Cochrane Library

Cochrane Database of Systematic Reviews

Interventions for infantile seborrhoeic dermatitis (including cradle cap) (Protocol)

Victoire A, Magin P, Coughlan J, van Driel ML

www.cochranelibrary.com

WILEY

TABLE OF CONTENTS

Interventions for infantile seborrhoeic dermatitis (including cradle cap)

Anousha Victoire[1], Parker Magin[1], Jessica Coughlan[2], Mieke L van Driel[3]

[1]Discipline of General Practice, School of Medicine and Public Health, The University of Newcastle, Newcastle, Australia. [2]c/o Cochrane Skin Group, The University of Nottingham, Nottingham, UK. [3]Discipline of General Practice, School of Medicine, The University of Queensland, Brisbane, Australia

Contact address: Anousha Victoire, Discipline of General Practice, School of Medicine and Public Health, The University of Newcastle, Callaghan, Newcastle, 2308, Australia. anousha.victoire@newcastle.edu.au.

ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

To assess the effects of interventions for infantile seborrhoeic dermatitis in children from birth to 24 months of age.

BACKGROUND

Description of the condition

Infantile seborrhoeic dermatitis (ISD) is a chronic, inflammatory scaling skin condition, which typically causes redness and a patchy, greasy scaling rash in babies and young children. It occurs on skin areas where sebaceous glands are more frequent, that is, hair-bearing and intertriginous areas (where the skin rubs together) (Schwartz 2006). It frequently involves the scalp, where it is commonly referred to as cradle cap, because the hard scaly patches on a red inflamed base can become thickened and confluent, resembling a cap (Elish 2006). The scalp scale can be white or yellow. Infantile seborrhoeic dermatitis can also affect the eyebrows, skin behind the ears, diaper or nappy area, and skin creases of the neck and under the arms. The appearance in the skin creases may be a moist red rash rather than the yellowish scaly rash seen on the scalp (eTG Complete 2013; Janniger 1993). The rash is not itchy or painful, and usually, babies are oblivious to it, though it may cause distress to parents. It is generally self-limiting, clearing by four to six months of age in most cases (Elish 2006; Gelmetti 2011).

The condition occurs worldwide and affects all ethnic groups (Palamaras 2012). It is very common, with the highest point prevalence - as reported in a large community-based study - observed in the first three months of life (71.7%) and a high prevalence in children under one year old (44.5%), reducing to 7.5% for the age range 12 to 23 months (Foley 2003). The majority of these cases are mild. Prevalence subsequently drops to < 1% in children aged three years old (Foley 2003). One community-based cohort study in Germany (Weisse 2012) documented the prevalence of cradle cap as at 58.4% in the first year of life. However, this study only reported doctor diagnosis of the condition, so may have underreported the true prevalence. An Indian study retrospectively reviewed outpatient paediatric dermatology clinic records and reported that 52.4% of children presenting at < 1 year of age had infantile seborrhoeic dermatitis (Sardana 2008).

Given the considerable prevalence of the condition at one year of age but low prevalence in children aged over two years, for the purposes of this review, we use the term 'infantile' loosely to refer to children aged 0 to 24 months. There is some debate about the degree to which ISD is the same entity as adult or adolescent seborrhoeic dermatitis, with some authors defining them as separate conditions bearing no relationship (eTG Complete 2013). Others claim that it is the same disease (Schwartz 2006) or at least similar enough to be able to extrapolate adult treatment data for the paediatric population (Cohen 2004). One study (Mimouni 1995) (with only 46% of participants followed up) cautiously suggested a possible link between ISD and later seborrhoeic dermatitis, although this conflicts with the results of another smaller retrospective cohort study (Menni 1989). Much of the literature on ISD cites research in adult populations when discussing both causes and treatments of the condition. There is similar debate about whether ISD is part of a spectrum leading to atopic dermatitis or psoriasis, a clinical syndrome presentation for several diseases, or a separate condition (Alexopoulos 2013; Elish 2006; Gelmetti 2011; Moises-Alfaro 2002; Neville 1975; Williams 2005). Infantile seborrhoeic dermatitis has been proposed as an umbrella term encompassing several unrelated diseases, such as atopic dermatitis, psoriasis, Langerhans' cell histiocytosis, and erythroderma (reddening due to inflammatory skin disease) (Gelmetti 2011). More traditionally, ISD is seen as a separate condition, with these other disorders considered in the differential diagnosis, i.e., ISD may share signs or symptoms with these other conditions, although it is generally accepted that it can be difficult to distinguish ISD, atopic dermatitis, and psoriasis in very young infants (Gelmetti 2011; Mimouni 1995). Other differential diagnoses include intertrigo (rash in the folds of the body); contact dermatitis; and multiple carboxylase deficiency, including biotinidase deficiency (Gelmetti 2011).

The cause of ISD is not well understood, but several factors are thought to play a role, involving an interplay between sebaceous gland secretions, microflora metabolism, and individual susceptibility (Ro 2005). One suggestion is that overactive sebaceous glands on the skin of newborn babies, under the influence of circulating maternal hormones, may secrete a greasy product that causes old skin cells to stay adherent to the scalp instead of falling off (New Zealand Dermatological Society 2012). It has also been suggested that the presence of increased fatty acids causes excess turnover of scalp cells leading to the flakes of ISD (Ro 2005). The bimodal occurrence of seborrhoeic dermatitis in infancy under the influence of maternal hormones then again in adolescence when androgen production increases with puberty (Ro 2005; Schwartz 2006) supports a hormonal aetiology.

There is an established association between seborrhoeic dermatitis and the yeast Malassezia (formerly Pityrosporum) (Gupta 2004; Zhang 2013). The yeast degrades sebum to release fatty acids, consuming saturated fatty acids as a food source and leaving the unsaturated fatty acids (Ro 2005). Recent studies have iden-

tified 10 species of Malassezia that can be present on the human head, the most common being M. restricta and M. globosa (Ro 2005). Malassezia globosa and M. restricta were identified in over 80% of seborrhoeic dermatitis patients of all ages attending an outpatient dermatology clinic (Zhang 2013). Malassezia furfur has been cultured in significantly higher frequency from children with ISD than children without the condition (Broberg 1995; Ruiz-Maldonado 1989). The response of ISD to antifungals provides supportive evidence of the yeast playing a causative role (Taieb 1990). In a small study, Ruiz-Maldonado cultured Malassezia from 73% of infants with seborrhoeic dermatitis and 53% of controls (Ruiz-Maldonado 1989). This high prevalence even in controls suggests that the condition is not due simply to presence of the yeast, but that individual susceptibility plays a role. In adults, as seborrhoeic dermatitis has been noted to occur even in the presence of normal numbers of yeast, some authors argue that an altered host response to Malassezia leads to the inflammatory skin condition, rather than an overgrowth of the yeast itself (Bergbrant 1989; Gupta 2004).

Severe generalised seborrhoeic dermatitis in children has been noted to be uncommon in otherwise healthy children and can be a presentation of underlying immunodeficiency. Desquamative erythroderma, previously known as Leiner's disease (Prigent 2002), is a rare condition involving severe ISD, which progresses to neonatal erythroderma. It can present with associated immunodeficiency, failure to thrive, and diarrhoea and is now thought to be a cutaneous expression of numerous underlying immunodeficiency disorders, rather than a disease in itself (Gelmetti 2011). Children with human t-cell leukaemia virus type 1 (HTLV-1) and human immunodeficiency virus (HIV) infection have a higher incidence of seborrhoeic dermatitis (Maloney 2004).

Historically, there has been some interest in the role of essential fatty acids in ISD as the skin lesions seen in essential fatty acid deficiency states are similar in appearance to ISD. Fatty acid deficiency was not present in infants with ISD in one study (Erlichman 1981). However, Tollesson and colleagues have described an altered pattern of serum essential fatty acids in children with ISD, which resolves in parallel with clinical resolution of the condition at any age (Tollesson 1993). This could in fact be related to Malassezia metabolism of fatty acids (Ro 2005).

Description of the intervention

While ISD is generally considered a benign and self-limiting condition, for which no treatment may be required (Arora 2007), many treatments have been proposed and are commercially available for it. Several treatments have been studied for adult seborrhoeic dermatitis (Kastarinen 2014). These include anti-inflammatory agents (e.g., topical steroids and calcineurin inhibitors); keratolytics (peeling agents) to soften and remove scale (e.g., salicylic acid, tar, zinc); antifungals to reduce yeast (e.g., ketoconazole, selenium sulfide); and alternative therapies, which may have mul-

tiple mechanisms of action (e.g., tea tree oil shampoo) (Schwartz 2006).

The role of treatments specifically for infantile seborrhoeic dermatitis is less clear. Topical ketoconazole (an antifungal) has been shown to be safe in infants, with minimal systemic absorption detected (Brodell 1998; Taieb 1990). Several authors recommend application of emollient creams or mineral or vegetable oils (e.g., olive oil, borage oil) to soften scale, with or without frequent washing with baby shampoo or medicated shampoo to lift scale, followed by brushing to mechanically remove scale (Elish 2006; Gelmetti 2011; Smoker 2007). Anti-inflammatories, such as topical hydrocortisone cream, have also been recommended for ISD, though concerns have been raised about side-effects (Arora 2007; Wannanukul 2004). Historically, biotin has also been postulated as a treatment, because similar scalp lesions to ISD are seen as part of biotinidase deficiency conditions (Erlichman 1981; Gelmetti 2011; Keipert 1976). Additionally, complementary and alternative medicines are also used to treat ISD. Recently, licochalcone (extracted from *Glycyrrheiza inflata*) has been studied as a treatment for ISD (Wananukul 2012).

Concerns have been raised about the use of olive oil to soften and lift scale, as it promotes a favourable environment for the yeast *Malassezia furfur* to proliferate and may theoretically worsen the condition (Siegfried 2012; Smoker 2007). Concerns have also been raised about keratolytics, such as salicylic acid, which are recommended by some (eTG Complete 2013; Smoker 2007), because of risks of systemic absorption, reportedly the cause of salicylate toxicity in infants after topical application for another condition (Abdel-Magid 1994). Similarly, selenium sulphide, which is used to treat other conditions (Chen 2010), has been reported to cause scalp discolouration (Fitzgerald 1997; Gilbertson 2012), and concerns have been raised about the dangers of systemic absorption (Gelmetti 2011). Additionally, some proposed treatments may have low acceptability for some cultural groups. For example, in people of African-American or African ethnicity with tightly curled hair that requires a lot of styling after washing, frequent hair-washing may be recommended despite indications that low hair-washing frequency is not associated with seborrhoeic dermatitis in African-American girls (Rucker Wright 2010).

How the intervention might work

Proposed treatments for infantile seborrhoeic dermatitis include topical antifungals aimed at reducing the yeast thought to be involved in the pathogenesis of the condition and known to be effective in treating adult seborrhoeic dermatitis. Some other treatments, such as topical steroids, aim to reduce inflammation. Other treatments rely on a mechanical effect, aiming to soften then lift away scale. These treatments include application of oils or keratolytics, followed by washing and brushing, or simply frequent washing with baby shampoos, followed by brushing.

Several studies of adult seborrhoeic dermatitis have noted topical steroids and topical antifungals (particularly ketoconazole) have both been effective, but they suggested that ketoconazole was better at preventing recurrences (Cohen 2004). It is unclear whether evidence for adult seborrhoeic dermatitis can indeed be applied to infantile seborrhoeic dermatitis. Treatments for adults with seborrhoeic dermatitis are the subject of two Cochrane publications: a published protocol, 'Interventions for seborrhoeic dermatitis' (Okokon 2009), and a published systematic review, 'Topical anti-inflammatory agents for seborrhoeic dermatitis of the face or scalp' (Kastarinen 2014).

Why it is important to do this review

While the condition is generally self-limiting and benign, causing no discomfort to the infant, it can cause considerable distress for parents. The myriad of commercially available and home remedies used by parents is evidence for the importance placed on infantile seborrhoeic dermatitis. Importantly, some of the currently used therapies may be harmful, as outlined above, so this review is needed to prevent harm to infants treated needlessly with those agents. Additionally, there has been no previous systematic review that we are aware of that specifically addresses seborrhoeic dermatitis in infants and children.

O B J E C T I V E S

To assess the effects of interventions for infantile seborrhoeic dermatitis in children from birth to 24 months of age.

M E T H O D S

Criteria for considering studies for this review

Types of studies

Only randomised controlled trials (RCTs) of interventions for infantile seborrhoeic dermatitis.

Types of participants

All children from birth to 24 months diagnosed with infantile seborrhoeic dermatitis or cradle cap, based on clinical diagnosis by a healthcare practitioner.

Types of interventions

All interventions, whether behavioural or pharmacological (including complementary and alternative medicines). We will compare the following:

1. any treatment versus no treatment or placebo; or
2. comparison of two or more treatments or combinations of treatments.

We will also group analyses into types of treatment (for example, anti-inflammatory agents, keratolytics, antifungals, or alternative therapies).

Types of outcome measures

We will include trials in the review even if they do not report relevant outcomes, but we will not include these trials in a meta-analysis. We will give reasons for exclusion from analysis.

Primary outcomes

1. Change in severity score from baseline to end of study (described by measures of surface area, redness, crust, or scale) (continuous outcome).
2. Percentage of persons treated who develop adverse effects or intolerance to treatment (dichotomous outcome).

Secondary outcomes

1. Improvement in quality of life (QoL) as reported by parents: either continuous (score on QoL scale) or dichotomous (improved or not).

If studies use different scales of severity or quality of life, we will either standardise these scales (so that they can be combined in a meta-analysis) or describe the outcomes narratively.

Search methods for identification of studies

We aim to identify all relevant RCTs regardless of language or publication status (published, unpublished, in press, or in progress).

Electronic searches

We will search the following databases for relevant trials:
- the Cochrane Skin Group Specialised Register;
- the Cochrane Central Register of Controlled Trials (CENTRAL) in *The Cochrane Library*;
- MEDLINE via Ovid (from 1946);
- Embase via Ovid (from 1974); and
- LILACS (Latin American and Caribbean Health Science Information database, from 1982).

We have devised a draft search strategy for RCTs for MEDLINE (Ovid), which is displayed in Appendix 1. This will be used as the basis for search strategies for the other databases listed.

Trials registers

We will search the following trials registers:
- The metaRegister of Controlled Trials (www.controlled-trials.com).
- The US National Institutes of Health Ongoing Trials Register (www.clinicaltrials.gov).
- The Australian New Zealand Clinical Trials Registry (www.anzctr.org.au).
- The World Health Organization International Clinical Trials Registry platform (www.who.int/ trialsearch).
- The EU Clinical Trials Register (www.clinicaltrialsregister.eu/).

Searching other resources

References from included studies

We will check the bibliographies of included studies for further references to relevant trials.

Unpublished literature

We will search unpublished RCTs and grey literature via web search engines and correspondence with authors and pharmaceutical companies.

Adverse effects

We will not perform a separate search for adverse effects of interventions used for the treatment of infantile seborrhoeic dermatitis. We will consider adverse effects and side-effects described in included studies only.

Data collection and analysis

Some parts of the methods section of this protocol uses text that was originally published in another Cochrane protocol on seborrhoeic dermatitis occurring in adolescents and adults: Okokon EO, Oyo-Ita A, Chosidow O. Interventions for seborrhoeic dermatitis (Protocol). Cochrane Database of Systematic Reviews 2009, Issue 4. Art. No.: CD008138. DOI: 10.1002/14651858.CD008138 (Okokon 2009).

We plan to include at least one 'Summary of findings' table in our review. In this, we will summarise the primary outcomes for the most important comparison. If we feel there are several major comparisons or that our findings need to be summarised for different populations, we will include further 'Summary of findings' tables.

Selection of studies

We will identify titles and abstracts that have been classed as randomised controlled trials on infantile seborrhoeic dermatitis (ISD) and assess if the studies meet the inclusion criteria. We will retrieve the full text of these studies and references that could not be assessed based on title or abstract alone. Two authors (AV and PJM) will independently carry out selection of studies for inclusion and resolve disagreement through discussion and consensus and, if necessary, further discussion with a third author (MVD). We will make attempts to obtain translations of studies not published in English. We will highlight excluded studies and state why we excluded these studies. If we find multiple reports of the same study, we will collate these so that the study, not the report, is the unit of analysis (Chandler 2013).

Data extraction and management

We will adapt the Cochrane Skin Group data extraction form for our review. PJM and AV will perform data extraction independently and make entries onto the form. A third author, MVD, will resolve any disagreements. A 'Characteristics of included studies' table for each study will include details of participant demographics, the type of intervention and comparators, outcomes reported, and the study design.

AV will check the data and enter it into RevMan (Review Manager (RevMan) 2014).

We will use data as presented in the available publications, calculate necessary data from other reported parameters (such as P values and confidence intervals), or request additional data from study authors.

We will compare direction and magnitude of effects reported by studies with how they appear in the review (Chandler 2013).

Assessment of risk of bias in included studies

Two authors (AV and PJM) will independently enter characteristics of studies and 'Risk of bias' assessments into appropriate tables, with any disagreement resolved by consensus and, if necessary, discussion with a third author (MVD).

We will assess the risk of bias in the following domains as outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011):

- method of random sequence generation - we will consider this adequate if generated centrally by means other than the immediate investigator;
- method of allocation concealment - we will consider this adequate if investigators or participants could not be foresee assignment;
- blinding of participants or carers, health professionals, or outcome assessors and whether the measurement of the outcome was likely to be affected if outcome assessors were not blinded;
- attrition bias - loss to follow up and whether intention-to-treat analysis was used;

- selective reporting; and
- other bias - for example, systemic contamination or carry-over effects with split lesion studies, baseline imbalance.

We will assess each item as low risk, high risk, or unclear risk if insufficient information is available to adequately assess the risk and summarise the results in a 'Risk of bias' table.

Measures of treatment effect

For dichotomous outcomes, we will express the results as risk ratios (RR) with a 95% confidence interval (CI) and as a number needed to treat where appropriate with a 95% CI and the baseline risk to which it applies. For continuous outcomes, we will express the results as mean differences (MD) with standard deviations (SD) when the same outcome scales are used, or as standardised mean differences (SMD) with SD when different scales are used in the pooled trials. Where different scales are used and those studies are combined, we will ensure the direction of the scale is the same for each study and report if we have had to reverse the direction to enable the studies to be combined.

Unit of analysis issues

Where there are multiple interventions within a trial, we will use pair-wise comparisons of two interventions or intervention versus placebo. We will avoid double-counting of placebo groups by splitting the placebo group participants evenly over the comparisons, as per the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

In the case of cross-over trials, we will only use the first comparison to avoid contamination due to carry-over effects, unless the risk of these has been assessed to be low, in which case, we will consider each of the treatment cycles for the analysis. We will analyse these combined treatment cycles as in a parallel group design, taking into account that this may underestimate the true effect. We will discuss the impact on the overall estimate in the discussion of the review. We will only pool results of studies of the same design.

We will analyse studies involving different interventions for different body parts on the same individual by considering each body part as the unit of analysis (Higgins 2011). We will evaluate studies involving different interventions for different parts of the same lesion for potential contamination effects, and if this is too high, we will not include the study in meta-analysis and we will provide reasons for our decision. If we assess the risk as low, we will analyse such studies in the same way as a cross-over trial (Higgins 2011). In cluster-randomised trials where the unit of analysis is not the same as the unit of randomisation, we will use analyses from the trials that adjust for clustering. If there are trials that do not adjust for clustering, we will attempt to account for the clustering in our analysis. This may be done through a number of methods ideally based on a direct estimate of the required effect measure, as stated in the *Cochrane Handbook for Systematic Reviews of Interventions*,

section 16.3.3 (Higgins 2011). We will use the generic inverse variance method in RevMan (Review Manager (RevMan) 2014) to pool data from cluster-randomised trials (Higgins 2011).

Dealing with missing data

We will attempt to contact authors of studies with missing data to obtain sufficient data for analysis and pooling. If insufficient information is available to enable 'Risk of bias' assessment, we will classify these studies as having either high risk (if it is likely that the missing information actually refers to absence of an appropriate study process) or unclear risk (if the absence of information could be a reporting issue). We will justify in the 'Risk of bias' table how we came to our decision.

If insufficient information is available for outcome data, we will perform an intention-to-treat (ITT) analysis. In the ITT analysis, we will analyse all participants in the group to which they were randomised, regardless of whether they changed over to another group.

In a sensitivity analysis, we will assess the impact of missing data and assumptions made on the overall estimate of effect (see Sensitivity analysis).

Assessment of heterogeneity

We will assess clinical heterogeneity of studies by examining participants, interventions, and outcomes in each study. If there is no face value heterogeneity (e.g., clearly different populations), we will perform a Chi² test with significance set at a P value of 0.10. We will assess statistical heterogeneity using I² statistic and consider heterogeneity significant where I² statistic is greater than 50%. Where statistical heterogeneity is > 80%, we will not perform a meta-analysis, but summarise studies individually.

Thresholds for the interpretation of the I² statistic can be misleading. We will use the following rough guide to interpretation (Higgins 2011):

- 0% to 40% might not be important;
- 30% to 60% may represent moderate heterogeneity;
- 50% to 90% may represent substantial heterogeneity; and
- 75% to 100% may represent considerable heterogeneity.

Assessment of reporting biases

If we find more than 10 RCTs for an outcome, we will draw a funnel plot to assess the risk of publication bias, which we will inspect for asymmetry.

Data synthesis

We will use the Mantel-Haenszel method for pooling dichotomous data. When pooling continuous data, we will use the mean difference (MD) when outcomes are measured on the same scale or a standardised mean difference (SMD) when different scales are used (Higgins 2011). In the absence of clinical and statistical heterogeneity, we will pool data using a fixed-effect model (Higgins 2011). If significant heterogeneity is present, we will either use a random-effects model, or we will not pool the studies. We will not pool cross-over studies and split body part study designs with parallel studies. Where it is not possible to perform a meta-analysis, we will summarise data from individual studies. Where it is not possible to perform a meta-analysis, we will summarise data from individual studies. We will regard a P value of </= 0.05 as statistically significant. We will interpret a higher P value as a finding of uncertainty, which is not the same as a lack of effect.

We will use the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system to assess the quality of the evidence for each outcome.

Subgroup analysis and investigation of heterogeneity

If substantial clinical or statistical heterogeneity exists amongst the included studies, we will explore the reasons for this by examining factors such as participant age, duration of the rash, and study design.

Where adequate information is given, we will perform further subgroup analyses of infants less than six months old and greater than or equal to six months old.

Sensitivity analysis

If we obtain sufficient evidence, we plan to conduct sensitivity analyses to explore the effects of risk of bias, assessing the effect of excluding poor-quality studies (those with a moderate or high risk of bias) and the effect of missing data (by comparing on-treatment and ITT analyses) on the overall estimate of effect.

ACKNOWLEDGEMENTS

REFERENCES

Additional references

Abdel-Magid 1994

Abdel-Magid EH, el-Awad Ahmed FR. Salicylate intoxication in an infant with ichthyosis transmitted through skin ointment--a case report. *Pediatrics* 1994;**94**(6 Pt 1):939–40. [MEDLINE: 7971016]

Alexopoulos 2013

Alexopoulos A, Kakourou T, Orfanou I, Xaidara A, Chrousos G. Retrospective analysis of the relationship between infantile seborrhoeic dermatitis and atopic dermatitis. *Pediatric Dermatology* 2014;**31**(2):125–130. [PUBMED: 24224924]

Arora 2007

Arora V, Arora S. Management of infantile seborrheic dermatitis. *American Family Physician* 2007;**75**(6):807. [MEDLINE: 17390592]

Bergbrant 1989

Bergbrant IM, Faergemann J. Seborrhoeic dermatitis and Pityrosporum ovale: a cultural and immunological study. *Acta Dermato-Venereologica* 1989;**69**(4):332–5. [MEDLINE: 2568055]

Broberg 1995

Broberg A. Pityrosporum ovale in healthy children, infantile seborrhoeic dermatitis and atopic dermatitis. *Acta Dermato-Venereologica Supplementum* 1995;**191**:1–47. [MEDLINE: 7537004]

Brodell 1998

Brodell RT, Patel S, Venglarcik JS, Moses D, Gemmel D. The safety of ketoconazole shampoo for infantile seborrheic dermatitis. *Pediatric Dermatology* 1998;**15**(5):406–7. [MEDLINE: 9796598]

Chandler 2013

Chandler J, Churchill R, Higgins J, Lasserson T, Tovey D. Methodological standards for the conduct of new Cochrane Intervention Reviews. //editorial-unit.cochrane.org/ sites/editorial-unit.cochrane.org/files/uploads/MECIR_ conduct_standards%202.3%2002122013.pdf (accessed 30 October 2014).

Chen 2010

Chen C, Koch LH, Dice JE, Dempsey KK, Moskowitz AB, Barnes-Eley ML, et al. A randomized, double-blind study comparing the efficacy of selenium sulfide shampoo 1% and ciclopirox shampoo 1% as adjunctive treatments for tinea capitis in children. *Pediatric Dermatology* 2010;**27**(5): 459–62. [MEDLINE: 20735804]

Cohen 2004

Cohen S. Should we treat infantile seborrhoeic dermatitis with topical antifungals or topical steroids?. *Archives of Disease in Childhood* 2004;**89**(3):288–9. [MEDLINE: 14977719]

Elish 2006

Elish D, Silverberg NB. Infantile seborrheic dermatitis. *Cutis* 2006;**77**(5):297–300. [MEDLINE: 16776285]

Erlichman 1981

Erlichman M, Goldstein R, Levi E, Greenberg A, Freier S. Infantile flexural seborrhoeic dermatitis: Neither biotin nor essential fatty acid deficiency. *Archives of Disease in Childhood* 1981;**56**(7):560–2. [MEDLINE: 6455969]

eTG Complete 2013

Dermatology Expert Group. Therapeutic guidelines: dermatology. Version 3. Infantile seborrhoeic dermatitis [revised 2009]. //etg.hcn.com.au/desktop/index.htm?acc= 36422 (accessed June 19 2013).

Fitzgerald 1997

Fitzgerald EA, Purcell SM, Goldman HM. Green hair discoloration due to selenium sulfide. *International Journal of Dermatology* 1997;**36**(3):238–9. [MEDLINE: 9159020]

Foley 2003

Foley P, Zuo Y, Plunkett A, Merlin K, Marks R. The frequency of common skin conditions in preschool-aged children in Australia: seborrheic dermatitis and pityriasis capitis (cradle cap). *Archives of Dermatology* 2003;**139**(3): 318–22. [MEDLINE: 12622623]

Gelmetti 2011

Gelmetti C, Grimalt R. Infantile seborrheic dermatitis. In: Irvine A, Hoeger P, Yan A editor(s). *Harper's Textbook of Pediatric Dermatology*. West Sussex, UK: Wiley-Blackwell, 2011:35.1–35.8.

Gilbertson 2012

Gilbertson K, Jarrett R, Bayliss SJ, Berk DR. Scalp discoloration from selenium sulfide shampoo: a case series and review of the literature. *Pediatric Dermatology* 2012;**29** (1):84–8. [MEDLINE: 21453309]

Gupta 2004

Gupta AK, Nicol K, Batra R. Role of antifungal agents in the treatment of seborrheic dermatitis. *American Journal of Clinical Dermatology* 2004;**5**(6):417–22. [MEDLINE: 15663338]

Higgins 2011

Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Janniger 1993

Janniger CK. Infantile seborrheic dermatitis: an approach to cradle cap. *Cutis* 1993;**51**(4):233–5. [MEDLINE: 8477601]

Kastarinen 2014

Kastarinen H, Oksanen T, Okokon EO, Kiviniemi VV, Airola K, Jyrkk J, et al. Topical anti-inflammatory agents for seborrhoeic dermatitis of the face or scalp. *Cochrane Database of Systematic Reviews* 2014, Issue 5. [DOI: 10.1002/14651858.CD009446.pub2]

Keipert 1976

Keipert JA. Oral use of biotin in seborrhoeic dermatitis of infancy: a controlled trial. *Medical Journal of Australia* 1976;**1**(16):584–5. [MEDLINE: 132601]

Maloney 2004

Maloney EM, Nagai M, Hisada M, Soldan SS, Goebel PB, Carrington M, et al. Prediagnostic human T lymphotropic virus type I provirus loads were highest in Jamaican children who developed seborrheic dermatitis and severe anemia. *Journal of Infectious Diseases* 2004;**189**(1):41–5. [MEDLINE: 14702151]

Menni 1989

Menni S, Piccinno R, Baietta S, Ciuffreda A, Scotti L. Infantile seborrheic dermatitis: seven-year follow-up and some prognostic criteria. *Pediatric Dermatology* 1989;**6**(1): 13–5. [MEDLINE: 2523038]

Mimouni 1995

Mimouni K, Mukamel M, Zeharia A, Mimouni M. Prognosis of infantile seborrheic dermatitis. *Journal of Pediatrics* 1995;**127**(5):744–6. [MEDLINE: 7472828]

Moises-Alfaro 2002

Moises-Alfaro CB, Caceres-Rios HW, Rueda M, Velazquez-Acosta A, Ruiz-Maldonado R. Are infantile seborrheic and atopic dermatitis clinical variants of the same disease?. *International Journal of Dermatology* 2002;**41**(6):349–51. [MEDLINE: 12100690]

Neville 1975

Neville EA, Finn OA. Psoriasiform napkin dermatitis- a follow-up study. *British Journal of Dermatology* 1975;**92**(3): 279–85. [MEDLINE: 125097]

New Zealand Dermatological Society 2012

New Zealand Dermatological Society. DermNet NZ: Cradle cap (infantile seborrhoeic dermatitis). www.dermnetnz.org/dermatitis/cradle-cap.html (accessed 26 June 2013).

Okokon 2009

Okokon EO, Oyo-Ita A, Chosidow O. Interventions for seborrhoeic dermatitis. *Cochrane Database of Systematic Reviews* 2009, Issue 4. [DOI: 10.1002/14651858.CD008138]

Palamaras 2012

Palamaras I, Kyriakis KP, Stavrianeas NG. Seborrheic dermatitis: lifetime detection rates. *Journal of the European Academy of Dermatology & Venereology* 2012;**26**(4):524–6. [MEDLINE: 21521374]

Prigent 2002

Prigent F. Seborrheic dermatitis of infancy [Dermite séborrhéique du nourrisson]. *Archives de Pédiatrie* 2002;**9** (9):970–1. [MEDLINE: 12416520]

Review Manager (RevMan) 2014 [Computer program]

The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Ro 2005

Ro BI, Dawson TL. The role of sebaceous gland activity and scalp microfloral metabolism in the etiology of seborrheic dermatitis and dandruff. *Journal of Investigative Dermatology Symposium Proceedings* 2005;**10**(3):194–7. [MEDLINE: 16382662]

Rucker Wright 2010

Rucker Wright D, Gathers R, Kapke A, Johnson D, Joseph CL. Hair care practices and their association with scalp and hair disorders in African American girls. *Journal of the American Academy of Dermatology* 2010;**64**(2):253–62. [MEDLINE: 20728245]

Ruiz-Maldonado 1989

Ruiz-Maldonado R, López-Matínez R, Pérez Chavarría EL, Rocio Castañón L, Tamayo L. Pityrosporum ovale in infantile seborrheic dermatitis. *Pediatric Dermatology* 1989; **6**(1):16–20. [MEDLINE: 2523039]

Sardana 2008

Sardana K, Mahajan S, Sarkar R, Mediratta V, Bhushan P, Koranne R, et al. The spectrum of skin disease among Indian children. *Pediatric Dermatology* 2009;**26**(1):6–13. [MEDLINE: 19250398]

Schwartz 2006

Schwartz RA, Janusz CA, Janniger CK. Seborrheic dermatitis: an overview. *American Family Physician* 2006; **74**(1):125–30. [MEDLINE: 16848386]

Siegfried 2012

Siegfried E, Glenn E. Use of olive oil for the treatment of seborrheic dermatitis in children. *Archives of Pediatrics & Adolescent Medicine* 2012;**166**(10):967. [MEDLINE: 22893193]

Smoker 2007

Smoker AL. On top of cradle cap. *Journal of Family Health Care.* 2007;**17**(4):134–6. [MEDLINE: 17824212]

Taieb 1990

Taieb A, Legrain V, Palmier C, Lejean S, Six M, Maleville J. Topical ketoconazole for infantile seborrhoeic dermatitis. *Dermatologica* 1990;**181**(1):26–32. [MEDLINE: 2144249]

Tollesson 1993

Tollesson A, Frithz A, Berg A, Karlman G. Essential fatty acids in infantile seborrheic dermatitis. *Journal of the American Academy of Dermatology* 1993;**28**(6):957–61. [MEDLINE: 8496460]

Wananukul 2012

Wananukul S, Chatproedprai S, Charutragulchai W. Randomized, double-blind, split-side comparison study of moisturizer containing licochalcone vs 1% hydrocortisone in the treatment of infantile seborrhoeic dermatitis. *Journal of the European Academy of Dermatology & Venereology* 2012; **26**(7):894–7. [MEDLINE: 21790793]

Wannanukul 2004

Wannanukul S, Chiabunkana J. Comparative study of 2% ketoconazole cream and 1% hydrocortisone cream in the treatment of infantile seborrheic dermatitis. *Journal of the*

Medical Association of Thailand 2004;**87**(Suppl 2):S68–71. [MEDLINE: 16083165]

Weisse 2012

Weisse K, Lehmann I, Heroux D, Kohajda T, Herberth G, Röder S, et al. The LINA cohort: indoor chemical exposure, circulating eosinophil/basophil (eo/B) progenitors and early life skin manifestations. *Clinical & Experimental Allergy* 2012;**42**(9):1337–46. [MEDLINE: 22925320]

Williams 2005

Williams JV, Eichenfield LF, Burke BL, Barnes-Eley M, Friedlander SF. Prevalence of scalp scaling in prepubertal children. *Pediatrics* Jan 2005;**115**(1):e1–6. [MEDLINE: 15629960]

Zhang 2013

Zhang H, Ran Y, Xie Z, Zhang R. Identification of *Malassezia* species in patients with seborrheic dermatitis in China. *Mycopathologia* 2013;**175**(1-2):83–9. [MEDLINE: 23247810]

* *Indicates the major publication for the study*

A P P E N D I C E S

Appendix 1. MEDLINE (Ovid) draft search strategy

1. cradle cap.ti,ab.
2. crusta lactea.ti,ab.
3. milk crust.ti,ab.
4. honeycomb disease.ti,ab.
5. or/1-4
6. pityriasis capitis.ti,ab.
7. seborrhea.ti,ab.
8. Dermatitis, Seborrheic/
9. seborrh$ dermatitis.ti,ab.
10. scalp dermatos$.ti,ab.
11. Scalp Dermatoses/
12. scalp dermatitis.ti,ab.
13. scalp eczema.ti,ab.
14. seborrh$ eczema.ti,ab.
15. or/6-14
16. neonatal.mp.
17. infant$.mp.
18. exp Infant/
19. 16 or 17 or 18
20. 15 and 19
21. 5 or 20
22. randomized controlled trial.pt.
23. controlled clinical trial.pt.
24. randomized.ab.
25. placebo.ab.
26. clinical trials as topic.sh.
27. randomly.ab.
28. trial.ti.
29. 22 or 23 or 24 or 25 or 26 or 27 or 28
30. exp animals/ not humans.sh.
31. 29 not 30
32. 21 and 31

WHAT'S NEW

Date	Event	Description
1 December 2014	Amended	Personal email address removed

CONTRIBUTIONS OF AUTHORS

AV was the contact person with the editorial base.

AV co-ordinated the contributions from the co-authors and wrote the final draft of the protocol.

AV and MvD worked on the methods sections.

AV and PM drafted the clinical sections of the background and responded to the clinical comments of the referees.

AV, PM, and MvD responded to the methodology and statistics comments of the referees.

AV, PM, and MvD contributed to writing the protocol.

JC was the consumer co-author and checked the protocol for readability and clarity. She also ensured that the outcomes are relevant to consumers.

AV is the guarantor of the final review.

The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the NIHR, NHS or the Department of Health, UK.

DECLARATIONS OF INTEREST

Anousha Victoire: nothing to declare.

Parker Magin: nothing to declare.

Jessica Coughlan: nothing to declare.

Mieke L van Driel: nothing to declare.

SOURCES OF SUPPORT

Internal sources

- Australasian Cochrane Centre, Australia.
Training workshop on writing Cochrane protocols and reviews

External sources

- The National Institute for Health Research (NIHR), UK.

The NIHR, UK, is the largest single funder of the Cochrane Skin Group.