National Institute for Health and Care Excellence

Draft for consultation

Acne vulgaris: management

[B] Skin care advice for people with acne vulgaris

NICE guideline number tbc

Evidence review underpinning recommendations 1.2.1 to 1.2.3 (recommendation 1.2.4 is underpinned by evidence report L) and research recommendation 4 in the NICE guideline

December 2020

Draft for Consultation

These evidence reviews were developed by the National Guideline Alliance which is a part of the Royal College of Obstetricians and Gynaecologists

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

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ISBN:

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Skin care advice for people with acne vulgaris

Review question

What skin care advice is appropriate for people with acne vulgaris?

Introduction

People with acne vulgaris need to look after their skin. This will include day-to-day care of the skin, for example cleansing, applying a moisturiser or a sunscreen and when necessary using active medical treatments. Effective skin care is of particular importance for people with acne vulgaris as it will help to ameliorate the effects of treatment and reduce the likelihood of everyday products worsening acne.

Summary of the protocol

Please see Table 1 for a summary of the Population, Intervention, Comparison and Outcome (PICO) characteristics of this review.

Table 1: Summary of the protocol

Population	People with acne vulgaris

Intervention	Advice regarding the use of the following skin care products or skin cleansing practices will be included:
	• Skin products:
	  ○ Cleansing products (e.g. cleansers, cloths, foam washes, soaps, washable solutions, washes)
	  ○ Other non-acne specific skin care products (e.g. make up; moisturisers; oily products; sun cream)
	• Skin cleansing practices/regimens (e.g. washing with water 5 times a day; cloth and no soap 3 times a day, and wash in evening)

Comparison	The following comparisons will be considered: • Any other skin care cleansing product, other non-acne specific skincare product or cleansing practice/regimen • Placebo/sham treatment/untreated

Outcomes	**Critical**
	• Change of acne severity during and at the end of treatment
	  ○ Investigator-reported status
	  ○ Self-reported status
	  ○ Reduction in inflammation of acne lesions
	  ○ Reduction in number of acne lesions
	• Health-related quality of life
	  ○ Disease-specific only
	• Skin-related adverse events (e.g. skin irritation)
	Important
	• Satisfaction with treatment

For further details see the review protocol in appendix A.

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A and the methods document (supplementary document 1).

Declarations of interest were recorded according to NICE's conflicts of interest policy.

Clinical evidence

Included studies

Overall three randomised controlled trials (RCTs) were included in this review, of which 2 were parallel group studies (Korting 1995, Santos-Caetano 2019) and 1 was a split-face trial (Choi 2010).

One study was conducted in South Korea (Choi 2010), 1 in Germany (Korting 1995) and 1 in the USA (Santos-Caetano 2019). All studies included both men and women. Two studies focused on people with mild acne vulgaris (Choi 2010, Korting 1995) and 1 on mild to moderate acne vulgaris (Santos-Caetano 2019). The sample size of the studies ranged from 13 to 122 participants.

All included studies compared different types of skincare products. One parallel-group study compared an acidic syndet (short for synthetic detergent which had a pH in solution: 5.5 to 5.6) bar called 'Sebamed compact' to a conventional 'Lux' soap bar (Korting 1995), whilst another compared reformulated 4% and 10% benzoyl peroxide face washes to an older (and no longer commercially available) 10% formulation face wash (Santos-Caetano 2019). One split-face study compared an enhanced face cleanser containing papain, proteomax, soap powder and 0.04% triclosan, 1% salicylic acid and 1% azelaic acid to a cleanser containing papain, proteomax and soap powder only (Choi 2010).

Evidence was identified for some outcomes such as change in acne severity (change in inflammatory and non-inflammatory lesion counts), skin-related adverse events and satisfaction with the study product.

No evidence was identified for self-reported change of acne severity and skin-specific quality of life. The included studies are summarised in Table 2.

Excluded studies

Studies not included in this review are listed, and reasons for their exclusion are provided in appendix K.

1 Summary of clinical studies included in the evidence review

2 Summaries of the studies that were included in this review are presented in Table 2.

3 **Table 2: Summary of included studies**

Study	Population	Intervention	Comparison	Outcomes
Choi 2010 Split-face RCT South Korea	N=13 (7 females and 6 males) Mean age: 26 Facial acne severity: mild (assessed using Cunliffe's grading system)	• Enhanced (acidic) skin cleanser containing papain, proteomax, soap powder and 0.04% triclosan, 1% salicylic acid and 1% azelaic acid Treatment: twice daily for 4 weeks Study duration: 8 weeks but cleansers were used for first 4 weeks	• Conventional skin cleanser containing papain, proteomax and soap powder	• Change in inflammatory lesion counts • Skin-related adverse events: - prurituis - scales - xerosis
Korting 1995 RCT Germany	N=114 (47 females and 67 males) Mean age (SD) in intervention group: 20.6 (3.4) Mean age (SD) in control group: 19.4 (3.2) Facial acne severity: mild (assessed using Plewig and Klingman's grading system)	• Acidic syndet bar, pH in solution ranging from 5.5 to 5.6, containing sodium cocoyl isethionate, disodium sulfo succinate, wheat starch, paraffin, stearic acid, glyceryl stearate, cetyl palmitate, cetearyl alcohol, water, lecithin, tocopheryl acetate, perfume, lactic acid, PEG-14, disodium EDTA, hydrogenatedcoco-glyceride (and) tocopherol, urea phosphate, glycine, aspartic acid, alanine, pyridoxine hydrochtoride, lysine, leucine, C.I.77891, C.I.47005, and C.I.61570. Treatment: twice daily for 12 weeks Study duration: 12 weeks	• Conventional soap bar	• Change in inflammatory lesion counts • Change in non-inflammatory lesion counts • Skin-related adverse events: - itching - redness - scaling
Santos-Caetano 2019 RCT	N=122 Mean age (SD) in intervention groups: 31.7 (7.7) and 31.4 (6.5)	• Reformulated 4% BPO face wash[1] • Reformulated 10% BPO face wash[1] Treatment: twice daily for	• Older formulation 10% BPO Acne Foaming Wash (no longer commercially	• Skin-related adverse events: - burning sensation - dryness - erythema

Study	Population	Intervention	Comparison	Outcomes
USA	Mean age (SD) in control group: 32.6 (7.7) Female gender (%) in: • 4% reformulated BPO wash group: 73 • 10% reformulated BPO wash group: 80 • 10% older formulation BPO group: 78 Facial acne severity: mild to moderate (defined as grade 2 or 3 on the 2005 IGA scale for acne severity suggested by the US Food and Drug Administration)	21 days (+/-2 days) Study duration: 21 days (3 weeks)	available)	• Study product acceptability (satisfied/very satisfied)

BPO: benzoyl peroxide; IGA: Investigator's Global Assessment; SD: standard deviation; syndet: synthetic detergent

[1] Reformulated products used the sugar-base surfactants sodium laurylglucosides hydroxypropylsulfonate and decyl glucoside instead of potassium lauryl sulphate and sodium lauryl sulphate, and contain a different source of BPO raw material that contains micronized BPO particles.

See the full evidence tables in appendix D. No meta-analysis was conducted (and so there are no forest plots in appendix E).

Quality assessment of clinical studies included in the evidence review

See the evidence profiles in appendix F.

Economic evidence

Included studies

A single economic search was undertaken for all topics included in the scope of this guideline but no economic studies were identified which were applicable to this review question. See the literature search strategy in appendix B and economic study selection flow chart in appendix G.

Excluded studies

No economic studies were reviewed at full text and excluded from this review.

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

Change of acne severity during and at the end of treatment (investigator reported or self-reported, reduction in inflammation and number of acne lesions) were prioritised by the committee as critical outcomes because they indicate whether the treatment is efficacious. Disease-specific health-related quality of life was another critical outcome because it indicates whether the person with acne vulgaris perceives an improvement in acne symptoms. Skin-related adverse events were chosen as a critical outcome and satisfaction with treatment as an important outcome because they indicate whether the intervention is safe in the short-term and the acceptability of the intervention.

The quality of the evidence

The quality of the evidence ranged from very low to moderate, with most of the evidence being of a low quality. This was predominately due to risk of bias of individual studies and imprecision of the effect estimates. Two studies were sponsored by industry.

Benefits and harms

Overall, the evidence on the use of skin care products was very limited. The committee recommended that advising the use of a syndet skin cleansing product for acne vulgaris affected areas, ideally twice daily, should be considered as the evidence suggests that this reduces inflammatory and non-inflammatory acne lesion counts. These bars have an acidic pH level, whereas soap bars are alkaline, therefore syndet skin cleansing products are more gentle to the skin than soap bars. The committee also discussed that, although the research was carried out on a syndet bar, many syndets are now available in different formulations such as liquid or foam, and they agreed that different formulations are probably similarly effective.

No relevant evidence on the use of other skin-care products such as oil-free products or make-up was identified. However, the committee agreed that it was important to say something about the use of skin care products as many people affected by acne vulgaris are concerned about them. Therefore, based on their knowledge and experience, they recommended that people with acne vulgaris should be advised to avoid applying oil-based products whenever possible as these could worsen their acne vulgaris. They agreed that any skin care product applied to the skin should be oil-free, in particular moisturisers, sunscreens and cleansers. They also recommended that people with acne vulgaris using make-up should be advised to use oil-free products and to remove them at the end of the day. They discussed that in their experience oil-based products can make acne vulgaris worse because acne is typified by excessively oily skin.

There was limited evidence of low quality on the use of acidic skin cleansers and benzoyl peroxide-based face washes. Although there was moderate quality evidence for the outcome of participants satisfied or very satisfied with the benzoyl peroxide from 1 study, the committee agreed that a recommendation could not be made based on this outcome. Furthermore, there was little evidence of benefit for other outcomes based on low quality evidence. Therefore, the committee did not make a recommendation about these products.

The committee discussed whether a research recommendation should be made for this topic. Clinicians are frequently asked for advice regarding skin care, such as what is appropriate and effective in people with acne vulgaris. Therefore it is an important topic for people with acne vulgaris. Due to the limited evidence the committee decided to prioritise this for a research recommendation (see appendix L).

Cost effectiveness and resource use

No economic evidence was identified for this review question. The recommendations made by the committee have minimal healthcare resource implications comprising health professionals' time to provide advice. The types of products advised for use are generic and thus incur small costs to people with acne. As skin care products are generally paid for by the person with acne, there are no costs to the health service.

Recommendations supported by this evidence review

This evidence review supports recommendations 1.2.1 to 1.2.3 (recommendation 1.2.4 is supported by evidence from evidence report L- risk factors for scarring) and research recommendation 4 on skin care advice in the guideline.

References

Choi 2010

Choi YS, Suh HS, Yoon MY, Min SU, Kim JS, Jung JY et al. A study of the efficacy of cleansers for acne vulgaris. J Dermatolog Treat 2010, 21(3):201-5

Korting 1995

Korting HC, Ponce-Pöschl E, Klövekorn W, Schmötzer G, Arens-Corell M, Braun-Falco O. The influence of the regular use of a soap or an acidic syndet bar on pre-acne. Infection 1995, 23(2):89-93

Santos-Caetano 2019

Santos-Caetano JP, Cargill MR. A Randomized Controlled Tolerability Study to Evaluate Reformulated Benzoyl Peroxide Face Washes for Acne Vulgaris. J Drugs Dermatol 2019, 18(4):350-356

Appendices

Appendix A – Review protocol

Review protocol for review question: What skin care advice is appropriate for people with acne vulgaris?

Table 3: Review protocol for skin care advice for people with acne vulgaris

Field	Content
PROSPERO registration number	CRD42019137733
Review title	Skin care advice for people with acne vulgaris
Review question	What skin care advice is appropriate for people with acne vulgaris?
Objective	The aim of this review is to determine what the best skin care advice is for people with acne vulgaris
Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE Searches will be restricted by: • Date: No restriction • Language of publication: English language only • Publication status: Conference abstracts will be excluded because these do not typically provide sufficient information to fully assess risk of bias • Standard exclusions filter (animal studies/low level publication types) will be applied • For each search (including economic searches), the principal database search strategy is quality assured by a second information specialist using an adaption of the PRESS 2015 Guideline Evidence-Based Checklist
Condition or domain being studied	• Acne vulgaris
Population	• Inclusion: People with acne vulgaris • Exclusion: Neonatal acne

Intervention	Advice regarding the use of the following skin care products or skin cleansing practices will be included:
	• Skin products:
	  ○ Cleansing products (for example cleansers, cloths, foam washes, soaps, washable solutions, washes)
	  ○ Other non-acne specific skin care products (for example make up, moisturisers, oily products, sun cream)

	• Skin cleansing practices/regimens (for example washing with water 5 times a day, cloth and no soap 3 times a day, and wash in evening) Note: The committee recognise that it is difficult to distinguish between topical and skin care products but will assume that the main difference is how long the relevant substance stays on the skin irrespective of their active ingredients. As such, products that are washed off or do not stay on the skin for very long (for example less than 15 minutes) will be included in this review, whilst products that stay on the skin (for example for more than 15 minutes) will be included in the topical treatment review. Generally, cleansing products that come in the form of cleansers, cloths, foam washes, and soaps will be included in this review, whilst products that come in the form of creams, non-washable foam, gels, lotions, and ointments, and non-washable solutions (topical treatments) will be examined in two network meta-analyses and 2 pairwise meta-analyses (E1/E2 for mild to moderate acne and F1/F2 for moderate to severe acne). The committee will be consulted regarding how a study should be categorised if the method of treatment is unclear or not described.
Comparator	The following comparisons will be considered: • Any other skin care cleansing product, other non-acne specific skincare product, or cleansing practice/regimen • Placebo/sham treatment/untreated
Types of study to be included	• Systematic reviews/meta-analyses of randomised controlled trials (RCTs) • Randomised or quasi-randomised controlled trials Note: For further details, see the algorithm in appendix H, Developing NICE guidelines: the manual.
Other exclusion criteria	Studies with indirect population: where studies with a mixed population [that is including people with acne vulgaris and another condition different to acne vulgaris] are identified, those with <66% of the relevant population will be excluded, unless subgroup analysis for acne vulgaris has been reported.
Context	Recommendations will apply to those receiving care in all healthcare settings (for example community, primary, secondary care).

Primary outcomes (critical outcomes)	**Critical outcomes**
	• Change of acne severity during and at the end of treatment:
	  ○ Investigator-reported status
	  ○ Self-reported status
	  ○ Reduction in inflammation of acne lesions
	  ○ Reduction in number of acne lesions
	• Health-related quality of life
	  ○ Disease-specific only
	• Skin-related adverse events (for example skin irritation)

Secondary outcomes (important outcomes)	**Important outcomes** • Satisfaction with treatment

Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into STAR and de-duplicated. Review questions selected as high priorities for health economic analysis (and those selected as medium priorities and where health economic analysis could influence recommendations) will be subject to dual weeding and study selection; any discrepancies above 10% of the dual weeded resources will be resolved through discussion between the first and second reviewers or by reference to a third person. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). All data extraction will quality assured by a senior reviewer. Draft excluded studies and evidence tables will be circulated to the Topic Group for their comments. Resolution of disputes will be by discussion between the senior reviewer, Topic Advisor and Chair.
Risk of bias (quality) assessment	Risk of bias of individual studies will be assessed using the preferred checklist as described in Developing NICE guidelines: the manual.
Strategy for data synthesis	**Synthesis of data:** • For dichotomous outcomes, intention-to-treat (ITT) data will be used if available; if not then available data will be used. • Meta-analysis will be conducted where appropriate. • Final and change scores will be pooled and if any study reports both, change scores will be used in preference over final scores. • If studies only report p-values from parametric analyses, and 95% CIs cannot be calculated from other data provided, the SMD will be calculated and plotted in RevMan using the generic inverse variance method. • If studies only report p-values from non-parametric analyses and mean/SE/SD cannot be calculated, this information will be included in GRADE tables but downgraded by one level as imprecision cannot be assessed for such analyses. **Sensitivity analysis** Sensitivity analysis will be conducted according to risk of bias of individual studies. Missing data will be accounted for in the risk of bias assessment. **Heterogeneity:** Heterogeneity will be assessed by visual examination of the forest plots and by the I2 statistic (where I2≥50% indicates serious heterogeneity and I2≥80 indicates very serious heterogeneity) **Minimal important differences (MIDs):** • Default MIDs will be used for risk ratios and continuous outcomes only, unless the committee pre-specifies published or other MIDs for specific outcomes • For risk ratios: 0.8 and 1.25. • For continuous outcomes: +/-0.5 times the baseline SD of the control arm. If there are 2 studies, the MID is calculated as +/- 0.5 times the mean of the SDs of the control arms at baseline. If there are 3 or more studies, the MID is calculated as +/- 0.5 times the median of the SDs of the control arms at baseline. If baseline SD is not available, then SD at follow up will be used. **Appraisal of methodological quality:** • The methodological quality of each study will be assessed using an

	appropriate checklist as per the NICE guidelines manual. • The quality of the evidence will be assessed by GRADE for each outcome according to the process described in the NICE guidelines manual. • If studies only report p-values from non-parametric analyses, this information will be included in GRADE tables but downgraded by one level as imprecision cannot be assessed for such analyses.		
Analysis of sub-groups	Stratified analysis will be conducted for the following groups: • Severity of acne o Mild o Moderate and severe Note: Recommendations will apply to all people with acne vulgaris unless there is evidence of difference for these subgroups. The guideline will look at inequalities relating to people of darker skin colour, people with pre-existing mental health conditions, transgender people and people whose first language is not English.		
Type and method of review	☒	Intervention	
	☐	Diagnostic	
	☐	Prognostic	
	☐	Qualitative	
	☐	Epidemiologic	
	☐	Service Delivery	
	☐	Other (please specify)	
Language	English		
Country	England		
Anticipated or actual start date	30 May 2019		
Anticipated completion date	13 January 2021		
Stage of review at time of this submission	**Review stage**	**Started**	**Completed**
	Preliminary searches	☑	☑
	Piloting of the study selection process	☐	☐
	Formal screening of search results against eligibility criteria	☑	☑
	Data extraction	☑	☑
	Risk of bias (quality) assessment	☑	☑
	Data analysis	☑	☑
Named contact	**5a. Named contact**		

	National Guideline Alliance **5b Named contact e-mail** AcneManagement@nice.org.uk **5e Organisational affiliation of the review** National Institute for Health and Care Excellence (NICE) and National Guideline Alliance
Review team members	National Guideline Alliance
Funding sources/sponsor	This systematic review is being completed by the National Guideline Alliance, which is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists. NICE funds the National Guideline Alliance to develop guidelines for those working in the NHS, public health, and social care in England.
Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/gid-ng10109/documents/committee-member-list
Other registration details	
Reference/URL for published protocol	https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=137733
Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
Keywords	Acne; advice; makeup; skin care; skin cleansing.
Details of existing review of same topic by same authors	Not applicable

Current review status	☒	Ongoing
	☒	Completed but not published
	☐	Completed and published
	☐	Completed, published and being updated
	☐	Discontinued
Additional information		
Details of final publication	www.nice.org.uk	

GRADE: Grading of Recommendations Assessment, Development and Evaluation; MID: minimally important difference; NHS: National health service; NICE: National Institute for Health and Care Excellence; RCT: randomised controlled trial; SD: standard deviation; SE: standard error; SMD: standard mean difference.

Appendix B – Literature search strategies

Literature search strategies for review question: What skin care advice is appropriate for people with acne vulgaris?

Clinical search

Date of search: 11/06/2019

Database(s): Embase Classic+Embase 1947 to 2019 June 04, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to June 04, 2019

Multifile database codes: emczd = Embase Classic+Embase; ppez= MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily

#	Searches
1	exp Acne Vulgaris/ use ppez
2	exp acne/ use emczd
3	acne.tw.
4	or/1-3
5	(exp counseling/ or education/ or health education/ or exp health promotion/ or medical information/ or patient education/ or patient information/ or patient preference/ or patient satisfaction/ or public health/) use emczd
6	(exp Counseling/ or Education/ or exp Health Education/ or Nurses Instruction/ or Patient Education as Topic/ or exp Patient Satisfaction/ or Programmed Instruction/) use ppez
7	(advice or advis* or counsel* or direct* or educat* or encourag* or guid* or indicat* or instruct* or promot* or recommend* or suggest*).tw.
8	or/5-7
9	(skin care/ or skin protection/) use emczd
10	exp Skin Care/ use ppez
11	hygiene/
12	(detergent/ or soap/) use emczd
13	exp water/
14	exp dermatological agent/ use emczd
15	topical antiinfective agent/ use emczd
16	exp Surface-Active Agents/ use ppez
17	exp Dermatologic Agents/ use ppez
18	exp Anti-Infective Agents, Local/ use ppez
19	exp Astringents/ use ppez
20	benzoyl peroxide/
21	salicylic acid/
22	(sunburn/pc or exp sunscreen/) use emczd
23	(Sunburn/pc or exp Sunscreening Agents/) use ppez
24	(antiseptic* or astringent* or cleans* or cloth*1 or cosmetic*1 or dermocosmetic* or detergent* or emollient* or hygien* or keratolytic* or lotion* or makeup or make-up or moisturi* or noncomedogenic or non-comedogenic or photoprotect* or photo-protect* or soap* or syndet or sunscreen* or sunblock* or (sun adj1 (block* or cream* or lotion* or protect*)) or wash* or water* or wipe*).tw.
25	(azelaic acid* or benzoyl peroxide* or hydroxy acid* or glycolate* or glycolic acid* or lactate* or lactic acid* or niacinamide or retinol or retinoid* or salicylic acid* or tea tree oil* or zinc acetate).tw.
26	(skincare or (skin adj2 (care or practic* or product* or regimen* or routine*))).tw.
27	or/9-26
28	4 and 8 and 27
29	limit 28 to english language
30	Letter/ use ppez
31	letter.pt. or letter/ use emczd
32	note.pt.
33	editorial.pt.
34	Editorial/ use ppez
35	News/ use ppez
36	exp Historical Article/ use ppez
37	Anecdotes as Topic/ use ppez
38	Comment/ use ppez
39	Case Report/ use ppez
40	case report/ or case study/ use emczd
41	(letter or comment*).ti.
42	or/30-41
43	randomized controlled trial/ use ppez

#	Searches
44	randomized controlled trial/ use emczd
45	random*.ti,ab.
46	or/43-45
47	42 not 46
48	animals/ not humans/ use ppez
49	animal/ not human/ use emczd
50	nonhuman/ use emczd
51	exp Animals, Laboratory/ use ppez
52	exp Animal Experimentation/ use ppez
53	exp Animal Experiment/ use emczd
54	exp Experimental Animal/ use emczd
55	exp Models, Animal/ use ppez
56	animal model/ use emczd
57	exp Rodentia/ use ppez
58	exp Rodent/ use emczd
59	(rat or rats or mouse or mice).ti.
60	or/47-59
61	29 not 60
62	clinical Trials as topic.sh. or (controlled clinical trial or pragmatic clinical trial or randomized controlled trial).pt. or (placebo or randomi#ed or randomly).ab. or trial.ti.
63	62 use ppez
64	(controlled clinical trial or pragmatic clinical trial or randomized controlled trial).pt. or drug therapy.fs. or (groups or placebo or randomi#ed or randomly or trial).ab.
65	64 use ppez
66	crossover procedure/ or double blind procedure/ or randomized controlled trial/ or single blind procedure/ or (assign* or allocat* or crossover* or cross over* or ((doubl* or singl*) adj blind*) or factorial* or placebo* or random* or volunteer*).ti,ab.
67	66 use emczd
68	63 or 65
69	67 or 68
70	Meta-Analysis/
71	exp Meta-Analysis as Topic/
72	systematic review/
73	meta-analysis/
74	(meta analy* or metanaly* or metaanaly*).ti,ab.
75	((systematic or evidence) adj2 (review* or overview*)).ti,ab.
76	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
77	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
78	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
79	(search* adj4 literature).ab.
80	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
81	cochrane.jw.
82	((pool* or combined) adj2 (data or trials or studies or results)).ab.
83	(or/70-72,74,76-81) use ppez
84	(or/72-75,77-82) use emczd
85	or/83-84
86	69 or 85
87	61 and 86

Date of search: 11/06/2019

Database(s): The Cochrane Library: Cochrane Database of Systematic Reviews, Issue 6 of 12, June 2019; Cochrane Central Register of Controlled Trials, Issue 6 of 12, June 2019

ID	Search
#1	MeSH descriptor: [Acne Vulgaris] explode all trees
#2	acne:ti,ab
#3	#1 or #2
#4	MeSH descriptor: [Counseling] explode all trees
#5	MeSH descriptor: [Education] this term only
#6	MeSH descriptor: [Health Education] explode all trees
#7	MeSH descriptor: [Nurses Instruction] this term only
#8	MeSH descriptor: [Patient Education as Topic] this term only
#9	MeSH descriptor: [Programmed Instruction] this term only
#10	MeSH descriptor: [Patient Satisfaction] explode all trees
#11	(advice or advis* or counsel* or direct* or educat* or encourag* or guid* or indicat* or instruct* or promot* or recommend* or suggest*):ti,ab
#12	{or #4-#11}
#13	MeSH descriptor: [Skin Care] explode all trees
#14	MeSH descriptor: [Hygiene] this term only

ID	Search
#15	MeSH descriptor: [Water] explode all trees
#16	MeSH descriptor: [Surface-Active Agents] explode all trees
#17	MeSH descriptor: [Dermatologic Agents] explode all trees
#18	MeSH descriptor: [Anti-Infective Agents, Local] explode all trees
#19	MeSH descriptor: [Astringents] this term only
#20	MeSH descriptor: [Benzoyl Peroxide] explode all trees
#21	MeSH descriptor: [Salicylic Acid] explode all trees
#22	MeSH descriptor: [Sunburn] this term only and with qualifier(s): [prevention & control - PC]
#23	MeSH descriptor: [Sunscreening Agents] explode all trees
#24	(antiseptic* or astringent* or cleans* or cloth or cloths or cosmetic or cosmetics or dermocosmetic* or detergent* or emollient* or hygien* or keratolytic* or lotion* or makeup or make-up or moisturi* or noncomedogenic or non-comedogenic or photoprotect* or photo-protect* or soap* or syndet or sunscreen* or sunblock* or (sun near/1 (block* or cream* or lotion* or protect*)) or wash* or water* or wipe*):ti,ab
#25	(azelaic acid* or benzoyl peroxide* or hydroxy acid* or glycolate* or glycolic acid* or lactate* or lactic acid* or niacinamide or retinol or retinoid* or salicylic acid* or tea tree oil* or zinc acetate):ti,ab
#26	(skincare or (skin near/2 (care or practic* or product* or regimen* or routine*))):ti,ab
#27	{or #13-#26}
#28	#3 and #12 and #27

Health Economics search

Date of initial search: 12/12/2018

Date of updated search: 06/05/2020

Database{s): Embase 1980 to 2020 May 05, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to May 05, 2020

Multifile database codes: emez = Embase; ppez = MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily

#	Searches
1	exp Acne Vulgaris/ use ppez
2	exp acne/ use emez
3	acne.tw.
4	or/1-3
5	Economics/
6	Value of life/
7	exp "Costs and Cost Analysis"/
8	exp Economics, Hospital/
9	exp Economics, Medical/
10	Economics, Nursing/
11	Economics, Pharmaceutical/
12	exp "Fees and Charges"/
13	exp Budgets/
14	(or/5-13) use ppez
15	health economics/
16	exp economic evaluation/
17	exp health care cost/
18	exp fee/
19	budget/
20	funding/
21	(or/15-20) use emez
22	budget*.ti,ab.
23	cost*.ti.
24	(economic* or pharmaco?economic*).ti.
25	(price* or pricing*).ti,ab.
26	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
27	(financ* or fee or fees).ti,ab.
28	(value adj2 (money or monetary)).ti,ab.
29	or/22-27
30	14 or 21 or 29
31	4 and 30
32	limit 31 to english language
33	limit 32 to yr="2004 -Current"
34	remove duplicates from 33

Date of initial search: 12/12/2018

Date of updated search: 06/05/2020

Databases(s): NIHR Centre for Reviews and Dissemination: Health Technology Assessment Database (HTA) and the NHS Economic Evaluation Database (NHS EED)

#	Searches
1	MeSH DESCRIPTOR Acne Vulgaris EXPLODE ALL TREES
2	(acne) IN NHSEED, HTA FROM 2004 TO 2018
3	#1 OR #2

Search for health utility values

Date of initial search: 29/01/2019

Date of updated search: 06/05/2020

Database{s): Embase 1980 to 2020 May 05, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to May 05, 2020

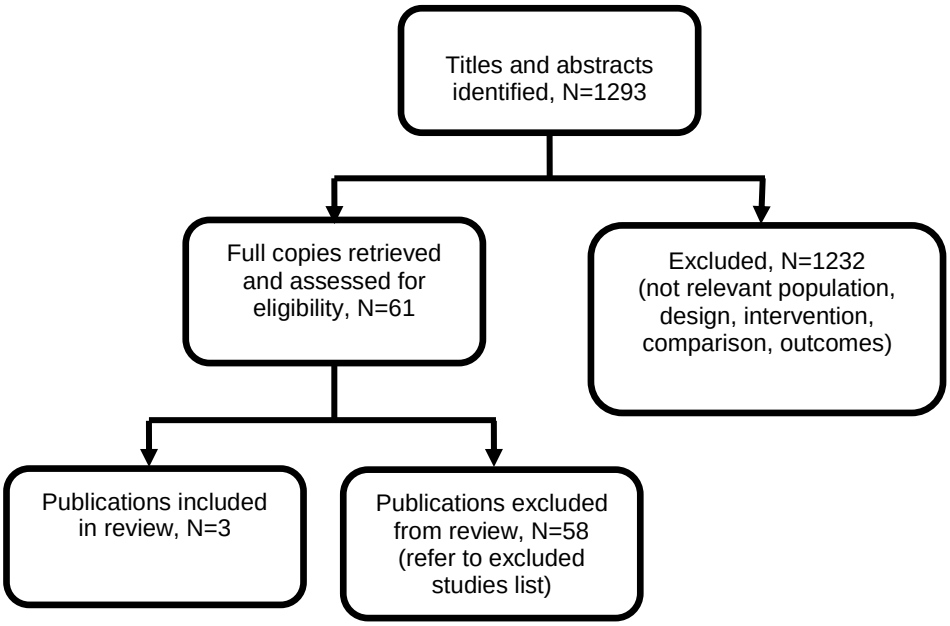
Multifile database codes: emez = Embase; ppez = MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily

#	Searches
1	exp Acne Vulgaris/ use ppez
2	exp acne/ use emez
3	acne.tw.
4	or/1-3
5	Quality-Adjusted Life Years/ use ppez
6	Sickness Impact Profile/
7	quality adjusted life year/ use emez
8	"quality of life index"/ use emez
9	(quality adjusted or quality adjusted life year*).tw.
10	(qaly* or qal or qald* or qale* or qtime* or qwb* or daly).tw.
11	(illness state* or health state*).tw.
12	(hui or hui2 or hui3).tw.
13	(multiattibute* or multi attribute*).tw.
14	(utilit* adj3 (score*1 or valu* or health* or cost* or measur* or disease* or mean or gain or gains or index*)).tw.
15	utilities.tw.
16	(eq-5d* or eq5d* or eq-5* or eq5* or euroqual* or euro qual* or euroqual 5d* or euro qual 5d* or euro qol* or euroqol*or euro quol* or euroquol* or euro quol5d* or euroquol5d* or eur qol* or eurqol* or eur qol5d* or eurqol5d* or eur?qul* or eur?qul5d* or euro* quality of life or european qol).tw.
17	(euro* adj3 (5 d* or 5d* or 5 dimension* or 5dimension* or 5 domain* or 5domain*)).tw.
18	(sf36 or sf 36 or sf thirty six or sf thirtysix).tw.
19	(time trade off*1 or time tradeoff*1 or tto or timetradeoff*1).tw.
20	Quality of Life/ and ((quality of life or qol) adj (score*1 or measure*1)).tw.
21	Quality of Life/ and ec.fs.
22	Quality of Life/ and (health adj3 status).tw.
23	(quality of life or qol).tw. and Cost-Benefit Analysis/ use ppez
24	(quality of life or qol).tw. and cost benefit analysis/ use emez
25	((qol or hrqol or quality of life).tw. or *quality of life/) and ((qol or hrqol* or quality of life) adj2 (increas* or decreas* or improv* or declin* or reduc* or high* or low* or effect or effects or worse or score or scores or change*1 or impact*1 or impacted or deteriorat*)).ab.
26	Cost-Benefit Analysis/ use ppez and cost-effectiveness ratio*.tw. and (cost-effectiveness ratio* and (perspective* or life expectanc*)).tw.
27	cost benefit analysis/ use emez and cost-effectiveness ratio*.tw. and (cost-effectiveness ratio* and (perspective* or life expectanc*)).tw.
28	*quality of life/ and (quality of life or qol).ti.
29	quality of life/ and ((quality of life or qol) adj3 (improv* or chang*)).tw.
30	quality of life/ and health-related quality of life.tw.
31	Models, Economic/ use ppez
32	economic model/ use emez
33	or/5-32
34	4 and 33
35	limit 34 to english language
36	limit 35 to yr="2004 -Current"
37	remove duplicates from 36

Appendix C – Clinical evidence study selection

Clinical study selection for: What skin care advice is appropriate for people with acne vulgaris?

Figure 1: Study selection flow chart



Appendix D – Evidence tables

Evidence tables for review question: What skin care advice is appropriate for people with acne vulgaris?

Table 4: Evidence table

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Choi, Y. S., Suh, H. S., Yoon, M. Y., Min, S. U., Kim, J. S., Jung, J. Y., Lee, D. H., Suh, D. H., A study of the efficacy of cleansers for acne vulgaris, Journal of Dermatological Treatment, 21, 201-5, 2010 **Ref Id** 868217 **Country/ies where the study was carried out** South Korea **Study type** split-face RCT (description in the paper: a split-face, double-blind, randomised controlled study) **Aim of the study**	**Sample size** N=13 **Characteristics** Mean age: 26 years; Gender: male = 6, female = 7 **Inclusion criteria** People aged 20-37 years with mild facial acne grades of 0.25 to 2 according to Cunliffe's grading system and otherwise healthy. **Exclusion criteria** Not reported	**Interventions** Intervention: Cleanser A: papain, proteomax and soap powder (made by NanoPharm Corporation, Seoul Korea) **Comparison:** Cleanser B: same as cleanser A plus 0.04% triclosan, 1% salicylic acid and 1% azelaic acid (made by NanoPharm Corporation, Seoul Korea) Treatment: Participants were instructed to use each cleanser for 4 weeks twice daily (morning and evening) and not to use these cleaners during the following 4 weeks. No use of other facial treatment was permitted during the study and all acne medications were stopped 6 weeks prior to the study.	**Details** Randomisation: At initial visit, the sides of patients' faces were randomly assigned to cleanser A or B, and they were provided with appropriately labelled cleansers. Outcome definition: 1) Change (%) in inflammatory lesion counts (baseline to week 8, that is 4 weeks after discontinuation of the intervention) 2) Skin-related adverse events): xerosis scales pruritus Time points of investigation:	**Results** **Change (%) in inflammatory lesion counts (baseline to week 8, that is 4 weeks after discontinuation of the intervention*):** *Cleanser A* (n=13): 53% of baseline *Cleanser B* (n=13): 13% of baseline, p<0.05** *no sufficient data reported to calculate a difference in the improvement of acne from baseline to 4-week follow-up between the 2 trial groups **this p-value was used by the NGA technical team to calculate a standard mean difference between the 2 study groups (conservative estimate as no exact p-value provided) **Skin-related adverse events (n=13):**	**Limitations** **Methodological limitations assessed using the Cochrane risk-of-bias tool for randomised trials (RoB2**) Selection bias: some concerns (no information provided about the allocation concealment) Performance bias: low risk of bias Attrition bias: low risk of bias Detection bias: some concerns (no information provided how the study product was used by the participants but assume a wash as it is a cleanser and the authors mention facial washing) Reporting bias: low risk of bias Other bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
To evaluate the efficacy and safety of an acne cleanser incorporating 0.04% triclosan, 1% salicylic acid, and 1% azelaic acid, and associated histopathologic changes in mild acne vulgaris patients. **Study dates** Not reported **Source of funding** This study was supported by Seoul National University Hospital Grant (06-2007-142-0)			Participants were evaluated over the course of the 8-week study period, that is baseline, week 2, 4 and 8 weeks. After 4 weeks participants discontinued using cleansers for the following 4 weeks. Analysis: Not reported but it looks like an intention-to-treat Adherence: All participants completed the study	Xerosis: Cleanser A: 0/13 Cleanser B: 0/13 Scales: Cleanser A: 0/13 Cleanser B: 0/13 Pruritus: Cleanser A: 0/13 Cleanser B: 0/13	Overall risk of bias: some concerns
Full citation Korting, H. C., Ponce-Poschl, E., Klovekorn, W., Schmotzer, G., Arens-Corell, M., Braun-Falco, O., The influence of the regular use of a soap or an acidic syndet bar on pre-acne, Infection, 23, 89-93, 1995 **Ref Id** 869052	**Sample size** N=120 randomised but n=114 analysed; of those n=57 received "Sebamed compact" an acidic bar syndet and n=57 received a conventional bar soap ("Lux") **Characteristics** Male gender: acidic syndet bar group = 32/57; conventional soap group = 35/57 Mean age (SD): acidic syndet	**Interventions** Intervention: skin cleanser "Sebamed compact" an acidic bar syndet (pH in solution: 5.5 to 5.6) composed of sodium cocoyl isethionate, disodium sulfo succinate, wheat starch, paraffin, stearic acid, glyceryl stearate, cetyl palmitate, cetearyl alcohol, water, lecithin, tocopheryl acetate, perfume, lactic acid, PEG-14, disodium EDTA, hydrogenatedcoco-glyceride (and) tocopherol, urea phosphate, glycine, aspartic acid, alanine,	**Details** Randomisation: intervention was assigned to the participants by an institution outside the trial centre according to a random plan in written form via telefax letter on an individual basis. Outcome definition: the number of	**Results** **Change in inflammatory lesions (mean (SD), baseline to 12 weeks):** *Acidic syndet bar group (n=57):* baseline = 13.4 (5.2) at 12 weeks = 10.4 (5.8) mean change (SD)* = -3 (3.68) *Conventional soap group (n=57):*	**Limitations** **Methodological limitations assessed using the Cochrane risk-of-bias tool for randomised trials (RoB2)** Selection bias: some concerns (not described what form of randomisation was used; it stated only that treatment was assigned to the participants by an institution outside the trial

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Country/ies where the study was carried out Germany **Study type** RCT (description in the paper: mono-centric, randomised, open, parallel-controlled trial in a dermatologic office) **Aim of the study** To assess the relative value of an acidic syndet bar and a conventional soap bar in the prevention of acne lesions in acne-prone patients. **Study dates** June 1992 to June 1993 **Source of funding** Supported by a grant from Sebapharma, Boppard, Germany	bar group = 20.6 (3.4); conventional soap group = 19.4 (3.2) **Inclusion criteria** Two to 20 inflammatory lesions of acne vulgaris, that is, papulopustules, on each side of the face (classification by Plewig and Kligman, 1975)*; age between 14 and 24 years; written informed consent after detailed explanation of the study protocol, with adolescents, in addition, written informed consent of the person responsible. *Assignment to this category is based solely on the prevalence of inflammatory lesions, regardless of the number of comedones: Grade I - less than 10 on one side Grade II - 10-20 on one side Grade III - 20-30 on one side Grade IV - more than 30 on one side (from https://link.springer.com/chapter/10.1007/978-3-642-96246-2_10) **Exclusion criteria** Known intolerance or	pyridoxine hydrochtoride, lysine, leucine, C.I.77891, C.I.47005, C.I.61570) **Comparison:** skin cleanser in a form of a bar soap ("Lux" soap) Treatment (12 weeks): During the following 12-week treatment period either Sebamed compact or Lux soap was to be used as follows: facial skin was to be washed in the morning and in the evening for 1 min, thereafter thoroughly rinsed with plain water and dried with a towel. Wash-out period: During the 2-week wash-out period (no treatment whatsoever) the face was only cleansed with water.	inflammatory lesions, that is papulopustules in the face; the number of non-inflammatory lesions, that is closed and open comedones (classification by Plewig and Kligman, 1975); adverse events (not defined). The number of inflammatory and non-inflammatory lesions in the face was recorded separately per side. Assessment was performed by the investigator. Time points of investigations: all participants were investigated on the day of enrolment (time point 0), a fortnight later (time point 1) and at 4-week intervals three times thereafter (time points 2 to 4). Analysis: intention to treat Adherence: acidic syndet bar group = all participants applied the trial preparation for the entire period of the study;	baseline = 14.6 (5.3) at 12 weeks = 15.3 (6) mean change (SD)* = 0.7 (3.75) **Change in non-inflammatory lesions (mean (SD), baseline to 12 weeks):** *Acidic syndet bar group (n=57):* baseline = 6.8 (5) at 12 weeks = 6 (5) mean change (SD)* = -0.8 (3.54) *Conventional soap group (n=57):* baseline = 6.7 (5.3) at 12 weeks = 8.8 (6) mean change (SD)* = 2.1 (3.75) *calculated by the NGA technical team using an internally developed calculator **Skin irritation (at 12 weeks)** Itching:	center according to a random plan in written form via telefax letter on an individual basis) Performance bias: some concerns (participants and personnel not blinded) Attrition bias: some concerns (drop-outs: 8.7% in the soap group (mainly because of acne exacerbation; 11% in the soap group did not conform to the trial protocol in full, in particular pre-treatment with a drug was sometimes not discontinued in time) Detection bias: some concerns (outcome assessors were aware of the intervention received) Reporting bias: low risk of bias Other bias Overall risk of bias: some concerns

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	hypersensitivity to soaps and syndets; diseases influencing ache; other treatment for acne whether physical or pharmaceutical, in particular drug treatment within the last month before enrolment; drugs potentially influencing ache, in particular systemic or topical antibiotics, with the exception of oral contraceptives; change of the contraceptive during the last 2 months, of the trial, the participants were not to be put on a contraceptive for the 1st time at the beginning of the trial, nor was the type of contraceptive to be changed within the trial period proper; use of ethanoic cleansers; change of cosmetic care habits during the study envisaged; predictable causes for non-compliance such as absence from home; inability to conform to the rules laid down in the trial protocol; addiction to ethanol or drugs; psychiatric disorders; participation in a clinical trial within the last 30 days or concurrent participation in a different clinical trial.		conventional soap bar = 5 participants discontinued application of the cleanser before the end of the trial period (4 because of acne exacerbation)	Acidic syndet bar group: 0/57 Conventional soap group: 12/57 (21.1%) Redness: Acidic syndet bar group: 1/57 (1.8%) Conventional soap group: 15/57 (26.3%) Scaling: Acidic syndet bar group: 1/57 (1.8%) Conventional soap group: 12/57 (21.1%)	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Santos-Caetano, J. P., Cargill, M. R., A Randomized Controlled Tolerability Study to Evaluate Reformulated Benzoyl Peroxide Face Washes for Acne Vulgaris, Journal of drugs in dermatology, 18, 350-356, 2019 **Ref Id** 1051092 **Country/ies where the study was carried out** USA **Study type** RCT (description in the paper: randomised, evaluator-blind, single-centre, parallel-group study) **Aim of the study** To confirm the modifications to the 2 reformulated face washes do not result in unacceptable local tolerance of the face washes.	**Sample size** N=133 randomised but n=122 completed the study: n=39 in 4% (reformulated) BPO cleanser group, n=40 in 10% (reformulated) BPO group, n=43 in reference product group containing 10% BPO **Characteristics** Mean age (SD): 4% BPO cleanser = 31.7 (7.7) 10% BPO cleanser = 31.4 (6.54) Reference product = 32.6 (7.72) Female gender: 4% BPO cleanser = 72.7% 10% BPO cleanser = 79.5% Reference product = 77.8% White race: 4% BPO cleanser = 63.6% 10% BPO cleanser = 59.1% Reference product = 48.9% Fitzpatrick skin type V (very rarely burns, tans very easily): 4% BPO cleanser = 25% 10% BPO cleanser = 34.1% Reference product = 35,6%	**Interventions** Interventions: reformulated 4% BPO (benzoyl peroxide) face wash reformulated 10% BPO (benzoyl peroxide) face wash Reformulated products use the sugar-base surfactants sodium laurylglucosides hydroxypropylsulfonate and decyl glucoside instead of potassium lauryl sulphate and sodium lauryl sulphate, and contain a different source of BPO raw material that contains micronized BPO particles. Comparison: older formulation 10% BPO (benzoyl peroxide) Acne Foaming Wash (no longer commercially available; referred to as the reference product) Treatment: Products were self-administered by the participants at home twice a day for 21 days (+-2 days) including the morning of the final visit. Participants were instructed to gently massage the product onto a wet face for 1-2 minutes before thoroughly rinsing the skin with water. The first application was conducted under supervision.	**Details** Randomisation: Randomisation was stratified by acne severity (IGA grade 2/IGA grade 3) and contact lens use/non-use. Randomisation schedule was generated by the GSK CH Biostatistics Department prior the start of the study using validated internal software. Randomisation numbers were assigned to participants in ascending numerical order within their respective strata. Branding on the reference product was obscured and all products were over-wrapped in opaque vinyl. Evaluators were blinded to product allocation. Outcome definition: Skin-related adverse events Product acceptability questionnaire (satisfied/very satisfied with the product)	**Results** **Skin-related adverse events:** Burning sensation: 4% BPO group: 0/44 10% BPO group: 0/44 Reference product: 1/45 Dry skin: 4% BPO group: 0/44 10% BPO group: 0/44 Reference product: 2/45 Erythema: 4% BPO group: 0/44 10% BPO group: 0/44 Reference product: 1/45 **Product acceptability questionnaire (satisfied/very satisfied with the product):** 4% BPO group: 31/44 (70.5%) 10% BPO group: 35/44 (79.5%) Reference product: 35/45 (77.8%)	**Limitations** **Methodological limitations assessed using the Cochrane risk-of-bias tool for randomised trials (RoB2)** Selection bias: low risk of bias Performance bias: low risk of bias Attrition bias: low risk of bias Detection bias: low risk of bias Reporting bias: low risk of bias Other bias Overall risk of bias: low risk of bias **Other information** Study's aim was to assess local tolerance of the intervention and not the efficacy

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates Between November 2016 and February 2017 **Source of funding** The authors are employees of GlaxoSmithKline	Acne severity 2 (mild): 4% BPO cleanser = 77% 10% BPO cleanser = 75% Reference product = 75.6% Acne severity 3 (moderate): 4% BPO cleanser = 22.7% 10% BPO cleanser = 25% Reference product = 24.4% Composite dermatologist score (sum of individual score for erythema, dryness, desquamation, oedema; mean (SD)): 4% BPO cleanser = 0.16 (0.37) 10% BPO cleanser = 0.09 (0.29) Reference product = 0.09 (0.29) **Inclusion criteria** Those aged between 18 and 45 years; mild to moderate acne vulgaris (defined as grade 2 or 3 on the 2005 Investigator Global Assessment (IGA) scale for acne severity suggested by the US Food and Drug Administration); Fitzpatrick skin type 1 to V; Dermatologist scores of <=1 for		Time points of assessment: Assessments by a dermatologist were conducted on the day of the first application (baseline) and during the final study visit at day 21 (+-2 days). Analysis: intention to treat Adherence: 4% BPO group: 5 drop-outs (reason - 1 due to adverse event, 4 due to other reason) 10% BPO group: 4 drop-outs (reason - not specified but not due to adverse event or lost to follow-up) Reference product: 2 drop-outs (reason - due to adverse event)		

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	erythema, and 0 for dryness, desquamation/peeling and oedema; Ophthalmologist scores of 0 for conjunctiva involvement and lacrimal intensity. **Exclusion criteria** Not reported				

BPO: benzoyl peroxide; NGA: National Guideline Alliance; RCT: randomised controlled trial

Appendix E – Forest plots

Forest plots for review question: What skin care advice is appropriate for people with acne vulgaris?

This section includes forest plots only for outcomes that are meta-analysed. No meta-analysis was conducted for this review question and so there are no forest plots.

Appendix F – GRADE tables

GRADE tables for review question: What skin care advice is appropriate for people with acne vulgaris?

Table 5: Clinical evidence profile for comparison of enhanced cleanser versus conventional cleanser

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Enhanced cleanser	Conventional cleanser	Relative (95% CI)	Absolute		
% change in inflammatory lesion counts at 4-week follow up (Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	13	13	-	SMD 0.81 lower (1.61 to 0.01 lower)	⊕⊕OO LOW	CRITICAL
Skin-related adverse events - Pruritus (follow-up 4 weeks)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/13 (0%)	0/13 (0%)	-	RD 0.00 (-0.14 to 0.14)	⊕OOO VERY LOW	CRITICAL
Skin-related adverse events - Scales (follow-up 4 weeks)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/13 (0%)	0/13 (0%)	-	RD 0.00 (-0.14 to 0.14)	⊕OOO VERY LOW	CRITICAL
Skin-related adverse events - Xerosis (follow-up 4 weeks)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/13 (0%)	0/13 (0%)	-	RD 0.00 (-0.14 to 0.14)	⊕OOO VERY LOW	CRITICAL

CI: confidence interval; MID: minimally important difference; RD: risk difference; SMD: standardised mean difference

[1] Choi 2010. Enhanced cleanser contains papain, proteomax, soap powder, 0.04% triclosan, 1% salicylic acid and 1% azelaic acid; conventional cleanser contains papain, proteomax, and soap powder only.

[2] Overall risk of bias judgement: some concerns as no information provided about allocation concealment and how the study product was used by the participants but assume a wash as it is a cleanser and the authors mention facial washing.

[3] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for SMD.
[4] Evidence downgraded by 2 levels due to risk of very serious imprecision due to no events.

Table 6: Clinical evidence profile for comparison of syndet bar versus conventional soap bar

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Syndet bar**	**Conventional soap bar**	**Relative (95% CI)**	**Absolute**		
Mean change in inflammatory lesion counts from baseline (Better indicated by lower values)												
1[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	57	57	-	MD 3.7 lower (5.06 to 2.34 lower)	⊕⊕OO LOW	CRITICAL
Mean change in non-infl. lesion counts from baseline (Better indicated by lower values)												
1[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	57	57	-	MD 2.9 lower (4.24 to 1.56 lower)	⊕⊕OO LOW	CRITICAL
Skin-related adverse events - Itching												
1[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/57 (0%)	12/57 (21.1%)	POR 0.11 (0.03 to 0.36)	182 fewer per 1000 (from 123 fewer to 203 fewer)	⊕⊕OO LOW	CRITICAL
Skin-related adverse events - Redness												
1[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	1/57 (1.8%)	15/57 (26.3%)	RR 0.07 (0.01 to 0.49)	245 fewer per 1000 (from 134 fewer to 261 fewer)	⊕⊕OO LOW	CRITICAL
Skin-related adverse events - Scaling												
1[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	1/57 (1.8%)	12/57 (21.1%)	RR 0.08 (0.01 to 0.62)	194 fewer per 1000 (from 80 fewer to 208 fewer)	⊕⊕OO LOW	CRITICAL

CI: confidence interval; MID: minimally important difference; MD: mean difference; POR: Peto odds ratio; RR: relative risk
[1] Korting 1995. Acidic syndet bar ('Sebamed compact') contains sodium cocoyl isethionate, disodium sulfo succinate, wheat starch, paraffin, stearic acid, glyceryl stearate, cetyl palmitate, cetearyl alcohol, water, lecithin, tocopheryl acetate, perfume, lactic acid, PEG-14, disodium EDTA, hydrogenatedcoco-glyceride (and) tocopherol, urea phosphate, glycine, aspartic acid, alanine, pyridoxine hydrochtoride, lysine, leucine, C.I.77891, C.I.47005, and C.I.61570.

[2] Overall risk of bias judgement: some concerns as it is not reported what form of randomisation was used; participants, personnel and outcome assessors were not blinded; 8.7% drop-outs in the control group.
MIDs were calculated for continuous outcomes (using baseline SD) and are as follows: change in inflammatory lesion counts +/-2.7; change in non-inflammatory lesion counts +/-2.7.

Table 7: Clinical evidence profile for comparison of reformulated 4% benzoyl peroxide face wash versus older formulation 10% benzoyl peroxide face wash

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Reformulated 4% BPO	Old formulation 10% BPO	Relative (95% CI)	Absolute		
Skin-related adverse events - Burning sensation												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	0/44 (0%)	0/45 (0%)	-	RD 0.00 (-0.04 to 0.04)	⊕⊕OO LOW	CRITICAL
Skin-related adverse events - Dry skin												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	0/44 (0%)	0/45 (0%)	-	RD 0.00 (-0.04 to 0.04)	⊕⊕OO LOW	CRITICAL
Skin-related adverse events - Erythema												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	0/44 (0%)	0/45 (0%)	-	RD 0.00 (-0.04 to 0.04)	⊕⊕OO LOW	CRITICAL
Satisfied or very satisfied with product												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	31/44 (70.5%)	35/45 (77.8%)	RR 0.91 (0.71 to 1.16)	70 fewer per 1000 (from 226 fewer to 124 more)	⊕⊕⊕O MODERATE	IMPORTANT

BPO: benzoyl peroxide; CI: confidence interval; RD: risk difference; RR: relative risk
[1] Santos-Caetano 2019. Reformulated 4% or 10% BPO face wash (these products use the sugar-base surfactants sodium laurylglucosides hydroxypropylsulfonate and decyl glucoside instead of potassium lauryl sulphate and sodium lauryl sulphate, and contain a different source of BPO raw material that contains micronized BPO particles; the older 10% BPO face wash is no longer commercially available.
[2] Evidence downgraded by 2 levels due to risk of very serious imprecision due to no events.
[3] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes.

Table 8: Clinical evidence profile for comparison of reformulated 10% benzoyl peroxide face wash versus older formulation 10% benzoyl peroxide face wash

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Reformulated 4% BPO	Old formulation 10% BPO	Relative (95% CI)	Absolute		
Skin-related adverse events - Burning sensation												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	0/44 (0%)	0/45 (0%)	-	RD 0.00 (-0.04 to 0.04)	⊕⊕OO LOW	CRITICAL
Skin-related adverse events - Dry skin												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	0/44 (0%)	0/45 (0%)	-	RD 0.00 (-0.04 to 0.04)	⊕⊕OO LOW	CRITICAL
Skin-related adverse events – Erythema												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	0/44 (0%)	0/45 (0%)	-	RD 0.00 (-0.04 to 0.04)	⊕⊕OO LOW	CRITICAL
Satisfied or very satisfied with product												
1[1]	randomised trials	no serious risk of	no serious inconsistency	no serious indirectness	serious[3]	none	31/44 (70.5%)	35/45 (77.8%)	RR 0.91 (0.71 to 1.16)	70 fewer per 1000 (from 226 fewer to	⊕⊕⊕O MODERATE	IMPORTANT

		bias								124 more)		

BPO: benzoyl peroxide; CI: confidence interval; RD: risk difference; RR: relative risk
[1] Santos-Caetano 2019. Reformulated 4% or 10% BPO face wash (these products use the sugar-base surfactants sodium laurylglucosides hydroxypropylsulfonate and decyl glucoside instead of potassium lauryl sulphate and sodium lauryl sulphate, and contain a different source of BPO raw material that contains micronized BPO particles; the older 10% BPO face wash is no longer commercially available.
[2] Evidence downgraded by 2 levels due to risk of very serious imprecision due to no events.
[3] Evidence downgraded by 1 level due to risk of very serious imprecision as 95% confidence intervals cross 1 default MID for dichotomous outcomes.

Table 9: Clinical evidence profile for comparison of reformulated 4% benzoyl peroxide face wash to reformulated 10% benzoyl peroxide face wash

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Reformulated 10% BPO**	**Old formulation 10% BPO**	**Relative (95% CI)**	**Absolute**		
Skin-related adverse events - Burning sensation												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	0/44 (0%)	0/45 (0%)	-	RD 0.00 (-0.04 to 0.04)	⊕⊕OO LOW	CRITICAL
Skin-related adverse events - Dry skin												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	0/44 (0%)	0/45 (0%)	-	RD 0.00 (-0.04 to 0.04)	⊕⊕OO LOW	CRITICAL
Skin-related adverse events - Erythema												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	0/44 (0%)	0/45 (0%)	-	RD 0.00 (-0.04 to 0.04)	⊕⊕OO LOW	CRITICAL
Satisfied or very satisfied with product												

1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	35/44 (79.5%)	35/45 (77.8%)	RR 1.02 (0.82 to 1.27)	16 more per 1000 (from 140 fewer to 210 more)	⊕⊕OO LOW	IMPORTANT

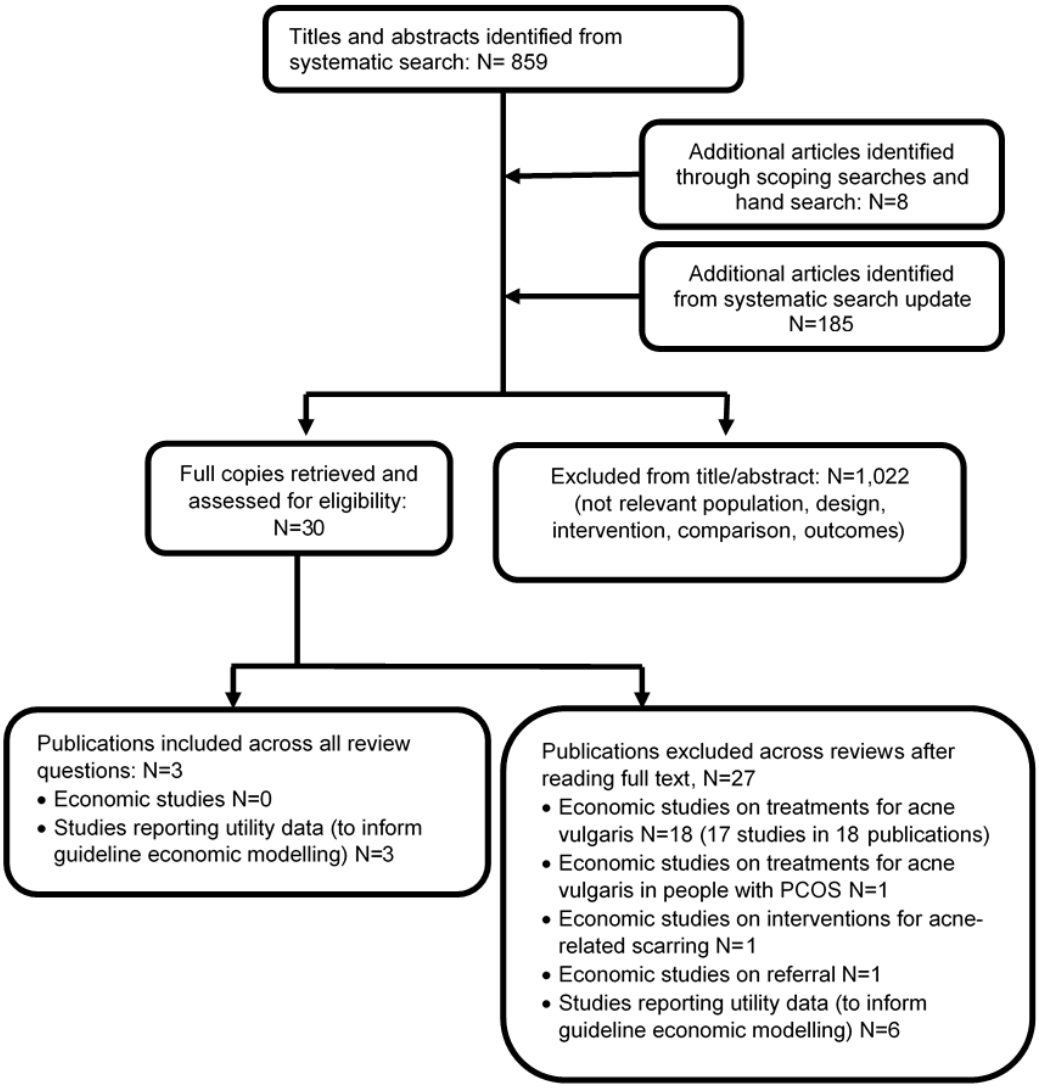
BPO: benzoyl peroxide; CI: confidence interval; RD: risk difference; RR: relative risk
[1] Santos-Caetano 2019. Santos-Caetano 2019. Reformulated 4% or 10% BPO face wash (these products use the sugar-base surfactants sodium laurylglucosides hydroxypropylsulfonate and decyl glucoside instead of potassium lauryl sulphate and sodium lauryl sulphate, and contain a different source of BPO raw material that contains micronized BPO particles.
[2] Evidence downgraded by 2 levels due to risk of very serious imprecision due to no events.
[3] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 1 default MIDs for dichotomous SMD outcomes.

Appendix G – Economic evidence study selection

Economic evidence study selection for review question: What skin care advice is appropriate for people with acne vulgaris?

A global health economics search was undertaken for all areas covered in the guideline. Figure 2 shows the flow diagram of the selection process for economic evaluations of interventions and strategies associated with the care of people with acne vulgaris and studies reporting acne vulgaris-related health state utility data.

Figure 2. Flow diagram of selection process for economic evaluations of interventions and strategies associated with the care of people with acne vulgaris and studies reporting acne vulgaris-related health state utility data



Appendix H – Economic evidence tables

Economic evidence tables for review question: What skin care advice is appropriate for people with acne vulgaris?

No economic evidence was identified which was applicable to this review question.

Appendix I – Health economic evidence profiles

Economic evidence profiles for review question: What skin care advice is appropriate for people with acne vulgaris?

No economic evidence was identified which was applicable to this review question.

Appendix J – Economic analysis

Economic analysis for review question: What skin care advice is appropriate for people with acne vulgaris?

No economic analysis was conducted for this review question.

Appendix K – Excluded studies

Excluded clinical and economic studies for review question: What skin care advice is appropriate for people with acne vulgaris?

Clinical studies

Table 10: Excluded studies and reasons for their exclusion

Study	Reason for Exclusion
Armitstead, R. L., Baillie, A. T. K., Banky, P., Retinoic acid in the treatment of acne. A report from the General Practitioner Research Group, Practitioner, 213, 387-390, 1974	Study product was left on the skin
Baumann, L. S., Oresajo, C., Yatskayer, M., Dahl, A., Figueras, K., Comparison of clindamycin 1% and benzoyl peroxide 5% gel to a novel composition containing salicylic acid, capryloyl salicylic acid, HEPES, glycolic acid, citric acid, and dioic acid in the treatment of acne vulgaris, Journal of Drugs in Dermatology, 12, 266-9, 2013	Study product was left on the skin. Participants also used a cleanser, sunscreen and moisturiser before applying study product
Bhatia, A. C., Jimenez, F., Rapid treatment of mild acne with a novel skin care system containing 1% salicylic acid, 10% buffered glycolic acid, and botanical ingredients, Journal of Drugs in Dermatology, 13, 678-683, 2014	Not a RCT
Bhatia, N., Pillai, R., Randomized, Observer-blind, Split-face Compatibility Study with Clindamycin Phosphate 1.2%/Benzoyl Peroxide 3.75% gel and Facial Foundation Makeup, The Journal of Clinical & Aesthetic Dermatology, 8, 25-32, 2015	Not the population of interest
Bissonnette, R., Bolduc, C., Seite, S., Nigen, S., Provost, N., Maari, C., Rougier, A., Randomized study comparing the efficacy and tolerance of a lipophillic hydroxy acid derivative of salicylic acid and 5% benzoyl peroxide in the treatment of facial acne vulgaris, Journal of Cosmetic Dermatology, 8, 19-23, 2009	Study product was left on the skin
Bojar, R. A., Cunliffe, W. J., Holland, K. T., The short-term treatment of acne vulgaris with benzoyl peroxide: Effects on the surface and follicular cutaneous microflora, British Journal of Dermatology, 132, 204-208, 1995	Study product was left on the skin
Capitanio, B., Sinagra, J. L., Weller, R. B., Brown, C., Berardesca, E., Randomized controlled study of a cosmetic treatment for mild acne, Clinical & Experimental Dermatology, 37, 346-9, 2012	Study describes a topical cream (applied twice a day) and left on the skin. The authors suggest that it is as a 'cosmetic' product as it has not been through the medicines agency or met the criteria for that; however, it is not makeup per se
Cestone, E., Michelotti, A., Zanoletti, V., Zanardi, A., Mantegazza, R., Dossena, M., Acne RA-1,2, a novel UV-selective face cream for patients with acne: Efficacy and tolerability results of a randomized, placebo-controlled clinical study, Journal of Cosmetic DermatologyJ, 16, 265-270, 2017	Not relevant intervention as it includes facial cleanser, base cream and cream designed to provide selective protection from daily UV light
Charakida, A., Charakida, M., Chu, A. C., Double-blind, randomized, placebo-controlled study of a lotion containing triethyl citrate and ethyl linoleate in the	Study product was left on the skin

treatment of acne vulgaris, British Journal of Dermatology, 157, 569-574, 2007	
Choi, J. M., Lew, V. K., Kimball, A. B., A single-blinded, randomized, controlled clinical trial evaluating the effect of face washing on acne vulgaris, Pediatric Dermatology, 23, 421-7, 2006	Not sufficient data reported to calculate a difference in the improvement of acne from baseline to follow-up between the trial groups
Chu, A., Huber, F. J., Plott, R. T., The comparative efficacy of benzoyl peroxide 5%/erythromycin 3% gel and erythromycin 4%/zinc 1.2% solution in the treatment of acne vulgaris, British Journal of Dermatology, 136, 235-8, 1997	Study product was left on the skin
Cullen, S. I., Childers, R. C., Tretinoin-sunscreen mixture in the treatment of acne vulgaris, Cutis, 41, 289-291, 1988	Not a RCT
Cunliffe, W. J., Fernandez, C., Bojar, R., Kanis, R., West, F., An observer-blind, parallel-group, randomized, multicentre clinical and microbiological study of a topical clindamycin/zinc gel and a topical clindamycin lotion in patients with mild/moderate acne, Journal of Dermatological Treatment, 16, 213-218, 2005	Study product was left on the skin
Del Rosso, J. Q., A 6% benzoyl peroxide foaming cloth cleanser used in the treatment of acne vulgaris: aesthetic characteristics, patient preference considerations, and impact on compliance with treatment, The Journal of Clinical & Aesthetic Dermatology, 2, 26-9, 2009	Data reported either in figures or descriptively
Del Rosso, J. Q., Gold, M., Rueda, M. J., Brandt, S., Winkelman, W. J., Efficacy, safety, and subject satisfaction of a specified skin care regimen to cleanse, medicate, moisturize, and protect the skin of patients under treatment for acne vulgaris, Journal of Clinical and Aesthetic Dermatology, 8, 22-30, 2015	Not a RCT
Draelos, Z., Hornby, S., Walters, R. M., Appa, Y., Hydrophobically modified polymers can minimize skin irritation potential caused by surfactant-based cleansers, Journal of Cosmetic Dermatology, 12, 314-21, 2013	Mixed population, that is those with acne, rosacea, eczema; not reported how many participants had acne
Dreno, B., Nocera, T., Verriere, F., Vienne, M. P., Segard, C., Vitse, S., Carre, C., Topical retinaldehyde with glycolic acid: study of tolerance and acceptability in association with anti-acne treatments in 1,709 patients, Dermatology, 210 Suppl 1, 22-9, 2005	Study product was left on the skin
Dunlop, K. J., Barnetson, R. S., A comparative study of isolutrol versus benzoyl peroxide in the treatment of acne, Australasian Journal of Dermatology, 36, 13-5, 1995	Study product was left on the skin
Eady, E. A., Burke, B. M., Pulling, K., Cunliffe, W. J., The benefit of 2% salicylic acid lotion in acne - A placebo-controlled study, Journal of Dermatological Treatment, 7, 93-96, 1996	Treatment consisted of 2% salicylic acid lotion which was left on the skin and not washed off
Eichenfield, L. F., Sugarman, J. L., Guenin, E., Harris, S., Bhatt, V., Novel tretinoin 0.05% lotion for the once-daily treatment of moderate-to-severe acne vulgaris in a preadolescent population, Pediatr Dermatol, 36, 193-199, 2019	Study product was left on the skin
Fabbrocini, G., Capasso, C., Donnarumma, M., Cantelli, M., Le Maitre, M., Monfrecola, G., Emanuele, E., A peel-off facial mask comprising myoinositol and trehalose-loaded liposomes improves adult female acne by reducing local hyperandrogenism and activating autophagy, Journal of cosmetic dermatology, 16, 480-484, 2017	Not a RCT

Feldman, S. R., Werner, C. P., Saenz, A. B. A., The efficacy and tolerability of Tazarotene foam, 0.1%, in the treatment of acne vulgaris in 2 multicenter, randomized, vehicle-controlled, double-blind studies, Journal of drugs in dermatology, 12, 438-446, 2013	Not relevant comparison as the study compares tazarotene 0.1% foam to vehicle foam which is more relevant for the topical treatment question
Francomano, M., Giusti, G., Bertoni, L., Seidenari, S., Instrumental and clinical assessment of the efficacy and tolerability of a topical product with benzoyl peroxide combined with a detergent for acneic skin, Giornale Italiano di Dermatologia e Venereologia, 135, 387-391, 2000	In Italian language
Gold, M. H., A multicenter efficacy and tolerability evaluation of benzoyl peroxide in a 10% urea vehicle for the treatment of acne vulgaris, Journal of Drugs in Dermatology, 5, 442-5, 2006	Not a RCT
Greenwood, R., Burke, B., Cunliffe, W. J., Evaluation of a therapeutic strategy for the treatment of acne vulgaris with conventional therapy, British Journal of Dermatology, 114, 353-8, 1986	Study product was left on the skin
Handojo, I., The combined use of topical benzoyl peroxide and tretinoin in the treatment of acne vulgaris, International Journal of Dermatology, 18, 489-96, 1979	Study product was left on the skin
Hensley, D., Meckfessel, M. H., Tolerability of a Skin Care Regimen Formulated for Acne-Prone Skin in Children, Pediatr Dermatol, 32, 501-5, 2015	Not a RCT
Hoffman, L. K., Del Rosso, J. Q., Kircik, L. H., The efficacy and safety of azelaic acid 15% foam in the treatment of truncal acne vulgaris, Journal of drugs in dermatology, 16, 534-538, 2017	Not a RCT
Holt, S., Beasley, R., Weatherall, M., Braithwaite, I., Holliday, M., Montgomery, B., Corin, A., Helm, C., Sheahan, D., Tofield, C., A single-blind randomised controlled trial of a topical kanuka honey formulation for the treatment of acne, Australasian Journal of Dermatology, 56 (4), a5, 2015	Conference abstract
Hughes, B. R., Norris, J. F., Cunliffe, W. J., A double-blind evaluation of topical isotretinoin 0.05%, benzoyl peroxide gel 5% and placebo in patients with acne, Clinical & Experimental Dermatology, 17, 165-8, 1992	Study product was left on the skin
Hulme, N. A., Parish, L. C., Witkowski, J. A., Skin cleansing as an accompaniment to acne therapy, 25, 505, 1986	Commentary
Iraji, F., Momeni, A., Naji, S. M., Siadat, A. H., The efficacy of topical cyproterone acetate alcohol lotion versus placebo in the treatment of the mild to moderate acne vulgaris: a double blind study, Dermatology Online Journal, 12, 26, 2006	Study product was left on the skin
Isoda, K., Takagi, Y., Endo, K., Miyaki, M., Matsuo, K., Umeda, K., Umeda-Togami, K., Mizutani, H., Effects of washing of the face with a mild facial cleanser formulated with sodium laureth carboxylate and alkyl carboxylates on acne in Japanese adult males, Skin Research & Technology, 21, 247-53, 2015	Not a RCT
Kim, M. R., Kerrouche, N., Combination of benzoyl peroxide 5% gel with liquid cleanser and moisturizer SPF 30 in acne treatment results in high levels of subject satisfaction, good adherence and favorable tolerability,	Not a RCT

Journal of Dermatological Treatment, 29, 49-54, 2018	
Kreusch, J., Bextermoller, R., Efficacy and tolerability of a topical erythromycin/tretinoin combination preparation in acne treatment: post-marketing surveillance study involving over 6500 patients, Current Medical Research & Opinion, 16, 1-7, 2000	Study product was left on the skin
Laquieze, S., Czernielewski, J., Rueda, M. J., Beneficial effect of a moisturizing cream as adjunctive treatment to oral isotretinoin or topical tretinoin in the management of acne, Journal of Drugs in Dermatology, 5, 985-90, 2006	Data reported either in figures or descriptively; no standard deviation or p-values reported
Mayr-Kanhauser, S., Kranke, B., Aberer, W., Efficacy of octenidine dihydrochloride and 2-phenoxyethanol in the topical treatment of inflammatory acne, Acta Dermatovenerologica Alpina, 17, 139-43, 2008	Not a RCT
Monfrecola, G., Capasso, C., Russo, G., Fabbrocini, G., UV-selective face cream (Acne RA-1,2) in acne patients: clinical study of its effects on epidermal barrier function, sebum production, tolerability and therapy adherence, Giornale Italiano di Dermatologia e Venereologia, 153, 26-32, 2018	Not a RCT
Moy, R. L., Levenson, C., So, J. J., Rock, J. A., Single-center, open-label study of a proprietary topical 0.5% salicylic acid-based treatment regimen containing sandalwood oil in adolescents and adults with mild to moderate acne, Journal of drugs in dermatology, 11, 1403-8, 2012	Not a RCT
Muizzuddin, N., Schnittger, S., Maher, W., Maes, D. H., Mammone, T., Enzymatically generated hydrogen peroxide reduces the number of acne lesions in acne vulgaris, Journal of Cosmetic Science, 64, 1-8, 2013	Article not available
Munehiro, A., Murakami, Y., Shirahige, Y., Nakai, K., Moriue, T., Matsunaka, H., Yoneda, K., Kubota, Y., Combination effects of cosmetic moisturisers in the topical treatment of acne vulgaris, Journal of Dermatological Treatment, 23, 172-6, 2012	Data reported either in figures or descriptively
NilFroushzadeh, M. A., Siadat, A. H., Baradaran, E. H., Moradi, S., Clindamycin lotion alone versus combination lotion of clindamycin phosphate plus tretinoin versus combination lotion of clindamycin phosphate plus salicylic acid in the topical treatment of mild to moderate acne vulgaris: a randomized control trial, Indian Journal of Dermatology, Venereology & Leprology, 75, 279-82, 2009	Study product was left on the skin
Ozgen, Z. Y., Gurbuz, O., A randomized, double-blind comparison of nadifloxacin 1% cream alone and with benzoyl peroxide 5% lotion in the treatment of mild to moderate facial acne vulgaris, Marmara Medical Journal, 26, 2013	Study product was left on the skin
Poli, F., Ribet, V., Lauze, C., Adhoute, H., Morinet, P., Efficacy and safety of 0.1% retinaldehyde/ 6% glycolic acid (diacneal) for mild to moderate acne vulgaris. A multicentre, double-blind, randomized, vehicle-controlled trial, Dermatology, 210 Suppl 1, 14-21, 2005	Study product was left on the skin
Schutte, H., Cunliffe, W. J., Forster, R. A., The short-term effects of benzoyl peroxide lotion on the resolution of inflamed acne lesions, British Journal of Dermatology, 106, 91-4, 1982	Study product was left on the skin
Shalita, A. R., Comparison of a salicylic acid cleanser and a benzoyl peroxide wash in the treatment of acne vulgaris,	No sufficient data reported to calculate the difference in comedone counts

11, 264-7, 1989	between the two interventions
Shalita, A. R., Rafal, E. S., Anderson, D. N., Yavel, R., Landow, S., Lee, W. L., Compared efficacy and safety of tretinoin 0.1% microsphere gel alone and in combination with benzoyl peroxide 6% cleanser for the treatment of acne vulgaris, Cutis, 72, 167-72, 2003	Not relevant comparison as the study compares cleanser gel vs gel which is more relevant for the topical treatment question
Shellow, W. V., pHresh 3.5: a new low pH liquid skin cleanser, Journal of International Medical Research, 9, 297-9, 1981	Not a RCT
Stoughton, R. B., Leyden, J. J., Efficacy of 4 percent chlorhexidine gluconate skin cleanser in the treatment of acne vulgaris, Cutis, 39, 551-3, 1987	Not a RCT
Stringer, T., Nagler, A., Orlow, S. J., Oza, V. S., Clinical evidence for washing and cleansers in acne vulgaris: a systematic review, Journal of Dermatological Treatment, 1-6, 2018	Systematic review mainly of prospective non-randomised studies. The references were checked for potentially relevant papers
Trelles, M. A., Allones, I., Rigau, J., Mordon, S., Effects of skin cleaning modes on the condition of collagen and elastin after laser resurfacing, Journal of cutaneous laser therapy, 2, 169-176, 2000	Not the population of interest, that is participants undergoing periocular and perioral resurfacing
Tyring, S. K., Kircik, L. H., Pariser, D. M., Guenin, E., Bhatt, V., Pillai, R., Novel Tretinoin 0.05% Lotion for the Once-Daily Treatment of Moderate-to-Severe Acne Vulgaris: Assessment of Efficacy and Safety in Patients Aged 9 Years and Older, Journal of drugs in dermatology : JDD, 17, 1084-1091, 2018	Study product was left on the skin
Wollina, U., Tirant, M., Bayer, P., Coburn, M., Anderson, P., Donnelly, B., Kennedy, T., Gaibor, J., Arora, M., Clews, L., Walmsley, S., Hercogova, J., Fioranelli, M., Gianfaldoni, S., Chokoeva, A. A., Tchernev, G., Novotny, F., Roccia, M. G., Maximov, G. K., Franca, K., Lotti, T., Successful treatment of mild to moderate acne vulgaris with Dr Michaels(R) (also branded as Zitinex(R)) topical products family: a clinical trial, J Biol Regul Homeost Agents, 30, 49-54, 2016	Article not available
Xu, L. H., Zhong, P., Yin-Nourishing and Lung-Clearing Formula for treating 45 cases with female postadolescent acne, Henan traditional chinese medicine [he nan zhong yi], 35, 1613-1615, 2015	In Chinese language
Zeichner, J. A., Wong, V., Linkner, R. V., Haddican, M., Efficacy and safety of tretinoin 0.025%/clindamycin phosphate 1.2% gel in combination with benzoyl peroxide 6% cleansing cloths for the treatment of facial acne vulgaris, Journal of Drugs in Dermatology, 12, 277-82, 2013	Not relevant comparison as the study compares gel vs cleansing cloth plus gel (combination therapy) which is more relevant for the topical treatment question

Economic studies

No economic evidence was identified for this review.

Appendix L – Research recommendations

Research recommendations for review question: What skin care advice is appropriate for people with acne vulgaris?

Research recommendation

What skincare advice is appropriate for people with acne vulgaris?

Why this is important

Clinicians are frequently asked regarding skin care advice that is appropriate and effective in people with acne vulgaris. There is currently very limited evidence to make such recommendations, however it is an important question as skin care advice may be helpful in combination with other treatment modalities in the management of acne.

Rationale for research recommendation

Table 11: Research recommendation rationale

Research question	What skincare advice is appropriate for people with acne?
Why is this needed	
Importance to 'patients' or the population	Clinicians are frequently asked for advice regarding skin care, such as what is appropriate and effective in people with acne vulgaris. Therefore it is an important topic for people with acne vulgaris. There is very limited current evidence to support making strong recommendations and given that this is likely to apply to the majority of people with acne, this is an area that requires further research.
Relevance to NICE guidance	There is some evidence for skincare advice for people with acne vulgaris, however this is insufficient for a strong recommendation. The benefits of appropriate skincare advice has not been adequately studied and with further research, the potential synergistic effect with other treatment modalities may become apparent. This may also be used to prolong acne-free skin post treatment.
Relevance to the NHS	Acne vulgaris is a very common skin condition affecting the majority of young people and skincare advice in addition to acne treatment may improve outcome for people with acne.
National priorities	There are 2 national priorities, one is to improve young people's mental health and another is to reduce antibiotic prescribing to prevent resistance. Improving the mental health of young people is a national priority. Simple interventions such as skin cleansing offer a degree of control back to young people which may impact beneficially on their mental health. Rates of depression and suicide are increasing in the under 25-year-old age group, especially amongst men 20-25 years old. (suicides in the UK 2019 ons.gov.uk). In 2018 the government produced a paper

Research question	What skincare advice is appropriate for people with acne?
	'Transforming children's and young people's mental health provision', including improving services for those 16-25 years old. This aligns with a need to understand support required for young people with acne vulgaris https://www.gov.uk/government/consultations/transforming-children-and-young-peoples-mental-health-provision-a-green-paper/quick-read-transforming-children-and-young-peoples-mental-health-provision Acne has traditionally been treated with long courses of antibiotics. If any particular cleansing product could be identified as having a positive impact on acne vulgaris, then it may lead to a decreased need for antibiotics. Antibiotic resistance is rising in the UK and the government wants to optimise antibiotic prescribing to prevent the development of superbugs. Keeping people well informed would therefore help to address this priority (Tackling antimicrobial resistance 2019–2024 The UK's five-year national action plan Published 24 January 2019. HM Government) https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/784894/UK_AMR_5_year_national_action_plan.pdf
Current evidence base	It is difficult to draw strong conclusions from the current evidence on appropriate skincare advice for people with acne vulgaris. The existing trials lacked consistency and have variable follow-up durations.
Equality	Access and acceptability of skincare advice may differ across socioeconomic groups and cultures.
Feasibility	Whilst there may be economic implications for recommending certain skin cleansing products, it should be relatively straight forward for individuals to incorporate recommended treatments into an already existing skin cleansing regime.
Other comments	Not applicable

Modified PICO table

Table 12: Research recommendation modified PICO table

Population	Male and female patients from all ethnic and socioeconomic backgrounds with acne vulgaris who are not using any other acne treatments.
Intervention	• Any skin cleansing product
Comparator	• Placebo or vehicle • Other same class products • Any other skin cleansing product
Outcome	• Change in severity of acne using a validated scoring system. • Improvement using patient rated measure
Study design	Randomised controlled trial Cross-over study

	Split-face study
Timeframe	• 3-6 months (intervention) • 6 month (follow-up)
Additional information	Not applicable