

1 **Economic evidence for the prevention and treatment of atopic eczema: a**
2 **protocol for a systematic review**

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25

26 **Abstract**

27 **Background**

28 Eczema, synonymous with atopic eczema or atopic dermatitis, is a chronic skin
29 disease that has a similar impact on health-related quality of life as other chronic
30 diseases. The proposed research aims to provide a comprehensive systematic
31 assessment of the economic evidence base available to inform economic modelling
32 and decision making on interventions to prevent and treat eczema at any stage of the
33 life course. Whilst the Global Resource of Eczema Trials (GREAT) database collects
34 together the effectiveness evidence for eczema there is currently no such systematic
35 resource on the economics of eczema. It is important to gain an overview of the current
36 state of the art of economic methods in the field of eczema in order to strengthen the
37 economic evidence base further.

38 **Methods/design**

39 The proposed study is a systematic review of the economic evidence surrounding
40 interventions for the prevention and treatment of eczema. Relevant search terms will
41 be used to search MEDLINE, EMBASE, Database of Abstracts of Reviews of Effects,
42 Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled
43 Trials, NHS Economic Evaluation Database, Health Technology Assessment,
44 Cumulative Index to Nursing and Allied Health Literature, Econ Lit, Scopus, Cost-
45 Effectiveness Analysis Registry and Web of Science in order to identify relevant
46 evidence. To be eligible for inclusion studies will be primary empirical studies
47 evaluating the cost, utility or full economic evaluation of interventions for preventing or
48 treating eczema. Two reviewers will independently assess studies for eligibility and
49 perform data abstraction. Evidence tables will be produced presenting details of study

50 characteristics, costing methods, outcome methods and quality assessment. The
51 methodological quality of studies will be assessed using accepted checklists.

52 **Discussion**

53 The systematic review is being undertaken to identify the type of economic evidence
54 available, summarise the results of the available economic evidence and critically
55 appraise the quality of economic evidence currently available to inform future
56 economic modelling and resource allocation decisions about interventions to prevent
57 or treat eczema. We aim to use the review to offer guidance about how to gather
58 economic evidence in studies of eczema and/or what further research is necessary in
59 order to inform this.

60 **Registration**

61 PROSPERO registration number: CRD42015024633

62 **Keywords:**

63 Eczema; Economics; Costs; Health-related quality of life; Cost effectiveness

64

65 **BACKGROUND**

66

67 In the UK the lifetime prevalence of eczema is estimated to be between 16% and 20%
68 making it the commonest inflammatory skin condition in children and it has been
69 increasing in “western style” environments (Williams et al. 2008, Williams 2005, Kay
70 et al 1994). In the UK, the age-sex standardised incidence and lifetime prevalence of
71 eczema has increased between 2001 and 2005 from 9.58 per 1000 to 13.58 per 1000
72 patients and 77.78 per 1000 to 115.26 per 1000 respectively (Simpson et al, 2009).
73 Up to 50% of childhood cases will experience recurrence in adulthood (Williams 2005).
74 Eczema is largely managed in primary care. Skin conditions are the commonest new

75 reason patients consult their GP (Schofield et al, 2011). Eczema has been found to
76 have a similar impact on health-related quality of life as other common childhood
77 conditions such as asthma and diabetes (Lewis-Jones, 2006). Eczema impacts quality
78 of life by causing itching, sleep loss and social stigma for the child. Families may also
79 suffer from sleep loss and time taken off work to accompany children to health
80 appointments (Paller et al, 2002). The condition is associated with atopy so children
81 with the condition are more likely to develop asthma and allergic rhinitis (Hon et al,
82 2012). It is also believed that eczema has large cost implications. For instance, in
83 1995-6 the total annual UK cost of eczema in children aged 5 years or younger was
84 estimated as £47 million (£80 per child) (Emerson et al, 2001). Looking at a broader
85 age range, the UK total annual cost was estimated to be around £465 million, of which
86 £125 million were NHS costs, £297 million costs incurred by patients and £42 million
87 by society in terms of lost productivity (price year not reported) (Herd et al, 1996).
88 These UK based estimates of the total annual UK costs of eczema are now dated, the
89 estimates were based on small samples [146 in Herd et al 1996 and 1523 in Emerson
90 et al 2001], and the range of treatments available has increased and is likely to
91 increase in the future with the addition of new biologics (Howell et al, 2015).

92

93 Despite Eczema being common there remain many unknowns about how to prevent
94 and treat the condition. The James Lind Alliance (JLA) Priority Setting Partnership
95 (PSP) on eczema illustrates this ([http://www.jla.nihr.ac.uk/priority-setting-](http://www.jla.nihr.ac.uk/priority-setting-partnerships/eczema)
96 [partnerships/eczema](http://www.jla.nihr.ac.uk/priority-setting-partnerships/eczema) and Batchelor et al, 2013). The JLA facilitates disease specific
97 PSPs that bring together patients, carers and health professionals to identify and
98 prioritise research for the treatment uncertainties of the disease of interest
99 (<http://www.jla.nihr.ac.uk/>). The eczema PSP was established in 2010 with partners

100 drawn from academic, NHS and charitable sectors and resulted in 14 treatment
101 uncertainties being prioritised (Batchelor et al., 2013).

102

103 In order to draw together the effectiveness evidence of interventions for eczema, The
104 Global Resource of Eczema Trials (GREAT) database was established (Nankervis et
105 al, 2011) and includes details of over 600 systematic reviews and randomised
106 controlled trials. It does not, however, identify or bring together the economic literature
107 on eczema and thus this review attempts to do this. There is likely to be less economic
108 evidence, compared to effectiveness data, for eczema. Indeed the English National
109 Institute of Health and Care Excellence (NICE) has only considered economic models
110 for two areas of eczema care: an educational intervention for those with eczema aged
111 under 12 (NICE, 2007) and Tacrolimus and pimecrolimus for atopic eczema (NICE,
112 2004). It is, therefore, important to identify the current state of economic evidence
113 addressing eczema in order to inform the design of future economic research in the
114 area.

115

116 The proposed systematic review will address the following four research questions:

117

118 1. What type of health economic evidence has been used in the evaluation of
119 the prevention and treatment of atopic eczema?

120

121 2. Are interventions to prevent and treat atopic eczema cost effective?

122

123 3. What is the quality of the health economic evidence for the prevention and
124 treatment of atopic eczema?

125

126 4. What are the current gaps in the existing research?

127

128 **METHODS/DESIGN**

129 **Protocol and registration**

130 The Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols
131 (PRISMA-P) statement recommendations were used to develop the methods for this
132 systematic review and will be used in reporting the results from the study (Shamseer
133 et al 2015). This protocol has been registered in the International Prospective Register
134 of Systematic Reviews (PROSPERO) CRD42015024633. Should protocol
135 amendments be necessary, these will be documented including details of the date,
136 changes made and the rationale for changes.

137

138 **Literature search**

139 The following electronic databases will be searched: MEDLINE, EMBASE, Cumulative
140 Index to Nursing and Allied Health Literature, Cochrane Central Register of Controlled
141 Trials, Database of Abstracts of Reviews of Effects, Cochrane Database of Systematic
142 Reviews, NHS Economic Evaluation Database, Econ Lit, Scopus, Health Technology
143 Assessment, Cost-Effectiveness Analysis Registry and Web of Science. Search
144 results will be downloaded to EndNote version 7 where duplicates will be identified
145 and removed.

146

147 Reference lists of potential eligible studies, reviews, guidelines or other sources will
148 be screened for additional literature. Authors of published abstracts and conference

149 proceedings will be contacted by email to establish if a full paper has since been
150 published in the grey literature.

151

152 The search strategy (with interface and coverage dates) is available in Appendix 1 to
153 this protocol.

154

155 **Eligible studies**

156 A study will be included if it reports primary data on cost and/or outcome (utility or
157 willingness to pay) data on atopic eczema. The primary interest is in full economic
158 evaluations (Cost effectiveness, cost utility, cost benefit, cost minimisation) although
159 other partial economic evidence will also be included where the study has an explicit
160 economic objective, this is likely to include cost consequence analyses, cost analyses,
161 utility assessment, or willingness to pay/accept studies. There will be no restriction on
162 the study designs used in the economic studies so, for example, economic studies
163 conducted alongside randomised controlled trials, as part of observational studies, or
164 as decision model-based analyses will be included. Nor will there be any restrictions
165 on type of setting. The search was undertaken on the 9th October 2015 so only studies
166 published before this date are included. Only full text articles published in the English
167 Language will be included, abstracts and letters will be excluded. Where two or more
168 studies appear to be reporting on the same dataset or using the same model, the most
169 comprehensive paper will be included unless each paper reports on a different aspect
170 or in relation to a different jurisdiction/population (in the case of modelling studies).

171

172 **DATA COLLECTION**

173 **Study selection**

174 Two independent reviewers will assess the titles and abstracts retrieved in the
175 literature search against our inclusion criteria. In a second stage, full-text articles for
176 those seeming to fit the criteria or where there is uncertainty about relevance will be
177 retrieved and their eligibility assessed according to criteria set out in Table 1. Where
178 disagreements occur a third reviewer will be involved.

179

180 **Data abstraction and management**

181 Data will be extracted independently by two reviewers and entered into an electronic
182 data extraction form developed in Microsoft Excel, with the third reviewer consulted in
183 case of disagreements that cannot be resolved between the two reviewers. A full list
184 of the extraction fields can be found in Table 2. The data extraction form was piloted,
185 modified (where necessary) and reviewers' responses calibrated on the basis of two
186 pre-identified studies (one modelling study and one non-model based paper). The data
187 extracted will be analysed in a narrative/descriptive manner focusing on the methods,
188 results and quality of studies included with the aim of identifying gaps in the evidence,
189 areas of strength and areas in need of methodological improvement.

190

191 If the necessary data are available, the results will be discussed as subsets for different
192 age groups (e.g. child/adult/elderly) and/or different skin disease severities and/or
193 world regions and/or health care settings.

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195 **Quality assessment and data presentation**

196 Two reviewers will independently evaluate the quality of included studies in order to
197 assess the risk of bias. Studies will be assessed using a published checklist based on
198 a modified version of the Consolidated Health Economic Evaluation Reporting

199 Standards (CHEERS) framework (Husereau et al, 2013) (see Table 3). In addition,
200 model based economic evaluations will also be assessed using the Phillips criterion
201 (Phillips et al, 2004, 2006) (see Table 4 for extraction table). Any discrepancies will be
202 discussed and resolved by a third reviewer. These evaluations will be included in any
203 publication as supplementary material.

204

205 Methodological variation between studies is likely to prevent a pooling of economic
206 data in the form of a meta-analysis and therefore, results of the studies will be
207 presented and discussed in a qualitative manner according to study type.

208

209 **DISCUSSION**

210 This systematic review will provide a comprehensive assessment of the type and
211 quality of economic research used in the evaluation of interventions to prevent and
212 treat eczema. The results of the review are likely to be written up in multiple
213 publications, one focusing on an overview of the state of the art with additional papers
214 focusing in more detail on particular methodologically aspects (for instance, the
215 methods used in modelling studies). The review will report the range of cost
216 effectiveness estimates found for interventions to prevent and treat atopic eczema,
217 which may be useful in informing clinicians and decision makers about the relative
218 value of different interventions for eczema and enable the value of eczema
219 interventions to be compared with the cost effectiveness for other interventions in other
220 disease areas. That is, it may help decision makers, on the basis of current information
221 (if sufficient), to be able to answer questions about how to allocate limited resources
222 between eczema and other disease areas and once allocated to eczema how to use
223 those limited resources efficiently to maximise outcomes from eczema care. The

224 review will also be of interest to methodologists interested in the range and quality of
225 economic studies in this clinical field. Finally this systematic review will help identify
226 gaps in the current evidence base surrounding the economics of eczema to inform
227 further research efforts in this area.

228

229 **Abbreviations**

230 CHEERS: Consolidated Health Economic Evaluation Reporting Standards; GP:
231 General Practitioner; GREAT: Global Resource for Eczema Trials; HQoL: Health-
232 related quality of life; ICER: Incremental Cost-Effectiveness Ratio; JLA: James Lind
233 Alliance; NA: Not applicable; NHS: National Health Service; NICE: National Institute
234 of Health and Care Excellence; PSP: Priority Setting Partnership; QALYs: Quality-
235 Adjusted Life Years; UK: United Kingdom.

236

237 **Competing interests**

238 The authors declare that they have no competing interests.

239

240 **Authors' contributions**

241 TS conceptualised the research plan for the proposed systematic review and wrote
242 the manuscript. EM and CM contributed to the writing of the manuscript. NL provided
243 expertise on eczema. All authors reviewed the manuscript for important intellectual
244 content and approved the final manuscript. TS is the guarantor.

245

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