

Supplementary Materials

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.

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

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 Psacharopoulos⁷ 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 $PV(\cdot)$ 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 Psacharopoulos⁷ 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 Psacharopoulos⁷ 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.	Table 11.1. Cost per hour, including qualifications.

Item	Unit cost	Source	Notes
Social worker, children's services	£52.00	<p>https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-of-health-and-social-care-2021/ (Accessed 4 Jan 2023).</p> <p>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).</p>	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).

Item	Unit cost	Source	Notes
Breast cancer screening	£190	GenesisCare. 2023. Mammogram for breast screening. https://www.genescare.com/uk/diagnostics/imaging-scans/mammography (Accessed 20 Feb 2023).	Cost of a private mammogram starts from £190.
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.

Item	Unit cost	Source	Notes
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).
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.

Item	Unit cost	Source	Notes
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.
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.

Item	Unit cost	Source	Notes
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.
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.

Item	Unit cost	Source	Notes
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.
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.

Item	Unit cost	Source	Notes
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.
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.nhs.uk/statistical-collections/prescription-cost-analysis-england/prescription-cost-analysis-england-2020-21 (Accessed 02 Oct 2023)	Totals by BNF Chapters

Item	Unit cost	Source	Notes
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.
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

Item	Unit cost	Source	Notes
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

See attached file

Supplementary Materials S7

Health Economics Analysis Plan

See attached file

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 treatment arm for missing items and, when appropriate, also conditional on other characteristics (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

See attached file

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.

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

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

Items	Treatment Groups							
	OSI+TS				C-TAU			
	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.

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
<i>Total Supervision time (minutes)</i>	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.

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.

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.

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.

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.

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.

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.

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.

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

Cost Types	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 overall NHS & PSS cost	801.63	946.83	66.49	821.65	926.93	68.95	-20.02	(-206.03, 165.99)	0.83	-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)	<0.001			
Therapy cost	253.69	114.81	8.69	319.85	186.20	13.55	-66.16	(-98.02, -34.31)	<0.001			
Supervision cost	54.32	61.20	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, 140.60)	0.34
Secondary Care	240.29	613.12	44.28	255.24	745.30	54.30	-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	18.60	1.36	2.75	(-1.83, 7.32)	0.24	2.79	(-1.62, 7.21)	0.21
Child out-of-pocket	31.20	82.06	6.02	37.43	146.12	10.10	-6.23	(-29.35, 16.88)	0.60	-6.82	(-29.83, 16.19)	0.56
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, 591.40)	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	395.00	27.65	86.42	310.90	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	45.57	106.14	7.58	42.12	148.30	10.26	3.45	(-21.51, 28.4)	0.79	0.58	(-23.69, 24.85)	0.96
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, 73.30)	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)	<0.001			
Parent opportunity cost of travelling	14.46	38.28	2.67	15.40	46.25	3.19	-0.94	(-9.06, 7.17)	0.82	-2.78	(-10.29, 4.74)	0.47
Total societal cost												
Excluding missed school human capital cost	1462.31	1868.53	129.07	1363.93	1541.42	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	3955.07	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

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.

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

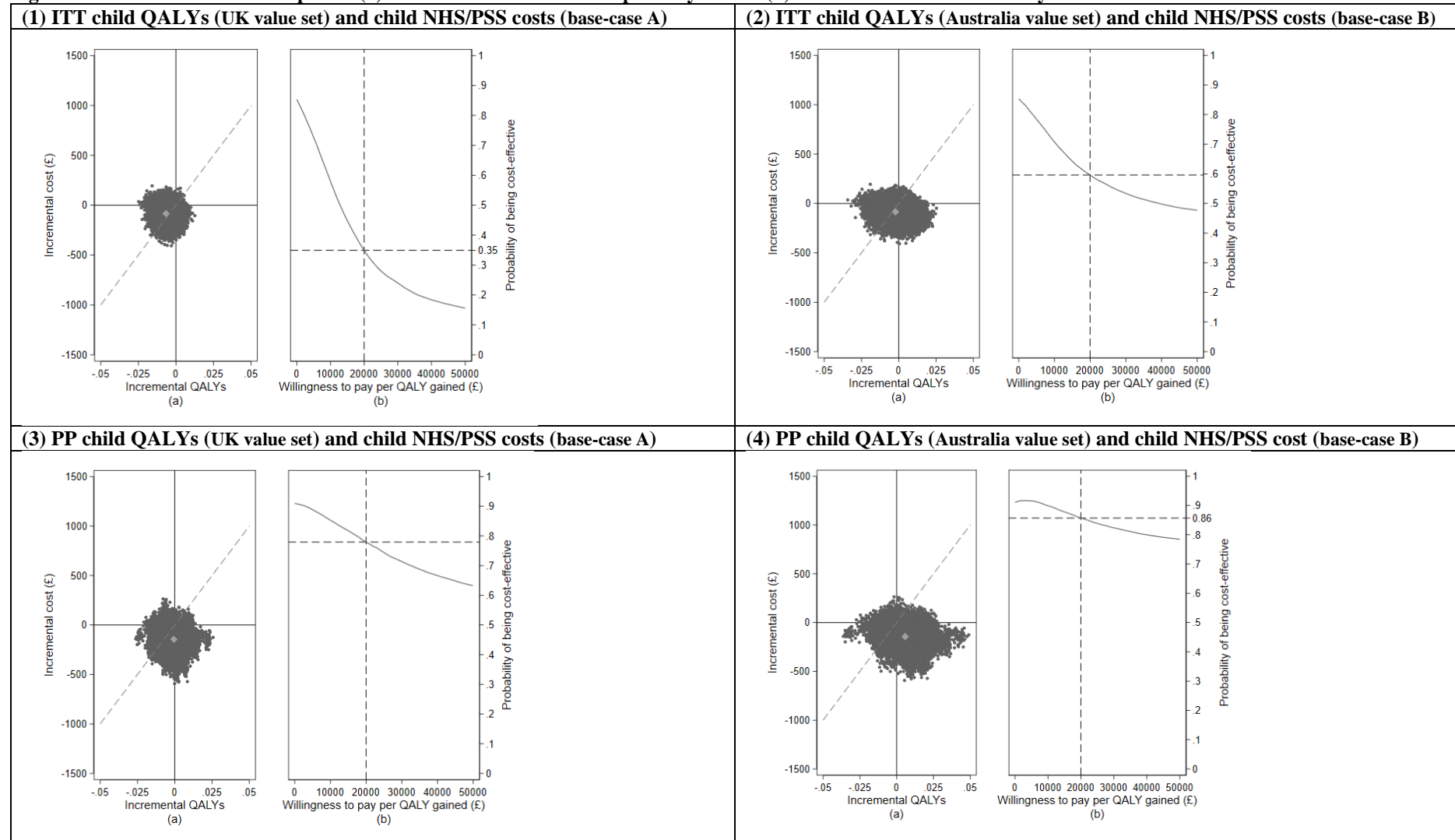
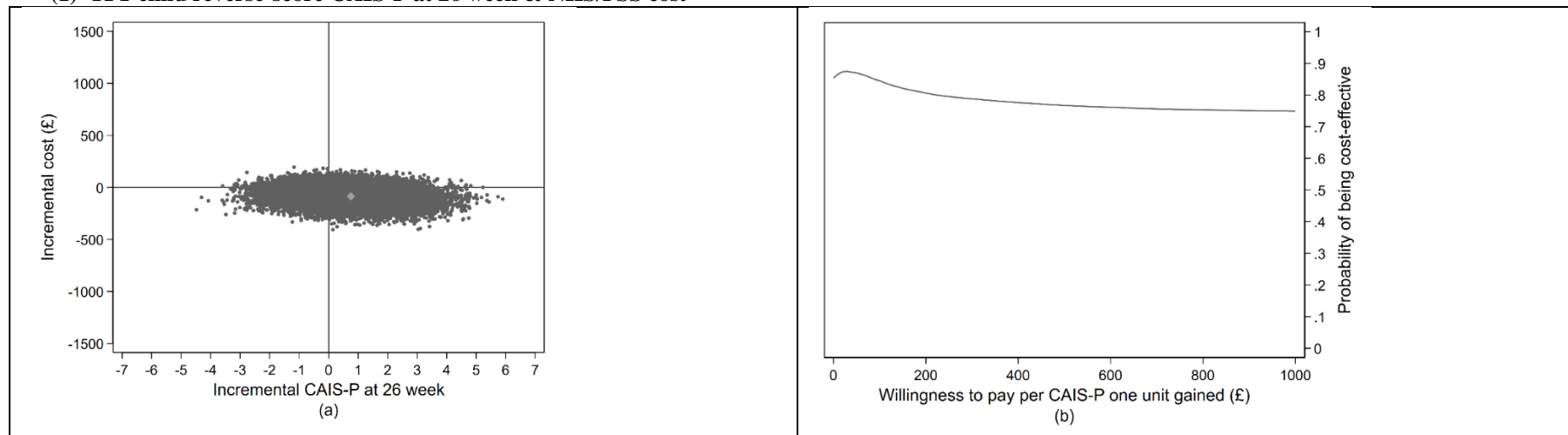


Figure S17.2: Cost-effectiveness planes (a) and cost-effectiveness acceptability curves (b) for the CEA base-case analyses

(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

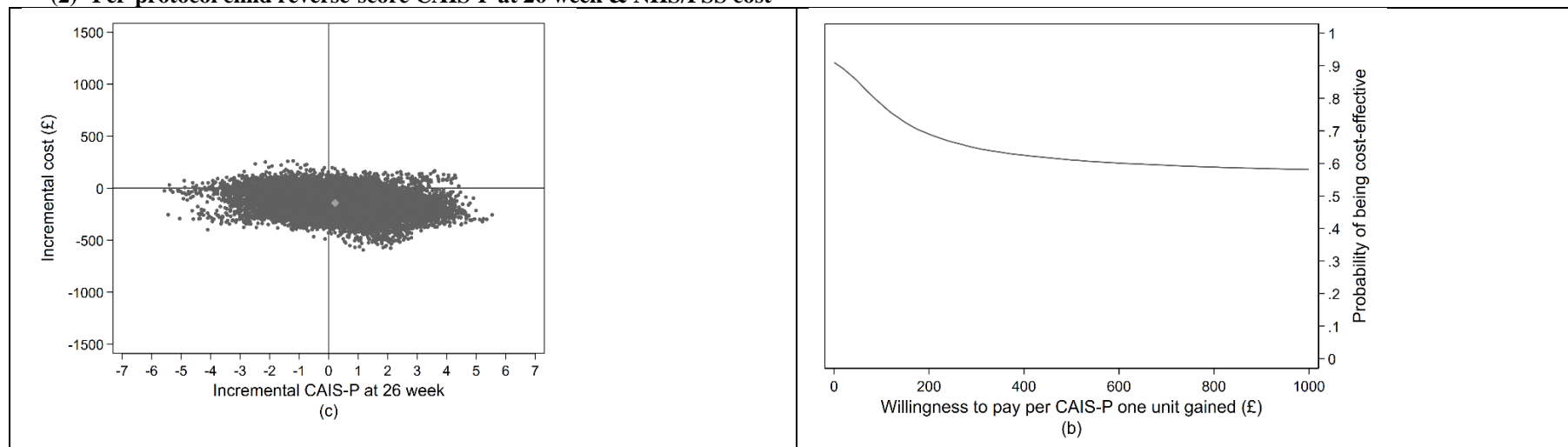


Table S17.2: Results of the cost-utility analyses sensitivity analyses (SAs)

	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.

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	<i>0.017</i>	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.				

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 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 (Table S17.2), 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 statistically 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.

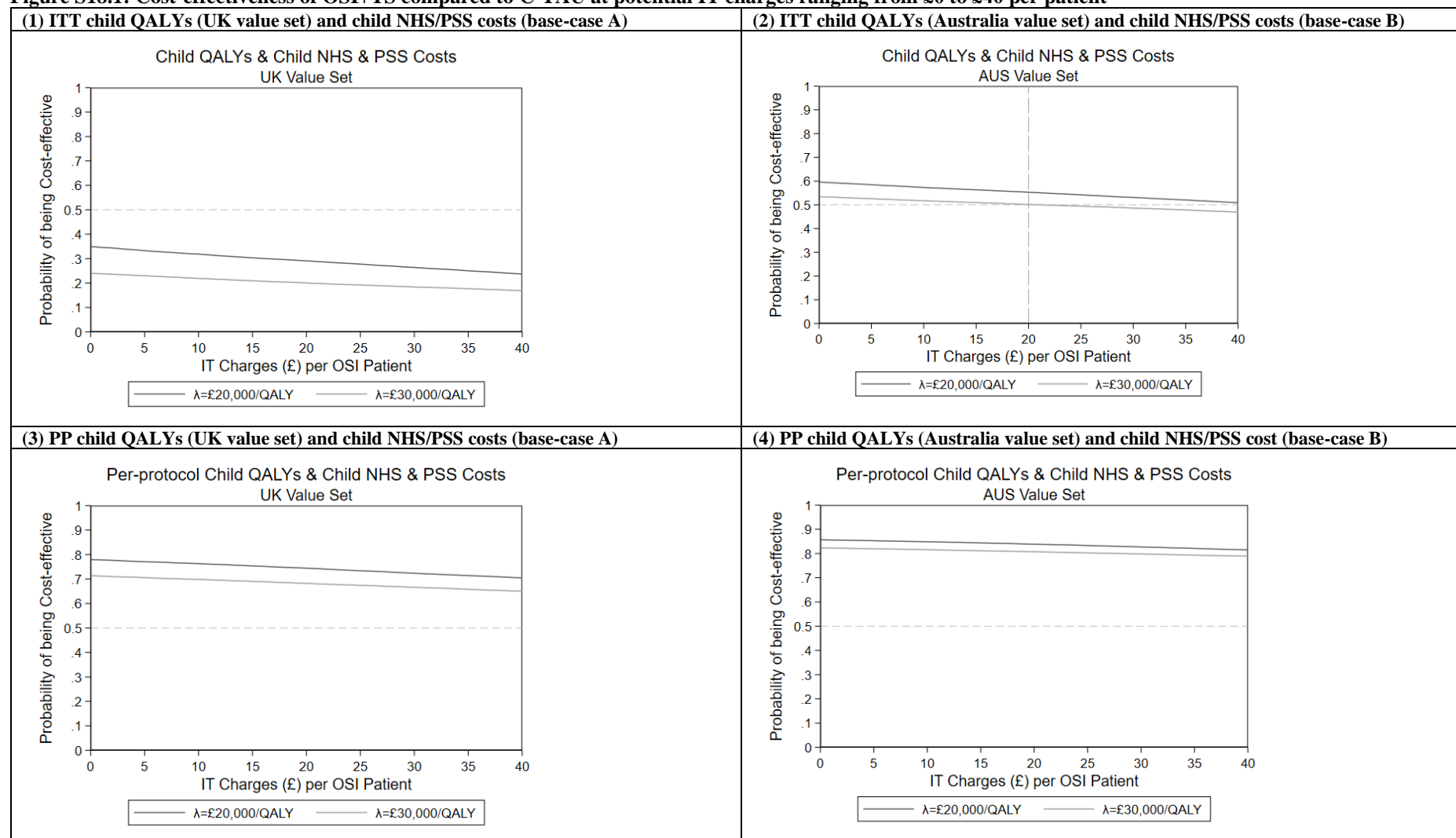
The base case ITT analyses in Figure S17.1 indicated that, even without IT charges, the probability that OSI was cost-effective was low, at 35% given a £20,000/QALY threshold, when the UK value set was used to obtain utility scores from the CHU-9D measure. Imposing IT charges ranging £0-£40 would further 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.

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



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.

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