1. PROTOCOL FULL TITLE

SOOTH-ED: Purrble's Soothing Touch for Eating Disorders and Autism

Protocol Short Title/ Acronym: SOOTH-ED

Trial Identifiers

ISRCTN:	https://doi.org/10.17605/OSF.IO/4UKFW		
REC Number:	Awaiting		
NIHR portfolio ID:			
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2. Study Synopsis

TITLE OF CLINICAL TRIAL:	PURRBLE'S SOOTHING TOUCH FOR EATING DISORDERS AND AUTISM
Protocol Short Title/ Acronym:	SOOTH-ED
Study Phase If Not Mentioned In Title:	Phase II
Sponsor Name:	EPSRC IAA Accelerating Impact Award
Chief Investigator:	Prof. Kate Tchanturia
UKCRN Number:	N/A
REC Number:	Awaiting
Medical Condition Or Disease Under Investigation:	Eating Disorders
Purpose Of Clinical Trial:	The purpose of this study is to explore the potential therapeutic benefits of the Purrble intervention, a tangible device designed to assist with in-situ emotion regulation, for individuals on the South London and Maudsley NHS Trust (SLaM) Eating Disorders outpatient service waiting list. By examining its effects on emotion regulation, sensory sensitivity, depression, anxiety, and motivation for treatment engagement, the study seeks to offer empirical evidence on the efficacy of the Purrble as a supportive tool while patients are on the waiting list for formal outpatient treatment.
Primary Objective:	The primary goal of this study is to determine whether there's a significant difference in outcomes (specifically in emotion regulation) between individuals on the EDs outpatient waiting list who receive the Purrble intervention and those who do not. This determination will guide clinicians and healthcare providers in understanding the potential value and application of Purrble in supporting patients with EDs during their waiting period.

Secondary Objective(s):	1. Sensory and Psychological Outcomes: To evaluate the influence of the Purrble intervention on sensory sensitivity, depression, anxiety, and motivation for treatment engagement. 2. User Experience and Feasibility: To evaluate participants' subjective experiences and feasibility levels of the Purrble intervention during their waiting period. 3. Correlations with Comorbid Conditions: To explore the differential effects of the Purrble intervention on participants with specific comorbid conditions, such as Autism.
Trial Design:	Randomized Control Trial (RCT)
Endpoints:	**Primary Endpoint:** Emotion regulation difficulties; measured with the Difficulties in Emotion Regulation Scale (DERS-8) T1. DERS-8 is a unidimensional measure of emotion regulation difficulties in adolescents and adults. The decrease in emotional dysregulation (as measured by DERS) will be compared between intervention and control groups. **Supportive Secondary Endpoints:** T2. Sensory sensitivity; measured with the Glasgow Sensory Questionnaire Short (GSQ-14) The GSQ-14 gauges hypo- and hyper-reactivity to senses in seven modalities: vision, audition, olfactory, gustation, tactile, proprioception and the vestibular sense. Change in sensory sensitivity differences will be compared between intervention and control groups. T3. Depression and anxiety; measured with Hospital Anxiety and Depression Scale (HADS) The HADS measures the severity of depression and anxiety symptoms. Change in depression and anxiety symptoms will be compared between the intervention and control groups. T4. Motivation and self-efficacy for ED recovery; measured with the Motivational Ruler The Motivational Ruler measures participants' self-reported importance to change (motivation) and ability to change (self-efficacy). Any improvement in motivation and self-efficacy to change will be compared between intervention and control groups. Other exploratory outcomes (not a clinical endpoint but will provide additional evidence for Purrble's user affinity and target population): T5. User experience and affinity with Purrble Participants' engagement will be measured post-intervention using an adapted version of the Twente Engagement With eHealth Technologies Scale [TWEETS]. T6. Autism traits; measured with the AQ10 The Autism Spectrum Quotient, short version (AQ10) will be used to measure participants' autistic characteristics, to gauge the difference in intervention effect in autistic and non-autistic patient population.

Sample Size:	200
Summary Of Eligibility Criteria:	**Inclusion Criteria:** • Currently enrolled on the South London and Maudsley NHS Foundation Trust (SLaM) Eating Disorders Outpatient Service waiting list • Confirmed diagnosis of an ED. • Participants aged 18 and above. • Must be on the waiting list for ED outpatient service. • Willing to commit to the duration of the study and provide informed consent. **Exclusion Criteria:** • Individuals currently dealing with substance abuse issues. • Individuals with active psychosis. • Individuals currently experiencing high suicidality or deemed to be at a high risk of self-harm. • Individuals currently undergoing a separate ED treatment. • Individuals who have previously been exposed to the Purrble intervention.
Intervention (Description, frequency, details of delivery)	**Study Groups Description:** All participants in this study are selected from the EDs Outpatient waitlist. Once they agree to participate in the study, they will be randomized into one of two groups: the Intervention or the Control group. **Intervention Group (Purrble):** The intervention takes the form of an interactive plush toy, which was co-designed with children to support in-the-moment soothing (Theofanopoulou et al., 2018; Slovak et al., 2019). The device is framed as an anxious creature, in need of care and attention when it feels distressed. This distress is indicated by a simulated heartbeat using embedded electronics to produce vibration patterns of i) frantic and anxious, to ii) slow, steady and relaxed. When held, the device emits a frantic heartbeat which can be slowed by stroking movements registered by embedded sensors. Once the device has been "soothed" for long enough, the heartbeat transitions into a purring vibration indicating a relaxed state. This transition can be achieved in under 1 minute but is dependent on the device-human interaction. The trial will span 6 weeks, followed by an 8-week follow-up, totaling 14 weeks: • 2 weeks are allocated for interest registration, consent, randomization, and baseline assessment. • 4 weeks are designated for Purrble deployment, with outcomes measured weekly. • An 8-week period is set aside for follow-ups. The intervention period will begin in the 3rd week, once the Purrble has been deployed to the intervention group. After the 8-week follow-up, participants in the intervention group will retain their Purrble devices.

Comparator Intervention:	**Control Group** The control group participants will not receive any specific intervention during the study period. This group serves as a "no treatment" comparator to assess the effects of the Purrble intervention. Control group participants will be monitored similarly to the Purrble intervention group for the outcomes of interest. At the end of the study, participants in the control group will also receive the Purrble device as a gift to thank them for their participation.
Maximum Duration Of Treatment Of A Subject:	4 weeks (about a month). * Participants will be given the Purrble device indefinitely. However, we will monitor participants outcomes for 4 weeks of the study.
Version And Date Of Final Protocol:	Version 1.0, December 12, 2023
Version And Date Of Protocol Amendments:	N/A

3. Revision History

Document ID - (Document Title) revision X.Y	Description of changes from previous revision	Effective Date
Document2	New Protocol	May 2012
N/A	N/A	N/A

4. Glossary of terms (Optional)

EDs – eating disorders.

SLaM – South London and Maudsley NHS Trust

T – Test

5. Protocol Contents

6. Background & Rationale

What is the Problem? The field of Eating Disorders (EDs) has noted a pronounced interplay with conditions like Autism (Westwood and Tchanturia, 2017). Individuals grappling with these disorders frequently manifest sensory difficulties (Kinnaird et al, 2019 & 2020) and face pronounced challenges in emotion regulation (Harrison et al. 2010; Brockmeyer et al. 2014). These challenges not only amplify the distress felt by those with EDs but can also pose significant obstacles to the therapeutic process, especially concerning patient retention and active engagement in treatment. Moreover, the high demand for specialized care in this field has resulted in prolonged waiting periods, often more than 18 months, before individuals can receive treatment (NHS England 2022). This prolonged wait intensifies the necessity for innovative interventions that can offer immediate relief and to ensure continuous care and support during the interim waiting period. Notably, single-session interventions have shown potential, with ED waitlist participants observing a three-fold increase in treatment completion rates (Keegan et al., 2023 In Press).
Study Description: The proposed study aims to evaluate the effects of the Purrble toy intervention on sensory sensitivity, emotion regulation, depression, anxiety, and motivation for treatment engagement among individuals on the ED service outpatient waiting list, and also investigate if the outcomes differ between patients with and without autistic characteristics. By comparing the outcomes with a waitlist control group, we aim to assess the feasibility of Purrble as an intervention used to soothe and better prepare patients for ED treatment.
Population Description: The study population will be drawn from the South London and Maudsley (SLaM) outpatient eating disorders service waitlist. These participants will be adults awaiting their treatment. All individuals included will have a confirmed diagnosis of an Eating Disorder (EDs). Additionally, a subset of the participants may present with a comorbidity of Autism.
Investigational Device: The intervention takes the form of an interactive plush toy (figure 1), which was co-designed with children to support in-the-moment soothing (Theofanopoulou et al., 2018; Slovak et al., 2019). The device is framed as an anxious creature, in need of care and attention when it feels distressed. This distress is indicated by a simulated heartbeat using embedded electronics to produce vibration patterns of i) frantic and anxious, to ii) slow, steady and relaxed. When held, the device emits a frantic heartbeat which can be slowed by stroking movements registered by embedded sensors. Once the device has been "soothed" for long enough, the heartbeat transitions into a purring vibration indicating a relaxed state. This transition can be achieved in under 1 minute but is dependent on the device-human interaction. For full details on the logic model underlying Purrble, see Theofanopoulou et al., (2018).

Figure 1. Purrble companion device

Findings from Previous Studies: The broader societal implications of EDs are equally significant. Estimates from 2015 suggested that the UK sees between 600,000-725,000 ED cases, costing the NHS between £3.9-4.6 billion and resulting in lost income between £6.8-8 billion (BEAT, 2015). Moreover, there's a glaring accessibility gap, with 80% of those with EDs not accessing care due to various barriers (Schleider et al, 2023). This disparity is further exacerbated by a 17-year lag in the practical implementation of developed interventions (Kazdin et al, 2017).
Purrble is an innovative technology-enabled intervention for mental health. Originating from the foundational work of Dr. Slovak and team, Purrble has emerged as a potent tool to deliver emotion regulation interventions, which are pivotal in reducing the incidence of mental health disorders. Since its inception in 2018, this innovative solution has seen commercial success with over 50k units sold, recognition from TIME Magazine, and a cumulative investment nearing $1.5M. Previous studies (Slovák et al, 2018, 2021; Theofanopoulou et al, 2019, 2022; Jess Williams et al, 2023) corroborate its efficacy, especially in enhancing emotion regulation.
Furthermore, Purrble has the potential to address a need for solutions to sensory disturbances associated with comorbid ED and Autism (Adamson et al, 2020; Tchanturia, 2021, 2022). With pathways like Prof Tchanturia's

PEACE (https://peacepathway.org/) already pioneering strides in this realm, Purrble has the potential to augment support beyond traditional therapeutic settings, amplifying the benefits of treatment.

7. Trial Objectives and Design

7.1 Trial Objectives

Primary Objective:

The primary goal of this trial is to assess if the Purrble intervention improves emotion regulation in individuals on the ED outpatient waiting list compared to those who do not receive the Purrble intervention while waiting. This assessment intends to provide clinicians and healthcare practitioners with a clearer insight into the potential benefits and practicality of incorporating Purrble to assist ED patients during their waiting phase.

Secondary Objective(s):

Sensory and Psychological Outcomes:

- Investigate the impact of the Purrble intervention on parameters like sensory sensitivity, depression, anxiety, and individuals' motivation and self-efficacy for ED treatment.

User Experience and Feasibility:

- Examine participants' subjective experiences and evaluate the practicality of the Purrble intervention throughout their waiting phase.

Impact of Comorbid Condition:

- Investigate whether outcomes differ between individuals with and without autistic characteristics.

7.1.1 Primary endpoints

T1. Emotion Regulation Difficulties:
Measurement Tool: Difficulties in Emotion Regulation Scale (DERS-8)
Description: The DERS-8 offers a unidimensional assessment of emotion regulation challenges in adolescents and adults. The study will juxtapose the shift in emotional dysregulation, as quantified by the DERS, between the intervention and control clusters.

7.1.2 Secondary endpoints

T2. Sensory Sensitivity:
Measurement Tool: Glasgow Sensory Questionnaire Short (GSQ-14)
Description: The GSQ-14 appraises both hypo- and hyper-reactivity across seven sensory modalities: vision, audition, olfactory, gustation, tactile, proprioception, and the vestibular sense. Variances in sensory sensitivity will be analyzed and contrasted between both study groups.

T3. Depression and Anxiety:
Measurement Tool: Hospital Anxiety and Depression Scale (HADS)
Description: The HADS evaluates the intensity of manifesting depression and anxiety symptoms. Changes in these parameters will be analyzed between the intervention and control cohorts.

T4. Motivation and Self-efficacy for ED Recovery:
Measurement Tool: Motivational Ruler
Description: The Motivational Ruler quantifies participants' self-professed urgency to alter behaviors (motivation) and perceived capability to initiate change (self-efficacy). Enhancements in these domains will be compared across both study groups.

Exploratory Outcomes (Supplementary insights supporting Purrble's user compatibility and demographical relevance):

T5. User Experience and Affinity with Purrble:

Measurement Tool: Twente Engagement With eHealth Technologies Scale [TWEETS] (adapted version)
Description: After the intervention, the study will measure participants' engagement levels with Purrble.

T6. Autism Traits:
Measurement Tool: Autism Spectrum Quotient, short version (AQ10)
Description: The AQ10 will discern participants' autistic traits. This will help evaluate the difference in the intervention's efficacy between autistic and non-autistic patient populations.

7.2 Trial Design

Design Type: The study is a 2-arm randomized controlled trial comparing an intervention group (Purrble) with a control group on the waiting list for EDs outpatient formal treatment. The trial spans 6 weeks, followed by 8 weeks of follow-ups. The trial consists of 5 pre-deployment assessments and 6 deployment assessments (see Table 1(a)). The intervention period begins once the Purrble is deployed to the intervention group. After the 2-month follow-up, participants in the intervention group can keep their Purrble devices. Outcome measures and corresponding timepoints for control group are summarised in Table 1(b). Control group participants will receive Purrble devices at the end of the intervention period.

Table 1(a). Summary of the outcome measures and assessment times for intervention group

Outcome measure	Pre-deployment (week 1-2)		Purrble deployment (week 3-6)				Follow-up (week 7+)
	T(-1)	T0	T1	T2	T3	T4	
Clinician referral & register interest	X						
Consent	X						
Difficulties in emotion regulation scale-8 (DERS8; Penner et al., 2022)		X	X	X	X	X	
Glasgow Sensory Questionnaire Short (GSQ-14; Millington & Simmons, 2023)		X	X	X	X	X	
Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983)		X	X	X	X	X	
Motivational Ruler (Miller & Rollnick, 2012)		X	X	X	X	X	
Autism Spectrum Quotient, short version (AQ-10, Allison et al., 2012)		X				X	
Twente Engagement With eHealth Technologies Scale (TWEETS)			X	X	X	X	
Purrble engagement questions 1.How many times have you used the Purrble this week 2.In what situations did you tend to use it			X	X	X	X	
Bespoke feedback form							X

Table 1(b). Summary of the outcome measures and assessment times for control group

Outcome measure	Week 1-2		Week 3-6			
	T (-1)	T0	T1	T2	T3	T4

Clinician referral & register interest	X					
Consent	X					
Difficulties in emotion regulation scale-8 (DERS8; Penner et al., 2022)		X	X	X	X	X
Glasgow Sensory Questionnaire Short (GSQ-14; Millington & Simmons, 2023)		X	X	X	X	X
Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983)		X	X	X	X	X
Motivational Ruler (Miller & Rollnick, 2012)		X	X	X	X	X
Autism Spectrum Quotient, short version (AQ-10, Allison et al., 2012)		X				X

Study Groups:

Intervention Group (Purrble): Participants in this group will be provided with the Purrble device, while waitlisted for eating disorder treatment.

Control Group: The control condition will be waitlist as usual. Participants in this arm will not receive the Purrble intervention and will serve as a reference group for comparison.

Blinding Method: Participants will not be blinded to the emotion regulation purpose of Purrble at the time of recruitment and will be informed about their assigned condition. The researcher responsible for participant randomization and the collection of outcome measures will be blinded to the intervention group allocation. The researcher tasked with sending out the Purrble devices will not be blinded.

Nature of the Study: We hypothesize that engagement with an in-situ, bottom-up emotion regulation intervention, providing in-the-moment support, will lead to measurable reductions in self-regulatory difficulties over time for members on the EDs outpatient treatment waiting list.

Cross-Over Design: There will be no cross-over in this study. Participants will remain in their initially assigned groups for the duration of the trial to ensure clarity in results and avoid any potential carry-over effects from one intervention to another.

Endpoint Measurement: To ascertain the efficacy of the intervention, primary and secondary endpoints will be measured using validated instruments as described in the objectives section. Measurements will be taken at baseline, during and post-intervention, and at follow-up timepoints to track changes over time and gauge the persistence of any observed effects.

By adopting an exploratory RCT design, this study aims to establish the potential benefits of the Purrble intervention in the context of emotion regulation, sensory sensitivity, and other related outcomes among individuals on the EDs outpatient waiting list.

7.3 Trial Flowchart

	Week 1	Week 2	Week 3-6	Week 7-14
Patient information and informed consent	X			

Enrolment, Baseline Assessment and Delivering Devices		X		
Purrble Deployment			X	
Follow-up				X

8. Trial Intervention

8.1 Therapy/Intervention Details

Name of the Intervention: Purrble Interactive Plush Toy.
Type of Therapy: Behavioral intervention using a therapeutic companion device.
Description: The intervention takes the form of an interactive plush toy, which was co-designed with children to support in-the-moment soothing (Theofanopoulou et al., 2018; Slovak et al., 2019). The device is framed as an anxious creature, in need of care and attention when it feels distressed. This distress is indicated by a simulated heartbeat using embedded electronics to produce vibration patterns of i) frantic and anxious, to ii) slow, steady and relaxed. When held, the device emits a frantic heartbeat which can be slowed by stroking movements registered by embedded sensors. Once the device has been "soothed" for long enough, the heartbeat transitions into a purring vibration indicating a relaxed state. This transition can be achieved in under 1 minute but is dependent on the device-human interaction.

Administration: One Purrble will be provided to each participant in the intervention group.
Duration: The intervention duration is set at 4 weeks. However, after the deployment period, participants can keep the device indefinitely.

Frequency: There is no set limit to the number of times a participant can interact with the Purrble within a day. They can use it as frequently as they feel necessary.

Method of Administration: Participants will be provided with the Purrble along with a user manual detailing its features and potential benefits. They will be instructed to engage with the toy during times of heightened emotional distress or sensory overload, or whenever they feel the need for emotional support.
Point of Delivery: The Purrble toy will be securely packaged and mailed directly to the participants' provided addresses from the the South London and Maudsley Eating Disorders Outpatient Service premises. Each package will contain:

- The Purrble therapeutic device.
- A user manual detailing how to use the Purrble effectively and safely.
- Link/QR Code for the Questionnaires (Assessment MS Form)A contact information sheet for the research team, should participants have any queries or face any issues during the intervention period.

Upon receiving the package, participants will need to confirm its receipt by completing the baseline measures online (https://forms.office.com/e/qCENYfpBAR) to ensure that all participants have received Purrble and can begin using the intervention as intended. This method of delivery aims to ensure that all participants, regardless of their location or potential mobility constraints, can access the intervention without any hindrance.

Guidance and Support: A helpline will be available for any questions or concerns regarding the use of the Purrble during the intervention period.

8.2 Frequency and duration of intervention

The total expected duration of subject participation is 4 weeks, from the day they receive the Purrble to the end of the intervention period. However, after the intervention, participants can keep the Purrble indefinitely.

Enrolment and Baseline Assessment:
Duration: 2 weeks
Description: Participants are enrolled in the study, assigned to either the intervention or control group, and complete baseline assessments. Participants in the intervention group receive the Purrble toy and a supplementary material – 'user manual' on its use.

Intervention Period:

Duration: 4 weeks
Description: Participants in the intervention group start using the Purrble toy as a part of their daily routine. They are encouraged to engage with the toy whenever they experience heightened emotional distress or sensory overload, or as frequently as they feel necessary.

Follow-up Period:
Duration: 8 weeks
Description: During the follow-up period, all participants (from both the intervention and control groups) will receive a bespoke feedback form.
Wash-out Period: N/A
* Given the nature of this study and the non-pharmacological intervention involved, a wash-out period is not deemed necessary.

8.3 Intervention records

Engagement with Purrble will be assessed using a bespoke survey that enquires about daily use of Purrble and perceived usefulness. The survey will also collect qualitative responses indicating situations where Purrble is helpful/unhelpful.

8.4 Subject Compliance.

Not applicable.

8.5 Study adherence

Not applicable.

8.6 5.5 Concomitant Medication

Individuals undergoing clinical treatment, or any other mental health intervention will be excluded from the study.

9. Research environment

Setting Description: The study will be conducted in a clinical research setting based in London, UK. Specifically, the primary site for this research will be the South London and Maudsley NHS Trust (SLaM) outpatient eating disorders service. Being the university hospital of King's College London, SLaM also serves as a hub for academic exploration and inquiry. The renowned faculty from the university not only provides clinical services at SLaM but also spearheads a myriad of research initiatives, making it a focal point for advancements in psychiatric and psychological care.

Research Participants: Individuals enrolled in the SLaM outpatient eating disorders service and subsequently placed on the waiting list serve as the pool of potential research participants. Given the reputation and reach of SLaM, this list encompasses a diverse range of individuals, providing a rich dataset for the proposed research.

Research Team Affiliation: The research team consists of experts affiliated with both institutions.

10. Selection and Withdrawal of Subjects

10.1 Inclusion Criteria

- Currently enrolled on the South London and Maudsley NHS Foundation Trust (SLaM) Eating Disorders Outpatient Service waiting list
- Confirmed diagnosis of an ED.
- Participants aged 18 and above.
- Must be on the waiting list for ED outpatient service.
- Willing to commit to the duration of the study and provide informed consent.

10.2 Exclusion Criteria

- Individuals currently dealing with substance abuse issues.
- Individuals with active psychosis.
- Individuals currently experiencing high suicidality or deemed to be at a high risk of self-harm.
- Individuals currently undergoing a separate ED treatment.
- Individuals who have previously been exposed to the Purrble intervention.

10.3 Selection of Participants and consent process details

Participants for this research study will be selected directly from the South London and Maudsley (SLaM) outpatient Eating Disorders (EDs) waiting list. This waiting list comprises individuals who have been assessed, diagnosed, and are awaiting specialized outpatient treatment for their EDs at the SLaM facility. Patients who are interested in taking part in research give Consent for Contact (C4C) as part of the standard intake process at SLaM outpatient ED service. The C4C list at the outpatient service will be used to identify potential participants for the study.

The decision to select from this specific waiting list ensures that participants have a confirmed diagnosis of an ED, thereby maintaining the integrity and specificity of the research study. Additionally, selecting from this list means participants are already engaged to some extent with the healthcare system, potentially improving adherence and follow-up rates.

Consent Process Details:

The Participant Information Sheet and the consent form, provided as an editable PDF file attachment, will be shared with participants via email. Participants will have the opportunity to arrange a digital Q&A forum or a live chat session (via MS Teams) to address any queries and concerns regarding the study. Following this, consent form will be countersigned once participants sign and return it via email. A fully signed copy will then be emailed back to participants for their records. Signed electronic consent forms will be stored in a dedicated folder for the project on a King's College London laptop.

10.4 Randomisation Procedure / Code Break

Participants will be 1:1 randomized to two groups through simple randomisation (with stratification of ED diagnoses) using Excel (Kim and Shin, 2014). The allocation key is recorded and managed by the researcher conducting the randomisation. The researcher sending out Purrbles will not be blinded to the intervention group allocation, as do participants receiving Purrbles in the intervention group.

10.5 Withdrawal of Subjects

Purrble intervention must be discontinued if:

- The participant misses Baseline Assessment, Purrble Delivery, or Follow-up assessment.
- The participant decides they no longer wish to continue.
- Discontinuation is recommended by the investigator.

Guidelines for Withdrawal:
Voluntary Withdrawal: Participants have the inherent right to withdraw from the study at any time without giving a reason. This approach prioritizes the autonomy and well-being of the participant.
Investigator-Initiated Withdrawal: The principal investigator may decide to withdraw a participant from the study due to:

- Protocol violations that could compromise the integrity of the study.
- Administrative or other scientifically valid reasons.
- Missed Study Stages: If a participant misses the Baseline Assessment, Purrble Delivery, or Follow-up assessment, they may be subject to withdrawal.

Post-Withdrawal Procedures:

- Participants will be instructed to send Purrble back if they withdraw during the trial.

- Reason for Withdrawal: Should a participant decide to withdraw from the study, every effort will be made to ascertain and document the reason for withdrawal in a detailed manner.
- Follow-Up After Withdrawal: For participants who choose to withdraw only from the therapeutic intervention but not from the study, efforts will be made to continue collecting follow-up data, with the participant's permission.
- Data Collection for Withdrawn Subjects: Participants who opt to withdraw from the therapy will be asked if they are willing to:
- Provide study-specific data during scheduled visits such as Baseline Assessment or Follow-up assessment.
- Permit the collection of specific data during Baseline Assessment or Follow-up assessment.

**Participants have the right to withdraw from the study at any time for any reason. The investigator also has the right to withdraw patients from the study drug in the event of inter-current illness, AEs, SAE's, SUSAR's, protocol violations, cure, administrative reasons or other reasons. It is understood by all concerned that an excessive rate of withdrawals can render the study uninterpretable; therefore, unnecessary withdrawal of patients should be avoided. Should a patient decide to withdraw from the study, all efforts will be made to report the reason for withdrawal as thoroughly as possible. Should a patient withdraw from study drug only, efforts will be made to continue to obtain follow-up data, with the permission of the patient.*

10.6 Expected Duration of Trial.

The full duration of the trial, including follow-up from enrollment, is 14 weeks. Here's a detailed breakdown of the trial phases:

Week 1. Patient Information and Informed Consent Acquisition.
During this phase, potential participants will be provided with comprehensive information about the trial and its objectives. After ensuring they have a clear understanding, they will be asked to give their informed consent if they wish to participate.

Week 2: Enrolment, Baseline Assessment, and Purrble Delivery for the Intervention Group.
Participants will be officially enrolled in the trial. They will undergo a comprehensive Baseline Assessment to collect preliminary data. Those in the intervention group will be delivered the Purrble for the therapy phase.

Week 3-6: Purrble Intervention.
The intervention group will engage with the Purrble therapeutic toy during this phase.

Week 7-14: Follow-Up and Purrble Delivery for the Control Group.
A follow-up assessment will be conducted for all participants to gauge post-intervention outcomes.
The control group will receive the Purrble toy after the main intervention phase to ensure ethical practices, offering them access to the therapeutic tool despite not being part of the primary intervention.

The trial will officially conclude marking the end of the follow-up. The end date of the study will be determined by the date of the final participant's follow-up.

11. Trial Procedures

11.1 By Visit

Throughout all phases of the trial - from initial contact through to post-intervention assessments - everything will be conducted exclusively online. We will be utilizing Microsoft Forms to compile questionnaire packs, which will be sent to participants' email addresses at each respective time point.

Week 1: Patient Information and Consent Acquisition
Objective: Introduction to the trial and acquisition of participant consent.
Online Activities:

- Release of the Participant Information Sheet (PIS).
- Digital Q&A forum or live chat session (via MS Teams) to address queries and concerns from potential participants.

- Distribution and submission of digital Informed Consent Forms for interested participants.

Week 2: Enrolment, Baseline Data Collection, and Purrble Distribution
Objective: Official enrollment of participants, gathering of initial data, and commencement of intervention.
Online Activities:

- Digital enrollment of confirmed participants.
- Online administration of baseline assessments using predefined tools and surveys.

Week 3-6: Purrble Intervention
Objective: Participants interact with Purrble.
Online Activities:

- Weekly assessments (questionaries) will be sent at the end of each week.

Week 7-14: Post-Intervention Follow-up and Purrble Distribution
Objective: Evaluation of outcomes and provision of Purrble to the control group.
Online Activities:

- Administering post-intervention assessments - Bespoke feedback form - to capture participant feedback. Link to complete questionnaires is emailed to participants.
- Notification to the control group about the delivery of Purrble as a gesture of appreciation.

11.2 Laboratory Tests

N/A

12. Assessment of Efficacy

N/A

12.1 Primary Efficacy Parameters

N/A

12.2 Secondary Efficacy Parameters

N/A

12.3 Procedures for Assessing Efficacy Parameters

N/A

13. Assessment of Safety

13.1 Specification, Timing and Recording of Safety Parameters.

Given the non-invasive nature of the Purrble intervention, traditional medical safety assessments like blood tests or physical examinations are not applicable. However, considering the emotional and sensory sensitivities of the target population, it is paramount to closely monitor any negative psychological or sensory responses to the intervention.

Safety Measures:

Adverse Event Reporting: Participants will be given a contact information sheet, enabling them to reach out to two members of the research team via email or phone call during the trial. They can promptly report any undesirable experiences or adverse reactions related to the Purrble intervention.

Regular Check-ins: Throughout the trial, clinicians will conduct periodic check-ins with participants in both groups via phone calls to assess their well-being.

Feedback after Purrble Interactions: After each recorded interaction with Purrble, participants will have the option to provide feedback. This will aid in capturing real-time data on any potential adverse reactions or positive benefits.

Post-Intervention Assessment: A comprehensive assessment will be conducted after the intervention to understand participants' overall experience, including any negative or adverse reactions they might have had.

13.2 Procedures for Recording and Reporting Adverse Events

Adverse Event (AE): Any untoward medical occurrence in a subject to whom a therapy has been administered including occurrences which are not necessarily caused by or related to that therapy.

Adverse Reaction (AR): Any untoward and unintended response in a subject to a therapy which is related to any duration of therapy administered to that subject.

Unexpected Adverse Reaction (UAR): An adverse reaction the nature and severity of which is not consistent with the information known about the therapy in question in the view of the investigator

In non-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 (CI) 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.

Reporting Responsibilities

All SAEs, SARs and SUSARs (excepting those specified in this protocol as not requiring reporting) should be reported immediately to the Chief Investigator and to the Sponsor.

Reports of Serious Adverse Events (SAEs) that are:

- **related** to the study (ie they resulted from administration of any of the research procedures) and
- **unexpected** (ie not listed in the protocol as an expected occurence)

Should be submitted to the REC using the Non-CTIMP safety report to REC form.

These should be sent within 15 days of the chief investigator becoming aware of the event. Reports of SAEs in double-blind trials should be unblinded. There is no requirement for annual safety reports in addition to the information provided through the annual progress report.

	Who	When	How	To Whom
SAE	Chief Investigator	Within 15 days of CI becoming aware of the event	SAE Report form for Non-CTIMPs, available from NRES website.	Main REC with a copy to the sponsor
Urgent Safety Measures	Chief Investigator	Immediately Within 3 days	By phone Notice in writing setting out reasons for the urgent safety measures and the plan for future action.	Main REC Main REC with a copy sent to the sponsor. The MREC will acknowledge this within 30 days of receipt.
Progress Reports	Chief Investigator	Annually (starting 12 months after the date of favourable opinion)	Annual Progress Report Form (non-CTIMPs) available from the NRES website	Main REC with a copy to the sponsor
Declaration of the conclusion or early termination of the study	Chief Investigator	Within 90 days (conclusion) Within 15 days (early termination) *The end of study should be defined in the protocol*	End of Study Declaration form available from the NRES website	Main REC with a copy to the sponsor

Summary of final Report	Chief Investigator	Within one year of conclusion of the Research	No Standard Format However, the following Information should be included:- Where the study has met its objectives, the main findings and arrangements for publication or dissemination including feedback to subjects	Main REC with a copy to be sent to the sponsor

13.2.1 Adverse events that do not require reporting

Given the nature of the Purrble intervention, it's primarily anticipated to be non-invasive and risk-free. However, considering the study's focus on individuals with Eating Disorders and potential comorbidity with Autism, there are certain expected responses due to their inherent conditions. The following outlines anticipated adverse events (AEs) or serious adverse events (SAEs) that, while essential for monitoring, may not require formal reporting within the context of this trial:

- **Minor Emotional Responses:** Given the nature of the disorders and the sensory and emotional challenges faced by participants, minor mood fluctuations or temporary emotional distress can be expected. This might manifest as mild anxiety, momentary sadness, or slight irritability.
- **Brief Sensory Discomfort:** Some participants, especially those with Autism, might initially find Purrble's tactile or auditory feedback slightly uncomfortable. However, if this discomfort persists or is severe, it should be reported.
- **Familiar Physical Responses:** Temporary, minor physical responses that are common for the participant due to their condition, such as mild stomachaches in ED individuals, are expected and may not require reporting unless they are unusually severe or prolonged.
- **Initial Skepticism or Disinterest:** A lack of initial interest or skepticism towards Purrble does not classify as an adverse event. However, persistent disengagement or a marked negative attitude would be of concern.

Period for AE Reporting:

The period for reporting adverse events will begin from the moment of participant consent and extend up to 30 days post the final interaction session with Purrble. This time frame ensures that any delayed reactions or longer-term impacts, both positive and negative, are adequately captured and assessed.

13.3 Stopping Rules

The trial may be prematurely discontinued by the Sponsor or Chief Investigator on the basis of new safety information or for other reasons given by the Data Monitoring & Ethics Committee / Trial Steering Committee regulatory authority or ethics committee concerned.

The trial may also be prematurely discontinued due to lack of recruitment or upon advice from a Trial Steering Committee (if applicable), who will advise on whether to continue or discontinue the study and make a recommendation to the sponsor. If the study is prematurely discontinued, active participants will be informed and no further participant data will be collected.

14. Statistics

Bias in research can significantly compromise the validity and reliability of results. In this study, we've implemented a range of measures to prevent or at least reduce potential biases:

Randomization: Subjects are randomized into either the intervention or control group. This process ensures that both known and unknown confounding variables are evenly distributed between the groups, which can help reduce selection bias. The researcher conducting this randomisation will be blind to intervention group allocation.

Standardized Assessment Tools: Using standardized tools for measuring outcomes ensures consistency in evaluation.

Objective Measurements: Wherever possible, we will rely on objective measurements instead of subjective self-reports. Objective measures minimize the risk of recall bias or response bias.

Transparent Reporting: All methods, deviations, and potential conflicts of interest will be transparently reported in the final publication.

14.1 Sample Size

For this study, we aim to enroll a total of 200 subjects.

Power Calculation: Assuming an alpha level of 0.05 for a two-sided test and a desired power of 80%, the sample size of 200 would allow us to detect significant differences between the intervention and control groups with medium effect sizes.

14.2 Randomisation

A simple randomisation with stratification of ED diagnoses between the two groups will be conducted. Participants will be 1:1 randomly assigned to either intervention or waitlist control group, using a computerised algorithm. Rationale for simple randomisation: subjects are allocated to each group purely randomly for every assignment to minimise bias. The risk of unequal allocation using simple randomisation is low given that we do not have a small sample size of under 100 (Kim and Shin).

Rationale for stratification: it is common for patients on the waiting list for ED outpatient treatment to have a variety of ED diagnoses, including anorexia nervosa, bulimia nervosa, and binge-eating disorder. To avoid bias caused by the different levels and presentation of emotion difficulties across these diagnoses, we aim to stratify ED diagnoses between intervention and control.

14.3 Analysis

General Approach: The data will be analyzed using both descriptive and inferential statistics. Descriptive statistics will offer insight into the central tendencies and dispersions within our data. Inferential statistics will determine the effectiveness of the Purrble intervention compared to the control group. Linear mixed models will be fitted for each outcome measure with time point and group as main effects, time x group interaction, and participant level random intercept. Baseline covariates will be adjusted for when appropriate.

Level of Significance: 0.05

Handling of Data:
Missing Data: We will employ multiple imputation techniques to handle missing data, ensuring that the conclusions are not biased due to any non-random missingness.
Unused and Spurious Data: Any outliers or spurious data will be identified using standard deviation methods. Sensitivity analyses will be conducted to understand their influence on the main findings.

Deviation from Original Statistical Plan: Any deviations from the initially proposed statistical plan will be thoroughly documented in the final report. The reason for each deviation will be justified, and its potential impact on the study's findings will be assessed.

Data Set for Analysis: The primary analysis will be performed on an "intent-to-treat" (ITT) basis, which will include all randomized participants regardless of their adherence or completion status. This approach maintains the randomization's benefits and provides a conservative estimate of treatment effect.

15. Trial Steering Committee

The Trial Steering Committee (TSC) has been constituted with the following distinguished members:

Chairperson (Independent):
Dr. Hubertus Himmerich: He serves as a Consultant Psychiatrist at the SLaM ED Service and holds the position of Senior Reader specializing in Eating Disorders. Dr. Himmerich brings a wealth of experience in treating Eating

Disorders and expertise in conducting randomised trials. Significantly, he is not a co-investigator on this trial, ensuring an unbiased oversight.

Chief Investigator:
Prof. Kate Tchanturia: A recognized Clinical Consultant Psychologist and a Professor of Eating Disorders. As the driving force behind this trial, Prof. Tchanturia is responsible for its conception, design, and execution.

Clinical Expert:
Dr. Ivana Picek: A Consultant Psychiatrist affiliated with the SLaM ED Service. Dr. Picek brings her profound clinical expertise and understanding of the treatment landscape to the committee.

Patient Representatives:
Zhuo Li: An advocate with firsthand experience of Eating Disorders, offering invaluable patient perspective to the committee. Zhuo is also co-investigator of this project.

Dorota Ali: An insightful representative with a background in the Autism spectrum, providing a comprehensive understanding of the challenges and nuances of Autism.

Each member of the TSC has been chosen to ensure the trial is guided by a combination of clinical expertise, research acumen, and patient-centric perspectives. The collaboration of these professionals is integral to the successful execution and meaningful impact of the study.

16. Data Monitoring Committee

The Data Monitoring Committee (DMC) for this project will consist of co-investigators Dr. Petr Slovak, Dr. Dimitri Chubinidze, and Zhuo Li.

Functions of the DMC:
Trial Progress: The DMC will regularly review the trial's overall progress, taking into account patient recruitment, data collection, and follow-up sessions.

Safety Monitoring: The committee will monitor and document any adverse events or unexpected problems that may pose risks to the participants.

Data Integrity: The DMC will ensure the data collected is both accurate and consistent, and that it's stored securely.

Interim Analyses: If necessary, the committee will carry out interim analyses to determine the safety and efficacy of the interventions.

Recommendations: Based on the data they monitor, the DMC will make recommendations on whether the trial should continue as planned, be modified, or be terminated.

Meeting Frequency:
The DMC plans to convene every week during the intervention phase and bi-monthly for the duration of the project. Additionally, if specific incidents arise or urgent issues need addressing, ad-hoc meetings will be scheduled.

17. Direct Access to Source Data and Documents

The Investigator(s) will permit trial-related monitoring, audits and REC review by providing the Sponsor(s), and REC direct access to source data and other documents (eg patients' case sheets).

18. Ethics & Regulatory Approvals

The trial will be conducted in compliance with the principles of the Declaration of Helsinki (1996), the principles of GCP and in accordance with all applicable regulatory requirements including but not limited to the UK policy framework for health and social care research and the Mental Capacity Act 2005.

This protocol and related documents will be submitted for review to XXXXXX Research Ethics Committee (REC)

The Chief Investigator will submit a final report at conclusion of the trial to the funder, the REC and the Sponsor

19. Quality Assurance

Monitoring of this trial will be to ensure compliance with Good Clinical Practice and scientific integrity will be managed by the study team (DETAIL METHODS). A clear reporting mechanism will be established for any issues, deviations, or non-compliances identified during the trial. Corrective and preventive action plans will be developed to address these issues.

20. Data Handling

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

Patient data will be pseudonymised.

- All pesudonymised data will be stored on a password protected computer.
- All trial data will be stored in line with the Data Protection Act 2018 and GDPR and archived in line with Sponsor requirements

21. Data Management

All outcome measures are collected electronically using Microsoft Forms, which automatically collates participant response (raw source data) onto an excel sheet only accessible by researchers on the project. For analysis upon completion of data collection, data will be exported to SPSS/R datasheet with denoted extraction date.
Database:
Our database will be hosted on the KCL protected server with encryption.
Only authorized personnel will have access, each with unique logins.
Regular backups will be taken, with audit trails maintained.

Data Finalization:
After trial completion and data verification, the database will be locked.
Data will be archived securely for future reference.

All data will be stored for 7 years as stipulated by the King's College London policy guidelines.

22. Publication Policy

It is intended that the results of the study will be reported and disseminated at international conferences and in peer-reviewed scientific journals.

23. Insurance / Indemnity

KCL and NHS indemnity will be in place. KCL insurance covers the design of the study, NHS indemnity covers conduct of the study.

24. Financial Aspects

Funding to conduct the trial is provided by EPSRC IAA (Accelerating Impact Award)

25. Signatures

Chief Investigator **Date:** November 2, 2023

Print name: Kate Tchanturia

26. References

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27. Appendixes

- Patient Information Sheet (PIS)
- Consent Form
- Inclusion/Exclusion Criteria
- Study Flowchart
- Questionaries
- IRAS Application
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