Using evidence to inform midwifery practice and advice to parents of well term babies in order to protect baby skin and prevent, or minimise, the risk of atopic disease and distress for young children and their parents in the United Kingdom

A review of evidence on skin care for healthy babies at term and to inform the development of practice guidance

REVIEW PROTOCOL

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Research team: Alison Cooke, Dr Carol Bedwell, Dr Malcolm Campbell, Prof Linda McGowan, Prof Steven Ersser, Prof Dame Tina Lavender

Named Contact: Alison Cooke

Contact e-mail: Alison.Cooke@manchester.ac.uk

Organisational Affiliation: The University of Manchester

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Conflicts of Interest: The research team members have some papers in the topic area which are published, under review or in press. No team members will review their own papers. Professor Dame Tina Lavender and Dr Carol Bedwell have both acted as advisors to Johnson and Johnson. The trials led by Professor Dame Tina Lavender were funded by Johnson and Johnson, although were investigator led and sponsored by the NHS Trusts.

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Contents

1. Introduction

Special care of baby skin is important due to the differences in biological composition between babies and adults; the stratum corneum is 30% thinner and the epidermis is 20% thinner in babies (Stamatas et al 2010). This contrast in the skin structure causes a propensity to increased permeability and dryness. Any topical agent used on baby skin can have a more intensive effect as the ratio of baby body surface to body weight is higher than that for adults (NIkolovski et al 2008). Baby skin is susceptible to increased trans-epidermal water loss (TEWL) and reduced stratum corneum hydration, which are established indicators of less effective skin barrier function. This is due to babies having less lipids, melanin and natural moisturising factors compared to adult skin (Chiou and Blume-Peytavi 2004; Nakagawa et al 2004). Babies also have an elevated skin surface pH (low acidity) which results in increased activity of proteases. These proteases break down corneodesmosomes, the supportive connective elements of the stratum corneum (Cork et al 2009; Hachem et al 2003). The baby skin barrier is developed sufficiently at birth to withstand extrauterine environment, but the barrier continues to be in a transitional state in the early years of life (Nikolovski et al 2008; Stamatas et al 2011; Fluhr et al 2011).

In view of a baby's propensity for reduced skin barrier function, clinical recommendations should incorporate evidence which ensures that only topical products which ensure that the epidermal barrier is not adversely altered or affected are advised. This is particularly important in consideration of the rising prevalence of childhood atopic eczema (Taylor et al 1984; Gupta et al 2004), which cannot be attributed to genetic pre-disposition, but may be linked to environmental factors including the increased availability and use of oils and inappropriately formulated skincare products (Danby et al 2013; 2011; Danby and Cork 2011).

It is known that 45% of diagnoses of atopic eczema occur in the first six months of life, and 60% in the first year (Bieber 2008). This is the period of time when maternity service health professionals have the most influence over parental practices. Parents want to use skin products (Furber et al 2012; Lavender et al 2009), but there is insufficient guidance for midwives, health visitors and other maternity service health professionals to give evidence-based advice on baby skincare. It is possible that current advice is doing more harm than good. A systematic review of the evidence, followed by recommendations for further research and updated clinical guidelines will be of value to health professionals and new parents and may also contribute to reducing the environmental effect of the rising prevalence of atopic eczema.

The University of Manchester, in collaboration with colleagues from the University of Leeds, aim to deliver a review of the evidence on skincare for babies from birth to 6 months, including bathing and cleansing, nappy care, management of dry skin, care of the hair and the scalp, and oils used for baby massage. A systematic review will provide an evidence base to inform parents and health professionals in their skin care practice with newborn term

babies and highlight any areas which require further investigation and research. The age range for the review (birth to six months) has been informed by the overall aim of providing evidence to protect the integrity of newborn infant skin and prevent atopic dermatitis. Atopic dermatitis is usually diagnosed at the earliest around six months of age (Ben-Gashir et al 2004; Wadonda-Kabondo et al 2003; Williams 2000; Kay et al 1994).

2. Review questions

2.1 Primary review questions

i. What is the current clinical practice in maternity units[1] (both hospital and community based settings) and the extent of variation? What are the concerns of health professionals with regard to baby skin care, research and commercial baby skin care products?

ii. What is the level of parental knowledge and behaviour in relation to normal aspects of baby skin care, such as bathing, cord care, nappy care, dry skin, hair and scalp care and baby massage? What concerns and preferences do parents have?

iii. What are the effects of skin care products and practices[2] used for bathing and cleansing, nappy care, hair and scalp care, management of dry skin and topical oils used for baby massage?

iv. What are the economic costs of current skincare practices?

2.2 Specific review questions for topic areas of interest

2.2.1 Bathing and cleansing

i. What are the benefits and risks of delaying baby bathing for a period of time after birth?

ii. What is the evidence for use of commercial baby skincare products for healthy term babies in the immediate postnatal period and up to six months of age?

iii. What are the benefits and risks of daily bathing?

iv. What is the social role of bathing the baby and how do family members feel about advice on bathing and skin care?

v. What is the evidence on the effect of water hardness on baby skin integrity / condition?

2.2.2 Nappy care

i. What is the evidence for efficacy of products for nappy area cleansing such as baby wipes, reusable cloth and water or disposable cotton wool and water?

[1] Scope of the review is healthy term newborn babies. Neonatal units have therefore been excluded.
[2] This will include water use and washing and drying techniques and aids such as cotton wool, gauze, towel etc.

ii. What are the effects on nappy area skin integrity of using products for nappy area cleansing such as baby wipes, reusable cloth and water and disposable cotton wool and water?

iii. What is the evidence for exposing the nappy area of skin to the air for a period of time after nappy changing in babies wearing cloth nappies and babies wearing absorbent gel or other disposable nappies?

iv. What is the evidence for using a nappy barrier cream in babies wearing cloth nappies and babies wearing absorbent gel or other disposable nappies?

v. What are parents' views of nappy care?

2.2.3 Management of dry skin

i. What is the evidence for using topical oil and emollients[3] for the prevention of healthy term baby dry skin from birth up to six months of age?

ii. What is the evidence for using topical oil and emollients for the treatment of healthy term baby dry skin from birth up to six months of age?

iii. What are the benefits and risks of applying topical oil and emollients from birth?

2.2.4 Care of hair and the scalp

i. What is the evidence for the 'soak and seal' approach to treating cradle cap?

ii. What is the evidence for the use of topical oils and emollients for treating cradle cap from birth up to six months of age?

2.2.5 Oils used for baby massage

i. What is the evidence for using natural vegetable oils or mineral oils for baby massage?

ii. What are the effects of topical oils used for baby massage on skin barrier function?

iii. What advice is given by health professionals and massage instructors to new parents with regard to oils for baby massage use?

iv. Which oils are acceptable and preferable to new parents?

3. Aims of the review

i. To highlight what is important for the protection of baby skin in healthy, term babies from birth to six months, with a focus on common aspects of baby care to include:

[3] Includes 'leave on' emollients and bath oils

- Bathing and cleansing
- Nappy care
- Management of dry skin
- Care of hair and the scalp
- Oils used for baby massage.

ii. To produce evidence-based practice guidance to inform health professionals and parents about what is important for the protection of baby skin in healthy, term babies from birth up to six months of age focusing on common aspects of normal baby skincare.

4. Methods

The methods will follow the guidance from NICE (2014).

4.4.1 Criteria for considering studies for this review

4.4.1.1 Types of studies

All randomised and quasi-randomised controlled trials (including cluster and parallel trials in which the baby serves as his / her own control) comparing the effects of any skincare regimen with an alternative regimen or with no treatment will be included. Other high quality observational studies will also be included if appropriate. Qualitative and economic research papers will be included and synthesised separately. Included papers will be published in English in the period 2000 to 2015. If any earlier key papers are deemed to be necessary for completeness of the review, these will be included if agreed by the whole review team.

4.4.1.2 Types of participants

Inclusion criteria: Newborn healthy term ($\geq 37^{+0}$ weeks of gestation) babies receiving common aspects of baby skincare from birth for durations up until six months of age will be included. There will be no upper gestational age limit for eligibility.

Exclusion criteria: Preterm ($<37^{+0}$ weeks of gestation) babies, term babies with nappy rash, term babies with atopic eczema (synonym atopic dermatitis), term babies receiving treatment for these conditions and poorly term babies on neonatal units will not be included.

Dry skin will be diagnosed using a validated skin assessment tool (Lane 1993; Lund 2001), stratum corneum hydration measurement tool (such as a Corneometer®), or by clinical observation by an appropriately trained health professional such as GP, health visitor, midwife, neonatologist, dermatologist or dermatology nurse. Consideration will also be given to parental diagnosis.

Diagnosis of nappy rash or atopic eczema will be made by an appropriately trained health professional such as GP, health visitor, midwife, neonatologist or dermatology professional.

Healthy babies and those with a family history of atopic eczema will be included. Family history of atopic eczema will be defined as 'at least one of mother, father or sibling with a medical diagnosis of atopic eczema/atopic dermatitis and having been prescribed topical steroidal treatment'. Normal baby skin variations such as erythema neonatorum, erythema toxicum, or milia will not be excluded from the review. Impairment of the skin barrier seen in conditions such as collodion baby or congenital ichthyosis, will be excluded.

4.4.1.3 Types of interventions

The following interventions will be reviewed separately:

Intervention:

a. Use of bathing cleanser compared with placebo or no cleanser (water only)

b. Use of napkin emollient compared with placebo or no emollient (water only)

c. Use of napkin wipe compared with no wipe (cotton wool and water only)

d. Use of topical oil compared with placebo or no topical applications

e. Use of topical emollient compared with placebo or no topical applications

f. Use of scalp treatment compared with placebo or no treatment (water only)

Comparators:

a. Intervention cleanser versus another cleanser

b. Intervention emollient versus another emollient

c. Intervention topical oil versus another topical oil

d. Intervention treatment versus another treatment

e. Intervention cleanser/emollient/oil/treatment versus another topical application

It is anticipated that other skincare products may be used by babies in trials. It is also anticipated that there will be diversity in the dose, frequency, body site and duration of application of the interventions. If there is heterogeneity between studies, data will not be pooled and will be reported separately. Where there is homogeneity between studies, meta-analysis will be conducted as appropriate.

4.4.1.4 Types of outcome measures

Where it is appropriate, for quantitative studies data will be pooled for meta-analysis. Where it is necessary, and appropriate, data may be dichotomised. Outcomes will be analysed at baseline and at further time points up to six months, for example, one, three and six months. For qualitative studies, data will be synthesised using the principles of meta-ethnography. If this is not possible, a narrative synthesis will be presented.

4.4.1.4.i *Primary outcomes*

a.) Change in stratum corneum hydration, measured by Corneometer® or similar validated tool, within six months following birth

b.) Change in TEWL, measured by Aquaflux, Tewameter® or similar validated tool, within six months following birth

c.) Change in skin surface pH, measured using a Skin pH meter or similar validated tool, within six months following birth

4.4.1.4.ii *Secondary outcomes*

a.) Change in skin assessment scores, measured using the Neonatal Skin Condition Score (NSCS; Lund et al 2001), or similar validated skin assessment tool, within six months following birth

b.) Change in clinical observation of adverse skin conditions such as erythema/rash, measured by Mexameter® or similar validated tool, or documented clinical examination by midwifery, neonatal or dermatology health professional, within six months following birth

c.) Maternal satisfaction with their baby's skin condition or products used (natural or commercially manufactured), and confidence in their baby's skin care, measured by questionnaire response or qualitative interview, within six months following birth

d.) Systemic or cutaneous infection, confirmed by diagnosis more than 48 hours after birth, as determined by blood culture or culture of swabs from a normally sterile skin site

e.) Atopic eczema, confirmed by clinical diagnosis by a dermatologist or an appropriately trained health professional

f.) Neonatal Behavioural Assessment Scale

g.) Cost (economic) analysis of skin care regimen

h.) Other skin-related outcomes not identified a priori by the research team, but reported by study authors

4.4.2 Search methods for identification of studies

The search protocol will be agreed with the RCM prior to undertaking the search (NICE 2014). The AWOHNN (2013) Neonatal Skincare evidence based guidelines (3rd edition) will be used as a starting point for the review search strategy. The search strategy will 'balance precision and sensitivity' as recommended by the Centre for Public Health Excellence (NICE 2012). This will produce a search that incorporates creating a precise search question, matching the search resources to the research question, adopting a pragmatic and flexible approach to allow continual review of the search process and maintaining an understanding of the evidence base (NICE 2012; 5.3.2).

The PICO search strategy tool (Booth et al 2000) will be used to identify quantitative studies and the SPIDER search strategy tool (Cooke et al 2012) will be used to identify qualitative research papers.

4.4.2.1 Electronic searches

Randomised controlled trials will be identified from the latest issue of the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library. Other trials and observational studies will be identified from MEDLINE, EMBASE, and CINAHL. We will identify ongoing clinical trials through a search of the Clinical Trials Registry (www.clinicaltrials.gov). Grey literature will be identified from ProQuest Dissertation and Theses, and OpenGrey. Searches will also be conducted in the British Nursing Index, Maternity and Infant Care, PsycINFO and AMED. Qualitative papers will also be identified through these databases. We will include studies presented in abstract form if sufficient data are available in the abstract, or from contact with the study author. We will list the full search strategies for each database in the review to ensure that the search process is transparent and reproducible (NICE 2014). References will be managed in Endnote.

Keywords and MeSH terms will be identified following a scoping search using the terms highlighted in tables 1 and 2.

Population	infant* OR bab* OR neonat* OR newborn*
Intervention	(skin* OR skin care OR scalp OR cord OR umbilic*) AND (oil* OR therap* OR treatment* OR bath* OR clean* OR nap* OR diaper* OR massag* OR soap* OR wash* OR detergent* OR shampoo* OR wipe* OR product*)
Comparison	(skin* OR skin care OR scalp OR cord OR umbilic*) AND (emollient* OR cream* OR moistur* OR lubricant* OR powder* OR lotion* OR ointment* OR cloth* OR towel* OR sponge* OR cotton wool OR gauze)
Outcome	skin barrier* OR TEWL OR trans epidermal water loss OR stratum corneum hydration OR skin surface hydration OR hydration OR water loss OR skin pH OR erythema OR rash* OR skin ADJ3 score* OR dry skin OR xerosis OR microbio* OR skin development OR vernix OR seborrh?eic
Quantitative Search using (P) AND (I OR C) AND (O)	

Table 1: PICO scoping search strategy (Booth et al 2000)

Sample	infant* OR bab* OR neonat* OR newborn* OR parent* OR mother* OR father* OR maternal OR paternal
Phenomenon of **I**nterest	(skin* OR skin care OR scalp OR cord OR umbilic* OR dry skin) AND (oil* OR therap* OR treatment* OR bath* OR clean* OR nap* OR diaper* OR massag* OR soap* OR wash* OR detergent* OR shampoo* OR wipe* OR product* OR emollient* OR cream* OR moistur* OR lubricant* OR powder* OR lotion* OR ointment* OR cloth* OR towel* OR sponge* OR cotton wool OR gauze)
Design	questionnaire* OR survey* OR interview* OR focus group* OR case stud* OR observ*
Evaluation	view* OR experience* OR opinion* OR attitude* OR perce* OR belie* OR feel* OR know* OR understand*
Research type	qualitative OR mixed method*
Qualitative Search using [S AND P of I] AND [D OR E OR R]	

Table 2: SPIDER scoping search strategy (Cooke et al 2012)

4.4.2.2 Searching other resources

A three-step search strategy will then be followed:

i.) Electronic database search will be conducted.

ii.) The reference lists of studies generated from the database search will be examined to determine any further relevant papers. The research web pages of major pharmaceutical and cosmetic companies related to baby skin care products will be examined.

iii.) An electronic search of the most relevant journals in the topic area, such as Pediatric Dermatology, Pediatrics, BMC Pediatrics, Journal of Obstetric, Gynecologic and Neonatal Nursing and British Journal of Midwifery, to confirm that any obscure titles not determined by the main search are identified.

4.4.3 Data extraction and quality assessment

The process of quality appraisal, data extraction and analysis will be guided by NICE (2014).

Two review authors will independently assess all of the titles and abstracts of the studies identified for inclusion as a result of the search strategy. Any disagreement will be resolved by consultation with a third review author.

A form will be designed for the extraction of data. For eligible studies, at least two review authors will extract data from the full text of the paper using the agreed form. Discrepancies will be resolved through a third author. Where the eligible studies are those authored by one of the team, an alternative member of the review team will extract the data. We will attempt to contact authors where study information is unclear.

Studies will be quality assessed independently by two review authors using the recommended checklists (NICE 2014: quantitative http://www.ephpp.ca/PDF/Quality%20Assessment%20Tool_2010_2.pdf ; qualitative http://dera.ioe.ac.uk/21069/2/a-quality-framework-tcm6-38740.pdf). Where the eligible studies are those authored by one of the team, an alternative member of the review team will quality appraise the study. For quantitative studies, quality assessment will be presented by outcome using the GRADE approach (Guyatt et al 2008). The quality of evidence is classified as high, moderate, low or very low:

- High – further research is very unlikely to change our confidence in the estimate of effect
- Moderate – further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
- Low – further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
- Very low – any estimate of effect is very uncertain.

For qualitative studies, quality assessment will be presented by individual study using the grading strategy developed by Downe et al (2009) based on the work by Lincoln and Guba (1985) (see appendix 1). If there is sufficient qualitative evidence an integrative review approach is proposed using Whittemore and Knafl's 5-stage methodology (2005): problem identification, literature search, data evaluation, data analysis and presentation. Integrative review methodology allows for the inclusion of studies using a range of methodological approaches.

4.4.4 Strategy for data synthesis

Evidence will be presented for each review question. Evidence tables will illustrate the similarities and differences between studies, and highlight the key characteristics of each study with quality rating. Evidence statements will be provided in order to help the guideline committee to formulate and prioritise recommendations (NICE 2014).

Quantitative synthesis: Meta-analysis will be presented if appropriate. The strength and direction of quantitative evidence will be illustrated using forest plots to highlight the individual study results together with the pooled estimate. If not, the summary of evidence will include descriptive statistics (mean values and standard deviations), effect sizes with confidence intervals, and *p*-values. A narrative summary will be presented which will highlight any gaps in the evidence, key factors affecting the results, an interpretation of the results, and a summary of the key findings.

Qualitative synthesis: Meta-synthesis will be presented if appropriate using the line of argument synthesis process of meta-ethnography (Noblit and Hare 1988). This will be conducted by assembling the findings of the individual studies (Level 1 findings), categorising these findings on the basis of similarity in meaning (Level 2 findings) and then subjecting to meta-synthesis in order to provide a new interpretation of the data as a whole (Level 3 findings) whilst remaining true to the individual study data. Where a new interpretation is not possible, data will be aggregated in narrative form.

The findings from the quantitative and qualitative parts of the review will be synthesised narratively. Relationships in the data will be explored to provide an understanding of the effects of infant skincare regimens and what the views and experiences of parents and health professionals are with regard to current skincare practice. The framework used for this synthesis will be structured using the guidance by Rodgers et al (2006), allowing conclusions to be drawn from the data in a transparent way.

4.4.5 Analysis of subgroups

The following sub-group analyses will be conducted if appropriate:

a) Setting: high resource setting (gross national income (GNI) per capita $4125 or more) versus low resource setting (gross national income (GNI) per capita $4124 or less) (World Bank 2015)

b) Ethnicity (white versus black and minority ethnic)

c) Family history of atopic eczema (at least one of mother, father or sibling with a medical diagnosis of atopic eczema/atopic dermatitis and having been prescribed topical steroidal treatment) versus no family history of atopic eczema

4.4.6 Sensitivity analysis

We will perform sensitivity analyses based on study quality, where appropriate. We will restrict sensitivity analyses to primary outcomes.

4.5 Dissemination

Progress reports will be submitted to the funder, Royal College of Midwives, every two months. Any delays in scheduled progress will be reported immediately with details of a proposed action plan.

The review will follow the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher et al 2009). The review will be presented to the multidisciplinary panel to contribute towards the development of evidence-based guidance.

5. Project plan / timescale

The project is anticipated to be complete within nine months. Work commences on the project the day following the meeting with the RCM and AWHONN. The first three weeks will be spent on refining and compiling the survey, review questions, protocol, conducting a scoping search and defining a search strategy. The protocol and search strategy will be agreed with the RCM prior to conducting the searches. During the second half of October, the searches will be run and examined and the survey will be piloted. During November, evidence will be gathered, and the survey will be made live. The review process will be documented throughout. Quality appraisal and data extraction will take place in December. Data synthesis will be conducted for the review and survey during January and February 2016. Any meta-analysis and sub group analysis will take place in March 2016. The results will then be written up for dissemination during the remaining time. We anticipate presenting the results to the stakeholders during May 2016. These timescales are illustrated in figure 1.

	2015																2016															
Task	September				October				November				December				January				February				March				April				May			
Weeks	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Meeting with RCM/AWHONN																																				
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Data synthesis: review																																				
Data analysis: survey results																																				
Meta-analysis																																				
Sub-group analysis																																				
Write up survey results/review																																				
Dissemination																																				

Figure 1: Project timescale

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7. Appendix 1

Qualitative Quality Assessment Grading System

A	**No, or few flaws. The study credibility, transferability, dependability and confirmability is high.**
B	**Some flaws, unlikely to affect the credibility, transferability, dependability and/or confirmability of the study.**
C	**Some flaws that may affect the credibility, transferability, dependability and/or confirmability of the study.**
D	**Significant flaws that are very likely to affect the credibility, transferability, dependability and/or confirmability of the study.**