Rapid Eczema Trials MASTER Protocol



Rapid Eczema Trials

Rapid & Efficient Eczema Trials – a citizen science approach to conducting eczema clinical trials

Short title: Rapid Eczema Trials

Protocol Version Number: 7.0

Protocol Version Date: 13 Aug 2026

This protocol contains details for the following:

Eczema Bathing Study – how often should we bathe?	Appendix B
Photo assessment of eczema – a Rapid Eczema Trials feasibility study	Appendix C
Keep Control of Eczema Study	Appendix D
Scratch Less Study	Appendix E

EudraCT number (CTIMPs only)	N/A
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CI and Sponsor Approval Page

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the trial in compliance with the approved protocol and will adhere to the principles outlined in the Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031), amended regulations (SI 2006/1928) and any subsequent amendments of the clinical trial regulations, GCP guidelines, the Sponsor's (and any other relevant) SOPs, and other regulatory requirements as amended.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of the Sponsor.

I also confirm that I will make the findings of the trial publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the trial will be given; and that any discrepancies and serious breaches of GCP from the trial as planned in this protocol will be explained.

This protocol has been approved by:	
Trial Name:	Rapid Eczema Trials
CI Name:	Prof Kim Thomas
Trial Role:	Chief Investigator
Signature and date:	KS Thomas KS Thomas (Aug 24, 2026 11:09:32 GMT+1)
Date:	24-Aug-2026

Sponsor statement:

Where Nottingham University Hospitals NHS Trust takes on the Sponsor role for oversight of protocol development, signing of the IRAS form by the Sponsor will serve as confirmation of approval of this protocol.

Statistical approval	
Statistician name:	Lucy Bradshaw
Signature and date:	Lucy Bradshaw
Date:	20-Aug-2026

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Protocol development and sign off

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Amendment number	Protocol version number	Type of amendment	Summary of amendment
SA001	2.0	Substantial	• Addition of Ms Firoza Davies as a protocol contributor • Clarification of criteria for identifying participants by GP practices. • Addition of Appendix B detailing the Eczema Bathing Study
SA002	3.0	Substantial	• Coordinating Centre contact details updated • Addition of Mr Devin Patel as a protocol contributor • Addition of section on feasibility studies. • Addition of ISRCTN registration for Eczema Bathing Study in Appendix B. • Addition of Appendix C detailing the Photo assessment of eczema feasibility study.
NSA007	3.1	Non-Substantial	• Update to Appendix C to permit scheduling and conducting of qualitative interviews before final follow-up timepoint.
SA003	4.0	Substantial	• Addition of Appendix D detailing the Keep Control of Eczema Study
NSA010	4.1	Non-substantial	• Update to Appendix D: Participants/eligibility criteria – revision of criteria for identifying participants by GP practices
NSA011	4.2	Non-substantial	• Update to Sponsor contact details • Update to Appendix D: Lay summary – addition that people may receive reminders to complete questionnaires and data may be collected over the phone. • Update to Appendix D: Trial flowchart – addition that phone calls may collect data if needed. • Update to Appendix D: Recruitment strategies – addition of details that each questionnaire gives an entry into the prize draw. • Update to Appendix D: Trial procedures – addition that data may be collected through other means.

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SA004	5.0	Substantial	• Addition of Appendix E detailing the Scratch Less Study
SM005	6.0	Substantial	• Update to Appendix E: Trial duration - Update to include a Minimum 4-Month Recruitment Period • Update to Appendix E: Sample size - Update to increase the sample size for the 13+ trial to 450. • Update to Appendix E: Addition of ISRCTN number
SM006	7.0	Substantial	• Appendix E: Update to blinding section • Appendix E: Process Evaluation - addition of token of appreciation for interview participants.

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Abbreviations

Abbreviation	Term
AE	Adverse Event
AI	Artificial Intelligence
AR	Adverse Reaction
CDLQI	Children's Dermatology Life Quality Index
CI	Chief Investigator
CONSORT	Consolidated Standards of Reporting Trials
CS	Citizen Science
DAP	Data Analysis Plan
DLQI	Dermatology Life Quality Index
DMC	Data Monitoring Committee
EASI	Eczema Area and Severity Index
CRF	Case Report Form
GCP	Good Clinical Practice
GP	General Practitioner
HOME	Harmonising Outcome Measures for Eczema
ICF	Informed Consent Form
IDQoL	Infant's Dermatitis Quality of Life Index
ISRCTN	International Standard Randomised Controlled Trials Number
NCTU	Nottingham Clinical Trials Unit. NCTU is a UKCRC fully-registered CTU with expertise in the design, conduct, analysis and reporting of randomised trials.
NHS	National Health Service
NIHR	National Institute for Health Research
NRS	Numerical Rating Scale
MCID	Minimal Clinically Important Difference
PI	Principal Investigator
PPI	Patient and Public Involvement
PPIE	Patient and Public Involvement and Engagement
PIS	Participant Information Sheet
POEM	Patient Oriented Eczema Measure
PO-SCORAD	Patient Oriented Scoring Atopic Dermatitis
PSG	Programme Steering Group
PSC	Programme Steering Committee
PSP	Priority Setting Partnership
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
RECAP	Recap of Atopic Eczema
REDCap	Research Electronic Data Capture
ROC	Receiver Operating Characteristics
TIDieR	Template for Intervention Description and Replication
TMF	Trial Master File
TMG	Trial Management Group
TSC	Trial Steering Committee

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Trial Summary

Trial Title	Rapid & Efficient Eczema Trials Programme
Trial Design	Master protocol for a series of prospective, pragmatic, randomised online eczema trials that have been prioritised and designed in partnership with members of the public. Details for each specific trial will be submitted for approval as a protocol amendment to this master protocol (see Appendix A). This novel programme of work has been designed to streamline the approach to conducting online clinical trials and improve efficiencies. The trials may be two-arm, parallel group trials or multi-arm trials depending on the topics prioritised for research by people living with eczema and the co-production groups designing the trials (members of the eczema research community with experience of living with eczema, researchers and healthcare professionals). All trials will be low risk behavioural interventions or advice trials . This could include trials that test self-management interventions (e.g. frequency of bathing), psychological interventions (e.g. stress management or mindfulness activities), advice on use of existing eczema treatments (e.g. how often to apply emollients), or testing of simple dietary intervention (e.g. low sugar diet).
Objectives	Aim: To improve the lives of people living with eczema by partnering with members of the public to co-produce and deliver multiple, efficient online randomised controlled trials (RCTs) and to share new knowledge with those who need it. Objective: To answer multiple research questions that members of the public and healthcare professionals have about the self-management of eczema.
Participants and eligibility criteria	People with lived experience of eczema (specific eligibility for each trial will be decided by the co-production groups).
Intervention and control	To be determined by the co-production groups and through consultation with the wider eczema citizen-science community.
Outcome measures	This project will include the core outcome set measurement instruments for patient-reported outcomes, as developed by Harmonising Outcome Measures for Eczema (HOME: www.homeforeczema.org). Since all trials will be completed online, it will not be possible to conduct face-to-face assessment of clinical signs (one of the HOME core outcome domains). Primary outcome: Choice of primary outcome to be determined by the co-production groups.

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	Secondary outcomes: self-reported eczema symptoms (Patient Oriented Eczema Measure (POEM)); itch intensity (Peak Pruritus Numerical Rating Scale (NRS 24-hour peak itch)); eczema control (Recap of atopic eczema (RECAP)); skin-specific quality of life (Infants' Dermatitis Quality of Life (IDQoL), Children's Dermatology Life Quality Index (CDLQI), Dermatology Life Quality Index (DLQI) depending on age). Additional outcomes: other secondary outcomes may include i) use of interventions, ii) acceptability of interventions, iii) use of eczema treatments (e.g. number of days topical corticosteroids/emollients have been used); iv) adverse reactions, plus up to two additional outcomes that are felt to be relevant to a particular intervention under investigation.
Sample size	Sample sizes will be calculated for each of the individual trials, as they are dependent upon the research question. The justification for the sample size for each trial will be included in the protocol amendment as new research questions are added.

Trial Flow Chart

A flow chart will be added for each trial as it is developed and submitted as a protocol amendment.

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1. Background and Rationale

1.1. Background

Eczema is an itchy, chronic skin condition. The main treatments are topical treatments such as moisturisers (emollients) and flare-control creams (e.g. topical corticosteroids and calcineurin inhibitors), but how best to use them is still uncertain. Inconsistent messages and confusion leads to poor treatment adherence[1]. Questions about skincare, washing and how to use eczema treatments are a high priority for patients[2], but are rarely the focus of large, high-quality randomised controlled trials (RCTs)[3].

Efficient methodologies are required to address these patient priorities in a timely and resource efficient manner, whilst providing robust evidence to inform management choices.

Citizen science (CS) has been variably defined[4], but here we mean the scientific method of working with members of the public to define, address and share answers to questions that are important to them. Citizen science democratises research[5], makes it more relevant, accessible and inclusive[5], and can improve uptake of study findings[6].

The Covid-19 pandemic has dramatically increased awareness of RCTs and the relevance of research to our daily lives, making this research both timely and achievable.

This research programme aligns with the Government's recent strategy document on the Future of UK Clinical Research Delivery[7], which calls for patient-centred research that is "streamlined, efficient and innovative", and supports the Government's agenda for reducing health inequalities in healthcare and research.

1.2. Overview of the whole Rapid Eczema Trials Programme

Aim of the Rapid programme: To improve the lives of people living with eczema by working with citizen scientists to deliver multiple, efficient online clinical trials and share new knowledge with those who need it.

Objectives:

- To establish an "Eczema Citizen Science Community" of people with lived experience of eczema who are willing to co-produce and help disseminate results of the RCTs.
- To embed strategies for engaging with people from diverse communities throughout the programme.
- To answer multiple prioritised research questions via online RCTs.
- To ensure new knowledge is shared rapidly and effectively with patients, health professionals and other stakeholders.
- To identify transferable learning for conducting trials co-produced with citizen scientists in other long-term conditions.

This work is configured across three distinct workstreams.

WORKSTREAM 1 (WS1): Prioritisation and development of citizen science trials

I. Establish cohort of people willing to contribute to citizen science eczema trials.
II. Prioritise research questions.
III. Co-design the research.
IV. Characterise and develop interventions.
V. Co-produce trials.

WORKSTREAM 2 (WS2): Online eczema trials

I. Conduct multiple, online trials.
II. Validate objective eczema severity assessment from digital images.

WORKSTREAM 3 (WS3)– Getting new knowledge to where it is needed.

I. Accelerate meaningful uptake of new knowledge.
II. Identify transferable learning for conducting citizen science trials in other health settings.
III. Identify factors in the implementation of interventions shown to be effective.

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This master protocol pertains to delivery of the online trials (workstream 2) and process evaluation (workstream 3). Requests for ethical approval for the specific trials to be conducted as part of the Rapid Eczema Trials project will be submitted as protocol amendments once key trial design decisions have been made by the co-production groups. See Appendix A for a summary of the aspects to be defined through subsequent protocol amendments.

In addition to the trials and process evaluation, various aspects of the Rapid Eczema Trials programme will employ different engagement/communication methods relevant to the specific activity being undertaken. Most of these activities constitute patient and public involvement, co-design and engagement activities, thus not meeting the definition of research and therefore not requiring specific-ethics approval. NOTE: Whilst these activities do not require specific ethics approval and consent for participation, we have briefly outlined the whole programme in this protocol to ensure appropriate governance of this innovative programme of work.

Methods used during the design of the Rapid Eczema Trials may include, but are not restricted to:

- Online surveys
- Discussion groups
- Workshops
- Engagement activities
- Piloting and testing of trial materials and methods
- Development of podcasts, blogs, infographics, animations and training materials
- Q&A sessions with experts

1.3. Trial Rationale

Why this research is important

Globally, eczema is the most common skin condition[8]. Eczema affects a quarter of infants[9], 1 in 5 children of school age, and often continues into adulthood[10]. It has high cost to both the healthcare provider and patients[11], and results in itch, sleep loss and psychological distress[12]. Eczema affects people of all ethnicities[13] and socio-economic groups[14], although diverse ethnic groups are under-represented in dermatology research[15].

This programme will provide robust answers to multiple questions about the management of eczema. Our programme will answer **multiple important questions** that can be addressed through randomised controlled trials conducted at scale and at pace, and we will rapidly mobilise new knowledge to people who need it.

We will engage with diverse communities, with health benefits to patients and the NHS within the timescale of the award.

Existing research

Our 2013 James Lind Alliance Priority Setting Partnership (PSP)[2], involved 399 people with eczema, and prioritised 14 topics. Of these, seven are suitable for inclusion in this project and remain unanswered[16]. A crowdsourcing prioritisation exercise by the Global Parents of Eczema Research initiative, using natural language processing of online social media posts[17], confirmed ongoing debate in these topics.

The specific focus for the first round of prioritisation will be determined by the Prioritisation Co-production team, but we anticipate that the programme will initially focus on **how best to use existing treatments for eczema** (topical corticosteroids (flare-control creams) and emollients/over-the-counter products) and **best ways of bathing/washing**. These topics cover four of the PSP priority areas for research and systematic reviews have confirmed evidence-gaps.

A systematic review of international eczema guidelines[18] highlights variability in the recommendations for using topical corticosteroids, emollients and bathing practices, and this variation is driven by lack of robust evidence to inform practice.

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Our Cochrane systematic review on the best and safest ways of using topical corticosteroids in eczema[19], confirms large gaps in our understanding of how to best use these common treatments, including questions like: how long to treat an eczema flare for; and whether topical corticosteroids and emollients can be applied concurrently.

Addressing these uncertainties will inform future updates of national and international eczema clinical guidelines and help ensure clear, consistent messages to patients and clinicians and improve the lives of people living with eczema.

1.3.1. Justification for participant population

Patient and public partner feedback has recommended that the trials be as inclusive as possible and so we will initially aim to include all people with eczema, regardless of age or eczema severity. However, the nature of interventions prioritised for testing, by patients and researchers, in the Rapid Eczema Trials may sometimes be more suitable to specific groups of people with eczema, in which case eligibility will be limited to those of most relevance for the question being addressed. This decision will be made by members of the co-production groups, with advice and support from the Trial Management Group (TMG) and Programme Steering Group (PSG).

1.3.2. Justification for design

This programme will combine the strengths of collaborative citizen science with robust trial design to rapidly and efficiently answer research questions through a series of pragmatic, parallel group online RCTs conducted according to this master protocol. Trial integrity and quality will be ensured by working in collaboration with the Nottingham Clinical Trials Unit (NCTU).

Our innovative approach ensures that trials can be conducted, and results implemented, more quickly (Table 1).

Table 1: Summary of efficiencies in Rapid Eczema Trial design and conduct

Stage of research	Traditional approach to eczema trials	Rapid Eczema Trials
Prioritisation of questions	• Usually prioritised by researchers	• Prioritised by people living with eczema
Funding	• Funding secured individually	• Funding agreed for whole programme from outset
Trial design	• Individual trials • Designed from scratch each time	• Multiple online trials based on a standardised master protocol
Trial set-up	• Bespoke per trial • Separate ethics approvals • Bespoke database • Typically, at least 6 months	• Standardised protocol, outcomes and analysis plan • Ethics approval for standardised template protocol with review of new research questions as amendments to the master protocol • Shared infrastructure for data collection and database

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		• New research questions added as prioritisation and intervention development is complete • Trials may be conducted in parallel
Recruitment	• Through GP surgeries or hospitals, with individual sites set up and trained • Face-to-face clinic visits for informed consent, randomisation and data collection • Usually takes 1 to 2 years	• Cohort of citizen scientists established and ready to advertise trials amongst a broad community of people with eczema • Online consent, randomisation and data collection allowing recruitment without geographical or socio-economic boundaries • Aim to recruit in 4 to 6 months per research question
Data cleaning	• Monitoring undertaken by trial team and data queries raised to recruiting sites	• Online data collection with patient-reported outcomes only
Analysis	• Bespoke per trial • Typically allow 6 months between completing follow up of all participants and submission of report	• Standardised statistical analysis plan • Aim to complete analysis within 2 months of final follow-up
Dissemination of results	• Delayed until academic publications completed and peer reviewed • Often takes 12+ months from last visit to publication	• Rapid sharing of results using accessible formats through Eczema Citizen Science Community • Aim to share results within 3 months of database lock
Knowledge Mobilisation / impact on practice	• Usually limited due to time and resource constraints at end of trial	• Knowledge mobilisation planned from outset and co-designed to facilitate rapid uptake of new knowledge
Time required per trial	• 4+ years	• 12 to 18 months

We aim to answer multiple research questions as efficiently as possible, with new research questions being added during the programme as they become available from workstream 1.

All trials will share this master protocol to address the questions prioritised and developed by the co-production groups, ensuring consistent data collection to facilitate speedy set-up and rapid analysis of results. Comparator interventions may vary according to the specific question being addressed (see table 2). Similarly, a standardised statistical analysis plan will be used across all trials.

Areas pre-specified in this standardised master protocol include: overall trial design; setting (online); trial conduct; details of the core outcomes; approach to randomisation, blinding and allocation concealment; broad approach to statistical analysis; PPIE involvement; and governance and oversight arrangements.

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Other aspects will be agreed by the co-production groups and will be submitted for ethics approval for each new research question as an appendix to the protocol. These aspects will include clarification of: i) the specific research question; ii) eligibility criteria (e.g. children/adults, severity of eczema); iii) recruitment strategies (ensuring inclusivity), iv) choice and definition of intervention and comparator; v) choice of outcomes, including likely adverse reactions, and vi) duration of follow-up.

Co-production groups will be supported by a multi-disciplinary TMG to ensure that the trial design is appropriate for the research question.

The co-production groups will decide the most appropriate duration of follow-up for specific research questions (up to a maximum 6 months) using the following general principles:

- **Proof of principle trials with 4-6 weeks follow-up** – little or no existing trial evidence, and rapid onset of intervention response is likely.
- **Definitive trials with 4 to 6 months follow-up** – some evidence exists, but a more robust evidence base demonstrating benefits for people with eczema over several months is required to change practice.

If a trial of longer duration is felt to be warranted (e.g. up to 12 months), this will be discussed with the TMG and approval sought from the independent PSG.

Examples of possible trials that would be suitable for delivery as Rapid Online Eczema Trials are shown in Table 2.

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Please note, these are examples only. Actual research questions and interventions are to be developed by the Eczema Citizen Science community.

Table 2: Examples of trials that would be feasible to conduct as Rapid Eczema Trials

Research question	Is it better for people with eczema to bathe frequently or less often?	How long should topical corticosteroids be applied for to control an eczema flare?	How often should moisturisers be applied to keep control of eczema?	Q1: Is avoidance of soap effective for the management of eczema? (Intervention A versus Comparator) Q2: Is avoidance of shampoo effective for the management of eczema? (Intervention B versus comparator)
Type of trial	Proof of principle	Definitive trial	Proof of principle	Proof of principle
Participant	Children with eczema, all eczema severities	People with eczema, all ages, all eczema severities (planned sub-group analysis based on eczema severity)	People with eczema, all ages, all eczema severities	People with eczema, all ages, all eczema severities
Intervention	Bathe weekly (plus usual eczema care)	Usual prescribed topical corticosteroid applied until symptoms resolve, plus additional 3 days (max of 14 days)	**Intervention A:** Emollients applied 2-3 times per day **Intervention B:** Emollients applied 4+ times per day	**Intervention A:** Usual prescribed leave-on emollient used as soap substitute when bathing **Intervention B:** avoid shampoo on the body when bathing (use mild soap/wash products during bathing)
Comparator	Bathe daily (plus usual eczema care)	Usual care - topical corticosteroid applied as required	Emollient applied once per day	Use mild soap/wash product during bathing and shampoo hair as normal
Outcome	Eczema symptoms (POEM)	Eczema control (RECAP)	Eczema Symptoms (POEM)	Eczema Symptoms (POEM)
Duration of follow-up	4 weeks	6 months	4 weeks	6 weeks

1.3.3. Choice of treatment

Interventions will be defined and characterised by co-production groups consisting of people with lived experience of eczema, healthcare professionals and researchers with experience of intervention development.

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Intervention materials and instructions will be designed to be accessible (including pictures and simple language) and inclusive (available in different languages and formats). Where relevant, the intervention will be described using the TIDieR checklist to allow replication of the intervention[20].

Comparator Interventions: Comparator groups will be defined as appropriate to the trial in questions. A control group using standard eczema care is defined as using treatments for eczema (e.g. emollients and flare-control creams) as advised by their treating clinician(s). This is likely to be the control intervention for most of the comparisons, but the co-production group will advise on choice and specification of the comparator intervention for specific research questions. For example, for a trial looking at frequency of bathing, the comparator group may be defined as daily bathing (plus usual eczema care) and the intervention group as weekly bathing (plus usual eczema care).

Details of the interventions to be compared will be provided as a protocol amendment for each new trial developed.

1.3.4. Sub-studies

Process evaluation: Nested process evaluation studies may be incorporated into individual trials depending on the nature of the interventions being tested and the perceived value of process evaluation insight.
These process evaluations will use a variety of methods including interviews, surveys and focus groups.

Feasibility studies: Feasibility studies may be conducted, and these may be randomised or non-randomised depending on the needs of the study. Details of any feasibility studies will be provided in an appendix and included in a protocol amendment.

2. Aims, Objectives and Outcome Measures

2.1. Aims and Objectives

Aim: To improve the lives of people living with eczema by partnering with citizen scientists to deliver collaborative research and to share new knowledge with those who need it.

Objective: To answer multiple questions that members of the public and healthcare professionals have about the self-management of eczema through multiple, efficient online RCTs.

2.2. Outcome Measures

2.2.1. Primary outcome

The primary outcome will be chosen by the co-production groups and is most likely to be one of the HOME-approved core outcome instruments.

2.2.2. Secondary outcomes

We will include the agreed patient-reported outcomes in the Eczema Core Outcome Set (www.homeforeczema.org). These include:

- eczema symptoms (Patient-oriented Eczema Measure (POEM)[21]) - 7 items, scored 0 to 28;
- itch intensity (Peak Pruritis Numerical Rating Scale (NRS)[22] 24-hour peak itch) - one item, scored 0 to 10;
- eczema control (RECAP)[23] – 7 items, scored 0 to 28;

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- skin-specific quality of life (Infants' Dermatitis Quality of Life Index (IDQoL)[24], Children's Dermatology Life Quality Index (CDLQI)[25] or Dermatology Life Quality Index (DLQI)[26]depending on age) – 10 items, scored 0 to 30

Since these will be online trials, it will not be possible to assess clinician-rated signs of eczema (one of the HOME core domains).

Other secondary outcomes, in additional to the core outcome set, will include i) reported use of intervention and control, ii) acceptability of intervention and control, iii) use of eczema treatments, e.g. number of days topical corticosteroids/emollients have been used; iv) adverse reactions (relevant adverse reactions to be defined by co-production groups).

In addition, up to two 'trial-specific' outcomes may be specified by the co-production working group if required (e.g. process outcomes for a behavioural intervention). Responder burden will be considered carefully when deciding on additional outcomes and baseline characteristics to include.

Participant prior beliefs about the effectiveness of the chosen interventions will be collected and used to inform sensitivity analysis.

Further details of the analysis metric, method of aggregation, and time point for each outcome will be provided as a protocol amendment once the trial design has been agreed with the co-production groups.

3. Trial Design and Setting

3.1. Trial Design

The programme will consist of a series of pragmatic, online, parallel group, randomised controlled trials.

3.2. Trial Setting

All participants will be recruited, provide consent and be randomised online, with digital follow-up data collection via a dedicated app/weblink or text messaging service (i.e. self-referral with no in person visits).

4. Eligibility

Full eligibility criteria will be defined by the co-production groups relevant to each intervention. Participants identified through GP practices will have a recorded diagnosis of eczema on their medical records and will have been issued a prescription for emollients or topical corticosteroids in the last 2 years. We will exclude people who are aged less than 1 year, report eczema only on the hands, eczema limited to locations where exposed to nickel (e.g. from jewellery) and people with eczema around varicose veins, as these characteristics most likely represent alternative or unclear diagnoses.

Exclusions will be kept to a minimum to ensure generalisable results, but participants will only be able to take part in one eczema intervention trial at any one time (this will be monitored centrally based on data provided at baseline). Recruitment will also be limited to one person per household per trial. Participants outside of the UK will not be able to take part.

4.1. Inclusion Criteria

To be determined by the co-production groups and included in protocol amendment.

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4.2. Exclusion Criteria

To be determined by the co-production groups and included in protocol amendment.

4.3. Participant identification

Participants will volunteer to take part in the Rapid Eczema Trials via the trial website www.RapidEczemaTrials.org. Signposting to the website will be through different methods, platforms and organisations (including, but not limited to):

- **Database search and mailout or text messages from GP practices**: may advertise Rapid Eczema Trials project or individual trials specifically
- **Eczema Citizen Science Community:** newsletters sent to people on the existing Rapid Eczema Trials mailing list with encouragement to promote the trial via their personal networks using snowballing recruitment.
- **Through existing mailing lists of people with eczema: e.g.** previous trial participants who provided consent to be re-contacted.
- **Social media:** Facebook, Instagram, Twitter, Reddit, Snapchat, TikTok, Youtube.
- **Eczema charities:** e.g. National Eczema Society (http://www.eczema.org/), Eczema Outreach Support (https://www.eos.org.uk/), Nottingham Support Group for Carers of Children with Eczema (http://www.nottinghameczema.org.uk/index.aspx).
- **Outreach and engagement events:** Throughout the Rapid Eczema Trials programme we will attend events to help mobilise knowledge about eczema and engage individuals who might be interested in joining our Eczema Research Community. If we have ongoing advertisements for an RCT during this time, we will take our advertisement flyers to these events.
- **Internal communication channels of partner organisations** (e.g. social media accounts, website, existing consented mailing lists and newsletters).
- **Call for Participants website** (https://www.callforparticipants.com). An open platform that brings together researchers to promote their trials and potential participants interested in taking part in trials.
- **NIHR People in Research website** (https://www.peopleinresearch.org/)
- **NIHR Be Part of Research website (**Be Part of Research.nihr.ac.uk)
- **Posters and flyers:** displayed in e.g**.** schools, clinical settings, community centres, grocery stores (with permissions from relevant staff members).
- **Other organisations/online platforms/ individuals** e.g. resharing via social media.

Advertising of the trials will be limited to the UK.

We are keen to minimise the risk of digital exclusion by engaging people offline as well as online: recruitment to all trials will include offline approaches such as working with community groups/leaders, snowballing techniques to enrol friends and family of our Eczema Research Community, targeted mail-out from GP surgeries and advertising materials in clinical settings.

To minimise social and culture exclusion, we will use inclusive images and language and recognise that eczema presents differently in people with darker skin tones. We will produce content in a variety of languages and formats to encourage uptake amongst different groups, with use of video content and infographics to avoid difficulties with written English.

Our citizen scientists (members of the Eczema Research Community) will be encouraged to lead on raising awareness of the project and encouraging others in their own networks and interest groups to join, thus continually renewing the membership of the Eczema Research Community over the duration of the programme. We will use a combination of paid social media advertisements to target diverse communities, in addition to unpaid methods (i.e. snowballing, tagging on social media

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platforms): including people of different ages, from diverse ethnic backgrounds and lower social-economic groups.

4.4. Screening

Eligibility screening will be conducted online prior to randomisation into the trial and will be based on self-report. The outcome of the eligibility screening will be displayed on screen to the potential participant, and if they are eligible the participant will be directed to complete the consent should they wish to take part.

Details of reasons for exclusion from the trial will be retained for reporting of the CONSORT flow diagram in trial reports.

We will instigate several strategies to address misrepresentation of eligibility during screening[27]. These include, but may not be limited to:

- sharing videos and information that explains the reasons for randomisation and why it is important in clinical trials to discourage people from trying to join multiple times in order to get the intervention of their choice;
- registration details will be monitored centrally for duplicate registrations.

All trials will be of simple advice to use existing treatments in specific ways, or different ways of managing eczema at home. As such, we do not anticipate misrepresentation of eligibility to be a major concern for the internal validity of the trials as the incentive to 'cheat' will be low.

5. e-Consent

These are low risk trials of interventions to support self-management of eczema at home. As such, our approach to gaining informed consent will be proportionate to the low level of risk and will be provided as e-Consent.

Potential participants will be guided to the trial website (www.RapidEczemaTrials.org), where they will be provided with online information about the trial. Information will be provided in a variety of engaging and formats appropriate for all ages (may include videos, infographics and/or printable materials).

Contact details will be provided for the trial team, should potential participants have questions that they would like to ask prior to signing the informed consent form for the trial or if they have any questions throughout the trial.

Following an initial self-reported eligibility screen completed by the participant online, electronic consent will be gained prior to completion of trial procedures and questionnaires. A completed online consent form from each participant will always be obtained prior to participating in the trial.

Throughout the trial the participant will have the opportunity to ask questions about the trial via the trial e-mail. Any new information that may be relevant to the participant's continued participation will be provided. Where new information becomes available which may affect the participants' decision to continue, participants will be given time to consider and if happy to continue will be re-consented. The participant's right to withdraw from the trial will remain.

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For children aged less than 16 years, e-consent will be provided by the parent/carer. In addition to providing e-consent, parents/carers will be asked to confirm that they have discussed participation in the trial with their child (if appropriate) and that their child is willing to take part. Children under 16 years will be provided with the opportunity to give optional assent on the e-consent form.

6. Enrolment and Randomisation

6.1. Enrolment/Registration

Enrolment will take place online via a dedicated website (www.RapidEczemaTrials.org) linked to a secure, bespoke online database hosted by NCTU. There will be no trial recruiting sites.

6.2. Randomisation

We will use a web-based randomisation service using restricted allocation methods (such as stratification and/or minimisation) to balance key variables likely to be associated with the primary outcome between groups.

Potential participants will be randomised online once consent has been provided, they have submitted their baseline information, including the outcomes specified above, and eligibility confirmed.

Randomisation will be provided by a secure online randomisation system at NCTU. The online randomisation system will be available 24 hours a day, 7 days a week, apart from short periods of scheduled maintenance.

Following randomisation, an email and/or text will be sent to the research team and to the participant confirming enrolment into the trial. Participants will be provided with details of their allocated treatment/intervention (if appropriate). The research team will not be aware of intervention allocation unless needed for distribution of interventions.

Participants will be randomised at the level of the individual in a 1:1 ratio to relevant trial arms. If a different ratio is deemed necessary for a specific trial, this will be clarified in a protocol amendment for that trial.

Groups will be balanced (using stratification and/or minimisation) for the following variables:

- Eczema severity POEM scores: 0-7 (mild), 8-16 (moderate), 17-28 (severe)
- Age (age bands to be defined per trial)
- Other variables specific to individual trials maybe agreed by the co-production group

Full details of the randomisation specification for each trial will be stored confidentially at NCTU.

6.3. Blinding and concealment

Due to the nature of the interventions being considered, participants will usually be aware of their treatment allocation, but the trial statisticians and majority of the research team, will be blinded to treatment allocation.

Participant prior beliefs about the effectiveness of the chosen interventions will be collected and used to inform sensitivity analysis.

7. Trial treatment / intervention

To be determined by the co-production groups and included in protocol amendment.

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8. Trial procedures and assessments

8.1. Summary of assessments

A summary of the trial schedule will be included in the trial amendment once details of individual trials are known.

8.2. Schedule of Assessments

All screening and assessments will take place online.

T0: Screening, randomisation and baseline assessment visit

Participants will complete a brief eligibility screen prior to completing the online consent form. The outcome of the eligibility assessment will be displayed on screen.

If eligible for the trial and consent is provided, participants will be asked to complete the following:

- Demographic information, randomisation variables, UK Diagnostic criteria[28], characteristics of eczema, use of eczema medications, prior belief about the interventions, previous involvement in the trial development, additional baseline information relevant to the specific trial interventions
- Core outcome instruments (POEM (7 items), NRS 24-hour itch (1 item), RECAP (7 items), quality of life instruments (10 items))
- Other outcome instruments: additional outcomes specific to the intervention, use of eczema treatments

For children who are unable to complete patient reported outcomes themselves, proxy reporting by a parent or carer will be accepted, but participants will be encouraged to complete patient reported outcomes in discussion with their child.

Follow-up data collection timepoints

The schedule of follow-up visits will vary depending on the duration of the trial.

For a 6-week proof of principle trial, this is likely to be at baseline, week 1, week 2 and week 6 (but maybe be more, or less, frequent depending on the views of the co-production group).

For a 6-month trial, this is likely to be at baseline, month 2, month 4 and month 6 (but maybe be more, or less, frequent depending on the views of the co-production group).

In addition to outcomes listed above, data will be collected on adherence to intervention and safety.

8.3. Trial Procedures

Face-to-face trial visits are not required for the eczema trials in this programme.

All trial procedures will be completed online with data collection through secure, bespoke links sent via email, text or other appropriate methods. Participants will be sent email and text reminders to complete their questionnaires (or notifications from within an app if used). Participants will be offered the opportunity to take part in an optional prize draw to encourage completion of trial outcomes. The need for additional payments to compensate for additional expense incurred by taking part in the trial will be decided on a trial-by-trial basis.

All data will be collected using the REDCap (Research Electronic Data Capture) platform. Data collection tools will be usable on a range of digital devices, including smartphones.

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Validated questionnaires will be used as recommended by the HOME core outcome set for eczema[29] as these have all been assessed as being feasible to use in a trial setting and having sufficient validity, reliability and responsiveness.

Other secondary outcomes and baseline characteristics will be assessed using bespoke questions if a validated instrument is not available. Details of exact questions for these will be included in protocol amendments for specific trials.

8.4. Collection, Storage and Analysis of Clinical Samples

We do not anticipate collecting any clinical samples as all assessments are made online with no face-to-face contact with the research team.

If a particular research question warrants collection of samples details of these arrangements will be included as a protocol amendment for the specific trial.

8.5. Sub studies

8.5.1.1. Process evaluation

Trials, even those delivered in partnership with citizen scientists, should generate new knowledge which might have a positive societal impact; any limitation or bias that might undermine this should be identified and addressed[30]. To this end (and when deemed appropriate by the co-production groups) we will undertake nested process evaluation within/alongside the trials.

For each Rapid Eczema Trial, we will work with the co-production groups to establish nested process evaluations. These will generate contextualised understanding of each intervention to support interpretation of trial outcomes and recommendations for implementation, specifically considering questions of acceptability, feasibility, and adherence with intervention. The co-production groups will define the scope and method of these evaluations. Trained research staff will undertake qualitative data collection and analysis; if citizen scientists wish to take part in these activities they will be appropriately trained and supported.

We will advocate a range of simple methods - online surveys, participant diaries, participant interviews, participant focus groups. The co-production groups will identify and refine appropriate evaluation methods for each intervention evaluation. We will provide training for the co-production groups where this is felt to be necessary.

The complexity of each intervention will shape the design of the bespoke evaluations. Online surveys may adequately assess the acceptability and feasibility of relatively simple interventions. Other methods (interviews, research diaries) may be required to explore the benefits and difficulties of more complex interventions.

The size of each Rapid Eczema Trial and the methods used in the intervention evaluations will inform the number of trial participants included in each process evaluation. Analysis will be shaped by the scale and scope of each evaluation, but we would expect descriptive statistics and/or qualitative thematic analysis as a minimum. We will ensure that the process evaluation findings are generalisable to the broader clinical population. We will ensure that the process evaluations are inclusive of all socio-demographic groups.

In addition, at the completion of each Rapid Eczema Trial, we will review recruitment, retention and data quality; specifically considering the diversity and appropriateness of the trial population for the intervention being tested. We will ask NCTU staff to maintain a log of issues or difficulties with trial delivery; we will reflect upon these in focus groups or structured interviews with NCTU staff.

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At the conclusion of each Rapid Eczema Trial, members of the research team will review findings with external experts/stakeholders (i.e. clinicians, researchers, members of the public not involved in the Rapid Eczema Trials programme delivery). These workshops will address the acceptability of trial findings, contribution to eczema care knowledge, and implementation of findings. They will directly feed into the Knowledge Mobilisation activities for the project and will conclude with recommendations for how best to operationalise learning for greatest effect.

8.5.1.2. Feasibility studies

Feasibility studies may be conducted, and these may be randomised or non-randomised depending on the needs of the study. Details of any feasibility studies will be provided in an appendix and included in a protocol amendment.

8.6. Withdrawal and discontinuation procedures

8.5.1 Withdrawal prior to randomisation

Any participant who does not provide consent during the recruitment process, **prior to randomisation**, will not be randomised, and no further data will be collected.

8.5.2 Discontinuation and withdrawal post randomisation

Participants may withdraw their consent for follow-up and/or other trial-related activities or receiving trial-related communications. To withdraw, participants will be asked to contact the research team so that appropriate action can be taken to ensure that the participant's wishes are followed.

Participants may withdraw from different activities.

Withdrawal type	Withdrawal procedure	Use of data
Discontinue follow-up questionnaires	Any participant that requests to discontinue from trial questionnaires will be marked as withdrawn from questionnaire collection on the trial database and no further contact will be made with the participant for the purpose of obtaining questionnaire follow-up data.	Any data collected prior to participant withdrawal will be retained and used.
Discontinue allocated intervention but continue with follow-up	Any participant that requests to discontinue their allocated intervention but is willing to continue questionnaire follow-up will be marked as withdrawn from allocated intervention on the trial database but contact will continue to be made with the participant for the purpose of	Any data collected will be used

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	obtaining questionnaire follow-up data.	

As these trials are being conducted online with minimal contact with the research team, participants wishing to stop completing the questionnaires or stop their allocated intervention, will probably simply stop. In these cases, participants will continue to receive links to the trial questionnaires through until the end of their planned follow-up and adherence data will be used to capture adherence with allocated interventions.

8.7. Post Trial Care

Once their participation in the trial is over, participants will be advised to revert to their usual self-management practice and use of eczema treatments as directed by their routine clinical care team.

9. Adverse Event Reporting

9.1. Reporting Requirements

The collection and reporting of Adverse Events (AEs) will be in accordance with the Research Governance Framework for Health and Social Care and the requirements of the National Research Ethics Service (NRES).

We do not anticipate AEs for the types of lifestyle and advice trials that the Rapid Eczema Trials programme will deliver, but our approach to reporting adverse events and identification of related adverse effects that could be attributed to the individual trials will be outlined in the protocol amendment for each trial (e.g slips in the bath or shower for a trial on frequency of bathing).

10. Data Handling and Record Keeping

10.1. Source Data

All data for the Rapid Eczema Trials will be via participant-report through electronic questionnaires and stored directly into the trial database, thus this is the source data. Participants' medical records will not be accessed.

10.2. CRF Completion

All data collection will be via online questionnaires completed by participants. There will be no Case Report Forms completed by sites. This section is therefore not applicable.

10.3. Data Management

Central data management for the Rapid Eczema Trials will be minimal as there will be no recruiting sites or source documentation. As such, data queries will not be raised for missing questionnaire responses.

All data will be handled according to the Rapid Eczema Trials Data Management Plan.

10.4. Archiving

It is the responsibility of the Chief Investigator to ensure all essential trial documentation are securely retained for at least 5 years.

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The Trial Master File and trial documents held by NCTU on behalf of the sponsor shall be archived using secure archive facilities at Nottingham University Hospitals NHS Trust. This archive shall include all trial databases and associated meta-data encryption codes.

10.5. Data Sharing

Individual participant medical information obtained as a result of this trial is considered confidential and disclosure to third parties is prohibited with the exceptions noted in this protocol.

Participants' contact details, including name, telephone/mobile number and email may be shared between NCTU and third parties (where required) for the sole purpose of issuing questionnaires and electronic reminders (text/email) for the trial.

Any personal data will be held in a secure database using encryption, with restricted password protected access. Only appropriate members of the research team will have access to these data.

Participant confidentiality will be further ensured by utilising identification code numbers to correspond to treatment data in computer files.

Data generated as a result of this trial will be available for inspection on request by Nottingham University Hospitals NHS Trust, the REC, local R&D departments and the regulatory authorities.

Anonymised participant datasets may be shared with researchers external to the trial research team on request.

Since one of the aims of the Rapid Eczema Trials programme is to share resources to allow others to run high-quality and efficient eczema trials for themselves, we will openly share this master protocol, master analysis plans, database coding, data dictionaries, analysis code and other relevant trial materials via an appropriate platform.

11. Quality control and quality assurance

11.1. Site Set-up and Initiation

N/A – no research sites are involved in this research programme

11.2. Monitoring

Monitoring will be carried out as required following a risk assessment and as documented in the monitoring plan.

11.3. Audit and Inspection

The Trial Master File and evidence of audits will be made available upon request for regulatory inspections.

11.4. Notification of Serious Breaches

The Sponsor is responsible for notifying the REC of any serious breach of the conditions and principles of GCP in connection with that trial or the protocol relating to this project.

11.5. End of Trial Definition

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The end of each trial will be the final database lock. NCTU will notify the REC once the final trial has ended and a summary of the clinical trial report will be provided within 12 months of the end of the final trial.

12. Statistical Considerations

12.1.1. Power Calculations / sample size calculation

The total number of participants for each trial required will depend on the questions prioritised and the chosen primary outcome. The justification for the sample size for each trial will be included in the protocol as new research questions are added. The principles of sample size calculation for each research question will be based on 90% power, 5% significance and also consider the family wise error rate if multi-arm trials with a shared control group are used. Target sample sizes will also account for potential loss to follow-up.

For some research questions, the co-production groups may feel that it is important to be able to detect an effect within different groups (e.g. adults/children), in which case the overall sample size will be determined to ensure sufficient power within each participant group.

12.2. Analysis of Outcome Measures

Analysis and reporting of each trial will be in accordance with CONSORT guidelines. A standardised statistical analysis plan will be developed and agreed with the independent programme steering committee. The analysis plan for each trial will be finalised prior to database lock and release of the treatment allocations.

Primary comparative analyses for each trial will be conducted according to randomised allocation regardless of adherence (e.g. intention to treat principle) with due emphasis on confidence intervals for between-arm comparisons. Primary and secondary outcomes will be analysed using appropriate regression models with adjustment for the randomisation variables and baseline score (if applicable)[31]. Where possible, regression models will also adjust for other baseline prognostic covariates (based on evidence considered by co-production groups).

Sensitivity analyses will be considered on a case-by-case basis for each trial including:

- Using multiple imputation for missing data
- Using the information on prior belief in the effectiveness of the proposed interventions.
- According to diagnosis of eczema based on the UK Diagnostic Criteria for eczema

The effect of adherence with the allocated intervention may also be investigated if appropriate.

12.2.1. Planned Interim Analysis

There are no planned interim statistical analyses for any of the trials in view of the short-anticipated recruitment period.

12.2.2. Planned Final Analyses

Data analysis for each trial will be performed when the target sample size for the trial has been reached, follow-up completed, and database locked.

12.2.3. Planned Subgroup Analyses

For some research questions, the co-production groups may feel that it is important to be able to detect an effect within different groups (e.g. adults/children), in which case the overall sample size will be determined to ensure sufficient power within each participant group and the intervention effect will be estimated for each participant group.

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In addition, the need for subgroup analysis to explore whether the intervention effect varies according to baseline characteristics will be considered on a case-by-case basis for each trial by the co-production groups. Where specified, these subgroup analyses will be performed by including appropriate interaction terms in the regression model for the primary outcome. Trials will not be powered to detect any interactions hence any subgroup analyses will be treated as exploratory.

13. Qualitative Process Evaluation Analysis

Data will be analysed thematically using a framework approach.

A standard Rapid Eczema Trials framework will be developed to incorporate three broad thematic areas which can be applied in all trial process evaluations. Thematic areas will be (i) acceptability of the intervention; (ii) benefits (or difficulties) experienced; (iii) improvements for the future.

Quantitative process evaluation may be conducted depending on the nature of the trial and process evaluation planned.

14. Trial Organisational Structure

The roles and responsibilities for each organisation are documented in the Contractual Agreement and the responsibilities of the Sponsor/CI/NCTU specifically are detailed in the Delegation of Responsibilities.

14.1. Sponsor

Nottingham University Hospitals NHS Trust

14.2. Trials Unit

The trials will be co-ordinated by NCTU.

14.3. Trial Management Group

The Trial Management Group (TMG) will include those individuals responsible for the day-to-day management of the trial, such as the Chief Investigator, Statistician, Trial Manager, Data Manager, plus members of the co-production groups and other co-applicants as appropriate. The role of the group is to ensure high quality trial conduct, to time and within budget, to monitor all aspects of the conduct and progress of the trial, ensure that the protocol is adhered to and take appropriate action to safeguard participants and the quality of the trial itself.

14.4. Programme Steering Committee

The role of the Programme Steering Committee (PSC) and its membership is outlined in the PSC Charter.

14.5. Data Monitoring Committee

Since the programme includes only low-risk trials it was agreed with the sponsor and funder that a Data Monitoring Committee was not required.

14.6. Finance

This project is funded by National Institute for Health & Care Research Programme Grants for Applied Research (NIHR203279).

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14.7. Participant gratitude and stipends

Participants will be offered the opportunity to enter a prize draw, but we do not anticipate making payments to individuals for participation. If a particular trial might result in costs to the individual, then the need to provide reimbursement for costs will be considered on a trial-by-trial basis.
No travel will be required as interventions and data collection are to be completed at home.

15. Ethical Considerations

The trials will be performed in accordance with the recommendations guiding physicians in biomedical research involving human participants, adopted by the 18th World Medical Association General Assembly, Helsinki, Finland, June 1964.

The trials will be conducted in accordance with the Research Governance Framework for Health and Social Care, and subsequent amendments and the Data Protection Act 2018 and Guidelines for Good Clinical Practice (GCP). The protocol will be submitted to and approved by the REC prior to use.

16. Confidentiality and Data Protection

Personal data recorded on all documents will be regarded as strictly confidential and will be handled and stored in accordance with the Data Protection Act 2018 and the UK General Data Protection Regulation (GDPR).

All participants will be assigned a unique trial number on randomisation into the trial. First names will be stored to allow personalised messages to individual participants when sending questionnaires and reminders. Details of ethnicity and other protected characteristics will be stored to enable monitoring of inclusivity.

Text messages and emails will be used to send participants reminders about trial procedures and to provide links to the required questionnaires using a unique personalised link. Participants who do not complete follow-up questionnaires will be sent text/email/phone reminders by the trial team as appropriate.

NCTU will maintain the confidentiality of all participant's data and will not disclose information by which participants may be identified to any third party (except where this is required for trial purposes e.g. to send interventions or text reminders to participants) or organisations for which the participant has given explicit consent for data transfer (e.g. Laboratory staff, competent authority, Sponsor).

Participants wishing to receive update newsletters will be added to the trial mailing list. All participants will be sent a summary of the results that will not include personal identifiers.

Reports of qualitative data findings may include direct quotes from participants, but these will not be identifiable to individuals.

17. Insurance and Indemnity

Nottingham University Hospitals NHS Trust will act as sponsor for the trial. Delegated responsibilities will be assigned to the NCTU and University of Nottingham. Insurance and indemnity for trial participants and NHS trial staff is covered within the NHS Indemnity Arrangements for clinical negligence claims in the NHS, issued under cover of HSG (96) 48. There are no special compensation arrangements, but trial participants may have recourse to the NHS complaints procedure.

The University of Nottingham has appropriate and typical insurance coverage in place (including, but

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not limited to Clinical Trials, Professional Indemnity, Employer's Liability and Public Liability policies) in relation to the Institution's Legal Liabilities arising from the University's activities and those of its staff, whilst conducting University business and research activity.

Nottingham University Hospitals NHS Trust is independent of any pharmaceutical company, and as such it is not covered by the Association of the British Pharmaceutical Industry (ABPI) guidelines for participant compensation.

18. Publication Policy

Results of these trials will be submitted for publication in a peer-reviewed journals, but it is anticipated that results will be released back to the Eczema Research Community as quickly as possible on completion of the trials, using lay-friendly formats. Prior to release, results will be quality checked according to the NCTU statistics standard operating procedure, and interpretation of the trial results will be discussed with members of the co-design groups, the Trial Management Group and the Trial Steering Group.

Since this is a citizen-science project, copies of the trial materials including the trial protocol, analysis plan, database code and analysis code will be made freely available for others to use.

Academic journal manuscript will be prepared by the research team and members of the co-production groups and authorship will be determined by mutual agreement. Copies of published manuscripts should be submitted to NIHR Programme Manager for information.

Authors must acknowledge that the trial was sponsored by Nottingham University Hospitals NHS Trust, was funded by NIHR and supported by the UK Dermatology Clinical Trials Network.

The following disclaimers should be included:

> "This study/project is funded by the National Institute for Health Research (NIHR) under its Programme Grants for Applied Research Programme (NIHR203279). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care."
>
> "This study/project was supported by the UK Dermatology Clinical Trials Network. The UK DCTN is grateful to the British Association of Dermatologists and the University of Nottingham for financial support of the Network."

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Appendices

Appendix A

Aspects to be confirmed in subsequent trial amendments for specific Rapid Eczema trials.

Aspect of protocol	Points to be clarified
Trial title	• Title of trial
Principal Investigators	• Each trial will have a research lead and a PPI lead who will be responsible for delivery of the trial
Contributors	• Any additional contributors
ISRCTN registration number	• Each trial will be registered on the ISRCTN clinical trial registry before recruitment commences
Trial flowchart	• Details to be confirmed specific to trial
Research question and hypotheses	• Limited to non-drug and advice trials that can be implemented at participants' home without medical supervision
Participants / eligibility criteria	• Eligibility criteria for specific trials
Trial design	• Minimum two-arm trials, but may include multiple trial arms • Details of any pilot phase and progression criteria
Trial duration	• Either short-term proof of principle trial (4 to 6 weeks) or definitive trial (6 months) • Timing of assessments
Recruitment strategies	• Details of how participants will be identified. • Clarification of payments for participants if applicable. • Details of any incentives or prize draws
Intervention and control	• Interventions developed to be pragmatic to reflect normal practice • Inclusive and accessible to as many people as possible • Consider whether participants are given access to alternative intervention at end of trial
Outcomes	• Summary of assessment timepoints and data collected • Clarification of primary outcome • Additional secondary outcomes relevant to the specific trial • Clarification of approach to adverse event reporting (including verification of ARs if necessary) • Wording of non-validated questionnaires and baseline variables
Trial procedures	• Consent process/requirements including assent for children • Details of assessments • Monitoring arrangements
Blinding	• Ability to blind (or not) the trial interventions clarified

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	• Clarify who will be blinded
Sample size	• Justification of sample size
Randomisation	• Randomisation method clarified • Stratification/minimisation variables confirmed (including age bandings) • Allocation ratio confirmed
Analysis	• Analysis metric, method of aggregation and timepoint for each outcome • Clarification of analysis method based on above • Baseline prognostic factors to adjust for in analysis • Sensitivity analysis and sub-group analyses • Definition of adherence to intervention
Process evaluation	• Details of evaluation to be included will be outlined if appropriate
Data sharing	• Details of data sharing arrangements if different to master protocol.
Study-specific documents	Checklist of any study-specific documents that have been developed to be included in amendment e.g. • Participant Information Sheet (PIS) • Participant video scripts • Participant questionnaires • Intervention information for participants • Wording for participant communication/reminders • GP invite letter • GP text message wording • Posters/advertising materials (if relevant) • Process Evaluation Interview PIS • Process Evaluation Interview ICF • Process Evaluation Interview invite letter Checklist of any master documents to be used without additions/amends e.g. • Informed Consent Form (ICF)

Summary of Assessments

Example of possible assessment timepoints (to be confirmed once trial design known)

	TRIAL PERIOD							
	Enrolment	**Randomisation**	**Post-randomisation**					**Follow-up**
TIMEPOINT**	**$-t_1$**	**0**	**t_1**	**t_2**	**t_3**	**t_4**		**t_x**
ENROLMENT:								NA

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Eligibility screen (including self-report of eczema diagnosis)	X							NA
Informed consent	X							NA
Minimisation variables	X							NA
Randomisation		X						NA
INTERVENTIONS:								NA
[Intervention A]								NA
[Intervention B]								NA
[Additional trial arms as agreed by co-production groups]								NA
ASSESSMENTS:								NA
Demographics and baseline characteristics		X						NA
UK Diagnostic criteria		X						
Prior belief in intervention		X						NA
POEM		X	X	X	X	X		NA
NRS 24-hour itch		X	X	X	X	X		NA
RECAP		X	X	X	X	X		NA
Quality of life (DLQI, CDLQI, IDQI as appropriate)		X				X		NA
EQ5D / CHU-9D if appropriate		X				X		NA
Use of eczema medications		X	X	X	X	X		NA
Acceptability of intervention						X		NA
Adherence to intervention			X	X	X	X		NA
Safety outcomes (reactions)			X	X	X	X		NA

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Additional outcomes specific to chosen intervention		X	X	X	X	X		NA

Contacts

For queries about specific trials:

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Appendix B
TITLE: Eczema Bathing Study – how often should we bathe? (Short title: Eczema Bathing Study)

Trial summary

Trial Title	Eczema Bathing Study – how often should we bathe? (Short title: Eczema Bathing Study)
Trial Design	Two-arm, parallel group, superiority randomised controlled trial, with internal pilot.
Objectives	AIM: To explore the impact of bathing frequency on eczema symptoms, quality of life and disease control in children and adults with eczema. OBJECTIVES: 1. To assess the impact of weekly bathing (1 or 2 times per week) compared to daily bathing (6 or more times per week) in people with atopic eczema over 4 weeks (syn. Atopic dermatitis, eczema). 2. To explore barriers and facilitators to changing bathing practices and to understand the impact of trial processes on trial participation.
Research question	Is weekly bathing better than daily bathing for people with eczema in terms of participant reported symptoms over 4 weeks?
Trial duration	Each participant will be enrolled for 4 weeks
Participants and eligibility criteria	People with eczema aged 1 year and older
Intervention and control	**Weekly bathing group**: no more than 1 or 2 times per week **Daily bathing group:** 6 or more times per week
Outcome measures	**Primary outcome:** • Eczema symptoms measured by Patient Oriented Eczema Measure (POEM).[21] Includes 7 items, scored 0 to 28. Assessed weekly over 4 weeks. **Secondary outcomes:** • Itch intensity (Peak Pruritis Numerical Rating Scale (NRS)[22] 24-hour peak itch) - one item, scored 0 to 10. Assessed at baseline and 4 weeks. • Eczema control (Recap of atopic eczema, RECAP)[23] – 7 items, scored 0 to 28. Assessed at baseline and 4 weeks.

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	• Skin-specific quality of life (Infants' Dermatitis Quality of Life Index (IDQoL)[24] (under 4 years), Children's Dermatology Life Quality Index (CDLQI)[25](from 4 years to 15 years) or Dermatology Life Quality Index (DLQI)[26](16 years and over) depending on age) – 10 items, scored 0 to 30. Assessed at baseline and 4 weeks.
	• Use of usual eczema treatments assessed weekly over 4 weeks:
	  ○ number of days in the last week flare control creams (topical corticosteroids or calcineurin inhibitors) used – this outcome will be used as an indication of days with eczema flares.[32]
	  ○ number of days in the last week moisturisers (emollients) used.
	• Proportion of participants who achieve an improvement in POEM at week 4 of ≥3 points compared to baseline.[33]
	• Global change in eczema compared to baseline. Assessed at week 4.
	• Adverse events: we do not anticipate adverse events related to changing bathing practices but will collect whether participants changed their eczema treatments or sought advice from a health care provider as a result of a worsening of the eczema.

Sample size / Number of participants	390 (195 per arm)

Lay Summary

This study is part of the Rapid Eczema Trials project. We hope to answer many questions about how to manage eczema through this project. People with eczema are helping to design and run these studies. This means that the project will answer important questions for people with eczema.

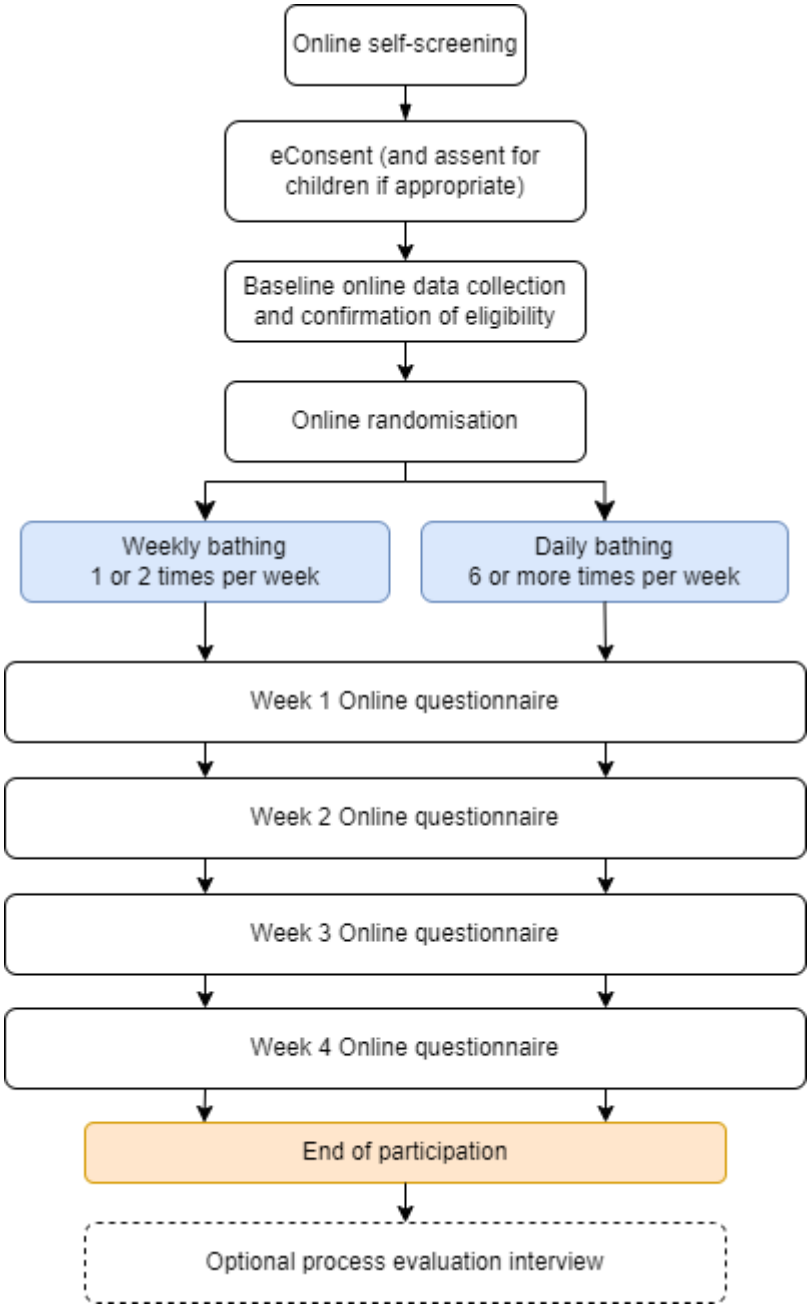
In this Eczema Bathing Study, we will test how often people with eczema should have a bath or a shower to best manage their eczema. People will join the study by signing up on the study's website. They will give information about their eczema and how they usually bathe. For this study, bathing means taking a bath or a shower. They will then be put into one of two groups by a computer. One group will be asked to have a bath or shower no more than 1 or 2 times a week. The other group will be asked to have a bath or shower 6 or more times a week. People will be asked to follow this advice for four weeks. They will be asked to complete some questions, sent to them by email/text message each week. People can take part from home and do not need to travel.

People aged 1 year or older, who have eczema, can join the study. We are encouraging people from all different backgrounds to take part.

As soon as the study results are known, we will share the results as quickly as possible on the study's website (www.RapidEczemaTrials.org).

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Trial flowchart



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Details of Eczema Bathing Study

Aspect of protocol	
Trial title	Eczema Bathing study – how often should we bathe? (Short title: Eczema Bathing Study)
Principal Investigators	Prof Kim Thomas (Chief investigator) and Ms Amanda Roberts (PPI lead)
Contributors	Co-applicants and contributors as outlined in Master Protocol PPI co-design team members: Tressa Davey, Tracy Owen, Joanne Harwood, Mars Eddis-Finbow, Fiona McOwen, Aaron Foulds, Devin Patel, Goldie Putrym, Kelly Hang, Tim Burton, Shakeela Riaz Other contributors: Nicholas Hilken, University of Nottingham; Eleanor Harrison, University of Nottingham; Leila Thuma, University of Nottingham
ISRCTN registration number	ISRCTN12016473
Research question and hypotheses	Is weekly bathing better than daily bathing for people with eczema in terms of participant reported symptoms over 4 weeks?
Trial aim and objectives	AIM: To explore the impact of bathing frequency on eczema symptoms, quality of life and disease control in children and adults with eczema. OBJECTIVES: 1. To assess the impact of weekly bathing (1 or 2 times per week) compared to daily bathing (6 or more times per week) in people with atopic eczema over 4 weeks (syn. Atopic dermatitis, eczema). 2. To explore barriers and facilitators to changing bathing practices and to understand the impact of trial processes on trial participation.
Participants / eligibility criteria	People with eczema aged 1 year and older. **Inclusion criteria** • Aged ≥1 year with self-report of eczema (syn. Atopic dermatitis, atopic eczema) • Usual residence in the UK • Able and willing to give informed consent (or parent/legal guardian able and willing to give informed consent for children under 16 years) **Exclusion criteria:** • None or very mild eczema symptoms (POEM score ≤2) • Eczema only present on hands (likely to be hand eczema or contact dermatitis); limited to locations where skin exposed to

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	nickel e.g. jewellery (likely to be contact dermatitis); or eczema only around varicose veins (likely to be varicose eczema) • Started a new eczema treatment (including antibiotics for eczema) other than emollients in the last 4 weeks • Taking part in another eczema intervention trial • Unable or unwilling to change bathing practices for 4 weeks • Planning to swim more than twice a week in the next 4 weeks (including surfing, scuba diving etc.) • Member of household already participating in this trial As per protocol section 4, participants identified through GP practices will have a recorded diagnosis of eczema on their medical records and have been issued a prescription for emollients or topical corticosteroids in the last 2 years.
Trial design	Two-arm, parallel group, superiority randomised controlled trial, with internal pilot. The internal pilot will assess: recruitment, adherence with intervention, completeness of data and any issues around online randomisation and consent. This trial has been co-designed by member of the Rapid Eczema Trials Research Community (www.RapidEczemaTrials.org).
Trial duration	Each participant will be in the trial for 4 weeks with weekly outcome assessment. Recruitment will take place for up to 12 months. The pilot phase will end once 20% of the target sample size has been recruited or after 4 months, whichever is the sooner. The end of trial is defined in protocol section 11.5.

Internal pilot progression criteria	The following criteria will be considered at the end of the pilot phase.
	
	Aspects that do not meet these milestones will be flagged as cause for concern. Remedial actions will be discussed and implemented with input from the wider programme team and Independent Programme Steering Committee.
	
	• Recruitment: < 20% of total sample size at 4 months
	• Adherence:
	  ○ Daily bathing group: > 25% of participants reported to have bathed/showered < 6 times per week for two or more of the follow-up weeks
	  ○ Weekly bathing group: > 25% of participants reported to have bathed/showered >2 times per week for two or more of the follow-up weeks

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	• Data completeness: <85% of participants with POEM scores at week 1 and <70% of participants with POEM scores at 4 weeks (for those who have reached this timepoint)
Recruitment strategies	Participants will be identified through online and offline methods, including the use of GP practices as Participant Identification Centres (PICs), as described in protocol section 4.3. Information about the trial will be available on the website (www.RapidEczemaTrials.org) in a variety of engaging formats appropriate for all ages. Payments will be made available for people financially disadvantaged by taking part in the trial (£20 per participant paid at the outset of the trial after randomisation). Participants wishing to access this fund will be asked to complete a short online form providing their contact details and preferred method of payment (bank transfer or vouchers). If participants choose to receive the payment by bank transfer, appropriate bank details will be requested. All data relating to payments will be stored securely, in a separate place to the main trial database. Access will be restricted to only those members of the team who will be managing the payments. Participants who complete questionnaires at week 4 will be offered the opportunity to enter a free prize draw to win £25, a child-friendly book about eczema, or both, according to their preference. Potential participants will be encouraged to contact the trial team if they have any questions prior to registering for the trial online.
Intervention and control	• **Weekly bathing group** = 1 or 2 times per week • **Daily bathing group** = 6 or more times per week Following randomisation, participants will be provided with intervention instructions detailing how often they should bathe according to their allocation. Participants should follow this for 4 weeks. Intervention materials have been designed to be accessible (including pictures and simple language) and inclusive (available in different formats). Participants will be asked not to change any of their other bathing practices e.g. method of bathing, use of wash products etc. Participants can wash their face and body using a flannel/sponge in the sink in between showers or baths, and can wash their hair in between showers or baths. Participants may use their usual eczema treatments (e.g. emollients and flare control creams) whenever they need to as per usual practice. They

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	will be asked not to change their usual eczema treatments (or start a new treatment) during the trial, if medically possible. Withdrawal procedures are as described in protocol section 8.6. Post-trial care is described in protocol section 8.7.

Outcomes	Outcomes include the Harmonizing Outcomes for Eczema (HOME) initiative's recommended core outcome set.
	
	Primary outcome:
	• Eczema symptoms measured by Patient Oriented Eczema Measure (POEM)[21]. Includes 7 items, scored 0 to 28. Assessed weekly over 4 weeks.
	
	Secondary outcomes:
	• Itch intensity (Peak Pruritis Numerical Rating Scale (NRS)[22] 24-hour peak itch) - one item, scored 0 to 10. Assessed at baseline and 4 weeks.
	• Eczema control (Recap of atopic eczema, RECAP)[23] – 7 items, scored 0 to 28. Assessed at baseline and 4 weeks.
	• Skin-specific quality of life (Infants' Dermatitis Quality of Life Index (IDQoL)[24](under 4 years), Children's Dermatology Life Quality Index (CDLQI)[25](from 4 years to 15 years) or Dermatology Life Quality Index (DLQI)[26](16 years and over) depending on age) – 10 items, scored 0 to 30. Assessed at baseline and 4 weeks.
	• Use of usual eczema treatments assessed weekly over 4 weeks:
	  ○ number of days in the last week flare control creams (topical corticosteroids or calcineurin inhibitors) used – this outcome will be used as an indication of days with eczema flares.[32]
	  ○ number of days in the last week moisturisers (emollients) used.
	• Proportion of participants who achieve an improvement in POEM at week 4 of ≥3 points compared to baseline.[33]
	• Global change in eczema compared to baseline. Assessed at week 4.
	• Adverse events: we do not anticipate adverse events related to changing bathing practices but will collect whether participants changed their eczema treatments or sought advice from a health care provider as a result of a worsening of the eczema.
	
	Additional variables will be collected to inform analysis and interpretation of the trial. These include:
	
	• Minimisation variables, prior belief on the frequency of bathing and eczema symptoms, demographics, UK Diagnostic Criteria for Eczema and usual bathing practices (e.g. usual temperature of the water, use of shampoo, use of emollient wash products, and application of emollients/flare control creams after bathing). Assessed at baseline only.

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	• Number of times had bath or shower in the previous week, assessed weekly over 4 weeks to evaluate adherence to allocated frequency of bathing routine. • Ease of bathing as allocated, willingness to continue, things that helped or made it difficult to bathe as allocated, experience of being in the trial (for process evaluation). Assessed at 4 weeks. For children under 16 years, proxy reporting by a parent or carer will be accepted as per protocol section 8.2.
Trial procedures	Informed e-consent will be obtained as per protocol section 5. For children under 16, consent will be obtained from the parent/carer but there will be an optional assent section for the child to complete if they wish. All assessments will be carried out online as per protocol section 8.3. For children who are unable to complete patient reported outcomes themselves, proxy reporting by a parent or carer will be accepted as per protocol section 8.2. Parents/carers will be advised that this should be the same adult throughout the trial if possible. Parents and children will be encouraged to complete the questionnaires together wherever possible. An email/text message with a unique link to the questionnaires will be sent each week to the participant/parent/carer. For weeks 1, 2 and 3 participants will receive a maximum of 2 reminders by email/text message for each questionnaire if it has not been completed. At the final 4-week timepoint, participants will receive text message, email or phone call reminders to complete the final follow-up questionnaires (for up to 2 weeks after the questionnaire is due). A summary of assessments diagram is provided below. We will regularly monitor attempts to re-randomise the same individual or enrol multiple people per household on an ongoing basis. Electronic forms collecting data for screening, consent and eligibility will be recorded and processed with automatic and/or manual checks. These checks will include ensuring identifiers and contact details are unique for participants, so no duplicate entries for the same participant may be made. Eligibility checks will ensure only those who meet all the prescribed inclusion and exclusion criteria can join the trial.
Blinding	Due to the nature of the intervention, it is not possible to blind trial participants to their randomised allocation. To mitigate the potential bias caused by lack of blinding, we will collect prior belief in the impact of bathing on eczema symptoms at baseline and explore this in a sensitivity analysis.

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	The trial statisticians, trial team at NCTU and members of the Trial Management Group will be blinded to treatment allocation.
Sample size	The sample size for the trial is based on POEM scores assessed weekly for 4 weeks and is designed to detect a difference of 2.2 in POEM scores between the two groups. A small difference of 2.2 has been chosen as it is not anticipated that there will be large effects from a change in bathing frequency, but even small differences could be important for people looking for self-management options to try at home. This difference represents a small change that is likely to be beyond measurement error.[33] Assuming a standard deviation in weekly POEM scores of 6.5 and a correlation between repeated measurements of 0.8 (based on data from previous eczema RCTs), a sample size of 156 per group is required to detect this difference with 90% power and 5% two-sided significance level. Allowing for 20% loss to follow-up, gives a total sample size of 390 participants.
Randomisation	Randomisation will be carried out by the participant using an online system managed by NCTU, as described in protocol section 6.2. Participants will be randomised 1:1 to either the intervention group (weekly bathing) or control group (daily bathing) using a minimisation algorithm with a probabilistic element balancing on the following factors: • Eczema severity POEM score (3-7 mild, 8-16 moderate, 17-28 severe). • Age (<4 years, 4-11 years, 12-15 years, 16-25 years, 26-55 years, >55 years) • Usual method of bathing (bath or not bath) The randomised allocated group will not be released to participants until after baseline variables have been entered and stored on the trial database.
Analysis	The analysis and reporting of the trial will be in accordance with CONSORT guidelines, with the primary comparative analyses being conducted according to randomised allocation regardless of actual frequency of bathing. A statistical analysis plan will be finalised prior to database lock and release of the treatment allocations. The primary analysis will use all available longitudinal outcome data and will use a linear mixed effects model to estimate the difference in mean POEM score over the 4-week trial period with 95% confidence interval. The model will include fixed effects for the minimisation variables (age, baseline POEM score and usual method of bathing) as well as frequency of bathing, whether participants usually wash their hair in the bath/shower, whether they use emollient wash products, use of moisturisers and flare control creams after bathing, diagnosis of eczema

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	according to the UK Diagnostic Criteria and whether participants are currently using systemic treatments. It will allow for observations nested within participants over time using random effects. If there is evidence of a differential effect over time, the difference in mean POEM score each week will be reported. Sensitivity analyses for the primary outcome will use multiple imputation for missing outcome data. Further supplementary analysis will investigate potential effects of compliance with allocated frequency of bathing to estimate the complier average causal effect (CACE). Participants will be considered as adherent if the number of times they report bathing/showering in the previous week is as per the allocated frequency of bathing strategy each week over the 4-week trial period. Subgroup analyses for the primary outcome will be performed according to age at randomisation, usual method of bathing (bath/shower/other), diagnosis of eczema according to UK Diagnostic Criteria and prior belief on the frequency of bathing and eczema symptoms by including an appropriate interaction term in the mixed effect model. The trial is not powered to detect any interactions hence the subgroup analyses will be treated as exploratory. Between-group comparison of secondary outcomes will use an appropriate regression model for the outcome (linear for continuous outcomes, logistic for binary) with adjustment as described above for the primary outcome and baseline outcome measure for continuous variables if available. For secondary outcomes assessed weekly, mixed effects models will be used to allow for observations nested within participants over time using random effects.
Process evaluation	A nested, qualitative interview study will consider questions of acceptability, feasibility, and adherence with regards to changed bathing practices. Interviews will also consider trial procedures. A purposive sample of those willing to take part in a research interview will be constructed to include a range of age, gender, ethnicity, prior belief in the impact of bathing on eczema symptoms and acceptability of the interventions after 4 weeks. Equal numbers will be recruited from each arm of the trial (n = 15 to 20 per arm). Only adults (aged 16+) will be included in this process evaluation. Additional consent will be taken from those that participate in a research interview. Online informed consent will be taken prior to the interview, and consent confirmed verbally at the start of the interview. Interviews will be undertaken online or by telephone, at a time convenient to the participant. Data will be digitally recorded if participants consent to this. Interviews will be timed to take place after an individual has completed their final follow-up assessment at four weeks.

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	Interviews will explore the participants (i) experience of changing bathing patterns; (ii) any difficulties or challenges that they experienced in this; (iii) any difference that this made to their eczema; (iv) their willingness to continue with their allocated bathing pattern; (v) their assessment of the effectiveness of the intervention and vi) their experience of taking part in the trial. Digital recordings will be transcribed (either internally or using an approved transcription service) and anonymised. Transcripts will be stored as per our Data Management Plan. Recordings will be destroyed once transcripts have been approved as an accurate record. An inductive, thematic approach will be taken in analysing the data. This will develop a more detailed and contextualised understanding of the bathing intervention. A trained researcher will lead the analysis, with the support of Dr Paul Leighton.
Data sharing	Data from the trial may be shared as per protocol section 10.5.
Trial-specific documents	The following documents have been developed for the Eczema Bathing Study and included in an amendment: • Eczema Bathing Study Participant Information Sheet (website text) • Eczema Bathing Study video script (suitable for older children, adults and people with low literacy) • Eczema Bathing Study child video script (suitable for young children) • Eczema Bathing Study intervention guidance - Weekly Bathing • Eczema Bathing Study intervention guidance - Weekly Bathing - Parent • Eczema Bathing Study intervention guidance - Daily Bathing • Eczema Bathing Study intervention guidance - Daily Bathing - Parent • Eczema Bathing Study participant communication wording • Eczema Bathing Study questionnaires • Eczema Bathing Study GP invite letter Adult • Eczema Bathing Study GP invite letter Parent • Eczema Bathing Study GP invite text message wording • Eczema Bathing Study Poster (for GP surgeries/pharmacies/schools etc) • Eczema Bathing Study Process Evaluation Interview PIS • Eczema Bathing Study Process Evaluation Interview Invitation letter • Eczema Bathing Study Process Evaluation Interview Topic Guide • Rapid Master Process Evaluation Interview ICF The Eczema Bathing Study will use the current version of the following approved Rapid Master documents with no additions/amendments:

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	• Rapid Master Adult Informed Consent Form • Rapid Master Parent Informed Consent Form (with child assent if appropriate) Additional advertising materials may be used e.g. social media posts, and these will adhere to the Rapid Principles for advertising materials document.

Summary of Assessments

	TRIAL PERIOD					
	Enrolment	Baseline	Follow-up			
TIMEPOINT	**0**	**0**	**Week 1**	**Week 2**	**Week 3**	**Week 4**
ENROLMENT:						
Eligibility screen (including self-report of eczema diagnosis)	X					
Informed e-consent (and child assent if appropriate)	X					
Eczema Symptoms (POEM) – exclude if POEM ≤2		X	X	X	X	X
Minimisation variables		X				
Randomisation		X				
INTERVENTIONS:						
Weekly bathing (1 or 2 times per week)			◆—	—	—	—◆
Daily bathing (6 or more times per week)			◆—	—	—	—◆
ASSESSMENTS:						
Demographics and baseline characteristics		X				
UK Diagnostic criteria		X				
Usual bathing practices		X				
Prior belief in intervention		X				
Peak Pruritis NRS		X				X
Eczema Control (RECAP)		X				X

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Quality of Life (DLQI, CDLQI, IDQI as appropriate)		X				X
Use of eczema medications		X	X	X	X	X
Global change in eczema compared to baseline						X
Acceptability of intervention						X
Adherence to intervention			X	X	X	X
Adverse events – changes in eczema treatments and healthcare professional contact due to worsening of eczema						X

Contacts

For queries about specific trials:
Rapid Eczema Trials Team
Nottingham Clinical Trials Unit
University Park
Nottingham
NG7 2RD
Email: RapidEczemaTrials@nottingham.ac.uk

For queries about payments for additional costs incurred:
Rapid Eczema Trials Team
Centre of Evidence Based Dermatology
School of Medicine
Applied Health Research Building
University Park
Nottingham
NG7 2RD

Email: eczema@nottingham.ac.uk

Tel: 0115 8468631

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Appendix C

TITLE: Photo assessment of eczema - a Rapid Eczema Trials feasibility study

Study Summary

Study Title	Photo assessment of eczema – a Rapid Eczema Trials feasibility study
Study Design	Online observational feasibility study, with nested qualitative study
Participants and eligibility criteria	People with eczema aged 1 year and older, who live in the UK
Planned sample size	A minimum of 100 participants will be recruited to the observational study. Nested qualitative study – 10 to 15 interviews or until the saturation of themes is achieved
Study duration	Each participant will be enrolled for 4 weeks. Recruitment will take place for up to 12 months.
Research Question/Aim(s)	What is the feasibility and acceptability of using photos to assess eczema severity in online clinical studies?
Outcomes	Feasibility outcomes: 1. Proportion of participants who provided consent and submitted at least one photo 2. Proportion of participants who submitted at least one photo at each time-point 3. Proportion of photos that were of sufficient quality to generate an EczemaNet[34] score 4. Time taken to take and upload photos Acceptability outcomes: 1. How easy/difficult was the photo taking and uploading process (assessed using closed and open questions) 2. Perceived benefits to participants (assessed using closed and open questions) 3. Perceived barriers to participants (assessed using closed and open questions)

Lay Summary

This study is part of the Rapid Eczema Trials project (www.RapidEczemaTrials.org). We hope to answer many questions about how to manage eczema through this project. People with eczema are helping to design and run these studies. This means that the project will answer important questions for people with eczema.

In this Photo Assessment of Eczema study, we are testing to see if people with eczema are willing and able to take photos of their eczema and to upload them to a secure web portal managed by

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researchers at Imperial College London. This will help to see if it is possible to use photo assessments as part of our next Rapid Eczema trial. The photos will be put through a computer programme that has been trained to assess eczema severity from photos.

People will be asked to answer questions and upload photos of their eczema for 4 weeks. People can take part in this online study from home and do not need to travel.

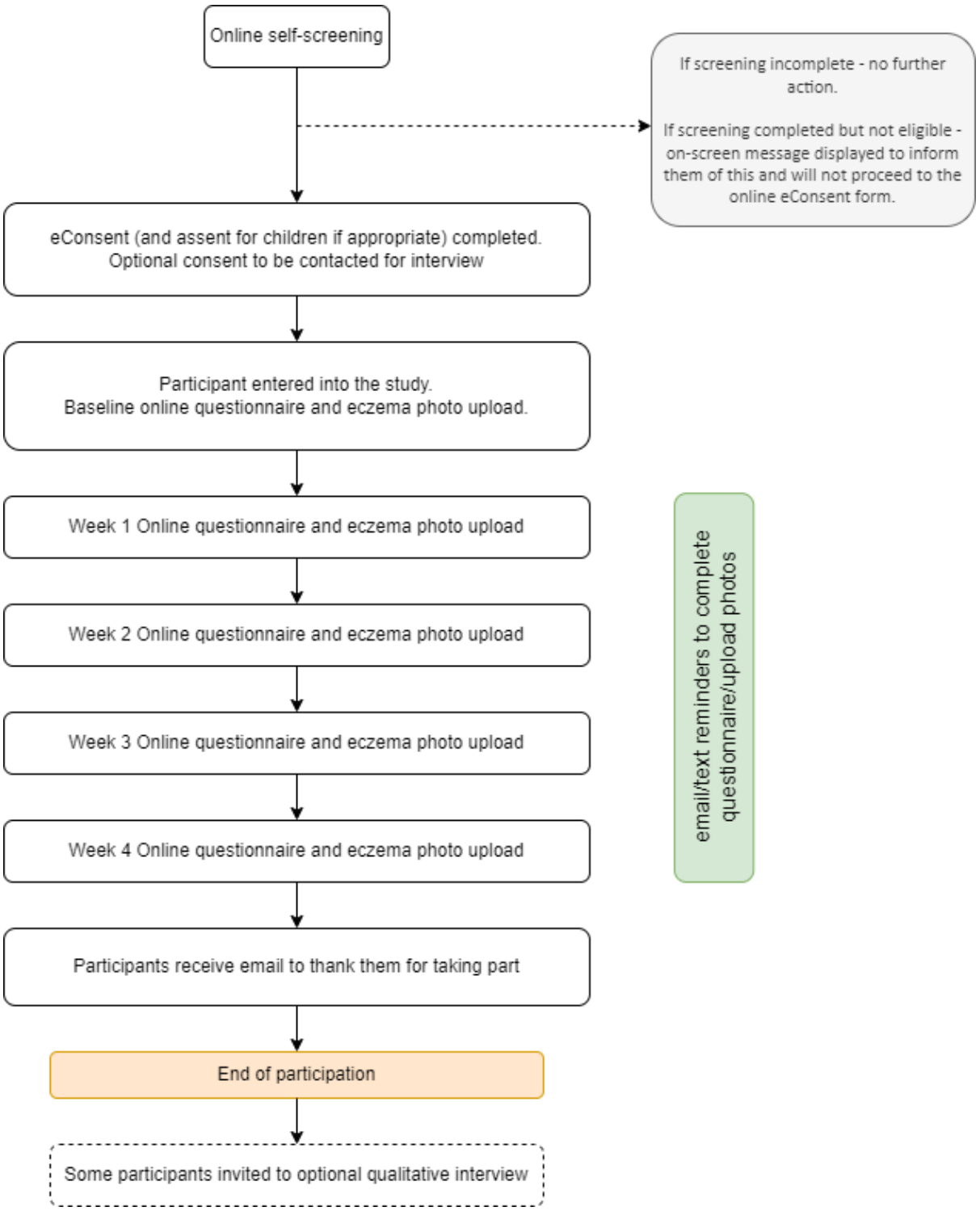
People aged 1 year or older, who have eczema, can join the study. We are encouraging people from all different backgrounds to take part.

As soon as the study results are known, we will share the results as quickly as possible, and will also post them on the study's website (www.RapidEczemaTrials.org).

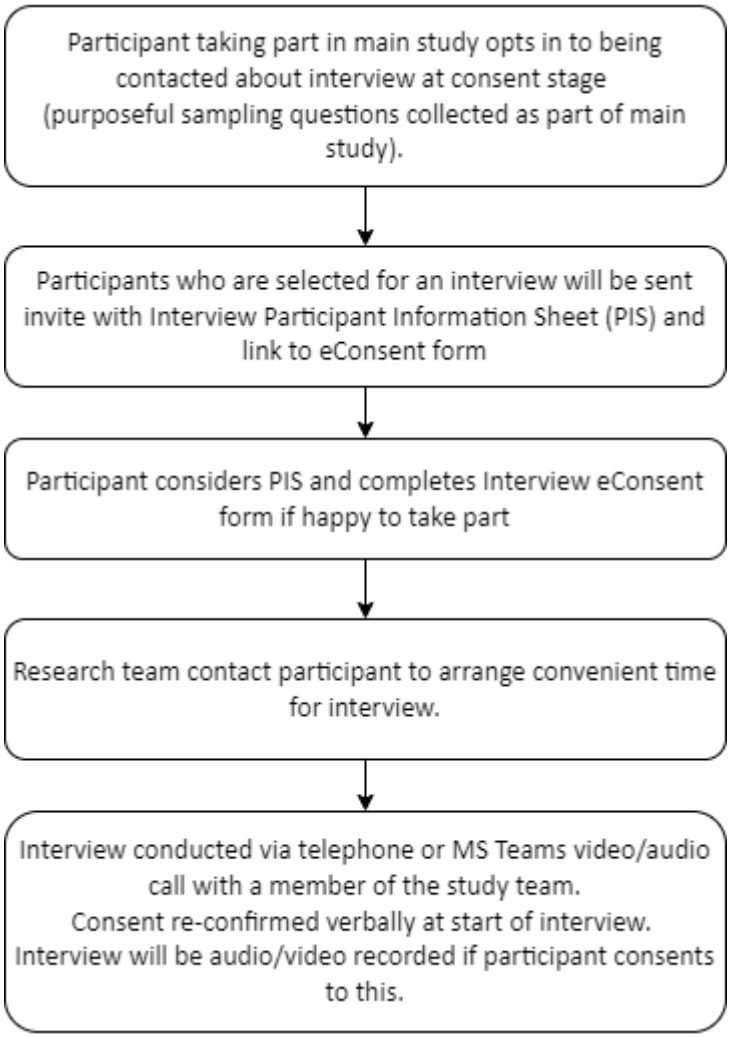
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Main study flowchart

This study will recruit people with eczema directly from the community. People willing to take part will self-refer online via the Rapid Eczema Trials website: www.RapidEczemaTrials.org



Nested Qualitative Study flowchart



Details of Photo Assessment study

Aspect of protocol	
Study title	Photo assessment of eczema – a Rapid Eczema Trials feasibility study
Principal Investigators	Prof Kim Thomas (Chief investigator) and Ms Amanda Roberts (PPI lead)
Contributors	Co-applicants and contributors as outlined in Master Protocol Other contributors: University of Nottingham (Nicholas Hilken, Eleanor Harrison, Leila Thuma, Liz Hartshorne, Richard Swinden, Emma Campbell, Lydia Tutt); Derby and Burton Foundation Hospitals NHS Trust (Gavin Fong)

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ISRCTN registration number	Not applicable (non-randomised feasibility study)
Research question and hypotheses	What is the feasibility and acceptability of using photos to assess eczema severity in online clinical studies?
Participants / eligibility criteria	Eligibility criteria are broad to ensure generalisable results. **Inclusion criteria** • Aged ≥1 year with self-report of eczema (syn. Atopic dermatitis, atopic eczema) • Usual residence in the UK • Have access to a device that can take and upload digital photos to the web portal • Able and willing to give informed consent (or parent/legal guardian able and willing to give informed consent for children under 16 years) **Exclusion criteria** • Eczema only present on hands (likely to be hand eczema or contact dermatitis); limited to locations where skin exposed to nickel e.g. jewellery (likely to be contact dermatitis); or eczema only around varicose veins (likely to be varicose eczema) Only adults will be included in the nested qualitative study (either as people with eczema or as parents/carers of children with eczema).
Study design	Online observational feasibility study, with a nested qualitative study.
Study duration	Each participant will be in the study for 4 weeks with weekly data collection. Recruitment will take place for up to 12 months. End of study will be the final database lock.
Recruitment strategies	Participants will be identified through online and offline methods, including the use of GP practices as Participant Identification Centres (PICs), as described in protocol section 4.3. Information about the trial will be available on the website (www.RapidEczemaTrials.org) in a variety of engaging formats appropriate for all ages. Potential participants will be encouraged to contact the study team if they have any questions prior to registering for the study online.

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Intervention and control	Not applicable (observational study only)
Outcomes	This study will help to determine if it is possible to use photos to assess eczema severity in future eczema clinical studies. Feasibility outcomes: 1. Proportion of participants who gave their consent and submitted at least one photo 2. Proportion of participants who submitted at least one photo at each time-point 3. Proportion of photos that were of sufficient quality to generate an EczemaNet score[34] 4. Time taken to take and upload photos Data will also be used to assess the feasibility of combining individual photo severity scores to produce a per person severity score suitable for use in clinical studies. Results will be compared with self-reported questionnaires for eczema control (RECAP),[23] eczema flares and use of eczema treatments (days when topical corticosteroids used). See section 2.2.2 of protocol. Acceptability outcomes: 1. How easy/difficult was the photo taking and uploading process (assessed using closed and open questions) 2. Perceived benefits to participants (assessed using closed and open questions) 3. Perceived barriers to participants (assessed using closed and open questions)
Study procedures	Informed e-consent will be obtained as per master protocol section 5. For children under 16, consent will be obtained from the parent/carer but there will be an optional assent section for the child to complete if they wish. Specific consent for data sharing (including photos) between University of Nottingham, Imperial College London and study sponsor (Nottingham University Hospitals NHS Trust) will be obtained. All assessments will be carried out online as per master protocol section 8.3, with the addition of photos that will be uploaded by participants to a platform hosted by Imperial College London. For children who are unable to complete patient-reported outcomes themselves, proxy reporting by a parent or carer will be accepted as per master protocol section 8.2. Parents/carers will be advised that this should be the same adult throughout the study if possible.

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	Parents and children will be encouraged to complete the questionnaires together wherever possible. Participants will be asked to take photos of their/their child's eczema and to upload the photos via a secure link to a platform hosted by Imperial College London. The uploaded photos will be used to assess eczema severity using a machine learning algorithm, called EczemaNet.[34] Scores and photos will be returned to Nottingham Clinical Trials Unit via a secure TLS1.2 link using a unique study ID. An email/text message with a unique link to the questionnaires/photo upload platform will be sent each week to the participant/parent/carer. For weeks 1, 2 and 3 participants will receive a maximum of 2 reminders by email/text for each questionnaire if it has not been completed. At the final 4-week timepoint, participants will receive text message, email or phone call reminders to complete the final follow-up questionnaires (for up to 2 weeks after the questionnaire is due). Participants who complete questionnaires at week 4 will be offered the opportunity to enter a free prize draw to win a £25 shopping voucher, a child-friendly book about eczema, or both, according to their preference. Participants can contact the research team to request to withdraw from the study at any point, but data already collected will be retained and used. Electronic forms collecting data for screening, consent and eligibility will be recorded and processed with automatic and/or manual checks. These checks will include ensuring identifiers and contact details are unique for participants, so no duplicate entries for the same participant may be made. Eligibility checks will ensure only those who meet all the prescribed inclusion and exclusion criteria can join the study.
Summary of assessments	The following information will be collected at baseline: • Demographics of the person with eczema (age, gender, ethnicity, postcode) • UK Diagnostic criteria for eczema[28] • Eczema severity assessed by the Patient Oriented Eczema Measure (POEM)[21] • Eczema control assessed by the Recap of atopic eczema (RECAP) questionnaire[23] • Global assessment of flares • Patient global assessment (PGA) of eczema severity

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	• Skin tone • Photos of eczema • Details of photos: whether photos were taken in artificial or natural light; what device was used to take the photos; time taken • Use of topical eczema treatments • Acceptability and ease of use of the photo upload portal The following information will be collected at week 1, 2, 3 and 4: • Eczema control assessed by the RECAP questionnaire (RECAP)[23] • Global assessment of flares • Patient global assessment (PGA) of eczema severity • Photos of eczema • Details of photos: whether photos were taken in artificial or natural light; what device was used to take the photos; time taken • Use of topical eczema treatments • Week 4 only: How easy participants found the process, perceived benefits and perceived barriers
Blinding	Not applicable (observational study only)
Sample size	The aim is to recruit a minimum of 100 participants. This number will provide estimated margins of error (half width of 95% confidence interval) for the proportion submitting photos of approximately 10%. We will aim to recruit from diverse backgrounds to enhance our opportunity of learning about the feasibility of using photos to assess eczema in future clinical studies.
Randomisation	Not applicable (observational study only)
Analysis	Feasibility outcomes will be summarised descriptively. Results will be presented both overall and according to participant characteristics (e.g. demographic characteristics, who is completing the task - parents on behalf of child or adults self-completing). Useability of the images will be assessed through a combination of visual inspection and automated quality assessment using a quality screening algorithm. A selection of scores and images will be reviewed by clinically trained members of the team to evaluate the quality of the scores as generated by the machine learning algorithm compared to trained healthcare professional assessment of the images.

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Nested qualitative interview	A nested, qualitative interview study will consider questions of acceptability, feasibility, and adherence with regards to providing photos of eczema and completing study outcomes. Interviews will also consider study procedures. Only adults (aged 16+) will be included in this qualitative study (either as people with eczema or as parents/carers of children with eczema). Additional consent will be taken from those that participate in a research interview. Online informed e-consent will be taken prior to the interview, and consent confirmed verbally at the start of the interview. We will interview approximately 10-15 participants or until saturation of themes is achieved. Purposeful sampling will be used to recruit individuals with a range of characteristics (gender, age, ethnicity, skin tone, level of engagement with the observational study as assessed by feasibility outcomes). Researchers from the University of Nottingham will conduct the interviews. The interviews will be undertaken online or by telephone, at a time convenient to the participant. Data will be digitally recorded if participants consent to this Interviews will explore the participants': • Experience of taking and uploading photos in the study • Concerns or barriers to taking part in a study involving uploading of photos • Suggestions for improving the EczemaNet upload platform and using photos to assess eczema severity in clinical studies (including better assessment of body surface area) • Other ideas for improving their experience of taking part or data collection methods used. Digital recordings will be collected and transcribed in-house using University of Nottingham approved software (MS Office 365, or an offline digital recorder). If an approved external transcription service is used, details of this will be added to the Data Protection Impact Assessment. Transcripts will be stored as per the Data Management Plan. Recordings will be destroyed once transcripts have been approved as an accurate record. Qualitative data will be analysed using NVivo software.[35] Data will be analysed using framework analysis.[36] A framework will be used to organise the data. Themes will be described and will help to understand the trends and findings in the quantitative data.

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	A trained researcher will lead the analysis, with the support of Dr Paul Leighton.
Data sharing/management	Data from the study may be shared as per master protocol section 10.5. The photos taken by participants and the machine learning eczema severity scores from these photos, will be stored at a secure server at Imperial College London maintained by Prof Reiko Tanaka and her team. With participants' consent, data transfer between the University of Nottingham and Imperial College London will be via secure TLS1.2 link using a unique study ID. See Figure 1: Data flowchart. Appropriate members of the team at the University of Nottingham and Imperial College London will have access to the data. Direct access will be granted to authorised representatives from the University of Nottingham, Nottingham University Hospitals NHS Trust (sponsor) and any host institution for monitoring and/or audit of the study to ensure compliance with regulations. Digital images will be subject to the same data protection requirements as for all the data collected e.g. encryption, back-up, secure access control. Where considered useful and appropriate, anonymised research data created by the project will be deposited in the University of Nottingham's research data archive (https://rdmc.nottingham.ac.uk) so that it can be used in further research. All patient documentation will reflect this data sharing approach. To comply with the Data Protection Act, personal data will be securely deleted as soon as possible after it is no longer needed for the study. To comply with Nottingham University Hospitals policy, personal data will be stored for a minimum of 5 years after the end of this project.
Assessment and management of risk	As the study has no planned in-person contact between study participants and the research team, there are no expected safeguarding risks. Participants will be offered clear instructions on the type of photos that are appropriate to upload (i.e. no genital or sensitive areas) and clear information on how their data will be stored and shared. We may ask for photos of the face as this is a commonly affected body site for people with eczema. People will be free to decide whether they feel comfortable about uploading identifiable photos of the face. Whilst we will do our best to ensure participants cannot be identified from photos this is not guaranteed if the photos

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	contain identifiable features i.e. a face, scarring, birthmarks, body art, piercings etc. People will be free to decide whether they feel comfortable about uploading identifiable photos. It will be made clear that all photos will be kept secure and will not be shared with other researchers unless consent is provided. There is also the potential risk of people being required to store their photos on their personal devices before they upload them to the secure web portal and that we have no way of controlling the security of their own device. Participants will be made aware of this.
Study-specific documents	The following documents have been developed for this photo assessment study and included in an amendment: • Photo Assessment Study Participant Information Sheet (website text) • Photo Assessment Study Informed Consent Forms (adult and parent) • Photo Assessment Study Video script (suitable for older children, adults and people with low literacy) • Photo Assessment Study Child video script (suitable for young children) • Photo Assessment Study participant communication wording • Photo Assessment Study questionnaires • Rapid Photo taking manual • Photo Assessment Study GP invite letter Adult • Photo Assessment Study GP invite letter Parent • Photo Assessment Study GP invite text message wording • Photo Assessment Study Interview PIS • Photo Assessment Study Interview Invitation letter • Photo Assessment Interview topic guide • Poster (for GP surgeries, pharmacies, schools, etc) • Photo Assessment Study Be Part of Research volunteer service email invitation This study will use the current version of the following approved Rapid Master documents with no additions/amendments: • Rapid Master Process Evaluation Interview ICF • Principles of advertising materials Additional advertising materials may be used e.g. social media posts, and these will adhere to the Rapid Principles for advertising materials document. Copies will be retained in the electronic Trial Master File.
Aspects of the Master Protocol that do not apply for	The following sections of the master protocol are not applicable for this observational study:

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this non-randomised observational study	Section 6.2 Randomisation Section 6.3 Blinding and concealment Section 7 Trial treatment/intervention Section 8.2 Schedule of assessments (not all aspects apply) Section 8.5.1.1 Process evaluation Section 9 Adverse event reporting Section 12 Statistical considerations Section 13 Qualitative process evaluation analysis

Schedule of Assessments

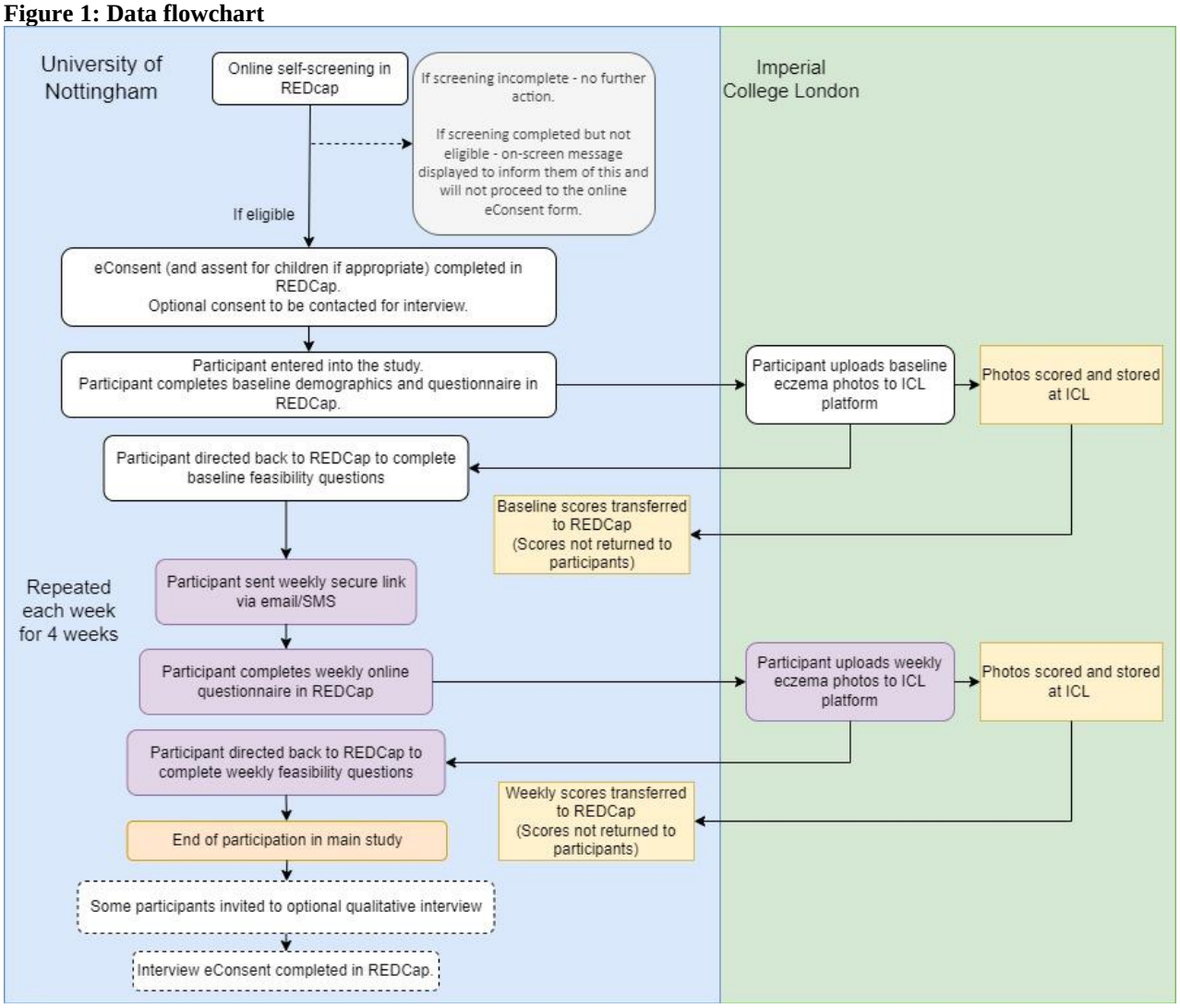
Procedures	**Timepoints**					
	Baseline	Week 1	Week 2	Week 3	Week 4	Week 5 onwards
Informed consent and eligibility screening	X					
Demographics and baseline variables	X					
Eczema severity (POEM)	X					
Eczema outcomes: control (RECAP), global assessment of flares and patient global assessment (PGA)	X	X	X	X	X	
Use of eczema treatments	X	X	X	X	X	
Upload photos of eczema	X	X	X	X	X	
Characteristics of photo upload (e.g. device used, lighting, time taken)	X	X	X	X	X	
Feasibility and acceptability of taking and uploading photos (closed and open questions)	X				X	
Perceived benefits and barriers (closed and open questions)					X	

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Qualitative interview arranged and conducted (if opted in and selected for interview)	x	x	x	x	x	X

Photo Assessment Data flowchart

Figure 1: Data flowchart



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Appendix D

TITLE: Keep Control of Eczema Study

Rationale for the study

Eczema in a chronic-relapsing itchy skin condition, that is characterised by period of flare-up and remission. People with eczema are usually able to self-manage their condition with a combination of topical treatments. These include topical corticosteroids (TCS) to get control of flares, and emollients to manage dry skin and to help prevent future flare-ups.

NICE and MHRA guidance recommends that people with eczema are given advice by healthcare professionals about how long to use their TCS treatments for,[37,38] but clinical guidelines vary in their recommendations and people are often given vague or unhelpful instructions, such as "use sparingly" or "use as required".[39]

This lack of clarity is partially driven by the lack of evidence to inform clinical practice. A recent Cochrane review of strategies for the use of TCS in eczema found no RCTs that addressed how long to apply TCS for an eczema flare-up.[40]

"How best to use topical corticosteroids?" was identified as the top priority for future research in the eczema James Lind Alliance Priority Setting Partnership[2], and the Rapid Eczema Trials project was established to answer patient-driven questions such as this.

Trial summary

Trial Title	Keep Control of Eczema Study
Trial Design	Pragmatic, two-arm, parallel group, superiority randomised controlled trial
Objectives	AIM: To compare different strategies for using TCSs for the self-management of eczema over a period of 4 months in children and adults with eczema OBJECTIVES: 1. To assess the impact of providing specific advice on how long to apply TCSs for during an eczema flare-up compared with no specific advice. 2. To explore barriers and facilitators in using the different strategies for controlling eczema flare-ups and to understand the impact of trial processes on trial participation. 3. To explore feasibility of using photos to assess eczema severity in online clinical trials
Research question	Does providing specific advice on "how long to apply TCSs for during an eczema flare-up" improve eczema control compared to "no specific advice", over 4 months?
Trial duration	Each participant will be enrolled for 16 weeks. Recruitment will take place for up to 12 months.

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Participants and eligibility criteria	People with eczema aged 1 year and older who currently use topical corticosteroids (TCS) to manage their eczema
Intervention and control	The study is an "advice trial". Whilst both treatment strategies align with current practice, advice varies, and people are often given conflicting or vague advice. For the purposes of this trial, two advice strategies will be tested: **Specific advice on duration of applying TCSs (treat flare-ups for longer):** • Use TCSs during a flare-up and for 2 days after the skin is eczema free. **No specific advice on duration of applying TCSs (treat flare-ups as usual):** • Use TCSs during a flare-up as you normally would. Participants will be advised to use their usual prescribed TCS and will remain under the care of their usual healthcare professional.

Outcome measures	**Primary outcome:**
	• Eczema control measured by Recap of atopic eczema (Recap)[23]. Includes 7 items, scored 0 to 28. Assessed weekly over 16 weeks.
	
	Secondary outcomes:
	• Eczema symptoms (Patient Oriented Eczema Measure, POEM).[21] Includes 7 items, scored 0 to 28. Assessed monthly.
	• Total days of TCS used (days of TCS use each week 0 to 7 days) – collected weekly
	• Skin-specific quality of life (Infants' Dermatitis Quality of Life Index (IDQoL)[24] (under 4 years), Children's Dermatology Life Quality Index (CDLQI)[25](from 4 years to 15 years) or Dermatology Life Quality Index (DLQI)[26](16 years and over) depending on age) – 10 items, scored 0 to 30. Assessed at baseline and week 16.
	• Number of weeks when TCS not used (based on the use of TCS questions- assessed weekly)
	• Number of well controlled weeks (defined as number of weeks with Recap score <6).
	• Global change in eczema compared to baseline. Assessed at week 16.
	• Adverse events:
	  ○ Contact with healthcare professional (HCP) because of a worsening of the eczema
	  ○ Contact with HCP due to concerns about side-effects.

Sample size / Number of participants	450 (225 per arm)

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Lay Summary

This study is part of the Rapid Eczema Trials project. We hope to answer many questions about how to look after eczema through this project. People with eczema are helping to design and run these studies. This means that the project will answer important questions for people with eczema.

Eczema is a long-term skin condition that causes itching and goes through cycles of flare-ups and remission. People with eczema can usually manage it themselves by applying treatments directly to their skin. These treatments include corticosteroid ("steroid") creams, which are the main way to control flare-ups. Advice given by healthcare professionals on how long to use steroid creams can often be vague with instructions like "use sparingly" or "use as needed". [39] This uncertainty is partly due to a lack of research on the best approach.[40]
In this Keep Control of Eczema Study, we will test if providing specific advice on how long to use a corticosteroid ("steroid") cream for during a flare-up can help keep eczema controlled for longer compared to no specific advice.

People will join the study by signing up on the study's website. They will give information about their eczema and how they currently treat their eczema flare-ups. They will then be put into one of two groups at random. One group will be given specific advice about how long to use their steroid creams for when they have an eczema flare-up. The other group will be asked to use steroid creams during a flare-up as they normally would.

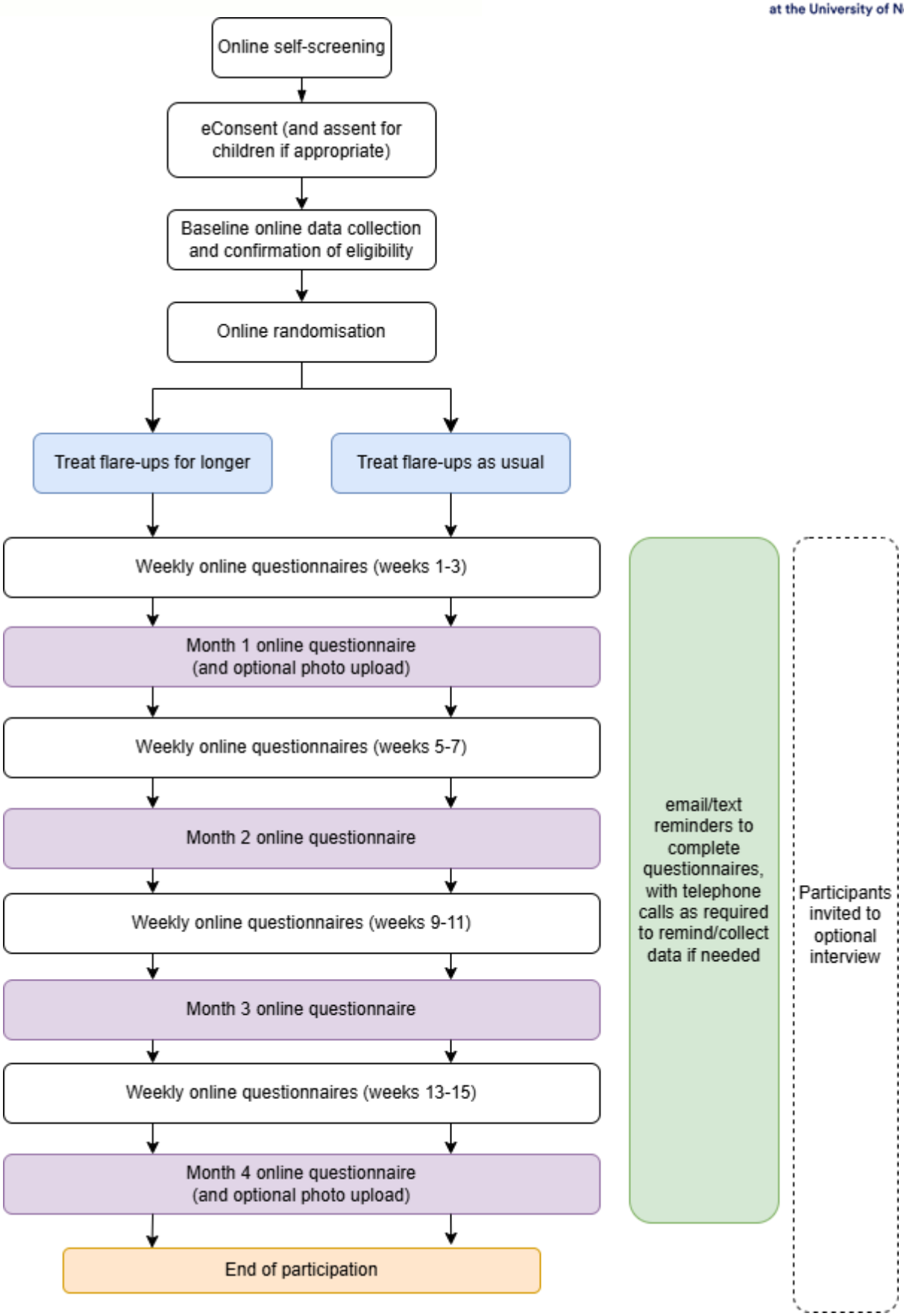
People will be asked to follow their advice strategy for 16 weeks. They will be asked to complete some questions, sent to them by email/text message each week. People will receive reminders to complete the questionnaires by email/text message/telephone call, and information may be collected over the phone if needed. People will be able to upload photos of their eczema if they would like to. These photos will be put through a computer programme that has been trained to assess eczema severity from photos to explore the accuracy of this approach. People can take part from home and do not need to travel.

People aged 1 year or older, who already use steroid creams or ointments to manage their eczema, can join the study. We are encouraging people from all different backgrounds to take part.

As soon as the study results are known, we will share the results as quickly as possible on the study's website (www.RapidEczemaTrials.org).

Trial flowchart

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Details of Keep Control of Eczema Study

Aspect of protocol	
Trial title	Keep Control of Eczema Study
Principal Investigators	Prof Kim Thomas (Chief investigator) and Ms Amanda Roberts (PPI lead)
Contributors	Co-applicants and contributors as outlined in Master Protocol PPI co-design team members: Fiona McOwan, Jemima Jackson, Amanda Roberts, Aaron Pull, Charlotte Wragg, Sonal Marner, Hamish Yewdall and Firoza Davies Other contributors: University of Nottingham (Leila Thuma, Eleanor Harrison, Liz Hartshorne)
ISRCTN registration number	ISRCTN29214215
Research question and hypotheses	Does providing specific advice on how long to apply TCS for during an eczema flare-up improve eczema control compared to no specific advice over 4 months?
Trial aim and objectives	AIM: To compare different strategies for using TCSs for the self-management of eczema over a period of 4 months in children and adults with eczema. OBJECTIVES: 1. To assess the impact of providing specific advice on how long to apply TCSs for during an eczema flare-up, compared to no specific advice. 2. To explore barriers and facilitators in using the two different strategies for controlling eczema flare-ups and to understand the impact of trial processes on trial participation. 3. To explore feasibility of using photos to assess eczema severity in online clinical trials
Participants / eligibility criteria	People with eczema, aged 1 year and older, who currently use TCSs to manage their eczema. **Inclusion criteria** • Aged ≥1 year with self-report of eczema (syn. Atopic dermatitis, atopic eczema) • Used topical corticosteroid on a total of at least 3 days to manage eczema flare up in the last 8 weeks • Willing to change how currently using TCS treatments whilst in the trial • Usual residence in the UK

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	• Able and willing to give informed consent (or parent/legal guardian able and willing to give informed consent for children under 16 years) **Exclusion criteria:** • Using a TCS preparation that includes antibiotics or antifungal (and have no other TCS available), as these products are not intended for long-term use. • Diagnosis unlikely to be atopic eczema: only present on hands (likely to be hand eczema or contact dermatitis); limited to locations where skin exposed to nickel e.g. jewellery (likely to be contact dermatitis); eczema only around varicose veins (likely to be varicose eczema) • Taking part in another eczema intervention trial • Member of household already participating in this trial • Eczema only present on the scalp (as this requires different topical steroid formulations) and/or only at sensitive body sites (e.g. groin, armpits or face (as the advice being tested is not applicable to treatment at sensitive sites, which may require a different potency and duration of treatment)) • Using clobetasol propionate 0.05% (trade name Dermovate), a very strong TCS - to ensure participant safety. Potential participants invited through GP practices will be identified using search criteria as per protocol section 4.
Trial design	Pragmatic, two-arm, parallel group, superiority randomised controlled trial This trial has been co-designed by member of the Rapid Eczema Trials Research Community (www.RapidEczemaTrials.org).
Trial duration	Each participant will be in the trial for 16 weeks with weekly outcome assessment. Recruitment will take place for up to 12 months. The end of trial is defined in protocol section 11.5.
Recruitment strategies	Participants will be identified through online and offline methods, including the use of GP practices as Participant Identification Centres (PICs), as described in protocol section 4.3. Information about the trial will be available on the website (www.RapidEczemaTrials.org) in a variety of engaging formats appropriate for all ages. Participants who complete the final questionnaires at week 16 will be offered the opportunity to enter a free prize draw to win £20, a child-friendly book about eczema, or both, according to their preference. Each

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	questionnaire completed during the study will count as one entry into the prize draw. This approach is intended to provide an incentive for participants to complete questionnaires throughout the study, rather than only the final week 16 questionnaire. Potential participants will be encouraged to contact the trial team if they have any questions prior to registering for the trial online.
Intervention and control	This is an "advice trial". Whilst both treatment strategies align with current practice and guidelines, advice varies, and people are often given conflicting or vague advice. For the purposes of this trial, two advice strategies will be tested: **Specific advice on duration of applying TCSs (treat flare-ups for longer):** • Use TCS during a flare-up, and for 2 days after the skin is eczema free. **No specific advice on duration of applying TCSs (treat flare-ups as usual):** • Use TCS during a flare-up as you normally would. The proposed "treat flare-ups for longer" advice has been taken from the NICE Clinical Knowledge Summary (last updated May 2024): https://cks.nice.org.uk/topics/eczema-atopic/prescribing-information/topical-corticosteroids/, which states that for flares on the body, people should be advised to continue treatment for 48 hours after the eczema has cleared. This is based on clinical opinion and without good research evidence. The advantage of doing so may be that it treats non-visible inflammation ("eczema under the skin") and so prolongs remission longer; a disadvantage is that it may lead to use of more TCS than is needed. Participants will be advised to use their usual prescribed TCS and will remain under the care of their usual healthcare professional. They will be asked to treat eczema on the face as they usually would (i.e. those in the treat for longer group will not be asked to treat eczema on the face for a longer period). Following randomisation, participants will be provided with intervention instructions attached to their welcome email, along with a link to access an online copy. This intervention guidance details how long they should treat their eczema flare-up for according to their allocation. Participants should follow this when they have a flare-up during the 4 months they are in the study. Both groups will receive information in the intervention guidance about: • What an eczema flare-up is • Using their usual topical corticosteroid creams or ointments

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	• Applying the creams or ointments in a thin layer • Seeing a healthcare professional if the eczema does not improve • Ordering repeat prescriptions as they normally would Intervention materials have been designed to be accessible (including pictures and simple language) and inclusive (available in different formats). Withdrawal procedures are as described in protocol section 8.6. Post-trial care is described in protocol section 8.7.

Outcomes	Participant reported outcomes include the Harmonizing Outcomes for Eczema (HOME) initiative's recommended core outcome set validated instruments, with the exception of itch intensity. This will be collected through the itch intensity questions in the weekly Recap questionnaires.
	
	Primary outcome:
	• Eczema control measured by Recap of atopic eczema (Recap)[23]. Includes 7 items, scored 0 to 28. Assessed weekly over 16 weeks.
	
	Secondary outcomes:
	• Eczema symptoms (Patient Oriented Eczema Measure ,POEM).[21] Includes 7 items, scored 0 to 28. Assessed monthly.
	• Total days of TCS used (days of TCS use each week 0 to 7 days) – collected weekly
	• Skin-specific quality of life (Infants' Dermatitis Quality of Life Index (IDQoL)[24] (under 4 years), Children's Dermatology Life Quality Index (CDLQI)[25](from 4 years to 15 years) or Dermatology Life Quality Index (DLQI)[26](16 years and over) depending on age) – 10 items, scored 0 to 30. Assessed at baseline and week 16.
	• Number of weeks when TCS not used (based on the use of TCS questions- assessed weekly)
	• Number of well controlled weeks (defined as number of weeks with Recap score <6).
	• Global change in eczema compared to baseline. Assessed at week 16.
	• Adverse Events:
	  ○ Contact with health care professional (HCP) because of a worsening of the eczema – assessed monthly
	  ○ Contact with HCP due to concerns about side-effects of TCS – assessed monthly
	
	Additional information will be collected to inform analysis and interpretation of the trial. These include:
	
	• Minimisation variables, prior belief in intervention strategy, demographics, UK Diagnostic Criteria for Eczema (baseline only).
	• Potency of TCS currently used on body, number of days TCS used to treat last flare-up, use of TCS to prevent flare-ups, strategy for

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	starting TCS, attitudes towards use of TCS, sensory issues that might influence use of eczema treatments, use of systemic eczema medications (not including antihistamine), use of other steroid formulations (for any condition) (baseline only) • Flares used to assess adherence (monthly) • Intervention group only - adherence to advice about TCS duration of use (monthly) • Changes in eczema treatments (monthly) For children under 16 years, proxy reporting by a parent or carer will be accepted as per protocol section 8.2.
Trial procedures	Informed e-consent will be obtained as per protocol section 5. For children under 16, consent will be obtained from the parent/carer but there will be an optional assent section for the child to complete if they wish. All assessments will be carried out online as per protocol section 8.3. To optimise completion rates, data may be collected through other means if necessary (e.g. by phone, SMS, or email), and entered directly into REDCap by the trial team. For children who are unable to complete patient reported outcomes themselves, proxy reporting by a parent or carer will be accepted as per protocol section 8.2. Parents/carers will be advised that this should be the same adult throughout the trial, if possible. Parents and children will be encouraged to complete the questionnaires together wherever possible. Participants will be invited to take photos of their/their child's eczema and, if they choose, to upload them via a secure link to a platform hosted by Imperial College London. The uploaded photos will be used to assess eczema severity using an artificial intelligence (AI) tool, called EczemaNet.[34] Scores and photos will be securely transferred to the Nottingham Clinical Trials Unit in accordance with the data management plan. The process of taking and uploading photos, as well as the use of EczemaNet, is consistent with the procedures previously approved in appendix C (Photo Assessment Study). An email/text message with a unique link to the questionnaires will be sent each week to the participant/parent/carer. Participants will receive email, text message or phone call reminders as appropriate if questionnaires have not been completed. A summary of assessments diagram is provided below. **Monitoring:** Recruitment, retention, % who reached week 16 and did not use TCS (surrogate for having a flare) and changes in eczema medication use

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	during the trial will be monitored by the TMG. To maintain blinding to treatment allocation, an independent statistician will produce reports to monitor duration of using TCSs during a flare. We will regularly monitor attempts to re-randomise the same individual or enrol multiple people per household on an ongoing basis. Electronic forms collecting data for screening, consent and eligibility will be recorded and processed with automatic and/or manual checks. These checks will include ensuring identifiers and contact details are unique for participants, so no duplicate entries for the same participant may be made. Eligibility checks will ensure only those who meet all the prescribed inclusion and exclusion criteria can join the trial.
Blinding	As this is an advice trial, it is not possible to mask trial participants to their randomised allocation. To mitigate the potential bias caused by lack of blinding, we will collect prior belief in the impact of intervention strategy at baseline and explore this in a sensitivity analysis. The trial statisticians, trial team at NCTU and members of the Trial Management Group will be blinded to treatment allocation.
Sample size	The sample size for the trial is based on Recap scores assessed weekly for 16 weeks and is designed to detect a difference of 2.2 in Recap scores between the two groups. A small difference of 2.2 has been chosen as this trial is evaluating a simple advice strategy. In this context, even a small improvement could be important to people living with eczema and could help them to self-manage their eczema more effectively. Although 2.2 is a small change, it is likely to be beyond measurement error[41]. Assuming a standard deviation in weekly Recap scores of 6.5 and a correlation between repeated measurements of 0.8 (based on data from previous eczema RCTs), a sample size of 150 per group is required to detect this difference with 90% power and 5% two-sided significance level. Randomised participants will follow their allocated treatment strategy when they have a flare-up during the trial, however some participants may join the trial and not have an eczema flare-up. Based on previous online trials, we assume 80% of participants randomised will have at least one flare up and need to use TCS over the 16-week follow-up period. Inflating for this and allowing for 15% loss to follow-up, a total sample size of 450 is required.
Randomisation	Randomisation will be carried out by the participant using an online system managed by NCTU, as described in protocol section 6.2. Participants will be randomised 1:1 to either the intervention group (treat flare-ups for longer) or control group (treat flare-ups as usual) using a minimisation algorithm with a probabilistic element balancing on the following factors: • Eczema severity POEM score (0-7 mild, 8-16 moderate, 17-28 severe).

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	• Age (<4 years, 4-11 years, 12-15 years, 16-25 years, 26-55 years, >55 years) • Potency of TCS (mild, moderate, potent) The randomised allocated group will not be released to participants until after baseline variables have been entered and stored on the trial database.
Analysis	The analysis and reporting of the trial will be in accordance with CONSORT guidelines, with the primary comparative analyses being conducted according to randomised allocation regardless of adherence to allocated TCS strategy during a flare-up. A statistical analysis plan will be finalised prior to database lock and release of the treatment allocations. The primary analysis will use all available longitudinal outcome data and will use a linear mixed effects model to estimate the difference in mean Recap score over the 16-week trial period with 95% confidence interval. The model will include fixed effects for the minimisation variables (age, baseline POEM score and potency of TCS) and baseline Recap score. The following potentially prognostic variables will also be included as fixed effects if technically possible: UK Diagnostic criteria, number of days TCS used to treat last flare-up, attitudes towards use of TCS, use of TCS to prevent flares and use of steroids (for any condition). It will allow for observations nested within participants over time using random effects. If there is evidence of a differential effect over time, the difference in mean Recap score each week will be reported. Sensitivity analyses for the primary outcome will use multiple imputation for missing outcome data. Subgroup analyses for the primary outcome will be performed according to age, potency of TCS, eczema severity, diagnosis of eczema according to UK Diagnostic Criteria and prior belief by including an appropriate interaction term in the mixed effect model. The trial is not powered to detect any interactions hence the subgroup analyses will be treated as exploratory. Between-group comparison of secondary outcomes will use an appropriate regression model for the outcome (linear for continuous outcomes, logistic for binary) with adjustment as described above for the primary outcome and baseline outcome measure for continuous variables if available. For secondary outcomes assessed weekly or monthly, mixed effects models will be used to allow for observations nested within participants over time using random effects. Scores generated from photos using EczemaNet will be used to evaluate the feasibility, validity and responsiveness of eczema severity assessments based on EczemaNet assessment of clinical images. This will include summarising descriptively the proportion of participants

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	uploading photos and whether they were of sufficient quality to generate an EczemaNet score and assessing the association between EczemaNet severity scores and patient-reported outcomes from the trial.
Process evaluation	A nested, qualitative interview study will consider questions of acceptability, feasibility, and adherence regarding different strategies for using TCS for the treatment of eczema flare-ups. Interviews will also consider trial procedures. A purposive sample of those willing to take part in a research interview will be constructed to include a range of age, gender, ethnicity, prior belief in the impact of length of flare-up treatment and acceptability of the interventions. We will recruit approximately 20 participants, purposefully selected to capture diverse participants and balanced reflection of the two groups. Only adults (aged 16+) will be included in this qualitative study (either as people with eczema or as parents/carers of children with eczema). Children who took part in the study may accompany their parent/carer during the interview if they wish to. Additional consent will be taken from those that participate in a research interview. Online informed consent will be taken prior to the interview, and consent confirmed verbally at the start of the interview. Interviews will be undertaken online or by telephone, at a time convenient to the participant. Data will be digitally recorded if participants consent to this. Interviews will explore the participants (i) experience with the provided treatment advice; (ii) any difficulties or challenges that they experienced in this; (iii) any difference that this made to their eczema; (iv) their willingness to continue with their allocated treatment advice; (v) their assessment of the effectiveness of the intervention and vi) their experience of taking part in the trial. Digital recordings will be collected and transcribed in-house using University of Nottingham approved software (MS Office 365, or an offline digital recorder), or by an approved external transcription service. Transcripts will be stored as per the Data Management Plan. Recordings will be destroyed once transcripts have been approved as an accurate record. Qualitative data will be analysed using NVivo software.[35] Data will be analysed using framework analysis.[36] A framework will be used to organise the data. Themes will be described and will help to understand the trends and findings in the quantitative data. A trained researcher will lead the analysis, with the support of Dr Paul Leighton.

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Data sharing	Data from the trial may be shared as per protocol section 10.5.
Trial-specific documents	The following documents have been developed for the Keep Control of Eczema Study and included in an amendment: • Keep Control Study Participant Information Sheet (website text) • Keep Control Study video script (suitable for older children, adults and people with low literacy) • Keep Control Study child video script (suitable for young children) • Keep Control Study intervention guidance – Specific Advice • Keep Control Study intervention guidance – Treat as usual • Keep Control Study questionnaire (draft) • Keep Control Study Poster (for GP surgeries/pharmacies/schools etc) • Keep Control Study Interview PIS • Keep Control Study Interview Topic Guide The Keep Control Study will use the following Rapid Master documents: • Rapid Master Adult Informed Consent Form • Rapid Master Parent Informed Consent Form (with child assent if appropriate) • Rapid Master GP invite letter Adult • Rapid Master GP invite letter Parent • Rapid Master GP invite text message wording • Rapid Master Process Evaluation Interview ICF • Rapid Master Interview Invitation Additional advertising materials may be used e.g. social media posts, and these will adhere to the Rapid Principles for advertising materials document.

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Summary of Assessments

	TRIAL PERIOD

	Enrolment	Baseline	Follow-up				
TIMEPOINT	**0**	**0**	**Month 1**	**Month 2**	**Month 3**	**Month 4**	**Weekly**
ENROLMENT:							
Eligibility screen (including self-report of eczema diagnosis)	X						
Informed e-consent (and child assent if appropriate)	X						
Minimisation variables		X					
Randomisation		X					
INTERVENTIONS:							
Treat flare-ups for longer			←	—	—	→	
Treat flare-ups as usual			←	—	—	→	
ASSESSMENTS:							
Demographics and baseline characteristics		X					
UK Diagnostic criteria		X					
Prior belief in intervention		X					
Eczema Control (RECAP)		X					X
Number of Days of TCS		X					X
Eczema Symptoms (POEM)		X	X	X	X	X	
Changes in eczema treatments		X	X	X	X	X	
Quality of Life (DLQI, CDLQI, IDQI as appropriate)		X				X	
Global change in eczema compared to baseline						X	
Acceptability of intervention/ process outcomes						X	
Flares and adherence to intervention			X	X	X	X	
Adverse events –contact with healthcare professional due to worsening of eczema			X	X	X	X	
Adverse events –contact with healthcare professional due			X	X	X	X	

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to concerns about side-effects							
Eczema signs from photos			X			X	

Contacts

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Appendix E

TITLE: Scratch Less Study

Rationale for the study

Eczema (syn. atopic eczema, atopic dermatitis) is a chronic itchy skin condition that changes and can worsen ("flare up"). Itching often leads to scratching, and scratching worsens the itch, so periods of disease activity can lead to an itch-scratch cycle, exacerbating the flare. Scratching disrupts the skin barrier making it more permeable to allergens and increasing susceptibility to skin infections, and chronic scratching leads to thickened leathery patches of skin with increase in nerve endings. Scratching has been shown to directly cause inflammation in experimental models, probably through release of neuropeptide 2 which in turn results in mast cell aggregation.[42] Stress has been shown to increase the urge to scratch.[43] The mainstay of treatment is topical treatments including emollients to manage the associated dry skin and topical corticosteroids or calcineurin inhibitors to get control of and prevent new flares. Literature documents a high treatment burden for patients, lack of consistent advice, and concerns about treatments.[44]

There is a strong interest amongst the patient community in psychological and behavioural approaches to managing eczema. The James Lind Alliance eczema priority setting partnership in 2012 identified 'What is the best psychological treatment for itching/scratching in eczema?' as a key patient priority.[45] The decision to test an intervention for 'breaking the itch-scratch cycle in eczema' was prioritised by members of the Rapid Eczema Trials community through a 6-month prioritisation process. This included an online survey, online prioritisation workshops, and co-design discussions to review the resulting data and to consider what question could be answered effectively in a clinical trial.

One behavioural approach to addressing itching and scratching in eczema is habit reversal. Habit reversal techniques were designed specifically for people with eczema in the 1980s using behavioural psychology principles to address the itch-scratch cycle. Although the term "habit" is perhaps undesirable as it apportions "blame" onto the person with eczema, the approach suggests that over time scratching behaviour becomes not just a response to the itch, but also becomes a habit and a response to mental state.[46] The approach includes education on the difference between itching and scratching, raising the patient awareness of their scratching, and behavioural modification to replace the scratching behaviour.[47]

Proponents of the habit reversal approach describe how it should be used as an adjunct to medical therapy as opposed to a stand-alone intervention, and refer to the 'combined approach' which should combine habit reversal techniques alongside best practice medical care.[48]

A systematic review in 2017 identified a lack of high-quality self-management interventions for eczema.[16] There is a need for a large high-quality trial comparing a habit reversal based intervention with usual care for eczema. To date, there have only been two very small RCTs (n=17 and n= 45) in adults[49,50] and one in children (n = 39).[51] These trials were identified from Cochrane reviews of educational and psychological interventions for eczema.[52,53]

Susannah Baron and team at King's College London developed an intervention called 'Kids in Control', which aims to educate children aged 8-12 years on how to use their topical treatments for eczema and learn habit reversal techniques in a three-part programme. The programme was designed to be done in three stages via online group delivery by a healthcare professional. Part 1 teaches people about eczema and how to use their treatments effectively and appropriately. Part 2 asks people to notice their scratching and instructs them on how to track their scratching over the next week. Part 3 teaches people new behaviours that can replace the scratching behaviour and instructs them how to continue tracking their scratching and trying out the new behaviours over the next week. Kids in Control has undergone a series of think aloud interviews with users to refine the intervention for the target age group. The Rapid Eczema Trials team have adapted the Kids in Control intervention to create Scratch Less. The key differences being: 1) developing it so that it can be used in a self-directed way online for the trial and 2) creating a version that is appropriate for people aged 13+.

Trial summary

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Trial Title	Scratch Less Study
Trial Design	Two, pragmatic, online, parallel group, superiority, randomised controlled trials.
Objectives	AIM: To assess the impact of a 3-part online intervention on eczema symptoms compared with usual care over a period of 16 weeks in children and adults with eczema. OBJECTIVES: 1) To assess the impact on eczema symptoms of an online intervention addressing the itch-scratch cycle compared with usual care alone in two populations: a) Children aged 8-12 years, and b) Adults and young people (aged 13 years and over) 2) To explore barriers and facilitators in using the online intervention and inform routes to implementation.
Research question	Does an online intervention addressing the itch-scratch cycle improve eczema symptoms compared with usual care over 16 weeks?
Trial duration	Each participant will be enrolled for 16 weeks. Recruitment will take place for up to 12 months (minimum 4 months).
Participants and eligibility criteria	People with eczema aged 8 years and older who are interested in reducing how much they scratch their eczema. There will be two trials conducted following the same design: one for children aged 8-12 years and one for adults and young people aged 13 years and over.
Intervention and control	**Intervention group: Scratch Less programme** • A 3-part online programme to support management of itch and scratch for people with eczema in addition to usual care **Control group: Usual care** • Usual eczema care The Scratch Less intervention is tailored by age. 8 to 12 years version is designed to be used with support from a parent or carer. 13+ years version is designed for self-completion. To encourage continued engagement with the trial, participants in the control group will be given access to the intervention after 16 weeks in study so that they can try it for themselves if they would like to.
Outcome measures	**Primary outcome:** • Eczema symptoms measured by Patient Oriented Eczema Measure (POEM).[21] Includes 7 items, scored 0 to 28. Assessed monthly over 16 weeks.

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	Secondary outcomes:
	• Eczema control measured by Recap of atopic eczema (RECAP).[23] Includes 7 items, scored 0 to 28. Assessed at baseline, week 4 and week 16.
	• Itch intensity (Peak Pruritis Numerical Rating Scale (NRS) 24-hour peak itch)[22] - one item, scored 0 to 10. Assessed monthly.
	• Scratching over the last week – assessed at baseline, week 4 and week 16.
	• Skin-specific quality of life (Children's Dermatology Life Quality Index (CDLQI)(from 4 years to 15 years)[25] or Dermatology Life Quality Index (DLQI)(16 years and over)[26] depending on age) – 10 items, scored 0 to 30. Assessed at baseline and week 16.
	• Patient Enablement Instrument (PEI)[54] – assessed at baseline and week 16
	• Adverse events:
	  ○ Contact with healthcare professional (HCP) because of a worsening of the eczema – week 16
	  ○ Open question to capture unexpected events – week 16
	• Frequency of skin bleeding due to eczema – assessed using POEM[21] item 3, monthly over 16 weeks.
	• Proportion of participants who achieve an improvement in POEM at week 16 of ≥3 points compared to baseline[33]

Sample size / Number of participants	278 children (8 to 12 years) 278 adults and young people (13+ years) After recruitment to the 13+ trial was completed within two months, recruitment was extended to up to four months and the sample size increased to 450 participants to confirm sample size assumptions, ensure diversity of participants, and to allow for approximately 20% non-engagement with the intervention.

Lay summary

This study is part of the Rapid Eczema Trials project. We hope to answer many questions about how to look after eczema through this project. People with eczema are helping to design and run these studies. This means that the project will answer important questions for people with eczema.

Itch is a common symptom of eczema, and scratching is a response to feeling itchy. Over time, the response of scratching can form a habit, where people scratch even if they don't feel itchy.

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Scratching can also lead to worsening of itch and make the eczema worse. There are various ways of helping people to reduce how much they scratch in the hope of breaking this itch-scratch cycle. One of these approaches – the Scratch Less programme is being tested in this study.

In the Scratch Less Study, we will test if a 3-part online programme can help improve eczema symptoms compared with usual eczema care over 4 months. The Scratch Less programme starts by helping people to treat their eczema, and then supports people to try to reduce their scratching behaviour. This involves becoming more aware of the scratching, identifying the situations and reasons scratching is occurring, and then replacing the scratching with doing something else instead.

The Scratch Less programme can be done at people's own pace, but is designed to be completed over 3 weeks. In part 1 people learn more about eczema and how to treat it, in part 2 people learn how to become aware of their scratching and how to start tracking their scratching, and in part 3 people learn new activities they can do instead of scratching and how to keep tracking their progress.

People will join the study by signing up on the study website. People can take part from home and do not need to travel. They will answer questions about their eczema and how they currently treat it. They will then be put into one of two groups at random. One group will be asked to follow the 3-part online programme. The other group will be asked to follow their usual care for their eczema. We don't yet know if the Scratch Less programme works, but people in the usual care group will be able to try it at the end of the study if they would like to.

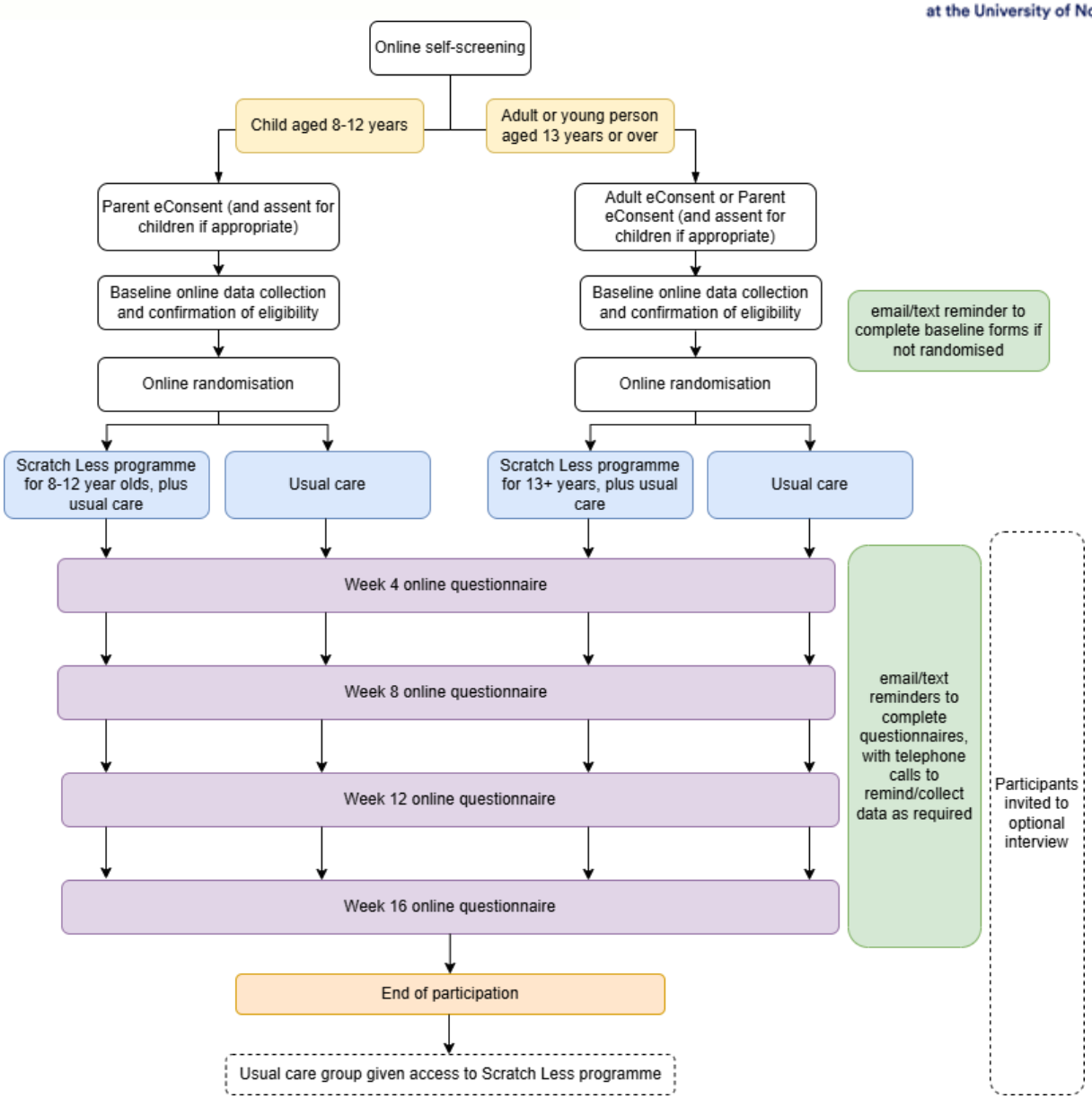
Everyone will be in the study for 4 months. They will be asked to complete some questions, sent to them by email/text message each month. People will receive reminders to complete the questionnaires by email/text message/telephone call, and information may be collected over the phone if needed.

People aged 8 years or older who have eczema and would like to reduce their scratching can join the studies. We are encouraging people from all different backgrounds to take part.

Soon after the study results are known, we will share the results on the study's website (www.RapidEczemaTrials.org).

Trial flowchart

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Details of Scratch Less Study

Aspect of protocol	
Trial title	Scratch Less Study

Scientific title	Impact of an online intervention to address the itch-scratch cycle on eczema symptoms, quality of life, disease control and patient enablement in children and adults with eczema: two online, superiority, randomised controlled trials
Principal Investigators	Professor Kim Thomas (Chief Investigator), Dr Laura Howells (Co-lead for Scratch Less Study) and Ms Amanda Roberts (PPI lead for Rapid Eczema Trials programme)
Contributors	Lead and co-applicants and contributors as outlined in Master Protocol, plus: Co-design team members: Clara Martins de Barros Hamish Yewdall Hugh Jarrett Wing-Zie Yim Tim Burton Leslie Ferrar Chloé Bodard-Williams Victoria Isom Umm Ilyaas Naheen (chosen not to share surname) Charlotte Wragg Laura Howells Lydia Tutt Kate Clement Kim Thomas Sonu Tamang Gemma Whicker Gavin Fong Grace Boyd Anthony Bewley Ella Guest Hywel Williams Lucy Bradshaw Corri Campbell Susannah Baron Liz Steed And other PPI members who have not yet consented to be acknowledged by name Nottingham Clinical Trials Unit staff: Eleanor Harrison Leila Thuma Susanne Spas Liz Hartshorne Lucy Bradshaw Corri Campbell Nick Hilken

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	Rich Swinden
ISRCTN registration number	ISRCTN15774173
Research question and hypotheses	Does an online intervention addressing the itch-scratch cycle improve eczema symptoms compared to usual care over 4 months?
Aim and objectives	AIM: To assess the impact of a 3-part online intervention on eczema symptoms compared with usual care over a period of 16 weeks in children and adults with eczema. OBJECTIVES: 1) To assess the impact on eczema symptoms of an online intervention addressing the itch-scratch cycle compared with usual care alone in two populations: a) Children aged 8-12 years, and b) Adults and young people (aged 13 years and over) 2) To explore barriers and facilitators in using the online intervention and inform routes to implementation.
Participants / eligibility criteria	People with eczema aged 8 years and older who are interested in reducing how much they scratch their eczema. Children aged 8-12 years will be enrolled into the trial for children. Individuals aged 13 years and over will be enrolled into the trial for adults and young people. **Inclusion criteria** • Aged ≥8 years with self-report of eczema (syn. atopic dermatitis, atopic eczema). • Able and willing to participate in the online intervention. • Usual residence in the UK. • Able and willing to give informed consent (or parent/legal guardian able and willing to give informed consent for children under 16 years). **Exclusion criteria:** • Diagnosis unlikely to be atopic eczema: only present on hands (likely to be hand eczema or contact dermatitis); limited to locations where skin exposed to nickel e.g. jewellery (likely to be contact dermatitis); eczema only around varicose veins (likely to be varicose eczema). • Taking part in another eczema intervention trial. • Member of household already agreed to take part in the Scratch Less trial. As per protocol section 4, potential participants identified through GP practices will have a recorded diagnosis of eczema on their medical records and will have been issued a prescription for emollients or topical corticosteroids in the last 2 years.

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	Participants identified via secondary care will have an eczema diagnosis in their medical records.
Trial design	Two pragmatic, online, parallel group, superiority randomised controlled trials. This trial has been co-designed by member of the Rapid Eczema Trials Research Community (www.RapidEczemaTrials.org).
Trial duration	Each participant will be in the trial for 16 weeks with monthly outcome assessment. Recruitment is expected to take place for up to 12 months (minimum 4 months to allow assessment of follow-up rates and engagement with the intervention). The end of trial is defined in protocol section 11.5.
Recruitment strategies	Participants will be signposted to the trial website through online and offline methods as described in protocol section 4.3. This will include using GP practices as Participant Identification Centres (PICs) and displaying trial materials e.g. posters in various locations including healthcare settings. Secondary/tertiary care settings will also be used as PICs, including but not limited to dermatology, allergy and paediatric departments. Trial advertising materials/invitation letters directing people to the trial website will be displayed in and/or given out to patients attending appointments or clinics, or sent out to people on waiting lists, on clinic lists, awaiting follow-up or recently discharged. Links may also be provided in Advice and Guidance responses to patients being managed in primary care. Repeat searches of patient lists may be required during the trial. Information about the trial will be available on the website (www.RapidEczemaTrials.org) in a variety of engaging formats appropriate for all ages. Screening, consent and randomisation will all take place online. Participants who complete questionnaires during the study will be offered the opportunity to enter a free prize draw to win £20, a child-friendly book about eczema, or both, according to their preference. Each questionnaire completed during the study will count as one entry into the prize draw to provide an incentive for participants to complete questionnaires throughout the study. Potential participants will be encouraged to contact the trial team if they have any questions prior to registering for the trial online.
Intervention and control	**Intervention group: Scratch Less programme** • A 3-part online programme to support management of itch and scratch for people with eczema plus usual care **Control group: Usual care**

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	• Usual eczema care alone The intervention is adapted from the 'Kids in Control' intervention developed by Dr Susannah Baron and team at King's College London. Kids in Control uses a combined approach of education about how to use eczema treatments alongside habit reversal techniques from behavioural psychology (raising awareness of scratching behaviour and replacing the behaviour). The Kids in Control intervention was designed to be delivered by a healthcare professional in an online group setting for 8-12 year olds. Therefore, to make it suitable for evaluation in this study, we have adapted the intervention (with user testing through think aloud interviews) to make it suitable for stand-alone self-directed online use and to create a version suitable for older children and adults aged 13+ years. The trial enrolling children aged 8-12 years will use the intervention for 8-12 year olds which is designed to be used with parental support. The trial enrolling adults and young people will use the intervention adapted for 13+ years which is designed to be used by the person with eczema, but could be supported by parents/carers if required. The online programme is divided into 3 parts. It is self-directed but is suggested that each part is completed a week apart, with activities completed between sessions to put the learning into practice. Part 1: Individuals learn more about eczema and how to use the two main topical treatments for eczema (emollients and topical corticosteroids). They are encouraged over the next week to label their topical treatments so they are clear which is an emollient and which is a topical steroid and use their treatments using the 'best practice' guidance they have learnt within the programme. Part 2: Individuals learn about the itch-scratch cycle in eczema and how to become aware of their scratching. They are instructed on how to track their scratching and are encouraged over the next week to use the scratching diary within the website to track their scratching. The aim is for them to become aware of what situations are likely to trigger their scratching and to be able to notice when they are scratching. Part 3: Individuals learn a series of new activities they can try out to replace their scratching behaviour (e.g. tracing their hand, deep breathing). They are encouraged over the next week to continue to notice situations where they are scratching and track their scratching in the online diary, alongside trying out replacing the scratching behaviour with a new activity. People are sent automatic reminders to complete the relevant part of the intervention via email to help them stay engaged.

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	Following randomisation, participants in the intervention group will be provided with access to the online programme via an individual user account that will be created for them. • Children aged 8-12 years will receive access to the 'child version' and use the intervention with parent/carer support. • Participants aged 13 years or over will receive access to the 13+ version and use the intervention independently (unless help is required on individual basis). Intervention materials and instructions have been through an extensive period of development and testing, informed by psychological theory and behaviour change techniques. Materials have been designed to be accessible for all ages and those with limited reading abilities and English language skills. All participants can use their usual eczema treatments (e.g. emollients and flare control creams) and will remain under the care of their usual healthcare professional during the trial. Withdrawal procedures are as described in protocol section 8.6. Post-trial care is described in protocol section 8.7. Participants in the control group will receive access to the intervention once they have completed their time in the study.
Outcomes	Participant reported outcomes include the Harmonizing Outcomes for Eczema (HOME) initiative's recommended core outcome set validated instruments. **Primary outcome:** • Eczema symptoms measured by Patient Oriented Eczema Measure (POEM).[21] Includes 7 items, scored 0 to 28. Assessed monthly over 16 weeks. **Secondary outcomes:** • Eczema control measured by Recap of atopic eczema (RECAP).[23] Includes 7 items, scored 0 to 28. Assessed at baseline, week 4 and week 16. • Itch intensity (Peak Pruritis Numerical Rating Scale (NRS) 24-hour peak itch)[22] - one item, scored 0 to 10. Assessed monthly. • Scratching over the last week – assessed at baseline, week 4 and week 16. • Skin-specific quality of life (Children's Dermatology Life Quality Index (CDLQI)(from 4 years to 15 years)[25] or Dermatology Life Quality Index (DLQI)(16 years and over)[26] depending on age) – 10 items, scored 0 to 30. Assessed at baseline and week 16. • Patient Enablement Instrument (PEI)[54] – assessed at baseline and week 16 • Adverse events:

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	○ Contact with healthcare professional (HCP) because of a worsening of the eczema – week 16 ○ Open question to capture unexpected events – week 16 • Frequency of skin bleeding due to eczema – assessed using POEM[21] item 3, monthly over 16 weeks. • Proportion of participants who achieve an improvement in POEM at week 16 of ≥3 points compared to baseline[33] Additional information will be collected to inform analysis and interpretation of the trial. These include: • Minimisation variables, prior belief in intervention strategy, demographics, UK Diagnostic Criteria for Eczema (baseline only) • Use of flare control creams (steroids and/or calcineurin inhibitors) – assessed monthly • Adherence to online programme (intervention group only) - week 4 and week 16 (including self-report and Scratch Less usage statistics) • Acceptability (intervention group only) – week 16 • Changes in eczema treatments – week 16
Trial procedures	Informed e-consent will be obtained as per protocol section 5. For children under 16, consent will be obtained from the parent/carer but there will be an optional assent section for the child to complete if they wish. Participants that complete e-consent but do not proceed to randomisation may be sent an email/text message reminder to complete the baseline forms and join the study. All assessments will be carried out online as per protocol section 8.3. To optimise completion rates, data may be collected through other means if necessary (e.g. by phone, SMS, or email). An email/text message with a unique link to the questionnaires will be sent each month to the participant/parent/carer. Participants will receive email, text message or phone call reminders as appropriate. Data may be collected over the phone if required. Email and text messaging may also be used periodically throughout the study to keep participants engaged and send updates/reminders to participants. It is anticipated that children aged 8-15 years will complete patient reported outcomes themselves, with parental support if required. For children who are unable to complete patient reported outcomes themselves, proxy reporting by a parent or carer will be accepted as per protocol section 8.2. Parents/carers will be advised that this should be the same adult throughout the trial, if possible.

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	Participants' email address, name, which version of the intervention they should receive, and their study ID will be shared (with consent) with We Create Digital for the purposes of providing access to the intervention. Data will be securely transferred between UoN and We Create Digital in accordance with the Data Management Plan (DMP) and Data Protection Impact Assessment (DPIA). A summary of assessments diagram is provided below. **Monitoring:** Recruitment, retention, and engagement with the intervention will be monitored by the TMG and adjustments made to procedures if necessary. We will regularly monitor attempts to re-randomise the same individual or enrol multiple people per household. Electronic forms collecting data for screening, consent and eligibility will be recorded and processed with automatic and/or manual checks. These checks will include ensuring identifiers and contact details are unique for participants, so no duplicate entries for the same participant may be made. Eligibility checks will ensure only those who meet all the prescribed inclusion and exclusion criteria can join the trial.
Blinding	As this trial involves completing an online self-directed programme, it is not possible to mask trial participants to their randomised allocation. To mitigate the potential bias caused by lack of blinding, we will collect prior belief in the impact of intervention strategy at baseline and explore this in a sensitivity analysis. The trial statisticians and members of the Trial Management Group (other than the NCTU trial management, data management and IT teams) will be blinded to treatment allocation.
Sample size	The sample size is based on POEM scores assessed monthly for 4 months and is designed to detect a difference of 2.5 in POEM scores between the two groups. A small difference of 2.5 has been chosen as we are testing a simple self-management strategy with minimal cost. Even small differences could be important for people looking for self-management options to try at home. This difference represents a change that is likely to be beyond measurement error.[33] Assuming a standard deviation in monthly POEM scores of 6.5 and a correlation between repeated measurements of 0.7 (based on data from previous eczema RCTs), a sample size of 111 per group in each of the two trials is required to detect this difference with 90% power and 5% two-sided significance level. Allowing for 20% loss to follow-

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	up, gives a total sample size of 278 participants in each of the two age groups. Since recruitment into the 13+ trial was completed in just two months, a protocol amendment was requested to allow recruitment to continue for an additional two months, so that assumptions around the sample size could be checked. At this point, to ensure sufficient power and diversity in the target population, the sample size was increased to 450 for the 13+ trial. This allows for around 20% of participants not engaging with the intervention and the consequent reduction in the expected difference between groups
Randomisation	Participants will be randomised using an online system managed by NCTU, as described in protocol section 6.2. Participants will be randomised 1:1 to either the intervention group (Scratch Less programme) or control group (usual care alone) separately for the two age groups (8-12 years and 13 years and over) using a minimisation algorithm with a probabilistic element balancing on the following factors: • Eczema severity POEM score (0-7 mild, 8-16 moderate, 17-28 severe). • Age (13+ years group only: 13 to 15, 16 to 25, 26 to 55, > 55 years) • Gender (male, female, other) • Use of systemic treatments or super potent topical corticosteroids (no, yes started less than 3 months ago, yes started 3 months ago or more) The randomised allocated group will not be released to participants until after baseline variables have been entered and stored on the trial database.
Analysis	The analysis and reporting of the trial will be in accordance with CONSORT guidelines, with the primary comparative analyses being conducted according to randomised allocation regardless of adherence to allocation to the online programme or usual care. A statistical analysis plan will be finalised prior to database lock and release of the treatment allocations. The trial is powered to detect treatment differences in the two age groups (ages 8 to 12 years and 13+ years) separately, and data will be analysed and presented separately for each age group. The primary analysis will use all available longitudinal outcome data and will use a linear mixed effects model to estimate the difference in mean POEM score over the 16-week trial period with 95% confidence interval. The model will include fixed effects for the minimisation variables (age, baseline POEM score, gender, and use of systemic treatments or super potent topical corticosteroids). The following potentially prognostic variable will also be included as fixed effects if technically possible: UK Diagnostic criteria. The model

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	will allow for observations nested within participants over time using random effects. If there is evidence of a differential effect over time, the difference in mean POEM score each month will be reported. Sensitivity analyses for the primary outcome will use multiple imputation for missing outcome data. Subgroup analyses for the primary outcome will be performed according to age (13+ only), gender, use of systemic treatments or super potent topical corticosteroids, diagnosis of eczema according to the UK Diagnostic Criteria, prior belief in the intervention, other atopic conditions (e.g. history of asthma/hay fever) and baseline eczema severity (using POEM). All subgroup analyses will be treated as exploratory since the trial is not powered to detect interactions. Between-group comparison of secondary outcomes will use an appropriate regression model for the outcome (linear for continuous outcomes, logistic for binary) with adjustment as described above for the primary outcome and baseline outcome measure for continuous variables if available. For secondary outcomes assessed monthly, mixed effects models will be used to allow for observations nested within participants over time using random effects. The overall effect of the Scratch Less intervention for people with eczema aged 8 or above will be estimated by pooling individual participant data from both age groups, using a mixed-effects model with a random intercept for age group to account for clustering.
Process evaluation	A nested, qualitative interview study will consider questions of acceptability, feasibility, and adherence regarding the online programme. Interviews will also consider trial procedures. A purposive sample of those willing to take part in a research interview will be constructed to include a range of age, gender, ethnicity, prior belief in the intervention and acceptability of the intervention. We will recruit approximately 20 participants, purposefully selected to capture diverse participants and experiences in the trial. Additional consent will be taken from those that participate in a research interview. Online informed consent will be taken prior to the interview, and consent confirmed verbally at the start of the interview. Children who took part in the study (aged 8-15 years) may take part in an interview, but a parent/carer must provide consent and be present during the interview. There will be an optional assent section on the online consent form for the child to complete if they wish.

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	Interviews will be undertaken online or by telephone, at a time convenient to the participant. Data will be digitally recorded if participants consent to this. A £20 shopping voucher will be offered to all interview participants upon interview completion, as a token of appreciation. Interviews will explore the participants' (i) experience of taking part in the study; (ii) any difficulties or challenges that they experienced; (iii) any difference taking part in the trial made to their eczema; (iv) their willingness to continue with their allocated intervention; (v) their assessment of the effectiveness of their allocated intervention. Digital recordings will be collected and transcribed in-house using University of Nottingham approved software (MS Office 365, or an offline digital recorder), or by an approved external transcription service. Transcripts will be stored as per the Data Management Plan. Recordings will be destroyed once transcripts have been approved as an accurate record. Qualitative data will be analysed using NVivo software.[35] Data will be analysed using framework analysis. A framework will be used to organise the data. Themes will be described and will help to understand the trends and findings in the quantitative data. A trained researcher will lead the analysis, with the support of Dr Paul Leighton.
Data sharing	Data from the trial may be shared as per protocol section 10.5.
Trial-specific documents	The following documents have been developed for the Scratch Less Study and included in an amendment: • Scratch Less Study Participant Information Sheet (website text) • Scratch Less Study video script (suitable for older children, adults and people with low literacy) • Scratch Less Study child video script (suitable for children aged 8-12 years) • Scratch Less Study Adult Informed Consent Form • Scratch Less Study Parent Informed Consent Form (with child assent if appropriate) • Scratch Less Study questionnaire (draft) • Scratch Less Study Poster (for GP surgeries/hospitals/pharmacies/schools etc) • Scratch Less Study flyer • Scratch Less Study Process Evaluation Interview PIS • Scratch Less Study Process Evaluation Interview Topic Guide The Scratch Less Study will use the following Rapid Master documents:

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	• Rapid Master GP invite letter Adult • Rapid Master GP invite letter Parent • Rapid Master GP invite text message wording • Rapid Master Process Evaluation Interview ICF • Rapid Master Process Evaluation Parent Interview ICF (with child assent if appropriate) • Rapid Master Interview Invitation Additional advertising materials may be used e.g. social media posts, and these will adhere to the Rapid Principles for advertising materials document.

Summary of Assessments

	TRIAL PERIOD					
	Enrolment	Baseline	Follow-up			
TIMEPOINT	**0**	**0**	**Week 4**	**Week 8**	**Week 12**	**Week 16**
ENROLMENT:						
Eligibility screen (including self-report of eczema diagnosis)	X					
Informed e-consent (and child assent if appropriate)	X					
Minimisation variables		X				
Randomisation		X				
INTERVENTIONS:						
Scratch Less online programme		◆—	—◆			
Usual care (access to online programme after 16 weeks)		◆—	—	—	—	—◆
ASSESSMENTS:						
Demographics and baseline characteristics		X				
UK Diagnostic criteria		X				
Eczema Symptoms (POEM)		X	X	X	X	X
Use of flare control creams		X	X	X	X	X
Use of systemic treatments and super potent TCS		X				

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	TRIAL PERIOD					
	Enrolment	**Baseline**	**Follow-up**			
Prior belief in intervention		X				
Scratching		X	X	X	X	X
Eczema Control (RECAP)		X	X			X
Itch intensity		X	X	X	X	X
Quality of Life (DLQI or CDLQI as appropriate)		X				X
Patient enablement		X				X
Adherence (intervention group only)			X			X
Changes in eczema treatments						X
Safety – contact with healthcare professional due to worsening of eczema						X
Safety – unexpected effects						X
Acceptability of intervention/ process outcomes						X

Contacts

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