0·0001**
Multiple Imputation					
Baseline	26·87 (15·26) [222]	25·96 (14·63) [221]	-	-	-
14 weeks	20·44 (15·19) [222]	19·84 (13·69) [221]	-0·05 [-1·78 to 1·68]	0·00 [-0·12 to 0·11]	<0·0001
26 weeks	**18·58 (14·93) [222]**	**17·81 (13·55) [221]**	**0·13 [-1.60 to 0·12]**	**0·01 [-0·11 to 0·12]**	**<0.0001**
Best Case (missing values = 0)					
Baseline	26·87 (15·26) [222]	25·96 (14·63) [221]	-	-	-
14 weeks	14·42 (16·34) [222]	12·39 (14·80) [221]	1·68 [-0·84 to 4·20]	0·11 [-0·06 to 0·28]	0·0058
26 weeks	**12·88 (15·34) [222]**	**10·64 (14·59) [221]**	**1·90 [-0·62 to 4·42]**	**0·13 [-0·04 to 0·30]**	**0·0093**
Worst Case (missing values = 75)					
Baseline	26·87 (15·26) [222]	25·96 (14·63) [221]	-	-	-
14 weeks	34·35 (28·08) [222]	38·19 (29·18) [221]	-4·33 [-9·48 to 0·82]	-0·29 [-0·63 to 0·05]	0·00021
26 weeks	**34·17 (28·86) [222]**	**41·52 (30·36) [221]**	**-7·85 [-12·99 to -2·70]**	**-0·53 [-0·87 to -0·18]**	**<0·0001**

Notes: OSI+TS=Online Support and Intervention for child anxiety plus therapist support; C-TAU=child mental health services treatment as usual. Multiple imputation was conducted using chained equations. Variables included in the MI model: random allocation, minimisation variables; child's age, child's gender, baseline anxiety associated interference, and service type (school/clinic), and factors found to be predictive of the primary outcome (partnered, and co-habiting). The best case scenario assumed and replaced all missing data with a score of 0, while the worst case scenario had a score of 75 for all missing data.

Supplementary Tables S12

Treatment approach followed for C-TAU where was provided

Therapists provided some information on the nature of C-TAU for 148/222 (67%) trial cases

	n
CBT	110
Family Therapy	0
Child Psychotherapy	1
Eclectic	5
Art Therapy	0
Psychoanalytic Psychotherapy	0
Brief Solution Focused Therapy	5
Other	9
No response	18
Total	148

C-TAU=child mental health services treatment as usual.

C-TAU format (multiple options per participant)

	n
Telephone	82
Video call	96
Clinic	40
Home	2
Total reports	148*

* 220 formats were reported: note that several formats were often selected.
C-TAU=child mental health services treatment as usual.

C-TAU modality (multiple options per participant)

	n
Parent group	13
Child group	1
Parent individual	134
Child individual	20
No response	1
Total reports	148*

* 168 modalities were reported: note that several formats were often selected.
C-TAU=child mental health services treatment as usual.

C-TAU sessions conducted with parent or child (multiple options per participant)

	n
Parent only	138
Child only	21
Together	42
No response	1
Total reports	148*

* 201 variations were reported: note that several formats were often selected.
C-TAU=child mental health services treatment as usual.

Supplementary Table S13

Summary statistics and the test of significance for the exploratory analyses of treatment credibility and expectation of improvement (CEI)

	OSI + TS (N=222)	C-TAU (N=221)	P-value*
Exploratory Analyses			
Credibility and Expectation of Improvement Scale – Parent Version (CEI-P)			
CEI-P: How logical do you consider this type of treatment to be?, median (IQR) [n]			
Post-randomisation	7·0 (6·0 to 9·0) [218]	7·0 (5·0 to 9·0) [209]	0·174
14 weeks	8·5 (7·0 to 10·0) [160]	8·0 (7·0 to 10·0) [143]	0·364
CEI-P: How certain are you that this method will be successful in the treatment of your child's anxiety?, median (IQR) [n]			
Post-randomisation	6·0 (5·0 to 7·0) [218]	5·0 (5·0 to 7·0) [209]	0·006
14 weeks	7·0 (5·0 to 9·0) [160]	7·0 (5·0 to 9·0) [143]	0·392
CEI-P: With that degree of confidence would you recommend this treatment to another family with a child with the same type of anxiety problems as your child has?, median (IQR) [n]			
Post-randomisation	6·0 (5·0 to 8·0) [218]	5·0 (5·0 to 7·0) [209]	0·155
14 weeks	8·0 (6·0 to 10·0) [160]	8·0 (5·0 to 10·0) [143]	0·193
Credibility and Expectation of Improvement Scale – Therapist Version (CEI-T)			
CEI-T: How logical did you consider the treatment to be?, median (IQR) [n]			
End of treatment	9·0 (7·0 to 10·0) [155]	8·0 (7·0 to 10·0) [128]	0·425
CEI-T: How comfortable did you feel in your therapist role in delivering the treatment?, median (IQR) [n]			
End of treatment	7·0 (6·0 to 9·0) [154]	8·0 (7·0 to 10·0) [127]	0·012
CEI-T: How well prepared did you feel to deliver the treatment?, median (IQR) [n]			
End of treatment	8·0 (6·0 to 9·0) [154]	8·0 (7·0 to 10·0) [127]	0·072
CEI-T: How certain are you that this method was successful in the treatment of children's anxiety problems?, median (IQR) [n]			
End of treatment	7·0 (5·0 to 9·0) [155]	7·0 (5·0 to 9·0) [126]	0·601
CEI-T: With what degree of confidence would you recommend this treatment to another therapist to treat child anxiety problems?, median (IQR) [n]			
End of treatment	8·0 (7·0 to 10·0) [155]	8·0 (7·0 to 10·0) [127]	0·288
CEI-T: How likely are you to use this method in the future to treat children's anxiety problems?, median (IQR) [n]			
End of treatment	8·0 (7·0 to 10·0) [155]	9·0 (7·0 to 10·0) [127]	0·003

*OSI + TS versus C-TAU· Mann-Whitney U test· Exact P-values· Level of statistical significance = 0·05.
OSI+TS=Online Support and Intervention for child anxiety plus therapist support; C-TAU=child mental health services treatment as usual.

Supplementary Table S14: Health economics data completeness (%)

Items	OSI+TS	C-TAU
Health outcomes		
Child CHU9D - baseline	100.00	100.00
Child CHU9D - 14 week	77.93	73.76
Child CHU9D - 26 week	77.48	73.30
Parent EQ-5D-5L - baseline	100.00	100.00
Parent EQ-5D-5L - 14 week	77.93	74.21
Parent EQ-5D-5L - 26 week	77.48	73.30
Service use		
Child service use - baseline	92.79	93.21
Child service use - 14 week	70.27	65.16
Child service use - 26 week	65.77	61.54
Parent service use - baseline	92.79	93.21
Parent service use - 14 week	70.27	65.16
Parent service use - 26 week	65.77	61.54
Medicine use		
Child medicine use - baseline	100.00	100.00
Child medicine use - 14 week	76.58	71.49
Child medicine use - 26 week	74.77	68.78
Parent medicine use - baseline	100.00	100.00
Parent medicine use - 14 week	76.58	71.49
Parent medicine use - 26 week	74.77	68.78
Treatment travel time and travel cost		
Treatment travel time/cost - 14 week	76.58	71.49
Treatment travel time/cost - 26 week	74.77	68.78
School Absence		
School absence - baseline	100.00	100.00
School absence - 14 week	76.58	71.95
School absence - 26 week	74.77	68.78
Employment		
Employment - baseline	100.00	100.00
Employment – 14 week	76.13	72.40
Employment – 26 week	75.23	71.04
Treatment and supervision logs		
Treatment logs	81.53	71.17
Supervision logs	56.31	45.95

Notes: percentages calculated with respect to 222 individuals in the OSI+TS arm and 221 individuals in the C-TAU arm. OSI+TS=Online Support and Intervention for child anxiety plus therapist support; C-TAU=child mental health services treatment as usual.

Supplementary Materials S15

Supplementary Table S15.1: Therapists' and Supervisors' time spent on treatment and supervision for users – complete case analysis

	Treatment Groups							
	OSI+TS				C-TAU			
Items	N	mean	sd	median (IQR)	N	mean	sd	median (IQR)
Total Treatment time (minutes)	181	374.39	154.73	365.00 (277 to 460)	158	502.04	268.86	479.02 (312.00 to 655.00)
Treatment Time (delivery)	181	181.98	81.00	175.00 (126.00 to 226.00)	158	307.05	172.77	315.00 (200.00 to 400.00)
Other time use related to treatment								
- *preparation*	181	108.09	65.24	100.00 (70.00 to 140.00)	158	95.74	83.64	79.58 (39.00 to 130.00)
- *admin*	181	83.74	73.20	65.13 (25.00 to 120.00)	158	90.63	88.62	70.00 (30.00 to 130.00)
- *travel*	181	0.57	4.47	0 (0 to 0)	158	8.62	34.00	0 (0 to 0)
Total Supervision time (minutes)	125	55.02	71.37	31.67 (0 to 81.17)	102	42.67	60.48	15.46 (0 to 68.36)
- case time by a therapist	125	23.12	29.73	15 (0 to 35.00)	102	18.85	28.02	6.37 (0 to 30.00)
- case time by a supervisor	125	23.83	31.53	15 (0 to 35.00)	102	17.33	23.74	6.44 (0 to 30.00)
Other time use related to supervision								
- preparation	125	3.89	6.14	1.25 (0 to 5.24)	102	3.85	6.34	0.83 (0 to 5.08)
- admin	125	4.18	7.24	1.25 (0 to 5.36)	102	2.65	5.13	0.19 (0 to 3.08)

Notes: This table summarises the time (minutes) spent on a patient in each treatment arm. This calculation is based on the patients who are recorded at least once in the treatment and supervision logs. OSI+TS=Online Support and Intervention for child anxiety plus therapist support; C-TAU=child mental health services treatment as usual.

Supplementary Table S15.2: Therapists' and Supervisors' time spent on treatment and supervision – Intention-to-Treat analysis

	Treatment Groups							
	OSI+TS (N=222)				C-TAU (N=221)			
	Mean	SD	SE	Median	Mean	SD	SE	Median
Treatment Time (minutes)	385.30	164.15	12.47	375.25	472.34	259.24	19.05	444.13
Supervision Time (minutes)								
- by clinicians	34.09	39.80	3.47	19.76	31.14	38.20	3.41	17.10
- by supervisors	25.76	30.43	2.53	14.99	20.74	25.45	2.44	11.83
Total Supervision time (minutes)	59.85	|67.55	5.7	36.18	51.89	59.82	5.43	31.17
Overall Treatment Time (Minutes)	445.15	193.74	14.42	435.54	524.22	280.03	20.75	488.26

Notes: SD = standard deviation, SE = standard error. OSI+TS=Online Support and Intervention for child anxiety plus therapist support; C-TAU=child mental health services treatment as usual.

Supplementary Table S15.3: Children's service use at the baseline – complete case analysis

Service (unit)	OSI+TS					C-TAU				
	n	Mean (SD)	Min	Max	% using	n	Mean (SD)	Min	Max	% using
Hospital										
A&E	206	0.13 (0.51)	0	4	7.77	206	0.04 (0.21)	0	1	3.88
Audiology	206	0.00 (0.00)	0	0	0.00	206	0.01 (0.12)	0	1	1.46
Day hospital	206	0.04 (0.31)	0	4	2.43	206	0.03 (0.30)	0	4	1.94
Inpatient (nights)	206	0.06 (0.71)	0	10	0.97	206	0.00 (0.00)	0	0	0.00
Ophthalmology	206	0.03 (0.17)	0	1	2.91	206	0.02 (0.14)	0	1	1.94
Paediatrician	206	0.15 (0.52)	0	4	9.22	206	0.17 (0.82)	0	9	6.31
Community and social care										
Advice lines	206	0.02 (0.22)	0	3	0.97	206	0.00 (0.00)	0	0	0.00
Alternative medicine	206	0.04 (0.56)	0	8	0.49	206	0.00 (0.07)	0	1	0.49
Child and adolescent mental health nurse	206	0.17 (0.96)	0	9	4.85	206	0.20 (1.17)	0	12	4.85
Community children's nurse	206	0.05 (0.33)	0	3	2.91	206	0.00 (0.07)	0	1	0.49
Education welfare officer	206	0.10 (1.10)	0	15	1.46	206	0.08 (0.88)	0	12	1.46
Educational psychologist	206	0.08 (0.40)	0	3	4.37	206	0.04 (0.33)	0	4	2.43
Family centre	206	0.04 (0.56)	0	8	0.49	206	0.01 (0.21)	0	3	0.49
Family liaison officer	206	0.56 (4.69)	0	57	3.88	206	0.29 (2.88)	0	40	3.40
Family therapist	206	0.07 (0.55)	0	6	1.94	206	0.01 (0.21)	0	3	0.49
GP	206	0.83 (2.31)	0	25	32.04	206	0.58 (1.24)	0	10	28.64
Home start	206	0.00 (0.00)	0	0	0.00	206	0.01 (0.21)	0	3	0.49
Occupational therapist	206	0.04 (0.43)	0	6	1.46	206	0.09 (0.65)	0	7	2.43
Paediatric dietician	206	0.02 (0.22)	0	3	0.97	206	0.02 (0.29)	0	4	0.97
Paediatric physiotherapist	206	0.02 (0.25)	0	3	0.97	206	0.04 (0.28)	0	3	2.43
Paediatric play specialist	206	0.00 (0.00)	0	0	0.00	206	0.02 (0.28)	0	4	0.49
Practice nurse	206	0.06 (0.43)	0	5	2.43	206	0.04 (0.43)	0	6	1.94
Primary mental health worker	206	0.14 (0.71)	0	8	5.83	206	0.22 (1.06)	0	9	5.83

Psychiatrist	206	0.07 (0.61)	0	8	1.94	206	0.00 (0.07)	0	1	0.49
Psychologist	206	0.26 (1.35)	0	12	5.83	206	0.16 (0.96)	0	10	3.88
Self help groups	206	0.00 (0.00)	0	0	0.00	206	0.02 (0.28)	0	4	0.49
Social worker	206	0.07 (0.68)	0	9	1.94	206	0.03 (0.26)	0	3	1.46
Speech and language	206	0.11 (0.99)	0	12	2.43	206	0.23 (2.82)	0	40	1.46
Teacher (additional contact)	206	0.72 (2.83)	0	25	14.56	206	0.55 (2.44)	0	30	12.14
Other services										
Autism assessment team	206	0.00 (0.07)	0	1	0.49	206	0.00 (0.00)	0	0	0.00
Child and adolescent mental health, other	206	0.07 (0.69)	0	9	1.46	206	0.07 (0.86)	0	12	0.97
Children's wellbeing practitioner	206	0.06 (0.55)	0	6	1.46	206	0.04 (0.41)	0	5	0.97
Community dentist	206	0.01 (0.14)	0	2	0.49	206	0.01 (0.14)	0	2	0.49
Community specialist nurse	206	0.02 (0.25)	0	3	0.97	206	0.00 (0.07)	0	1	0.49
Education mental health practitioner	206	0.00 (0.07)	0	1	0.49	206	0.00 (0.00)	0	0	0.00
Endocrinology	206	0.02 (0.35)	0	5	0.49	206	0.00 (0.00)	0	0	0.00
Family support worker	206	0.01 (0.14)	0	2	0.49	206	0.00 (0.00)	0	0	0.00
Orthotics	206	0.01 (0.14)	0	2	0.49	206	0.00 (0.00)	0	0	0.00
Pastoral support officer	206	0.00 (0.00)	0	0	0.00	206	0.04 (0.56)	0	8	0.49
Private counsellor	206	0.01 (0.21)	0	3	0.49	206	0.00 (0.00)	0	0	0.00
School nurse	206	0.00 (0.07)	0	1	0.49	206	0.04 (0.33)	0	3	1.46
SENCO	206	0.00 (0.00)	0	0	0.00	206	0.02 (0.35)	0	5	0.49
Wheelchair services	206	0.01 (0.14)	0	2	0.49	206	0.00 (0.00)	0	0	0.00
Educational loss										
School days off	222	1.23 (4.16)	0	40	0.25	221	1.06 (4.40)	0	55	0.19

Notes: OSI+TS=Online Support and Intervention for child anxiety plus therapist support; C-TAU=child mental health services treatment as usual.

Supplementary Table S15.4: Children's service use at 14 weeks – complete case analysis

Service (unit)	OSI+TS					C-TAU				
	n	Mean (SD)	Min	Max	% using	n	Mean (SD)	Min	Max	% using
Hospital										
A&E	156	0.06 (0.33)	0	3	3.85	144	0.16 (0.76)	0	8	8.33
Audiology	156	0.02 (0.18)	0	2	1.28	144	0.01 (0.12)	0	1	1.39
Day hospital	156	0.02 (0.18)	0	2	1.28	144	0.03 (0.34)	0	4	1.39
Ophthalmology	156	0.03 (0.21)	0	2	2.56	144	0.02 (0.14)	0	1	2.08
Paediatrician	156	0.13 (0.57)	0	5	7.69	144	0.19 (1.38)	0	16	6.25
Community and social care										
Advice lines	156	0.00 (0.00)	0	0	0.00	144	0.03 (0.34)	0	4	1.39
Child and adolescent mental health nurse	156	0.03 (0.25)	0	3	1.28	144	0.12 (0.85)	0	8	2.08
Community children's nurse	156	0.01 (0.16)	0	2	0.64	144	0.01 (0.08)	0	1	0.69
Education welfare officer	156	0.06 (0.38)	0	3	2.56	144	0.00 (0.00)	0	0	0.00
Educational psychologist	156	0.02 (0.18)	0	2	1.28	144	0.08 (0.71)	0	7	1.39
Family liaison officer	156	0.19 (1.00)	0	8	4.49	144	0.13 (1.06)	0	9	1.39
Family therapist	156	0.07 (0.62)	0	6	1.28	144	0.00 (0.00)	0	0	0.00
GP	156	0.58 (1.50)	0	11	24.36	144	0.56 (1.39)	0	8	21.53
Occupational therapist	156	0.01 (0.08)	0	1	0.64	144	0.02 (0.19)	0	2	1.39
Paediatric dietician	156	0.01 (0.08)	0	1	0.64	144	0.01 (0.08)	0	1	0.69
Paediatric physiotherapist	156	0.00 (0.00)	0	0	0.00	144	0.01 (0.17)	0	2	0.69
Paediatric play specialist	156	0.03 (0.32)	0	4	0.64	144	0.00 (0.00)	0	0	0.00
Practice nurse	156	0.10 (1.20)	0	15	1.28	144	0.03 (0.18)	0	1	3.47
Primary mental health worker	156	0.15 (0.85)	0	7	3.85	144	0.06 (0.53)	0	5	1.39
Psychiatrist	156	0.10 (0.79)	0	8	1.92	144	0.03 (0.33)	0	4	0.69
Psychologist	156	0.19 (1.24)	0	11	3.85	144	0.15 (1.16)	0	13	3.47
Social worker	156	0.04 (0.30)	0	3	1.92	144	0.06 (0.59)	0	7	1.39
Speech and language	156	0.12 (1.14)	0	14	1.92	144	0.13 (1.26)	0	15	2.08

Teacher (additional contact)	156	0.45 (2.25)	0	25	9.62	144	0.62 (5.07)	0	60	7.64
Other services										
Cardiology	156	0.00 (0.00)	0	0	0.00	144	0.01 (0.17)	0	2	0.69
Charity groups	156	0.00 (0.00)	0	0	0.00	144	0.01 (0.17)	0	2	0.69
Children's wellbeing practitioner	156	0.04 (0.34)	0	3	1.28	144	0.00 (0.00)	0	0	0.00
Community dentist	156	0.03 (0.32)	0	4	0.64	144	0.01 (0.17)	0	2	0.69
Community specialist nurse	156	0.01 (0.08)	0	1	0.64	144	0.01 (0.08)	0	1	0.69
Counsellor	156	0.08 (0.68)	0	6	1.28	144	0.06 (0.48)	0	5	1.39
Hospital dentist	156	0.00 (0.00)	0	0	0.00	144	0.01 (0.08)	0	1	0.69
Neurology	156	0.01 (0.08)	0	1	0.64	144	0.00 (0.00)	0	0	0.00
Outreach worker	156	0.00 (0.00)	0	0	0.00	144	0.02 (0.25)	0	3	0.69
Private counsellor	156	0.06 (0.80)	0	10	0.64	144	0.00 (0.00)	0	0	0.00
SENCO	156	0.01 (0.16)	0	2	0.64	144	0.00 (0.00)	0	0	0.00
Urology	156	0.01 (0.08)	0	1	0.64	144	0.00 (0.00)	0	0	0.00
Educational loss										
School days off	170	1.87 (5.73)	0	40	0.24	159	1.59 (6.55)	0	60	0.22

Notes: OSI+TS=Online Support and Intervention for child anxiety plus therapist support; C-TAU=child mental health services treatment as usual.

Supplementary Table S15.5: Children's service use at 26 weeks – complete case analysis

Service (unit)	OSI+TS					C-TAU				
	n	Mean (SD)	Min	Max	% using	n	Mean (SD)	Min	Max	% using
Hospital										
A&E	146	0.03 (0.25)	0	2	2.05	136	0.13 (0.57)	0	5	8.09
Audiology	146	0.08 (0.91)	0	11	0.68	136	0.00 (0.00)	0	0	0.00
Day hospital	146	0.01 (0.08)	0	1	0.68	136	0.03 (0.17)	0	1	2.94
Ophthalmology	146	0.03 (0.16)	0	1	2.74	136	0.05 (0.60)	0	7	0.74
Paediatrician	146	0.16 (0.57)	0	4	9.59	136	0.11 (0.48)	0	3	6.62
Community and social care										
Advice lines	146	0.02 (0.25)	0	3	0.68	136	0.00 (0.00)	0	0	0.00
Alternative medicine	146	0.01 (0.12)	0	1	1.37	136	0.00 (0.00)	0	0	0.00
Child and adolescent mental health nurse	146	0.11 (0.60)	0	5	4.11	136	0.14 (1.05)	0	10	2.94
Community children's nurse	146	0.01 (0.17)	0	2	0.68	136	0.00 (0.00)	0	0	0.00
Education welfare officer	146	0.05 (0.48)	0	5	1.37	136	0.02 (0.26)	0	3	0.74
Educational psychologist	146	0.03 (0.20)	0	2	2.05	136	0.11 (0.82)	0	8	2.21
Family centre	146	0.00 (0.00)	0	0	0.00	136	0.04 (0.43)	0	5	0.74
Family liaison officer	146	0.91 (7.00)	0	80	4.11	136	0.06 (0.69)	0	8	0.74
Family therapist	146	0.03 (0.23)	0	2	1.37	136	0.00 (0.00)	0	0	0.00
GP	146	0.51 (2.12)	0	22	15.75	136	0.55 (1.65)	0	13	19.85
Occupational therapist	146	0.03 (0.20)	0	2	2.05	136	0.01 (0.12)	0	1	1.47
Paediatric dietician	146	0.03 (0.23)	0	2	1.37	136	0.00 (0.00)	0	0	0.00
Paediatric physiotherapist	146	0.01 (0.17)	0	2	0.68	136	0.01 (0.09)	0	1	0.74
Paediatric play specialist	146	0.00 (0.00)	0	0	0.00	136	0.06 (0.69)	0	8	0.74
Practice nurse	146	0.03 (0.20)	0	2	2.05	136	0.01 (0.12)	0	1	1.47
Primary mental health worker	146	0.03 (0.34)	0	4	1.37	136	0.00 (0.00)	0	0	0.00
Psychiatrist	146	0.08 (0.99)	0	12	0.68	136	0.03 (0.34)	0	4	0.74
Psychologist	146	0.08 (0.64)	0	6	1.37	136	0.14 (1.22)	0	13	1.47
Self help groups	146	0.01 (0.08)	0	1	0.68	136	0.03 (0.34)	0	4	0.74

Social worker	146	0.07 (0.38)	0	3	3.42	136	0.02 (0.19)	0	2	1.47
Speech and language	146	0.05 (0.38)	0	4	2.05	136	0.01 (0.09)	0	1	0.74
Teacher (additional contact)	146	0.20 (0.92)	0	6	6.16	136	0.13 (0.67)	0	6	4.41
Other services										
Cardiology	146	0.01 (0.08)	0	1	0.68	136	0.00 (0.00)	0	0	0.00
Child and adolescent mental health, other	146	0.05 (0.66)	0	8	0.68	136	0.01 (0.17)	0	2	0.74
Children's wellbeing practitioner	146	0.07 (0.83)	0	10	0.68	136	0.00 (0.00)	0	0	0.00
Counsellor	146	0.03 (0.33)	0	4	0.68	136	0.00 (0.00)	0	0	0.00
Family support worker	146	0.05 (0.66)	0	8	0.68	136	0.00 (0.00)	0	0	0.00
Orthodontist	146	0.00 (0.00)	0	0	0.00	136	0.01 (0.09)	0	1	0.74
Orthopaedics	146	0.00 (0.00)	0	0	0.00	136	0.02 (0.26)	0	3	0.74
Educational loss										
School days off	166	1.20 (6.64)	0	60	0.10	153	0.97 (5.70)	0	67	0.14

Notes: OSI+TS=Online Support and Intervention for child anxiety plus therapist support; C-TAU=child mental health services treatment as usual.

Supplementary Table S15.6: Parents' service use at the baseline – complete case analysis

Service (unit)	OSI+TS					C-TAU				
	n	Mean (SD)	Min	Max	% using	n	Mean (SD)	Min	Max	% using
Hospital										
A&E	206	0.13 (0.97)	0	10	2.91	206	0.04 (0.25)	0	3	2.91
Day hospital	206	0.01 (0.12)	0	1	1.46	206	0.01 (0.10)	0	1	0.97
Inpatient (nights)	206	0.01 (0.21)	0	3	0.49	206	0.00 (0.00)	0	0	0.00
Ophthalmology	206	0.03 (0.35)	0	5	0.97	206	0.00 (0.07)	0	1	0.49
Paediatrician	206	0.09 (0.68)	0	9	3.88	206	0.03 (0.25)	0	2	1.94
Community and social care										
Advice lines	206	0.12 (0.94)	0	10	1.94	206	0.03 (0.31)	0	4	0.97
Alternative medicine	206	0.02 (0.21)	0	2	1.46	206	0.02 (0.22)	0	3	0.97
Child and adolescent mental health nurse	206	0.18 (1.42)	0	18	3.40	206	0.10 (0.53)	0	4	3.88
Citizens advice bureau	206	0.01 (0.14)	0	2	0.49	206	0.01 (0.21)	0	3	0.49
Community children's nurse	206	0.01 (0.21)	0	3	0.49	206	0.00 (0.00)	0	0	0.00
Education welfare officer	206	0.12 (0.98)	0	13	2.91	206	0.00 (0.00)	0	0	0.00
Educational psychologist	206	0.05 (0.29)	0	3	2.91	206	0.01 (0.10)	0	1	0.97
Family centre	206	0.00 (0.00)	0	0	0.00	206	0.04 (0.56)	0	8	0.49
Family liaison officer	206	0.50 (5.45)	0	77	4.37	206	0.06 (0.37)	0	3	3.40
Family planning	206	0.00 (0.00)	0	0	0.00	206	0.11 (1.28)	0	18	0.97
Family therapist	206	0.01 (0.16)	0	2	0.97	206	0.03 (0.42)	0	6	0.49
GP	206	0.68 (1.70)	0	12	21.36	206	0.74 (1.71)	0	12	24.76
Home start	206	0.05 (0.70)	0	10	0.49	206	0.02 (0.28)	0	4	0.49
Housing department	206	0.02 (0.28)	0	4	0.49	206	0.01 (0.14)	0	2	0.49
Occupational therapist	206	0.04 (0.33)	0	4	1.94	206	0.04 (0.29)	0	3	1.94
Paediatric dietician	206	0.02 (0.22)	0	3	0.97	206	0.00 (0.00)	0	0	0.00
Paediatric physiotherapist	206	0.00 (0.00)	0	0	0.00	206	0.01 (0.14)	0	2	0.49
Paediatric play specialist	206	0.00 (0.00)	0	0	0.00	206	0.01 (0.14)	0	2	0.49
Practice nurse	206	0.06 (0.37)	0	4	3.88	206	0.06 (0.31)	0	2	3.88

Primary mental health worker	206	0.18 (0.90)	0	7	5.83	206	0.09 (0.56)	0	5	2.91
Psychiatrist	206	0.03 (0.20)	0	2	2.43	206	0.00 (0.07)	0	1	0.49
Psychologist	206	0.07 (0.53)	0	6	2.91	206	0.05 (0.36)	0	3	2.43
Self help groups	206	0.01 (0.21)	0	3	0.49	206	0.10 (1.03)	0	11	0.97
Social worker	206	0.17 (2.03)	0	28	0.97	206	0.12 (0.93)	0	10	1.94
Speech and language	206	0.04 (0.41)	0	6	1.46	206	0.10 (1.39)	0	20	0.97
Teacher (additional contact)	206	0.95 (4.33)	0	40	14.56	206	0.76 (2.90)	0	30	14.56
Other services										
Breast cancer screening	206	0.01 (0.14)	0	2	0.49	206	0.00 (0.00)	0	0	0.00
Charity groups	206	0.00 (0.00)	0	0	0.00	206	0.02 (0.35)	0	5	0.49
Child and adolescent mental health, other	206	0.05 (0.70)	0	10	0.49	206	0.00 (0.00)	0	0	0.00
Children's wellbeing practitioner	206	0.01 (0.14)	0	2	0.49	206	0.02 (0.28)	0	4	0.49
Complementary therapist	206	0.00 (0.00)	0	0	0.00	206	0.00 (0.07)	0	1	0.49
Group therapy	206	0.00 (0.00)	0	0	0.00	206	0.07 (1.05)	0	15	0.49
Gynaecological oncology	206	0.01 (0.14)	0	2	0.49	206	0.00 (0.00)	0	0	0.00
IAPT	206	0.01 (0.14)	0	2	0.49	206	0.00 (0.00)	0	0	0.00
Oncology	206	0.00 (0.07)	0	1	0.49	206	0.00 (0.00)	0	0	0.00
Orthopaedics	206	0.00 (0.00)	0	0	0.00	206	0.00 (0.07)	0	1	0.49
School nurse	206	0.00 (0.00)	0	0	0.00	206	0.03 (0.30)	0	3	1.46
Productivity loss										
Working days off	222	0.52 (2.21)	0	25	0.12	221	0.47 (2.29)	0	25	0.10

Notes: OSI+TS=Online Support and Intervention for child anxiety plus therapist support; C-TAU=child mental health services treatment as usual.

Supplementary Table S15.7: Parents' service use at 14 weeks – complete case analysis

Service (unit)	OSI+TS					C-TAU				
	n	Mean (SD)	Min	Max	% using	n	Mean (SD)	Min	Max	% using
Hospital										
A&E	156	0.05 (0.36)	0	3	2.56	144	0.02 (0.19)	0	2	1.39
Audiology	156	0.00 (0.00)	0	0	0.00	144	0.01 (0.08)	0	1	0.69
Day hospital	156	0.04 (0.37)	0	4	1.92	144	0.05 (0.38)	0	4	2.08
Ophthalmology	156	0.00 (0.00)	0	0	0.00	144	0.01 (0.08)	0	1	0.69
Paediatrician	156	0.15 (0.89)	0	8	3.85	144	0.03 (0.28)	0	3	2.08
Community and social care										
Advice lines	156	0.03 (0.25)	0	3	1.28	144	0.06 (0.41)	0	4	2.78
Alternative medicine	156	0.00 (0.00)	0	0	0.00	144	0.02 (0.19)	0	2	1.39
Child and adolescent mental health nurse	156	0.17 (1.38)	0	14	2.56	144	0.08 (0.65)	0	6	1.39
Citizens advice bureau	156	0.01 (0.08)	0	1	0.64	144	0.02 (0.25)	0	3	0.69
Community children's nurse	156	0.04 (0.36)	0	4	1.28	144	0.00 (0.00)	0	0	0.00
Education welfare officer	156	0.15 (1.00)	0	10	3.21	144	0.00 (0.00)	0	0	0.00
Educational psychologist	156	0.03 (0.33)	0	4	1.28	144	0.01 (0.08)	0	1	0.69
Family centre	156	0.01 (0.16)	0	2	0.64	144	0.09 (0.67)	0	6	2.08
Family liaison officer	156	0.14 (0.88)	0	9	3.21	144	0.02 (0.19)	0	2	1.39
Family therapist	156	0.10 (0.80)	0	8	1.92	144	0.00 (0.00)	0	0	0.00
GP	156	0.63 (2.54)	0	27	16.67	144	0.60 (2.24)	0	22	15.28
Home start	156	0.03 (0.32)	0	4	0.64	144	0.00 (0.00)	0	0	0.00
Occupational therapist	156	0.01 (0.16)	0	2	0.64	144	0.00 (0.00)	0	0	0.00
Paediatric play specialist	156	0.01 (0.16)	0	2	0.64	144	0.00 (0.00)	0	0	0.00
Practice nurse	156	0.20 (2.17)	0	27	2.56	144	0.07 (0.54)	0	6	2.78
Primary mental health worker	156	0.19 (1.02)	0	7	3.85	144	0.10 (0.64)	0	5	2.78
Psychiatrist	156	0.06 (0.46)	0	4	1.92	144	0.00 (0.00)	0	0	0.00
Psychologist	156	0.06 (0.49)	0	5	1.92	144	0.19 (1.56)	0	18	3.47
Self help groups	156	0.02 (0.18)	0	2	1.28	144	0.33 (3.13)	0	37	2.78

Social worker	156	0.03 (0.40)	0	5	0.64	144	0.10 (1.09)	0	13	1.39
Speech and language	156	0.02 (0.24)	0	3	0.64	144	0.02 (0.14)	0	1	2.08
Teacher (additional contact)	156	0.48 (1.73)	0	15	12.82	144	0.68 (5.08)	0	60	10.42
Other services										
Charity groups	156	0.03 (0.32)	0	4	0.64	144	0.03 (0.42)	0	5	0.69
Child and adolescent mental health, other	156	0.00 (0.00)	0	0	0.00	144	0.01 (0.17)	0	2	0.69
Children's wellbeing practitioner	156	0.03 (0.23)	0	2	1.28	144	0.00 (0.00)	0	0	0.00
Chiropractor	156	0.00 (0.00)	0	0	0.00	144	0.08 (1.00)	0	12	0.69
Community specialist nurse	156	0.00 (0.00)	0	0	0.00	144	0.01 (0.08)	0	1	0.69
Counsellor	156	0.02 (0.24)	0	3	0.64	144	0.00 (0.00)	0	0	0.00
Family support worker	156	0.01 (0.08)	0	1	0.64	144	0.00 (0.00)	0	0	0.00
NVR Practitioners Consortium	156	0.02 (0.24)	0	3	0.64	144	0.00 (0.00)	0	0	0.00
Outpatient	156	0.01 (0.08)	0	1	0.64	144	0.00 (0.00)	0	0	0.00
Outreach worker	156	0.00 (0.00)	0	0	0.00	144	0.03 (0.42)	0	5	0.69
Police	156	0.00 (0.00)	0	0	0.00	144	0.01 (0.08)	0	1	0.69
Private counsellor	156	0.06 (0.80)	0	10	0.64	144	0.00 (0.00)	0	0	0.00
SENCO	156	0.01 (0.11)	0	1	1.28	144	0.00 (0.00)	0	0	0.00
VOICE programme	156	0.03 (0.40)	0	5	0.64	144	0.00 (0.00)	0	0	0.00
Productivity loss										
Working days off	169	0.63 (2.18)	0	15	0.14	160	0.26 (1.02)	0	8	0.10

Notes: OSI+TS=Online Support and Intervention for child anxiety plus therapist support; C-TAU=child mental health services treatment as usual.

Supplementary Table S15.8: Parents' service use at 26 weeks – complete case analysis

Service (unit)	OSI+TS					C-TAU				
	n	Mean (SD)	Min	Max	% using	n	Mean (SD)	Min	Max	% using
Hospital										
A&E	146	0.01 (0.17)	0	2	0.68	136	0.06 (0.43)	0	4	2.21
Day hospital	146	0.01 (0.12)	0	1	1.37	136	0.04 (0.36)	0	4	2.21
Ophthalmology	146	0.04 (0.31)	0	3	2.05	136	0.01 (0.09)	0	1	0.74
Paediatrician	146	0.06 (0.41)	0	4	2.74	136	0.08 (0.66)	0	7	2.21
Community and social care										
Advice lines	146	0.00 (0.00)	0	0	0.00	136	0.01 (0.09)	0	1	0.74
Alternative medicine	146	0.05 (0.58)	0	7	0.68	136	0.01 (0.17)	0	2	0.74
Child and adolescent mental health nurse	146	0.15 (0.82)	0	5	3.42	136	0.03 (0.24)	0	2	1.47
Citizens advice bureau	146	0.00 (0.00)	0	0	0.00	136	0.03 (0.24)	0	2	1.47
Education welfare officer	146	0.05 (0.44)	0	5	1.37	136	0.02 (0.26)	0	3	0.74
Educational psychologist	146	0.01 (0.08)	0	1	0.68	136	0.07 (0.86)	0	10	0.74
Family centre	146	0.01 (0.08)	0	1	0.68	136	0.04 (0.43)	0	5	0.74
Family liaison officer	146	0.90 (7.00)	0	80	4.11	136	0.04 (0.43)	0	5	0.74
GP	146	0.47 (2.12)	0	22	12.33	136	0.38 (1.03)	0	6	17.65
Housing department	146	0.00 (0.00)	0	0	0.00	136	0.04 (0.51)	0	6	0.74
Occupational therapist	146	0.01 (0.08)	0	1	0.68	136	0.01 (0.09)	0	1	0.74
Practice nurse	146	0.01 (0.08)	0	1	0.68	136	0.04 (0.24)	0	2	3.68
Primary mental health worker	146	0.01 (0.08)	0	1	0.68	136	0.00 (0.00)	0	0	0.00
Psychologist	146	0.01 (0.17)	0	2	0.68	136	0.10 (1.03)	0	12	1.47
Self help groups	146	0.02 (0.25)	0	3	0.68	136	0.01 (0.09)	0	1	0.74
Social worker	146	0.11 (0.96)	0	10	1.37	136	0.08 (0.57)	0	5	2.21
Speech and language	146	0.05 (0.38)	0	4	2.05	136	0.00 (0.00)	0	0	0.00
Teacher (additional contact)	146	0.24 (0.96)	0	6	6.85	136	0.09 (0.58)	0	5	2.94
Other services										
Autism assessment team	146	0.01 (0.08)	0	1	0.68	136	0.00 (0.00)	0	0	0.00

Charity groups	146	0.03 (0.33)	0	4	0.68	136	0.00 (0.00)	0	0	0.00
Child and adolescent mental health, other	146	0.00 (0.00)	0	0	0.00	136	0.01 (0.09)	0	1	0.74
Children's wellbeing practitioner	146	0.03 (0.33)	0	4	0.68	136	0.00 (0.00)	0	0	0.00
Counsellor	146	0.03 (0.41)	0	5	0.68	136	0.00 (0.00)	0	0	0.00
Family support worker	146	0.05 (0.66)	0	8	0.68	136	0.00 (0.00)	0	0	0.00
Neurology	146	0.00 (0.00)	0	0	0.00	136	0.01 (0.17)	0	2	0.74
Productivity loss										
Working days off	167	0.51 (1.87)	0	15	0.13	157	0.60 (1.83)	0	12	0.15

Notes: OSI+TS=Online Support and Intervention for child anxiety plus therapist support; C-TAU=child mental health services treatment as usual.

Supplementary Table S15.9: Mean and mean difference in CHU9D and EQ-5D-5L utility scores, and QALYs by trial arm

	OSI+TS (N=222)			TAU (N=221)			Unadjusted difference			Adjusted difference*		
	Mean	SD	SE	Mean	SD	SE	Mean	95% CI	p-value	Mean	95% CI	p-value
Child CHU9D score UK value set												
Baseline	0.771	0.132	0.009	0.793	0.119	0.008	-0.022	(-0.045, 0.002)	0.071			
14 week	0.828	0.128	0.009	0.842	0.115	0.008	-0.013	(-0.037, 0.011)	0.279	-0.002	(-0.022, 0.019)	0.882
26 week	0.832	0.135	0.009	0.849	0.112	0.008	-0.016	(-0.041, 0.009)	0.200	-0.005	(-0.027, 0.017)	0.648
Total child QALYs	0.428	0.065	0.004	0.443	0.062	0.004	-0.014	(-0.027, -0.002)	0.020	-0.007	(-0.015, 0.002)	0.135
Child CHU9D score Australia value set												
Baseline	0.541	0.256	0.017	0.578	0.234	0.016	-0.037	(-0.083, 0.009)	0.111			
14 week	0.660	0.259	0.018	0.674	0.240	0.017	-0.015	(-0.064, 0.035)	0.556	0.007	(-0.034, 0.049)	0.736
26 week	0.672	0.266	0.018	0.690	0.231	0.017	-0.018	(-0.067, 0.031)	0.469	0.001	(-0.043, 0.044)	0.969
Total child QALYs	0.331	0.121	0.008	0.347	0.108	0.008	-0.016	(-0.038, 0.006)	0.161	-0.002	(-0.017, 0.012)	0.760
Parent EQ-5D-5L score												
Baseline	0.792	0.215	0.014	0.835	0.175	0.012	-0.043	(-0.08, -0.006)	0.022			
14 week	0.830	0.214	0.015	0.851	0.173	0.013	-0.021	(-0.06, 0.018)	0.288	0.004	(-0.029, 0.038)	0.799
26 week	0.851	0.193	0.014	0.873	0.141	0.011	-0.022	(-0.056, 0.012)	0.201	-0.002	(-0.031, 0.027)	0.897
Total parent QALYs	0.434	0.102	0.007	0.454	0.080	0.006	-0.021	(-0.038, -0.003)	0.023	-0.005	(-0.017, 0.007)	0.391

**Adjusted for baseline utility using linear regression. OSI+TS=Online Support and Intervention for child anxiety plus therapist support; C-TAU=child mental health services treatment as usual.*

Supplementary Table S15.10: Mean and mean difference in cost of service use between baseline and 26 week follow-up by trial arm

	OSI+TS (N=222)			TAU (N=221)			Unadjusted difference			Adjusted difference*		
Costs Types	Mean	SD	SE	Mean	SD	SE	Mean	95% CI	p-value	Mean	95% CI	p-value
Child overall NHS & PSS cost	**801.63**	**946.83**	**66.49**	**821.65**	**926.93**	**68.95**	**-20.02**	**(-206.03, 165.99)**	**0.832**	**-85.87**	**(-248.06 ,76.31)**	**0.30**
Intervention	**308.00**	**142.45**	**10.62**	**366.46**	**206.12**	**15.21**	**-58.45**	**(-94.85, -22.06)**	**p<0.001**			
Therapy cost	253.69	114.81	8.69	319.85	186.2	13.55	-66.16	(-98.02, -34.31)	p<0.001			
Supervision cost	54.32	61.2	5.17	46.61	53.79	4.94	7.71	(-5.5, 20.92)	0.25			
Child NHS and PSS	**493.63**	**926.84**	**65.13**	**455.20**	**899.65**	**66.35**	**38.43**	**(-142.72, 219.59)**	**0.68**	**-26.69**	**(-183.97, 130.58)**	**0.74**
Primary/community care	245.95	611.66	42.66	195.33	443.36	35.23	50.63	(-59.05, 160.3)	0.36	45.71	(-49.17, 140.6)	0.34
Secondary Care	240.29	613.12	44.28	255.24	745.3	54.3	-14.94	(-150.72,120.84)	0.83	-62.94	(-191.32, 65.44)	0.34
Medications	7.38	27.51	1.90	4.63	18.6	1.36	2.75	(-1.83, 7.32)	0.24	2.79	(-1.62, 7.21)	0.21
Child out-of-pocket	**27.66**	**79.89**	**5.90**	**32.00**	**141.46**	**9.78**	**-4.34**	**(-26.78, 18.11)**	**0.70**	**-4.87**	**(-27.26, 17.53)**	**0.67**
Child missed school	**895.25**	**2998.75**	**207.41**	**774.37**	**3227.36**	**227.24**	**120.88**	**(-484.8, 726.57)**	**0.69**	**83.01**	**(-495.31, 661.33)**	**0.78**
School opportunity cost	94.66	317.07	21.93	81.88	341.24	24.03	12.78	(-51.26, 76.82)	0.69	8.78	(-52.37, 69.92)	0.78
Human capital cost (loss of future earnings)	800.59	2681.68	185.48	692.49	2886.12	203.22	108.10	(-433.54, 649.75)	0.69	74.23	(-442.94, 591.4)	0.78
Parent NHS and PSS	**331.17**	**796.07**	**55.42**	**228.29**	**530.06**	**38.83**	**102.89**	**(-30.81, 236.59)**	**0.13**	**68.09**	**(-60.43, 196.61)**	**0.30**
Primary/community care	211.33	605.11	42.22	135.57	388.36	28.70	75.76	(-25.88, 177.4)	0.14	38.78	(-48.46, 126.01)	0.38
Secondary care	111.79	395	27.65	86.42	310.9	23.10	25.37	(-46.02, 96.77)	0.48	23.83	(-48.02, 95.68)	0.51
Medications	8.05	24.75	1.70	6.30	18.84	1.34	1.75	(-2.47, 5.97)	0.41	1.87	(-2.11, 5.85)	0.36
Parent out-of-pocket	**43.83**	**103.81**	**7.42**	**39.39**	**146.14**	**10.12**	**4.44**	**(-20.13, 29)**	**0.72**	**1.65**	**(-22.24, 25.54)**	**0.89**
Parent missed work	**103.38**	**286.95**	**20.52**	**78.70**	**199.71**	**15.53**	**24.68**	**(-25.44, 74.81)**	**0.33**	**23.76**	**(-25.77, 73.3)**	**0.35**
Parent opportunity cost of treatment	**40.24**	**19.13**	**1.49**	**58.46**	**31.65**	**2.36**	**-18.23**	**(-23.8, -12.65)**	**p<0.001**			
Total societal cost												
Excluding missed school human capital cost	1462.31	1868.53	129.07	1363.93	1363.93	112.05	98.38	(-237.82, 434.58)	0.57	-52.58	(-353.87, 248.71)	0.73
Including missed school human capital cost	2262.90	4183.08	287.27	2056.42	2056.42	277.61	206.48	(-575.66, 988.62)	0.60	-35.30	(-753.01, 682.42)	0.92

**For the mean difference, we adjusted for the baseline value of each variable except for intervention cost, treatment cost, supervision cost and parent opportunity cost of treatment, where their baseline value is unavailable. OSI+TS=Online Support and Intervention for child anxiety plus therapist support; C-TAU=child mental health services treatment*
as usual.

Health economics outcomes

Table S15.9 shows mean child CHU9D utilities, using the Australia adolescent and UK adult value sets, respectively, and parents EQ-5D-5L utility scores across the two trial arms at each time point, as well as the associated QALYs. Utility scores were slightly lower (i.e. worse) in the OSI+TS arm at baseline, with child utility 0.022 (95% CI: -0.045, 0.002) and 0.037 (95% CI: -0.083, 0.009) lower on the UK adult and Australia adolescent value sets, respectively, and parent utility 0.043 lower (95% CI: -0.08, -0.006). None of the above differences were statistically significant. Child and parent utility scores improved at each time point on each of the three measures, although they remained slightly lower in the OSI+TS arm. However, after adjusting for baseline values, there was little difference between utility scores in the two arms at 14 and 26 weeks. In fact, both unadjusted and adjusted mean differences in utility at all time points approximated zero in magnitude and were not statistically significant. Given the lower utility scores in the OSI+TS arm throughout the trial, QALYs gained were also lower. Unadjusted child QALYs were 0.014 (95% CI: -0.027, -0.002) and 0.016 (95% CI: -0.038, 0.006) lower in the OSI+TS arm, using the UK adult and Australia adolescent value sets respectively, while parent QALYs were 0.021 (95% CI: -0.038, -0.003) lower. Again, after adjusting for baseline values, there was minimal differences in child QALYs, with the difference ranging from -0.007 (95% CI: -0.015, 0.002) to -0.002 (95% CI: -0.017, 0.012) in OSI+TS compared to C-TAU, using the UK adult and Australia adolescent value sets respectively. Parent QALYs were 0.014 (95% CI: -0.031, 0.002) lower in the OSI+TS arm after adjusting for baseline differences. None of the child and parent QALYs differences were statistically significant.

Costs

Mean trial costs for key resource types by trial arm and mean differences are presented Table S15.10. On average, the overall OSI+TS intervention cost was £308, whereas C-TAU cost was £366.46, with OSI+TS generating a statistical significant cost-saving of £58.45 (95% CI: -94.85, -22.06). The main cost driver of both interventions was therapist time spent delivering the intervention, including preparation, administrative and travel time, resulting in a cost of £253.69 and £319.85 for OSI+TS and C-TAU respectively, meaning OSI+TS was associated with a statistically significant saving of £66.16 (95% CI: -98.02, -34.31: p-value<0.0001). We utilised the actual band/grade of all therapists taking part in the trial to identify their hourly rates for use in our cost calculations (Supplementary Materials S5: Unit costs (2020/21 prices, page 21). The mean hourly rates for therapists in each arm were £39.87 (SD: 6.636) and £40.36 (SD: 6.609) for OSI+TS and C-TAU, respectively.

While the difference in therapists' hourly rate was negligible and not statistically significant (mean difference (£): -0.492; (95% CI: -1.729, 0.744; p-value: 0.435), it may partially drive the difference in Therapy cost. We did some further analyses to examine the extent to which the therapy cost difference was driven by differential therapist's delivery time. We calculated an alternative "Therapy cost" using a common unit cost for all therapists across the two arms, setting this common unit cost equal to the average hourly rate of all involved therapists in both arms, which was £40.11 (SD: 6.6202). We found that the mean "Therapy cost" difference using this common unit costs was £-58.38 (95% CI: -88.63, -28.12; p-value <0.0001) versus -£66.16 in Table S15.10, which is unlikely to be due to the differential therapist's time. This alternative mean "Therapy cost" difference (i.e. -£58.38) was around 88.2% of the one presented Table S15.10 (i.e. -£66.16). Therefore, we can reasonably conclude that about 88% of the mean "Therapy cost" difference was attributable to the therapists' time-saving in treatment delivery.

The cost of supervision time for therapists delivering the intervention was similar in both arms (mean difference: £7.71; 95% CI: -5.5, 20.92).

With respect to service costs beyond the intervention (Table S15.10), there were some differences between the two trial arms, but none of those were statistically significant, with the only exception being the parent's opportunity cost of taking part in the treatment. In particular, child NHS and PSS costs were £38.43 (95% CI: -142.72, 219.59) higher in the OSI+TS arm, but after controlling for baseline costs, child NHS and PSS costs were actually £26.69 (95% CI: -183.97, 130.58) lower in the OSI+TS arm. Parent NHS and PSS costs were £102.89 (95% CI: -30.81, 236.59) greater in the OSI+TS arm, and remained higher, but reduced in magnitude, after controlling for baseline costs (adjusted mean difference: £68.09; 95% CI: -60.43, 196.61). Out-of-pocket expenditure was similar in both arms for children and parents. The cost of child missed school and the productivity loss of parent missed work remained higher, but reduced in magnitude, in the OSI+TS arm, after controlling for baseline differences. However, the parent opportunity cost of taking part in the treatment was significantly lower in the OSI+TS arm (mean difference: -£18.23: 95% CI: -23.8, -12.65). Overall, total societal costs (excluding missed school human capital costs) were £1,462.31 in the OSI+TS arm and £1,363.93 in the C-TAU arm across the 26 weeks of follow-up. However, after controlling for baseline costs, OSI+TS provided a £52.58 (95% CI: -353.87, 248.71) cost saving. Uncertainty around most of these mean values was large.

Supplementary Table S16

Treatment initiation and completion

	OSI+TS	C-TAU
Number (%) of participants that started allocated treatment within trial	181 (82%)	168 (76%)
Number (%) of participants that started within 12 weeks of randomisation	172 (77·5%)	151 (68·3%)
Number of sessions completed, median (IQR, range)	8 (6-8, 0-12)	6 (4-8, 0-33)
Number (%) of participants that started treatment who received minimum treatment dose (≥5 sessions)	154 (85·08%)	120 (71·42%)
Weeks between treatment completion and 14 week assessment (median (IQR, range)	-2 (-6.14-1.71, -39.43-14.43)	-0.29 (-5-2.57, -60.43-17.43)
Weeks between treatment completion and 26 week assessment (median (IQR, range))	10.14 (6.25-14.43, -29.43-33.86)	12 (7.07-15.93, -49.43-32.14)

Note: number of sessions, minimum dose, therapist minutes and weeks between treatment completion and assessment is based on available data provided for participants, assigned according to their allocated treatment arm. OSI+TS=Online Support and Intervention for child anxiety plus therapist support; C-TAU=child mental health services treatment as usual.

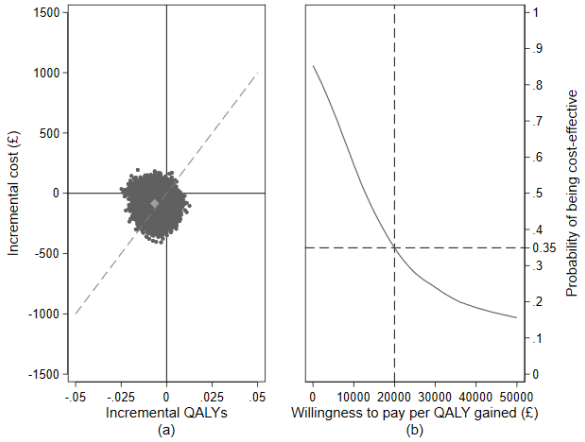
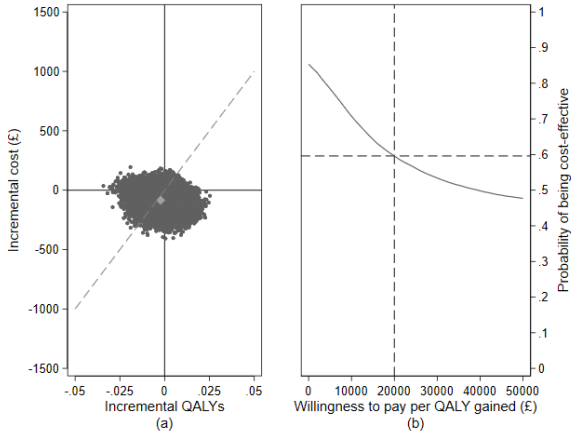
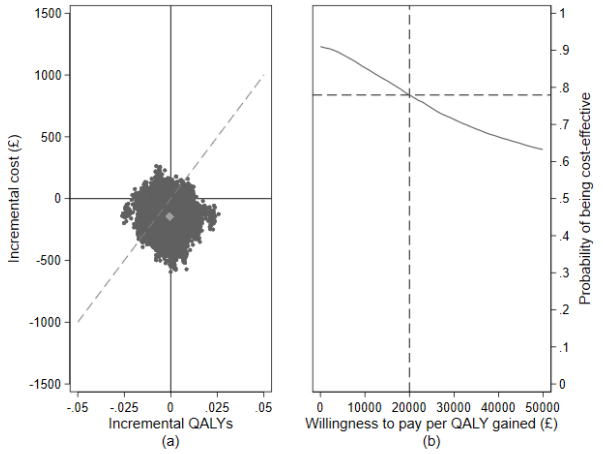
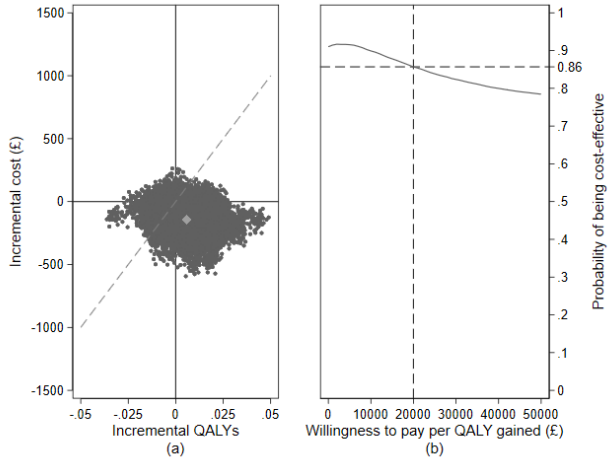
Supplementary Materials S17

Supplementary Table S17.1: Results of the economic evaluation (ITT and PP approaches) base-case analyses

	Cost mean difference (£)	95% CI	Effect mean difference	95% CI	ICER (£)	Probability cost-effective at £20,000 WTP per QALY gained	Probability cost-effective at £30,000 WTP per QALY gained
CUA analyses – ITT							
Child QALY (UK value set- primary valuation) & NHS/PSS costs (base-case A)	-85.87	(-248.06, 76.31)	-0.0067	(-0.0154, 0.0021)	12,883.06	35%	24%
Child QALY (AU value set- secondary valuation) & NHS/PSS costs (base-case B)	-85.87	(-248.06, 76.31)	-0.0023	(-0.0169, 0.0123)	37,895.43	60%	53%
CUA analyses – PP							
Child QALY (UK value set- primary valuation) & NHS/PSS costs (base-case A)	-142.96	(-383.77, 97.84)	-0.0008	(-0.0131, 0.0114)	170,501.10	78%	71%
Child QALY (AU value set- secondary valuation) & NHS/PSS costs (base-case B)	-142.96	(-383.77, 97.84)	0.0054	(-0.0147, 0.0256)	OSI dominates	86%	82%
CEA analyses – ITT							
Child reverse-score CAIS-P at 26 week & NHS/PSS cost (base-case)	-85.87	(-248.06, 76.31)	0.7354	(-1.6723, 3.1432)	N/A	N/A	N/A
CEA analyses – PP							
Child reverse-score CAIS-P at 26 week & NHS/PSS cost (base-case)	-142.96	(-383.77, 97.84)	0.2083	(-2.958, 3.3746)	N/A	N/A	N/A

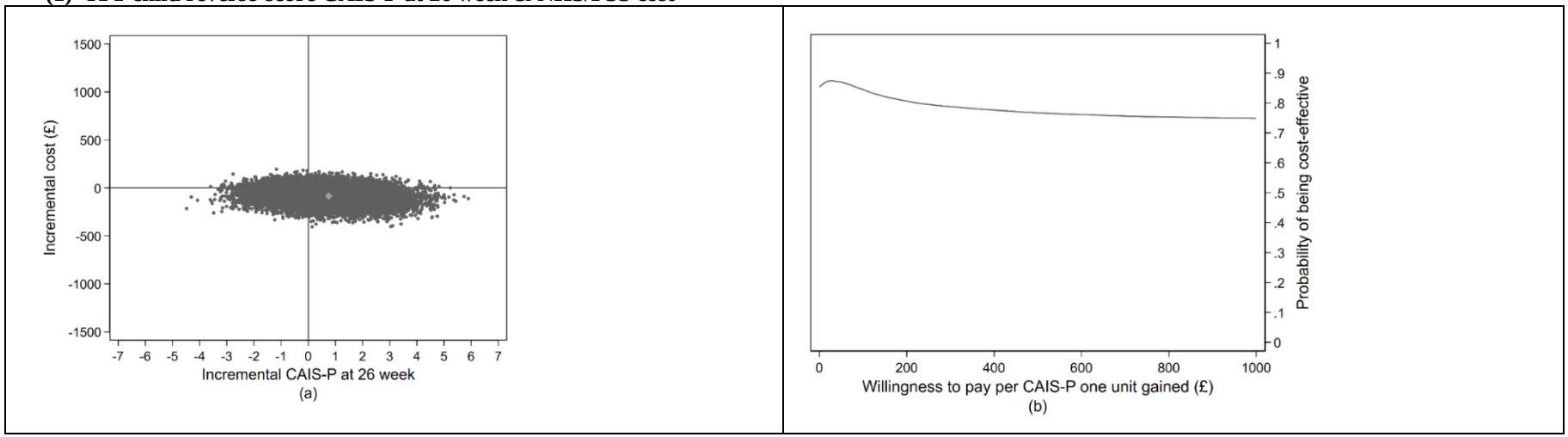
Notes: ITT = intention-to-treat; PP = per-protocol; CUA = cost-utility analysis; CEA = cost-effectiveness analysis; UK = United Kingdom; AU = Australia. OSI+TS=Online Support and Intervention for child anxiety plus therapist support; C-TAU=child mental health services treatment as usual.

Supplementary Figure S17.1: Cost-effectiveness planes (a) and cost-effectiveness acceptability curves (b) for the CUA base-case analyses

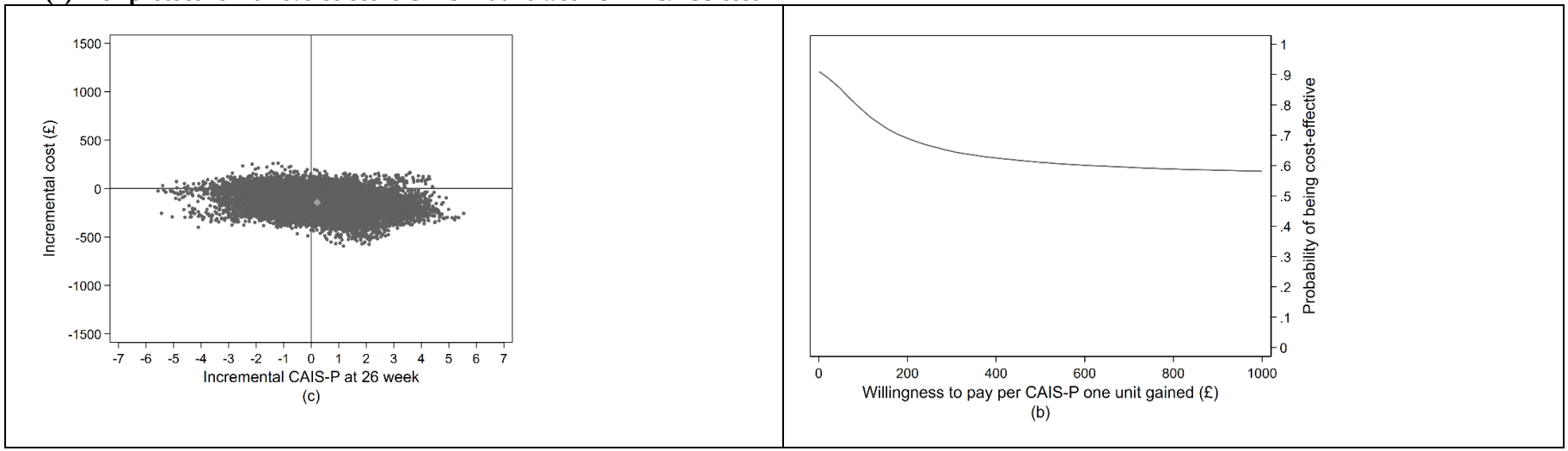
(1) ITT child QALYs (UK value set) and child NHS/PSS costs (base-case A)	(2) ITT child QALYs (Australia value set) and child NHS/PSS costs (base-case B)
	
(3) PP child QALYs (UK value set) and child NHS/PSS costs (base-case A)	**(4) PP child QALYs (Australia value set) and child NHS/PSS cost (base-case B)**
	

Supplementary Figure S17.2: Cost-effectiveness planes (a) and cost-effectiveness acceptability curves (b) for the CEA base-case analyses

(1) ITT child reverse-score CAIS-P at 26 week & NHS/PSS cost



(2) Per-protocol child reverse-score CAIS-P at 26 week & NHS/PSS cost



Supplementary Table S17.2: Results of the cost-utility analyses sensitivity analyses (SAs)

	Cost mean difference (£)	95% CI	Effect mean difference (QALYs)	95% CI	ICER (£)	Probability cost-effective at £20,000 WTP per QALY gained	Probability cost-effective at £30,000 WTP per QALY gained
ITT analyses							
SA1: ITT child QALY (UK) & NHS/PSS costs with optimum OSI delivery	-169.36	(-331.1, -7.62)	-0.0067	(-0.0154, 0.0021)	25,407.62	62%	42%
SA2: ITT child QALY (AU) & NHS/PSS costs with optimum OSI delivery	-169.36	(-331.1, -7.62)	-0.0023	(-0.0169, 0.0123)	74,736.31	76%	67%
SA3: ITT child QALY (UK) & societal costs	-52.58	(-353.87, 248.71)	-0.0067	(-0.0154, 0.0021)	7,887.78	32%	23%
SA4: ITT child QALY (AU) & societal costs	-52.58	(-353.87, 248.71)	-0.0023	(-0.0169, 0.0123)	23,201.84	52%	48%
SA5: ITT child QALY (UK) & societal costs, incl. missed school human capital costs	-35.30	(-753.01, 682.42)	-0.0067	(-0.0154, 0.0021)	5,295.28	39%	33%
SA6: ITT child QALY (AU) & societal costs, incl. missed school human capital costs	-35.30	(-753.01, 682.42)	-0.0023	(-0.0169, 0.0123)	15,576.01	49%	47%
SA7: ITT child-parent dyad QALYs (UK) & societal costs	-52.58	(-353.87, 248.71)	-0.0100	(-0.0281, 0.0082)	5,276.61	29%	24%
SA8: ITT child-parent dyad QALYs (AU) & societal costs	-52.58	(-353.87, 248.71)	-0.0042	(-0.0264, 0.018)	12,496.06	47%	44%

Complete case analyses							
SA9: Complete case child QALY (UK) & NHS/PSS costs	-39.68	(-336.49, 257.14)	0.0008	(-0.0154, 0.0169)	OSI dominates	60%	59%
SA10: Complete case child QALY (AU) & NHS/PSS costs	-39.68	(-336.49, 257.14)	0.0129	(-0.0131, 0.0390)	OSI dominates	82%	83%
PP analyses*							
SA11: PP child QALY (UK) & NHS/PSS costs with optimum OSI delivery	-229.24	(-467.99, 9.5)	-0.0008	(-0.0131, 0.0114)	273,403.30	90%	82%
SA12: PP child QALY (AU) & NHS/PSS costs with optimum OSI delivery	-229.24	(-467.99, 9.5)	0.0054	(-0.0147, 0.0256)	OSI dominates	92%	88%
SA13: PP child QALY (UK) & societal costs	-83.29	(-559.23, 392.66)	-0.0008	(-0.0131, 0.0114)	99,332.01	57%	56%
SA14: PP child QALY (AU) & societal costs	-83.29	(-559.23, 392.66)	0.0054	(-0.0147, 0.0256)	OSI dominates	71%	72%
SA15: PP child QALY (UK) & societal costs, incl. missed school human capital costs	38.64	(-1331.44, 1408.72)	-0.0008	(-0.0131, 0.0114)	TAU dominates	45%	45%
SA16: PP child QALY (AU) & societal costs, incl. missed school human capital costs	38.64	(-1331.44, 1408.72)	0.0054	(-0.0147, 0.0256)	7,124.85	53%	56%
SA17: PP child-parent dyad QALYs (UK) & societal costs	-83.29	(-559.23, 392.66)	0.0013	(-0.0219, 0.0246)	OSI dominates	63%	63%
SA18: PP child-parent dyad QALYs (AU) & societal costs	-83.29	(-559.23, 392.66)	0.0096	(-0.0194, 0.0385)	OSI dominates	78%	78%

Notes: * The per-protocol population included participants who had (i) received five or more treatment sessions, (ii) received the treatment they were originally assigned to, (iii) submitted their final questionnaire within 30 weeks of randomisation, and (iv) started treatment within 12 weeks of being randomised. OSI+TS=Online Support and Intervention for child anxiety plus therapist support; C-TAU=child mental health services treatment as usual.

Supplementary Table S17.3: Net Health Benefit (NHB) and Net Monetary Benefit (NMB) of the cost-utility analyses base-case and sensitivity analyses (SAs)

	NHB £20,000 WTP	**NHB £30,000 WTP**	**NMB £20,000 WTP**	**NMB £30,000 WTP**
CUA analyses – ITT				
Child QALY (UK value set- primary valuation) & NHS/PSS costs (base-case A)	-0.002	-0.004	-47.44	-114.10
Child QALY (AU value set- secondary valuation) & NHS/PSS costs (base-case B)	0.002	0.001	40.55	17.89
CUA analyses – PP				
Child QALY (UK value set- primary valuation) & NHS/PSS costs (base-case A)	0.006	0.004	126.19	117.81
Child QALY (AU value set- secondary valuation) & NHS/PSS costs (base-case B)	0.013	0.010	251.43	305.66
ITT analyses				
SA1: ITT child QALY (UK) & NHS/PSS costs with optimum OSI delivery	0.002	-0.001	36.05	-30.61
SA2: ITT child QALY (AU) & NHS/PSS costs with optimum OSI delivery	0.006	0.003	124.04	101.38
SA3: ITT child QALY (UK) & societal costs	-0.004	-0.005	-80.74	-147.39
SA4: ITT child QALY (AU) & societal costs	0.0004	-0.001	7.26	-15.41
SA5: ITT child QALY (UK) & societal costs, incl. missed school human capital costs	-0.005	-0.005	-98.02	-164.67
SA6: ITT child QALY (AU) & societal costs, incl. missed school human capital costs	-0.001	-0.001	-10.03	-32.69

SA7: ITT child-parent dyad QALYs (UK) & societal costs	-0.007	-0.008	-146.71	-246.35
SA8: ITT child-parent dyad QALYs (AU) & societal costs	-0.002	-0.002	-31.57	-73.65
Complete case analyses				
SA9: Complete case child QALY (UK) & NHS/PSS costs	0.003	0.002	55.68	63.68
SA10: Complete case child QALY (AU) & NHS/PSS costs	0.015	0.014	297.68	426.68
PP analyses				
SA11: PP child QALY (UK) & NHS/PSS costs with optimum OSI delivery	0.011	0.007	212.47	204.09
SA12: PP child QALY (AU) & NHS/PSS costs with optimum OSI delivery	*0.017*	0.013	337.71	391.94
SA13: PP child QALY (UK) & societal costs	0.003	0.002	66.52	58.13
SA14: PP child QALY (AU) & societal costs	0.010	0.008	191.75	245.99
SA15: PP child QALY (UK) & societal costs, incl. missed school human capital costs	-0.003	-0.002	-55.41	-63.79
SA16: PP child QALY (AU) & societal costs, incl. missed school human capital costs	0.003	0.004	69.83	124.06
SA17: PP child-parent dyad QALYs (UK) & societal costs	0.005	0.004	109.77	123.02
SA18: PP child-parent dyad QALYs (AU) & societal costs	0.014	0.012	274.63	370.30

Notes: NHB=Net Health Benefit; WTP=Willingness To Pay: NMB: Net Monetary Benefit. OSI+TS=Online Support and Intervention for child anxiety plus therapist support; C-TAU=child mental health services treatment as usual.

Supplementary Table S17.4: Results of the cost-effectiveness analysis sensitivity analyses

	Cost mean difference (£)	95% CI	Effect mean difference (reverse-score CAIS-P at 26 week)	95% CI
ITT analyses				
SA19: ITT child reverse-score CAIS-P at 26 week & NHS/PSS costs with optimum OSI delivery	-169.36	(-331.1, -7.62)	0.735	(-1.67, 3.14)
SA20: ITT child reverse-score CAIS-P at 26 week & societal costs	-52.58	(-353.87, 248.71)	0.735	(-1.67, 3.14)
SA21: ITT child reverse-score CAIS-P at 26 week & societal costs, incl. missed school human capital costs	-35.30	(-753.01, 682.42)	0.735	(-1.67, 3.14)
PP analyses				
SA22: PP child reverse-score CAIS-P at 26 week & NHS/PSS costs with optimum OSI delivery	-229.24	(-467.99, 9.5)	0.208	(-2.96, 3.38)
SA23: PP child reverse-score CAIS-P at 26 week & societal costs	-83.29	(-559.23, 392.66)	0.208	(-2.96, 3.38)
SA24: PP child reverse-score CAIS-P at 26 week & societal costs, incl. missed school human capital costs	38.64	(-1331.44, 1408.72)	0.208	(-2.96, 3.38)

Notes: OSI+TS=Online Support and Intervention for child anxiety plus therapist support; C-TAU=child mental health services treatment as usual.

Cost-utility analysis results (primary analysis)

In the intention-to-treat (ITT) base-case CUAs, OSI+TS was cost saving while the mean difference in QALYs across trial arms approximated to zero (Table S17.1, ITT base-case A and B, and Table S17.3). There were not statistically significant differences in QALYs across the trial arms, but the almost null difference slightly varied depending on the value set used to obtain utilities from the CHU-9D instrument. The adjusted mean difference equalled to -0.0067 (95% CI: -0.0154, 0.0021) QALYs when using the UK adult value set (primary valuation), and was -0.0023 (95% CI: -0.0169, 0.0123) QALYs when using the Australian adolescent value set (secondary valuation). After controlling for baseline costs, OSI+TS costed £85.87 (95% CI: -248.06, 76.31) less than C-TAU, taking the NHS and PSS perspective (which included both treatment costs and child wider NHS and PSS costs), but the difference was not statistically significant. The 20,000 bootstrapped pairs of incremental costs and incremental QALYs were plotted in the CE plane for the two value sets (Figure S17.1, quadrants (1) and (2), graphs (a) in both quadrants). The majority of bootstrapped estimates were below the £20,000 WTP threshold for the Australia adolescent value set, suggesting that OSI+TS is likely to be cost-effective, whereas most were above the threshold for the UK adult value set. This was more clearly summarised by the CEACs (Figure S17.1, quadrants (1), and (2), graphs (b) in both quadrants), with the probability of cost-effectiveness at the £20,000 WTP threshold being 35% for the UK adult value set and 60% for the Australia adolescent value set.

The per-protocol (PP) group included 195 participants, 111 in OSI+TS and 84 in C-TAU. In the PP base-case CUAs, OSI+TS was highly likely to be cost-effective (Table S17.1, PP base-case A and B, and Table S17.3), independently from the value set used to value the CHU-9D. Taking the NHS and PSS perspective, OSI+TS cost £142.96 (95% CI: -383.77, 97.84) less than C-TAU, and the difference was not statistically significant. The OSI+TS arm lost a non-statistically significant amount of QALYs equal to 0.0008 (95% CI: -0.0131, 0.0114) when using the UK adult value set, while it gained a non-statistically significant amount of 0.0054 (95% CI: -0.0147, 0.0256) QALYs when using the Australia adolescent value set, meaning that OSI+TS dominated C-TAU in this last specific scenario. When considering the joint distributions of costs and effects, most bootstrapped estimates fell below the £20,000 WTP threshold in the CE planes (Figure S17.2, quadrants (3) and (4), graphs (a) in both quadrants) and the probability of OSI+TS being cost-effective compared to C-TAU was 78% and 86% for the UK adult and Australia adolescent value sets respectively (Figure S17.2, quadrants (3) and (4), graphs (b) in both quadrants).

Results from the sensitivity analyses are summarised in Table S17.2 and S17.3 for the CUA and CEA respectively. When assuming that the optimum delivery of OSI+TS was achieved, which is expected to happen when therapists achieve familiarity with the OSI+TS treatment delivery (Table S17.2, SA1 and SA2), the probability that OSI+TS was cost-effective was 62% and 76% for UK adult and Australia adolescent value sets respectively, based on the UK NICE WTP threshold of £20,000 per QALY gained. OSI+TS would cost £169.36 (95% CI: -331.1, -7.62) less than C-TAU and this cost difference was statistically significant, while the mean difference in QALYs would be close to zero and still not statistically significant. When taking a societal perspective on costs (SA3 to SA6) and then on both costs and outcomes (i.e. child-parent dyad QALYs) (SA7 and SA8), cost savings associated with OSI+TS reduced but were not statistically significant, while mean differences in QALYs remained close to zero and not statistically significant. When the joint distribution of costs and effects was considered, with costs included from the societal perspective, sensitivity analyses using the UK value set (SA3 and SA5) suggested that that OSI-+TS was not likely to be cost-effective, while the probability of cost-effectiveness ranged between 49-52% when the Australia adolescent value set was used (SA6 and SA4 respectively), suggesting that both treatments are likely to achieve comparable outcomes. Complete case analyses for both value sets (SA9 and SA10) suggested that OSI+TS was likely to be cost effective at UK NICE WTP threshold of £20,000 per QALY gained, with probabilities of 60% and 82% for or UK adult and Australia adolescent value sets respectively. Per-Protocol sensitivity analyses (Table S17.2, SA11 to SA18) using both value sets, suggest that OSI+TS was likely to be cost effective compared to C-TAU, with probabilities ranging from 57% to 90% for the UK value set (SA11. SA13, and Sa17) and from 53% to 92% for the Australia adolescent value set (SA12, SA14, SA16, SA18) at the UK NICE WTP threshold of £20,000 per QALY gained. The only exception was SA15 (UK value set) where the probability that OSI+TS was cost-effective was only 45%.

Cost-effectiveness analysis results (secondary analysis)

In the ITT base-case CEA (Table S17.1), OSI+TS dominated C-TAU, as costs were £85.87 (95% CI -248.06, 76.31) lower and CAIS-P at 26 weeks improved by 0.74 (95% CI: -1.67, 3.14). It also dominated C-TAU in the PP base-case CEA, as costs were £142.96 (95% CI -383.77, 97.84) lower and CAIS-P at 26 weeks improved by 0.21 (95% CI: -2.98, 3.37). When considering the joint distribution of costs and effects in the ITT analysis (Figure S17.2, panel 1)), the probability that OSI+TS was cost-effective compared to C-TAU increased from 85.4% to 87.4% as the willingness-to-pay for a unit improvement in CAIS-P increased from £0 to £30, for then

decreasing to 74.9% at a willingness-to-pay of £1,000, remaining stable at 74% for higher willingness-to-pay. When considering the joint distribution of costs and effects in the PP CEA analysis (Figure S17.2, panel 2)), the probability that OSI+TS was cost-effective compared to C-TAU decreased from 91% to 58.1% when 87.4% as the willingness-to-pay for a unit improvement in CAIS-P increased from £0 to £1000 and remained stable at 58% for willingness-to-pay larger than £1,000. However, the maximum threshold value a decision maker is willing to pay for a unit improvement in the CAIS-P is unknown.

Results of the sensitivity analyses are presented in supplementary Table S17.4. OSI+TS dominated C-TAU in all of the ITT CEA sensitivity analyses (SA19 to SA21) as OSI+TS remained cost saving in all scenarios and the outcome improvement was unchanged in all SAs. In the per-protocol CEA sensitivity analyses (SA22 to SA24), OSI-+TS dominated C-TAU in all but one of the scenarios, i.e. where a societal perspective was taken including child missed school human capital costs (SA24).

Discussion of health economic results

This is the first study analysing the cost-effectiveness of a digitally augmented psychological treatment, compared to treatment as usual for child anxiety problems. OSI+TS was found to be cost-saving in all of our base-case CUAs (Table S17.1 and Table S17.3) and the vast majority of our sensitivity analyses (Table S17.2 and Table S17.3), but the differences were not statistically significant. Similarly, the mean QALY difference across the trial arms approximated to zero throughout the analyses, was not statistically significant, but was sensitive to the different value sets (UK adult population and Australian adolescents) used to value the CHU-9D instrument from which QALYs were derived. When considering the joint distribution of costs and effects, OSI+TS was found to be cost-effective in three of our four CUA base-case analyses (Table S17.1 and Table S17.3) and the majority of our sensitivity analyses (TableS17.2), but was not cost-effective in the ITT analysis using the CHU9D UK adult value set. In secondary analyses, OSI+TS dominated C-TAU in both of the base-case (Table S17.1 and Figure S17.2) and sensitivity (Table S17.4) CEAs, as it was cost-saving and reduced anxiety problems on the CAIS-P. When looking at the joint distribution of costs and effects (Tables S17.1 and Figure S17.2), the probability of OSI+TS being cost-effective compared to C-TAU ranged from more than 80% to about 60%, when the policy-maker willingness to pay increased from £0 to £1,000+ per unit improvement on

the CAIS-P. However, the maximum threshold value a decision maker is willing to pay for a unit improvement in the CAIS-P is not established.

While overall the primary analyses results (CUAs), which are those more likely to inform policy-making, indicated that OSI+TS may be likely to be cost-effective under certain scenarios, they need to be considered with caution, due to their sensitivity to the underlying values sets used for deriving QALYs, and the large uncertainty surrounding the cost-effectiveness estimates.

In relation to the value set used to derive QALYs, we presented both the UK adult set (primary valuation) and the Australian adolescent value set (secondary valuation) as part of our base-case analyses, because no guidelines are available as to which is more appropriate to use. The two value sets were derived using different preference elicitation methods (standard gamble for the UK adult valuation; best-worst scaling for the Australia adolescents valuation), and systematic differences between adults' and adolescents' preferences were initially attributed to the different methods [29]. However, it was then shown that they persisted when the same method of preference elicitation (i.e. best-worst scaling) was applied to both populations, concluding that adults, in general, weighted less on impairments in the CHU-9D mental health domains (i.e., worried, sad, annoyed) and weighted more moderate to severe levels of pain relative to adolescents [30]. Given the importance of the CHU-9D mental health domains in this trial, it may be that the Australian value set may be more appropriate on this occasion, but without any further methodological research, this interpretation can only remain speculative, given also the fact that the children in the Co-CAT trial are pre-adolescent. More methodological research is warranted on the impact of different value sets, given the importance for policy recommendations. However, it has to be noted that, in this study, with both value sets the differences in QALYs approximated zero and were not statistical significant, suggesting no differential impact of the two treatments on health-related quality of life of the participants. This specific health economic outcome, in isolation, keeps in line with the clinical outcome results of non-inferiority of OSI+TS compared to C-TAU.

Our cost-effectiveness estimates were characterised by large levels of uncertainty, which may explain why minimal and non-statistically significant changes in the mean differences in QALYs across the two trial arms (such as those due to the different value sets for the CHU-9D), made OSI+TS not likely to be cost-effective in the ITT analyses using the UK value sets. However, it has to be kept in mind that the primary objective of an

economic evaluation is not hypothesis testing, but rather the estimation of the incremental cost-effectiveness ratio alongside the pertinent representation of uncertainty around those estimates [31]. This is why we are interested in the joint distribution of costs and effects, rather than the individual test of the mean differences in costs and effects.

The CoCAT trial was a non-inferiority randomised controlled trial powered on the primary clinical outcome. However, the economic analyses attempted to identify whether OSI+TS was a cost-effective intervention compared to C-TAU, as it is standard in economic evaluations alongside non-inferiority trial [32]. There are no well established guidelines for economic evaluations within a non-inferiority clinical trial, with the only clear advice being to present both ITT and per-protocol results with equal importance [19], which we have followed. This is because although ITT analysis is generally conservative in superiority trials, as the inclusion of dropouts and protocol violators makes the two treatment groups more similar, the same is not true in inferiority trials. Any blurring of the difference between the two groups increases the chance of achieving equivalence, while the trial may in fact have had poor discriminatory power, meaning the ITT analysis is no longer conservative. Including only patients who met the per-protocol criteria should enhance any differences between the two treatment groups, decreasing the chance of declaring equivalence [19,20]. We found that OSI+TS was highly likely to be cost-effective in the PP base-case CUA analyses, and likely to be cost-effective in all but one of our PP CUA SAs, although sample sizes were reduced in both arms.

Our economic analyses present some strengths. Unlike many economic evaluations alongside clinical trials, we considered the spill over effects of OSI+TS and C-TAU on parents and the wider society by collecting information on their health-related quality of life, primary and secondary healthcare use, social care use, medication use, time in spent while taking part in the treatment, associated travel time and direct costs for this resource utilisation, as well as missed days at work due to their child's anxiety (loss of productivity). We utilised this information to estimate the cost-effectiveness of OSI+TS considering costs from a societal perspective, i.e. including all child and parent costs, which is an important sensitivity analysis to be conducted in light of the fact that the impact of poor mental health extends beyond the individual experiencing mental health problems to include consequences on the family and the society at large. Furthermore, in a sensitivity analysis, we attempted to estimate and included the human capital cost of child missed school in terms of loss in lifetime earnings, going beyond the usual way of costing them simply as opportunity cost for the school/educational

systems. Finally, we undertook a comprehensive analytical approach that followed the established guidelines [17], and conducted extensive sensitivity analyses to explore uncertainties around assumptions made in the base-case analyses and test the robustness of the results.

The health economic analyses also need to be considered in light of some potential weaknesses. Firstly, follow-up questionnaires were planned for 14 weeks and 26 weeks post-randomisation. However, in some instances actual follow-up time differed from this. The per-protocol analyses accounted for this, as one of the criteria was achieving expected follow-up time, with the results favouring OSI+TS over C-TAU. Secondly, when we estimated the human capital loss, the applied model and the calibration method were relatively simple and relied on strong assumptions. For example, child anxiety may mainly occur in a selected socio-economic group [33]. Hence, the UK median income may not be an accurate value to generate the lifetime earnings of children with anxiety problems. Future work may consider more advanced and sophisticated methods to calibrate the models. Furthermore, the value of children's forgone time and how and whether to account for it in economic evaluations is a large unexplored area and more methodological research and guidelines would be welcome [34]. Thirdly, as with all economic evaluations alongside randomised controlled trials, respondents may suffer from recall bias [35]. Ideally, we would have drawn on administrative data to identify participant's accurate resource use. In practice this is hardly feasible given the burden of accessing such data and problems associated with the management, curation, processing and use of such data [36]. Finally, economic evaluations alongside non-inferiority randomised controlled trials suffer in general from a lack of appropriate guidelines, and future methodological research is warranted to further explore these important issues, given the importance it has for policy recommendations.

In conclusion, our economic results are encouraging as they suggest that OSI+TS may be likely to represent a cost-effective intervention for the treatment of anxiety problems in preadolescent children, when compared to C-TAU, under certain assumptions/perspectives. However, our cost-effectiveness results should be considered with caution, due to their sensitivity to the underlying values sets used for deriving QALYs, and the large uncertainty surrounding the cost-effectiveness estimates.

Supplementary material S18

IT charges

An integral part of the OSI intervention is the IT platform that hosts OSI. In our economic analyses, we have not included any IT charges. As a novel digitally-augmented intervention, OSI does not have a confirmed IT service fee yet. However, similarly to all digital interventions that may be expanded at scale, it is expected that the per-patient IT commercial price of the OSI IT platform will decrease as the number of users increases, due to benefits arising from economies of scale and competition among potential suppliers. Starting from this assumption, the maximum fee of £40 per patient was an "educated guess" based on preliminary informal discussions with potential IT companies that may support the OSI IT platform, should the OSI+TS treatment be rolled-out at scale. To explore how the cost-effectiveness of OSI may be impacted by different values of the OSI IT fee per-patient, we repeated the base case analyses (i.e. ITT and PP approaches for CUA according to the child NHS & PSS perspective) assuming that the IT charges might vary between £0-£40. We then reported, in Figure S18.1, the probability of OSI being cost-effective for each IT charge in the interval £0-£40.

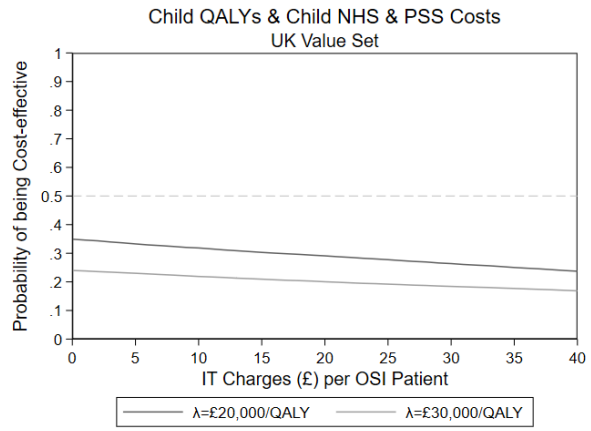
The base case ITT analyses in Figure S17.1 indicated that, even without IT charges, the probability that OSI was cost-effective was low, at 35% given a £20,000/QALY threshold, when the UK value set was used to obtain utility scores from the CHU-9D measure. Imposing IT charges ranging £0-£40 would further reduce the chance of OSI being cost-effective (Figure S18.1, top left panel, base-case A). In contrast, results that used the Australian value set to derive CHU-9D utility scores could tolerate a £40 IT charge while remaining cost-effective at 50% given a £20,000/QALY threshold (Figure S18.1, top right panel, base-case B). The tolerance would be £20 when considering a £30,000/QALY threshold.

The base case PP analyses in Figure S17.1 indicated that, independently from the value set used to value the CHU-9D measure, OS+TS was likely to be cost-effective compared with C-TAU. These results would be maintained also when adding potential IT fees ranging from £0-£40 (Figure S18.1, bottom left and right panels, base-cases A and B). In particular, when applying our hypothesised maximum IT charge of £40 per-patient, the likelihood of OS+TS remaining cost-effective would be about 70% for both £20,000/QALY and £30,000/QALY thresholds, when the UK value set is used (Figure S18.1, bottom left panel, base-case A). When using the Australia value set, the probability of OSI+TS remaining cost-effective would still hold and would be at around 80% for both thresholds of £20,000/QALY and £30,000/QALY (Figure S18.1, bottom right panel, base-case B).

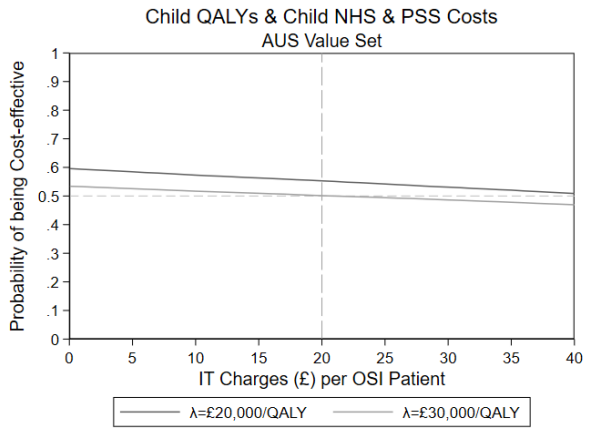
All of these results, however, are only exploratory and need to be considered with caution, because they are based on IT charges that are, to some extent, arbitrary and will remain so until a definite commercial price has been agreed

Supplementary Figure S18.1: Cost-effectiveness of OSI+TS compared to C-TAU at potential IT charges ranging from £0 to £40 per patient

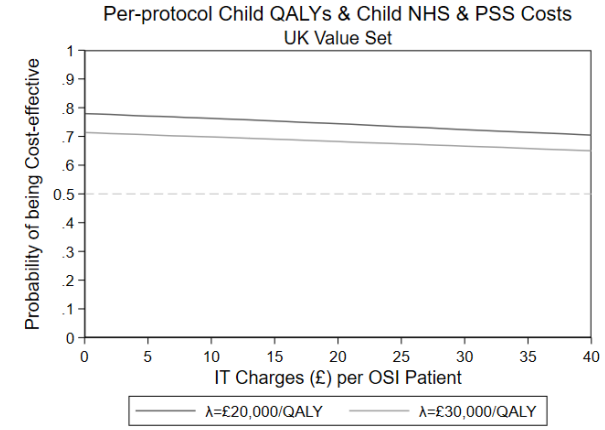
(1) ITT child QALYs (UK value set) and child NHS/PSS costs (base-case A)



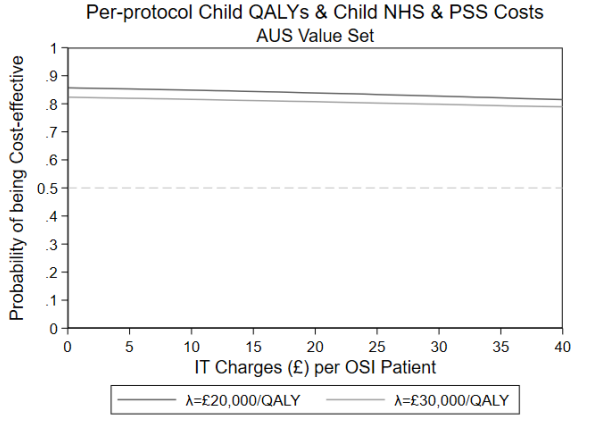
(2) ITT child QALYs (Australia value set) and child NHS/PSS costs (base-case B)



(3) PP child QALYs (UK value set) and child NHS/PSS costs (base-case A)



(4) PP child QALYs (Australia value set) and child NHS/PSS cost (base-case B)



Notes: ITT: intention-to-treat; PP: Per-protocol; UK: United Kingdom; AUS: Australia; OSI+TS=Online Support and Intervention for child anxiety plus therapist support; C-TAU=child mental health services treatment as usual.

References for the health economic supplementary materials and tables

1. NHS England. National Cost Collection for the NHS. 2022. [Available from: https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/] (accessed 11/12/2023).
2. Jones KC, Burns A. Unit Costs of Health and Social Care 2021, Personal Social Services Research Unit, University of Kent, Canterbury. 2021.
3. NHS Business Services Authority. Prescription Cost Analysis – England 2020/21. 2021.
4. Gov.uk. NHS prescription charges from 1 April 2020. [Available from: https://www.gov.uk/government/speeches/nhs-prescription-charges-from-1-april-2020] (accessed 11/12/23).
5. Gov.uk. School funding statistics. 2023. [Available from: https://explore-education-statistics.service.gov.uk/find-statistics/school-funding-statistics] (accessed 02/10/2023).
6. Long R. The school day and year. 2021.
7. Psacharopoulos G, Collis V, Patrinos HA, Vegas E. The COVID-19 cost of school closures in earnings and income across the world. Comparative Education Review. 2021;65(2):271-87.
8. Office for National Statistics. Measures of employee earnings based on SOC 2020, UK: 2021. Earnings and hours worked, all employees: ASHE Table 1.5a 2022 [Available from: https://www.ons.gov.uk/releases/annualsurveyofhoursandearnings2021basedonsoc2020] (accessed 02/10/2023).
9. Personal Social Services Research Unit. Unit Costs of Health and Social Care 2021.
10. Shemilt I, Thomas J, Morciano M. A web-based tool for adjusting costs to a specific target currency and price year. Evid Policy. 2010;6(1):51-9.
11. Gov uk. School funding statistics 2023 [Available from: https://explore-education-statistics.service.gov.uk/find-statistics/school-funding-statistics] (accessed 02/10/2023).
12. Welch F. Human Capital Theory - Education, Discrimination, and Life Cycles. Am Econ Rev. 1975;65(2):63-73.
13. Office for National Statistics. Employee earnings in the UK: 2021 2021 [Available from: https://www.ons.gov.uk/employmentandlabourmarket/peopleinwork/earningsandworkinghours/bulletins/annualsurveyofhoursandearnings/2021] (accessed 02/10/2023).
14. Creswell C, Violato M, Fairbanks H, White E, Parkinson M, Abitabile G, et al. Clinical outcomes and cost-effectiveness of brief guided parent-delivered cognitive behavioural therapy and solution-focused brief therapy for treatment of childhood anxiety disorders: a randomised controlled trial. Lancet Psychiat. 2017;4(7):529-39.
15. Hobbs FDR, Bankhead C, Mukhtar T, Stevens S, Perera-Salazar R, Holt T, et al. Clinical workload in UK primary care: a retrospective analysis of 100 million consultations in England, 2007-14. Lancet. 2016;387(10035):2323-30.
16. Kuyken W, Ball S, Crane C, Ganguli P, Jones B, Montero-Marin J, et al. Effectiveness and cost-effectiveness of universal school-based mindfulness training compared with normal school provision in reducing risk of mental health problems and promoting well-being in adolescence: the MYRIAD cluster randomised controlled trial. Evid-Based Ment Heal. 2022;25(3):99-109.
17. Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, et al. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) statement: updated reporting guidance for health economic evaluations. International journal of technology assessment in health care. 2022;38(1):e13.
18. Thorn JC, Davies CF, Brookes ST, Noble SM, Dritsaki M, Gray E, et al. Content of Health Economics Analysis Plans (HEAPs) for Trial-Based Economic Evaluations: Expert Delphi Consensus Survey. Value Health. 2021;24(4):539-47.
19. Bosmans JE, De Bruijne MC, Van Hout HP, Hermens ML, Adèr HJ, Van Tulder MW. Practical guidelines for economic evaluations alongside equivalence trials. Value in Health. 2008;11(2):251-8.
20. Rhodes S, Richards DA, Ekers D, McMillan D, Byford S, Farrand PA, et al. Cost and outcome of behavioural activation versus cognitive behaviour therapy for depression (COBRA): study protocol for a randomised controlled trial. Trials. 2014;15.
21. European Medicines Agency. European Medicines Agency Committee For Medicinal Products For Human Use (CHMP): guideline on the choice of the non-inferiority margin. 2005.
22. Faria R, Gomes M, Epstein D, White IR. A guide to handling missing data in cost-effectiveness analysis conducted within randomised controlled trials. Pharmacoeconomics. 2014;32(12):1157-70.
23. Rubin D. Multiple imputation for nonresponse in surveys (Vol.81). John Wiley & Sons. 2004.
24. Leurent B, Gomes M, Faria R, Morris S, Grieve R, Carpenter JR. Sensitivity analysis for not-at-random missing data in trial-based cost-effectiveness analysis: a tutorial. Pharmacoeconomics. 2018;36(8):889-901.

25. Fenwick E, Marshall DA, Levy AR, Nichol G. Using and interpreting cost-effectiveness acceptability curves: an example using data from a trial of management strategies for atrial fibrillation. BMC health services research. 2006;6(1):1-8.
26. National Institute for Health and Care Excellence. NICE health technology evaluations: the manual. Process and methods [PMG36]. 2022.
27. Consortium YHE. Net Health Benefit [online] 2016 [Available from: http://www.yhec.co.uk/glossary/net-health-benefit/ (accessed 06/12/2023)
28. Consortium YHE. Net Monetary Benefit [online] 2016 [Available from: https://yhec.co.uk/glossary/net-monetary-benefit/ (accessed 06/12/2023)
29. Ratcliffe J, Flynn T, Terlich F, Stevens K, Brazier J, Sawyer M. Developing Adolescent-Specific Health State Values for Economic Evaluation An Application of Profile Case Best-Worst Scaling to the Child Health Utility 9D. Pharmacoeconomics. 2012;30(8):713-27.
30. Ratcliffe J, Huynh E, Stevens K, Brazier J, Sawyer M, Flynn T. Nothing about us without us? A comparison of adolescent and adult health-state values for the child health utility-9D using profile case best–worst scaling. Health Economics. 2016;25(4):486-96.
31. Gray AM, Clarke PM, Wolstenholme JL, Wordsworth S. Applied methods of cost-effectiveness analysis in healthcare: OUP Oxford; 2010.
32. Wang H-I, Wright B, Tindall L, Cooper C, Biggs K, Lee E, et al. Cost and effectiveness of one session treatment (OST) for children and young people with specific phobias compared to multi-session cognitive behavioural therapy (CBT): results from a randomised controlled trial. BMC Psychiatry. 2022;22(1):1-12.
33. Reiss F. Socioeconomic inequalities and mental health problems in children and adolescents: a systematic review. Soc Sci Med. 2013;90:24-31.
34. Andronis L, Maredza M, Petrou S. Measuring, valuing and including forgone childhood education and leisure time costs in economic evaluation: Methods, challenges and the way forward. Soc Sci Med. 2019;237:112475.
35. Petrou S, Gray A. Economic evaluation alongside randomised controlled trials: design, conduct, analysis, and reporting. BMJ. 2011;342.
36. Astle DE, Moore A, Marryat L, Viding E, Mansfield KL, Fazel M, et al. We need timely access to mental health data: implications of the Goldacre review. The Lancet Psychiatry. 2023;10(4):242-4.

Example search terms

PsycINFO 1806 to present (26/01/23)		
Search Number	**Search Terms**	**Number of Results**
1	(child* or youth* or adolescen* or preadolescen* or paediatric* or pediatric* or peadiatric* or boy or boys or girl or girls or preteen* or pre-teen* or teen* or young or preschool* or student* or offspring or toddler* or minor* or pubescen* or school* or "junior high" or "senior high").ti,ab.	1700241
2	exp parents/	132016
3	caregivers/	34800
4	family/	58613
5	(parent* or family* or families or mother* or father* or matern* or patern* or care-giver* or caregiver* or carer or carers or stepparent* or step-parent*).ti,ab.	729770
6	2 or 3 or 4 or 5	737161
7	exp anxiety disorders/	57451
8	anxiety management/	1191
9	(anxio* or anxiet* or phobi* or agoraphobi* or panic or GAD or "selective mut*" or ocd or "obsessive compulsive disorder*" or "neurotic disorder*" or neurosis or neuroses).ti,ab.	276244
10	7 or 8 or 9	281147
11	exp cognitive behavior therapy/	25839
12	cognitive therapy/	13956
13	(CBT or "cognitive behaviour*" or "I-C/BT" or "cognitive behavior*" or "cognitive and behavi*" or "cognitive therap*" or "cognition therap*" or icbt* or i-cbt*).ti,ab.	62097
14	11 or 12 or 13	69254
15	exp randomized controlled trials/	1343
16	random sampling/	937
17	(RCT* or random*).ti,ab.	234420
18	15 or 16 or 17	234561
19	1 and 6 and 10 and 14 and 18	565