# 8-year surveillance 2016 - Atopic eczema in under 12s (2007) NICE guideline CG57

# Appendix A: decision matrix

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact	
<u>Diagnosis</u>				
57 - 01 What criteria should be used	to diagnose atopic eczema in children a	nd how do they vary between ethnic grou	ıps? ( <u>1.1.1.1-1.1.1.2</u> )	
Surveillance decision This review question should not be update	d.			
4-year surveillance (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.	
Assessment of severity, psychologic	cal and psychosocial wellbeing and	quality of life		
57 - 02 What measures should be us	sed to classify the severity of atopic ecze	ma in children in the setting of clinical m	anagement? ( <u>1.2.1.1, 1.2.1.3, 1.2.1.6</u> )	
Surveillance decision This review question should not be updated.				
4-year review (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	Topic expert feedback noted an initiative for standardising outcomes in eczema which found systematic reviews indicating the Eczema Area and Severity Index (EASI) and the objective Scoring Atopic Dermatitis (SCORAD) index as extensively validated and that EASI is the	New evidence is unlikely to impact on guideline recommendations.  New evidence was identified reporting that EASI and SCORAD are extensively validated and EASI was recommended to use in clinical trials. The current guideline looked at the available evidence for EASI	

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact
		preferred core instrument to measure clinical signs in AE trials <sup>1</sup> .  A topic expert referred to the Choice of Moisturiser in Eczema Treatment (COMET) feasibility trial of emollients (moisturisers) for the treatment of children with eczema. One of the publications from COMET <sup>2</sup> reported that the Patient-Oriented Eczema Measure (POEM) was responsive to changes in eczema severity in young children with eczema. The minimal clinically importance difference of the POEM was around 3. POEM scores ranged from 0 (clear) to 28 (very severe eczema).	and SCORAD but both tools were ruled out because the Guideline Committee considered POEM to be the best tool as it was short, easy for parents or caregivers to complete and easily accessible via the internet. There was also new evidence about the use of POEM indicating it is responsive to changes in eczema severity. Therefore, the new evidence is unlikely to impact in the guideline recommendations.
57 – 03 How can psychological and p (1.2.1.1, 1.2.1.4-1.2.1.6)	osychosocial effects in children with atop	pic eczema and their families/carers be id	entified in everyday clinical settings?
Surveillance decision This review question should not be updated	d.		
4-year surveillance (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact	
57 – 04 How should the impact of atopic eczema on families'/carers' quality of life be assessed, and how effective is it to use quality of life and other health-related scales in routine clinical management? (1.2.1.4, 1.2.1.6)				
Surveillance decision				
This review question should not be update	ed.			
4-year review (2011) A study looked at Italian versions of the Infants' Dermatitis Quality of Life Index (IDQoL) and Dermatitis Family Impact	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.  At the 4-year surveillance review the evidence showed that the CADIS	
(DFI) finding both had satisfactory psychometric properties and can be used to evaluate quality of life of infants with atopic dermatitis and their families <sup>3</sup> .			measure had adequate reliability, validity and responsiveness but the current guideline recommendation suggests othe tools to measure quality of life which are	
A study found that the Childhood Atopic Dermatitis Impact Scale (CADIS) measure had adequate test-retest reliability, concurrent validity, and discriminative validity. A responsiveness evaluation demonstrated that the CADIS also accurately measures change in patients whose disease improves <sup>4</sup> .			validated, shorter, and less complicated to use in routine clinical practice (Children's Dermatology Life Quality Index (CDLQI), IDQoL and DFI). There was also evidence about satisfactory psychometric properties of the IDQOL and FDI which is in line with the current guideline recommendation. At the 6-year	
New evidence was considered unlikely to impact on guideline recommendations.  6-year surveillance (2014)  A systematic review of the quality of life literature in children with atopic dermatitis was identified <sup>5</sup> . Most studies utilised an			surveillance review the evidence showed that inverse correlation between QOL and severity as well as correlation between various instruments which is in line with the current guideline recommendation. No new evidence was identified in the 8 year surveillance review to change these	

atopic dermatitis specific tool with the

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8- year surveillance	Impact
majority of studies indicating an inverse correlation between quality of life (QOL) and severity as well as correlation between various instruments. The review concluded that most atopic dermatitis-specific tools do not provide a standard, quantitative measurement in relation to perfect health as would do preference based studies required for cost-utility analyses. It was concluded at the 6 year surveillance review that this new evidence was unlikely to impact on guideline recommendations.			conclusions.
57 – 05 How effective are behavioura	al therapy techniques for children with at	opic eczema and what other effective psy	chological interventions are available

# (<u>1.7.1.4</u>)

# Surveillance decision

	1		
4-year review (2011)	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that
One meta-analysis revealed that			would affect recommendations.
psychological interventions had a significant ameliorating effect on eczema			At the 4-year surveillance review the
severity, itching intensity and scratching			evidence showed that psychological
in atopic dermatitis patients, but definite			interventions had a significant
conclusions about their effectiveness			ameliorating effect on eczema severity,
seem premature <sup>6</sup> .			itching intensity and scratching in atopic
This new evidence was considered			dermatitis patients. This evidence was considered unlikely to impact on guideline
unlikely to impact on guideline			recommendations because the guideline
uninkely to impact on guideline			recommendations because the guideline

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact
recommendations.  6-year surveillance (2014)  No relevant evidence identified.			recommends referring for psychological advice when the impact of the atopic eczema on quality of life and psychosocial wellbeing has not improved.  No new evidence was identified in the 8 year surveillance review to change this conclusion.

# **Epidemiology**

57 – 06 What are the epidemiological characteristics of atopic eczema in children (including prevalence, age of onset and resolution, frequency, location and extent of flare-ups, associations with asthma, hay fever and food allergies, and variations in different ethnic groups)? (1.1.1.2, 1.3.1.1-1.3.1.2)

# Surveillance decision

A-year surveillance (2011)  No relevant evidence identified.  6-year surveillance (2014)  No relevant evidence identified.  No relevant evidence identified.  One meta-analysis of epidemiological data reported that the prevalence of having asthma, allergic rhinitis and eczema is higher than could be expected by chance and supports a close relationship of these disorders in children 7.  One RCT reported that infants with eczema under 6 months of age are at high risk of allergic reactions with their first introduction of egg, including severe symptoms of Food Protein-Induced Enterocolitis Syndrome (FPIES) and	A meta-analysis demonstrated that     early life food sensitisation is related.	New evidence is consistent with guideline recommendations.  New evidence was identified about the association between eczema and asthma / allergic rhinitis / food allergy which is in line with the current guideline recommendation which states that children with atopic eczema can often develop asthma and / or allergic rhinitis and that sometimes food allergy is associated with atopic eczema.

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8- year surveillance	Impact
	anaphylaxis <sup>8</sup> .	<ul> <li>allergy and 11 times more likely to have peanut allergy by 12 months than infants without eczema <sup>11</sup>.</li> <li>An RCT on early peanut introduction in infants with eczema leading to 86% reduction in peanut allergy at 5 years <sup>12</sup>.</li> <li>One topic expert referred to a review of epidemiologic studies and meta-analysis reporting that indoor dampness or mould is associated consistently with current and ever diagnosis of eczema but it is unclear from the abstract if studies in children were included in the review <sup>13</sup>.</li> <li>One topic expert referred to an observational study concluding that atopic dermatitis is the main skin-related risk factor for food sensitisation in young infants <sup>14</sup>.</li> </ul>	

# **Identification and management of trigger factors**

57 – 07 What are the potential triggering factors for atopic eczema in children (including environmental irritants and allergens, dietary and psychological factors)? (1.4.1.1)

# Surveillance decision

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact	
4-year surveillance (2011)  No relevant evidence identified.  6-year surveillance (2014)  No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.	
57 – 08 How should triggering factors for atopic eczema in children be identified and managed? (1.4.1.1-1.4.1.11)  Surveillance decision  This review question should not be updated.				

# 4-year surveillance (2011)

No relevant evidence identified.

#### 6-year surveillance (2014)

No relevant evidence identified.

A systematic review of RCTs assessed the effects of all house dust mite reduction and avoidance measures for the treatment of eczema including participants of any age <sup>15</sup>. Two of the seven trials included only children, four included children and adults, and one included only adults. Overall, the included studies had a high risk of bias. Most studies reported no differences between the interventions. The abstract does not include specific results in children.

One topic expert referred to a systematic review of treatments for atopic eczema. This publication is an update of a previous version published in 2000. The systematic review found new evidence suggesting no clinically useful benefit for enzyme washing power avoidance <sup>16</sup>.

New evidence is unlikely to impact on guideline recommendations.

New evidence was identified during the 8 year surveillance review about house dust mite reduction and avoidance measures for the treatment of eczema reporting no difference between interventions and no clinically useful benefit for enzyme washing power avoidance.

The Guideline Committee concluded during guideline development that house dust mite elimination strategies may not be practical in many cases and no new evidence was identified through surveillance to counter this view.

57 – 09 What clinical tests should be used to identify relevant allergens and which children with atopic eczema would benefit from their use? (1.4.1.2-1.4.1.6)

#### Surveillance decision

Summary of evidence from previous urveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact
his review question should not be update	ed.		
In relevant evidence identified.  In relevant evidence identified.  In relevant evidence identified.  In relevant evidence (2014)  In is area was highlighted by the evideline Committee as an area with new evidence. However the guideline cross effers to CG116 which would include this inopulation.  It we evidence/feedback is unlikely to impact on guideline recommendations.	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.  This area was highlighted by the Guideline Committee as an area with new evidence during the 6 year surveillance review. However the guideline cross refers to CG116: Food allergy in under 19s: assessment and diagnosis (Februar 2011) which would include this population.

#### How should food allergies in children with atopic eczema be identified and managed? (1.4.1.2, 1.4.1.5-1.4.1.10, 1.7.1.5)

#### Surveillance decision

This review question should not be updated.

# 4-year review (2011)

Results from 2 small poorly reported studies indicated that there may be some benefit in using an egg-free diet in infants with suspected egg allergy who have positive specific IgE to eggs. However, there was little evidence to support the use of various exclusion diets in unselected people with atopic eczema, but this may be because they were not allergic to those substances in the first

One RCT evaluated the effects of a new thickened amino acid-based formula (TAAF, Novalac), containing a pectinbased thickener, and a reference amino acid-based formula (RAAF, Neocate) on allergy symptoms and safety, through blood biochemistry analysis and growth in infants <18 months with cow's-milk allergy symptoms <sup>19</sup>. The intervention group (TAAF) showed more improvements on the dominant allergic symptom, the

A stakeholder suggested to add a piece of evidence under this question which was already included under clinical guestion number 6. This is an RCT on early peanut introduction in infants with eczema leading to 86% reduction in peanut allergy at 5 years 12.

New evidence is unlikely to impact on guideline recommendations.

The evidence identified at the 4 year surveillance review was considered unlikely to impact on guideline recommendations because there was no high quality evidence and the guideline already includes a recommendation to refer children with suspected food allergy for a specialist investigation and management of the atopic eczema and

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact
place <sup>17,18</sup> .  At the 4 year surveillance review, this evidence was considered unlikely to impact on guideline recommendations.  6-year surveillance (2014)  No relevant evidence identified.	Scoring Atopic Dermatitis Index, the quality of night time, and the frequency of irritability signs. The TAAF group also had normal stools compared to the RAAF group. All of the biochemical parameters were within normal ranges with both formulas. There were no differences between the 2 groups in any of the anthropometric z scores.		allergy.  New evidence identified at the 8 year surveillance review showed improvements in infants who took an amino acid-based formula in place of cow's milk which is in line with the current guideline recommendation which states that 'Healthcare professionals should offer a 6–8 week trial of an extensively hydrolysed protein formula or amino acid formula in place of cow's milk formula for bottle-fed infants aged under 6 months with moderate or severe atopic eczema that has not been controlled by optimal treatment with emollients and mild topical corticosteroids.'
Treatment - Stepped approach to m 57 – 11 What management strategies 1.5.6.3, 1.6.1.2)	nanagement es are appropriate for different ages and c	ultural groups? ( <u>1.4.1.3, 1.4.1.7, 1.4.1.9, 1</u>	1.5.2.4, 1.5.3.6-1.5.3.7, 1.5.4.2-1.5.4.4,
Surveillance decision This review question should not be update	ed.		
4-year surveillance (2011)  No relevant evidence identified.  6-year surveillance (2014)  No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8- year surveillance	Impact		
	57 – 12 What is the most effective and safe way of combining different forms of therapy (for example, emollients, topical corticosteroids, bandaging techniques and calcineurin inhibitors)? (1.5.2.1-1.5.2.2, 1.5.2.8, 1.5.5.2-1.5.5.3, 1.5.5.5, 1.5.7.6-1.5.7.7)				
Surveillance decision This review question should not be update	d.				
4-year surveillance (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.		
57 – 13 How should atopic eczema in Surveillance decision This review question should not be update	n children be managed and monitored be	tween flare-ups (maintenance therapy)? (	1.5.1.1-1.5.1.3, 1.5.3.9)		
4-year surveillance (2011)  No relevant evidence identified.  6-year surveillance (2014)  No relevant evidence identified.	No relevant evidence identified.	A topic expert referred to a systematic review of RCTs of proactive treatment for atopic eczema with topical corticosteroids and calcineurin inhibitors <sup>20</sup> . This systematic review concluded that topical tacrolimus, fluticasone propionate and methylprednisolone aceponate were more efficacious to prevent flares than topical corticosteroids and calcineurin inhibitors vehicle alone. This indirect evidence from vehicle-controlled trials suggested that twice weekly application of the potent topical corticosteroid fluticasone propionate may be more efficacious to	New evidence is consistent with guideline recommendations. The guideline already recommends the use of topical corticosteroids to prevent flares.		

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8- year surveillance	Impact
		prevent AE flares than tacrolimus ointment. It was noted that the included trials did not allow firm conclusions about long-term safety. From the information in the abstract, it is unclear if children were included.	
57 – 14 How should flare-ups of atop	oic eczema in children be identified and n	nanaged? ( <u>1.4.1.3, 1.4.1.11, 1.5.1.1-1.5.1.3</u>	, 1.5.3.2, 1.5.3.9, 1.5.5.3, 1.5.6.3, 1.7.1.3)
Surveillance decision This review question should not be update.	d.		
4-year review (2011) One study evaluated the use of an	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.
evidence based treatment algorithm, finding it to be effective and applicable for the management of atopic eczema. However it did not show clear advantages compared to individualised treatment in a dermatological setting <sup>21</sup> .			The evidence identified at the 4 year surveillance review was considered unlikely to impact on guideline recommendations. No new evidence was identified in the 8-year surveillance review to change this conclusion.
At the 4 year surveillance review this evidence was considered unlikely to impact on guideline recommendations.			to change this condusion.
6-year surveillance (2014) No relevant evidence identified.			

### **Treatment - Emollients**

57 – 15 What types of emollients are available for atopic eczema in children, how effective are they, what quantities should be used, and how often should they be used? (1.5.1.1, 1.5.2.1-1.5.2.8, 1.5.5.2-1.5.5.3, 1.5.5.5, 1.5.9.4-1.5.9.5)

#### Surveillance decision

This review question should not be updated.

#### 4-year review (2011)

Three studies addressed the effectiveness of emollients.

One study indicated emollient use during corticosteroid treatment improves xerosis and puritus, and maintains clinical improvements after therapy discontinuation <sup>22</sup>. Triclosan-containing leave-on emollient was safe and highly acceptable to patients. However, the overall benefit on day 27 was not significant <sup>23</sup>. A study looking at a ceramide-dominant, physiological-lipid based formulation found it was an effective stand-alone or ancillary therapy for many paediatric patients with atopic dermatitis (AD) <sup>24</sup>.

In addition, two studies were highlighted through stakeholder consultation undertaken at the 4 year surveillance. One study found that both an emollient or an emollient enriched with furfuryl

Three RCTs investigated the effect of a range of emollients in the treatment of atopic dermatitis in children.

One RCT compared 3% glycerine against a basic emollient<sup>28</sup>. The second RCT compared four emollients: emulsifying ointment, glycerine/petroleum (proportion 1:2), cetomacrogol, white petroleum jelly <sup>29</sup>. The third RCT compared a pro-AMP cream (containing rhamnosoft, ceramides, and L-isoleucine) against an emollient cream <sup>30</sup>.

The studies reported significant improvements on SCORAD score <sup>28,29</sup>, Patient Oriented-SCORAD score <sup>28</sup>, Facial Eczema Severity Score <sup>30</sup>, the number of relapses and their intensity, skin moisturising, itching sensations, and quality of life of children and of the whole family <sup>28</sup>. One study included children aged from 6 months to 15 years but it is unclear, from an assessment of the

One topic expert referred to an intervention study which concluded that emollient aqueous cream BP used as a leave-on emollient caused severe damage to the skin barrier in volunteers with a previous history of atopic dermatitis. However, the abstract did not report the age of participants <sup>31</sup>.

One topic expert referred to a safety issue from the MHRA which warns healthcare professionals about adverse effects from aqueous cream containing sodium lauryl sulfate: <a href="https://www.gov.uk/drug-safety-update/aqueous-cream-may-cause-skin-irritation">https://www.gov.uk/drug-safety-update/aqueous-cream-may-cause-skin-irritation</a>. This MHRA warning includes different evidence to the evidence reported during the 4-year surveillance review. One topic expert provided further evidence about adverse effects of chronic use of aqueous cream which was associated with increased desquamatory and inflammatory protease activity <a href="https://www.gov.uk/drug-safety-update/">22</a>.

New evidence is unlikely to impact on guideline recommendations.

The 4 year surveillance review concluded that it would be pertinent to await further evidence, particularly on the harms associated with emollients, before an update is commissioned.

New evidence was identified at the 8 year surveillance about the beneficial effects of a range of emollients on atopic eczema. However, evidence from an updated systematic review was mixed and meta-analyses were not considered adequate. Therefore, the evidence was not considered to affect current recommendations which state that 'emollients should form the basis of atopic eczema management and should always be used, even when the atopic eczema is clear'. An MHRA safety alert was identified through this surveillance which warns about adverse effects from

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8- year surveillance	Impact
palmitate were efficacious in treating atopic dermatitis in children, but the emollient cream not containing furfuryl palmitate showed better clinical efficacy <sup>25</sup> . Topic expert feedback suggested that furfuryl palmitate is not available to prescribe in the UK. A further study indicated that pale sulfonated shale oil cream is capable to treat mild to moderate atopic eczema in children more efficaciously than vehicle and is well tolerated <sup>26</sup> . A study found that MPA twice weekly plus an emollient provides an effective maintenance treatment regimen to control AD <sup>27</sup> . It was concluded at the 4 year surveillance review that it would be pertinent to await further evidence, particularly on the harms associated with emollients, before an update is commissioned.  6-year surveillance (2014)  No relevant evidence identified.	abstract, how many children under 12 years old were included <sup>28</sup> .	One topic expert referred to a systematic review of treatments for atopic eczema. This publication is an update of a previous version published in 2000. The systematic review 16 found new evidence from trials including children (7 trials). The results were mixed with 2 trials showing benefits and 5 trials reporting no differences between interventions and comparisons. There were also 3 trials in children evaluating Atopiclair. Atopiclair was listed under 'other topical treatments' but described as a 'medical device emollient cream'. Therefore, these 3 trials were considered as new evidence for emollients. The results from these trials were also mixed with 2 trials showing benefits and 1 trial reporting no differences between intervention and comparison.	aqueous cream containing sodium lauryl sulfate. It would be useful to include a link from the guideline recommendations on emollients to the MHRA safety alert:  Aqueous cream: may cause skin irritation in Drug Safety Update March 2013

# **Treatment** - Topical corticosteroids

57 – 16 How effective and safe are topical corticosteroids for atopic eczema in children, and when and how often should they be used? (1.5.1.1, 1.5.3.1-1.5.3.10, 1.5.4.2-1.5.4.4, 1.5.4.8, 1.5.5.3, 1.5.5.5, 1.5.7.6, 1.5.7.8)

# Surveillance decision

# Summary of evidence from previous surveillance

# Summary of new evidence from 8-year surveillance

# Summary of new intelligence from 8-year surveillance

# Impact

This review question should not be updated.

#### 4-year review (2011)

Results from 1 study demonstrated the safety and efficacy of Hydrocortisone butyrate (HCB) 0.1% lotion in four weeks of treatment for the treatment of mild to moderate AD in children 3 months to 18 years of age <sup>33</sup>. A second study found that HCB 0.1% in a lipocream (LCr) vehicle is more effective than LCr vehicle alone in paediatric populations down to 3 months of age without significant adverse events when used twice a day for up to 1 month <sup>34</sup>

A study of fluticasone propionate (FP) ointment showed that the addition of twice weekly FP to standard maintenance therapy significantly reduces the risk of relapse in children with moderate severe AD <sup>35</sup>.

At the 4 year surveillance review this evidence was considered unlikely to impact on guideline recommendations.

#### 6-year surveillance (2014)

No relevant evidence identified.

An RCT compared pimecrolimus 1% cream (including short-term topical corticosteroids for disease flares) with topical corticosteroids in infants with atopic dermatitis <sup>36</sup>. After 5 years, more infants with topical corticosteroids achieved overall and facial treatment success. The pimecrolimus group required substantially fewer steroid days than the topical corticosteroids group. The profile and frequency of adverse events was similar in the 2 groups. This RCT concluded that pimecrolimus was safe and effective as a first-line treatment of mild-to-moderate atopic eczema in infants and children 3 months and older. Longterm management of mild-to-moderate AD in infants with PIM or TCSs was safe without any effect on the immune system.

There was a comment from one topic expert related to the study by Sigurgeirsson et al. (2015)<sup>36</sup> stating that the main rationale for introducing topical pimecrolimus was that it is does not cause skin thinning (on the premise that normal use of mild to moderate topical corticosteroids do) but only one patient (out of 1205) had clinical skin thinning i.e. there does not appear to be a problem with skin thinning of topical corticosteroids use for mild to moderate eczema.

One topic expert referred to an RCT comparing betamethasone valerate (0.1%) cream (BMVc) against tacrolimus (0.1%) ointment (TACo) <sup>37</sup>. It was concluded that the results supported the proactive use of TACo to promote reparation of the subclinical barrier defect in atopic dermatitis. However, the abstract did not report the age of participants.

One topic expert referred to a systematic review of treatments for atopic eczema. This publication is an update of a previous version published in 2000. The systematic review<sup>16</sup> found new evidence from trials including children with mixed

New evidence is unlikely to impact on guideline recommendations.

Through surveillance reviews, evidence was identified providing mixed results about the beneficial effects of topical corticosteroids for the treatment of eczema and flare prevention. The current guideline recommends to use topical corticosteroids and to discuss benefits and harms with children with atopic eczema and their parents or carers. Current guidance on topical corticosteroids is included in the technology appraisal TA81: Frequency of application of topical corticosteroids for atopic eczema (August 2004) which is mentioned in the guideline. This information was passed onto the Technology Appraisals team for consideration when the topic undergoes the review proposal process.

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact
		results about the benefit of topical corticosteroids for the treatment of eczema and flare prevention (4 trials showed benefit, 3 trials reported no differences between topical corticosteroids and active treatments, and 2 trials did not report results for severity of atopic eczema). This systematic review <sup>16</sup> also found evidence suggesting no clinically useful benefit of corticosteroids containing antimicrobials for non-infected eczema.	

# **Treatment** - Topical calcineurin inhibitors

What are the indications and precautions for using topical calcineurin inhibitors (pimecrolimus and tacrolimus) for atopic eczema in children and how 57 – 17 effective and safe are they? (1.5.1.1, 1.5.4.1-1.5.4.8)

#### Surveillance decision

This review question should not be updated.

#### 4-year review (2011)

Six studies reported topical calcineurin inhibitors (TCIs) were effective at preventing flares and their use was at no additional cost for moderate eczema, and increased cost effectiveness for severe eczema <sup>38-43</sup>. Four studies reported that TCIs were safe and effective for long term use up to 4 years 40,44-46. Ten studies found that TCI's were safe and effective.

An RCT reported that 0.03% tacrolimus ointment was effective at reducing the eczema area and severity index (EASI) score and well tolerated 67.

An RCT compared pimecrolimus 1% cream (including short-term topical corticosteroids for disease flares) with topical corticosteroids in infants with atopic dermatitis <sup>36</sup>. After 5 years, more

One topic expert referred to a study with new data on safety and efficacy of TCIs in guideline recommendations. children. This longitudinal cohort study reported that it seems unlikely that topical pimecrolimus is associated with an increased risk of malignancy <sup>68</sup>.

There was a comment from one topic expert related to the study by Sigurgeirsson et al. (2015)<sup>36</sup> stating that New evidence is unlikely to impact on

The evidence identified at the 4 year surveillance review was not considered to contradict current recommendations on the use of TCIs to treat moderate to severe atopic eczema.

During the 8 year surveillance, new evidence was identified evaluating the

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact
relieving itch and improving QoL <sup>47-56</sup> . Eight additional studies found no increase in adverse effects such as, lymphoma, systemic absorption, malignancy, skin infections, and growth in children who had or were using TCIs <sup>44,57-63</sup> .  One study reported that maintenance therapy with tacrolimus ointment (0.03% or 0.1%) was associated with significantly more flare-free days compared with tacrolimus vehicle <sup>64</sup> . A commentary on this study found that similar results were seen with topical fluticasone propionate which is a topical corticosteroid <sup>65</sup> . However, it was noted that the study on maintenance therapy with tacrolimus only included participants who responded to topical tacrolimus in the stabilisation phase of the trial <sup>64,65</sup> . One study found tacrolimus to be more effective than topical corticosteroid in 72 of the 93 children (77%) who completed the study <sup>66</sup> .  Overall, the identified new evidence was not considered to contradict current recommendations on the use of TCIs to treat moderate to severe atopic eczema. However, the new evidence also suggested that TCIs may be effective in	success. The pimecrolimus group required substantially fewer steroid days	the main rationale for introducing topical pimecrolimus was that it is does not cause skin thinning (on the premise that normal use of mild to moderate topical corticosteroids do) but only one patient (out of 1205) had clinical skin thinning i.e. there does not appear to be a problem with skin thinning of topical corticosteroids use for mild to moderate eczema.  One topic expert referred to an RCT comparing betamethasone valerate (0.1%) cream (BMVc) against tacrolimus (0.1%) ointment (TACo) <sup>37</sup> . It was concluded that the results supported the proactive use of TACo to promote reparation of the subclinical barrier defect in atopic dermatitis. However, the abstract did not report the age of participants.  One topic expert referred to a systematic review of treatments for atopic eczema. This publication is an update of a previous version published in 2000. The systematic review <sup>16</sup> found new evidence from trials including children reporting mixed results about the benefit of topical tacrolimus and pimecrolimus for the treatment of eczema and flare prevention (19 trials). Topical calcineurin inhibitors were better than placebo in 5 out of 6	use of tacrolimus and pimecrolimus in children and adults moderate to severe atopic eczema. Current guidance on tacrolimus and pimecrolimus is included in the technology appraisal TA82:  Tacrolimus and pimecrolimus for atopic eczema (August 2004) which is mentioned in the guideline. This information was passed onto the Technology Appraisals team for consideration when the topic undergoes the review proposal process.

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact
preventing flares, is safe for long-term use, and could be more effective than corticosteroids. This evidence was considered to suggest there are developments in this area of the guideline.  The 4 year surveillance noted that the licensing of this intervention has changed since the current guideline was published However, it was concluded that this is a small area of the guideline, and may not be significant enough to warrant an update of the guideline. The guideline incorporates the recommendations from the technology appraisal TA82:  Tacrolimus and pimecrolimus for atopic eczema (August 2004) which states that pimecrolimus and tacrolimus should be used within their licensed indications as second line treatments when conventional therapies have failed. Long term safety data was noted to be lacking at the 4 year surveillance. Therefore the existing guideline recommendations were considered to still stand.		trials. There were no differences between topical calcineurin inhibitors and other active treatments in 5 trials out of 6 trials. Tacrolimus and pimecrolimus were compared in 7 trials: 3 trials reported that tacrolimus was better, 1 trial reported that pimecrolimus was better, and 3 trials reported no differences.	
6-year surveillance (2014) A meta-analysis comparing tacrolimus with pimecrolimus in the treatment of AD was identified at the 6 year surveillance			

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact
but we have subsequently found out that it has been retracted.			

# **Treatment** - Dry bandages and medicated dressings including wet wrap therapy

57 – 18 What types of dry bandages and medicated dressings (including wet wrap therapies) are available for atopic eczema in children, how effective and safe are they (particularly when combined with topical corticosteroids), and when and how often should they be used? (1.5.1.1, 1.5.5.1-1.5.5.5)

#### Surveillance decision

4-year surveillance (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	A topic expert referred to a systematic review of treatments for atopic eczema. This publication is an update of a previous version published in 2000. The systematic review <sup>16</sup> found new evidence from 5 trials including children about the use of topical corticosteroids with occlusive therapy (wet wrap bandages). The studies reported mixed results regarding the beneficial effect of using topical corticosteroids with occlusive therapy: 2 trials reported benefits with wet wrap bandages, 1 trial reported benefits without wet wrap bandages, 1 trial reported no differences and 1 trial did not conduct a comparison between treatment groups.	New evidence is unlikely to impact on guideline recommendations.  During the 8-year surveillance review, evidence was identified providing mixed results about the beneficial effects of topical corticosteroids with occlusive therapy (wet wrap bandages) for the treatment of eczema. The current guideline recommends the use of medicated dressings or dry bandages with topical corticosteroids for short treatment of flares or areas of chronic lichenified atopic eczema in children or for longer with specialist dermatological advice.
---	----------------------------------	--	--

Summary of evidence from previous
surveillance

Summary of new evidence from 8-year surveillance

Summary of new intelligence from 8year surveillance

Impact

### **Treatment - Antihistamines**

#### 57 – 19 How effective and safe are antihistamines in the management of atopic eczema in children of different ages? (1.5.6.1-1.5.6.3)

#### Surveillance decision

This review question should not be updated.

#### 4-year surveillance (2011)

No relevant evidence identified.

#### 6-year surveillance (2014)

No relevant evidence identified.

Two RCTs reported contradictory results on 4% sodium cromoglicate cutaneous emulsion compared to its vehicle <sup>69,70</sup>. One RCT reported significant reduction in SCORAD and Six Area, Six Sign Atopic Dermatitis (SASSAD) and treatment success with sodium cromoglicate and that application site discomfort was reported similarly between the 2 groups <sup>69</sup>. The other RCT reported that there were no differences in the reduction of SCORAD scores, symptom severity, quality of life, concomitant treatment usage, and global assessments between the 2 groups <sup>70</sup>. Thirty-two children reported treatment related events (abstract does not mention what these are) and eleven children reported application site discomfort 70.

Topic expert feedback suggested that there is no licensed UK preparation of 4% sodium cromoglicate cutaneous emulsion.

A topic expert referred to a systematic review of treatments for atopic eczema. This publication is an update of a previous version published in 2000. The systematic review<sup>16</sup> found new evidence about the use of antihistamines for the treatment of atopic eczema in children (6 trials). Five of these trials did not provide evidence of a beneficial effect of using antihistamines in children.

New evidence is unlikely to impact on guideline recommendations.

During the 8-year surveillance review, new evidence was identified on treatment with 4% sodium cromoglicate cutaneous emulsion reporting contradictory results. Sodium cromoglicate was considered in the guideline but no recommendations were made as the Guideline Committee did not feel there was good evidence to support its use. New evidence on sodium cromoglicate was identified through the 8 vear surveillance but the results were inconsistent. There was also new evidence on the lack of effect using antihistamines and the severity of atopic eczema of children participating in these RCTs was unclear. NICE guideline CG57 recommends that oral antihistamines should not be used routinely in the management of atopic eczema in children. Overall, there is a lack of consistent evidence in this area to impact

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact		
			on the guideline at this time.		
57 – 20 How effective and safe are o made in the guideline)					
Surveillance decision					
This review question should not be update	ed.				
4-year surveillance (2011)  No relevant evidence identified.  6-year surveillance (2014)  No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.		
<b>Treatment</b> - Treatments for infection	าร				
57 – 21 What types of clinically sign <u>1.5.7.8, 1.5.7.12</u> )	ificant secondary infections occur in atop	oic eczema in children and how should th	ney be identified? ( <u>1.5.3.6, 1.5.7.1-1.5.7.3,</u>		
Surveillance decision This review question should not be update	d.				
4-year surveillance (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.		
57 – 22 Which antimicrobial agents (including antiseptics) are effective and appropriate for treating infected atopic eczema in children? (1.5.7.4-1.5.7.7. 1.5.7.9-1.5.7.11)					
Surveillance decision	Surveillance decision				

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8- year surveillance	Impact
This review question should not be update	ed.		
4-year review (2011) Seven studies addressing the question were identified. Two studies found a beneficial effect of silk garments treated with an antibacterial agent <sup>71,72</sup> . Overall evidence for the effectiveness of topical and systemic antibiotics/ antimicrobials was mixed <sup>21,73-75</sup> .  Overall, the identified new evidence was considered to support current guideline recommendations that systemic antibiotics should be used to treat widespread infections and topical antibiotics should be reserved for cases of localised infection. There was felt to be a lack of robust evidence on the effectiveness of silk fabrics treated with an antibacterial agent.  6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	A topic expert referred to a systematic review of treatments for atopic eczema. This publication is an update of a previous version published in 2000. The systematic review 16 found new evidence about the use of antimicrobials including antibiotics, antiseptics and antifungal agents. However, the results from 5 RCTs provided contradictory results with the use of different antimicrobials in children with eczema.  A topic expert referred to a small RCT <sup>76</sup> comparing 7 days of oral flucloxacillin, topical fusidic acid and placebo in children who had infected eczema (n=113). The ChildRen with Eczema Antibiotic Management (CREAM) trial reported that these antibiotics had no effect or a worse effect on eczema symptoms measured with the Patient-Oriented Eczema Measure (POEM). There were important limitations in this trial which should be considered to interpret the results such as exclusions (children with severe infection) and lack of power due to problems during recruitment.	New evidence is unlikely to impact on guideline recommendations.  The evidence identified at the 4 year surveillance review was considered unlikely to impact on guideline recommendations because this evidence supports current guideline recommendations that systemic antibiotics should be used to treat widespread infections and topical antibiotics should be reserved for cases of localised infection.  During the 8-year surveillance review, new evidence was found regarding the use of antimicrobials but the evidence showed contradictory results. Therefore, this evidence was not considered to affect current recommendations.

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact
57 – 23 How should antiseptic and a the risk of resistance developing? (	•	nildren with infected atopic eczema and w	hat measures can be taken to reduce
Surveillance decision This review question should not be update	d.		
4-year surveillance (2011)  No relevant evidence identified.  6-year surveillance (2014)  No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.
	nt should be offered? (1.5.1.1, 1.5.8.1-1.5	atopic eczema in children, how effective a	and sale is it and what form of
4-year review (2011) One study indicated that phototherapy is an effective and well-tolerated treatment modality in children and it should be considered a possible treatment option for children with diseases including atopic dermatitis <sup>77</sup> .  Overall, the new evidence identified does not contradict current recommendations on the use of phototherapy only for the	No relevant evidence identified.	One topic expert referred to a systematic review of treatments for atopic eczema. This publication is an update of a previous version published in 2000. The systematic review <sup>16</sup> found new evidence from trials including children about the benefit of full-spectrum light treatments (1 trial) for eczema and mixed results about the benefit of ultraviolet A/B treatments (2 trials).	New evidence is unlikely to impact on guideline recommendations.  During the 4 year surveillance review, new evidence was identified about the effectiveness and tolerance of phototherapy.  During the 8 year surveillance, new evidence was found about the benefit of phototherapy with mixed results.  The evidence identified at the 4 year and

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact
	effective and safe are they, and how sho	e suppressants (such as ciclosporin, azat uld their use be monitored? (1.5.1.1, <u>1.5.8</u>	
4-year surveillance (2011)  No relevant evidence identified.  6-year surveillance (2014)  No relevant evidence identified.	One RCT estimated the effectiveness of basic therapy + immune modulator compared to basic therapy in children with exacerbation of moderate atopic dermatitis and to investigate the serum level-time profiles of antiinflammatory.	One topic expert referred to a critical appraisal <sup>80</sup> of an RCT. This RCT concluded that both methotrexate and ciclosporin in low doses are clinically effective, relatively safe, and well	New evidence is unlikely to impact on guideline recommendations.  New evidence was identified during the 8 year surveillance review showing that methotrexate and ciclosporin in low doses

tolerated as treatments for severe atopic

2mg.ml is not licensed for use in children

and not licensed for eczema either. See

license here. Methotrexate is listed in the

However, methotrexate oral solution

eczema in children 81.

level-time profiles of antiinflammatory

assessment of the abstract how many

children were under 12. There was a

years old but it is unclear from an

cytokines and neutrophil phagocytic rate

<sup>78</sup>. The study included children from 5-17

are clinically effective, relatively safe, and

atopic eczema in children. However, this

new evidence comes from a small study

(n=40 children with atopic eczema)

well tolerated as treatments for severe

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact
	significant reduction of inflammation, no skin lesions, decreased severity of atopic eczema, normalisation of phagocytic index and phagocytic number, and IFN elevation in the intervention group. The addition of basic therapy + immune modulator in children with exacerbation of moderate atopic dermatitis lead to significant clinic immunological improvement.  One RCT compared the clinical effect of sublingual allergen immunotherapy with placebo in the severity of atopic dermatitis in children sensitised to D. pteronnyssinus (the dust mite species with the highest prevalence) <sup>79</sup> . The SCORAD score decreased significantly more in the sublingual allergen immunotherapy group compared to the placebo group.	BNFC but only for severe resistant psoriasis. Mycophenolate mofetil is also listed in the BNFC for severe refractory eczema.  One topic expert referred to a systematic review of treatments for atopic eczema. This publication is an update of a previous version published in 2000. The systematic review found new evidence from trials including children about the benefit of systemic immune suppressants such as montelukast (2 trials), sensitisation to house dust mite allergens (2 trials), and intravenous immunoglobulin (1 trial).	conducted in Egypt.  There was also new evidence about the addition of basic therapy + immune modulator in children with exacerbation of moderate atopic dermatitis which lead to significant clinic immunological improvement. However, this evidence comes from one RCT and it is unclear how many children under 12 years old were included.  A systematic review found new evidence about the benefit of systemic immune suppressants such as montelukast, sensitisation to house dust mite allergens, and intravenous immunoglobulin.  The current guideline already recommends considering systemic treatments for the treatment of severe atopic eczema in children when other management options have failed or are inappropriate and where there is a significant negative impact on quality of life.
<b>Treatment</b> - Complementary therap	ies		

How effective and safe is homeopathy for managing atopic eczema in children? (1.5.9.1-1.5.9.3-1.5.9.4) 57 – 26

Surveillance decision

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact	
This review question should not be updated.				
4-year surveillance (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.	

#### 57 - 27How effective and safe are Chinese, Western and other herbal medicines for managing atopic eczema in children? (1.5.9.1-1.5.9.4)

#### Surveillance decision

This review question should not be updated.

#### 4-year review (2011)

that a traditional Chinese herbal medicine (TCHM) concoction is efficacious in improving quality of life and reducing topical corticosteroid use in children with moderate-to-severe AD 52 . This evidence was considered unlikely to impact on guideline recommendations.

#### 6-year surveillance (2014)

No relevant evidence identified.

One RCT compared three treatments: 1) One study was identified which concluded oral administration of the Chinese herbal formula Pei Tu Qing Xin Tang (PTQXT); 2) oral administration of PTQXT combined with an external application of Chinese herbs; 3) oral administration of antihistamine and a placebo of PTQXT pills added to topical 1% mometasone furoate for treating patients aged 5-25 years with moderate-to-severe atopic dermatitis 82. The abstract did not report the number of children under 12 years old. The mean SCORAD decreased significantly and gradually in all three groups at short term but at long term there was a significantly greater decrease in the mean SCORAD for the Chinese herbal medicine-treated groups compared

One topic expert mentioned that it is difficult to find a document on the MHRA website which was linked to footnote 4 [4] See 'Using herbal medicines: advice to consumers'. July 2006, MHRA within the CG57 online. This document may have been removed and this may need to link to something else. The MHRA published information about the safety of herbal medicines in 2008: Herbal medicines: new help available when advising patients about safe use. This new publication relates to the previous publication in 2006.

One topic expert mentioned a systematic review of RCTs of Chinese herbal medicines (oral and topical) for the

New evidence is unlikely to impact on quideline recommendations.

New evidence was identified about a Chinese herbal medicines showing inconclusive evidence about improvements in atopic eczema. The current guideline states that the effectiveness and safety of complementary therapies have not yet been adequately assessed in clinical studies and warns about the use of herbal medicines in children and to be wary of any herbal product that is not labelled in English or does not come with information about safe usage. On that basis, it would be premature to consider for inclusion in the guideline at this time.

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact
	to the control group. The difference in quality of life scores showed a significantly greater improvement in both Chinese herbal medicine-treated groups compared to the control group.	management of eczema in children and adults <sup>83</sup> . It was concluded that there was no conclusive evidence that Chinese herbal medicines taken by mouth or applied topically to the skin could reduce the severity of eczema in children or adults.  One topic expert referred to a systematic review of treatments for atopic eczema. This publication is an update of a previous version published in 2000. The systematic review <sup>16</sup> found new evidence from trials including children about the lack of benefit of Chinese herbal medicines (2 trials).	

# 57 – 28 How effective and safe are other complementary therapies (for example, hypnotherapy) for managing atopic eczema in children? (1.5.9.1)

#### Surveillance decision

This review question should not be updated.

# 4-year review (2011)

Ten studies addressed the use of probiotics for managing and treating eczema in children. Four studies showed a beneficial effect <sup>84-87</sup>. Five studies showed no beneficial effect <sup>88-92</sup>. Overall, the review concluded that there is still insufficient conclusive evidence on the

#### **Probiotics**

Three RCTs reported that probiotics improved SCORAD <sup>93,94</sup>, FDLQI, CDLQI <sup>94</sup>, EASI and visual analogue scale for pruritus (VASP) scores <sup>95</sup> compared to placebo in children with atopic dermatitis.

# Vitamin supplements

Two RCTs reported that vitamin

One topic expert mentioned an RCT reporting that water softeners for the treatment of eczema in children provide no benefit <sup>102</sup>.

One topic expert referred to a systematic review which concluded that there was no convincing evidence of the benefit of dietary supplements on eczema but it is

New evidence is unlikely to impact on guideline recommendations.

#### **Probiotics**

During the 4 year surveillance, new evidence was identified about the use of probiotics for managing and treating eczema in children but it was concluded that there was insufficient conclusive

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8- year surveillance	Impact
effectiveness of probiotics.  6-year surveillance (2014)  No relevant evidence identified.	supplements improved SCORAD <sup>96</sup> and EASI scores as well as Investigator's Global Assessment <sup>97</sup> in children with atopic dermatitis compared to placebo. Camargo (2014) reported a mean age of 9 years (standard deviation 5) <sup>97</sup> .  Other topical treatments Three RCTs investigated the effect of a range of topical therapies in the treatment of atopic dermatitis in children.  One RCT compared topical virgin coconut oil against a mineral oil <sup>98</sup> . The second RCT compared a moisturiser containing licochalcone A (Lic A) against 1% hydrocortisone <sup>99</sup> . The third RCT compared a moisturiser containing spent grain wax, Butyrospermum parkii extract and Argania spinosa kernel oil (S cream) against 1% hydrocortisone cream (HC cream) <sup>100</sup> .  The studies reported significant improvements on SCORAD score <sup>98-100</sup> , transepidermal water loss <sup>98,99</sup> , and skin capacitance <sup>98</sup> . Wananukul (2013) included children between 3 months and 14 years but is unclear, from an assessment of the abstract, how many children were under 12 years old <sup>99</sup> .	unclear, from an assessment of the abstract, if studies in children were included <sup>103</sup> .  One topic expert mentioned a systematic review of the effects of oral primrose oil and borage oil for treating the symptoms of atopic eczema <sup>104</sup> . The systematic review included randomised controlled, parallel, and cross-over trials. It was concluded that both oral borage oil and evening primrose oil lack effect on eczema; improvement was similar to respective placebos used in trials. The included studies did not examine possible adverse effects of long-term use of both oral borage oil and evening primrose oil. From the information in the abstract, it is unclear if children were included.  One topic expert mentioned a study which included adult volunteers reporting that olive oil damaged the skin compared to sunflower seed oil. The abstract included a sentence about infants suggesting that 'the use of olive oil for the treatment of dry skin and infant massage should therefore be discouraged' <sup>105</sup> .  One topic expert referred to a United States (US) population-based study	evidence on the effectiveness of probiotics. New evidence was identified during the 8 year surveillance showing improvements in severity of eczema and quality of life.  Vitamin supplements  New evidence was identified during the 8 year surveillance about the beneficial effects of vitamin supplements on atopic eczema.  Other topical treatments  New evidence was identified during the 8 year surveillance about the beneficial effects of a range of topical therapies on atopic eczema and the harmful effect of complementary therapies to the skin like olive oil.  Clothing  New evidence was identified during the 8 year surveillance about the beneficial effects of clothing made of cellulose fibres with seaweed enriched with silver ions, DermaSilk sleeves, anion textiles, and silver textile with prednicarbate ointment.  Water softeners  New evidence was identified during the 8 year surveillance showing no benefit of

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact
	Jirabundansuk (2014) included participants aged between 2 and 15 years old but the abstract did not report the number of children under 12 years old 100.  Clothing  One RCT evaluated the efficacy and safety of clothing made of cellulose fibres with seaweed enriched with silver ions in the treatment of children with atopic dermatitis 101. The SCORAD index significantly improved in the group with the fibre under study and there was also a significantly relevant reduction of the intensity of pruritus and an improvement in the sleep quality compared with the control group wearing placebo clothing.	concluding that complementary and alternative medicine may be harmful to the skin and be associated with higher eczema prevalence in children 0 to 17 years in the US <sup>106</sup> .  One topic expert mentioned that an unlicensed topical preparation of Vaseline contaminated with faecal bacteria and corticosteroid has been purchased in the UK by some parents of children with atopic eczema. However, the guideline recommendations already advise that children with atopic eczema and their parents and carers should be informed that the effectiveness and safety of complementary therapies have not yet been adequately assessed in clinical studies.  One topic expert referred to a systematic review of treatments for atopic eczema. This publication is an update of a previous version published in 2000. The systematic review <sup>16</sup> found new evidence from trials including children on:  Dietary interventions  The included trials in the systematic review showed mixed evidence about the use of dietary interventions such as	water softeners on atopic eczema.  Dietary supplements  New evidence was identified during the 8 year surveillance showing no convincing evidence of the benefit of dietary supplements on atopic eczema.  Other interventions  New evidence was identified during the 8 year surveillance showing no convincing evidence of the benefit of other interventions on atopic eczema such as dermatology nurse consultations, support groups, e-health portal, ion-exchange water softeners, house dust mite reduction, living in a different climate, additional visits to a doctor, vaccines, massage, P. leucotomos extract, and balneotherapy.  Overall, the clinical guideline warns against the use of complementary therapies because the effectiveness and safety of these therapies have not yet been adequately assessed in clinical studies. On that basis, it would be premature to consider this evidence for inclusion in the guideline at this time.

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8- year surveillance	Impact
		probiotics, prebiotics, synbiotics, fatty acid supplementation, oral evening primrose and borage oil, vitamin D and E, goat's milk and hypoallergenic formula. Most of the trials (19 trials out of 32) reported no significant difference in severity of eczema between interventions and comparisons.	
		Other topical treatments There were 14 trials evaluating other topical treatments. However, 3 of these trials have been reported under clinical question 57-15 because the topical treatment was an emollient (Atopiclair). The evidence was mixed for the rest of the topical treatments including antibacterial bath additives, furfuryl palmitate, pill mask, shale oil, vitreoscilla filiformis, topical vitamin B12, carbohydrate-derived fulvic acid, bacterial antigens, lipoxin A4, licochalcone A, and AR-GG27.	
		Specialised clothing Most of the trials (4 trials out of 6) reported benefits with specialised clothing, such as DermaSilk sleeves, anion textiles, and silver textile with prednicarbate ointment. No differences were reported with ethylene vinyl alcohol	

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8- year surveillance	Impact
		fibre fabric and silver filaments.	
		Other interventions The included trials in the systematic review showed mixed evidence about the use of other interventions such as dermatology nurse consultations, support groups, e-health portal, ion-exchange water softeners, house dust mite reduction, living in a different climate, additional visits to a doctor, vaccines, massage, P. leucotomos extract, and balneotherapy. Most of the trials (9 trials out of 15) reported no significant difference in severity of eczema between interventions and comparisons.	
Education and adherence to therapy	<u>v</u>		
57 - 29 What factors contribute to no	on-adherence to therapy and how can ad	herence be improved? ( <u>1.6.1.1-1.6.1.2</u> )	
Surveillance decision This review question should not be update	d.		
4-year surveillance (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	One topic expert suggested 2 studies on treatment adherence. A qualitative study found that barriers to treatment adherence included carer beliefs around eczema treatment, the time consuming nature of applying topical treatments, and child resistance to treatment. The family	New evidence is unlikely to impact on guideline recommendations.  New evidence was identified relating to treatment adherence which is in line with the current guideline recommendation which states that healthcare professionals should address factors that affect

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact
		strategies reported were focused on working around children's resistance to treatment <sup>107</sup> . A literature search identified factors leading to poor treatment adherence and effective strategies to increase treatment adherence but it is unclear from the abstract whether this is a systematic review <sup>108</sup> .	adherence.

#### 57 – 30 How effective are education programmes for children with atopic eczema and their families/carers? (1.6.1.1-1.6.1.3)

#### Surveillance decision

This review question should not be updated.

# 4-year review (2011)

Four studies were identified which found a beneficial effect of educational programmes however none compared different types of interventions 109-112. The studies found that training/education programmes had effects on all explored psychological variables and long term disease management. Nurse practitioners delivered care that improved eczema severity and quality of life to that provided by dermatologists and attendance at support groups improved pruritus and QoL. Overall the evidence identified at the 4 year surveillance was considered unlikely to impact on guideline

A systematic review of educational interventions to improve quality of life in people with skin conditions included 2 studies in children with atopic eczema (the other included studies (n=5) were in adults). This systematic review reported that carers of children in one RCT of eczema showed improvement in HRQoL but another RCT evaluating a website intervention did not find effects on HRQoL 113

One expert topic suggested 2 studies (an RCT and a systematic review) related to patient and family education. Both studies reported that educational interventions lead to improvements in disease severity and quality of life <sup>114,115</sup>.

A stakeholder suggested a pilot RCT of a Web-based intervention to support families of children with eczema <sup>116</sup>. This pilot RCT reported that the severity of atopic eczema in children was decreased more in the website only group compared to the usual care group and the website plus health care professional group.

One topic expert referred to a systematic

New evidence is consistent with guideline recommendations.

Taken together, the evidence identified through the 4 year and 8 year surveillance reviews indicated that educational interventions lead to improvements in disease severity and quality of life. This is supportive of the guideline which recommends that healthcare professionals should spend time educating children with atopic eczema and their parents or carers about atopic eczema and its treatment.

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact	
recommendations.  6-year surveillance (2014)  No relevant evidence identified.		review of treatments for atopic eczema. This publication is an update of a previous version published in 2000. The update <sup>16</sup> found new evidence from trials including children on education interventions with mixed results but most trials showed a benefit using education interventions (4 trials out of 6).		
57 – 31 What information and support 1.5.9.2, 1.6.1.1-1.6.1.3)	rt should be offered to children with atop	ic eczema and their families/carers? (1.2.	1.2, 1.2.1.4, 1.5.1.2, 1.5.7.1, 1.5.7.12,	
Surveillance decision This review question should not be updated	d.			
4-year surveillance (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.	
Indications for referral				
57 – 32 What are the indications for r	referral for specialist paediatric dermatol	ogical advice? ( <u>1.5.3.6, 1.5.7.10, 1.5.7.11,</u>	<u>1.7.1.1-1.7.1.3</u> )	
Surveillance decision This review question should not be updated.				
4-year surveillance (2011) No relevant evidence identified. 6-year surveillance (2014)	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.	

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact
No relevant evidence identified.			

# 57 – 33 What factors are involved in growth disturbance in children with atopic eczema and how should they be managed? (1.7.1.6)

#### Surveillance decision

This review question should not be updated.

4-year review (2011) One study was identified which found that short-term growth was not affected in children with mild to moderate atopic eczema <sup>60</sup> . This evidence was considered unlikely to impact on guideline recommendations.	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.  The evidence identified at the 4 year surveillance review was considered unlikely to impact on guideline recommendations because the guideline recommends referring children with atopic
6-year surveillance (2014)  No relevant evidence identified.			eczema for specialist advice relating to growth when they fail to grow at the expected growth trajectory, as reflected by UK growth charts.
			No new evidence was identified in the 8- year surveillance review to change this conclusion.

# **Research recommendations**

# Diagnosis

# RR - 01 What is the validity of currently used diagnostic criteria for atopic eczema when used in different ethnic groups?

# Surveillance decision

This research recommendation will be considered again at the next surveillance point.

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8- year surveillance	Impact
4-year surveillance (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect this research recommendation.
Assessment of severity, psychological	and psychosocial wellbeing and quality o	of life	
	s in the assessment of atopic eczema in egies, increasing clinical response) and i		
Surveillance decision This research recommendation will be con	sidered again at the next surveillance point.		
4-year surveillance (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect this research recommendation.
RR – 03 What is the optimal method (clinical practice?	(in terms of ease of use, accuracy and se	nsitivity) of measuring the severity of ato	pic eczema in children in routine
Surveillance decision This research recommendation will be con	sidered again at the next surveillance point.		
4-year surveillance (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	See 57–02 for new evidence.	See 57-02 for assessment of the impact of the new evidence.

			1				
Summary of evidence from previous surveillance		Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8- year surveillance	Impact			
RR – 04	Which psychological and quality of life scales are the most appropriate for use in clinical practice in children with atopic eczema in terms of guiding management or for outcomes of treatment and is their use effective and cost-effective?						
Surveillance decision							
This research recommendation will be considered again at the next surveillance point.							
4-year rev	view (2011)	No relevant evidence identified.	None identified relevant to this question.	See 57-04 for assessment of the impact			
See 57-04	4 for new evidence.			of the new evidence.			
6-year su	rveillance (2014)						
See 57–04	4 for new evidence.						
Identification and management of trigger factors							
RR – 05 How effective and cost-effective is the use of house dust mite avoidance strategies in the treatment of childhood atopic eczema and which strategies, if any, are the most effective?							
Surveillar	nce decision						
This research recommendation will be considered again at the next surveillance point.							
4-year su	rveillance (2011)	See 57–08 for new evidence.	See 57–08 for new evidence.	See 57-08 for assessment of the impact			
No relevant evidence identified.				of the new evidence.			
6-year su	rveillance (2014)						
No relevar	nt evidence identified.						
RR – 06 When and how should children with atopic eczema be tested for allergies (skin prick tests, allergen-specific immunoglobulin E), and how can the diagnostic accuracy and effect on clinical outcomes of the tests be improved?							
Surveillance decision							
This research recommendation will be considered again at the next surveillance point.							
	view (2011)	No relevant evidence identified.	None identified relevant to this question.	See 57-09 for assessment of the impact			
No relevant evidence identified.				of the new evidence.			
		1	1	1			

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact			
6-year surveillance (2014) See 57–09 for new evidence.						
RR - 07 How should exposure to pet	s be managed in children with atopic ecz	ema; at what age does allergy occur and	does tolerance develop?			
Surveillance decision This research recommendation will be considered again at the next surveillance point.						
4-year surveillance (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect this research recommendation.			
RR – 08 What is the optimal feeding regimen in the first year of life for children with established atopic eczema?						
Surveillance decision This research recommendation will be considered again at the next surveillance point.						
4-year surveillance (2011) See 57-10 for new evidence. 6-year surveillance (2014) No relevant evidence identified.	See 57-10 for new evidence.	None identified relevant to this question.	See 57-10 for assessment of the impact of the new evidence.			
Treatment						
Stepped approach to management						
RR - 09 How should flares of atopic eczema be defined/recognised, what pattern do they take and how useful is this to clinical practice?						
Surveillance decision This research recommendation will be considered again at the next surveillance point.						

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact
4-year surveillance (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect this research recommendation.
RR – 10 Which are the best, most cos	st-effective treatment strategies for mana	ging and preventing flares in children wi	th atopic eczema?
Surveillance decision This research recommendation will be con	sidered again at the next surveillance point.		
4-year surveillance (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	See 57-13 for new evidence.	See 57-13 for assessment of the impact of the new evidence.
	the control of atopic eczema in the first y d severity of food allergy, asthma and all		and severity of atopic eczema and the
Surveillance decision This research recommendation will be con	sidered again at the next surveillance point.		
4-year surveillance (2011) See 57–10 for new evidence. 6-year surveillance (2014) No relevant evidence identified.	See 57–10 for new evidence.	None identified relevant to this question.	See 57-10 for assessment of the impact of the new evidence.

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact	
Treatment				
Emollients				
RR - 12 Which are the most effective	and cost-effective combinations of emol	lient products to use for the treatment o	f childhood atopic eczema?	
Surveillance decision This research recommendation will be con	sidered again at the next surveillance point.			
4-year surveillance (2011) See 57–15 for new evidence. 6-year surveillance (2014) No relevant evidence identified.	See 57–15 for new evidence.	See 57–15 for new evidence.	See 57-15 for assessment of the impact of the new evidence.	
RR – 13 Does the regular use of emoin children?	llients reduce the severity and frequency	of flares and the need for other topical a	ngents in the treatment of atopic eczema	
Surveillance decision This research recommendation will be cor	sidered again at the next surveillance point.			
4-year surveillance (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect this research recommendation.	
Treatment				
Topical corticosteroids				
RR – 14 What are the long-term effects (when used for between 1 and 3 years) of typical use of topical corticosteroids in children with atopic eczema?				
Surveillance decision This research recommendation will be considered again at the next surveillance point.				

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8- year surveillance	Impact		
4-year surveillance (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	See 57–16 for new evidence.	See 57–16 for new evidence.	See 57-16 for assessment of the impact of the new evidence.		
RR - 15 What are the optimal treatme	nt regimens for using topical corticoster	oids in the treatment of atopic eczema in	children?		
Surveillance decision This research recommendation will be cons	sidered again at the next surveillance point.				
4-year review (2011) See 57–16 for new evidence. 6-year surveillance (2014) No relevant evidence identified.	See 57–16 for new evidence.	See 57–16 for new evidence.	See 57-16 for assessment of the impact of the new evidence.		
Treatment					
Topical calcineurin inhibitors	Topical calcineurin inhibitors				
	RR – 16 What are the most effective, cost-effective and safe ways of using combinations of topical calcineurin inhibitors with topical corticosteroids of different potencies in the treatment of atopic eczema in children, with particular reference to areas of thin skin such as the face and flexures?				
Surveillance decision This research recommendation will be considered again at the next surveillance point.					
4-year review (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	See 57–17 for new evidence.	None identified relevant to this question.	See 57-17 for assessment of the impact of the new evidence.		

Summary	of evidence from previous	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact	
RR – 17	What is the effectiveness and	d safety of using topical calcineurin inhib teroids and does this differ in various bo	itors for treating children with atopic ecz	zema in comparison with using different	
	nce decision	sidered again at the next surveillance point.	•		
See 57–17	view (2011) 7 for new evidence. rveillance (2014) nt evidence identified.	See 57–17 for new evidence.	See 57–17 for new evidence.	See 57-17 for assessment of the impact of the new evidence.	
RR – 18		and safe is the use of topical tacrolimus (	0.1% ointment for treating children with a	atopic eczema?	
	nce decision arch recommendation will be con	sidered again at the next surveillance point.			
See 57–17	view (2011) 7 for new evidence. rveillance (2014) nt evidence identified.	See 57–17 for new evidence.	See 57–17 for new evidence.	See 57-17 for assessment of the impact of the new evidence.	
RR – 19	RR – 19 What are the optimal treatment durations when using topical pimecrolimus and tacrolimus in the treatment of children with atopic eczema?				
	Surveillance decision This research recommendation will be considered again at the next surveillance point.				
See 57–17 6-year sur	view (2011) 7 for new evidence. rveillance (2014) nt evidence identified.	See 57–17 for new evidence.	See 57–17 for new evidence.	See 57-17 for assessment of the impact of the new evidence.	

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact
RR – 20 How safe are topical calcine	eurin inhibitors for long-term therapy (1–3	years) in the treatment of atopic eczema	in children?
Surveillance decision This research recommendation will be con	nsidered again at the next surveillance point.		
4-year review (2011) See 57–17 for new evidence. 6-year surveillance (2014) No relevant evidence identified.	See 57–17 for new evidence.	See 57–17 for new evidence.	See 57-17 for assessment of the impact of the new evidence.
Treatment			
Dry bandages and medicated dressing	s (including wet wrap therapy)		
RR – 21 What are the benefits and h eczema in children?	arms of the different bandaging therapies	(for example, wet, dry and medicated ba	ndages) in the treatment of atopic
Surveillance decision This research recommendation will be con	nsidered again at the next surveillance point.		
4-year surveillance (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect this research recommendation.
RR – 22 How effective, cost-effective and safe are wet wrap dressings with emollients alone or in combination with various potencies of topical corticosteroids, for the longer term management (greater than 5 days consecutively) of atopic eczema in children and how do they compare with the use of other topical therapies alone?			
Surveillance decision			
This research recommendation will be co	nsidered again at the next surveillance point.		

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact	
4-year surveillance (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect this research recommendation.	
	opical corticosteroids of different potenci fective, for how long can they safely be u		occlusion for the treatment of atopic	
Surveillance decision This research recommendation will be con	sidered again at the next surveillance point.			
4-year surveillance (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect this research recommendation.	
Treatment				
Antihistamines and other antipruritics				
	ness, cost-effectiveness and safety of us and night-time sleep disturbance?	ing sedating and non-sedating antihistar	nines in children with atopic eczema in	
Surveillance decision This research recommendation will be considered again at the next surveillance point.				
4-year surveillance (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	See 57–19 for new evidence.	See 57–19 for new evidence.	See 57-19 for assessment of the impact of the new evidence.	

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact			
Treatment	Freatment					
Treatment for infections associated wit	h atopic eczema					
	What are the prevalence and patterns of antibiotic resistance in children with atopic eczema and how clinically meaningful are these in terms of clinical management and the emergence of multiresistant bacteria?					
Surveillance decision						
This research recommendation will be con	nsidered again at the next surveillance point.					
4-year surveillance (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect this research recommendation.			
antimicrobial agents in term	eted atopic eczema in children be defined s of their clinical effectiveness (including					
Surveillance decision This research recommendation will be cor	nsidered again at the next surveillance point.					
4-year surveillance (2011) See 57–22 for new evidence. 6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	See 57-22 for assessment of the impact of the new evidence.			
Treatment						
Phototherapy and systemic treatments						
R – 27 How effective, cost-effective and safe is phototherapy in children with severe atopic eczema? How and when should it be used and should it be combined with other topical therapies?						
Surveillance decision						

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact	
This research recommendation will be con	sidered again at the next surveillance point.			
4-year review (2011) See 57–24 for new evidence. 6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	See 57-24 for assessment of the impact of the new evidence.	
	and safe are systemic treatment options iclosporin, methotrexate, mycophenolate			
Surveillance decision This research recommendation will be con	sidered again at the next surveillance point.			
4-year review (2011) No relevant evidence identified. 6-year surveillance (2014) No relevant evidence identified.	See 57–25 for new evidence.	See 57–25 for new evidence.	See 57-25 for assessment of the impact of the new evidence.	
Treatment				
Complementary therapies				
RR – 29 How effective, cost-effective and safe are complementary therapies for the management of atopic eczema in children and how do they compare with conventional Western therapies?				
Surveillance decision  This research recommendation will be considered again at the next surveillance point.				
4-year surveillance (2011) See 57–28 for new evidence. 6-year surveillance (2014)	See 57–28 for new evidence.	See 57–28 for new evidence.	See 57-28 for assessment of the impact of the new evidence.	

Summary of evidence from previous surveillance	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8-year surveillance	Impact		
No relevant evidence identified.					
Treatment	1				
Behavioural therapies					
	ological interventions, for example habit relible and cost-effective in clinical practice		gement of atopic eczema in children		
Surveillance decision This research recommendation will be con	nsidered again at the next surveillance point.				
4-year surveillance (2011) See 57–05 for new evidence. 6-year surveillance (2014) No relevant evidence identified.	No relevant evidence identified.	None identified relevant to this question.	See 57-05 for assessment of the impact of the new evidence.		
Education and adherence to therapy					
RR – 31 How effective and cost-effective					
Surveillance decision This research recommendation will be considered again at the next surveillance point.					
4-year surveillance (2011) See 57–30 for new evidence. 6-year surveillance (2014) No relevant evidence identified.	See 57–30 for new evidence.	See 57–30 for new evidence.	See 57-30 for assessment of the impact of the new evidence.		

Summary surveillar	of evidence from previous	Summary of new evidence from 8-year surveillance	Summary of new intelligence from 8- year surveillance	Impact	
Monitorin	ng growth				
RR – 32	Which factors contribute to growth delay in children with severe atopic eczema, how should they be managed and does this impact on their expected final adult height?				
	nce decision arch recommendation will be con	sidered again at the next surveillance point.			
See 57–3	view (2011) 3 for new evidence.  rveillance (2014) nt evidence identified.	No relevant evidence identified.	None identified relevant to this question.	See 57-33 for assessment of the impact of the new evidence.	
RR – 33	What is the impact of food a	llergy on growth in infants with atopic ec	zema and how should it be managed?		
	Surveillance decision This research recommendation will be considered again at the next surveillance point.				
No releva	nrveillance (2011) nt evidence identified. nrveillance (2014) nt evidence identified.	No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect this research recommendation.	

## References

- Schmitt J, Spuls PI, Thomas KS et al. (2014) The Harmonising Outcome Measures for Eczema (HOME) statement to assess clinical signs of atopic eczema in trials. J Allergy Clin Immunol 134:800-807.
- Gaunt DM, Metcalfe C, and Ridd M. (2016) The Patient-Oriented Eczema Measure in young children: responsiveness and minimal clinically important difference. Allergy.
- Baranzoni N, Scalone L, Mantovani LG et al. (2007) Validation of the Italian version of the Infants' Dermatitis Quality of Life and Family Dermatitis Indexes. Giornale Italiano di Dermatologia e Venereologia 142:423-432.
- 4. Chamlin SL, Lai JS, Cella D et al. (2007) Childhood Atopic Dermatitis Impact Scale: reliability, discriminative and concurrent validity, and responsiveness. Arch.Dermatol. 143:768-772.
- Iskedjian M, Navarro V, Khondoker F et al. (2011) Systematic review of the quality of life literature in children with atopic dermatitis. Value in Health 14:A57.
- 6. Chida Y, Steptoe A, Hirakawa N et al. (2007) The effects of psychological intervention on atopic dermatitis. A systematic review and meta-analysis. Int.Arch.Allergy Immunol. 144:1-9.
- Pols DH, Wartna JB, van Alphen EI et al. (2015) Interrelationships between Atopic Disorders in Children: A Meta-Analysis Based on ISAAC Questionnaires. PloS one 10:e0131869.
- 8. Metcalfe J, Palmer D, and Prescott S. (2013) Food allergy and anaphylaxis-2042. High rates of egg reactivity in infants with eczema randomised to receive egg under 6 months of age. World Allergy Organization Journal 6.
- Alduraywish SA, Lodge CJ, Campbell B et al. (2016) The march from early life food sensitization to allergic disease: a systematic review and meta-analyses of birth cohort studies. Allergy 71:77-89.
- Ben-Shoshan M, Soller L, Harrington DW et al. (2015) Eczema in early childhood, sociodemographic factors and lifestyle habits are associated with food allergy: a nested casecontrol study. Int Arch Allergy Immunol 166:199-207.
- 11. Martin PE, Eckert JK, Koplin JJ et al. (2015) Which infants with eczema are at risk of food allergy? Results from a population-based cohort. Clin Exp Allergy 45:255-264.
- Du TG, Roberts G, Sayre PH et al. (2015) Randomized trial of peanut consumption in infants at risk for peanut allergy. N Engl J Med 372:803-813.
- Mendell MJ, Mirer AG, Cheung K et al. (2011) Respiratory and allergic health effects of dampness, mold, and dampness-related agents: a review of the epidemiologic evidence. Environ Health Perspect. 119:748-756.
- 14. Flohr C, Perkin M, Logan K et al. (2014) Atopic dermatitis and disease severity are the main risk factors for food sensitization in exclusively breastfed infants. J Invest Dermatol 134:345-350.
- Nankervis H, Pynn EV, Boyle RJ et al. (2015) House dust mite reduction and avoidance measures for treating eczema. Cochrane Database of Systematic Reviews 1:CD008426.
- Nankervis H, Thomas KS, Delamere FM et al. (2016) Scoping systematic review of treatments for eczema. Programme Grants Appl Res 4.
- Bath-Hextall F, Delamere FM, and Williams HC. (2008) Dietary exclusions for established atopic eczema. Cochrane.Database.Syst.Rev. CD005203.
- 18. Bath-Hextall F, Delamere FM, and Williams HC. (2009) Dietary exclusions for improving established atopic eczema in adults and children: systematic review. Allergy 64:258-264.

- Dupont C, Kalach N, Soulaines P et al. (2015) Safety of a New Amino Acid Formula in Infants Allergic to Cow's Milk and Intolerant to Hydrolysates. Journal of Pediatric Gastroenterology & Nutrition 61:456-463.
- Schmitt J, von KL, Svensson A et al. (2011) Efficacy and tolerability of proactive treatment with topical corticosteroids and calcineurin inhibitors for atopic eczema: systematic review and metaanalysis of randomized controlled trials. Br.J Dermatol. 164:415-428.
- 21. Schmitt J, Meurer M, Schwanebeck U et al. (2008) Treatment following an evidence-based algorithm versus individualised symptom-oriented treatment for atopic eczema. A randomised controlled trial. Dermatology 217:299-308.
- Szczepanowska J, Reich A, and Szepietowski JC. (2008) Emollients improve treatment results
  with topical corticosteroids in childhood atopic dermatitis: a randomized comparative study.
  Pediatr.Allergy Immunol. 19:614-618.
- Tan WP, Suresh S, Tey HL et al. (2010) A randomized double-blind controlled trial to compare a triclosan-containing emollient with vehicle for the treatment of atopic dermatitis. Clin.Exp.Dermatol. 35:e109-e112.
- 24. Sugarman JL and Parish LC. (2009) Efficacy of a lipid-based barrier repair formulation in moderate-to-severe pediatric atopic dermatitis. J.Drugs Dermatol. 8:1106-1111.
- Tripodi S, Di Rienzo BA, Panetta V et al. (2009) Lack of efficacy of topical furfuryl palmitate in pediatric atopic dermatitis: a randomized double-blind study. J.Investig.Allergol.Clin.Immunol. 19:204-209.
- Korting HC, Schollmann C, Cholcha W et al. (2010) Efficacy and tolerability of pale sulfonated shale oil cream 4% in the treatment of mild to moderate atopic eczema in children: a multicentre, randomized vehicle-controlled trial. J.Eur.Acad.Dermatol.Venereol. 24:1176-1182.
- Peserico A, Stadtler G, Sebastian M et al. (2008) Reduction of relapses of atopic dermatitis with methylprednisolone aceponate cream twice weekly in addition to maintenance treatment with emollient: a multicentre, randomized, double-blind, controlled study. Br.J.Dermatol. 158:801-807.
- Gayraud F. (2014) Comparative, randomized, double-blinded study assessing the efficacy of a new kind of dermocosmetic product containing skin barrier therapy on infants and children with moderate atopic dermatitis. JDDG - Journal of the German Society of Dermatology 12:14-15.
- 29. Hlela C, Lunjani N, Gumedze F et al. (2015) Affordable moisturisers are effective in atopic eczema: A randomised controlled trial. South African Medical Journal Suid-Afrikaanse:780-784.
- Marseglia A. (2014) Local rhamnosoft, ceramides and L-isoleucine in atopic eczema: A randomized, placebo controlled trial. Pediatric allergy and immunology 25:271-275.
- 31. Danby SG, Al-Enezi T, Sultan A et al. (2011) The effect of aqueous cream BP on the skin barrier in volunteers with a previous history of atopic dermatitis. Br J Dermatol 165:329-334.
- Mohammed D, Matts PJ, Hadgraft J et al. (2011) Influence of Aqueous Cream BP on corneocyte size, maturity, skin protease activity, protein content and transepidermal water loss. Br J Dermatol 164:1304-1310.
- 33. Matheson R, Kempers S, Breneman D et al. (2008) Hydrocortisone butyrate 0.1% lotion in the treatment of atopic dermatitis in pediatric subjects. J.Drugs Dermatol. 7:266-271.
- 34. Abramovits W and Oquendo M. (2010) Hydrocortisone butyrate 0.1% lipocream in pediatric patients with atopic dermatitis. Skinmed. 8:72-79.
- 35. Glazenburg EJ, Wolkerstorfer A, Gerretsen AL et al. (2009) Efficacy and safety of fluticasone propionate 0.005% ointment in the long-term maintenance treatment of children with atopic dermatitis: differences between boys and girls? Pediatr.Allergy Immunol. 20:59-66.

- Sigurgeirsson B, Boznanski A, Todd G et al. (2015) Safety and efficacy of pimecrolimus in atopic dermatitis: A 5-year randomized trial. Pediatrics 135:597-606.
- 37. Chittock J, Brown K, Cork MJ et al. (2015) Comparing the effect of a twice-weekly tacrolimus and betamethasone valerate dose on the subclinical epidermal barrier defect in atopic dermatitis. Acta Dermato-Venereologica.95 (6) (pp 653-658), 2015.Date of Publication: 2015. 653-658.
- 38. Healy E, Bentley A, Fidler C et al. (2011) Cost-effectiveness of tacrolimus ointment in adults and children with moderate and severe atopic dermatitis: twice-weekly maintenance treatment vs. standard twice-daily reactive treatment of exacerbations from a third party payer (U.K. National Health Service) perspective. Br.J.Dermatol. 164:387-395.
- Kubota Y, Yoneda K, Nakai K et al. (2009) Effect of sequential applications of topical tacrolimus and topical corticosteroids in the treatment of pediatric atopic dermatitis: an open-label pilot study. J.Am.Acad.Dermatol. 60:212-217.
- Langley RG, Eichenfield LF, Lucky AW et al. (2008) Sustained efficacy and safety of pimecrolimus cream 1% when used long-term (up to 26 weeks) to treat children with atopic dermatitis. Pediatr.Dermatol. 25:301-307.
- Paller AS, Eichenfield LF, Kirsner RS et al. (2008) Three times weekly tacrolimus ointment reduces relapse in stabilized atopic dermatitis: a new paradigm for use. Pediatrics 122:e1210e1218.
- 42. Thaci D, Reitamo S, Gonzalez Ensenat MA et al. (2008) Proactive disease management with 0.03% tacrolimus ointment for children with atopic dermatitis: results of a randomized, multicentre, comparative study. Br.J.Dermatol. 159:1348-1356.
- Thaci D, Chambers C, Sidhu M et al. (2010) Twice-weekly treatment with tacrolimus 0.03% ointment in children with atopic dermatitis: clinical efficacy and economic impact over 12 months. J.Eur.Acad.Dermatol.Venereol. 24:1040-1046.
- 44. Reitamo S, Rustin M, Harper J et al. (2008) A 4-year follow-up study of atopic dermatitis therapy with 0.1% tacrolimus ointment in children and adult patients. Br.J.Dermatol. 159:942-951.
- 45. Remitz A, Harper J, Rustin M et al. (2007) Long-term safety and efficacy of tacrolimus ointment for the treatment of atopic dermatitis in children. Acta Derm. Venereol. 87:54-61.
- Zuberbier T and Brautigam M. (2008) Long-term management of facial atopic eczema with pimecrolimus cream 1% in paediatric patients with mild to moderate disease.
   J.Eur.Acad.Dermatol.Venereol. 22:718-721.
- Chen SL, Yan J, and Wang FS. (2010) Two topical calcineurin inhibitors for the treatment of atopic dermatitis in pediatric patients: a meta-analysis of randomized clinical trials.
   J.Dermatolog.Treat. 21:144-156.
- 48. Doss N, Kamoun MR, Dubertret L et al. (2010) Efficacy of tacrolimus 0.03% ointment as secondline treatment for children with moderate-to-severe atopic dermatitis: evidence from a randomized, double-blind non-inferiority trial vs. fluticasone 0.005% ointment. Pediatr.Allergy Immunol. 21:321-329.
- 49. Fowler J, Johnson A, Chen M et al. (2007) Improvement in pruritus in children with atopic dermatitis using pimecrolimus cream 1%. Cutis 79:65-72.
- Gontijo B, Duarte IAG, Sittart JAD et al. (2008) Evaluate of the efficacy and safety of tacrolimus ointment 0,03% to treat atopic dermatitis in pediatric patients. Anais Brasileiros de Dermatologia 83:511-519.
- 51. Hoeger PH, Lee KH, Jautova J et al. (2009) The treatment of facial atopic dermatitis in children who are intolerant of, or dependent on, topical corticosteroids: a randomized, controlled clinical trial. Br.J.Dermatol. 160:415-422.

- 52. Hon KL, Leung TF, Ng PC et al. (2007) Efficacy and tolerability of a Chinese herbal medicine concoction for treatment of atopic dermatitis: a randomized, double-blind, placebo-controlled study. Br.J.Dermatol. 157:357-363.
- 53. Kirsner RS, Heffernan MP, and Antaya R. (2010) Safety and efficacy of tacrolimus ointment versus pimecrolimus cream in the treatment of patients with atopic dermatitis previously treated with corticosteroids. Acta Derm. Venereol. 90:58-64.
- 54. Kondo Y, Nakajima Y, Komatsubara R et al. (2009) Short-term efficacy of tacrolimus ointment and impact on quality of life. Pediatr.Int. 51:385-389.
- 55. Meurer M, Eichenfield LF, Ho V et al. (2010) Addition of pimecrolimus cream 1% to a topical corticosteroid treatment regimen in paediatric patients with severe atopic dermatitis: a randomized, double-blind trial. J.Dermatolog.Treat. 21:157-166.
- Ring J, Abraham A, de CC et al. (2008) Control of atopic eczema with pimecrolimus cream 1% under daily practice conditions: results of a > 2000 patient study.
   J.Eur.Acad.Dermatol.Venereol. 22:195-203.
- 57. Arana A, Wentworth CW, Rivero E et al. (2011) Lymphoma among patients with atopic dermatitis treated with topical corticosteroids and/or topical calcineurin inhibitors. Journal of the American Academy of Dermatology 64:AB3.
- 58. Arellano FM, Wentworth CE, Arana A et al. (2007) Risk of lymphoma following exposure to calcineurin inhibitors and topical steroids in patients with atopic dermatitis. J.Invest Dermatol. 127:808-816.
- 59. Eichenfield LF, Thaci D, de PY et al. (2007) Clinical management of atopic eczema with pimecrolimus cream 1% (Elidel) in paediatric patients. Dermatology 215 Suppl 1:3-17.
- 60. Gradman J and Wolthers OD. (2007) Short-term growth in children with eczema during treatment with topical mometasone furoate and tacrolimus. Acta Paediatr. 96:1233-1237.
- Krueger GG, Eichenfield L, Goodman JJ et al. (2007) Pharmacokinetics of tacrolimus following topical application of tacrolimus ointment in adult and pediatric patients with moderate to severe atopic dermatitis. J.Drugs Dermatol. 6:185-193.
- 62. Leung DY, Hanifin JM, Pariser DM et al. (2009) Effects of pimecrolimus cream 1% in the treatment of patients with atopic dermatitis who demonstrate a clinical insensitivity to topical corticosteroids: a randomized, multicentre vehicle-controlled trial. Br.J.Dermatol. 161:435-443.
- 63. Yang LP and Curran MP. (2009) Topical pimecrolimus: a review of its use in the management of pediatric atopic dermatitis. Paediatr. Drugs 11:407-426.
- 64. Breneman D, Fleischer AB, Jr., Abramovits W et al. (2008) Intermittent therapy for flare prevention and long-term disease control in stabilized atopic dermatitis: a randomized comparison of 3-times-weekly applications of tacrolimus ointment versus vehicle. J Am Acad Dermatol 58:990-999.
- Spergel JM. (2008) Intermittent Therapy for Flare Prevention and Long-term Disease Control in Stabilized Atopic Dermatitis: A Randomized Comparison of 3-Times-Weekly Applications of Tacrolimus Ointment Versus Vehicle. Pediatrics 122.
- 66. Arkwright PD, Gillespie MC, Ewing CI et al. (2007) Blinded side-to-side comparison of topical corticosteroid and tacrolimus ointment in children with moderate to severe atopic dermatitis. Clin.Exp.Dermatol. 32:145-147.
- Rahman MF, Nandi AK, Kabir S et al. (2015) Topical Tacrolimus versus Hydrocortisone on Atopic Dermatitis in Paediatric Patients: A Randomized Controlled Trial. Mymensingh Medical Journal: MMJ 24:457-463.
- 68. Margolis DJ, Abuabara K, Hoffstad OJ et al. (2015) Association Between Malignancy and Topical Use of Pimecrolimus. JAMA Dermatol 151:594-599.

- 69. Berth-Jones J, Pollock I, Hearn RM et al. (2015) A randomised, controlled trial of a 4% cutaneous emulsion of sodium cromoglicate in treatment of atopic dermatitis in children. Journal of Dermatological Treatment 26:291-296.
- 70. Edwards AM, Bibawy D, Matthews S et al. (2015) Long-term use of a 4% sodium cromoglicate cutaneous emulsion in the treatment of moderate to severe atopic dermatitis in children. Journal of Dermatological Treatment 26:541-547.
- 71. Koller DY, Halmerbauer G, Bock A et al. (2007) Action of a silk fabric treated with AEGIS in children with atopic dermatitis: a 3-month trial. Pediatr.Allergy Immunol. 18:335-338.
- 72. Stinco G, Piccirillo F, and Valent F. (2008) A randomized double-blind study to investigate the clinical efficacy of adding a non-migrating antimicrobial to a special silk fabric in the treatment of atopic dermatitis. Dermatology 217:191-195.
- 73. Bell MC, Stovall SH, Harik NS et al. (2010) Resistance Patterns of Microbes Causing Superinfection and Antimicrobial Prescribing Practice in Children with Atopic Dermatitis in a Tertiary Pediatric Allergy Clinic. Journal of Allergy and Clinical Immunology 125:AB92.
- 74. Birnie AJ, Bath-Hextall FJ, Ravenscroft JC et al. (2008) Interventions to reduce Staphylococcus aureus in the management of atopic eczema. Cochrane Database Syst Rev CD003871.
- 75. Schena D, Papagrigoraki A, and Girolomoni G. (2008) Sensitizing potential of triclosan and triclosan-based skin care products in patients with chronic eczema. Dermatol.Ther. 21 Suppl 2:S35-S38.
- 76. Francis NA, Ridd MJ, Thomas-Jones E et al. (2016) A randomised placebo-controlled trial of oral and topical antibiotics for children with clinically infected eczema in the community: the ChildRen with Eczema, Antibiotic Management (CREAM) study. Health Technol Assess 20.
- 77. Clayton TH, Clark SM, Turner D et al. (2007) The treatment of severe atopic dermatitis in childhood with narrowband ultraviolet B phototherapy. Clin.Exp.Dermatol. 32:28-33.
- 78. Slavyanskaya TA. (2013) Immunotherapy rationale in children with exacerbation of moderate atopic dermatitis. Allergy: European Journal of Allergy and Clinical Immunology 68:161.
- Luna-Pech JA. (2013) Efficacy of sublingual immunotherapy in the severity of atopic dermatitis in children with allergic sensitization to dermatophagoides pteronyssinus. Annals of Allergy, Asthma and Immunology 111:A8.
- 80. Tsakok T and Flohr C. (2014) Methotrexate vs. ciclosporin in the treatment of severe atopic dermatitis in children: a critical appraisal. Br J Dermatol 170:496-498.
- El-Khalawany MA, Hassan H, Shaaban D et al. (2013) Methotrexate versus cyclosporine in the treatment of severe atopic dermatitis in children: a multicenter experience from Egypt. Eur J Pediatr 172:351-356.
- Liu J, Mo X, Wu D et al. (2015) Efficacy of a Chinese herbal medicine for the treatment of atopic dermatitis: A randomised controlled study. [Review]. Complementary Therapies in Medicine 23:644-651.
- 83. Gu S, Yang AW, Xue CC et al. (2013) Chinese herbal medicine for atopic eczema. Cochrane.Database.Syst.Rev. 9:CD008642.
- Betsi GI, Papadavid E, and Falagas ME. (2008) Probiotics for the treatment or prevention of atopic dermatitis: a review of the evidence from randomized controlled trials.
   Am.J.Clin.Dermatol. 9:93-103.
- 85. Gerasimov SV, Vasjuta VV, Myhovych OO et al. (2010) Probiotic supplement reduces atopic dermatitis in preschool children: a randomized, double-blind, placebo-controlled, clinical trial. Am.J.Clin.Dermatol. 11:351-361.
- Hoang BX, Shaw G, Pham P et al. (2010) Lactobacillus rhamnosus cell lysate in the management of resistant childhood atopic eczema. Inflamm. Allergy Drug Targets. 9:192-196.

- 87. Michail SK, Stolfi A, Johnson T et al. (2008) Efficacy of probiotics in the treatment of pediatric atopic dermatitis: a meta-analysis of randomized controlled trials. Ann.Allergy Asthma Immunol. 101:508-516.
- 88. Boyle RJ, Bath-Hextall FJ, Leonardi-Bee J et al. (2008) Probiotics for treating eczema. Cochrane.Database.Syst.Rev. CD006135.
- 89. Brothers S, Asher MI, Jaksic M et al. (2009) Effect of a Mycobacterium vaccae derivative on paediatric atopic dermatitis: a randomized, controlled trial. Clin.Exp.Dermatol. 34:770-775.
- 90. Lee J, Seto D, and Bielory L. (2008) Meta-analysis of clinical trials of probiotics for prevention and treatment of pediatric atopic dermatitis. J.Allergy Clin.Immunol. 121:116-121.
- Shafiei A, Moin M, Pourpak Z et al. (2011) Synbiotics could not reduce the scoring of childhood atopic dermatitis (SCORAD): a randomized double blind placebo-controlled trial. Iran J.Allergy Asthma Immunol. 10:21-28.
- 92. van der Aa LB, Heymans HS, van Aalderen WM et al. (2010) Effect of a new synbiotic mixture on atopic dermatitis in infants: a randomized-controlled trial. Clin.Exp.Allergy 40:795-804.
- 93. Lin R-J, Qiu L-H, Guan R-Z et al. (2015) Protective effect of probiotics in the treatment of infantile eczema. Experimental and therapeutic medicine 9:1593-1596.
- 94. Wang I-J and Wang J-Y. (2015) Children with atopic dermatitis show clinical improvement after Lactobacillus exposure. Clinical and experimental allergy 45:779-787.
- 95. Yang H-J. (2014) Efficacy of probiotic therapy on atopic dermatitis in children: A randomized, double-blind, placebo-controlled trial. Allergy, Asthma and Immunology Research 6:208-215.
- Oh SY. (2013) Antioxidant supplement had a lower effect of atopic dermatitis in young children: A randomized, double-blind, placebo-controlled, clinical trial. Annals of Nutrition and Metabolism 63:1358.
- Camargo CA, Jr., Ganmaa D, Sidbury R et al. (2014) Randomized trial of vitamin D supplementation for winter-related atopic dermatitis in children. J.Allergy.Clin.Immunol. 134:831-835.
- 98. Evangelista MTP AC. (2014) The effect of topical virgin coconut oil on SCORAD index, transepidermal water loss, and skin capacitance in mild to moderate pediatric atopic dermatitis: A randomized, double-blind, clinical trial. International Journal of Dermatology 53:100-108.
- Wananukul S. C. (2013) Randomized, double-blind, split-side, comparison study of moisturizer containing licochalcone a and 1% hydrocortisone in the treatment of childhood atopic dermatitis. Journal of the Medical Association of Thailand 96:1135-1142.
- 100. Jirabundansuk P. (2014) Comparative trial of moisturizer containing spent grain wax, Butyrospermum parkii Extract, Argania spinosa kernel oil vs. 1% hydrocortisone cream in the treatment of childhood atopic dermatitis. Journal of the Medical Association of Thailand 97:820-826.
- 101. Araujo CP. (2013) A proposal for the use of new silver-seaweed-cotton fibers in the treatment of atopic dermatitis. Cutaneous and Ocular Toxicology 32:268-274.
- 102. Thomas KS, Koller K, Dean T et al. (2011) A multicentre randomised controlled trial and economic evaluation of ion-exchange water softeners for the treatment of eczema in children: the Softened Water Eczema Trial (SWET). Health Technol Assess 15:v-156.
- 103. Bath-Hextall FJ, Jenkinson C, Humphreys R et al. (2012) Dietary supplements for established atopic eczema. Cochrane Database Syst Rev 2:CD005205.
- Bamford JT, Ray S, Musekiwa A et al. (2013) Oral evening primrose oil and borage oil for eczema. Cochrane. Database. Syst. Rev. 4:CD004416.

- 105. Danby SG, AlEnezi T, Sultan A et al. (2013) Effect of olive and sunflower seed oil on the adult skin barrier: implications for neonatal skin care. Pediatr Dermatol 30:42-50.
- Silverberg JI, Lee-Wong M, and Silverberg NB. (2014) Complementary and alternative medicines and childhood eczema: a US population-based study. Dermatitis 25:246-254.
- Santer M, Burgess H, Yardley L et al. (2013) Managing childhood eczema: qualitative study exploring carers' experiences of barriers and facilitators to treatment adherence. J Adv Nurs 69:2493-2501.
- Sokolova A and Smith SD. (2015) Factors contributing to poor treatment outcomes in childhood atopic dermatitis. Australas J Dermatol 56:252-257.
- 109. Kupfer J, Gieler U, Diepgen TL et al. (2010) Structured education program improves the coping with atopic dermatitis in children and their parents-a multicenter, randomized controlled trial. J.Psychosom.Res. 68:353-358.
- 110. Schuttelaar ML, Vermeulen KM, Drukker N et al. (2010) A randomized controlled trial in children with eczema: nurse practitioner vs. dermatologist. Br.J.Dermatol. 162:162-170.
- 111. Staab D, Diepgen TL, Fartasch M et al. (2006) Age related, structured educational programmes for the management of atopic dermatitis in children and adolescents: multicentre, randomised controlled trial. BMJ 332:933-938.
- Weber MB, Fontes Neto PT, Prati C et al. (2008) Improvement of pruritus and quality of life of children with atopic dermatitis and their families after joining support groups.
   J.Eur.Acad.Dermatol.Venereol. 22:992-997.
- 113. Pickett K, Loveman E, Kalita N et al. (2015) Educational interventions to improve quality of life in people with chronic inflammatory skin diseases: systematic reviews of clinical effectiveness and cost-effectiveness. Health Technology Assessment (Winchester, England) 19:1-176.
- 114. Ersser SJ, Farasat H, Jackson K et al. (2013) A service evaluation of the Eczema Education Programme: an analysis of child, parent and service impact outcomes. Br J Dermatol 169:629-636.
- 115. Ersser SJ, Cowdell F, Latter S et al. (2014) Psychological and educational interventions for atopic eczema in children. Cochrane Database Syst Rev 1:CD004054.
- 116. Santer M, Muller I, Yrdley L et al. (2014) Supporting self-care for families of children with eczema with a web-based intervention plus health care professional support: pilot randomized controlled trial. Journal of Medical Internet Research 16:e70.