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

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

Health Economics Analysis Plan

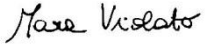
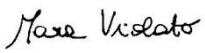
Co-CAT

Child Anxiety Treatment in the context of COVID-19

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

Essential items

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Optional items

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

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

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

References

1. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry. 2005;62(6):593-602.
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