Health Economic Analysis Plan for the TREAT trial

Content:

SECTION 1: ADMINISTRATIVE INFORMATION

1.1 Title:

Health Economic Analysis Plan for the TREAT (TREatment of Severe Atopic Eczema Trial) study: A randomised controlled trial assessing the effectiveness, safety and cost-effectiveness of methotrexate versus ciclosporin in the treatment of severe atopic eczema in children.

1.2 Trial registration number:

Trial Registration Number: ISRCTN15837754 (registered 09/03/2016)

1.3 Source of funding:

The main TREAT trial is funded by the MRC-NIHR Efficacy and Mechanism Evaluation (EME) Board of the Department of Health (grant code 13/50) whilst the economic evaluation for TREAT is funded by a grant from the NIHR Research for Patient Benefit Programme (grant code PB-PG-1215-20019).

The TREAT Trial is also supported by the South London NIHR Comprehensive Research Network (CRN) and the core facilities of the NIHR Biomedical Research Centre at Guy's & St Thomas' NHS Foundation Trust and King's College London.

1.4 Purpose of HEAP:

The purpose of this HEAP is to describe the methods, analysis and reporting procedure for the economic evaluation undertaken alongside the TREAT trial. It will be finalised and reviewed prior to the trial database being locked. This analysis plan is designed to be consistent with and read in conjunction with the study protocol and associated statistical analysis plan (SAP).

1.5 Trial protocol version

This document has been written based on information contained in the trial protocol version 3.0, dated 23/10/2015.

1.6 Trial statistical analysis plan (SAP) version

SAP version: 3.0, Date: 19/10/2015.

1.7 Trial HEAP version:

HEAP version: 1.0, Date: 25/3/2021

1.8 HEAP revisions

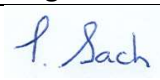
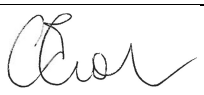
Revisions to the HEAP revision can be seen in the table below:

Protocol version	Updated HEAP version No.	Section number changed	Description of and reason for change	Name of individual making change	Date changed

1.9 Roles and responsibilities

The HEAP was prepared by Professor Tracey Sach (Lead health economist) with contributions from Dr Adam Wagner (trial health economist until date 1st October 2019) and Dr Charlotte Davies (trial health economist after 1st October 2019 and until 28th May 2021). In the absence of a trial health economist the senior lead health economist (Prof Sach) is responsible for conducting the analysis and reporting the economic evaluation in accordance with the HEAP.

1.10 Signatures and date of persons writing and approving the TREAT HEAP

The following people have reviewed the Health Economic Analysis Plan and are in agreement with the contents			
Name	**Role**	**Signature**	**Date**
Prof Tracey Sach	Author, Lead Health Economist		11/11/22
Prof Carsten Flohr	Chief Investigator		11/11/22

1.11 Abbreviations

Please see the list below for all abbreviations and/or acronyms used within the HEAP alongside their definitions.

Acronym	Definition
(S)AE	(Serious) Adverse Event
CEA	Cost effectiveness analysis
CEAC	Cost Effectiveness Acceptability Curve
CHU-9D	Child Health Utility – Nine Dimensions
CRF	Case Report Form
CUA	Cost Utility Analysis
CyA	Ciclosporin

EASI	Eczema Area and Severity Index
EME	Efficacy and Mechanism Evaluation programme
EVPI	Expected Value of Perfect Information
HEAP	Health Economics Analysis Plan
ICER	Incremental Cost Effectiveness Ration
MTX	Methotrexate
NICE	National Institute for Health and Care Excellence
o-SCORAD	Objective Scoring Atopic Dermatitis
QALYs	Quality-Adjusted Life Years
SAP	Statistical Analysis Plan
VOI	Value of Information

SECTION 2: TRIAL INTRODUCTION AND BACKGROUND

2.1 Trial background and rationale

Atopic eczema is a chronic, pruritic inflammatory skin disease affecting around 20% of UK children, 16% of whom have moderate-to-severe disease. Around 2% of children require intervention beyond the more typical use of emollients and anti-inflammatory treatments. Most physicians in Europe choose to treat these patients with Ciclosporin (CyA) though current treatment options are limited and there is no clear consensus on which treatment is the most appropriate. The European TREatment of severe Atopic eczema in children Taskforce survey of 765 consultant dermatologists and paediatricians from eight European countries was conducted to establish which systemic treatment options are available. The survey showed that the first-choice systemic immunosuppressive agent was CyA with 43%, compared with the U.K. where 39% use azathioprine (AZA) and 35% use CyA. MTX was only the third most commonly used systemic treatment in the survey in the U.K. However, MTX is increasingly being used as a first-line systemic agent, giving rise to the need for a randomised controlled trial to test whether the different treatments provide (dis)similar outcomes in terms of disease severity. Both drugs have previously been shown to reduce atopic eczema severity and improve quality of life [1].

TREAT is a Phase III, multi-centre, randomised, superiority, observer-blind trial assessing the safety and cost-effectiveness of MTX versus CyA in the treatment of severe atopic eczema in children over the 60 weeks follow-up (including the 36 week treatment phase). Details of the trial methods have been published [2], a summary is provided here.

2.2 Aim(s) of the trial

The TREAT trial aims to evaluate the treatment efficacy and safety of oral MTX versus CyA in the treatment of severe child atopic eczema during the 36 weeks of treatment and to compare disease control post-treatment cessation for a further 24 weeks. It also includes a mechanistic component to examine the effect of MTX and CyA on systemic and cutaneous markers of inflammation during and up to 6 months after treatment.

2.3 Objectives and/or research hypotheses of the trial

The study has two co-primary objectives.

1. To assess the change in atopic eczema severity between baseline and 12 weeks of treatment in the two treatment arms, and

2. To examine disease remission during the 24 weeks after treatment cessation in the MTX versus CyA groups.

A range of secondary objectives have been set out as follows:

(i) To examine atopic eczema severity using the EASI, IGA, o-SCORAD & POEM scores between 0 and 12, 36, 48, 60 weeks and using the o-SCORAD at 36, 48 and 60 weeks

(ii) To compare the number of flares in each study arm during the trial period as well as the proportion of children who re-flared during the 24 weeks after treatment cessation

(iii) To study the impact on quality of life as measured by a change in CDLQI/IDQOL, DFI and CHU-9D scores between 0, 12, 36, 48 and 60 weeks

(iv) To determine the proportion of participants achieving a 50% improvement in the o-SCORAD index at 12, 36, 48, and 60 weeks

(vi) To capture the proportion of participants who withdraw from treatment because of adverse events

(vii) To assess the cost-effectiveness of CyA vs MTX

(viii) To study the immuno-metabolic effects of MTX and CyA, especially in relation to markers of glycolytic activation and T cell cytokine signature, at baseline, during treatment and up to 24 weeks after completion of treatment.

(IX) To compare the drug side effects/toxicity profiles of both MTX and CyA,

(X) To examine the association between MTX polyglutamate and CyA trough levels and reduction in atopic eczema severity

(XI)To study the impact of FLG carriage (yes/no) on reduction in atopic eczema severity

2.4 Trial population

102 children aged 2-16 years with severe atopic eczema and inadequately responding to moderate (face) and potent (body) topical treatment will form the participant population.

To be eligible for the trial children must be aged between 2 and 16 years and have severe recalcitrant atopic eczema, defined as an o-SCORAD≥40 despite regular use of potent topical anti-inflammatory treatment. Children should live within travelling distance of a recruiting centre and have a presence of eczema confirmed in accordance with the UK refinement of

the Hanifin & Rajka criteria [3]. Children should not have received any systemic immuno-suppressive therapy previously (oral corticosteroids for acute flare management would not result in exclusion).

Children will not be eligible for the trial if they have a serious underlying condition (such as immune compromise or autoimmune disease); are pregnant/lactating; have insufficient parental ability to understand or consent to the trial intervention; are in receipt of either systemic corticosteroids for less than 1 month or UV therapy for less than 6 months prior to participation.

2.5 Intervention and comparator

2.5.1 Intervention

The intervention group will be given MTX as given by the following formula below taken from the trial protocol:

Arm	IMPs	Formulations
MTX	Methotrexate	Brand: any brand with marketing authorisation within EEA Tablets: 2.5mg
	Methotrexate	Brand: any brand with marketing authorisation within EEA Injection: 50mg/ml prefilled pen

MTX should be prepared and administered with the dosage detailed below:

<table>
<tr><th></th><th>Methotrexate tablets / subcutaneous injection</th></tr>
<tr><td>Dose</td><td>Initial dose of 0.1mg/kg/week, then 0.4mg/kg/week (maximum 25mg/week)
Where applicable, doses should be rounded to the nearest whole tablet as follows:
<table>
<tr><th>Weight band</th><th>0.1mg/kg test dose</th><th>0.4mg/kg dose</th></tr>
<tr><td>22 to <29 kg</td><td>2.5mg</td><td>10mg</td></tr>
<tr><td>29 to <36 kg</td><td>2.5mg</td><td>12.5mg</td></tr>
<tr><td>36 to <43 kg</td><td>5mg</td><td>15mg</td></tr>
<tr><td>43 to <50 kg</td><td>5mg</td><td>17.5mg</td></tr>
<tr><td>50 to <57 kg</td><td>5mg</td><td>20mg</td></tr>
<tr><td>57 to <63kg</td><td>5mg</td><td>22.5mg</td></tr>
<tr><td>63kg +</td><td>7.5mg</td><td>25mg</td></tr>
<tr><td></td><td></td><td></td></tr>
</table></td></tr>
<tr><td>Frequency</td><td>Weekly</td></tr>
<tr><td>Duration</td><td>36 weeks</td></tr>
<tr><td>Route</td><td>Oral or subcutaneous</td></tr>
<tr><td>Formulation</td><td>Decision about formulation used to be made by local clinician, taking into account patient’s preference</td></tr>
</table>

Note	The methotrexate dosing regimen reflects current clinical practice across European paediatric dermatology departments (based on TREAT survey among >300 paediatric dermatologists from 8 European countries)[1]. It is also in keeping with the British National Formulary guidance for the treatment of severe cutaneous inflammatory disease in children [2], and that of the American Academy of Dermatology for severe paediatric eczema [3]. It is acknowledged that extra precaution is necessary when prescribing and dispensing MTX and the following additional measures as listed below should be implemented for this trial in line with standard clinical care: - The child and their parents/carers must be carefully advised of the dose and frequency and the reason for taking MTX and folic acid at each visit. - Only the 2.5mg strength of the MTX tablet will be prescribed and dispensed. - The prescription and the dispensing label will clearly show the dose and frequency of MTX administration. - The child and their parents/carers will be provided with a MTX drug monitoring booklet which will provide additional supporting information on dose, frequency and adverse effects monitoring.

Patients will remain on the full treatment dose (0.4mg/kg/week for MTX – maximum dose of 25mg/week) for 8 weeks. After that, modifications to dose are permitted and will depend upon treatment response (maximum dose of 25mg/week). A dose increase is acceptable for growth (at same dose/kg as at trial entry).

Where there are clinical reasons indicating a need for MTX treatment to be suspended this may happen. However, only for up to a maximum cumulative period of 4 weeks throughout the duration of the protocol treatment phase. Where intermittent or continuous suspension of methotrexate treatment for a cumulative period longer than 4 weeks is required by a patient this will be considered a treatment failure and trial treatment should discontinue.

2.5.2 Comparator

The control arm will be given CyA as given by the following approved formula taken from the trial protocol:

Arm	IMP	Formulation
CyA	Ciclosporin	Brand: Neoral® Capsules: 10mg, 25mg, 50mg, 100mg

CyA capsules should be prepared and administered with the dosage detailed below:

	Ciclosporin capsules - Neoral® brand only
Dose	2mg/kg (total: 4mg/kg/day) (rounded to the nearest whole capsule where applicable)
Frequency	Twice daily
Duration	36 weeks
Route	Oral
Notes	Advise participants to avoid grapefruit juice

Patients will remain on the full treatment dose (4mg/kg/day for CyA) for 8 weeks. After which time the dose may increase to a maximum of 5mg/kg/day or decrease according to the treatment response.

Where there are clinical reasons indicating a need for CyA treatment to be suspended this may happen. However, only for up to a maximum cumulative period of 4 weeks throughout the duration of the protocol treatment phase. Where intermittent or continuous suspension of CyA treatment for a cumulative period longer than 4 weeks is required by a patient this will be considered a treatment failure and trial treatment should discontinue.

CyA blood levels will be occasionally monitored where Neoral is co-administered with medicines that are known to interact with CyA or where the patient is not responding to the treatment. The local investigator will assess this on a per patient basis and implement where deemed clinically appropriate.

2.6 Trial design

The TREAT study is a phase III, multi-centre parallel group, assessor-masked pragmatic randomised trial comparing MTX and CyA. Treatment duration is for 36 weeks and participants will be followed up for a further 24 weeks following treatment cessation. Participants will be randomised applying a ratio of 1:1. A total of 102 patients from 5 secondary care centres will be recruited into the trial. Study sites are in 13 secondary and tertiary care paediatric dermatology departments across the UK and Ireland.

2.7 Trial start and end dates

Recruitment started in May 2016 and concluded in February 2019. The follow up period concluded in May 2020.

SECTION 3: ECONOMIC APPROACH/OVERVIEW

3.1 Aim(s) of economic evaluation

The aim of this economic evaluation is to estimate the cost-effectiveness of MTX compared to CyA in children with severe atopic eczema from an NHS perspective over a 60 week time horizon in order to assess which treatment represents best value for money for NHS provision.

3.2 Objectives of economic evaluation

The four economic objectives are as follows:

(Objective 1) To measure resource use and estimate costs for children with severe atopic eczema in the MTX arm compared to the CyA arm.

(Objective 2) To estimate the Quality-Adjusted Life Years (QALYs) in children with severe atopic eczema in the MTX arm compared to the CyA arm.

(Objective 3) To undertake a cost-effectiveness and cost-utility analysis to assess which of the two treatment options (MTX versus CyA) for children with severe atopic eczema would represent best value for money for provision by the UK NHS.

(Objective 4) To estimate the level of uncertainty associated with the decision about which treatment to provide.

3.3 Overview of economic analysis

The within-trial economic analysis will be performed using individual patient level data from the TREAT trial. The primary analytical approach will take the form a cost-utility analysis, with secondary analysis taking a cost-effectiveness analysis approach. Using trial data, the mean incremental cost and mean incremental effect of MTX compared to CyA will be estimated. Separate mean incremental effects will be estimated for the CHU-9D (QALY gain), change in o-SCORAD and flare number. Adjusted analyses will use a regression-based approach (for instance seemingly-unrelated regression equations if assumptions are met, [4]) to estimate incremental costs and QALYs.

The evaluation will adhere to published guidelines for the economic evaluation of health care interventions as appropriate [5-9].

3.4 Jurisdiction

The trial is largely conducted in the UK, the one exception being the Dublin centre in Ireland. In the UK the NHS is publicly funded and provides health care largely free of charge at the point of use. In Ireland, although a large percentage of health care funding is via the public system individuals are often required to subsidise certain types of care at the point of use.

3.5 Perspective(s)

Since the funder of the research is primarily interested in a UK NHS perspective, the economic evaluation will be from an NHS and Personal social services (PSS) perspective. The process of care for the drugs being considered is not dissimilar between the UK and Ireland, therefore participants data from the Irish centre will be included in the analysis but costed from a UK perspective. Data on time off work for parents/carers and school for the children will be presented separately.

3.6 Time horizon

The primary economic analysis will compare the costs and outcomes of each arm over 60 weeks.

SECTION 4: ECONOMIC DATA COLLECTION AND MANAGEMENT

4.1 Statistical software used for HE analysis

Excel will be used for exploratory analysis and Stata 17 for the main analysis.

4.2 Identification of resources

In accordance with NICE [8] guidance, costs will be estimated from the perspective of the NHS. The clinical team did not feel this group of patients were likely to incur any Personal Social Services (PSS) as a result of their eczema. We will monitor levels of resource use associated with both interventions (including drug costs, monitoring costs and adverse event costs over the 36 weeks treatment period) alongside other potentially eczema-related NHS and PSS resource items, including primary care visits, prescriptions, and other health care contacts. Separately, we will record the time-off work parents take because of their child's eczema and children's time away from school.

4.3 Measurement of resource use data

Use of medications is being monitored by the clinical trials unit. Wider NHS disease specific resource use is being recorded via questions in study diaries at 4, 8, 12, 20, 28, 36, 48 and 60 weeks. These will be administered either by the trial research nurses at each recruitment site or via postal questionnaires which will be entered by the central research team at the University of Liverpool. In case of poor completion rates for the resource use data, consent will be sought to contact participants GP practices in order to collect this data.

4.4 Valuation of resource use data

The cost of the medications will be estimated using data collected by the trial research nurse and costed using the published unit costs for MTX and CyA in the Prescription Cost Analysis [10].

Unit Costs:

Wider disease specific 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 Prescription Cost Analysis [10], Unit Costs of Health and Social Care [11] and NHS Reference Costs [12]. A table of unit costs, together with their sources will be produced. Time-off work parents take because of their child's eczema will be costed using the human capital approach using published average wages [13].

Total Costs:

The cost of all reported resource use (relevant to an NHS perspective) will be calculated for each participant. A mean overall cost per participant by study group 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 Child Health Utility Nine Dimension (CHU-9D). The CHU-9D is a generic preference-based measure of health-related quality of life instrument that asks how a child is today on nine questions (worries, sad, pain, tired, annoyed, schoolwork/ homework, sleep, daily routine, activities) each with five response levels (ranging from no difficulty through to a lot or cannot do). Additional guidance given to us by the developer of the CHU-9D will be used. This guidance provides extra wording to help parents of younger children understand how to answer questions for a child of pre-school age. Utility ranges from 0.33 (worst health-related quality of life) through to 1 (best health-related quality of life) [14,15]. The CHU-9D will be completed by parental/guardian proxy for all participants aged 2-7 years only.

o-SCORAD

The Objective Scoring Atopic Dermatitis (o-SCORAD) measure is one of the co-primary outcomes in the TREAT trial, where the study seeks to detect a difference of 8 points. O-SCORAD is one of only three validated severity outcome measures for eczema. It measures the extent and intensity of eczema and the score can range from 0 to 83 (where mild 0–14, moderate 15–39, severe 40–83 [16]).

Flares

The number of flares each participant experiences across the 60 weeks will be recorded.

4.6 Measurement of outcomes

Utility measurements will be collected in person or by paper-based questionnaires at baseline, 12, 36, 48 and 60 weeks post study initiation.

4.7 Valuation of outcomes

In the base case cost utility analysis, the responses received on the quality-of-life instrument (CHU-9D) will be converted to utility scores using the valuation set published by Stevens [17]. Following this, the utility values will be used to calculate the number of quality adjusted life years (QALYs) generated over the trial period of 60 weeks, using both linear interpolation and area under the curve analysis with and without baseline adjustment [18].

Secondary cost-effectiveness analyses will be undertaken where the outcome is either change in eczema severity measured by the change in the o-SCORAD between baseline and 60 weeks or by the number of reflares.

SECTION 5: ECONOMIC DATA ANALYSIS

5.1 Analysis population

The economic base-case analysis will be undertaken using a chained-equations multiple imputation model [18] so that all 102 children are included in the analysis.

5.2 Timing of analyses

The base case analysis will be a within-trial analysis, taking a 60 week time horizon.

5.3 Discount rates for costs and benefits

If the data permits, costs and benefits will be discounted between weeks 53 and 60 reflecting the study time horizon. We will use the recommended discount rates at the time of analysis, these are currently 3.5% for both costs and benefits [8].

5.4 Cost-effectiveness threshold(s)

The main base case analysis is a cost utility analysis to estimate both the mean incremental cost and mean incremental effect (in terms of QALYs) of MTX compared to CyA. The reported economic analysis will use a cost-effectiveness threshold (ʎ) of £30,000 (£20,000) per QALY [8].

The secondary analysis will be a cost-effectiveness analysis on the change in o-SCORAD and number of flares.

5.5 Statistical decision rule(s)

As appropriate, all statistical tests will be two-sided, and the statistical significance level will be 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 resource use per participant between groups (MTX vs CyA) 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 (MTX vs CyA) will be estimated. This Analysis will fulfil objective 1 in Section 3.2.

5.8 Analysis of outcomes

The primary outcome for the economic evaluation will be the CHU-9D [14, 15, 17] where responses will be requested at baseline, 12, 36, 48 and 60 weeks from parents for children under 7 years and from young people directly if aged ≥7 at time of recruitment. The utility score from the CHU-9D will be used to estimate QALYs for the trial period using linear interpolation and area under the curve analysis adjusting for baseline [18]. 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 groups (MTX vs CyA) will be estimated.

The secondary outcomes will be change in eczema severity as measured using the change in o-SCORAD between baseline and 60 weeks and number of reflares will also be assessed to enable cost effectiveness analyses to be conducted. Mean (sd) change in o-SCORAD score between baseline and 60 weeks per participant per randomised group will be estimated along with the mean difference (95% CI) in the change in o-SCORAD score between groups (MTX vs CyA). Mean (sd) number of flares between baseline and 60 weeks per participant per randomised group will be estimated along with the mean difference (95% CI) in the number of flares between groups (MTX vs CyA).

This Analysis will fulfil objective 2 in Section 3.2.

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

The level of missing data will be reported and the frequency and pattern of missing data will be examined following the approach adopted by Faria et al [19] to missing data. The economic base case analysis will undertake multiple imputation.

5.11 Analysis of cost-effectiveness

Incremental cost and outcome data (QALYs in the base case cost utility analysis and change in o-SCORAD score/number of flares in the secondary cost effectiveness analyses) will be combined for the trial to estimate an incremental cost-effectiveness ratio (ICER) from the NHS perspective comparing MTX to CyA. A regression-based approach (such as seemingly

unrelated regression equations if appropriate) [4] 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 cost/utility/o-SCORAD (as appropriate), gender, age, and recruiting centre. This Analysis will fulfil objective 3 in Section 3.2.

In certain circumstances it may not be appropriate to conduct an incremental cost-utility analysis or cost-effectiveness analysis for the trial. For instance, if there is no clinical benefit or the assumptions of multiple imputation (MAR) may not hold. In this situation, section 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. However, where the assumptions of multiple imputation may hold for a subset of costs it may be possible to conduct the incremental analysis from a narrower perspective (i.e. focusing just on intervention costs).

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 (showing the probability of each treatment being cost-effective at various levels of willingness-to-pay for health benefits). 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. This Analysis will fulfil objective 4 in Section 3.2.

5.13 Subgroup analysis/Analysis of heterogeneity

No subgroup analyses are planned.

5.14 Sensitivity analyses

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 multiple imputation to a complete case analysis if appropriate. (See section 5.10)

2. If the intervention is found to be effective but not cost-effective, we will undertake a threshold analysis to explore at what drug cost the result would switch to being cost effectiveness.

SECTION 6: MODELLING AND VALUE OF INFORMATION ANALYSES

6.1 Extrapolation or Decision analytic modelling

Decision analytic modelling to extrapolate costs and outcomes beyond the period trial period will not be undertaken. The TREAT trial is longer in time frame (60 weeks) than most previous eczema trials (see http://www.greatdatabase.org.uk/GD4/Home/Index.php), even so it will not provide evidence beyond the 60 weeks with which to inform a longer term economic model. If other forms of longer-term data, such as observational data, become available then the TREAT economic evaluation may help inform future longer term modelling of the cost effectiveness of systemic medications for severe eczema in future studies.

SECTION 7: REPORTING/PUBLISHING

7.1 Reporting standards

CHEERS guidelines will be followed when reporting the health economic evaluation, in a format appropriate to stakeholders and policy makers [7].

7.2 Reporting deviations from the HEAP

Any deviation from the HEAP will be described and justified in the final report.

SECTION 8: APPENDICES AND REFERENCES

Example tables for reporting results

Table 1 Unit Costs Table (UK£ sterling, Price Year)

Cost Item	Unit Cost (£)	Source
Intervention		
Methotrexate		
Ciclosporin		
NHS Care		
GP		
Practice Nurse		
Hospital Doctor		
Hospital Nurse		
Medication		

Table 2 Mean (sd) resource use and mean (95% CI) difference in resource use over 60 weeks

Cost Item	MTX (n=)	CyA (n=)	Mean difference (95% CI)
Intervention			
Methotrexate			
Ciclosporin			
NHS Care			
GP			
Practice Nurse			
Hospital Doctor			
Hospital Nurse			
Medication			
Time off work			

Table 3 Mean (sd) cost and mean (95% CI) difference in cost over 60 weeks

Cost Item	Intervention (n=) MTX	Usual care (n=) CyA	Mean difference (95% CI)
Intervention			
Methotrexate			
Ciclosporin			
NHS Care			
GP			
Practice Nurse			
Hospital Doctor			
Hospital Nurse			
Medication			
Total NHS cost			
Time off work			

Table 4: Mean (sd) outcomes and mean (95% CI) difference in outcomes over 60 weeks

	Intervention (n=) MTX		**Usual Care (n=) CyA**		
	Mean	**Std dev**	**Mean**	**Std dev**	**Mean difference (95% CI)**
Child participants (all ages n=)					
CHU-9D baseline					
CHU-9D at 12 weeks					
CHU-9D at 36 weeks					
CHU-9D at 48 weeks					
CHU-9D at 60 weeks					
QALYs (all ages)					
Child participants (aged <7 years, proxy completed, n=)					
CHU-9D (under 7) baseline					
CHU-9D (under 7) at 12 weeks					
CHU-9D (under 7) at 36 weeks					
CHU-9D (under 7) at 48 weeks					
CHU-9D (under 7) at 60 weeks					
QALYs (aged <7)					
Child participants (aged 7 years or over, proxy completed, n=)					
CHU-9D (over 7) baseline					
CHU-9D (over 7) at 12 weeks					
CHU-9D (over 7) at 36 weeks					
CHU-9D (over 7) at 48 weeks					
CHU-9D (over 7) at 60 weeks					

QALYs (aged 7+)					
Child participants (all ages n=)					
o-SCORAD at baseline					
O_SCORAD at 60 weeks					
Child participants (all ages n=)					
Number of flares over 60 weeks					

References

[1] Proudfoot, L.E., et al., The European TREatment of severe Atopic eczema in children Taskforce (TREAT) survey. Br J Dermatol, 2013. 169(4): p. 901-9.

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