1. Title

1.1 Protocol Full Title:

A cluster randomised, 16-week, parallel-group multicentre trial to compare the effectiveness of a digital school-based cognitive behavioural resilience/wellbeing-building intervention (CUES for schools) targeting emotional and behavioural problems in vulnerable year 4 primary school children in whole classes, to the usual school curriculum.

1.2 Protocol Short Title/Acronym:

Building Resilience in Children: The CUES-Ed research project: Cluster randomised controlled trial of the CUES for schools programme.

2. Trial registration

Identifiers:

ISRCTN – ISRCTN11445338

REC Number – HR/DP-21/22-28344

3. Protocol version: V1 12/09/22

4. Funding

Funding to conduct the trial is provided by a grant from the Monday Charitable Trust.

5. Roles and responsibilities

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Appendix 1: Study Synopsis

Title of clinical trial	A cluster randomised, 16-week, parallel-group multicentre trial to compare the effectiveness of a digital school-based cognitive behavioural resilience/wellbeing-building intervention (CUES for schools) targeting emotional and behavioural problems in vulnerable year 4 primary school children in whole classes, to the usual curriculum
Protocol Short Title/Acronym	Building Resilience in Children: The CUES-Ed research project: Cluster randomised controlled trial of the CUES for schools programme.
Study Phase if not mentioned in title	Phase III
Sponsor name	SLaM/KCL
Chief Investigator	Dr. Debbie Plant
REC number	HR/DP-21/22-28344
Medical condition or disease under investigation	Emotional and behavioural problems in vulnerable children (scoring at or above a predefined cut-off on the Me and My Feelings (MMF) questionnaire at baseline) receiving the intervention in whole classes.
Purpose of clinical trial	To compare the effectiveness of the CUES for schools intervention in reducing emotional/behavioural problems in vulnerable children to the usual school curriculum at 16 weeks post-randomisation.
Primary objective	Evaluate the effectiveness of CUES for schools in reducing emotional/behavioural problems in vulnerable children at 16-weeks post-randomisation.
Secondary objective (s)	Explore the effectiveness of CUES for schools on: - Reducing emotional/behavioural problems in vulnerable children at 8-weeks post-randomisation. - Reducing emotional/behavioural problems in all children (both vulnerable and non-vulnerable) at 16-weeks post-randomisation. - Improving whole class behaviour at 16-weeks post-randomisation, as indicated by teacher ratings. - Improving teacher's self-rated management of children's emotional upset within the classroom at 16-weeks post-randomization, as indicated by teacher ratings. - Improving emotional/behavioural understanding across all children (both vulnerable and non-vulnerable) at 16-weeks post randomisation.

Trial Design	A cluster randomised, 16-week, parallel group, multicentre RCT.
Endpoints	Primary endpoint: 16 weeks post-randomisation. Secondary endpoint: 8 weeks post-randomisation.
Sample Size	We plan to enrol 2,220 vulnerable children across 74 schools.
Summary of eligibility criteria	*Inclusion criteria:* In Year 4 of a participating school No parental opt-out Child assent *Exclusion criteria:* None
Intervention	A cognitive behavioural resilience/wellbeing building intervention, comprising seven modules with 24 learning objectives, delivered weekly to whole classes, on a digital platform, facilitated by teachers (Digital CUES for schools programme, teacher led). The intervention lasts 12 weeks. The delivery window will be 16 weeks to fit school terms. Assessments will be completed at baseline (0 weeks), 8-weeks post-randomisation (primary outcome only) and 16-weeks post-randomisation, within a 6-week window (2-weeks pre scheduled assessment point to 4-weeks post).
Maximum duration of treatment of a Subject	16-weeks
Version and date of protocol amendments	V1 12/09/22

CONTENTS

6. Background & Rationale

6.1 Study Background

6.1.1 Context and need for CUES-Ed

CUES-Ed is an innovative prevention and early intervention programme rooted in evidence-based Cognitive Behaviour Therapy (CBT) and designed by clinical psychologists from the South London and Maudsley National Health Service Foundation Trust in response to direct feedback – about the need to learn how to look after mental health from a young age - gathered over many years from children and adolescents we have worked with.

As many as 1 in 8 school aged children will experience a mental health problem, such as anxiety and depression, with many more experiencing significant emotional difficulties which impact on learning, behaviour, social relationships, motivation and increase vulnerability to mental health difficulties in later adolescence and adult life. 75% of adult mental illness is present by the age of 21, and 50% by the age of 15. Worldwide, mental health conditions account for 16% of the global burden of disease and injury in young people (World Health Organisation [WHO], 2018).

However, according to the Association of School and College Leaders, 65% of head teachers say they struggle to get mental health services for pupils. Additionally, the National Society for the Prevention of Cruelty to Children (NSPCC) reports that up to 20% of referrals to Child and Adolescent Mental Health Services (CAMHS) are rejected. Across King's Health Partners, our services are seeing significant rises in demand and these are forecast to grow by 41% between 2018 and 2028.

CUES-Ed was born out of recognition that children need access to effective early intervention to manage these difficulties, build emotional resilience and prevent mental health difficulties escalating. Teaching children independent skills and effective strategies is fundamental to building this resilience and the capacity they need to move into healthy adolescence and adult life.

We want to reduce stigma and raise awareness of mental health issues for children and young people by starting developmentally appropriate interventions early - normalising emotional experience and expression and providing accessible, cost-effective, evidence-based treatment. Tackling children's wellbeing and mental health within their school setting enables us to have a far greater, non-stigmatising reach and build strong links between health and education.

Clinicians originally delivered the programme to whole classes in primary schools – reaching over 6,500 children to date. The programme teaches primary-aged children (7-10 years) cognitive strategies and simple but effective behavioural techniques with the help of multi-media and fun hands-on activities that make abstract concepts more concrete and memorable. Flexible and adaptive responses to difficulties are promoted, including self-regulation (the ability to monitor and manage thoughts, behaviours and emotions; especially important when things are difficult or when strong emotions take over) and support-seeking - recognising when extra help is needed. These approaches encourage children to learn useful ways of looking after themselves and their mental health. They are taught to understand when things are not going well and develop life-long skills to help manage any difficulties now and those that might emerge later in adolescence or adulthood.

Feedback from children:

"I think my mind is a whole lot calmer and I'm much more aware of my thoughts, my feelings and my behaviours. You have inspired me to tell my family and friends about what we have been doing..."

"I never thought there were so many ways to calm down!"

"CUES has made me understand more about my feelings and also how to handle my emotions when times are tough. I am very grateful for the CUES team because they have helped me very much."

Qualitative feedback from pilot suggests the key clinical content of the programme has been successfully translated into the digital platform.....

'CUES has helped me with a lot of things but most of all helped me learn how to keep myself happy and healthy' Yr4 child

'CUES has helped me to worry less and it has things to distract me when I am worrying' Yr 4 child

'CUES has taught me how to stop unhelpful thoughts and to make helpful thoughts' Yr 4 child

'It's like I've learnt a secret language after many years of teaching.....this is really going to help the children' Yr 4 teacher

Feedback from parents/carers:

"I think the content covered is invaluable and should definitely be delivered to every child in the country. Thank you."

"Really excellent project which has prompted many useful conversations with our children and helped us all. Great characters used in the sessions that captured the attention of our daughter."

Service evaluation (Redfern, Jolley et al., 2018) showed high rates of acceptability by children and teachers and improvements on whole class well-being. Importantly, children identified as more vulnerable (those scoring within a clinical range on self-report measures of wellbeing/distress and emotional and behavioural difficulties) consistently showed significant improvement following CUES-Ed.

This finding that 'those who need it most, benefit most' strengthens our overall vision to reduce stigma, raise awareness and improve the mental health resources available to children in the UK, particularly in areas of high disadvantage.

6.1.2 Digital programme

The content, aims and objectives of CUES-Ed fit the statutory guidance outline of mental and physical health and offer a comprehensive programme using evidence-based techniques in an accessible format for both teachers and children.

However, cost barriers associated with expert delivery have limited implementation: expert delivery is not a suitable model for widescale implementation. Most recently, we have designed a digital version of the programme, now called CUES for schools, for teachers to deliver. In-service piloting has shown preliminary acceptability and feasibility of this format.

Development of the digital programme has required a highly iterative process with children and teachers to ensure a robust and accessible resource.

It involves an interactive digital platform – with the programme being delivered to the whole class and led by a teacher. Each of the CUES for schools learning objectives has been translated into a combination of real-life video, animation, plus interactive exercises. This is accompanied by a hard copy workbook and home access to an engaging website.

6.1.3 Feasibility pilot

We recently completed a feasibility study of trial procedures which randomised 11 schools (1:1), 5schools and 299 students to receive CUES, and 6 schools and 419 students to usual curriculum (waitlist control).

From the feasibility study all progression criteria (Table 1) were met with the exception of the proportion of children completing baseline assessments (35.9%) which was limited by low return rates for parental consent forms (40.9%). It was established that low parental consent rates were the result of an opt-in procedure which required parents to explicitly confirm their consent into the trial, as opposed to parents actively not consenting. In light of these findings, we have amended trial procedures within the current trial such that parental consent is opt-in by default, with non-consenters required to explicitly opt-out of the trial. It is expected that with this adjustment considered, the current study would meet all feasibility parameters.

Table 1. Feasibility outcomes with 95% confidence intervals.

Feasibility parameter	N	Proportion - %	95% CI - %	Numbers used
Total number of schools randomised	11	100 (11/11)	71-100	Green
Parental Consent	294	40.9 (294/718)	37-45	Amber
Child Assent	551	76.7 (551/718)	73-80	Green
Proportion consent + assent	258	35.9 (258/718)	32-39	Red
Retained participants (non-withdrawal)	249	96.5 (249/258)	93-98	Green
Retained participants (non-withdrawal + no loss to follow-up)	217	84.1 (217/258)	79-88	Green

The feasibility trial also allowed us to estimate the proportion of children within schools who met the criterion for being vulnerable at baseline. Vulnerable children were defined as those scoring >9 on the Me and My Feelings (M&MF, Deighton et al 2013) emotional sub-scale (M&MF-E) and/or scoring >5 on the M&MF behavioural subscale (M&MF-B) at baseline (see section 12.1 below). Under this definition, 40% of the total school population were estimated to meet the threshold for vulnerability within the main trial. As the aim of the CUES for schools programme is to improve emotional and behavioural problems within this vulnerable sub-population more specifically, and effect sizes are expected to be larger within this group as opposed to the wider school population, a decision was therefore made to define a modified ITT population for which the main study would be powered to detect an effect within. To achieve this, two populations are defined within the main (current) trial, with this study being powered in accordance to the primary (sub-) population, as opposed to the wider school population:

1. The primary population, consisting of a sub-population of school children who meet the criterion for vulnerability at baseline.
2. The secondary population, consisting of all school children randomised within the study.

Within the feasibility trial, an effect size of d=-0.21 (95% CI= -0.88,0.45), which translates to a one-point decrease on the M&MF total score, was observed within the vulnerable primary population.

6.1.4 The current study

We will now conduct the planned adequately powered trial comparing CUES for schools to the usual curriculum in its effectiveness to improve emotional/behavioural problems in vulnerable school children participating as part of a whole class.

6.2 Choice of comparators

We will compare CUES for schools to a waitlist control intervention. The current state of evidence leaves open the question of whether whole class wellbeing interventions can be helpfully delivered at scale in schools. We are not yet at the stage of choosing between interventions, or identifying the helpful or active components, which would indicate an active control. Asking if delivering is better than not delivering will provide helpful information. A waitlist control intervention is therefore an appropriate choice for a large scale trial.

7. Trial Objectives

7.1 Trial Objectives

Aims: To evaluate the effectiveness of the CUES for schools intervention, as an adjunct to the usual school curriculum, compared to the usual school curriculum alone, in reducing emotional and behavioural problems in vulnerable Year 4 school children in England, receiving the intervention as part of a whole class.

7.1.1. Primary objective

The primary objective of this trial is to evaluate the effectiveness of CUES for schools compared to the usual school curriculum in improving emotional/behavioural problems for vulnerable year 4 children at 16-weeks post-randomisation, as measured using the M&MF total score. This objective relates to the primary sub-population of children meeting the threshold for vulnerability (M&MF-E >9 and/or M&MF-B >5) at baseline assessment (see section 12.1 below). A between group effect size of *d*=0.2 will be considered a minimum clinically significant effect, with this translating to a difference of approximately 1 point on the M&MF total scale.

7.1.2. Secondary objectives

Secondary aims will be to investigate the impact of the CUES for schools intervention on secondary wellbeing outcomes and on teacher-rated classroom behaviour, as well as exploring the effectiveness of CUES for schools across the wider school population (both vulnerable and non-vulnerable), as measured using the M&MF. More specifically, we will explore change in the CUES for schools group compared to the usual curriculum on:

Vulnerable sub-population:

- M&MF behavioural sub-scores at 16-weeks.
- M&MF emotional sub-scales at 16-weeks.
- The Children's Outcome Rating Scale (CORS) (Duncan, Miller & Sparks, 2003) at 16-weeks.
- Child workbook well-being scores at 16-weeks.
- Child workbook cognitive scores at 16-weeks.

Whole school population:

- M&MF total scores at 16-weeks.
- CORS at 16-weeks.
- Child workbook well-being scores at 16-weeks.
- Child workbook cognitive scores at 16-weeks.

- Teacher ratings of whole class behaviour at 16-weeks.
- Teacher ratings – self-rated coping scale at 16-weeks.

8. Trial Design

8.1 Design

The design will be a 16-week, multi-centre, parallel group cluster RCT with random allocation of schools to one of two arms, in a 1:1 ratio.

The usual school curriculum will be delivered without interference in both conditions, with assessments at baseline (0-weeks, T0), 8-weeks (primary outcome only, T1) and 16-weeks (post intervention, primary endpoint, T2) and a primary outcome of emotional/behavioural problems (M&MF total scores) for vulnerable children at 16-weeks. Waitlist control schools will be offered the intervention later in the term or the following school year. The intervention will be delivered to whole classes. Schools usually have between one and three year 4 classes, with 20-30 children in each class. The sample size calculation has been based on 75 children participating/school. As the exact composition of consenting schools cannot be determined in advance, we will review after the first wave of recruitment, and will recruit more schools as required.

Schools will be randomised to receiving CUES for schools in addition to the usual school curriculum, either now (CUES) or later (waitlist control, WL). The usual school curriculum is nationally set, with limited scope for variation by school. We will record what is delivered in the usual curriculum but will not interfere with usual delivery. In particular, as CUES will not comprise additional hours of teaching, we will record any difference arising in the routine curriculum delivered in intervention and WL schools.

Trained research workers will complete assessments with children and teachers at T0, T1, and T2 (see Figure 1).

8.2 Trial Flowchart

	Engagement with school	Baseline 0-weeks	Pre-intervention	8-weeks	16-weeks
Headteacher consent	X				
Parent letter, opt-out	X				
Teacher liaison/consent	X				
Child assent		X			
Randomisation			X		
Intervention		→	→	→	→
Assessment measures					
Primary outcome: Child-rated emotional and behavioural problems (Me and My Feelings)		X		X	X
Secondary outcome: Child-rated wellbeing (Child outcome rating scale)		X			X
Secondary outcome: Teacher-rated outcomes		X			X
Secondary outcome: Child-rated workbook measures		X			X

9-15: METHODS: PARTICIPANTS, INTERVENTIONS, OUTCOMES

9. Study setting

We will approach the Senior Leadership Teams (SLTs, i.e. the Headteacher and their nominated deputies) of primary schools in inner and outer London and, if needed, extend recruitment out to the home counties. Schools will be mainstream and run by local authorities. We expect to approach schools to express interest in participating around 6-weeks before the anticipated randomisation date.

SLTs will be asked for their agreement to participate on behalf of their school. SLTs will consult with teachers of Year 4 children before agreeing to participate, to ensure willingness

to deliver the intervention. Once SLTs have consented on behalf of the school, we will liaise directly with teachers to ask formally for their separate consent.

Once the SLT and teachers have consented, the school will be considered to be participating in the study.

At least two weeks before randomisation, participating schools will send information sheets to parents by their usual method for sending school-based permissions (paper letter and/or email). Parents will also have access to a video, similar to that to be shown to children (see below), explaining the study and the process of opt-out for each aspect (i.e. via the school for the intervention and assessments, via the research team for research use of data).

- Information sheets will inform parents of the school's decision to deliver the intervention as part of a randomised controlled study, and to complete evaluation measures. Parents will be offered the option to remove their child from the CUES teaching and assessments if they wish, by liaising directly with the school.

- Parents will be offered the opportunity to opt-out of their child's self-report measures being used for a research purpose. This will be by direct communication with the research team, using an online form.

Once parent information sheets have been sent out, children will be told about the study by their teacher, using a video from the study team to standardise the information provided across all schools.

Baseline assessments will commence at least *two weeks after* parental information sheets are sent out, to ensure parents have time to opt out of CUES teaching and assessments, and/or research use of data, should they wish to.

Children will be asked for their assent for data use for research purposes, and also given the opportunity to withdraw from the CUES intervention and assessment at the first baseline assessment. If any child is considered by the class teacher to be expressing a wish not to participate, in either the intervention or assessment, this will be dealt with at the teacher's discretion, as the teacher is responsible for the children's wellbeing and safety during the school day. As part of the school consent, withdrawn children will be found an alternative classroom activity. The teacher information sheet will make clear to teachers that participation in the study should not change their usual treatment of children, outside delivery of the intervention. We expect requests to remove children to be rare: in-service delivery of CUES to 6,500 children has generated only two parental opt-outs, and no child withdrawals.

In our feasibility pilot, numbers of parent and child withdrawals from the procedure were similar.

Unless withdrawn from CUES sessions or assessments, children will otherwise complete the intervention and assessments, even if their parents opt out, or they decline assent for the use of their data for research purposes. In this way, children will not feel stigmatised by being excluded from the class-based intervention and evaluation by not agreeing to the use of data for research. Data will be returned to the research team by courier upon completion by each class. Data for children with parental opt-out or not assenting will be securely destroyed upon receipt by the research team. Within our feasibility trial, we had previously requested that schools arrange this so that data was not sent to the research team without parent and child agreement for research use. However, schools reported finding this a burden and on occasion, this resulted in completed assessments being lost. They, therefore reported a preference for management to be handled by the research team. Current trial procedures therefore reflect this learning.

Teacher ratings are based on a whole class and the collection and use of these for a research purpose will be covered by the SLT consent. School consents will include agreement for the school office to follow-up any parental requests for further information and support, and ensure the research team are aware of these, and to ask permission for the research team to be in touch to support completion if appropriate (i.e. if requested by the parent).

10. Eligibility

10.1 Inclusion Criteria

The school and child inclusion criteria are shown as follows:

School (cluster) inclusion criteria:

- Run by the Local Authority/borough (i.e. a state school), providing mainstream education.
- In London or the home counties
- With an intake at Year 4 (children aged 8-9 years) and Year 5 (children aged 9-10 years), so that waitlist control schools, delivering the intervention after completing the 16-week assessment, will definitely have time to deliver the intervention.

Child inclusion criteria:

- All children in Year 4 (aged 8-9 years)

10.2 Exclusion Criteria

Student exclusion criteria:

- None

11. Trial Intervention

11.1 Interventions

11.1.1 Waitlist control Schools

The usual school curriculum for emotional and social learning will be delivered to all children, irrespective of receipt of CUES. The usual school curriculum is nationally set, with limited scope for variation by school. We will ask school senior leadership how they teach these aspects of the curriculum and record what is delivered in the usual curriculum, but will not interfere with usual delivery. In particular, as CUES will not comprise additional hours of teaching, we will record any difference arising in the routine curriculum delivered in intervention and waitlist control schools.

11.1.2 Intervention Schools

CUES comprises 7 modules, with 25 lessons delivered over 12 weeks (within a 16-week window), in sessions of 20 minutes, two or three times/week. Schools will be asked to incorporate CUES into their social and emotional learning provision, so children do not have additional time in the classroom. The programme consists of digital interactive sessions. Teachers guide their class through the sessions using the content and interactivities that are part of the package. The package incorporates appealing branding, and engaging characters in a mix of animation and video. Children in the intervention arm will receive CUES straight away. Children in the waitlist control arm will receive CUES later in the term or in the following academic year.

11.2 Teachers

The intervention is designed to be delivered by teachers with minimal training. Initial instructions for the use of the programme will be provided in a short video compiled by the research team. This will be given to teachers after randomisation. Teachers will also receive a delivery schedule – outlining which lessons to complete each week. Further delivery notes for teachers are embedded within the programme.

11.3 Adherence

Teacher adherence to the programme will be assessed by a self-report checklist of completed sessions. The intervention material itself is pre-prepared, so providing it is delivered to the class, adherence has been achieved.

Child attendance will be recorded by teachers at T2 as a binary report of whether children attended half or more of the taught sessions, or less than half.

Teachers and SLTs will agree as part of the school/teacher consent process to collect that information and send to the research team.

12. Outcomes

12.1 Primary outcome

We will use the M&MF (Deighton et al., 2013) total scale between group difference of vulnerable children at 16-weeks.

This measure comprises 16 items, each rated 0 (best) to 2 (worst), with total scores ranging from 0 – 32. The total score is made up from two subscales – emotional difficulties (M&MF-E, 10 items) and behavioral difficulties (M&MF-B, 6 items) – with children meeting the criterion for being vulnerable based on M&MF-E >9 and/or M&MF-B >5. The measure is designed specifically for use in schools to evaluate public health initiatives, and has been widely used with children of this age group.

12.2 Secondary outcomes

Vulnerable sub-population:

- M&MF-E 10 item subscale (M&MF items 1-10) at 16 weeks. Scores range from 0-20, with lower scores indicating more positive outcomes (clinical cut-off >9).

- M&MF-B 6 item subscale (M&MF items 11-16) at 16 weeks. Scores range from 0-12, with lower scores indicating more positive outcomes (clinical cut-off >5).

- CORS (Duncan, Miller & Sparks, 2003) four item total scale at 16 weeks. This scale is designed to measure wellbeing and distress, with each item rated 0 (worst) to 10 (best) with scores below 32 considered to represent clinical levels of distress/poor wellbeing.

- Child workbook 7 item wellbeing rating scores at 16 weeks. Each item is rated from 0 (worst) to 10 (best), with total scores ranging from 0-70. Items have been designed as a means to assess the learning from CUES (see Appendix 1). The items have been completed by large numbers of children during in-service delivery of CUES, and our feasibility pilot.

- Child workbook 8 item cognitive rating scores at 16-weeks. Each item is rated from 0-1, with one item rated from 0-2. Total scores range from 0-9. As with child workbook wellbeing rating scores, this outcome is designed to assess the learnings from CUES (Appendix 1).

Whole school population:

- M&MF-E 10 item subscale (M&MF items 1-10) at 16 weeks.

- M&MF-B 6 item subscale (M&MF items 11-16) at 16 weeks.

- CORS 4 item total scale at 16 weeks.

- Child workbook 7 item wellbeing rating scores at 16 weeks.

- Child workbook 8 item cognitive rating scores at 16-weeks.

- Teachers ratings of whole class behaviour (ratings I-II) at 16 weeks. This involves estimates of the proportion of the class displaying positive behaviours, rated as the total number of students within class who ‘often’ or ‘sometimes’ display these behaviours.

- Teachers 4 item coping scale at 16 weeks. Each item is rated from 0 (worst) to 4 (best), with total scores range from 0-16. This scale is designed to indicate how well the teacher feels they are able to manage emotional upset experienced by children within the classroom.

In addition, the following measures will be collected by the research team but will not be formally analysed by the trial statisticians:

- *Teacher adherence* data will be collected from a self-report checklist.
- *Child attendance* data will be collected from the class teacher.

School leadership report of usual emotional and social learning curriculum and impact of incorporating CUES

13. Participant timeline

The delivery timeline needs to fit school terms, so has been designed to accommodate breaks.

Week	Study phase	Activity
-6+	Pre-engagement	• Approach schools to assess preliminary interest
-4+	Engagement	• Approach SLTs. • As part of consent, SLTs check teacher availability/willingness to participate. • SLT consent • Teacher liaison and consent
-3 to -2	Participation, pre-randomisation	• Letter, information sheet and opt-out information sent to parents • Classes informed of study by teacher using video from research team
-1 to 0	Baseline	• Child assent • Child measures • Teacher measures
0	Randomisation	• Research team informs school of allocation
<2	Intervention start (intervention arm only)	• Intervention arm teachers watch training video and commence CUES delivery
8	8-weeks assessment	• Child measures – primary outcome only
16	16-weeks assessment	• Child measures • Teacher measures
16+	Waitlist control arm offered CUES at convenient point for school	

The table above summarises the study timeline from first contact.

Following randomisation:

For CUES schools, teachers will watch the instructional video, and start the CUES programme. CUES delivery should start within two weeks of randomisation and proceed at an hour each week. There are 12 hours of teaching to deliver within the 16-week window. Measures will be completed at T1 and T2.

For WL schools, the outcome measures at T1 (primary outcome only) and T2 will be completed without the class receiving the CUES programme.

The end of the trial will be defined as the last follow-up assessment at T2. WL participants will then receive CUES, at a time suitable in the context of the usual curriculum. This will not be part of the outcomes of the study.

All assessments will be overseen remotely or in-person by a member of the research team who can answer any teacher or child questions and ensure correct administration. Remote oversight will be a member of the research team joining the class by video conferencing platform. Following the pandemic, schools all have this resource routinely available. The procedure was piloted during our feasibility study. Data will be returned securely by courier to the research team after each assessment point.

13.3 Table of contacts

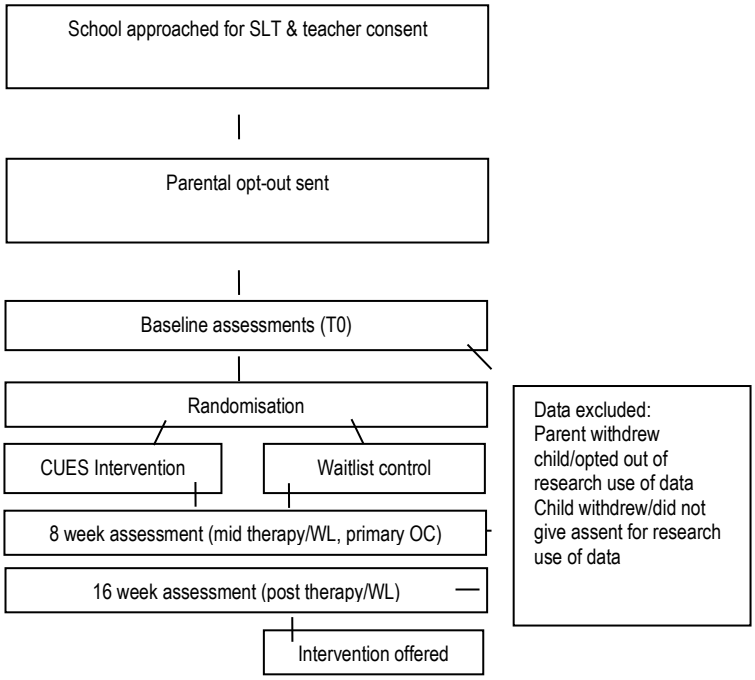
	Engagement with school	Baseline assessment 0-weeks	Pre-intervention	0-16 weeks	8-weeks	16-weeks
SLT consent	X (Research lead/ SLT 30 minutes*)					
Parent letter, opt-out	X (School/parent 30 minutes*)					
Teacher liaison and consent	X (Research team/ SLT/ Teacher 30 minutes*)					
Assessment		X (Children 15-30 minutes) (Teacher, 20 minutes)			X (Children 5-10 minutes)	X (Children 15-30 minutes) (Teacher 20 minutes)
Randomisation			X (Researcher 24 hours)			
Intervention				X (Teacher/ children 12 x 1 hour**)		
Adherence				X (Teacher/ teacher 1 hour)		

**30 minutes includes 15 minutes to read the information and 15 to discuss/decide*

***Teaching takes places during three 20 minute sessions/week for 12 weeks; with school holidays, the delivery window is expected to be up to 16 weeks*

13.4 Study flow diagram

Figure 1: Design



14. Sample size

Using information from our previous feasibility trial (Plant et al., 2022; ISRCTN12486546), we estimate a between group difference effect size of 0.2 between CUES and usual curriculum. Assuming a type-1 error=0.05 (two-sided test) with 90% power and an intraclass coefficient (ICC) of 0.025, a total of 68 schools are needed to be included in the analysis population, each with 25 vulnerable children.

After accounting for a loss-to-follow up at 5% of schools, then a loss of 15% of vulnerable children, we will randomise 74 schools (1:1) to enrol 2,220 vulnerable children.

We estimate within a typical school there are approximately 75 children, of which 40% are vulnerable, thus 30 vulnerable children per school. A total of 5,550 children will be enrolled in total for the whole-school secondary population.

15: Recruitment

15.1 Schools:

We will recruit schools through local authority listings, contacting all schools in inner and outer London to inform them of the study and invite an expression of interest before formally liaising with SLTs and teachers for consent. Each school will be approached for SLT consent, with discussion with the research team as needed. Teachers will be approached by their SLT to discuss participation. However, as the SLT is also their management, they will each have a separate discussion with the research team to ensure they have the opportunity to decline participation should they wish to. SLTs will agree, as part of their consent on behalf of the school, to teachers being free to decide to participate or otherwise without this compromising their relationship with their school in any way.

15.2 Parents:
Once SLT and teacher consent is secured, letters will be sent to all parents in the target year group explaining the study and offering the opportunity to opt out of CUES sessions and/or assessments by liaising with the school, or the use of child-reported outcome measures for a research purpose, by liaising with the research team. If parents wish, they request a discussion with the research team directly using the email provided in the information sheet, or via the school office or teacher.

15.3 Children:
All children will be invited to attend CUES sessions and complete outcomes, unless parents, or the children themselves request not to participate. This is because it is important that the parental opt-out process for research use of data does not result in children feeling excluded or stigmatised. Children will give assent for the use of their measures for research. This will be given as privately as possible, again to avoid any stigma. We will only use data when parents have not opted out and children have assented.

METHODS: ASSIGNMENT OF INTERVENTIONS

16. Randomisation

16.1 Sequence generation

Randomisation will be carried out following SLT/teacher consent, the sending of parental information sheets, and when teachers and children have completed baseline assessment and prior to the start of the intervention. Cluster randomisation will be managed by the study statistician and the King's Clinical Trials Unit (KCTU). We will randomise using covariate constrained cluster randomisation balancing on school deprivation and school size (Carter and Hood, 2008).

16.2 Concealment mechanism

Randomisation will be managed by the study statistician and KCTU. Cluster characteristics needed by the statistician in order to perform the randomisation will be sent through by the trial manager once the school is confirmed as taking part in the study. Allocations will then be sent to the trial manager once all baseline data has been collected from the participants.

16.3 Implementation

Schools will be randomised once baseline assessments are completed. The member of the study team overseeing the collecting and return of T0 measures will alert the study statistician who will send the allocation to the study PI or an allocated deputy from within the research team. This person will communicate with the school and ensure that appropriate steps are initiated (i.e. teacher induction and onboarding so they can deliver CUES for intervention schools).

17. Blinding, emergency unblinding

We will not be able to blind participants to treatment group. Similarly, the teachers cannot be blind to allocation as they will deliver the intervention. The RAs/research team members overseeing outcome assessments will be exposed to school interiors decorated with CUES materials and children's chatter about the intervention (or the absence of these indicators) and thus will not be blind to allocation. However, once collected, data will be processed by RAs blind to allocation. Information on allocation will be restricted to the trial co-ordinator and maintained in a separate database from outcome measures. The senior statistician will remain fully blind throughout the study and will only have access to pooled data. The junior statistician will be fully blind until the SAP has been signed off and prior to seeing any accumulating outcome data. Once the SAP has been signed off they will be fully unblinded. Breaks of blind procedure will be monitored, and an alternative data processor identified for the subsequent assessments. We will ask RAs to guess allocation group for each school as a test of the success of our efforts to maintain blindness. We will report any instances of unblinding in subsequent publications

Emergency unblinding will not be necessary.

18. Data collection

18.1 Data collection methods

Outcome measures (child emotional/behavioural problems, child wellbeing, teacher rated class behaviour) will be completed by children and teachers at T0, T1, and T2, on paper, with support from a research worker online or in-person as required. Measures will be

completed as a group in the classroom. Assessments should occur within a 6-week window of their calendar date (up to 2-weeks earlier or up to 4-weeks later), counted from the day of randomisation. Assessments will be collected by teachers and returned securely by courier to the research team, who will check parental opt-out and child assent. Assessment packs for assenting children, whose parents have not opted out will be stored in a secure office on NHS trust premises and entered into the research database. The research team will confidentially destroy, without access, data for children with opt-out or without assent for research use.

18.2 Retention

Children will be assessed in the classroom. Absent children and teachers will be followed up on their return to school, providing this falls within the 1-month window. Both schools and children are, however, permitted to withdraw at any point during the study. All withdrawals and loss to follow-ups will be monitored and reported to the DMC and TSC, with reasons for withdrawal provided where possible for full transparency.

19. Data management

19.1 Data forms and entry

Data will be collected in paper format and will be entered onto a secure web application REDCap, with integrated participant and range checks. Teacher adherence, student attendance, and school reports of usual curriculum delivery will be held in a separate Excel database by unblinded members of the research team. Paper forms will be stored securely by the research team until the end of the study (January 2024).

19.2 Data transmission and editing

Separate databases will be created for school level data, child level data, teacher adherence data, and allocation. The database will be designed to only accept within range responses. Range and value checks and spot checks against paper copies will be employed to check 20% of entered data.

19.3 Discrepancy checks

Data discrepancies that cannot be resolved by simple checking and reference to paper copies will be referred to the trial steering committee, blind to allocation, for discussion of a resolution.

19.4 Security and back-up of data

Data will be stored on password protected systems in SLaM and KCL. The allocation database will be accessible only to the lead research worker (who will not conduct post-baseline assessments) and the CI (DP) until the study is completed. Outcome data processing will be carried out by researchers who do not have access to allocation, intervention or feedback data. Once all data is entered, cleaned and checked, blind to allocation, the database will be locked. A final database will be returned to the statistician, who will combine with allocation data for analysis.

The Chief Investigator will act as custodian for the trial data. The following guidelines will be strictly adhered to:

Child/teacher data will be pseudonymised for the duration of the study and fully anonymised at the end of the study. The fully anonymised data will be kept indefinitely. Fully identifiable personal details will be kept for parents opting out on paper in a locked filing cabinet in a locked or occupied office and on university servers (as responses are returned using a university based system) until the end of the study (January 2024). Teachers will generate a class list of initials, using as many letters as required to uniquely identify each child, and the research team will allocate a study number, creating a pseudonymised list that can be decoded by the teacher/school for all children, and by the research team only when child details are provided (e.g. name and class provided by parents for the purpose of opting out). Pseudonymised paper data (identified by number and initials) will kept in the same way as personal details. Pseudonymised electronic data, identifiable by number only will be kept on secure Trust computers; and, encrypted, on password protected computers in the university until the end of the study (January 2024).

Pseudonymised data will be stored on personal laptop computers, using MHRN recommended encryption (Trucrypt).

All trial data will be stored in line with the Data Protection Act and archived in line with the relevant institutional policies.

19.5 End of the trial

The end of the trial will be defined as database hard lock. This will be defined as the removal of editing user access for those entering data into the REDCap database.

20. Statistical methods

Prior to the database lock a statistical analysis plan (SAP) will be developed following KCTU Standard Operating procedures (KCTU ST:02 – Developing a statistical analysis plan) and approved by the Trial Team and independent steering committee independent statistician.

Briefly, all statistical analyses will adopt an intention-to-treat principle (ITT) whereby all students will be analysed in accordance to the condition in which they were randomised, with this being a modified ITT for the primary outcome to allow for the inclusion of only the vulnerable sub-sample. All analyses will be conducted after data collection has been completed and pre-processed, the SAP has been signed off and the database has been locked. All variables will first be summarised using descriptive statistics (e.g. means and SDs for normally distributed continuous variables, and median and interquartile ranges skewed continuous data), prior to inferential analyses, and MMF descriptive will be further sub-divided to confirm the proportion of children meeting the criteria for vulnerability at each timepoint.

20.1 Primary outcome analysis

The primary outcome (difference in M&MF scores between CUES and WL at 16-weeks) will be analysed within the vulnerable sub-population using a multi-level, mixed effects linear regression. Here, two random intercepts will be modelled - one at the school level to account for cluster randomisation, and one at the participant level to account for repeated outcome measurement over time. Time, baseline M&MF scores, participant sex, participant age, a dummy variable indicating treatment group, and the balancing variables used for randomisation will be included as fixed effect covariates. A treatment group by time

interaction will also be included to allow for the treatment effect to differ at 8- and 16-week follow-up.

Participants who do not contribute any outcome measurements of the primary outcome at either follow-up time point will not be included in the modified ITT population. Modelling assumptions will be checked and missing outcome data will be handled using maximum likelihood estimation.

20.2 Secondary outcome analysis

Secondary outcomes measures, like the primary outcome, will be analysed using mixed effects linear models in order to account for school level cluster randomisation. However, as secondary outcomes are measured at one follow-up time period only, no participant level random effect will be included within the model. Instead, time will be accounted for using fixed effects, with baseline outcome scores, participant sex, participant age, a dummy variable indicating treatment group, the balancing variables used for randomisation, and any additional baseline variables found to predict missingness in the primary outcome variable included as fixed effect covariates. Participants who do not contribute follow-up outcome data will be omitted from these analyses.

20.3 Missing data and population under investigation

Data will be explored for structural missingness and reported accordingly. The primary population under investigation will be the modified intention to treat (ITT). The ITT population will be defined as all children with at least one post baseline timepoint.

20.3.1 Primary analysis population

This will include only the vulnerable children, as defined

21. Data monitoring

Data monitoring will be the responsibility of the study research lead (SJ), overseen by the trial management group and the steering committee. As data will be collected over a relatively short period of time, there will be no interim analyses. As we do not anticipate risks to participant safety as a direct result of the study and will not be conducting any interim data analysis, we will not convene a separate Data Monitoring Committee, and will devolve these functions to the trial steering committee (TSC) which will be detailed in the TSC charter. The study will be subject to the standard local and national governance frameworks of SLaM R&D, CAMHS clinical services and research co-ordination, and our ethics committee.

An independent steering committee will be established to oversee trial conduct.

22. Harms

We will ask teachers to report to the study team any concerns about CUES or the assessment protocol or any other aspect of the study, expressed by teachers themselves, parents, or children. These will be reviewed by the steering committee for severity, and attributability to the study in liaison with the school, and parents if relevant. Adverse events judged serious and attributed to participation in the study will be reported as below. We do not envisage, given the extensive delivery to date, without any adverse events, that these will be a frequent occurrence, or that an event will trigger cessation of the study.

22.1 Procedures for Recording and Reporting Adverse Events

In other research other than CTIMPs, a *serious adverse event* (SAE) is defined as an untoward occurrence that:
(a) results in death;
(b) is life-threatening;
(c) requires hospitalisation or prolongation of existing hospitalisation;
(d) results in persistent or significant disability or incapacity;
(e) consists of a congenital anomaly or birth defect; or
(f) is otherwise considered medically significant by the investigator.

An SAE occurring to a research participant should be reported to the main REC where in the opinion of the Chief Investigator the event was:
• *Related* – that is, it resulted from administration of any of the research procedures, and
• *Unexpected* – that is, the type of event is not listed in the protocol as an expected occurrence.

	Who	When	How	To Whom
SAE	Chief Investigator (CI) or sponsor.	Within 15 days of the CI becoming aware of the event.	SAE report form for non-CTIMPs, available from NRES website.	Main REC for the trial.
Urgent safety measures	Chief Investigator or sponsor. *Or exceptionally by local Principal Investigator (PI).*	(i) Immediately. (ii) Within 3 days.	(i) By telephone. (ii) Notice in writing setting out the reasons for the urgent safety measures and the plan for further action.	Main REC for the trial. REC Co-ordinator will acknowledge within 30 days. *If notified by PI, relevant local REC should also be informed.*

Type	Who	When	How	To Whom
Progress reports	To be submitted by sponsor, sponsor's legal representative or Chief Investigator (CI). Must always be signed by CI.	Annually (starting 12 months after the date of the favourable opinion) *Main REC may exceptionally request more frequent reports.*	Annual progress report form (non-CTIMPs), available from NRES website.	Main REC for the study.
Declaration of the conclusion or early termination of the research	Sponsor or CI.	Within 90 days (conclusion). Within 15 days (early termination). *The end of the study should be defined in the protocol.*	End of study declaration form, available from the NRES website.	Main REC for the study.
Summary of final report	Sponsor or CI.	Within one year of the conclusion of the research.	No standard format. The summary should include information on whether the study achieved its objectives, the main findings and arrangements for publication or dissemination including feedback to participants.	Main REC for the study.

We do not anticipate safety concerns arising as a direct result of CUEs, which is usually perceived as helpful by children, schools and families. However, we will monitor adverse events carefully, and ensure they are appropriately documented and addressed. Any that arise as a result of the intervention, however unlikely this may be, will be escalated to represented governing bodies for review, and opinion as to necessary adjustments to protocol. Adverse events and progress will be reported by the study team to the main REC and the local Trust R&D, following the schedule above.

22.2 Adverse events that do not require reporting

We will review all adverse events with the reporting school, and report these in study publications, and to the main REC, the TSC, and the local authority as required, following the schedule above.

22.3 Treatment Stopping Rules

The trial may be prematurely discontinued by the Sponsor, Chief Investigator or REC on the basis of new safety information or for other reasons given by the Ethics Committee or the steering/oversight group.

If the trial is prematurely discontinued, active participants will be informed and no further participant data will be collected. Arrangements will be made directly with participating schools and the local authority to ensure that the education and wellbeing of children is not compromised by this process. The Research Ethics Committee will be informed following the schedule above.

22.4 Withdrawal of participants

Schools will have the right to withdraw from the study at any time up until the start of delivery for any reason. Once delivery has begun, both children and parents will also be involved and a school opt out will need to take their wellbeing and expectations into account. Teachers can choose to opt out at any time: schools undertake to find a replacement at the point of consent, however, should this prove problematic, any school withdrawal will be reviewed by the TSC to ensure no undue pressure to participate is placed upon teachers. Parents may choose to opt their child out of the use of data for research purposes at any point prior to full anonymisation of the data. Children can also withdraw their assent at any time up until full anonymisation. If children are absent on the day of assessment, we will make every effort to follow up within the one month assessment window, being led by the school or parents as to any restrictions on this (e.g. the child being severely unwell).

It is understood by all concerned that an excessive rate of withdrawals can render the study uninterpretable; therefore, unnecessary withdrawal of participants should be avoided. Should a participant of any kind decide to withdraw from the study, all efforts will be made to report the reason for withdrawal as thoroughly as possible. Should a participant withdraw from the study intervention only, efforts will be made to continue to obtain follow-up data, providing consent and assent for data use remain in place.

Parents who wish to withdraw their child from the study intervention will be asked to confirm whether they are still willing for their child to attend assessments and contribute data to the study.

23. Auditing

As we do not anticipate risks to participant safety as a direct result of the study and will not be conducting any interim data analysis, we will not convene a Data Monitoring Committee. The study will be subject to the standard local and national governance

frameworks of SLaM R&D, CAMHS clinical services and research co-ordination, and our ethics committee.

Auditing will take place as required by funder/governing bodies, overseen by the study team and independent advisors. The data collection period is expected to be short, so we do not expect any auditing meetings to be required.

ETHICS AND DISSEMINATION

24. Ethical approval

Ethical approval has been granted by King's College London Research Ethics Committee (ref. HR/DP-21/22-28344).

25. Protocol amendments

These will be submitted for regulatory body approval and documented in the protocol log of amendments.

26. Consent or assent

26.1 Consent or assent– we will seek school and teacher consent to participate, and offer parents the opportunity to opt their child out of the intervention, assessments, and/or use of their child's information for a research purpose, with child assent. Should any child prefer not to participate in the CUES teaching or data collection this will be addressed at the teacher's discretion, as they are responsible for the child's safety and wellbeing during the school day. Information sheets will make clear that usual practice in this regard should not be compromised by participation in the research.

26.2 Ancillary studies: These will require a separate consent.

27. Confidentiality

Children may provide new personal information to the research team on their written questionnaires. Where this concerns their care and safety, it will be passed on to school, parental (or other, as appropriate) authorities.

28. Declaration of interests

The PI runs the CUES service. However, this is primarily funded by SLaM, so there is no direct financial conflict of interest. Otherwise, no member of the research team has a conflict of interest.

29. Access to Data

Data will be stored in a King's College repository, and made available upon request. The Investigator(s) will permit trial-related monitoring, audits, REC review, and regulatory inspections by providing the Sponsor(s) and REC direct access to source data and other

documents providing this is within the bounds of data protection and the protection of participants' confidentiality.

30. Ancillary and post-trial care

This is unlikely to be required, but schools will be able to contact the research team with concerns if they wish, following the end of the trial.

31. Dissemination policy

Findings will be communicated to participating school SLTs, who will be free to choose the best method for their school for dissemination. We will present the findings of the research at conferences and will publish in peer-reviewed journals. Locally, we will present to services within our Academic Health Sciences Network, where we have close practice and training links.

31.1 Trial results – these will be reported at the end of the study for all schools.

31.2 Authorship – will be determined by contribution to the paper in question

31.3 Reproducible research – data will be placed in the KCL repository once anonymised.

32-33. Appendices & figures: none

Signatures

To be signed by Chief Investigator minimum and statistician if applicable.

Chief Investigator Suzanne Jolley Date 12/09/22
Print name

Statistician (if applicable) Date
Print name

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