Supporting self-care for eczema: two randomised controlled trials of online interventions (ECO Trials): Health Economic Analysis Plan

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Section 1: Administrative Information

1.1 Title: Supporting self-care for eczema: two randomised controlled trials of online interventions (ECO Trials): Health Economic Analysis Plan

1.2 Trial registration number: ISRCTN 79282252

1.3 Source of funding:

This study is funded by the National Institute for Health Research (NIHR) under its Programme Grants for Applied Research programme (grant ref No RP-PG-0216-20007). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

1.4 Purpose of HEAP:

This document will outline the methods to be used in the economic evaluations to be conducted alongside the ECO Trials, including how data will be collected, analysed and reported. It will be finalised and reviewed prior to the trial database being locked. This HEAP has been written in line with the trial protocol and SAP in order to ensure there is consistency.

1.5 Trial protocol version*:*

This document has been written based on information contained in the trial protocol version 4, dated 08/10/2020.

1.6 Trial statistical analysis plan (SAP) version

SAP version 2, dated 7th November 2020

1.7 Trial HEAP version

HEAP version: 1.0, Date: 28th April 2021

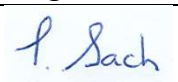
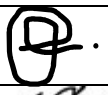
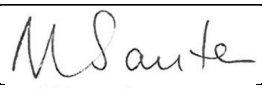
1.8 HEAP revisions

Protocol Version	Updated HEAP version No	Section number changed	Description of and reason for change	, Individual making the change	, Individual making the change

1.9 Roles and responsibilities

This HEAP was written by the senior health economist (TS), who is a co-applicant on the grant. TS has inputted into the design of the wider trial as well as taken the lead on designing the economic evaluation component. TS will be overseeing the analysis and writing up the economic evaluation. The trial health economists (HC and MO) will undertake the analysis under supervision and review the write-up for accuracy.

1.10 Signature(s):

The following people have reviewed the Health Economic Analysis Plan and are in agreement with its contents			
Name	**Role**	**Signature**	**Date**
Professor Tracey Sach	Lead Health Economist		30 Sept 2022
Holly Clarke	Trial Health Economist		30 Sept 2022
Mary Onoja	Trial Health Economist		30 Sept 2022
Professor Beth Stuart	Senior Clinical Trial Statistician		30 Sept 2022
Professor Miriam Santer	Chief Investigator		30 Sept 2022
Professor Kim Thomas	Chief Investigator		30 Sept 2022

1.11 Abbreviations/glossary of terms/definitions

List any abbreviations and/or acronyms used within the HEAP alongside their meanings/definitions

Abbreviation	Meaning
CEA	Cost Effectiveness Analysis
CEAC	Cost Effectiveness Acceptability Curve
CHU-9D	Child Health Utility - Nine Dimensions
CUA	Cost Utility Analysis
EQ-5D-5L	EuroQol Five Dimensions Five Levels
ICER	Incremental Cost Effectiveness Ratio
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
QALY	Quality-Adjusted Life Year
QOL	Quality Of Life
SAE	Serious Adverse Event

SECTION 2: TRIAL INTRODUCTION AND BACKGROUND

2.1 Trial background and rationale

Eczema is a common skin disorder causing itchy skin and dryness. Eczema leads to poor quality of life (sore or bleeding skin, itching and poor sleep). Most people with eczema benefit from two treatments: (1) moisturisers (emollients) for dry skin, which need to be applied daily; and (2) topical corticosteroids for inflamed skin and eczema flares. Commonly, if eczema is not well-controlled it is because treatments are not used appropriately. There are many reasons why people may find it difficult to use eczema treatments: they can be time-consuming to apply; treatments may sting when first applied to inflamed skin; there are concerns about the safety of some treatments; and because people often receive conflicting or insufficient advice about how and when to use treatments.

Two online toolkits to support self-management of eczema: (1) for parents/carers of children with eczema (aged 0-12 years); and (2) for young people with eczema (aged 13-25 years) have been developed. Toolkits cover a range of topics relevant to people with eczema.

2.2 Aim(s) of the trial:

The aims of the two trials is to determine the clinical and cost-effectiveness of online interventions for eczema: trial-PC for parents/carers of children aged 0-12 with eczema (intervention-PC) and trial-YP for young people aged 13-25 with eczema (intervention-YP).

2.3 Objectives and/or research hypotheses of the trial

To determine the clinical and cost-effectiveness of digital self-care interventions compared to standard clinical care for PC and YP. This is one of five workstreams being undertaken as part of the PGfAR.

2.4 Trial population

Inclusion criteria:

Participants will be eligible for inclusion in trial-PC if:

- They are a parent / carer of a child aged 0-12 years with eczema
- Their child was identified from GP records as having eczema and has obtained a relevant prescription in the past 12 months
- Their child has a POEM score greater than 5 to include mild to severe eczema, but exclude those with very mild or inactive eczema

- They have internet access

Only 1 person per household will be able to take part in one of the trials. If a parent/carer in trial-PC has more than one child who meets the inclusion criteria they will be asked to specify one child to participate.

Participants will be eligible for inclusion in trial-YP if:

- They are aged 13-25 years with eczema
- They were identified from GP records as having eczema and have obtained a prescription for eczema treatment in the past 12 months
- They have a POEM score greater than 5 to include mild to severe eczema, but exclude those with very mild or inactive eczema to avoid floor effects
- They have internet access

Exclusion criteria:

Potential participants will be excluded from trial-YP and trial-PC if:

- They are unable to give informed consent
- They are unable to read and write English as the intervention content and outcome measures are in English
- They have taken part in another eczema study in the past 3 months
- They took part in think aloud interviews as part of ECO intervention development. Qualitative interviewees who did not view intervention materials will not be excluded.

2.5 Intervention and comparator(s)
Usual care group

Participants randomised to usual care will continue to receive their usual medical advice and prescriptions. They will not be prevented from seeking additional online support but will not be supported in doing so by the study team and will not have access to the trial online interventions during the trial. Participants allocated to the usual care group will receive access to either intervention-PC or intervention-YP (depending on which trial they are in) after the 52-week follow-up.

intervention-PC and Intervention-YP groups

Participants randomised to the intervention group will receive access to an online behavioural intervention to support eczema self-care in addition to usual eczema care, as above. The online interventions target core behaviours linked to eczema treatment use (regular use of emollients and appropriate use of topical corticosteroids), eczema irritants and triggers, scratching, and emotional management. The interventions use behavioural techniques to support eczema self-care by building on aspects like knowledge, skills, self-efficacy, social support, and addressing environmental factors such as social and physical opportunity.

Intervention-PC has been developed for parents of children aged 0 to 12 years with eczema. This intervention covers the same wide range of topics relevant to eczema, as well as sections that are specifically relevant to parents and co-management of eczema, such as transitioning to co-management, dealing with child resistance, and managing your child's eczema at nursery and school.

Intervention-YP has been developed for people aged 13 to 25 years with eczema. The intervention covers a wide range of topics that are important to people with eczema, as well as additional sections that are important particularly to this age group, such as information about finances, school / university /work, and cosmetics.

2.6 Trial design

This study includes two independent randomised controlled trials (RCTs):

1. Trial-PC: to assess the effectiveness of an online intervention (intervention-PC) in parents and carers of children with eczema aged 0-12 years

2. Trial-YP: to assess the effectiveness of an online intervention (intervention-YP) in young people with eczema aged 13-25 years

Both RCTs include an internal pilot phase and nested health economic and process evaluation studies. A minimum of 200 participants are being recruited to each trial-YP and trial-PC. All participants will be recruited via GP surgeries (recruited through the local Clinical Research Networks) in Wessex, West of England, East Midland, Thames Valley and South Midlands.

Potential participants for trial-PC and potential participants for trial-YP aged 16-25 years are sent an invitation pack containing information about the study. To take part they follow the link provided, they are asked to provide informed consent and complete initial screening and baseline measures.

Parents or carers of potential participants for trial-YP aged 13-15 years are sent a different mail pack enclosing information about the study, information about how to contact the study team and a URL to complete consent online if they are happy for their child to take part. The child is then sent an invitation pack containing information about the study and a link to go online if they would like to take part. If they follow the link, they are asked to provide assent and complete initial screening and baseline measures.

Participants are then randomised to one of two groups:
1. Usual care (with access to the online intervention after 52 weeks of follow-up)
2. Usual care plus immediate access to the online intervention

LifeGuide software will be used to collect all participant reported outcome measures and intervention usage data. Outcome measures are very similar across trial-PC and trial-YP. Table 1 in Muller et al 2021 shows the schedule of observations. Missing questionnaires (at 4, 8, 12, 24 and 52 weeks) will be followed up by phone, text or email.

The primary outcome for both trials is the difference in eczema severity between the intervention and usual care group as measured by POEM (Patient-Oriented Eczema Measure) every 4 weeks over 24 weeks (Charman et al 2013, 2004). 24 weeks has been shown in previous NIHR-funded eczema trials to be a sufficient duration to capture the chronic-relapsing nature of eczema. Loss to follow-up is likely to be greater at 52 weeks – this is particularly important for a trial in which consent and follow-up assessments are all conducted online.

POEM, a patient reported outcome that measures symptoms that are important to the patient, consists of 7 questions about the frequency of eczema symptoms over the previous week which when summed give a score from 0 (no eczema) to 28 (worst possible eczema). The secondary outcomes include:

- Difference in POEM scores captured 4-weekly over 52 weeks.
- Quality of Life measured at baseline, 24 and 52 weeks in both trials. In trial-PC, Quality of Life will be measured by proxy using the Child Health Utility - Nine Dimensions (CHU-9D) for those children aged 2 to 12 years. In trial-YP, Quality of Life will be measured using the EQ-5D-5L self-completed by the young person.
- Eczema control will be measured by RECAP (Recap for atopic eczema patients) measured at baseline, 24 and 52 weeks.
- Itch intensity measure (worst itch in last 24 hours) at baseline, 24 and 52 weeks using a numeric rating scale, is validated in adults only and will therefore be collected in trial-YP only.

At baseline we also ask about:

- Prior belief about the effectiveness of the intervention.
- Use of other websites for eczema.

Full details of the trial can be found in the published protocol (Muller et al 2021).

2.7 Trial start and end dates

Trial recruitment started on the 8th December 2019 for trial-PC and finished recruitment on

26th November 2020 (n=340). The dates for the trial-YP were 5th December 2019 and 29th November 2020 respectively (n=337). The follow up period will run until the end of November 2021.

SECTION 3: ECONOMIC APPROACH/OVERVIEW

3.1 Aim(s) of economic evaluation

The aim of the two economic evaluations is to determine the cost-effectiveness of the intervention-PC and Intervention-YP compared to usual care alone for children and young people with atopic eczema from an NHS perspective.

3.2 Objectives(s)/hypotheses of economic evaluation

The primary objective of the two cost utility analyses is to estimate the cost-effectiveness of i) Intervention-PC compared to usual care and separately ii) Intervention-YP compared to usual care in terms of incremental cost per QALY at 12 months in the self-management of eczema using individual level data collected within the trial.

The secondary objective is to undertake a cost effectiveness analysis for each of the two trials at the end of trial follow-up at 12 months using the trial primary outcome measure Patient Oriented Eczema Measure (POEM).

This outcome will be used to estimate the incremental cost per 2-point change on the POEM. It should be noted that the decision makers willingness to pay to for a 2-point change improvement on the POEM is unknown.

3.3 Overview of economic analysis

The within-trial economic analyses (12-month time frame) will use individual participant level data from the ECO trials. For each trial a separate cost utility analysis will be undertaken from an NHS and PSS perspective as the base case analysis. Since the clinical outcome measure is the same in both trials secondary analyses will include cost-effectiveness analysis for participants of all ages combined (trial PC and trial YP) analysed together and separately using the primary clinical outcome POEM.

The evaluation will adhere to published guidelines for the economic evaluation of health care interventions as appropriate (Drummond et al 2015; Ramsey et al 2015; Glick et al 2014; Husereau, D., 2013; NICE 2013).

3.4 Jurisdiction

The trials are being conducted in the UK which has a national health service (NHS), providing publicly funded healthcare which is largely free of charge at the point of use.

3.5 Perspective(s)

Primarily, the analysis will take an NHS perspective. This is in keeping with the NICE reference case (NICE 2013) since the clinical team felt that Personal Social Services (PSS) were unlikely to be relevant to those with childhood eczema.

3.6 Time horizon

The base case economic analysis will compare the costs and outcomes over 12 months.

SECTION 4: ECONOMIC DATA COLLECTION AND MANAGEMENT

4.1 Statistical software used for HE analysis

Stata MP version 17

4.2 Identification of resources

In keeping with the chosen perspective the base case will capture the likely ongoing intervention costs to the NHS and the participant's wider use of the NHS (including health care visits and prescriptions). Only those resources that will be incurred if the interventions are rolled out will be included in the analysis. Costs associated exclusively with research activities related to the trial will not be included in the analysis.

4.3 Measurement of resource use data

Resource use for the intervention phase will be collected via medical notes review at GP practices for medication use and service use (primary and secondary care) for the entire 52-week period of study plus a 3-month pre-baseline period in order to be able to adjust for baseline costs in adjusted analyses.

4.4 Valuation of resource use data

Intervention development resources/costs are the costs required to design and set up the intervention. They include the costs of consulting researchers, professionals, clinicians, patient representatives to develop the interventions, time to create content e.g. audio-visual features, and the programming costs. Other costs incurred are registering a domain name, licensing software used for the intervention and hardware purchases. In line with other economic evaluations these sunk costs (costs that do not recur if the intervention is rolled out) are not going to be included in the economic evaluations because the interventions were developed using research funding and so do not represent an NHS/PSS cost. Instead these prior sunk costs will be estimated and reported separately as recommended (Tate et al, 2009). However, the maintenance costs likely to be incurred to keep the intervention running will be included in the analysis. This will include email support, software updates, hardware maintenance, service provider costs, Webhosting/Domain name costs, security, activities to improve uptake. The intervention

costs are mainly fixed costs, that is costs which are the same no matter how many participants use the intervention. With the exception of activities to promote uptake which may vary. The maintenance costs will therefore be apportioned to participants equally although we acknowledge that in reality if rolled out the per participant maintenance cost is likely to be very small given the expected number of intervention users. Sensitivity analyses will explore how many participants need to use the intervention to ensure it is cost-effective.

Unit Costs:

All resource use relevant to the NHS perspective will be valued using UK unit costs (in £Sterling) from the most current price year available at the time of the analysis. Unit costs will be identified from published sources, such as Unit Costs of Health and Social Care (Jones and Burns, 2021), Prescription Cost Analysis (NHS Business Services Authority, 2021) and NHS Reference Costs (NHS England, 2021). A table of unit costs, together with their sources will be produced.

Total Costs:

The cost of all reported resource use will be calculated for each participant. These figures will then be summed for each participant, giving a total cost over the 12-month period. For each of the trial group, a mean cost per participant will be calculated.

4.5 Identification of outcome(s)

Quality of Life:

Quality Adjusted Life Years (QALYs) will be estimated using utility scores obtained using the EQ-5D-5L instrument for the analysis of the trial-YP and the CHU-9D in the analysis of the trial-PC. The CHU-9D will be completed by parental/guardian proxy for all participants aged 2-12 years only in the Trial-PC due to the fact that in this trial it is parents whom consent to participate and the intervention itself is aimed at the parent/guardian as a means to improve their child's management of their eczema.

Patient-Oriented Eczema Measure (POEM):

The primary outcome in both trials is the difference in eczema severity between the intervention and usual care group as measured by POEM (Patient-Oriented Eczema Measure). POEM consists of 7 questions about the frequency of eczema symptoms over the previous week which when summed give a score from 0 (no eczema) to 28 (worst possible eczema). A secondary cost effectiveness analysis will be undertaken using change from baseline in the POEM.

4.6 Measurement of outcome(s)

Utility measurements will be collected at baseline, 24 and 52 weeks via online questionnaire.

4.7 Valuation of outcome(s)

In the cost utility analysis, the responses received on the quality-of-life instruments will be converted to utility scores using UK preference weights in line with current recommendations (NICE 2013; Van Hout et al 2012). Following this, the utility values will be used to calculate the number of quality adjusted life years (QALYs) generated over the trial treatment period of 12 months, using both linear interpolation and area under the curve analysis with and without baseline adjustment (Manca, 2005). Separate cost-utility analysis will report the incremental cost per QALY based on the EQ-5D-5L responses (for trial-YP) and the CHU-9D responses (for trial-PC).

SECTION 5: ECONOMIC DATA ANALYSIS

5.1 Analysis population

The economic base-case analysis will be performed on the full analysis set, that is a complete case analysis. In line with the statistical analysis plan we will not impute data missing in the base case analysis. The impact of missing data will be explored in sensitivity analyses.

5.2 Timing of analyses

The base case analysis will be a within-trial analysis, taking a 12-month time horizon.

5.3 Discount rates for costs and benefits

As the time horizon being evaluated is 12 months in all analyses, costs and benefits will not be discounted.

5.4 Cost-effectiveness threshold(s)

The main base case analysis is a cost utility analysis for each trial separately, combining estimated mean costs and QALYs for each intervention group in an incremental analysis to compare with a decision makers willingness to pay (ʎ) per QALY. The reported economic analysis will use a cost-effectiveness threshold (ʎ) of £30,000 (£20,000) per QALY (NICE 2013).

The secondary analysis will be a cost effectiveness analysis for each trial and both trials combined, where decision makers will need to make a value judgement about the acceptable willingness to pay value of a per 2-point change on POEM.

5.5 Statistical decision rule(s)
As appropriate, all statistical tests will be two-sided with the statistical significance level set at 5%.

5.6 Analysis of resource Use
Mean (sd) resource use per participant will be estimated for each randomised group. Mean difference (95% CI) in mean resource use between groups (online intervention compared to usual care alone) will be presented.

5.7 Analysis of costs
Mean (sd) cost per participant will be estimated for each randomised group. Mean difference (95% CI) in cost per participant between groups (online intervention compared to usual care alone) will be estimated.

5.8 Analysis of outcomes
The primary outcome for the economic evaluations will be quality-adjusted life years (QALYs) of participants over 12 months. Mean (sd) utility and mean (sd) QALYS per participant per randomised group will be presented and mean difference (95% CI) in utility and QALYs between arms (online intervention compared to usual care alone) will be estimated.

Mean (sd) change in POEM score between baseline and 12 months per participant per randomised group will be estimated along with the mean difference (95% CI) in the change in POEM score between groups (online intervention compared to usual care alone). The secondary outcome for the economic evaluation will be per 2-point change on the POEM.

5.9 Data cleaning for analysis

Before carrying out analyses, plausibility checks will be performed on the relevant data fields, such as resource use and reported outcome measures, such as quality of life. Where problems are identified, the health economist will contact the data manager of the trial for clarification.

5.10 Missing data
Trial data will be examined for any missing data, in particular the amount of missing data and the likely mechanism of missingness. If appropriate, sensitivity analysis will be undertaken using a multiple imputation model. Data will be imputed using a chained equations approach with a model including outcome variables, baseline utility scores,

randomisation group, recruitment region, age, gender, ethnicity, prior belief in the intervention, education (or carers education in the trial-PC), and prior use of a website or app for information about eczema. Comparing different approaches will enable us to assess the impact the results and conclusions reached.

5.11 Analysis of cost-effectiveness

If no clinical benefit is found for the online intervention then costs and outcomes will not be combined in an economic evaluation for that trial. Instead, 5.7 and 5.8 will be presented for the benefit of future researchers working in this area whom may wish to develop an economic model for eczema.

Treating the two trials as separate analyses, if a clinical benefit is found for the online intervention then Cost and outcome data (QALYs in the base case cost utility analysis and change in POEM score in the secondary cost effectiveness analysis) will be combined for the trial to estimate an incremental cost-effectiveness ratio (ICER) from the NHS perspective comparing the online intervention to usual care alone. A regression-based approach (such as seemingly unrelated regression equations if appropriate) (Willan et al 2004) will be used in the base case cost utility and secondary cost effectiveness analyses.

Both unadjusted and adjusted results will be presented. The adjusted analyses will be the main base case analysis and will adjust for baseline POEM/utility/cost (as appropriate), recruitment region and the following covariates which have been pre-specified in the statistical analysis plan as possible confounders: age, gender, ethnicity, prior belief in the intervention, education (or carer education for children) and prior use of a website or app for information or advice about the child/young person's eczema.

We will also run a secondary cost effectiveness analysis combining data from both trials as POEM is a common outcome measure unlike utility which was captured using a different instrument in each trial to reflect age of participants.

5.12 Sampling uncertainty

If costs and outcomes are skewed, non-parametric bootstrapping will be used to determine the level of sampling uncertainty surrounding the mean ICERs by generating 10,000 estimates of incremental costs and benefits. These estimates will be plotted on a cost-effectiveness plane. In addition, Cost-Effectiveness Acceptability Curves will be produced, which will show the probability that each of the intervention arms is cost effective at different values of willingness to pay.

5.13 Subgroup analysis/Analysis of heterogeneity

There are no plans to undertake subgroup analysis in the economic study. However, although the clinical analysis is not powered to look at subgroups, the statistical analysis plan (see section 8 of the SAP) sets out some exploratory analyses exploring the impact of

key subgroups that could plausibly modify intervention effectiveness. Should any of these prove significant it would be possible to undertake a sub-group analysis in the cost utility analysis if the study team believe it would be informative.

5.14 Sensitivity analyses

A number of sensitivity analyses will be undertaken to explore key uncertainties around important parameters in the economic evaluation.

1. The impact of missing data will be explored by comparing base case results using a complete case analysis to multiple imputation. (See section 5.10)

2. If the intervention is found to be effective but cost-ineffective for the trial population, we will undertake a threshold analysis to explore whether the cost effectiveness result changes if the number of users of the online intervention increases as might be expected when the intervention is rolled out. The fixed costs of maintenance would effectively be spread across more participants once the intervention is rolled out.

3. Additional sensitivity analysis may be undertaken to explore uncertainties informed by the process evaluation.

SECTION 6: MODELLING AND VALUE OF INFORMATION ANALYSES

6.1 Extrapolation or Decision analytic modelling

The within-trial base case time horizon will be 12 months. If found cost-effective over this time period the intervention is likely to be more cost-effective over a longer time period such that extrapolation or modelling would not be worth undertaking as it would not change the conclusion reached. If the online intervention is found effective but not cost effective over 12 months, we will explore the value of extrapolating our results in order to see if the conclusion would change if the intervention effect lasted over a longer period.

SECTION 7: REPORTING/PUBLISHING

7.1 Reporting standards

The CHEERS reporting quality guidelines will be followed when writing up the health economic evaluation.

7.2 Reporting deviations from the HEAP

Any deviations necessary from the HEAP will be described and justified in the main study report.

SECTION 8: Appendices

Appendix 1: Example Unit cost Table

Unit Costs Table (UK£ sterling, Price Year)

Cost Item	Unit Cost (£)	Source
Intervention		
Ongoing delivery costs		
Maintenance costs		
Primary Care		
GP		
Practice Nurse		
Pharmacist		
Secondary Care		
Hospital Doctor		
Hospital Nurse		
Inpatient stay		
A&E visit		
Other		
Medication		

Appendix 2: Example mean resource use and cost tables

Example Table: Mean (Standard Deviation) Resource Use and Mean Difference in Resource Use per Patient (95% Confidence Interval) over 12 months for the Intervention arm compared to usual care arm for Trial-PC

	Online intervention (n=)		Usual Care (n=)		Mean difference
	Mean	Std dev	Mean	Std dev	(95% CI)
GP visits related to intervention (number of visits)*					
GP (number of visits)					
Practice Nurse (number of visits)					
Pharmacist (number of visits)					
Hospital Doctor (number of visits)					
Hospital Nurse (number of visits)					
A&E (number of visits)					
Inpatient stay (number of nights)					

Medication – Prescriptions items (number)					

Example table: Mean (Standard Deviation) Cost and Cost Difference (95% Confidence Interval) Per Patient over the 24-week treatment period for the Intervention arm compared to usual care arm (in 2021 UK pounds sterling) for Trial-PC

	Online intervention (n=)		**Usual Care (n=)**		**Mean difference**
	Mean	**Std dev**	**Mean**	**Std dev**	**(95% CI) £'s**
Intervention					
Intervention maintenance and ongoing delivery costs					
Primary Care and Community					
GP visits					
Practice Nurse					
Pharmacist					
Secondary Care					
Hospital Doctor					
Hospital Nurse					
A&E					
Therapist					
Other					
Medication					
Total health care costs					

Example Table: Mean (Standard Deviation) Resource Use and Mean Difference in Resource Use per Patient (95% Confidence Interval) over 12 months for the Intervention arm compared to usual care arm for Trial-YP

	Online intervention (n=)		**Usual Care (n=)**		**Mean difference**
	Mean	**Std dev**	**Mean**	**Std dev**	**(95% CI)**
GP visits related to intervention (number of visits)*					
GP (number of visits)					
Practice Nurse (number of visits)					
Pharmacist (number of visits)					
Hospital Doctor (number of visits)					

Hospital Nurse (number of visits)					
A&E (number of visits)					
Inpatient stay (number of nights)					
Medication – Prescriptions items (number)					

Example table: Mean (Standard Deviation) Cost and Cost Difference (95% Confidence Interval) Per Patient over the 24-week treatment period for the Intervention arm compared to usual care arm (in 2021 UK pounds sterling) for Trial-YP

	Online intervention (n=)		**Usual Care (n=)**		**Mean difference**
	Mean	**Std dev**	**Mean**	**Std dev**	**(95% CI) £'s**
Intervention					
Intervention maintenance and ongoing delivery costs					
Primary Care and Community					
GP visits					
Practice Nurse					
Pharmacist					
Secondary Care					
Hospital Doctor					
Hospital Nurse					
A&E					
Therapist					
Other					
Medication					
Total health care costs					

Appendix 3: Example outcome tables

Utility and QALYs for base case analysis for Trial-PC

	Online intervention (n=)		**Usual care (n=)**		**Mean difference**
	Mean	**Std dev**	**Mean**	**Std dev**	**(95% CI)**
Trial-PC					
CHU-9D Baseline					
CHU-9D 24 weeks					
CHU-9D 52 weeks					
QALYs at 52 weeks					

Utility and QALYs for base case analysis for Trial-YP

	Online intervention (n=)		Usual care (n=)		Mean difference
	Mean	**Std dev**	**Mean**	**Std dev**	**(95% CI)**
Trial-YP					
EQ-5D-5L Baseline					
EQ-5D-5L 24 weeks					
EQ-5D-5L 52 weeks					
QALYs at 52 weeks					

POEM for secondary cost effectiveness analysis for Trial-PC

	ECO intervention (N=)		Standard care (n=)		Mean difference (95% CI)
	Mean	**Std dev (n)**	**Mean**	**Std dev (n)**	
Baseline POEM					
52 weeks POEM					
Change in POEM at 52 weeks					

POEM for secondary cost effectiveness analysis for Trial-YP

	ECO intervention (N=)		Standard care (n=)		Mean difference (95% CI)
	Mean	**Std dev (n)**	**Mean**	**Std dev (n)**	
Baseline POEM					
52 weeks POEM					
Change in POEM at 52 weeks					

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