CALM Research Protocol

The CALM trial: the clinical and cost-effectiveness of a guided self-help cognitive behavioural therapy intervention to reduce dental anxiety in children

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Glossary of frequently used abbreviations

CARIES-QC	A measure of child oral health-related quality of life
CBT	Cognitive behavioural therapy
CHU9D	Child Health Utility-9D – a measure of child health-related quality of life
CGI-I	Clinical Global Impressions: Improvement
CONSORT	Consolidated Standards of Reporting Trials
DA	Dental anxiety
DMFT	Decayed, missing and filled permanent teeth
DP	Dental professional
GA	General anaesthesia
GRC	Global Rating of Change
HRQoL	Health-related quality of life
HRA	Health Research Authority
MCDAS	Modified Child Dental Anxiety Scale
MCID	Minimal Clinically Important Difference
MDAS	Modified Dental Anxiety Scale
MRC	Medical Research Council
OHRQoL	Oral Health Related Quality of Life
PI	Principal Investigator
PPIE	Patient and public involvement and engagement
QALY	Quality Adjusted Life Year
RCT	Randomised controlled trial
SDCEP	Scottish Dental Clinical Effectiveness Programme
YTU	York Trials Unit

Table of Protocol Amendments

Version	Protocol section	Brief description of change
V2.0 22 March 2022	6.3	Clarification of initial assessment by dental professional.
	6.4	Clarification of screening process for dental anxiety.
	6.6	Re-ordering of inclusion and exclusion criteria to reflect the order dental professionals will assess potentially eligible patients.
	6.6	Removal of wording 'based on a screening question' in the inclusion criteria to ‘self-reported dental anxiety’ to allow other forms of assessment to be included.
	6.7.2	Removal of ‘cancelled’ from the list of ‘attended, cancelled and missed appointments’ based on advice from dental professionals on how these data are recorded.
	6.7.3	Removal of 'date of previous dental attendance prior to this one' from baseline participant characteristics, as this will not provide useful data due to the impact of the pandemic on routine dental attendance
	6.8.2	Removal of ‘cancelled appointments’ as in section 6.7.2 above.
	17	Appendix 1: Re-ordering of inclusion criteria and removal of ‘cancelled’ from the bottom table of the flowchart
V3.0 7 June 2022	6.6	Additional clarifcation to the inclusion criteria 'Found to require a course of treatment (categorised as level one complexity by NHS England) involving at least two additional visits' to include the wording 'and within the scope of practice of the CALM dental professional'. Additonal exclusion criteria: 'a sibling of a child patient recruited to the trial', to avoid contamination if siblings were recruited to different arms of the trial. Additional exclusion criteria in relation to the inclusion criteria added above: 'requiring procedures duing the course of treatment that fall outside of the scope of practice of the dental professional involved.'

The CALM trial: the clinical and cost-effectiveness of a guided self-help cognitive behavioural therapy intervention to reduce dental anxiety in children

1. Project details

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2. Research summary

Acronym	The CALM trial
Long title	The CALM trial: the clinical and cost-effectiveness of a guided self-help cognitive behavioural therapy intervention to reduce dental anxiety in children
Research question	What is the clinical and cost-effectiveness of a guided self-help cognitive behavioural therapy (CBT) intervention delivered to dentally anxious children by primary care dental professionals, compared to usual care?

Aim	The trial will determine the clinical and cost-effectiveness of a guided self-help cognitive behavioural therapy (CBT) intervention to reduce dental anxiety in children
Type of trial	Non-CTIMP
Study design	A multi-region, individually randomised, two-arm trial
Number and type of participants	600 children aged 9-16 years with self-reported dental anxiety We will also aim to recruit parent/carers of child participants to capture their dental anxiety. We anticipate 80% of parent/carers will agree to take part, (n=480) bringing an estimated total sample size of 1080.
Setting and sites	30 primary dental care sites across the UK
Study population	Children aged 9-16 years attending primary dental care sites in the UK and a parent/carer.
Intervention	A guided self-help CBT intervention 'Your teeth, you are in control' and accompanying parental resources delivered by the primary care dental professional
Primary Objective	To investigate the effect of the intervention on children's dental anxiety
Primary Outcome (outcome measure)	Modified Child Dental Anxiety Scale (MCDAS) score at 12 months post-randomisation.
Secondary Outcomes (outcome measure)	• Dental anxiety (MCDAS) measured at the end of the course of treatment. • Child health-related quality of life and oral health-related quality of life (Child Health Utility-9D and CARIES-QC) at the end of the course of treatment and 12 months post-randomisation. • Dental anxiety of the parent/carer (Modified Dental Anxiety Scale) measured at the end of the course of treatment and 12 months post-randomisation. • Attended, cancelled and missed appointments will be recorded during the course of treatment and for the 12 month follow up period. • The need for referral to secondary care and use of sedation or general anaesthesia (GA) will be recorded for children in both groups along with treatment provided.
Cost-effectiveness	Cost and outcome data for the economic evaluation will be collected at baseline, end of the course of treatment and 12 months post-randomisation via a combination of participant and parent/carer completed questionnaires, and data recorded by dental professionals. A cost-utility analysis (using CHU9D data) and a cost-effectiveness analysis (using MCDAS data) will be undertaken.

Process evaluation	A mixed-method process evaluation following MRC guidance will complement the outcome evaluation. The process evaluation will investigate implementation (particularly fidelity and adaptations made by different dental professionals), mechanisms of impact (including acceptability to patients, parent/carers and dental professionals, impact of parent/carer's dental anxiety as potential mediator) and context, such as how dental practice factors influence the delivery of the intervention and how patient factors such as deprivation influence how the intervention is experienced.
Estimated recruitment period	24 months (internal pilot trial during the first 12 months)
Estimated duration per participant	12 months
Estimated total trial duration	48 months

3. Abstract

Globally, around 13% of children are reported to experience dental anxiety (DA) and its associated negative impacts for the individual, their family and dental team. Children with DA frequently miss dental appointments, even when experiencing symptoms, consequently having poorer oral health and oral health-related quality of life (OHRQoL) than their non-anxious peers. Each year, thousands of children with DA are referred from primary dental care to secondary care to complete treatment. In 2018/19 there were 59,011 paediatric admissions to hospital for dental extractions costing around £50 million. In recent years, a low intensity cognitive behavioural therapy (CBT) based self-help approach has been recommended for management of childhood anxiety disorders. In 2015, NIHR funded the development and feasibility study of a guided self-help CBT resource to reduce DA in children referred to secondary care. The study confirmed key feasibility parameters and when used with 48 children, the guided self-help CBT approach reduced self-reported DA, improved OHRQoL, improved attendance and reduced need for general anaesthesia (GA). The effectiveness of this approach when delivered in primary dental care to reduce children's DA, now warrants investigation.

Aims and objectives

The aim is to establish the clinical and cost-effectiveness of a guided self-help CBT intervention to reduce DA in children attending primary dental care sites across the UK, compared to usual care.

Objectives are to:

- conduct an internal pilot trial
- determine effects of the intervention on DA, HRQoL, secondary care referrals, attendance and cost-effectiveness
- undertake a process evaluation.

Study design and timeline

This 4-year study is a multi-region, randomised controlled trial involving 600 children (aged 9-16 years), and where agreeable a parent/carer, in 30 primary dental care sites. A 12-month internal pilot will assess recruitment rates (of dental sites and participants) and engagement with the intervention, before progressing to the main trial. In each site, two dental professionals will take part, one randomly assigned to receive the CBT training and deliver the intervention and the other will deliver usual care. Children with DA attending these sites, in need of treatment, will be randomly allocated to be treated by the CBT dental professional or the control dental professional. Children will complete questionnaires relating to DA, OHRQoL and HRQoL before treatment, just after treatment completion and 12 months post-randomisation. Attendance rates, need for sedation/GA and the costs of the two different approaches will be compared. The primary outcome, DA, will be measured using the Modified Child Dental Anxiety Scale (MCDAS); scores will be compared between groups using a covariance pattern linear mixed model, adjusting for baseline value, other pertinent baseline covariates, time and an interaction between treatment group and time as fixed effects. A cost-utility analysis will estimate the mean differences in costs and quality-adjusted life years (QALYs), using the CHU9D to generate utilities.

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Impact and dissemination

The study will inform future guidelines, clinical practice and commissioning decisions for the management of children with DA. Findings will be published in high impact, peer-reviewed dental journals and presented at scientific meetings.

4. Aim of the study

The aim is to establish the clinical and cost-effectiveness of a guided self-help cognitive behavioural therapy intervention to reduce dental anxiety in children attending primary dental care sites across the UK, compared to usual care.

Objectives of the RCT are to:

- Conduct an internal pilot trial to assess:
    - trial feasibility
    - recruitment rates (of dental sites and participants)
    - dental professional and participant engagement with the intervention
- Investigate the effect of the intervention on DA (of child and parent/carer), health-related quality of life (HRQoL), OHRQoL, referral to secondary care and dental appointment attendance
- Investigate cost-effectiveness
- Undertake a process evaluation

5. Background

5.1 What is the problem being addressed?

Dental anxiety (DA) is common with a prevalence of 13% in adolescents globally [1]. Children with DA are more likely to miss/delay appointments until they experience pain/infections and subsequently children with dental anxiety have worse oral health and oral health-related quality of life (OHRQoL) than their non-anxious counterparts [1]. Children's dental anxiety is a risk factor for dental caries, which is a major public health problem, with almost half of 15-year-olds in the UK experiencing dental caries in their permanent teeth [2]. DA often continues into adulthood and anxious children are more likely to become symptomatic users of dental services when adults if DA is not addressed [3, 4] .

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5.2 Why is the research important?

Treating dentally anxious patients can be challenging and costly [5]. With children, basic 'behaviour shaping' techniques such as ‘tell-show-do' and positive reinforcement are routinely used but these techniques alone often have limited effectiveness at managing children's DA and therefore many children who have dental anxiety are referred by primary care dentists to secondary care paediatric dentists for treatment with pharmacological interventions (sedation, general anaesthesia [GA]) [6, 7]. Referrals for anxiety management using pharmacological treatments can result in anxious children having to wait longer, prolonging symptoms and travelling further for dental treatment [8]. As such this creates additional potential barriers to dental care and can contribute to increased healthcare inequalities given that children who are referred to specialist services for DA/behaviour management are more likely to be from lower socioeconomic backgrounds [9, 10]. Children who receive dental treatment under GA also continue to be at high risk for poor oral health and dental anxiety in later life [11]. Dental extractions remain the most common reason for a child hospital admission in England. In 2018/19 there were 59,011 admissions to hospital for dental extractions in children (0-19 years) costing around £50 million, with DA being one of the most common reasons why the dental treatment could not be performed in primary dental care [12, 13].

This research question addresses two of the research priorities identified by the James Lind Alliance for dental research, namely research to identify the best way to treat patients who are dentally anxious and improve communication between dental teams and patients (http://www.jla.nihr.ac.uk/priority-setting-partnerships/oral-and-dental-health/).

5.3 How does the literature support this proposal?

Greater effort should be directed towards interventions that can reduce a patient’s DA long-term [7]. Psychological interventions, such as psychologist-led Cognitive Behavioural Therapy (CBT) have shown promising results in reducing dental anxiety in adults in terms of effectiveness, acceptability and long-term benefits [14, 15]. However, the costs and availability of expert psychologists prohibit its widespread use and it is not feasible for primary care dentists to deliver complex psychological interventions within the NHS system [16]. To improve access to CBT in primary care a 'stepped care' approach can be used, which involves offering children the least intensive form of CBT in the first instance and 'stepping up' CBT interventions/support for children whose anxiety does not respond to these low intensity treatments [17]. The stepped care approach has been found to be an effective approach in the management of childhood anxiety [18] and NICE (2011) recommends CBT-based self-help as one of the low intensity treatment options which could be used as part of a stepped care approach for the management of a range of anxiety disorders [19]. However, there is very limited evidence about the use of low-intensity CBT self-help interventions delivered by primary care dentists and whether they are effective at reducing children's dental anxiety and thus the need to refer this group of children to specialist services for more complex and costly pharmacological interventions including GA [20].

Recently, a self-help CBT intervention ‘Your teeth, you are in control’ has been developed to be delivered by dental professionals (funded by NIHR Research for Patient Benefit). The intervention aims to use a range of evidence-based psychological techniques for the reduction of DA in children with guidance provided by dental professionals. The intervention includes a self-help guide for children aged 9-16 years with accompanying resources for parent/carers and the dental team. It was developed using a ‘person-based' approach involving dentally anxious children, parent/carers and dental health professionals to ensure the perspectives and needs of children were taken into

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account. A feasibility study was conducted in which 48 children with self-reported DA were given the intervention by paediatric dentists in hospital and primary care settings. Children reported a mean Modified Child Dental Anxiety Scale (MCDAS) score at baseline of 25.0 (SD 6.5) and at follow-up of 17.4 (SD 6.1). There was a significant reduction in DA (mean score difference = 7.7, P < 0.001, 95% CI = 5.7 to 9.6, Cohen's d ES = 1.2) and an increase in health-related quality of life (HRQoL) (mean score difference = -0.03, P < 0.05, 95% CI = -0.06 to -0.00, Cohen's d ES = 0.3) following the use of the CBT resource. There was a 66% recruitment rate, 86% completion rate and high levels of acceptability for children, parent/carers and clinicians. There was an excellent attendance rate with 90% of dental appointments kept. This compared favourably with the 74% attendance rate of children who met the study inclusion criteria but who were not recruited. Although 80% of participants were specifically referred for a GA only 15% of these went on to require one so the intervention may reduce the need for treatment under GA [21]. When a sample of these participants were followed-up one year later, 91% reported feeling less worried about dental visits, than previously, and described a change in cognition, behaviours and feelings that allowed them to manage their anxiety better [22].

Bux et al. (2019), in a single-centre service evaluation, found this guided CBT approach was feasible to deliver in a general dental setting. All of the children in the general dental practice who were offered the guided CBT, and returned for their dental treatment, engaged with the approach (N=77) [23]. Following the use of the guided CBT self-help there was a significant decrease in children's dental anxiety scores and the effect size of this reduction in anxiety was large (Cohen's d ES = 1.8). These positive findings support further evaluation in a definitive multi-centre randomised controlled trial in primary dental care.

6. Plan of the investigation

6.1 Methodology

A multi-region, randomised controlled trial with an internal pilot trial, involving a total of 600 children and where agreeable their parent/carers, in 30 primary dental care sites. A trial flowchart is included as appendix 1.

6.2 Design

6.2.1 Internal pilot/feasibility trial

A 12-month internal pilot trial (from start of recruitment) is proposed to assess trial feasibility, recruitment rates (of dental sites and participants), and engagement with the intervention (where possible). To recruit 600 children with a parent/carer (where agreeable) over 24 months requires an average monthly recruitment rate of 25 children; it is anticipated that the recruitment rate will start modestly and increase as more dental sites open to recruitment.

After 12 months the following criteria will be assessed against traffic light-style thresholds (Table 1):

- Number of dental sites open to recruitment: GREEN = 30; AMBER = 25-29 (unless sites are recruiting on average >1.1 participants a month); RED = <25 (unless sites are recruiting on average >1.1 participants a month).
- Average recruitment rate per site per month: GREEN = 1.1; AMBER = 0.5-1, RED = <0.5.

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- Percentage of participants in the intervention group engaging with the intervention based on completion of the 'message to dentist' component of the guided self-help CBT resources: GREEN = 100%; AMBER = 70-99.9%; RED = <70%.

Several variables will be considered:

1) the number of dental sites open to recruitment and the rate at which these are opened
2) the average per site/per month participant recruitment rate; and
3) how long each site is open to recruitment for.

Not all of the dental sites will be opened to recruitment at once, they will have to be staggered due to the time and trial staff resources required to grant a site the green light to commence recruitment.

The strategies for recruiting and engaging children (and parent/carers) will be reviewed and amended in collaboration with the Trial Steering Committee, who will consider the progression criteria holistically to advise whether the trial should continue, continue with minor/major amendments, or stop.

If all progression criteria are green, then, unless other unanticipated factors are at play, the trial will continue seamlessly with no or minimal changes.

If all progression criteria are amber or red, then we will discuss, with the independent Trial Steering Committee (TSC) and the funder, the viability of completing the trial with and without major modifications and/or strategies to improve recruitment and intervention engagement or address other unforeseen barriers. The trial may be deemed not to be feasible and the TSC may recommend to the funder that the trial is stopped.

If there is a mix of red, amber and green (at least one green), then the trial may be considered viable to continue but with some modifications to improve recruitment and intervention engagement or to address other unforeseen barriers. This would be subject to discussion with the independent TSC and funder.

Proposed length of internal pilot phase: 12 months from start of recruitment

	Red	Amber	Green
Recruitment rate per dental site per month	<0.5	0.5-1.09	1.1+
Number of dental sites opened	<25	25-29	30
Total number of participants recruited	<80	80-199	200
Participants in the intervention group engaging with the intervention based on completion of the 'message to dentist' component of the self-help CBT resources	<70%	70-99.9%	100%

Table 1 Criteria for progression criteria with traffic light-style thresholds

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6.2.2 Intervention and comparator

Intervention: is a guided self-help CBT intervention 'Your teeth, you are in control' (which will be made available as paper-based and online [via a website] formats) and accompanying parental resources delivered by the primary care dental professional.

The intervention:

- helps children, parent/carers and dental team members understand the factors that may be maintaining the child's dental anxiety
- includes information on the dental team and basic procedures
- describes a variety of cognitive and behavioural tools/strategies that children can use to help them feel less anxious (e.g. challenging unhelpful thinking, goal setting/graded treatment planning, relaxation exercises)
- suggests activities to increase children's feelings of control and self-efficacy in their ability to undertake dental treatment (including a 'message to dentist' and signed stop signal agreement)
- prompts them to reflect on what went well about each visit to build a memory bank of positive experiences
- provides structure and guidance on how to incorporate the use of individualised positive reinforcement techniques into dental treatment/visits
- promotes effective communication and shared decision-making between children, parent/carer and dental team members.

The intervention includes a two hour online training package for dental professionals and a step-by-step guide.

Meaningful engagement with CBT requires children to be capable of concrete operational thought which is typically acquired between 7 to 12 years [24]. Furthermore the effectiveness of a CBT intervention is dependent on the techniques being presented to children in a way which is appropriate for their developmental level and cognitive functioning [25]. For this reason, the intervention was developed with children aged 9-16 years and the content specifically designed around their needs and capabilities.

Comparator: usual care for this group will typically comprise basic behavioural approaches. The basic behavioural approaches are described by various national [26] and international guidelines [27] and include: "tell-show-do" where children are first told about an anxiety-inducing aspect of dental treatment, then this is demonstrated before the procedure is performed; "reinforcement" (usually positive) of behaviour using praise and non-verbal signals; "modelling" where the child observes another having dental treatment undertaken; "distraction" which can take many forms; "voice control" where the dental team alter their tone and volume of speaking to produce desired effects and "enhanced control" where a specific signal from the child allows them to communicate with the dentist. These non-pharmacological approaches have traditionally been framed in terms of encouraging acceptance of dental treatment and the "correct" behaviour rather than attempting to reduce child DA.

The pharmacological approaches of sedation or GA are used where the anxiety cannot be managed using the usual care non-pharmacological approaches described above. Sedation and GA in the UK are generally conducted in secondary care following referral.

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6.3 Setting

Participants will be recruited from 30 primary dental care sites, including general dental practices and primary dental care community clinics. These sites will be located across the UK, mainly from the East Midlands, South Yorkshire, West Yorkshire, North East and Wales. These five regions have been chosen as they contain some of the most deprived areas of the UK, where the prevalence of dental caries is above average, to ensure a socio-economically diverse and multi-ethnic mix of participants are recruited, and allow us to test the intervention in different devolved nations to increase generalisability. Previous successful primary dental care research has been conducted in these regions before by the applicants. Sites in other regions will be considered according to patient needs and where it will facilitate research in an underserved region.

Local research teams comprising a clinical lead with support from a research dental nurse in each of the five regions will oversee site and participant recruitment.

Primary dental care sites will be recruited using existing research networks, local dental committees and via NIHR Clinical Research Network dental leads. Sites will be asked to submit an expression of interest form to confirm they meet the inclusion criteria below. Following the expression of interest, an introductory meeting will be held to review the sites' ability to recruit participants, the patient population demographics (including proportion of children seen and area-based deprivation) and type of NHS contract. Only dental sites with no previous utilisation of the intervention will be recruited. Appropriate training, including the principles of Good Clinical Practice will be provided to recruited dental professionals.

Inclusion criteria for primary dental care sites:

- Providing NHS dental treatment to children aged 9-16 years
- 80% of sites will have a postcode in areas in 3rd, 4th or 5th quintile of deprivation based on the Index of Multiple Deprivation
- No previous utilisation of the guided self-help CBT intervention with child patients
- At least two dental professionals willing to be involved who are not on the specialist list for paediatric dentistry and who are providing a tier one or equivalent service.
  At least one of the dental professionals must have within their scope of practice the ability to conduct the initial assessment and make a treatment plan

Within each dental site, at least two dental professionals will be involved; one dental professional will be randomly assigned to receive the training and deliver the intervention; and the other to deliver usual care. At least one of the dental professionals must have within their scope of practice the ability to conduct the initial assessment and make a treatment plan. The provision of usual care, of the nature typically provided to eligible patients, should be within the scope of practice of both dental professionals involved. Randomisation of children will be 1:1 and stratified by site using variable block sizes. The randomisation sequences will be generated by an independent trial statistician at the York Trials Unit (YTU). Children will be randomised via the secure, remote web or telephone-based randomisation service at YTU.

NB. Randomising at the practitioner level, within a site, is more powerful than the alternative, which is to randomise at the site-level, because it will control for the wider site covariates (e.g. socioeconomic catchment, reception staff, quality of premises, ethos of the site, variation in waiting times for secondary care referrals etc) as well as site-level differences that might attract

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professionals with certain characteristics. Indeed, it will mean that it is more likely to address significant differences between dental professionals (DP) themselves, and more efficiently, because if we used site-level allocation we would need a greater number of sites to balance these issues.

6.4 Participants

The target population will include children, aged 9-16 years, attending primary dental care sites in the UK with a parent/carer. This age group has been primarily chosen because the evidence-base for the effectiveness and appropriateness of CBT for anxiety management in children is most persuasive in children older than 7-years [28]. The use of psychologist-led CBT has been shown to be effective in a previous blinded parallel dental trial involving children aged 10-16 years [29]. In addition the guided self-help CBT resources were originally developed with children aged 9-16 years [21]. In line with previous research, self-reported DA will be used to assess study eligibility [21]. All children who indicate they feel worried about visiting the dentist in response to a written or verbal question will be invited to participate in the study. The use of a simple self-reported question has the additional benefit of being easily translatable post-trial into clinical practice.

6.5 Sample size for the outcome evaluation

There is little reliable information to be confident what the minimal clinically important difference (MCID) is for the MCDAS. From the feasibility study [21], the MCID for the MCDAS was calculated at 5 points using the anchor-based method, and the standard deviation was 6.5. Given the low sample size of the feasibility trial, we have decided to power the trial to detect a more conservative difference of 2.5. The clustering of patients within dental professional's lists within sites, using an average cluster size of 20 (patients per dental site), and an intra-cluster correlation coefficient (ICC) of 0.03 is used in the sample size calculation. Assuming 90% power, 5% alpha, SD of 6.5, average cluster size of 20, ICC of 0.03 and 20% attrition then to detect a 2.5 point difference we would need to recruit 600 children (30 dental sites, 60 dental professionals).

We will also aim to recruit parent/carers of child participants to capture their dental anxiety. Based on the literature, we estimate 80% of parent/carers will agree to take part, (n=480) bringing an approximate sample size of 1080 [30, 31].

6.6 Recruitment

Sites will be asked to screen their patient lists for potentially eligible children and send, to their parent/carer, the participant documentation prior to their child's next dental assessment appointment. Following confirmation of eligibility at the dental assessment, parent/carer consent and child assent will be obtained (at the site during or after the dental appointment, or afterwards and returned by post). The children recruited at each site will be randomly allocated either to be treated by the dental professional allocated to deliver the intervention or the control dental professional.

Consent will be obtained from the child's parent/carer and assent will be obtained from children for participation in the trial. Every effort will be made to support a parent/carer to provide consent for their child if they wish to take part. In response to consent statements, initials or ticks will be accepted as valid. Where a participant has used crosses throughout on non-optional statements (rather than a mixture of ticks and crosses) and signed the consent form, this will also be accepted as valid consent. Support for recruitment will be provided by dental professionals in the form of an interpreter

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and multimedia participant information resources hosted on a patient-facing trial website. Dental professionals have existing experience of working with their local communities to facilitate consent with families where literacy can be problematic. Our PPIE work has suggested several ways to improve involvement of children and parent/carers including using a multimedia participant information resource, offering branded stationery appealing to children and thank you vouchers. Each child and parent/carer participant will be given a £10 shopping voucher at the final follow up appointment to thank them for taking part.

Inclusion criteria for participants:

- patients aged 9-16 years, inclusive
- child self-reported dental anxiety
- not requiring urgent dental treatment
- attending for a dental assessment and found to require a course of treatment for their presenting dental condition (categorised as level one complexity by NHS England), involving at least two additional visits and within the scope of practice of the CALM dental professional
- child able to read and use written English, required to receive the intervention and complete questionnaires
- parent/carer able to complete consent forms (with the support of an interpreter if necessary)

Exclusion criteria:

- patients younger than 9 years or older than 16 years
- a sibling of a child patient recruited to the trial
- no self-reported dental anxiety
- seen for an assessment with an acute presentation and in need of immediate dental treatment
- have previously been seen for an assessment and part-way through a prescribed course of dental treatment
- seen for an assessment but not requiring more than one further visit to complete any necessary treatment
- requiring procedures during the course of treatment that fall outside of the scope of the practice of the dental professionals involved
- requiring referral to a specialist for more complex treatment needs (categorised as level two or three complexity by NHS England)
- parent/carer unable to complete consent forms (even with support).
- child unable to read and use written English

The geographic location, selection criteria for the dental sites and broad eligibility criteria will ensure the sample is inclusive of participants who may not often get the opportunity to participate in research.

One parent/carer of each eligible and participating child will be invited to participate as a participant in their own right. Information on this element of the study will be included with participant documentation, sent before the initial dental appointment. Consent will be obtained from the parent/carer for them to be a participant in their own right.

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Exclusion criteria for parents/carers

- parent/carer unable to complete consent forms (even with support).

6.7 Outcomes and outcome measures

The outcomes are i) child dental anxiety (DA) ii) child HRQoL iii) child OHRQoL iv) parent DA v) referral and use of pharmacological approaches and vi) attendance patterns.

6.7.1 Primary outcome and outcome measure:

i) Primary outcome – child dental anxiety

The Modified Child DA Scale (MCDAS) measured at baseline (B), end of the course of treatment (follow up 1 (FU1)) and 12 months post randomisation (FU2). The MCDAS is one of the mostly widely used measures of child dental anxiety and assesses severity of dental anxiety in relation to a variety of dental situations/stimuli (e.g. having an injection in the gum, having a tooth taken out). It is an 8-item measure and therefore is quick to administer and complete, was developed with input from children and has been validated for use with children over 8 years old [32]. The MCDAS has high internal consistency, good test-retest reliability, concurrent validity and has demonstrated relationships with the clinical outcomes of interest within this study (e.g. caries experience, GA) [33]. It has been used in longitudinal research and has demonstrated its responsiveness to detect changes in dental anxiety over time [21].

6.7.2 Secondary outcomes and outcome measures:

ii) Health Related Quality of Life (HRQoL)

Child HRQoL will be assessed using the Child Health Utility 9D (CHU9D) [34] at baseline, end of the course of treatment (FU1) and 12 months post randomisation (FU2). It consists of nine dimensions (worried, sad, pain, tired, annoyed, schoolwork/homework, sleep, daily routine and activities), each represented by a single question with five response options. The recall period is today/last night, and the questionnaire is completed by the child. The responses to each of the nine questions can be taken together as a description of the HRQoL of the child and is termed a “health state”. There are many different health states defined by the CHU9D descriptive system (due to different combinations of response options on each of the nine dimensions), and each unique health state has a preference weight associated with it. These preference weights give a utility value (on a 0–1 scale where 1 is perfect health and 0 is a state equivalent to being dead) and can be used in economic analysis to estimate the cost per quality-adjusted life year (QALY).

iii) Oral Health Related Quality of Life (OHRQoL)

Child Oral HRQoL will be assessed using the CARIES-QC [35], a measure of the impact of caries validated in children aged 5-16 years, at baseline, end of the course of treatment (FU1) and 12 months post randomisation (FU2). CARIES-QC contains 12 items and one global question. The items are scored on a 3-point Likert scale from 0 to 2, with a higher score indicating increased impact (possible total score range 0-24). As the measure is unidimensional, a conversion scale is available to convert the raw ordinal score to an interval score to allow accurate calculation of change scores

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and effect sizes.

iv) Parent dental anxiety

DA of the parent/carer will be assessed at baseline, at the end of the course of the child's treatment (FU1) and 12 months post-randomisation (FU2) using the Modified Dental Anxiety Scale (MDAS) [36]. Each of the five items in the scale have response categories 1=not anxious to 5=extremely anxious. A total score is calculated by summing the five item responses from 5 to 25; a score of 19 or above indicates a highly dentally anxious patient.

v) Referral and use of pharmacological approaches

The need for referral to secondary care and use of sedation or GA will be recorded for children in both groups, along with treatment provided (e.g. prevention, restoration, extraction, local anaesthesia) throughout the 12 month follow up period.

vi) Detail on delivery of intervention including any deviation from the intervention step-by-step guide (including engagement with completion of the 'message to dentist') or detail on usual care provided. This data will be recorded on a case report form by the dental professional throughout the 12 month follow up period.

vii) Attendance patterns

Attended and missed appointments will be recorded during the course of treatment and for the 12-month follow up period. The duration of the appointments will also be recorded. This data will be recorded on a case report form by the dental professional along with the type of dental professional seen at each visit (e.g. dentist or dental therapist).

viii) Anchor ratings

As part of the CALM trial, an anchor-based approach will be used to determine the change in MCDAS that represents the minimum clinically important difference (MCID) [37]. The anchors will include: the single-item Global Rating of Change (GRC) outcome measure used to gain the participant's perspective on how meaningful the change to their anxiety has been. The GRC item asks participants to rate their condition (DA) following the intervention ("very much worse", "much worse", "a little worse", "no change", "a little better", "much better", or "very much better") compared with baseline [38] . Participants can then be further categorised based on whether they report that their DA has improved/not changed/deteriorated using this anchor.

The Clinical Global Impressions: Improvement (CGI-I) item will be used as an anchor to capture 'meaningful' change in children's dental anxiety levels from the perspective of the dental professionals [39]. The dental professional will be asked to rate the participant's DA after the intervention compared to baseline using a 7-point response scale (1=very much improved since the initiation of intervention; 2=much improved; 3=minimally improved; 4=no change; 5=minimally worse; 6=much worse; 7=very much worse since the initiation of the intervention). This data will be recorded on a case report form by the dental professional.

6.7.3 Baseline participant characteristics

Following recruitment, dental professionals will also provide baseline data on 1) the socio-demographic characteristics of participants, including age, gender, ethnicity and postcode, 2) their clinical status including: caries experience (number of decayed, missing and filled teeth (dmft/DMFT)), and previous experience of local anaesthetic, sedation or GA, and 3) information on past history of whether dental professionals involved in the trial from that site have previously seen

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the patient.

6.7.4 Resource use and cost data

Costs and resource use related to dental anxiety for inclusion in the economic evaluation will be collected from parent/carers via questionnaires at baseline, FU1 and FU2 and from dental sites (for the base case analysis; NHS perspective) throughout the 12 month follow up period. Further costs (e.g. travel time/costs for attending appointments, time missed from school, time off work for parent/carer/carers, out of pocket expenditure on medications) will also be collected via parent/carer questionnaires (for the secondary analysis; societal perspective).

6.7.5 Data collection methods

Questionnaires will be completed by children and by parent/carers: at baseline (B), end of the course of treatment (FU1) and 12 months post-randomisation (FU2). Questionnaire data may be collected via paper methods at the time of dental appointment or following the appointment via post where parent/carers have provided their consent for this information to be held and to be contacted in this way.

Data from dental sites will be collected at baseline, and throughout the 12 month follow up period via paper-based or electronic questionnaires/CRFs

The feasibility of the use of routine dental practice data to follow-up participants' dental attendance patterns and need for referral to secondary care will be explored with dental sites and the NHS Business Services Authority. While the research team know the data linkage needed to use routine data in this way is not currently possible, opportunities to use routine data in this way in future will be re-visited by the research team with the NHS Business Services Authority and other relevant stakeholders.

6.7.6 Process evaluation

A mixed-method process evaluation following MRC guidance [40] will complement the outcome evaluation and will include implementation, mechanisms of impact and context. A detailed plan for the process evaluation will be developed. In summary, the process evaluation will investigate:

Implementation: the process through which the intervention and usual care are delivered in dental sites, the appropriateness of the training to equip dental professionals for implementation, what is delivered in different sites, fidelity (including deviations from the intervention step-by-step guide), dose (duration of appointment), reach, and adaptations made by different dental professionals and the elements of the resources actually used.

Mechanisms of impact: how the intervention and usual care are experienced by children, parent/carers and dental professionals delivering it, including acceptability and how the child, parent and dental professional triad triggers changes in dental anxiety and any unintended positive or negative effects.

Context: the influence of external factors on the delivery of the intervention and usual care including dental site factors (contractual arrangements) and patient factors such as deprivation and how the intervention is experienced.

The process evaluation will include data from the questionnaires, participant characteristic data and CRFs described above and qualitative interviews with children, parent/carers, dental professionals and key stakeholders.

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6.7.7 Process evaluation - qualitative interviews – children and parent/carer

A sample of child and parent/carer participants will be interviewed to explore their experiences of the intervention and usual care. Participants will be asked during the initial consent process if they agree to being approached to take part in a qualitative interview via post or telephone and for this information to be held by the research team. A purposive sample will be taken to ensure a range of participants in terms of age, region, engagement with the treatment approach, parental anxiety, patterns of dental attendance and need for secondary care referral. Parent/carer will be sent an information sheet and consent form then contacted by an experienced researcher via telephone or email to arrange the interview. Interviews will ideally be conducted face-to-face in a location convenient to participants although telephone/video conference interviews will be offered for convenience. Before the start of each interview the researcher will obtain written informed consent from the parent for their child and themselves to be interviewed and assent will also obtained from the child. Recruitment will continue until no new themes emerge.

Previous similar studies have involved 26-30 participants (13-15 children and 13-15 parent/carers) in qualitative interviews [41]. Each child and parent/carer participant will be given a £10 shopping voucher to thank them for their time taking part in the interview. The interviews will be guided by the concept of patient acceptability using a topic guide developed by the research team. The interviews will be audio-recorded and transcribed verbatim by a professional transcription service who has been approved by the sponsor.

6.7.8 Process evaluation - qualitative interviews – dental stakeholders

A sample of dental professionals and other key stakeholders will be interviewed to explore their views about the intervention and usual care within their dental practice and primary dental care more generally. Dental professionals and stakeholders will be purposively sampled based on region, dental contractual arrangements, previous experience of treating children and role. The sample will include those who had recorded instances of having deviated from the intervention step-by-step guide to explore fidelity. The CALM research team will give potential dental professional and stakeholder participants an information sheet about the component and inviting them to participate. They will also be given a consent form. They will then be contacted by a member of the CALM research team to answer any questions they may have and if they agree to take part, arrange a suitable time and location to hold an interview. The interviews will either be face-to-face or telephone/video conference. Before beginning a face-to-face interview, the researcher conducting it will obtain written informed consent from the participant. For telephone/video conference interviews consent for audio recording will be obtained before the interview. Video recording will not take place.

Recruitment will continue until no new themes emerge. Previous similar studies have involved 25-30 stakeholders in qualitative interviews [42]. Each stakeholder participant will be given a £10 shopping voucher to thank them for their time taking part in the interview.

The interviews will be guided by the theoretical domains framework (TDF) [43] which has been used previously in implementation research to understand the motivations and behaviours of dental professionals when implementing evidence-based practice [44] [45]. A topic guide based on the TDF will be developed by the research team. The interviews will be audio-recorded and transcribed verbatim by a professional transcription service who has been approved by the sponsor.

The results of the process evaluation will be reported alongside those of the outcome evaluation.

6.7.9 Blinding

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Due to the open nature of the intervention, it will not be possible to blind participants, their parent/carers or treating DP to group allocation. Members of the research team, the statistician or health economist will not be blinded.

6.8 Data analysis

Analyses will be described in detail in a Statistical Analysis Plan drafted by the trial statisticians, agreed with the trials independent groups and signed off by the CI. Analyses will be conducted in accordance with YTU SOPs and will be undertaken in Stata v16 or later (to be confirmed in the final report). Statistical tests will be two-sided at the 5% significance level. All analyses will be conducted on an intention to treat basis, including all children in the groups to which they were randomised irrespective of deviations based on non-compliance.

6.8.1 Internal pilot trial

Relevant data from the internal pilot trial will be analysed prior to progression to the main trial to help determine whether progression is warranted. This will include descriptive examination of the number of dental sites open to participant recruitment, the participant (and parent/carer) recruitment rate in total and by site and month, and the number and percentage of participants randomised to receive the intervention who are engaging in the intervention (based on completion of the 'message to dentist' component of the self-help CBT resources).

In addition, as well as monitoring participant recruitment rates, we will also monitor recruitment of participants living in deprived areas, based on the Index of Multiple Deprivation quintiles derived from participant's postcodes, to ensure those living in the most deprived areas of England and Wales are included. This will be reported along with the progression criteria and changes will be made to the recruitment strategy for the main trial to improve recruitment of those living in the most deprived areas if required.

At the end of the internal pilot, the response rate for the parent/carer questionnaire, which includes the resource use questionnaire will be presented and the choice of approach to data collection reviewed.

6.8.2 Main trial

The flow of participants through the trial will be presented in a CONSORT diagram. The numbers of dental practices and children withdrawing from treatment and/or the trial will be summarised together with the reasons where available. All baseline data will be summarised descriptively by treatment group. No formal statistical testing will be conducted on baseline data.

The MCDAS scores at the end of treatment (FU1) and at 12 months (FU2) will be compared between groups using a covariance pattern linear mixed model, adjusting for baseline value, other pertinent baseline covariates, time, and an interaction between treatment group and time as fixed effects. Participant, treating dental professional and region will be included as random effects. The adjusted mean difference in MCDAS score at each time point will be extracted with its 95% confidence interval and p-value; the treatment effect at 12 months will be the primary endpoint, while the difference at the end of the course of treatment is a secondary endpoint. We will present a Complier Average Causal Effect sensitivity analysis for the primary outcome to account for non-compliance with the intervention, with engagement determined by participant self-report and dentist's assessment including evidence of completion of the 'message to dentist' component of the intervention [46]. A subgroup analysis will consider whether children with lower or higher baseline DA benefit more from the intervention, by including an interaction between baseline MCDAS score and treatment group in

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the analysis model.

As part of the CALM trial, an anchor-based approach and established analysis methods, will be used to determine the change in MCDAS that represents the minimum clinically important difference (MCID). The use of multiple, independent anchors is recommended to produce a range of MCID scores for the MCDAS based on the different anchors. The 'anchors' will include the GRC item, the CGI-I item and clinical outcomes, including referral to specialist services and the use of sedation or general anaesthesia.

CARIES-QC and parent/carer DA will be analysed in an analogous way to that described for the MCDAS.

The need for referral to secondary care and use of sedation or GA will be analysed by mixed effect logistic regression, adjusting for baseline MCDAS value and other pertinent baseline covariates as fixed effects, and dental team member and dental site as random effects. Treatment provided (e.g. prevention, restoration, extraction), attendance patterns (attended or missed appointments), and duration of attended appointments will be summarised for the two groups.

Quantitative analysis for the process evaluation will examine whether baseline characteristics or changes in process variables could affect the primary outcome between participants who received the intervention and participants who received usual care. Baseline and follow-up questionnaires will be analysed using linear regression modelling to measure mechanisms of impact. Data from CRFs will be compared within and between intervention and usual care to measures aspects of implementation.

6.8.3 Cost-utility and cost-effectiveness analyses

The economic evaluation will assess the cost-effectiveness of the intervention versus usual care, by means of (1) a within-trial economic analysis over the trial's 12-month time horizon, and (2) a decision analytic model, which will model beyond the trial to explore longer-term cost-effectiveness (subject to the findings of the trial). For both the within-trial and model-based analyses, an NHS and personal social services perspective will be taken in the base case, with a secondary analysis exploring a broader perspective whereby further costs incurred by other members of the household are incorporated. NICE recommendations on the methods of cost-effectiveness analyses will be followed wherever possible [47].

<u>1. Within-trial economic analysis</u>

The primary economic analysis will take the form of a cost-utility analysis, which will estimate the mean differences in costs and quality-adjusted life years (QALYs), using the CHU9D to generate utilities. In addition, the trial's primary outcome will be incorporated in a cost-effectiveness analysis, using MCDAS score as the effectiveness measure. Analyses will be undertaken on an intention-to-treat basis, in Stata v16 or later, and will utilise patient level trial data and data recorded by dental practices.

Data regarding participants' outcomes, resource use and costs will be collected over a 12-month follow-up period, via study questionnaires (completed by participants and parent/carers) and CRFs completed by dental practices. Specifically, resource use data obtained using questionnaires will be completed by parents/carers at baseline, and at dental appointments at the end of the course of treatment and at 12 months. Due to the potential for variability in the timing for the end of treatment appointment, the analysis will primarily focus on data obtained from the 12 month questionnaire.

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Unit costs, sourced from established databases [48] [49], will be applied to each resource item to estimate a total cost per participant. Cost estimates of the intervention will incorporate the time spent delivering the intervention and undertaking the associated training, with the costs of sedation/GA referrals also included. In addition to health-related costs, further costs incurred by parents/carers of participants will be collected for the secondary analysis: direct costs (e.g. out-of-pocket expenditure on medications) and indirect costs (e.g. parent/carer time off work to care for a child/attend appointments, travel costs for appointments). Time missed from school in relation to appointments/DA will be listed as a 'consequence' and compared between groups, but not formally valued in monetary terms.

Utilities will be derived from participants' CHU9D responses from questionnaires completed at baseline, end of the course of treatment and 12 months. QALYs will be estimated for each participant using the area under the curve approach [50]. Discounting of costs and outcomes will not be required for the within-trial analysis due to the trial follow-up not exceeding 12 months, and costs will be presented in UK £ for the appropriate year. Mean within-trial estimates of costs and health benefits will be calculated using regression methods, adjusting for covariates and allowing for correlation between costs and benefits. Multiple imputation methods will be used to deal with missing data [51], with sensitivity analysis exploring a complete case analysis. The results will be presented as mean costs and effects for both groups, and in terms of incremental cost-effectiveness ratios and net health benefit at 12 months. Uncertainty will be described using confidence intervals and cost-effectiveness acceptability curves [52], and sensitivity analyses will explore the impact of underlying assumptions and key parameters of the analysis in terms of the cost-effectiveness results. A pre-specified health economics analysis plan will be agreed with the trial's independent groups and signed off by the PI.

2. Decision analytic model

Dependent on the trial's findings, the economic results will be modelled beyond the time horizon of the trial, making assumptions of a longer-term impact. Prior to the within-trial economic analysis being undertaken, a modelling plan will be developed. This will set out conditions that are required to be met in order for a longer-term economic model to be considered feasible; namely, the clinical effectiveness findings and the availability of data inputs required for a model.

The model will use data collected from the trial (outcomes, resource use, attendance patterns, referrals), supplemented by published data, thereby enabling the estimation of longer-term cost-effectiveness of the intervention. Future costs and health benefits will be discounted in line with NICE recommendations [47]. Sensitivity analyses, both deterministic and probabilistic, will explore uncertainty around model parameters, with the robustness of results tested using different scenarios.

6.8.4 Qualitative data analysis

Qualitative interviews, as part of the process evaluation, will be analysed using framework analysis.

Framework analysis will be used as it provides a pragmatic approach which produces results that can be easily incorporated into mixed-method studies, process evaluations and RCTs [30-32]. The analysis will involve the following stages: identifying initial themes, labelling the data, sorting the data by theme, and synthesising the data. The analysis will be conducted by an experienced research associate with support from ZM and HDR. In addition, during the analysis, regular meetings will be held amongst the research team to discuss the emergent themes and consider the implication of

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these for the implementation and delivery of the intervention.

6.9 Data management and confidentiality

Sheffield Teaching Hospital (STH) and the York Trials Unit, University of York will hold joint data controller responsibilities. York Trials Unit will in most cases be responsible for responding to Subject Access Requests. Sheffield Teaching Hospital shall be the contact for data subjects.

Data processing notices are provided via the Participant Information Sheet, with links to STH and University of York privacy information.

STH, YTU and collaborators will comply with all aspects of the General Data Protection Regulation 2016 applicable in the UK from May 2018. Personal data will be processed under Article 6 (1) (e) (Processing necessary for the performance of a task carried out in the public interest) and Special Category data under Article 9 (2) (j) (Processing necessary for scientific research purposes) of the General Data Protection Regulation 2016.

A bespoke trial management database will be created for the trial which will house information on questionnaire due and return dates, as well as site and participant level-data. A unique trial identification number (Trial ID) will be generated for each participant and their parent/carer when their details are entered into the trial management system.

To ensure participant confidentiality, discussions about the trial and obtaining consent will be conducted in a private area of the dental site. This was felt to be particularly important by our PPI co-applicant.

The dental practices follow their own Information Governance policies. The dental practices will ensure copies of the consent and assent forms are securely stored in a locked cabinet, with access only for research staff. Any other paper documents (identified by Trial ID only) that need to be stored temporarily (before return to YTU), will be stored separately and securely (in locked cabinet).

Paper consent forms and outcome data – identified only by Trial ID (collected using electronic and/or paper-based methods) will be returned separately to YTU via post and/or secure electronic transfer (e.g. University of York Drop Off Service, Qualtrics). Sites can return data directly to YTU. Local research teams can support sites in collecting and returning data (acting as data processors) to YTU via post. Local research teams will therefore have access to identifiable participant data (including contact information) for participants based in sites in their areas.

Paper based forms collecting outcome data – identified only by Trial ID, returned to YTU will be logged and then scanned using optical scanning techniques (Cardiff Teleform). Scanned data will be 100% validated and cross-checked with the information in the management database. If electronic data collection is utilised this will be collected via Qualtrics survey software (or similar).

Once received by YTU, paper consent forms and paper data (identified by Trial ID only) will be held separately and securely in a controlled access area in locked cabinets, at the University of York. Sites will keep a paper copy of consent forms for their records. This is the only participant documentation that will be retained at the sites.

Both the trial management system and the data management systems are held on secure University

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of York servers, access will be limited to specified members of YTU staff as detailed on a delegation log.

University of Sheffield (acting as a data processor) will have access to participant personal data in order to select and approach for participation in qualitative research elements.

Interview transcript data will be anonymised by the use of participant study numbers and removal of any other identifying material. Participants will be asked to provide a name that is different from their real names to be used in transcription and analysis. The audio data will be stored as password-protected computer files on the University of Sheffield network and the transcripts, and consent forms will be stored securely in a locked filing cabinet at the University of Sheffield. Only the members of the research team will have access to the data. The transcription will be conducted by a professional transcription service called Dictate2us Limited. Dictate2us Limited use several methods to ensure security and confidentiality with the highest level of data protection at the Information Commissioner's Office (ICO). Their secure systems allow users to upload confidential audio files for transcription which are only accessible with the use of secure login credentials. A non disclosure agreement has been signed with Dictate2Us.

All identifiable trial data will be kept for ten years following the publication of the CALM trial final report. Anonymous trial data will be kept indefinitely.

YTU, University of York will be responsible for secure data archiving, and secure data deletion.

6.10 Safety Assessment

Based on findings from the literature on guided self-help CBT, the feasibility study and discussions with the sponsor and PPI representatives it has been agreed that any adverse events from the study intervention and procedures are extremely unlikely so it can be justified not to include adverse event reporting.

6.11 Participant withdrawal

Participants and their parents/carers are able to withdraw from the research at any point, and will be informed of this in the participant information sheets. If a participant explicitly states they do not wish to contribute further data to the study or to complete any future questionnaires (full withdrawal), they will be withdrawn from the trial and no further data will be collected, however participants will be informed (at the time of consent) that data already collected will be retained and used in the analysis. If a participant does volunteer a reason for their withdrawal, this will be documented.

Participants are able to fully withdraw by letting the dental professional know at the time of a dental assessment, or by contacting the research team directly, contact details are provided on participant information sheets.

Local research teams and sites will be provided with a procedure document detailing how to inform YTU of any such withdrawals and/or will be able to action withdrawals themselves via the trial management database.

All participants will be free to withdraw at any time from the intervention arm without giving reasons and without prejudicing further treatment, by letting the dental professional know at the time of dental assessment. They will still remain in the trial unless they specifically request to fully withdraw from

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the trial. If a participant no longer wants to engage with the 'intervention' (but are willing to continue to contribute data to the study/complete questionnaire), this will be recorded by the dental professional on CRFs throughout the 12 month follow up period.

7. Project management

The Gantt chart for the project has been added as Appendix 2.

7.1 Sponsor

Sheffield Teaching Hospital Foundation NHS Trust will be the study Sponsor. Marshman is the Chief Investigator and responsible for clinical elements of the trial. YTU is responsible for project management. Sheffield Teaching Hospital and the University of York will hold joint data controller responsibilities.

7.2 Trial Management Group (TMG)

The TMG is the executive decision-making body and is responsible for the day -to-day running and management of the trial. Led by the PI, it consists of members of the YTU (trial manager, statistician), and other co-applicants. The team meets on a monthly basis over teleconference and plan to meet face-to-face at least once a year. A Senior Management Team from within the TMG will convene by teleconference fortnightly to closely monitor milestones and deliverables. Findings from meetings of the youth forum, parent panel and PPIE co-applicants will be fedback into the TMG meetings by ZM and JP. The day to day co-ordination of the study will be supervised by an experienced trial manager.

7.3 Trial Steering Committee (TSC)

A TSC has been set up including an independent chair, three other independent members, as well as PPIE representatives and representatives of the funder and the sponsor. The TSC is likely to meet every six months but the committee will decide on the frequency of meetings. The committee will provide overall supervision of the trial and ensure that the study is conducted according to the protocol and within the overarching ethical framework through its independent chair. PPIE updates will be a standing agenda item for the TSC meetings. Members will also provide advice outside these meetings according to their area of expertise at key stages via e-mail, phone or if needed, face- to-face.

7.4 Independent Data Monitoring Ethics Committee (DMEC*)*

An independent DMEC has been formed, which will be the only group who sees the confidential, accumulating data for the trial. Reports to the DMEC will be produced by the YTU statisticians and trial manager. The DMEC will meet within 6 months of the trial opening; the frequency of meetings will be decided at the first meeting. The DMEC will consider data using the statistical analyses and will advise the TSC. The DMEC can recommend premature closure or reporting of the trial.

The establishment of the TSC and DMEC will further ensure equipoise on the trial question is maintained in terms of study conduct.

8. Expertise

We have assembled a team with expertise in the area of child oral health, psychology, trials methods, medical statistics, health economics, primary dental care, process evaluation and patient and public involvement. MARSHMAN is the Chief Investigator and Professor of Dental Public Health. She has expertise in dental clinical trials involving children, being Co-PI on the NIHR-HTA BRIGHT trial and

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is involved in four other dental trials with children and young people. She has published over 90 peer reviewed papers. Marshman will be the co-PPIE lead.

8.1 Trial methodology

TORGERSON is the Director of YTU and provides expertise in trial design. He is currently chief investigator and co-investigator on a large number of NIHR grants. HEWITT leads the quantitative portfolio in YTU she is co-applicant on a large number of NIHR grants, has vast experience of analysing trials and will oversee the statistical design and analysis of the trial. FAIRHURST is an experienced trial statistician and will lead and conduct the statistical design and analysis. RONALDSON is an experienced health economist and will be the lead for health economics. AINSWORTH is a research fellow with experience of more than 15 RCTs, with most trials involving children. She is currently Chief Investigator for two trials and will provide expertise in trial design and conduct. An experienced senior trial manager in YTU will provide day-today support and oversee the conduct of this trial.

8.2 Clinical leadership

RODD is a Professor of Paediatric Dentistry and will act as the clinical lead for South Yorkshire. DAY is an Associate Professor in Paediatric Dentistry and will act as the clinical lead in West Yorkshire. He is the joint lead of the NIHR CRN oral and dental specialty group in the Yorkshire and Humber. DAWETT is a dental practice owner and NIHR doctoral research fellow. He has experience of four NIHR HTA funded dental trials and is the lead for the NIHR CRN oral and dental specialty group in the East Midlands. VERNAZZA is a Senior Lecturer in Paediatric Dentistry, NIHR Clinician Scientist Fellow and will act as the clinical lead in the North East. He is the lead for the NIHR CRN oral and dental specialty group in the North East and North Cumbria. He is Director of the Newcastle Dental Clinical Research Facility. INNES is a Professor of Paediatric Dentistry and will act as the clinical lead for Wales. She worked in general dental practice for seven years. Innes has expertise on clinical trials involving children, young people and families. She has been PI on two NIHR trials with young people; FiCTION, set in general dental practices across the UK (responsible for successful recruitment of practices across Scotland) and BRIGHT. Innes has experience of other dental based clinical trials as steering group members in Brazil, Lithuania, Australia and Brazil.

8.3 Psychology

PORRITT is a registered Health Psychologist (HCPC) with specific expertise in dental anxiety assessment and management. Porritt has clinical experience of treating people with a range of anxiety disorders using cognitive behavioural therapy (CBT) based self-help interventions. Porritt will be the co-PPIE lead. NEWTON is Professor of Psychology with experience of the design and evaluation of theory based interventions in the dental field. BAKER is Professor of Psychology Applied to Dentistry with expertise in the application of psychological theories, methods and techniques to the field of dentistry.

8.4 Expert advisors

In addition, two academics with experience of conducting trials of cognitive behavioural therapy interventions, including low intensity interventions and those for child anxiety have agreed to act as expert advisors: Professor Cathy Creswell, University of Oxford and Professor Chris Williams, University of Glasgow.

9. Ethical issues

The project is not considered to raise any additional ethical concerns. The project does involve an intervention, but it is considered ‘low’ risk. However, the following specific ethical issues will be given

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due consideration as detailed below.

9.1 Informed consent

Due to the age of participants involved in the trial, informed consent will be requested from participant's parent or carer. Children will also be asked to assent to take part. Consent and assent will be required from both parties for the child to be able to participate.

Parents/carers will give separate consent for their own involvement to complete parental questionnaires.

Potential participants will be informed in understandable terms of the potential benefits and inconveniences that are associated with agreeing to participate in the study using age-appropriate information sheets and a multimedia information resource is being developed with input from the youth forum and parent panel.

After the participant has entered the trial the dental professional remains free to give alternative treatment at any stage if he/she feels it is in the participant's best interest, but the reasons for doing so will be recorded.

9.2 Protection from harm

All researchers that have contact with participants will have the appropriate level of disclosure obtained from the Disclosure and Barring Service and letters of access/research passports where applicable.

Dental teams have a statutory duty of care to all patients which includes ensuring that safeguarding arrangements are in place. Therefore, dental sites are required to maintain their own safeguarding policies. In any instance where there is a safeguarding concern regarding a participant or their parent, this will take precedence and anonymity will be broken to allow for appropriate reporting and/or recording of concerns. According to the Preventing Harm in Research and Innovation (Safeguarding) policy of the University of Sheffield, the designated safeguarding contact for the trial is RODD, a Professor /Honorary Consultant of Paediatric Dentistry (University of Sheffield/STH) who is trained to Safeguarding Children and Young People Level 3.

A Health and Safety risk assessment has been undertaken in line with University of Sheffield policy including consideration of lone working for researchers who are working off campus.

Measures taken by the team, such as the emphasis on good clinical practice and standardised protocols are likely to reduce risk of harm. We will adhere to the Research Governance Framework and Good Clinical Practice Guidance. The information sheet/multimedia information for the study have been developed with the involvement of the youth forum, parent panel and PPIE representatives. They state explicitly that the child's dental treatment will not be compromised if they do not enter the trial or withdraw their consent.

In terms of the qualitative component, the interviews will be conducted by qualitative researchers who have experience of conducting similar interviews with children, parent/carers and professionals. Should participants feel upset, distressed or uncomfortable the interviewers will ask the participants if they would like to stop the interview. All participants will be advised that they have the right to

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withdraw from the interviews at any time without providing a reason for doing so.

All research will be carried out in accordance with the current Government COVID guidelines.

10. Patient and Public Involvement and Engagement

We have worked with children, parent/carers and Patient and Public Involvement and Engagement (PPIE) members to develop the study. The PPIE work with children has included group discussions and one-to-one meetings with 20 children with different experiences of dental anxiety attending primary dental care settings. Children described how worried they felt about going to the dentist, the sights, smells, sounds and thoughts about what treatment they would need and how painful it might be. They described wanting to let the dental professional know how anxious they felt but also feeling embarrassed to admit it and feeling there was nothing the dentist could do to help them. They welcomed the idea of a resource given to them by the dentist, the opportunity to complete a 'message to dentist' proforma and being given more choice and control about what happens during the appointment. They felt the resource should be available in paper form and via a website. Some children said they preferred not to have a lot of reading to do so would like both paper-based and multimedia study information available. To thank participants for their time taking part in the trial, children would welcome a thank you voucher and branded small gifts. The young person co-applicant suggested that children should be discretely asked if they wanted to sign up for the trial in order to avoid potentially embarrassing conversations audible to other families.

Discussions were held with ten parent/carers of children with dental anxiety. Parent/carers also welcomed this study and the opportunity to test an intervention of this kind. They described frustration at not feeling able to support their own child before, during and after visits. Most parent/carers described how they themselves were anxious; some parent/carers described trying to hide their dental anxiety from their child but others talking openly about it in front of their child. Parent/carers felt that the inclusion of a measure of their own dental anxiety was useful and this may influence how well the child intervention worked. PPIE representatives endorsed the parent/carer's view that including a measure of adult dental anxiety would be beneficial. As a consequence, the design of the study was changed to include recruiting parent/carers to complete measures of their dental anxiety. PPIE representatives suggested a multimedia information resource may help parent/carers with limited ability to read English to understand the trial so multimedia information will be provided. The PPIE representatives raised the possibility of trying to follow-up young people longer-term to assess whether any changes in dental anxiety remained in adulthood. The use of routine data to capture future dental attendance patterns and acceptance of treatment be explored as part of the study. Finally, the PPIE representatives suggested having a PPIE co-applicant in addition to the young person co-applicant to reduce the burden on that individual. A PPIE co-applicant has been included. The views of children, parent/carers and PPIE representatives were obtained to choose the trial acronym.

Children, parent/carers and PPIE co-applicants will be actively involved throughout the trial. The trial team includes a young person co-applicant who has experience of dental anxiety and has previously been a member of a youth PPIE panel advising on other dental projects. An experienced PPIE representative will share the workload with the young person co-applicant.

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In addition, a youth forum involving four children and young people has been convened. A parent panel of four parent/carers has also been convened to include parent/carers of children with dental anxiety. The forum and panel will meet on average three times per year. To date, the forum and panel have chosen the design of the logo, had input into the format of questionnaires and participant information resources (including the multimedia resources) and thank you gifts. As the trial progresses they will advise on participant recruitment (of participants with a range of socio-demographic characteristics), ways to promote questionnaire completion and drafting of lay summaries. The youth forum and parent panel will be involved in the design of the dissemination strategy. The youth forum and parent panel will be given options in terms of meeting face-to-face, holding virtual meetings or a combination of the above. If there are differences in preferences between PPIE group members around the format of the meetings we will attempt to accommodate these preferences by offering both face-to-face and virtual meetings where possible and exchanging views between members facilitated by the two co-applicants jointly leading the PPIE activities.

This approach will improve recruitment, participants' experience, response rates, dissemination and ensure issues pertinent to child and parent participants are considered at each stage. PPI activities are co-ordinated by ZM and JP as the joint PPIE leads for the trial. They will provide ongoing tailored training and support throughout the trial for the PPIE co-applicants, youth forum and parent panel. ZM and JP will feed the findings of the PPIE activities into the Trial Management Group meetings, report them to the Trial Steering Committee, write annual reports of PPIE activities to NIHR and write the PPIE section of the HTA monograph. Guidance from the University of the West of England on evaluating PPIE in research will be followed and the Public Involvement Impact Assessment Framework used. The GRIPP2 reporting checklist will be used to improve the reporting of the PPIE.

Resources have been allocated to remunerate their time, provide refreshments and cover expenses based on INVOLVE guidance.

AMANUEL is the young person co-applicant who has experience of dental anxiety and has previously been a member of a youth PPIE panel advising on other dental projects.

CHARLES is the PPIE representative co-applicant. She is an experienced PPIE representative with prior involvement in child dental research projects.

11. Dissemination

The CALM trial will inform national clinical guidelines, commissioning decisions and clinical practice for the management of children with dental anxiety in primary dental care. The results will be published in an HTA monograph in accordance with NIHR guidelines.

The dissemination strategy will be developed as the trial progresses with the PPIE members, trial team and engagement with stakeholder groups. The trial team have existing national and international relationships and networks that will be used in addition to building new project-specific links.

The key stakeholders will be:

Policy makers, guideline producers and commissioners: the four Chief Dental Officers, NHS England, NHS Wales, NICE and Scottish Dental Clinical Effectiveness Programme (SDCEP).

One of the key impacts will be for the findings of the trial to be incorporated into commissioning guides produced by NHS England and guidelines produced by NICE and SDCEP. To facilitate this

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media releases will be issued. At the end of the trial a dissemination event is planned to which policy makers will be invited and a summary briefing will be produced. The research team will also liaise with the Cochrane Oral Health Group to ensure the findings feed into the relevant Cochrane review.

Dental professional organisations and dental professionals: the British Society of Paediatric Dentistry, the Faculty of Dental Surgery, the British Dental Association and dental professionals will be engaged throughout the trial via dental media releases, social media accounts describing the study progress and through clinical conference presentations. A summary of the findings will be shared with all those dental professionals involved with the trial. Depending on the outcome of the trial, the trial team will make the resources and online training freely available.

Patients and the public: a trial website has been developed, media releases will be issued and a social media presence will be maintained throughout the trial to describe the study progress. Regular easy read reports will be developed for participating children, their parent/carers and children more generally. We will produce a lay summary of the findings to share with all those involved with the trial. The findings will also be shared via public engagement events hosted by the participating Universities.

Academic community: the protocol for the trial will be published as an open access publication. The findings will be published in a peer-reviewed, high impact journal and presented at national and international oral health conferences such as those hosted by the International Association of Dental Research. The implications of the trial findings will also be shared with academic teaching units to ensure the impact of undergraduate and postgraduate teaching is maximised.

12. Success criteria and barriers to proposed work

The key success criteria: approvals and trial set-up on time; recruitment of dental practices; successful internal pilot study; recruitment of participants to time and target; impactful PPIE; deliver monograph on time, publication of academic papers; successful dissemination activities including event and incorporation of findings into commissioning guides/guidelines.

The main barriers to these successes are i) delays in approvals and/or set up, ii) difficulty with recruitment and retention of dental practices and participants and iii) prolonged impact of the COVID-19 pandemic. We intend to mitigate against risks to the trial through use of the experience of the research team, by the realistic estimates of the timeframes required and careful planning and anticipation of the next steps in the timeline. The inclusion of the internal pilot study will ensure relevant issues are identified early. The clinical leads have extensive experience of primary dental care based trials to draw on if recruitment or retention proves problematic.

In terms of the risks from the current pandemic, as the trial does not involve aerosol generating procedures and is based on a guided self-help approach the risks are already reduced compared to other dental intervention and electronic data capture and offering interviews via telephone or video conference will minimise these further.

13. Intellectual Property

The guided self-help cognitive behavioural therapy intervention ‘Your teeth you are in control’ was developed from an NIHR Research for Patient Benefit grant with Background Intellectual Property (IP) for the intervention held by Sheffield Teaching Hospitals. Background IP held by Sheffield Teaching Hospitals will be provided royalty-free, non-exclusive license, for the duration of the project. Any non-severable arising foreground IP will be managed by Sheffield Teaching Hospitals

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and the University of Sheffield as set out in the collaboration agreement.

14. Funding arrangements

Funding has been awarded by NIHR Health Technology Assessment (HTA) NIHR131805

15 Study documents

Participant Information Sheets • Child • Parent / Carer • Multimedia information resource
Trial Participant Consent/Assent Forms • Child assent form • Parent/Carer consent form
Qualitative Components Participant Information Sheets • Child • Parent / Carer • Dental stakeholders
Qualitative Components Participant Consent/Assent Forms • Child assent form • Parent/carer consent form • Dental stakeholders
Questionnaires/ Case Report Forms • Site Baseline and End Point CRF • Participant Screening Log • Child Baseline, Follow up (FU) 1 and FU2 CRFs • Parent/carer Baseline, FU1 and FU2 CRFs • Dental Practice per child CRFs
Intervention • CBT resources • Usual care – national clinical guidelines
Interview topic guide • Child • Parent/carer • Dental stakeholders

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17. Appendices

Appendix 1 Trial flowchart

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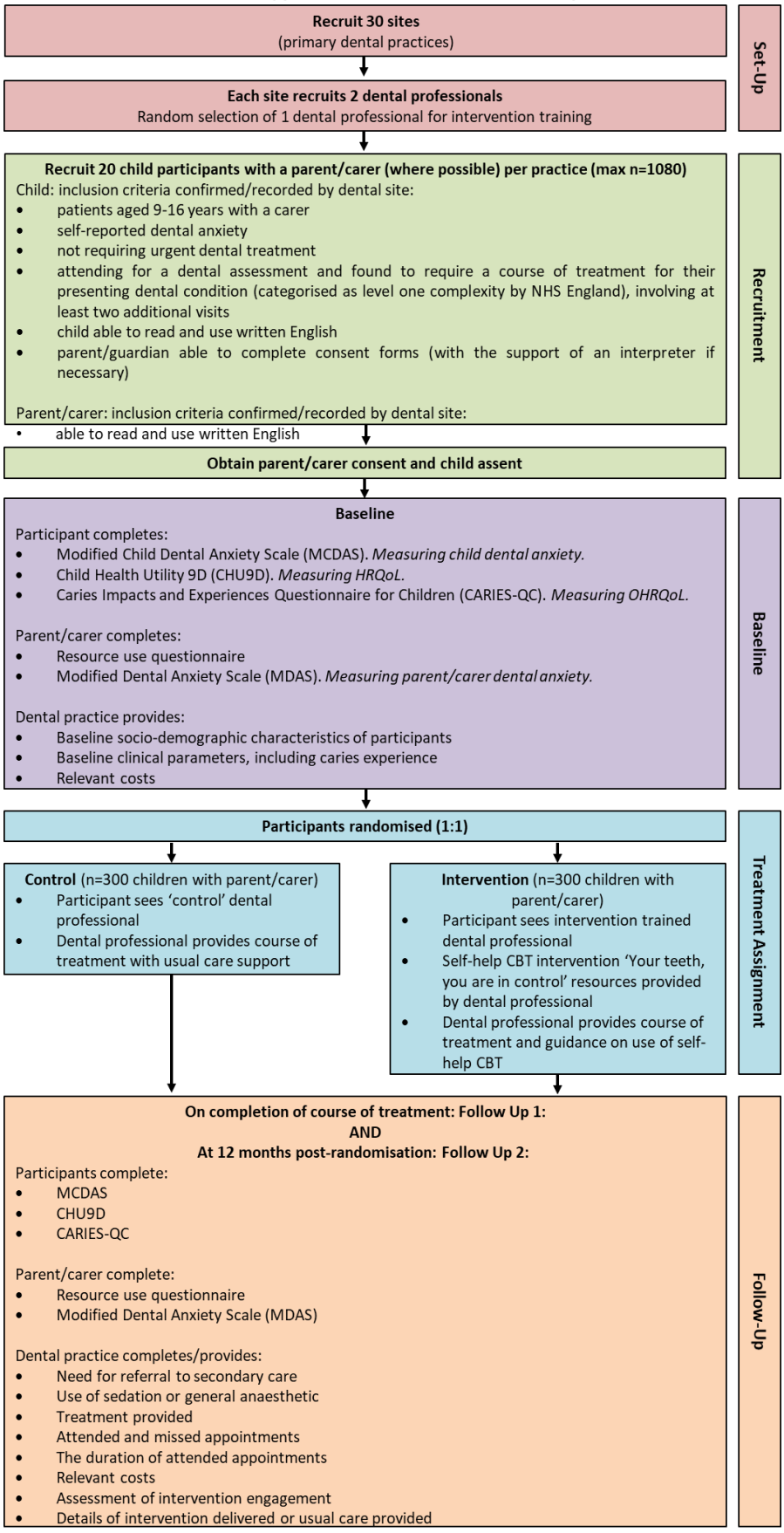
The CALM trial: the clinical and cost-effectiveness of a guided self-help cognitive behavioural therapy intervention to reduce dental anxiety in children



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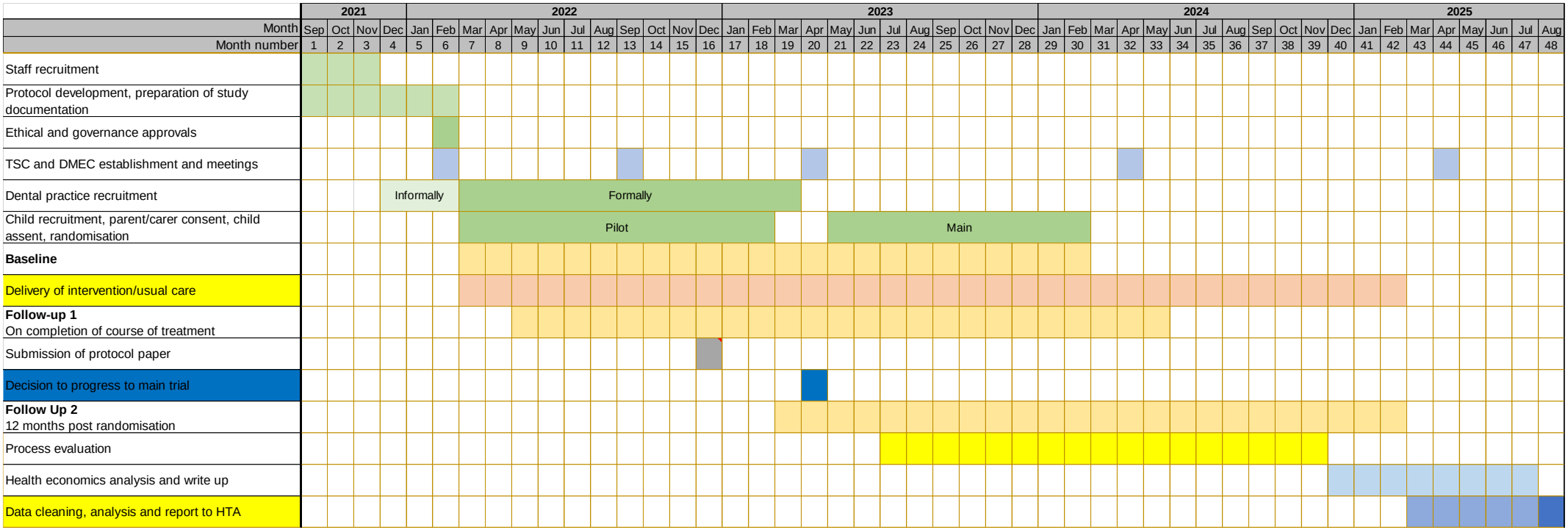
Appendix 2 Gantt chart



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