# National Institute for Health and Care Excellence

Final

# Acne vulgaris: management

## [I] Maintenance treatments for acne vulgaris

*NICE guideline number NG198*

*Evidence review underpinning recommendations 1.7.1 to 1.7.5 in the NICE guideline*

*June 2021*

*Final*

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

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# Contents

# 1 Maintenance treatment for acne vulgaris

## 2 Review question

3 What is the effectiveness of topical or oral pharmacological and physical interventions as
4 maintenance treatment for acne vulgaris?

### 5 Introduction

6 For some people acne is a relapsing condition that once treated may recur. This review
7 sought to identify whether any treatment could be effectively used to maintain good
8 outcomes once other treatments (including oral isotretinoin) had been discontinued.

### 9 Summary of the protocol

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

12 **Table 1: Summary of the protocol**

| | |
|---|---|
| **Population** | People of all ages whose acne is 'in remission', have had their acne treated successfully, or whose acne has responded to treatment. |
| **Intervention** | • Topical treatments including abrasive/cleaning agents, anthelmintics, antibacterials, antibiotics, antiseptics, dicarboxylic acids, vitamin B3, retinoids or retinoid-like agents, or any combination of these.<br>• Oral antibiotics including, for example, carbapenems, cephamycins/cephalosporins, sulphones, fucidic acid, lincosamides, macrolides, monobactams, penicillins, or any combination of these.<br>• Oral isotretinoin.<br>• Hormonal treatments including (monophasic and phasic) progestogen-only contraceptives, co-cyprindiol, and combined oral contraceptives.<br>• Hormone-modifying agents including, for example, aldosterone antagonists (for example, spironolactone), class 5α-reductase inhibitor (for example, dutasteride), other non-steroidal anti-androgens (for example, flutamide), and metformin.<br>• Physical treatments including chemical peels (for example, salicylic acid), comedone extraction, and treatments using energy-based devices (for example, photochemical therapy, photodynamic therapy, photopneumatic therapy, photothermal therapy, radiofrequency therapy). |
| **Comparison** | • Any other active acne treatment<br>• No treatment<br>• Placebo (for example, vehicle capsule, gel, solution, tablet)<br>• Sham physical treatment<br>• Waiting list |
| **Outcomes** | **Critical**<br>• Clinician-rated improvement at treatment endpoint:<br>  ○ Percentage change in acne lesion count<br>  ○ Change from baseline or final score on a validated acne severity scale.<br>• Prevention of scarring at any follow-up:<br>  ○ Change from baseline or final number of scars |

| | |
|---|---|
| | ○ Incidence of scarring.<br>• Participant-reported improvement:<br>○ Change in acne severity or symptoms (for example, assessed using global acne score).<br>**Important**<br>• Relapse<br>○ Relapse during or after maintenance treatment.<br>• Acceptability<br>○ Treatment discontinuation for any reason.<br>• Tolerability<br>○ Treatment discontinuation due to side effects.<br>• Side effects<br>○ Specific short-term side effects for comparisons of treatments. |

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 8 randomised controlled trials (RCTs) (Kawashima 2018; Leyden 2006; Poulin 2011; Thiboutot 2006; Thielitz 2007; Thielitz 2015; Truchuelo 2015; Vender 2012) and 1 open-label controlled study (Zhang 2004) were included in this review.

One RCT (Kawashima 2018) compared adapalene gel versus benzoyl peroxide gel in participants who had previously been treated with either benzoyl peroxide plus clindamycin, benzoyl peroxide plus adapalene, or adapalene plus clindamycin.

One RCT (Leyden 2006) compared tazarotene gel plus placebo versus tazarotene gel plus minocycline versus vehicle gel plus minocycline in participants who had previously been treated with tazarotene gel plus minocycline capsule.

One RCT (Truchuelo 2015) was a split-face study comparing retinoid combination versus vehicle in participants who had previously been treated with isotretinoin. One RCT (Vender 2012) compared tretinoin versus vehicle in participants who had also previously been treated with isotretinoin. One RCT (Thielitz 2015) compared azelaic acid versus observation; this study included a third treatment arm that was not included in the review because participants received adapalene gel for 9 months, which did not meet protocol eligibility criteria for treatment duration. Evidence from these 3 studies was analysed separately.

Two RCTs (Poulin 2011; Thielitz 2007) and 1 open-label study (Zhang 2004), although assessing adapalene, either reported certain outcomes that were not sufficiently similar to enable pooling (Poulin 2011; Zhang 2004) or compared adapalene regimens versus comparator regimens that were not sufficiently similar to other adapalene regimens to enable pooling (Thielitz 2007). Evidence from these 3 studies was therefore analysed separately. Poulin (2011) compared adapalene benzoyl peroxide (adapalene-BPO) versus vehicle to assess Investigator's Global Assessment (IGA) success rate (percentage of participants

rated worse from baseline), irritation (including erythema, scaling, dryness and stinging/burning) after 24 weeks of treatment. Zhang (2004) compared adapalene versus no treatment to assess the difference in mean percentage reduction in total lesions after 12 weeks of treatment. Thielitz (2007) compared adapalene gel/adapalene gel or vehicle versus vehicle/adapalene gel or vehicle.

However, it was possible to combine certain outcome data from 4 studies (3 RCTs and 1 open-label study) comparing adapalene regimens versus vehicle, no treatment or observation (Poulin 2011; Thiboutot 2006; Thielitz 2007; Zhang 2004). Treatment durations varied across the studies, ranging from 12 weeks to 24 weeks, and a subgroup analysis by treatment duration was therefore conducted.

The included studies are summarised in Table 2.

See the literature search strategy in appendix B and study selection flow chart in appendix C.

### Excluded studies

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

## Summary of clinical studies included in the evidence review

Summary of the studies included in this review are presented in Table 2.

**Table 2: Summary of included studies**

| Study | Population | Intervention | Comparison | Outcomes |
|---|---|---|---|---|
| Kawashima 2018<br><br>RCT<br><br>Japan | N=92 randomised to:<br>• Adapalene gel (n=47)<br>• Benzoyl peroxide gel (n=45)<br><br>Participants with moderate to severe facial acne vulgaris who had less than mild (≤ 5 inflammatory eruptions on the entire face with ≤ 3 on one side of the face)<br><br>Mean age (years): NR for maintenance phase<br>Sex (male): NR for maintenance phase | • 0.1% adapalene gel applied once a day<br><br>Applied after washing face before sleep | • 2.5% benzoyl peroxide applied once a day<br><br>Applied after washing face before sleep | • Relapse/aggravation of symptoms after 12 weeks<br>• Adverse events-Erythema<br>• Adverse events-Dryness |
| Leyden 2006<br><br>RCT<br><br>US | N=110 randomised to:<br>• Tazarotene gel plus placebo capsule (n=36)<br>• Vehicle gel plus minocycline hydrochloride capsule (n=37)<br>• Tazarotene gel plus minocycline capsule (n=37) | • 0.1% tazarotene gel each evening plus placebo capsule twice daily<br>• 0.1% tazarotene gel each evening plus a 100 mg minocycline capsule twice | • Vehicle gel each evening plus a 100 mg minocycline hydrochloride capsule twice daily | • Percentage change in inflammatory and non-inflammatory lesion count after 12 weeks<br>• Participants maintaining ≥70% reduction in inflammatory and non-inflammatory lesion count |

| Study | Population | Intervention | Comparison | Outcomes |
|---|---|---|---|---|
| | Participants with moderately severe to severe facial acne who had 75% or greater global improvement at the end of the initial open-label treatment phase<br><br>Mean age (years): 22<br>Sex (female): 55% | daily<br><br>Tazarotene gel was applied to the face as a pea-sized amount in a thin film 15 to 20 minutes after washing with a mild non-medicated cleanser and drying with a soft towel. | | achieved in the initial treatment phase, after 12 weeks (relapse rate calculated)<br>• Acceptability (treatment discontinuation for any reason) after 12 weeks<br>• Tolerability (treatment discontinuation due to side effects) after 12 weeks |
| Poulin 2011<br><br>RCT<br><br>US, Canada, Puerto Rico | N=243 randomised to:<br>• Adapalene plus BPO (n=123)<br>• Vehicle gel (n=120)<br><br>Participants with severe acne and who had shown at least 50% global improvement with previous treatment (doxycycline and adapalene-BPO or its vehicle gel for 12 weeks).<br><br>Mean (± SD) age (years):<br>Adapalene-BPO: 19.1 (5.89)<br>Vehicle: 18.2 (5.23)<br>Sex (male):<br>Adapalene-BPO: n=65<br>Vehicle: n=67 | • Fixed dose combination gel 0.1% adapalene plus 2.5% benzoyl peroxide (adapalene-BPO) once daily in the evening<br><br>Participants were encouraged to use sun protection factor 15 daily facial moisturiser and a gentle skin cleanser | • Vehicle gel once daily in the evening<br><br>Participants were encouraged to use sun protection factor 15 daily facial moisturiser and a gentle skin cleanser | • Percentage change in lesion count from baseline to 24 weeks<br>• IGA success rate (% of participants rated better or same as baseline) at 24 weeks<br>• Participants having at least 50% improvement from at 24 weeks in total lesions<br>• Treatment-related adverse effects at 24 weeks<br>• Irritation at 24 weeks (including erythema, scaling, dryness, stinging/burning<br>• Acceptability (treatment discontinuation for any reason) at 24 weeks<br>• Tolerability (treatment discontinuation due to side effects) at 24 weeks |
| Thiboutot 2006<br><br>RCT<br><br>US | N=253 randomised to:<br>• Adapalene (n=126)<br>• Vehicle gel (n=127)<br><br>Participants with severe acne and who showed at least moderate improvement from baseline (50% | • 0.1% adapalene gel once daily in the evening<br><br>Participants were provided with a daily facial moisturiser with sun protection factor 15 to use as | • Vehicle gel once daily in the evening<br><br>Participants were provided with a daily facial moisturiser with sun protection | • Percentage of participants maintaining at least 50% improvement after 16 weeks (total lesions)<br>• Treatment-related adverse effects after 16 weeks<br>• Acceptability |

| Study | Population | Intervention | Comparison | Outcomes |
|---|---|---|---|---|
| | improvement) to after treatment with either adapalene plus doxycycline, 100 mg once daily, or doxycycline, 100 mg once daily, plus gel vehicle in a previous 12-week study<br><br>Mean (± SD) age (years):<br>Adapalene: 18.1 (4.2)<br>Vehicle: 17.8 (3.9)<br>Sex (male):<br>Adapalene: n=65<br>Vehicle: n=73 | needed for the symptomatic relief of skin dryness or irritation | factor 15 to use as needed for the symptomatic relief of skin dryness or irritation | (treatment discontinuation for any reason) after 16 weeks<br>• Tolerability (treatment discontinuation due to side effects) after 16 weeks |
| Thielitz 2007<br><br>RCT<br><br>Germany | N=49 randomised to:<br>• Adapalene (n=16)<br>• Adapalene alternately with vehicle (n=16)<br>• Vehicle gel (n=17)<br><br>Participants with mild to moderate acne and with a presence of at least 250 microcomedones per $cm^2$ on the forehead at screening (counted via cyanoacrylate strips)<br><br>Mean (± SD) age (years):<br>Adapalene: 18.33 (5.0)<br>Adapalene alternately with vehicle: 16.47 (2.4)<br>Vehicle: 19.58 (5.4)<br>Sex (male): 59.2% | • 0.1% adapalene gel once daily applied to the face<br>• 0.1% adapalene gel alternately with vehicle once daily every other day applied to the face<br><br>Participants applied the same skin cleanser and moisturiser immediately before treatments and were advised to avoid excessive exposure to sunlight | • Vehicle once daily applied to the face<br><br>Participants applied the same skin cleanser and moisturiser immediately before treatments and were advised to avoid excessive exposure to sunlight | • Percentage change in microcomedone count after 12 weeks (total lesions)<br>• Treatment-related adverse events<br>• Treatment discontinuations |
| Thielitz 2015<br><br>RCT<br><br>Germany | N=36 randomised to:<br>• Azelaic acid (n=17)<br>• Observation (n=19)<br><br>Participants with mild to moderate acne including those with 'late-type acne'<br><br>Mean (± SD) age (years):<br>Azelaic acid: 30.58 (9.28) | • 15% azelaic acid gel twice daily for 9 months (6 months maintenance)<br><br>Participants were not permitted to take any other topical or systemic anti-acne medication including systemic oral | • 6 months observation following 3 months 15% azelaic acid gel twice daily<br><br>Participants were not permitted to take any other topical or systemic anti-acne medication | • Relative change in total lesions after 24 weeks<br>• Absolute change after 24 weeks maintenance in ISGA<br>• Absolute change after 24 weeks maintenance in LRAGS<br>• SGCA after 24 weeks<br>• Relapse during 24 |

| Study | Population | Intervention | Comparison | Outcomes |
|---|---|---|---|---|
| | Observation: 28.14 (4.56)<br>Sex (female): 100% | corticosteroids during the study period | including systemic oral corticosteroids during the study period | weeks<br>• Acceptability (treatment discontinuation for any reason - treatment and maintenance phase)<br>• Tolerability (treatment discontinuation due to side effects during 24 weeks |
| Truchuelo 2015<br><br>RCT (Split face)<br><br>Spain | N=30 – sides of the face randomised to:<br>• Retinoid combination<br>• Vehicle<br><br>Participants with mild acne and completed treatment with oral isotretinoin (including participants who had or had not reached the conventional target dose of 120 to 150 mg/kg) in the previous 6 months<br><br>Mean (± SD) age (years):<br>Male: 18.4 (5.2)<br>Female: 23.5 (5.6)<br>Sex (male): 40.6% | • Retinoid combination (retinol encapsulated in glycospheres and hydroxypinacolone retinoate) applied to one side of the face at night | • Vehicle applied to the other side of the face at night | • Relapse (global count) after 3 months<br>• Number of total lesions after 3 months<br>• Global lesions after 3 months<br>• IGA after 3 months<br>• Adverse events<br>• Discontinuations |
| Vender 2012<br><br>RCT<br><br>Canada | N=20 randomised to:<br>• Tretinoin (n=10)<br>• Vehicle (n=10)<br><br>Participants previously treated for moderate to severe acne and who successfully completed acne treatment with oral isotretinoin (minimum 4 months/maximum 6 months with an average of 5 months and a total of 120 to 150 mg/kg/course)<br><br>Mean age (years):<br>Tretinoin: 21<br>Vehicle: 22.4<br>Sex (male): 100% | • 0.04% Tretinoin gel (microsphere) applied once daily to the whole face (and left on for a minimum of 8 hours)<br><br>Participants were instructed to wash their face first and allow the areas to fully dry for approximately 20 to 30 minutes before applying treatment in a sufficient amount to cover the entire face. Treatments were to be applied consistently either | • Vehicle applied once daily to the whole face (and left on for a minimum of 8 hours)<br><br>Participants were instructed to wash their face first and allow the areas to fully dry for approximately 20 to 30 minutes before applying treatment in a sufficient amount to cover the entire face. | • Lesion count at 24 weeks<br>• ISGA at 24 weeks<br>• SGCA at 24 weeks<br>• Acceptability (treatment discontinuation for any reason) at week 24<br>• Serious adverse events or adverse events<br>• Tolerability |

| Study | Population | Intervention | Comparison | Outcomes |
|---|---|---|---|---|
| | | in the morning or in the evening throughout the study duration.<br><br>Participants were permitted to use moisturiser and cleanser on the face provided | Treatments were to be applied consistently either in the morning or in the evening throughout the study duration.<br><br>Participants were permitted to use moisturiser and cleanser on the face provided | |
| Zhang 2004<br><br>Open-labelled controlled trial<br><br>China | N=241 randomised to:<br>• Adapalene (n=122)<br>• No treatment (n=119)<br><br>Participants with moderate to moderately severe acne and who achieved at least moderate improvement in initial treatment phase. Specific treatment not described, but participants taking certain topical and systemic treatments were required to complete specified washout periods before they could enter the study.<br><br>Mean age (years): NR for maintenance phase<br>Sex (male): NR for maintenance phase | • 0.1% adapalene gel once daily in the evening after gentle cleaning of the face | • No treatment (simple and gentle washing of the face) | • Mean percentage reduction after 12 weeks maintenance phase (total lesions)<br>• Global assessment of change (further improved and much improved/clear) at the end of 12 weeks maintenance phase<br>• Adverse events |

*BPO: benzoyl peroxide; IGA: Investigator's Global Assessment; ISGA: Investigator's Static Global Assessment; LRAGS: Leeds Revised Acne Grading Scale; N: number; NR: not reported; RCT: randomised controlled trial; SD: standard deviation; SGCA: Subjects' Global Change Assessment*

See the full evidence table in appendix D and 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 conducted for this review question, 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*

Clinician-rated and participant-reported improvement were prioritised by the guideline committee as critical outcomes because these indicate effectiveness of a specific intervention and also whether the person receiving the intervention perceives an improvement in acne vulgaris. Prevention of scarring was also chosen as a critical outcome because it may be associated with physical and psychological distress.

Relapse, acceptability, tolerability and side effects were important outcomes as they indicate effectiveness of the intervention and how likely people are to adhere to a treatment regime.

### *The quality of the evidence*

The quality of the evidence ranged from very low to moderate quality, with most of the evidence being of low or very low quality. This was predominately due to risk of bias of studies and imprecision in the effect estimates. The committee noted that a number of studies did not report allocation concealment or blinding and there were high attrition rates in a couple of studies, all of which lowered their confidence in the findings. There were also some small studies which made the effect size uncertain due to large confidence intervals.

### *Benefits and harms*

The committee agreed that there was little evidence to inform decision making on the most effective maintenance treatment because it only investigated a small number of all possible maintenance options. So they used their expertise and experience, as well as the evidence, to make recommendations.

Based on their knowledge and experience, the committee decided to recommend good, continued skin care for all people with acne. The committee agreed that it is important to encourage good skin care regimens because this would help maintain the improvements achieved by the acne treatment.

The committee discussed that maintenance treatment is not always necessary for everyone who has achieved acne clearance following completion of treatment, as in many cases acne is unlikely to return after successful treatment. Also, in some people the acne may be mild after treatment which may no longer be a problem for the person and they might prefer not to

have maintenance treatment. Therefore, the committee decided that it was good clinical practice to explain to the person with acne following completion of treatment that maintenance treatment may not always be required for everyone.

Based on evidence from 2 studies where acne had improved rather than cleared and treatment was effectively maintaining this improvement, the committee decided that it could be appropriate for people where acne frequently relapses after treatment because a maintenance treatment could also reduce the likelihood of acne recurring.

There was some limited evidence of very low quality reporting clinician rated improvement using topical retinoid (adapalene) combined with benzoyl peroxide versus a sham treatment. Since this combination was also found to be effective as a first-line treatment (see evidence reports E1, E2, F1 and F2) the committee decided to made a weak recommendation for this topical combination to be considered as a maintenance treatment.

Even though the committee agreed that the combination treatment of adapalene and benzoyl peroxide demonstrated the best clinical effect, they discussed that other options should be available for those unable to tolerate this treatment. There was some evidence of moderate to low quality suggesting that topical retinoids (adapalene, tretinoin) or topical azelaic acid had some benefit for small numbers of people versus sham treatment or placebo. Although there was no evidence of discontinuation or discontinuation due to side effects for people using topical retinoids for up to 24 weeks, from their knowledge and experience, the committee agreed that retinoids can cause skin dryness and irritation, and are light sensitising so there is potential for side effects. Furthermore, the committee discussed that retinoids should not be used in pregnancy and that there are possible resource implications associated with retinoid use (for example in relation to the pregnancy prevention programmes for people with child bearing potential). Very low quality evidence from one study comparing benzoyl peroxide to a topical retinoid (adapalene) showed no difference between the two interventions on relapse or the side effects of erythema and dryness. The committee discussed that benzoyl peroxide is commonly prescribed in clinical practice and provides more options as it is available in different strengths. Therefore, the committee agreed to make a weak recommendation for the use of a topical monotherapy of adapalene, azelaic acid, or benzoyl peroxide maintenance treatments if a fixed combination of topical benzoyl peroxide and topical adapalene or either of the component parts is not tolerated.

The committee noted that the majority of the evidence reviewed participants at 12 weeks and discussed that 6 to 8 weeks is the minimum time required to see a response to a treatment. Therefore, the committee agreed that a review should take place at 12 weeks.

**Cost effectiveness and resource use**

No economic evidence was identified for this review question. The recommendations made by the committee on discussing the value of continued appropriate skin care to all people with acne and the value of maintenance treatment, in particular to specific subgroups of people with acne, have minimal healthcare resource implications relating to the health professionals' time to provide advice. The committee expressed the view that offering maintenance treatment to people with a history of frequent relapse after treatment is likely to lead to health benefits for these populations at a relative low cost (as drug acquisition costs of the recommended topical treatments are low), and potential future cost-savings, as these populations, without maintenance treatment, may need to contact health services for refractory or relapsing acne and require more costly treatment in the future. The committee agreed that reviewing maintenance treatment after 12 weeks in order to decide whether to continue or not ensured efficient use of resources by avoiding prolonged use of treatment that is not effective or not needed anymore.

**Other factors the committee took into account**

The committee discussed their experience with low dose isotretinoin as a maintenance treatment. There is variation in clinical practice with some healthcare providers prescribing this whereas other do not. Given a lack of evidence the committee decided not to make a recommendation, but recommended further research to investigate the effectiveness of a reduced dose of oral isotretinoin which could potentially also be used as maintenance treatment (see appendix L in evidence review F1 related to more severe forms of acne where isotretinoin can be prescribed).

## Recommendations supported by this evidence review

This evidence review supports recommendations 1.7.1 to 1.7.5 in the guideline.

## References

**Kawashima 2018**

Kawashima M., Miyachi Y., Efficacy of BPO 2.5% Gel in the Acute and Maintenance Periods for Moderate or Severe Facial Acne Vulgaris, J Dermatol Dis, 5, 273, 2018

**Leyden 2006**

Leyden, J., Thiboutot, D. M., Shalita, A. R., Webster, G., Washenik, K., Strober, B. E., Shupack, J., Comparison of tazarotene and minocycline maintenance therapies in acne vulgaris: a multicenter, double-blind, randomized, parallel-group study, Arch Dermatol, 142, 605-12, 2006

**Poulin 2011**

Poulin, Y., Sanchez, N. P., Bucko, A., Fowler, J., Jarratt, M., Kempers, S., Kerrouche, N., Dhuin, J. C., Kunynetz, R., A 6-month maintenance therapy with adapalene-benzoyl peroxide gel prevents relapse and continuously improves efficacy among patients with severe acne vulgaris: results of a randomized controlled trial, Br J Dermatol, 164, 1376-82, 2011

**Thiboutot 2006**

Thiboutot, D. M., Shalita, A. R., Yamauchi, P. S., Dawson, C., Kerrouche, N., Arsonnaud, S., Kang, S., Adapalene gel, 0.1%, as maintenance therapy for acne vulgaris: a randomized, controlled, investigator-blind follow-up of a recent combination study, Arch Dermatol, 142, 597-602, 2006

**Thielitz 2007**

Thielitz, A., Sidou, F., Gollnick, H., Control of microcomedone formation throughout a maintenance treatment with adapalene gel, 0.1%, J Eur Acad Dermatol Venereol, 21, 747-53, 2007

**Thielitz 2015**

Thielitz, A., Lux, A., Wiede, A., Kropf, S., Papakonstantinou, E., Gollnick, H., A randomized investigator-blind parallel-group study to assess efficacy and safety of azelaic acid 15% gel vs. adapalene 0.1% gel in the treatment and maintenance treatment of female adult acne, J Eur Acad Dermatol Venereol, 29, 789-96, 2015

**Truchuelo 2015**

Truchuelo, M. T., Jimenez, N., Mavura, D., Jaen, P., Assessment of the efficacy and safety of a combination of 2 topical retinoids (RetinSphere) in maintaining post-treatment response of acne to oral isotretinoin, Actas Dermo-Sifiliograficas, 106, 126-32, 2015

**Vender 2012**

Vender, R., Double-blinded, vehicle-controlled proof of concept study to investigate the recurrence of inflammatory and noninflammatory acne lesions using tretinoin gel (Microsphere) 0.04% in male patients after oral isotretinoin use, Dermatology Research and Practice (no pagination), 2012

**Zhang 2004**

Zhang, J., Li, L. F., Tu, Y. T., Zheng, J., A successful maintenance approach in inflammatory acne with adapalene gel 0.1% after an initial treatment in combination with clindamycin topical solution 1% or after monotherapy with clindamycin topical solution 1%, Journal of Dermatological Treatment, 15, 372-378, 2004

# Appendices

## Appendix A – Review protocol

### Review protocol for review question: What is the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris?

**Table 3: Review protocol for topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris**

| Field | Content |
|---|---|
| PROSPERO registration number | CRD42020165925 |
| Review title | Topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris. |
| Review question | What is the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris? |
| Objective | The objective of this review is to establish the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris. |
| Searches | The following databases will be searched:<br>• Cochrane Central Register of Controlled Trials (CENTRAL)<br>• Cochrane Database of Systematic Reviews (CDSR)<br>• Embase<br>• MEDLINE<br>Searches will be restricted by:<br>• Date: No restriction.<br>• Language of publication: English language only.<br>• Publication status: Conference abstracts will be excluded because these do not typically provide sufficient information to fully assess risk of bias. Unpublished data will also be excluded.<br>• Standard exclusions filter (animal studies/low level publication types) will be applied .<br>• For each search, the principal database search strategy is quality assured by a second information specialist using an adaption of the PRESS 2015 Guideline Evidence-Based Checklist.<br>• Other search methods will involve scanning the reference lists of all eligible systematic reviews for published studies meeting inclusion criteria. |
| Condition or domain being studied | • Acne vulgaris |
| Population | Inclusion:<br>• People of all ages whose acne is 'in remission', have had their acne treated successfully, or whose acne has responded to treatment.<br><br>All settings (community, primary, secondary, and tertiary healthcare) will be considered.<br><br>Exclusion:<br>• Neonatal acne |

| Field | Content |
|---|---|
| | • People with post-inflammatory dyspigmentation<br>• Trials in people with PCOS. |
| Intervention | • Topical treatments including abrasive/cleaning agents, anthelmintics, antibacterials, antibiotics, antiseptics, dicarboxylic acids, vitamin B3, retinoids or retinoid-like agents, or any combination of these.<br>• Oral antibiotics including, for example, carbapenems, cephamycins/cephalosporins, sulphones, fucidic acid, lincosamides, macrolides, monobactams, penicillins, or any combination of these.<br>• Oral isotretinoin.<br>• Hormonal treatments including (monophasic and phasic) progestogen-only contraceptives, co-cyprindiol, and combined oral contraceptives.<br>• Hormone-modifying agents including, for example, aldosterone antagonists (for example spironolactone), class 5α- reductase inhibitor (for example dutasteride), other non-steroidal anti-androgens (for example flutamide), and metformin.<br>• Physical treatments including chemical peels (for example salicylic acid), comedone extraction, and treatments using energy-based devices (for example photochemical therapy, photodynamic therapy, photopneumatic therapy, photothermal therapy, radiofrequency therapy).<br>• |
| Comparator | Comparisons include:<br>• Any other active acne treatment<br>• No treatment<br>• Placebo (for example vehicle capsule, gel, solution, tablet)<br>• Sham physical treatment<br>• Waiting list |
| Types of study to be included | Included study designs:<br>• Systematic reviews/meta-analyses of randomised controlled trials (RCTs).<br>• RCTs (individual or cluster parallel group, or split-face/-body trials).<br><br>Studies that do not report the level of acne severity in the study sample, or that include all ranges of severity, from mild to severe, without providing sub-group analyses by level of acne severity, will be excluded.<br><br>Excluded study designs:<br>• Quasi-randomised or non-randomised controlled trials<br>• Case-control studies<br>• Cohort studies<br>• Cross-sectional studies<br>• Epidemiological reviews or reviews on associations<br>• Non-comparative studies<br><br>Note: For further details, see the algorithm in appendix H, Developing NICE guidelines: the manual. |
| Other exclusion criteria | • Trials that have specifically recruited people who have not responded to previous treatment (refractory or resistant acne) for the same episode of acne; however, trials of people with recurrent or persistent acne, who are treated for a new episode of acne, will be included.<br>• Trials with <50% completion data.<br>• Trials that do not report the level of acne severity in the study sample, or they include all ranges of severity. |

| Field | Content |
|---|---|
| | • Trials with indirect population: Where studies with a mixed population (that is include people with acne vulgaris and another condition, for example hirsutism) are identified, those with <66% of the relevant population will be excluded, unless subgroup analysis for acne vulgaris is reported. |
| Context | Pharmacological interventions listed above, alone or in combination, will be included if administered in fixed or flexible doses within the therapeutic range recommended by the British National Formulary (BNF), or, if not available in the UK, recommended by the US Food and Drug Administration (FDA). The only exception will be oral isotretinoin, for which we will allow lower doses to be considered, as there is indication that these are efficacious while the rate of isotretinoin-related side effects is lower.<br><br>The short-term safety of interventions in the treatment of acne vulgaris as reported in studies (for example at end of treatment or follow up) will be covered in this review. The long-term safety of interventions will not be covered in this review. Please see the BNF and MHRA for further information. Relevant legislation and national policy will also be used to inform the guideline, as detailed on p.102 of Developing NICE guidelines: the manual.<br><br>Recommendations will apply to those receiving care in any healthcare settings (for example community, primary, secondary, and tertiary care). If any antibiotic intervention is found to be effective, the committee will consider the evidence in conjunction with considerations regarding antimicrobial resistance patterns (for example ESPAUR report), the safety of the specific antibiotic as determined by any relevant MHRA Drug Safety Update (https://www.gov.uk/drug-safety-update) and Summary of Product characteristics (https://www.medicines.org.uk/emc), and the principle that the use of antibiotics should be limited or optimised where possible. |
| Primary outcomes (critical outcomes) | **Critical outcomes**<br>Efficacy:<br>Efficacy of acne treatments will be assessed by the following three outcomes:<br>• Clinician-rated improvement at treatment endpoint<br>  ○ Percentage change in acne lesion count<br>  ○ Change from baseline or final score on a validated acne severity scale<br>• Prevention of scarring at any follow up<br>  ○ Change from baseline or final number of scars<br>  ○ Incidence of scarring<br>• Participant-reported improvement<br>  ○ Change in acne severity or symptoms (for example assessed using global acne score)<br>Note: For clinician-rated improvement, total lesion counts will be preferred but counts for lesion types (for example papules, pustules) or for inflammatory and non-inflammatory lesions may be included if these are not reported. |
| Secondary outcomes (important outcomes) | **Important outcomes**<br>• Relapse<br>  ○ Relapse during or after maintenance treatment<br>• Acceptability<br>  ○ Treatment discontinuation for any reason |

| Field | Content |
|---|---|
| | • Tolerability<br>  ○ Treatment discontinuation due to side effects<br>• Side effects<br>The following specific short-term side effects will be assessed for comparisons of treatments within the same class or those that involve an inactive arm (for example placebo, no or sham treatment):<br>  ○ Topical treatments, oral antibiotics or combination treatments: skin irritation (for example burning or tingling, dryness/irritation, swelling).<br>  ○ Topical retinoids: sensitivity to light.<br>  ○ Oral antibiotics: gastrointestinal side effects; thrush candidiasis.<br>  ○ Hormonal contraceptives and hormone-modifying agents: breast tenderness; neurological side effects (headache/migraine, mood disturbance, nausea); sexual dysfunction.<br>  ○ Hormonal contraceptives: breakthrough bleeding; mood disturbance.<br>  ○ Hormone-modifying agents: hepatobiliary side effects. For aldosterone receptor antagonists: renal side effects.<br>  ○ Metformin: gastrointestinal side effects.<br>  ○ Oral isotretinoin: change in mucosal and/or cutaneous condition (for example new cheilitis); change in participant's mood (as assessed by score on validated scale); diagnosis of any psychiatric disorder (for example depressive disorder); suicidality.<br>  ○ Physical treatments: persistent skin redness of 'treated' area; changes in pigmentation (for example hypopigmentation).<br>  ○ Chemical peels: heart, kidney or liver damage; infection of 'treated' area.<br>  ○ Comedone extraction: infection of 'treated' area; pain of 'treated' area.<br>  ○ Energy-based devices: skin irritation.<br><br>Note: Treatment discontinuation for any reason will be assessed by the number of participants leaving study before completion of treatment or who are lost to follow up. |
| Data extraction (selection and coding) | • All references identified by the searches and from other sources will be uploaded into STAR and de-duplicated. Titles and abstracts of the retrieved citations will be screened to identify studies that potentially meet the inclusion criteria outlined in the review protocol.<br>• Dual sifting will be performed on at least 10% of records; 90% agreement is required.<br>• Disagreements will be resolved via discussion between the 2 reviewers, and consultation with senior staff if necessary.<br>• Full versions of the selected studies will be obtained for assessment. Studies that fail to meet the inclusion criteria once the full version has been checked will be excluded at this stage. Each study excluded after checking the full version will be listed, along with the reason for its exclusion. A standardised form will be used to extract data from studies, including study reference, study characteristics (for example design, type of statistical analysis), participant characteristics (for example age, ethnicity, sex, scale/method used to assess acne severity, concurrent acne treatment skin type [for example Fitzpatrick type]), intervention(s) characteristics (intervention details, for example dosage, length, duration, frequency, mode), outcomes, and risk of bias. One reviewer will extract relevant data into a standardised form, and this will be quality |

| Field | Content | | |
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| | assessed by a senior reviewer. | | |
| Risk of bias (quality) assessment | Risk of bias of individual studies will be assessed using the relevant version of the Cochrane RoB tool, v.2 checklist (that is for parallel group or individually-randomised cross-over trials) as described in Developing NICE guidelines: the manual. | | |
| Strategy for data synthesis | • Depending on the availability of the evidence, the findings will be summarised narratively or quantitatively. Where possible, meta-analyses will be conducted using Cochrane's Review Manager software. A fixed effect meta-analysis will be conducted and data will be presented as risk ratios or odds ratios for dichotomous outcomes, and mean differences or standardised mean differences for continuous outcomes.<br>• Heterogeneity in the effect estimates of the individual studies will be assessed using the $I^2$ statistic. $I^2$ values of greater than 50% and 80% will be considered as serious and very serious heterogeneity, respectively. Heterogeneity will be explored as appropriate using sensitivity analyses and pre-specified subgroup analyses. If heterogeneity cannot be explained through subgroup analysis then a random effects model will be used for meta-analysis, or the data will not be pooled.<br>• Default MIDs will be used for risk ratios and continuous outcomes only, unless the committee pre-specifies published or other MIDs for specific outcomes<br>○ For risk ratios: 0.8 and 1.25.<br>○ 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.<br>• The confidence in the findings across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group: https://www.gradeworkinggroup.org/. | | |
| Analysis of sub-groups | Stratified analysis will be conducted for the following groups:<br>• Severity of acne<br>○ Mild to moderate<br>○ Moderate to severe | | |
| Type and method of review | ☒ | Intervention | |
| | ☐ | Diagnostic | |
| | ☐ | Prognostic | |
| | ☐ | Qualitative | |
| | ☐ | Epidemiologic | |
| | ☐ | Service Delivery | |
| | ☐ | Other (please specify) | |
| Language | English | | |
| Country | England | | |
| Anticipated or actual start date | 20 October 2019 | | |
| Anticipated completion date | 13 January 2021 | | |
| Stage of review | Review stage | Started | Completed |

| Field | Content | | |
|---|---|---|---|
| at time of this submission | 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<br>National Guideline Alliance (NGA)<br>5b Named contact e-mail<br>AcneManagement@nice.org.uk<br>5e Organisational affiliation of the review<br>National Institute for Health and Care Excellence (NICE) and National Guideline Alliance: https://www.nice.org.uk; https://www.rcog.org.uk/en/about-us/nga/. | | |
| Review team members | National Guideline Alliance | | |
| Funding sources/sponsor | This systematic review is being completed by the NGA, which is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists. NICE funds the NGA 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/NG198/history | | |
| Other registration details | Not applicable | | |
| Reference/URL for published protocol | https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=165925 | | |
| Dissemination plans | NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as:<br>• notifying registered stakeholders of publication<br>• publicising the guideline through NICE's newsletter and alerts<br>• 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. | | |

| Field | Content | |
|---|---|---|
| Keywords | Acne vulgaris; Benzoyl Peroxide; Humans; Physical Examination. | |
| 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 | https://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; NGA: National Guidelines Alliance; PCOS: polycystic ovary syndrome; RCT: randomised controlled trial; SD: standard deviation*

# Appendix B – Literature search strategies

## Literature search strategies for review question: What is the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris?

## Clinical search

### Topical interventions (including topical retinoids)

Date of initial search: 07/08/2019

Additional terms added and searched: 10/09/2019

Last searched: 07/05/2020

Database(s): Embase Classic+Embase 1947 to 2020 May 06, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to May 06, 2020

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 topical antiinfective agent/ use emczd |
| 6 | exp Anti-Infective Agents, Local/ use ppez |
| 7 | 5 or 6 |
| 8 | exp antibiotic agent/ use emczd |
| 9 | exp Anti-Bacterial Agents/ use ppez |
| 10 | exp anthelmintic agent/ use emczd |
| 11 | exp Anthelmintics/ use ppez |
| 12 | (antibiotic* or anti biotic* or anti bacteri* or antibacteri* or bacteriocid*).tw. |
| 13 | (anthelminti* or antihelmint?i* or anti-helmint?i* or antiparasit* or anti-parasit* or vermifug*).tw. |
| 14 | adapalene/ |
| 15 | aluminum oxide/ use emczd |
| 16 | amoxicillin/ |
| 17 | ampicillin/ |
| 18 | avermectin/ use emczd |
| 19 | azelaic acid/ |
| 20 | benzoyl peroxide plus clindamycin/ use emczd |
| 21 | benzoyl peroxide/ |
| 22 | (Benzoyl Peroxide/ and Clindamycin/) use ppez |
| 23 | cefaclor/ |
| 24 | cefadroxil/ |
| 25 | cefalexin/ use emczd |
| 26 | Cephalexin/ use ppez |
| 27 | cefixime/ |
| 28 | cefotaxime/ |
| 29 | cefradine/ use emczd |
| 30 | Cephradine/ use ppez |
| 31 | ceftaroline/ use emczd |
| 32 | ceftazidime/ |
| 33 | ceftriaxone/ |
| 34 | cefuroxime/ |
| 35 | chlorhexidine gluconate/ |
| 36 | clarithromycin/ |
| 37 | clindamycin/ |
| 38 | dapsone/ |
| 39 | doxycycline/ |
| 40 | erythromycin/ |
| 41 | erythromycin plus isotretinoin/ use emczd |
| 42 | flucloxacillin/ use emczd |
| 43 | Floxacillin/ use ppez |

| # | Searches |
|---|---|
| 44 | fusidic acid/ |
| 45 | isotretinoin/ |
| 46 | isotretinoin/ and clindamycin/ |
| 47 | ivermectin/ |
| 48 | lymecycline/ |
| 49 | metronidazole/ |
| 50 | minocycline/ |
| 51 | nadifloxacin/ |
| 52 | nicotinamide/ use emczd |
| 53 | Niacinamide/ use ppez |
| 54 | nitroimidazole/ use emczd |
| 55 | ozenoxacin/ |
| 56 | oxytetracycline/ |
| 57 | penicillin G/ |
| 58 | penicillin V/ |
| 59 | (phenol/ and chlorhexidine digluconate/) use emczd |
| 60 | (phenol/ and chlorhexidine/) use ppez |
| 61 | piperacillin/ |
| 62 | (pleuromutilin/ or pleuromutilin antibiotic agent/) use emczd |
| 63 | praziquantel/ |
| 64 | pseudomonic acid/ use emczd |
| 65 | Mupirocin/ use ppez |
| 66 | retapamulin/ use emczd |
| 67 | retinol/ use emczd |
| 68 | Vitamin A/ use ppez |
| 69 | tetracycline/ |
| 70 | ticarcillin/ |
| 71 | retinoic acid/ use emczd |
| 72 | tazarotene/ use emczd |
| 73 | temocillin/ use emczd |
| 74 | tretinoin/ use ppez |
| 75 | triclocarban/ use emczd |
| 76 | triclosan/ |
| 77 | trimethoprim/ |
| 78 | zinc acetate/ |
| 79 | (adapalene or aluminum oxide or ampicillin or amoxicillin or avermectin or az?laic acid or benzylpenicillin or benzyl penicillin or benzoyl peroxide or cefaclor or cefadroxil or cefalexin or cephalexin or cefixime or cefotaxime or cefradine or ceftaroline or ceftazidime or ceftriaxone or cefuroxime or cephalexin or cephalosporin* or cephamycin* or cephradine or chlorhexidine digluconate or chlorhexidine gluconate or clarithromycin or clindamycin or dapsone or diaminodiphenyl sulfone or doxycyclin* or erythromycin or floxacillin or flucloxacillin or fucidin or fusidic acid or fusidate sodium or sodium fusidate or germolene or isotretinoi* or ivermectin or lincosamide* or lymecycline or macrolide* or metronidazole or minocycline or nadifloxacin or niacinamide or nicotinamide or nitroimidazole or ozenoxacin or oxytetracyline or penicillin* or phenol or phenoxymethylpenicillin or piperacillin or pleuromutilin or praziquantel or cysticide or pseudomonic acid or mupirocin or quinoderm or quinolon* or retapamulin or retinoi* or retinol or tazarotene or temocillin or tetracyclin* or ticarcillin or tretinoin or triclocarban or triclosan or triclozan or trimethoprim or vitamin a or vitamin b3 or zinc acetate).tw. |
| 80 | or/7-79 |
| 81 | (topical or topically or cream? or emulsi* or gel? or foam? or ointment* or solution? or lotion? or pad?).tw. |
| 82 | (ointment/ or exp gel/) use emczd |
| 83 | (Ointments/ or exp Gels/) use ppez |
| 84 | skin cream/ |
| 85 | (cutaneous drug administration/ or topical drug administration/) use emczd |
| 86 | (Administration, Topical/ or Administration, Cutaneous/) use ppez |
| 87 | topical drug administration.fs. |
| 88 | (cutaneous or dermal or skin or transcutaneous or transdermal or percutaneous).tw. |
| 89 | or/81-88 |
| 90 | 4 and 80 and 89 |
| 91 | limit 90 to english language |
| 92 | Letter/ use ppez |
| 93 | letter.pt. or letter/ use emczd |
| 94 | note.pt. |
| 95 | editorial.pt. |
| 96 | Editorial/ use ppez |
| 97 | News/ use ppez |
| 98 | exp Historical Article/ use ppez |
| 99 | Anecdotes as Topic/ use ppez |
| 100 | Comment/ use ppez |
| 101 | Case Report/ use ppez |
| 102 | case report/ or case study/ use emczd |
| 103 | (letter or comment*).ti. |
| 104 | or/92-103 |

| # | Searches |
|---|---|
| 105 | randomized controlled trial/ use ppez |
| 106 | randomized controlled trial/ use emczd |
| 107 | random*.ti,ab. |
| 108 | or/105-107 |
| 109 | 104 not 108 |
| 110 | animals/ not humans/ use ppez |
| 111 | animal/ not human/ use emczd |
| 112 | nonhuman/ use emczd |
| 113 | exp Animals, Laboratory/ use ppez |
| 114 | exp Animal Experimentation/ use ppez |
| 115 | exp Animal Experiment/ use emczd |
| 116 | exp Experimental Animal/ use emczd |
| 117 | exp Models, Animal/ use ppez |
| 118 | animal model/ use emczd |
| 119 | exp Rodentia/ use ppez |
| 120 | exp Rodent/ use emczd |
| 121 | (rat or rats or mouse or mice).ti. |
| 122 | or/109-121 |
| 123 | 91 not 122 |
| 124 | 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. |
| 125 | 124 use ppez |
| 126 | (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. |
| 127 | 126 use ppez |
| 128 | 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. |
| 129 | 128 use emczd |
| 130 | 125 or 127 |
| 131 | 129 or 130 |
| 132 | Meta-Analysis/ |
| 133 | exp Meta-Analysis as Topic/ |
| 134 | systematic review/ |
| 135 | meta-analysis/ |
| 136 | (meta analy* or metanaly* or metaanaly*).ti,ab. |
| 137 | ((systematic or evidence) adj2 (review* or overview*)).ti,ab. |
| 138 | ((systematic* or evidence*) adj2 (review* or overview*)).ti,ab. |
| 139 | (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. |
| 140 | (search strategy or search criteria or systematic search or study selection or data extraction).ab. |
| 141 | (search* adj4 literature).ab. |
| 142 | (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. |
| 143 | cochrane.jw. |
| 144 | ((pool* or combined) adj2 (data or trials or studies or results)).ab. |
| 145 | (or/132-134,136,138-143) use ppez |
| 146 | (or/134-137,139-144) use emczd |
| 147 | or/145-146 |
| 148 | network meta-analysis/ |
| 149 | ((network adj (MA or MAs)) or (NMA or NMAs)).tw. |
| 150 | ((indirect or mixed or multiple or multi-treatment* or simultaneous) adj1 comparison*).tw. |
| 151 | or/148-150 |
| 152 | 131 or 147 or 151 |
| 153 | 123 and 152 |

Database(s): The Cochrane Library: Cochrane Database of Systematic Reviews, Issue 5 of 12, May 2020; Cochrane Central Register of Controlled Trials, Issue 5 of 12, May 2020

| # | Searches |
|---|---|
| #1 | MeSH descriptor: [Acne Vulgaris] explode all trees |
| #2 | acne:ti,ab |
| #3 | #1 or #2 |
| #4 | (topical or topically or cream or creams or emulsi* gel or gels or foam or foams or ointment* or solution or solutions or lotion or lotions or pad or pads):ti,ab |
| #5 | MeSH descriptor: [Ointments] this term only |
| #6 | MeSH descriptor: [Gels] explode all trees |
| #7 | MeSH descriptor: [Skin Cream] this term only |
| #8 | MeSH descriptor: [Administration, Topical] this term only |
| #9 | MeSH descriptor: [Administration, Cutaneous] this term only |
| #10 | (cutaneous or dermal or skin or transcutaneous or transdermal or percutaneous):ti,ab |
| #11 | {or #4-#10} |

| # | Searches |
|---|---|
| #12 | MeSH descriptor: [Anti-Bacterial Agents] explode all trees |
| #13 | MeSH descriptor: [Anthelmintics] explode all trees |
| #14 | (antibiotic* or "anti biotic*" or "anti bacteri*" or antibacteri* or bacteriocid*):ti,ab |
| #15 | (anthelminti* or antihelminthi* or antithelminti* or anti-helminthi* or anti-helminti* or antiparasit* or anti-parasit* or vermifug*):ti,ab |
| #16 | MeSH descriptor: [Adapalene] this term only |
| #17 | MeSH descriptor: [Aluminum Oxide] this term only |
| #18 | MeSH descriptor: [Amoxicillin] this term only |
| #19 | MeSH descriptor: [Ampicillin] this term only |
| #20 | MeSH descriptor: [Benzoyl Peroxide] this term only |
| #21 | MeSH descriptor: [Cefaclor] this term only |
| #22 | MeSH descriptor: [Cefadroxil] this term only |
| #23 | MeSH descriptor: [Cephalexin] this term only |
| #24 | MeSH descriptor: [Cefixime] this term only |
| #25 | MeSH descriptor: [Cefotaxime] this term only |
| #26 | MeSH descriptor: [Cephradine] this term only |
| #27 | MeSH descriptor: [Ceftazidime] this term only |
| #28 | MeSH descriptor: [Ceftriaxone] this term only |
| #29 | MeSH descriptor: [Cefuroxime] this term only |
| #30 | MeSH descriptor: [Clarithromycin] this term only |
| #31 | MeSH descriptor: [Clindamycin] this term only |
| #32 | MeSH descriptor: [Dapsone] this term only |
| #33 | MeSH descriptor: [Doxycycline] this term only |
| #34 | MeSH descriptor: [Erythromycin] this term only |
| #35 | MeSH descriptor: [Floxacillin] this term only |
| #36 | MeSH descriptor: [Fusidic Acid] this term only |
| #37 | MeSH descriptor: [Isotretinoin] this term only |
| #38 | MeSH descriptor: [Ivermectin] this term only |
| #39 | MeSH descriptor: [Lymecycline] this term only |
| #40 | MeSH descriptor: [Minocycline] this term only |
| #41 | MeSH descriptor: [Mupirocin] this term only |
| #42 | MeSH descriptor: [Niacinamide] this term only |
| #43 | MeSH descriptor: [Oxytetracycline] this term only |
| #44 | MeSH descriptor: [Penicillin G] this term only |
| #45 | MeSH descriptor: [Penicillin V] this term only |
| #46 | MeSH descriptor: [Phenol] this term only |
| #47 | MeSH descriptor: [Piperacillin] this term only |
| #48 | MeSH descriptor: [Praziquantel] this term only |
| #49 | MeSH descriptor: [Vitamin A] this term only |
| #50 | MeSH descriptor: [Tetracycline] this term only |
| #51 | MeSH descriptor: [Ticarcillin] this term only |
| #52 | MeSH descriptor: [Tretinoin] this term only |
| #53 | MeSH descriptor: [Trimethoprim] this term only |
| #54 | MeSH descriptor: [Zinc Acetate] this term only |
| #55 | (adapalene or aluminum oxide or ampicillin or amoxicillin or avermectin or azaelaic acid or azelaic acid or benzylpenicillin or benzyl penicillin or benzoyl peroxide or cefaclor or cefadroxil or cefalexin or cephalexin or cephalosporin* or cephamycin* or cefixime or cefotaxime or cefradine or ceftaroline or ceftazidime or ceftriaxone or cefuroxime or cephalexin or cephradine or chlorhexidine digluconate or chlorhexidine gluconate or clarithromycin or clindamycin or dapsone or diaminodiphenyl sulfone or doxycyclin* or erythromycin or floxacillin or flucloxacillin or fucidin or fusidic acid or fusidate sodium or sodium fusidate or germolene or isotretinoi* or ivermectin or lincosamide* or lymecycline or macrolide* or minocycline or mupirocin or pseudomonic acid or nadifloxacin or niacinamide or nicotinamide or nitroimidazole or ozenoxacin or oxytetracyline or penicillin* or phenol or phenoxymethylpenicillin or piperacillin or pleuromutilin or praziquantel or cysticide or quinoderm or quinolone* or retapamulin or retino* or retinol or temocillin or tetracyclin* or ticarcillin or tretinoin or trimethoprim or vitamin a or zinc acetate):ti,ab |
| #56 | {or #12-#55} |
| #57 | #3 and #11 and #56 |

### Oral antibiotics and oral isotretinoin

Database(s): Embase Classic+Embase 1947 to 2020 May 06, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to May 06, 2020

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 |

| # | Searches |
|---|---|
| 5 | exp antibiotic agent/ use emczd |
| 6 | exp Anti-Bacterial Agents/ use ppez |
| 7 | (antibiotic* or anti biotic* or anti bacteri* or antibacteri* or bacteriocid*).tw. |
| 8 | exp carbapenem derivative/ use emczd |
| 9 | exp Carbapenems/ use ppez |
| 10 | exp cephalosporin derivative/ use emczd |
| 11 | exp Cephalosporins/ use ppez |
| 12 | exp cephamycin derivative/ use emczd |
| 13 | exp Cephamycins/ use ppez |
| 14 | dapsone/ |
| 15 | exp lincosamide/ use emczd |
| 16 | exp Lincosamide/ use ppez |
| 17 | exp macrolide/ use emczd |
| 18 | exp Macrolides/ use ppez |
| 19 | exp monobactam derivative/ use emczd |
| 20 | exp Monobactams/ use ppez |
| 21 | exp penicillin derivative/ use emczd |
| 22 | exp Penicillins/ use ppez |
| 23 | exp quinoline derived antiinfective agent/ use emczd |
| 24 | exp Quinolones/ use ppez |
| 25 | exp retinoid/ use emczd |
| 26 | exp Retinoids/ use ppez |
| 27 | exp tetracycline derivative/ use emczd |
| 28 | exp Tetracyclines/ use ppez |
| 29 | trimethoprim/ |
| 30 | (carbapenem* or biapenem or doripenem or ertapenem or imipenem or meropenem or panipenem or betamipron or tebipenem).tw. |
| 31 | (cephamycin* or cephalosporin* or carbacephem or loracarbef or cefacetrile or cefaclor or cefadroxil or cefalexin or cefaloglycin or cefalonium or cefaloridine or cefalotin or cefamandole or cefapirin or cefatrizine or cefazaflur or cefazedone or cefazolin or cefbuperazone or cefcapene or cefdaloxime or cefdinir or cefditoren or cefepime or cefetamet or cefixime or cefmenoxime or cefmetazole or cefminox or cefodizime or cefonicid or cefoperazone or cefoperazone or ceforanide or cefotaxime or cefotetan or cefotiam or cefozopran or cefpiramide or cefpirome or cefpodoxime or cefprozil or cefquinome or cefradine or cefroxadine or cefsulodin or ceftaroline fosamile or ceftazidime or ceftazidime or cefteram or ceftezole or ceftibiprole or ceftibuten or ceftiolene or ceftolozane or ceftolozane or ceftraroline or ceftriaxone or cefuroxime or cefuzonam or cephamycin or depfimizole or flomoxef or latamoxef or oxacephem).tw. |
| 32 | dapsone.tw. |
| 33 | (isotretinoi* or iso tretinoin or isoretinoin or isotren or isotrex* or accutane or roaccutan* or roaccuttan* or roacuttan* or roacutan* or retinoic acid).tw. |
| 34 | (lincosamide* or clindamycin or lincomycine or linkomycine).tw. |
| 35 | (macrolide* or azithromycin or carbomycin a or clarithromycin or erythromycin or fidaxomicin or josamycin or kitasamycin or midecamycin or oleandomycin or roxithromycin or solithromycin or spiramycin or telithromycin or troleandomycin).tw. |
| 36 | (monobactam* or mono- bactam* or aztreonam).tw. |
| 37 | (penicillin* or almecillin or amoxicillin or ampicillin or azlocillin or bacampicillin or benzathine benzylpenicillin or benzylpenicillin sodium or carbenicillin or carindacillin or cloxacillin or co-amoxiclav or co-fluampicil or co-trimoxazole or dicloxacillin or epicillin or flucloxacillin or hetacillin or mecillinam or metampicillin or methicillin or mezlocillin or nafcillin or oxacillin or phenoxymethylpenicillin or piperacillin or pivampicillin or pivmecillinam hydrochloride or procaine benzylpenicillin or sultamicillin or talampicillin or temocillin or ticarcillin).tw. |
| 38 | (quinolone* or balofloxacin or besifloxacin or ciprofloxacine or clinafloxacin or delafloxacin or enoxacin or fleroxacin or gatifloxacin or gemifloxacin or grepafloxacin or levofloxacin or lomefloxacin or moxifloxacin or nadifloxacin or norfloxacin or ofloxacin or oxolinic acid or ozenoxacin or pazufloxacin or pefloxacin or prulifloxacin or rosoxacin or rufloxacin or sitafloxacin or sparfloxacin or temafloxacin or tosufloxacin).tw. |
| 39 | (tetracylcline* or chlortetracycline or demeclocycline or doxycycline or eravacycline or lymecycline or methacycline or minocycline or omadacycline or oxytetracycline or rolitetracycline or sarecycline or tetracycline or tigecycline).tw. |
| 40 | trimethoprim.tw. |
| 41 | or/5-40 |
| 42 | oral drug administration/ use emczd |
| 43 | Administration, Oral/ use ppez |
| 44 | oral drug administration.fs. |
| 45 | (oral* or per os).tw. |
| 46 | or/42-45 |
| 47 | 4 and 41 and 46 |
| 48 | Letter/ use ppez |
| 49 | letter.pt. or letter/ use emczd |
| 50 | note.pt. |
| 51 | editorial.pt. |
| 52 | Editorial/ use ppez |
| 53 | News/ use ppez |
| 54 | exp Historical Article/ use ppez |
| 55 | Anecdotes as Topic/ use ppez |
| 56 | Comment/ use ppez |

| # | Searches |
|---|---|
| 57 | Case Report/ use ppez |
| 58 | case report/ or case study/ use emczd |
| 59 | (letter or comment*).ti. |
| 60 | or/48-59 |
| 61 | randomized controlled trial/ use ppez |
| 62 | randomized controlled trial/ use emczd |
| 63 | random*.ti,ab. |
| 64 | or/61-63 |
| 65 | 60 not 64 |
| 66 | animals/ not humans/ use ppez |
| 67 | animal/ not human/ use emczd |
| 68 | nonhuman/ use emczd |
| 69 | exp Animals, Laboratory/ use ppez |
| 70 | exp Animal Experimentation/ use ppez |
| 71 | exp Animal Experiment/ use emczd |
| 72 | exp Experimental Animal/ use emczd |
| 73 | exp Models, Animal/ use ppez |
| 74 | animal model/ use emczd |
| 75 | exp Rodentia/ use ppez |
| 76 | exp Rodent/ use emczd |
| 77 | (rat or rats or mouse or mice).ti. |
| 78 | or/65-77 |
| 79 | 47 not 78 |
| 80 | limit 79 to english language |
| 81 | 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. |
| 82 | 81 use ppez |
| 83 | (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. |
| 84 | 83 use ppez |
| 85 | 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. |
| 86 | 85 use emczd |
| 87 | 82 or 84 |
| 88 | 86 or 87 |
| 89 | Meta-Analysis/ |
| 90 | exp Meta-Analysis as Topic/ |
| 91 | systematic review/ |
| 92 | meta-analysis/ |
| 93 | (meta analy* or metanaly* or metaanaly*).ti,ab. |
| 94 | ((systematic or evidence) adj2 (review* or overview*)).ti,ab. |
| 95 | ((systematic* or evidence*) adj2 (review* or overview*)).ti,ab. |
| 96 | (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. |
| 97 | (search strategy or search criteria or systematic search or study selection or data extraction).ab. |
| 98 | (search* adj4 literature).ab. |
| 99 | (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. |
| 100 | cochrane.jw. |
| 101 | ((pool* or combined) adj2 (data or trials or studies or results)).ab. |
| 102 | (or/89-91,93,95-100) use ppez |
| 103 | (or/91-94,96-101) use emczd |
| 104 | or/102-103 |
| 105 | network meta-analysis/ |
| 106 | ((network adj (MA or MAs)) or (NMA or NMAs)).tw. |
| 107 | ((indirect or mixed or multiple or multi-treatment* or simultaneous) adj1 comparison*).tw. |
| 108 | or/105-107 |
| 109 | 88 or 104 or 108 |
| 110 | 80 and 109 |

Database(s): The Cochrane Library: Cochrane Database of Systematic Reviews, Issue 5 of 12, May 2020; Cochrane Central Register of Controlled Trials, Issue 5 of 12, May 2020

| # | Searches |
|---|---|
| #1 | MeSH descriptor: [Acne Vulgaris] explode all trees |
| #2 | acne:ti,ab |
| #3 | #1 or #2 |
| #4 | MeSH descriptor: [Anti-Bacterial Agents] explode all trees |
| #5 | (antibiotic* or "anti biotic*" or "anti bacteri*" or antibacteri* or bacteriocid*):ti,ab |
| #6 | MeSH descriptor: [Amoxicillin] this term only |
| #7 | MeSH descriptor: [Ampicillin] this term only |

| # | Searches |
|---|---|
| #8 | MeSH descriptor: [Azithromycin] this term only |
| #9 | MeSH descriptor: [Azlocillin] this term only |
| #10 | MeSH descriptor: [Penicillin G] this term only |
| #11 | MeSH descriptor: [Carbenicillin] this term only |
| #12 | MeSH descriptor: [Cefaclor] this term only |
| #13 | MeSH descriptor: [Cefadroxil] this term only |
| #14 | MeSH descriptor: [Cephalexin] this term only |
| #15 | MeSH descriptor: [Cefixime] this term only |
| #16 | MeSH descriptor: [Cefotaxime] this term only |
| #17 | MeSH descriptor: [Cephradine] this term only |
| #18 | MeSH descriptor: [Ceftazidime] this term only |
| #19 | MeSH descriptor: [Ceftriaxone] this term only |
| #20 | MeSH descriptor: [Chlortetracycline] this term only |
| #21 | MeSH descriptor: [Clarithromycin] this term only |
| #22 | MeSH descriptor: [Clindamycin] this term only |
| #23 | MeSH descriptor: [Cloxacillin] this term only |
| #24 | MeSH descriptor: [Amoxicillin-Potassium Clavulanate Combination] this term only |
| #25 | MeSH descriptor: [Trimethoprim, Sulfamethoxazole Drug Combination] this term only |
| #26 | (amoxicillin or ampicillin or azithromycin or azlocillin or bacampicillin or benzylpenicillin sodium or "penicillin g" or biapenem or carbenicillin or carbomycin or cefaclor or cefadroxil or cefalexin or cephalexin or cefixime or cefotaxime or cephotaxim* or cefradine or cephradine or ceftaroline or ceftazidime or ceftriaxone or cefuroxime or chlortetracyline or clarithromycin or clindamycin or cloxacillin or co amoxiclav or coamoxiclav or co fluampcil or cofluampcil or co trimoxazole or cotrimoxazole):ti,ab |
| #27 | MeSH descriptor: [Demeclocycline] this term only |
| #28 | MeSH descriptor: [Dicloxacillin] this term only |
| #29 | MeSH descriptor: [Doripenem] this term only |
| #30 | MeSH descriptor: [Doxycycline] this term only |
| #31 | MeSH descriptor: [Ertapenem] this term only |
| #32 | MeSH descriptor: [Erythromycin] this term only |
| #33 | MeSH descriptor: [Fidaxomicin] this term only |
| #34 | MeSH descriptor: [Floxacillin] this term only |
| #35 | (demeclocycline or dicloxacillin or doripenem or doxycycline or epicillin or eravacycline or ertapenem or erythromycin or fidaxomicin or floxacillin or flucloxacillin):ti,ab |
| #36 | MeSH descriptor: [Imipenem] this term only |
| #37 | MeSH descriptor: [Cilastatin, Imipenem Drug Combination] this term only |
| #38 | MeSH descriptor: [Josamycin] this term only |
| #39 | MeSH descriptor: [Kitasamycin] this term only |
| #40 | MeSH descriptor: [Lymecycline] this term only |
| #41 | MeSH descriptor: [Meropenem] this term only |
| #42 | MeSH descriptor: [Methacycline] this term only |
| #43 | MeSH descriptor: [Methicillin] this term only |
| #44 | MeSH descriptor: [Mezlocillin] this term only |
| #45 | MeSH descriptor: [Miocamycin] this term only |
| #46 | MeSH descriptor: [Nafcillin] this term only |
| #47 | (hetacillin or imipenem or isotretinoi* or josamycin* or kitasamycin or leucomycin or lymecycline or meropenem or metampicillin or methampicillin or metacycline or methacycline or methicillin or mezlocillin or midecamycin or minocycline or miocamycin* or miokamycin* or nafcillin):ti,ab |
| #48 | MeSH descriptor: [Oleandomycin] this term only |
| #49 | MeSH descriptor: [Oxacillin] this term only |
| #50 | MeSH descriptor: [Oxytetracycline] this term only |
| #51 | MeSH descriptor: [Penicillin V] this term only |
| #52 | MeSH descriptor: [Piperacillin] this term only |
| #53 | MeSH descriptor: [Piperacillin, Tazobactam Drug Combination] this term only |
| #54 | MeSH descriptor: [Amdinocillin Pivoxil] this term only |
| #55 | MeSH descriptor: [Rolitetracycline] this term only |
| #56 | MeSH descriptor: [Roxithromycin] this term only |
| #57 | MeSH descriptor: [Spiramycin] this term only |
| #58 | MeSH descriptor: [Talampicillin] this term only |
| #59 | MeSH descriptor: [Tetracycline] this term only |
| #60 | MeSH descriptor: [Ticarcillin] this term only |
| #61 | MeSH descriptor: [Tigecycline] this term only |
| #62 | MeSH descriptor: [Trimethoprim] this term only |
| #63 | MeSH descriptor: [Troleandomycin] this term only |
| #64 | (oleandomycin or omadacycline or "PTK-0796" or oxacillin* or oxytetracycline or panipenem or betamipron or carbenin or phenoxymethylpenicillin or "penicillin v" or piperacillin or pivmeillinam or amdinocillin pivoxil or retinoi* or rolitetracycline or roxithromycin or sarecycline or solithromycin or spiramycin or talampicillin or tebipenem or telithromycin or temocillin or tetracylin* or ticarcillin or timentin or tigecycline or trimethoprim or troleandomycin):ti,ab |
| #65 | {or #4-#64} |
| #66 | #3 and #65 |
| #67 | MeSH descriptor: [Administration, Oral] explode all trees |
| #68 | (oral or per os):ti,ab |

| # | Searches |
|---|---|
| #69 | #67 or #68 |
| #70 | #66 and #69 |

### Hormonal interventions

Database(s): Embase Classic+Embase 1947 to 2020 May 06, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to May 06, 2020

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 aldosterone antagonist/ use emczd |
| 6 | exp Mineralocorticoid Receptor Antagonists/ use ppez |
| 7 | spironolactone/ |
| 8 | hydroflumethiazide plus spironolactone/ use emczd |
| 9 | canrenone/ |
| 10 | eplerenone/ |
| 11 | furosemide plus spironolactone/ use emczd |
| 12 | (aldactone or spironolactone or canrenone or co-flumactone or coflumactone or eplerenon* or furosemide).tw. |
| 13 | or/5-12 |
| 14 | exp alpha adrenergic receptor blocking agent/ use emczd |
| 15 | exp Adrenergic alpha-Antagonists/ use ppez |
| 16 | alfuzosin/ use emczd |
| 17 | doxazosin/ |
| 18 | indoramin/ |
| 19 | prazosin/ |
| 20 | tamsulosin/ |
| 21 | dutasteride plus tamsulosin/ use emczd |
| 22 | solifenacin plus tamsulosin/ use emczd |
| 23 | terazosin/ use emczd |
| 24 | (alfuzosin or doxazosin or uroprost or indoramin or prazosin or tamsulosin or terazosin).tw. |
| 25 | or/14-24 |
| 26 | exp steroid 5alpha reductase inhibitor/ use emczd |
| 27 | exp 5-alpha Reductase Inhibitors/ use ppez |
| 28 | dutasteride/ |
| 29 | finasteride/ |
| 30 | (5a reductase inhibitor* or 5-alpha reductase inhibitor* or dutastaride or finasteride).tw. |
| 31 | or/26-30 |
| 32 | exp antiandrogen/ use emczd |
| 33 | exp Androgen Antagonists/ use ppez |
| 34 | metformin/ |
| 35 | abiraterone acetate/ |
| 36 | apalutamide/ use emczd |
| 37 | bicalutamide/ use emczd |
| 38 | cyproterone acetate plus ethinylestradiol/ use emczd |
| 39 | cyproterone acetate/ |
| 40 | enzalutamide/ use emczd |
| 41 | flutamide/ |
| 42 | (antiandrogen* or anti-androgen* or androgen antagonist* or abiraterone acetate or apalutamide or bicalutamide or cocyprindiol or co-cyprindiol or cyproterone acetate or enzalutamide or flutamide or metformin).tw. |
| 43 | or/32-42 |
| 44 | exp oral contraceptive agent/ use emczd |
| 45 | exp Contraceptives, Oral, Combined/ use ppez |
| 46 | exp gestagen/ use emczd |
| 47 | exp Progestins/ use ppez |
| 48 | (chlormadinone acetate plus ethinylestradiol/ or desogestrel plus ethinylestradiol/ or dienogest plus ethinylestradiol/ or drospirenone plus ethinylestradiol/ or dydrogesterone plus estradiol/ or estradiol plus levonorgestrel/ or estradiol plus nomegestrol acetate/ or estradiol plus norethisterone acetate/ or ethinylestradiol plus etonogestrel/ or ethinylestradiol plus gestodene/ or ethinylestradiol plus levonorgestrel/ or ethinylestradiol plus norelgestromin/ or ethinylestradiol plus norethisterone/ or ethinylestradiol plus norgestimate/) use emczd |
| 49 | Ethinyl Estradiol-Norgestrel Combination/ use ppez |
| 50 | (Ethinyl Estradiol/ use ppez and (Chlormadinone Acetate/ or Desogestrel/ or Levonorgestrel/ or Norethindrone/ or Norgestrel/)) use ppez |
| 51 | (Mestranol/ and (Norethindrone/ or Norethynodrel/)) use ppez |
| 52 | (Estradiol/ and (Dydrogesterone/ or Levonorgestrel/ or Medroxyprogesterone Acetate/ or Norethindrone/)) use ppez |

| # | Searches |
|---|---|
| 53 | ((oral* adj contracept*) or progest?gen* or gestagen* or progestin*).tw. |
| 54 | ((ethinyl?estradiol or ethinyl estradiol or ethinyl oestradiol) adj3 (chlormadinone acetate or desogestrel or dienogest or drospirenone or etonogestrel or gestodene or levonorgestrel or nomogestrol or norelgestromin* or norethindrone or norethisterone or norgestimate or norgestrel)).tw. |
| 55 | (mestranol adj3 (norethindrone or norethisterone or noretynodrel or norethynodrel)).tw. |
| 56 | ((estradiol or oestradiol) adj3 (dienogest or dydrogesterone or levonorgestrel or medroxyprogesterone acetate or nomegestrol or norethindrone or norethisterone)).tw. |
| 57 | or/44-56 |
| 58 | or/13,25,31,43,57 |
| 59 | 4 and 58 |
| 60 | limit 59 to english language |
| 61 | Letter/ use ppez |
| 62 | letter.pt. or letter/ use emczd |
| 63 | note.pt. |
| 64 | editorial.pt. |
| 65 | Editorial/ use ppez |
| 66 | News/ use ppez |
| 67 | exp Historical Article/ use ppez |
| 68 | Anecdotes as Topic/ use ppez |
| 69 | Comment/ use ppez |
| 70 | Case Report/ use ppez |
| 71 | case report/ or case study/ use emczd |
| 72 | (letter or comment*).ti. |
| 73 | or/61-72 |
| 74 | randomized controlled trial/ use ppez |
| 75 | randomized controlled trial/ use emczd |
| 76 | random*.ti,ab. |
| 77 | or/74-76 |
| 78 | 73 not 77 |
| 79 | animals/ not humans/ use ppez |
| 80 | animal/ not human/ use emczd |
| 81 | nonhuman/ use emczd |
| 82 | exp Animals, Laboratory/ use ppez |
| 83 | exp Animal Experimentation/ use ppez |
| 84 | exp Animal Experiment/ use emczd |
| 85 | exp Experimental Animal/ use emczd |
| 86 | exp Models, Animal/ use ppez |
| 87 | animal model/ use emczd |
| 88 | exp Rodentia/ use ppez |
| 89 | exp Rodent/ use emczd |
| 90 | (rat or rats or mouse or mice).ti. |
| 91 | or/78-90 |
| 92 | 60 not 91 |
| 93 | 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. |
| 94 | 93 use ppez |
| 95 | (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. |
| 96 | 95 use ppez |
| 97 | 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. |
| 98 | 97 use emczd |
| 99 | 94 or 96 |
| 100 | 98 or 99 |
| 101 | Meta-Analysis/ |
| 102 | exp Meta-Analysis as Topic/ |
| 103 | systematic review/ |
| 104 | meta-analysis/ |
| 105 | (meta analy* or metanaly* or metaanaly*).ti,ab. |
| 106 | ((systematic or evidence) adj2 (review* or overview*)).ti,ab. |
| 107 | ((systematic* or evidence*) adj2 (review* or overview*)).ti,ab. |
| 108 | (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. |
| 109 | (search strategy or search criteria or systematic search or study selection or data extraction).ab. |
| 110 | (search* adj4 literature).ab. |
| 111 | (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. |
| 112 | cochrane.jw. |
| 113 | ((pool* or combined) adj2 (data or trials or studies or results)).ab. |
| 114 | (or/101-103,105,107-112) use ppez |
| 115 | (or/103-106,108-113) use emczd |

| # | Searches |
|---|---|
| 116 | or/114-115 |
| 117 | network meta-analysis/ |
| 118 | ((network adj (MA or MAs)) or (NMA or NMAs)).tw. |
| 119 | ((indirect or mixed or multiple or multi-treatment* or simultaneous) adj1 comparison*).tw. |
| 120 | or/117-119 |
| 121 | 100 or 116 or 120 |
| 122 | 92 and 121 |

Database(s): The Cochrane Library: Cochrane Database of Systematic Reviews, Issue 5 of 12, May 2020; Cochrane Central Register of Controlled Trials, Issue 5 of 12, May 2020

| # | Searches |
|---|---|
| #1 | MeSH descriptor: [Acne Vulgaris] explode all trees |
| #2 | acne*:ti,ab |
| #3 | #1 or #2 |
| #4 | MeSH descriptor: [Mineralocorticoid Receptor Antagonists] explode all trees |
| #5 | MeSH descriptor: [Spironolactone] this term only |
| #6 | MeSH descriptor: [Eplerenone] this term only |
| #7 | (aldactone or spironolactone or co-flumactone or coflumactone or eplerenon* or furosemide):ti,ab |
| #8 | {or #4-#7} |
| #9 | MeSH descriptor: [Adrenergic alpha-Antagonists] explode all trees |
| #10 | MeSH descriptor: [Doxazosin] this term only |
| #11 | MeSH descriptor: [Indoramin] this term only |
| #12 | MeSH descriptor: [Prazosin] this term only |
| #13 | MeSH descriptor: [Tamsulosin] this term only |
| #14 | (alfuzosin or doxazosin or uroprost or indoramin or prazosin or tamsulosin or terazosin):ti,ab |
| #15 | {or #9-#14} |
| #16 | MeSH descriptor: [5-alpha Reductase Inhibitors] explode all trees |
| #17 | MeSH descriptor: [Dutasteride] this term only |
| #18 | MeSH descriptor: [Finasteride] this term only |
| #19 | ("5a reductase inhibitor*" or "5-alpha reductase inhibitor*" or dutastaride or finasteride):ti,ab |
| #20 | {or #16-#19} |
| #21 | MeSH descriptor: [Androgen Antagonists] explode all trees |
| #22 | MeSH descriptor: [Metformin] this term only |
| #23 | MeSH descriptor: [Abiraterone Acetate] this term only |
| #24 | MeSH descriptor: [Cyproterone Acetate] this term only |
| #25 | MeSH descriptor: [Flutamide] this term only |
| #26 | (antiandrogen* or "anti androgen*" or "androgen antagonist*" or "abiraterone acetate" or apalutamide or bicalutamide or cocyprindiol or "co cyprindiol" or "cyproterone acetate" or enzalutamide or flutamide or metformin):ti,ab |
| #27 | {or #21-#26} |
| #28 | MeSH descriptor: [Contraceptives, Oral, Combined] explode all trees |
| #29 | MeSH descriptor: [Progestins] explode all trees |
| #30 | MeSH descriptor: [Ethinyl Estradiol-Norgestrel Combination] this term only |
| #31 | MeSH descriptor: [Ethinyl Estradiol] this term only |
| #32 | MeSH descriptor: [Estradiol] this term only |
| #33 | MeSH descriptor: [Mestranol] this term only |
| #34 | ((oral* next contracept*) or progestogen* or progestagen* or gestagen* or progestin*):ti,ab |
| #35 | ((ethinylestradiol or ethinyloestradiol or ethinyl estradiol or ethinyl oestradiol) near/3 (chlormadinone acetate or desogestrel or dienogest or drospirenone or etonogestrel or gestodene or levonorgestrel or nomogestrol or norelgestromin* or norethindrone or norethisterone or norgestimate or norgestrel)):ti,ab |
| #36 | ((estradiol or oestradiol) near/3 (dienogest or dydrogesterone or levonorgestrel or medroxyprogesterone acetate or nomegestrol or norethindrone or norethisterone)):ti,ab |
| #37 | (mestranol near/3 (norethindrone or norethisterone or noretynodrel or norethynodrel)):ti,ab |
| #38 | {or #28-#37} |
| #39 | #8 or #15 or #20 or #27 or #38 |
| #40 | #3 and #39 |

### Physical interventions

Database(s): Embase Classic+Embase 1947 to 2019 August 12, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to May 06, 2020

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

| # | Searches |
|---|---|

| # | Searches |
|---|---|
| 1 | exp Acne Vulgaris/ use ppez |
| 2 | exp acne/ use emczd |
| 3 | acne.tw. |
| 4 | or/1-3 |
| 5 | chemexfoliation/ |
| 6 | (amino acid/ or 2 hydroxyacid/) use emczd |
| 7 | (Amino Acids/ or Hydroxy Acids/) use ppez |
| 8 | glycolic acid/ use emczd |
| 9 | Glycolates/ use ppez |
| 10 | lactic acid/ |
| 11 | mandelic acid/ use emczd |
| 12 | Mandelic Acids/ use ppez |
| 13 | pyruvic acid/ |
| 14 | salicylic acid/ |
| 15 | trichloroacetic acid/ |
| 16 | (chemical adj1 (exfoliat* or peel* or resurfac*)).tw. |
| 17 | (chemoexfoliat* or chemexfoliat* or chemo exfoliat*).tw. |
| 18 | ((amino or glycol* or lactic or mandelic or pyruvic or salicylic or trichloroa?cetic or salicylic-mandelic or alpha hydroxy or "amino fruit") adj acid*).tw. |
| 19 | (hydroxyacid* or hydroxy acid*).tw. |
| 20 | ((Jessner* or phenol or pheno or Baker-Gordon) adj (peel* or solution*)).tw. |
| 21 | or/5-20 |
| 22 | comedo/th use emczd |
| 23 | ((blackhead* or comedo* or whitehead*) adj (extract* or remov*)).tw. |
| 24 | triamcinolone acetonide/ |
| 25 | (adrenal cortex hormone* or triamcinolone acetonide).tw. |
| 26 | or/22-25 |
| 27 | exp laser/ |
| 28 | exp phototherapy/ |
| 29 | exp photodynamic therapy/ |
| 30 | exp photochemotherapy/ |
| 31 | exp photolysis/ |
| 32 | exp sunlight/ |
| 33 | exp photosensitizing agent/ |
| 34 | radiofrequency/ or radiofrequency ablation/ |
| 35 | aminolevulinic acid/ |
| 36 | methylene blue/ |
| 37 | aminolevulinic acid methyl ester/ |
| 38 | (or/27-37) use emczd |
| 39 | exp Lasers/ |
| 40 | exp Phototherapy/ |
| 41 | exp Laser Therapy/ |
| 42 | exp Photochemotherapy/ |
| 43 | exp Photolysis/ |
| 44 | exp Sunlight/ |
| 45 | exp Ultraviolet Therapy/ |
| 46 | exp Photosensitizing Agents/ |
| 47 | exp Radiofrequency Therapy/ |
| 48 | Aminolevulinic Acid/ |
| 49 | Methylene Blue/ |
| 50 | (or/39-49) use ppez |
| 51 | (laser* or light therap* or light treatment* or aminolevulinic acid or blue light* or red light* or intense pulsed light* or IPL or methyl aminolevulinate or methylene blue gel or microneedl* or micro needl* or photochemical therap* or photochemical treatment* or photo chemical therap* or photo chemical treatment* or photochemotherap* or photodynamic therap* photodynamic treatment* or photo dynamic therap* or photo dynamic treatment* or photolysis or photopneumatic therap* or photopneumatic treatment* or photo pneumatic therap* or photo pneumatic treatment* or photosensiti?ing agent* or photo-sensiti?ing agent* or phototherap* or photo-therap* or photothermal therap* or photothermal treatment* or photo-thermal therap* or photo-thermal treatment* or radiofrequenc* or radio frequenc* or smoothbeam or sunlight or ultraviolet).tw. |
| 52 | or/21,26,38,50-51 |
| 53 | 4 and 52 |
| 54 | Letter/ use ppez |
| 55 | letter.pt. or letter/ use emczd |
| 56 | note.pt. |
| 57 | editorial.pt. |
| 58 | Editorial/ use ppez |
| 59 | News/ use ppez |
| 60 | exp Historical Article/ use ppez |
| 61 | Anecdotes as Topic/ use ppez |
| 62 | Comment/ use ppez |
| 63 | Case Report/ use ppez |

| # | Searches |
|---|---|
| 64 | case report/ or case study/ use emczd |
| 65 | (letter or comment*).ti. |
| 66 | or/54-65 |
| 67 | randomized controlled trial/ use ppez |
| 68 | randomized controlled trial/ use emczd |
| 69 | random*.ti,ab. |
| 70 | or/67-69 |
| 71 | 66 not 70 |
| 72 | animals/ not humans/ use ppez |
| 73 | animal/ not human/ use emczd |
| 74 | nonhuman/ use emczd |
| 75 | exp Animals, Laboratory/ use ppez |
| 76 | exp Animal Experimentation/ use ppez |
| 77 | exp Animal Experiment/ use emczd |
| 78 | exp Experimental Animal/ use emczd |
| 79 | exp Models, Animal/ use ppez |
| 80 | animal model/ use emczd |
| 81 | exp Rodentia/ use ppez |
| 82 | exp Rodent/ use emczd |
| 83 | (rat or rats or mouse or mice).ti. |
| 84 | or/71-83 |
| 85 | 53 not 84 |
| 86 | limit 85 to english language |
| 87 | 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. |
| 88 | 87 use ppez |
| 89 | (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. |
| 90 | 89 use ppez |
| 91 | 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. |
| 92 | 91 use emczd |
| 93 | 88 or 90 |
| 94 | 92 or 93 |
| 95 | Meta-Analysis/ |
| 96 | exp Meta-Analysis as Topic/ |
| 97 | systematic review/ |
| 98 | meta-analysis/ |
| 99 | (meta analy* or metanaly* or metaanaly*).ti,ab. |
| 100 | ((systematic or evidence) adj2 (review* or overview*)).ti,ab. |
| 101 | ((systematic* or evidence*) adj2 (review* or overview*)).ti,ab. |
| 102 | (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. |
| 103 | (search strategy or search criteria or systematic search or study selection or data extraction).ab. |
| 104 | (search* adj4 literature).ab. |
| 105 | (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. |
| 106 | cochrane.jw. |
| 107 | ((pool* or combined) adj2 (data or trials or studies or results)).ab. |
| 108 | (or/95-97,99,101-106) use ppez |
| 109 | (or/97-100,102-107) use emczd |
| 110 | or/108-109 |
| 111 | network meta-analysis/ |
| 112 | ((network adj (MA or MAs)) or (NMA or NMAs)).tw. |
| 113 | ((indirect or mixed or multiple or multi-treatment* or simultaneous) adj1 comparison*).tw. |
| 114 | or/111-113 |
| 115 | 94 or 110 or 114 |
| 116 | 86 and 115 |

Database(s): The Cochrane Library: Cochrane Database of Systematic Reviews, Issue 5 of 12, May 2020; Cochrane Central Register of Controlled Trials, Issue 5 of 12, May 2020

| # | Searches |
|---|---|
| #1 | MeSH descriptor: [Acne Vulgaris] explode all trees |
| #2 | acne*:ti,ab |
| #3 | #1 or #2 |
| #4 | MeSH descriptor: [Chemexfoliation] this term only |
| #5 | MeSH descriptor: [Amino Acids] this term only |
| #6 | MeSH descriptor: [Hydroxy Acids] this term only |
| #7 | MeSH descriptor: [Glycolates] this term only |
| #8 | MeSH descriptor: [Lactic Acid] this term only |

| # | Searches |
|---|---|
| #9 | MeSH descriptor: [Mandelic Acids] this term only |
| #10 | MeSH descriptor: [Pyruvic Acid] this term only |
| #11 | MeSH descriptor: [Salicylic Acid] this term only |
| #12 | MeSH descriptor: [Trichloroacetic Acid] this term only |
| #13 | (chemical near/1 (exfoliat* or peel* or resurfac*)):ti,ab |
| #14 | (chemoexfoliat* or chemexfoliat* or chemo exfoliat*):ti,ab |
| #15 | ((amino or glycol* or lactic or mandelic or pyruvic or salicylic or trichloroaecetic or trichloroacetic or "salicylic mandelic" or "alpha hydrox" or "amino fruit") next acid*):ti,ab |
| #16 | (hydroxyacid* or "hydroxy acid*").ti,ab |
| #17 | ((Jessner* or phenol or pheno or "Baker Gordon") next (peel* or solution*)).ti,ab |
| #18 | {or #4-#17} |
| #19 | ((blackhead* or comedo* or whitehead*) near/2 (extract* or remov*)):ti,ab |
| #20 | MeSH descriptor: [Triamcinolone Acetonide] this term only |
| #21 | ("adrenal cortex hormone*" or "triamcinolone acetonide").ti,ab |
| #22 | {or #19-#21} |
| #23 | MeSH descriptor: [Lasers] explode all trees |
| #24 | MeSH descriptor: [Phototherapy] explode all trees |
| #25 | MeSH descriptor: [Photochemotherapy] explode all trees |
| #26 | MeSH descriptor: [Photochemotherapy] explode all trees |
| #27 | MeSH descriptor: [Photolysis] explode all trees |
| #28 | MeSH descriptor: [Sunlight] explode all trees |
| #29 | MeSH descriptor: [Photosensitizing Agents] explode all trees |
| #30 | MeSH descriptor: [Radiofrequency Therapy] explode all trees |
| #31 | MeSH descriptor: [Aminolevulinic Acid] this term only |
| #32 | MeSH descriptor: [Methylene Blue] this term only |
| #33 | MeSH descriptor: [Ultraviolet Therapy] explode all trees |
| #34 | (laser* or light therap* or light treatment* or aminolevulinic acid or blue light* or red light* or intense pulsed light* or IPL or methyl aminolevulinate or methylene blue gel or microneedl* or micro needl* or photochemical therap* or photochemical treatment* or photo chemical therap* or photo chemical treatment* or photochemotherap* or photodynamic therap* photodynamic treatment* or photo dynamic therap* or photo dynamic treatment* or photolysis or photopneumatic therap* or photopneumatic treatment* or photo pneumatic therap* or photo pneumatic treatment* or photosensitising agent* or photosensitizing agent* or photo-sensitising agent* or photo-sensitizing agent* or phototherap* or photo-therap* or photothermal therap* or photothermal treatment* or photo-thermal therap* or photo-thermal treatment* or radiofrequenc* or radio frequenc* or smoothbeam or sunlight or ultraviolet):ti,ab |
| #35 | {or #23-#34} |
| #36 | #18 or #22 or #35 |
| #37 | #3 and #18 |

## Economic 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/ |

| # | Searches |
|---|---|
| 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 |

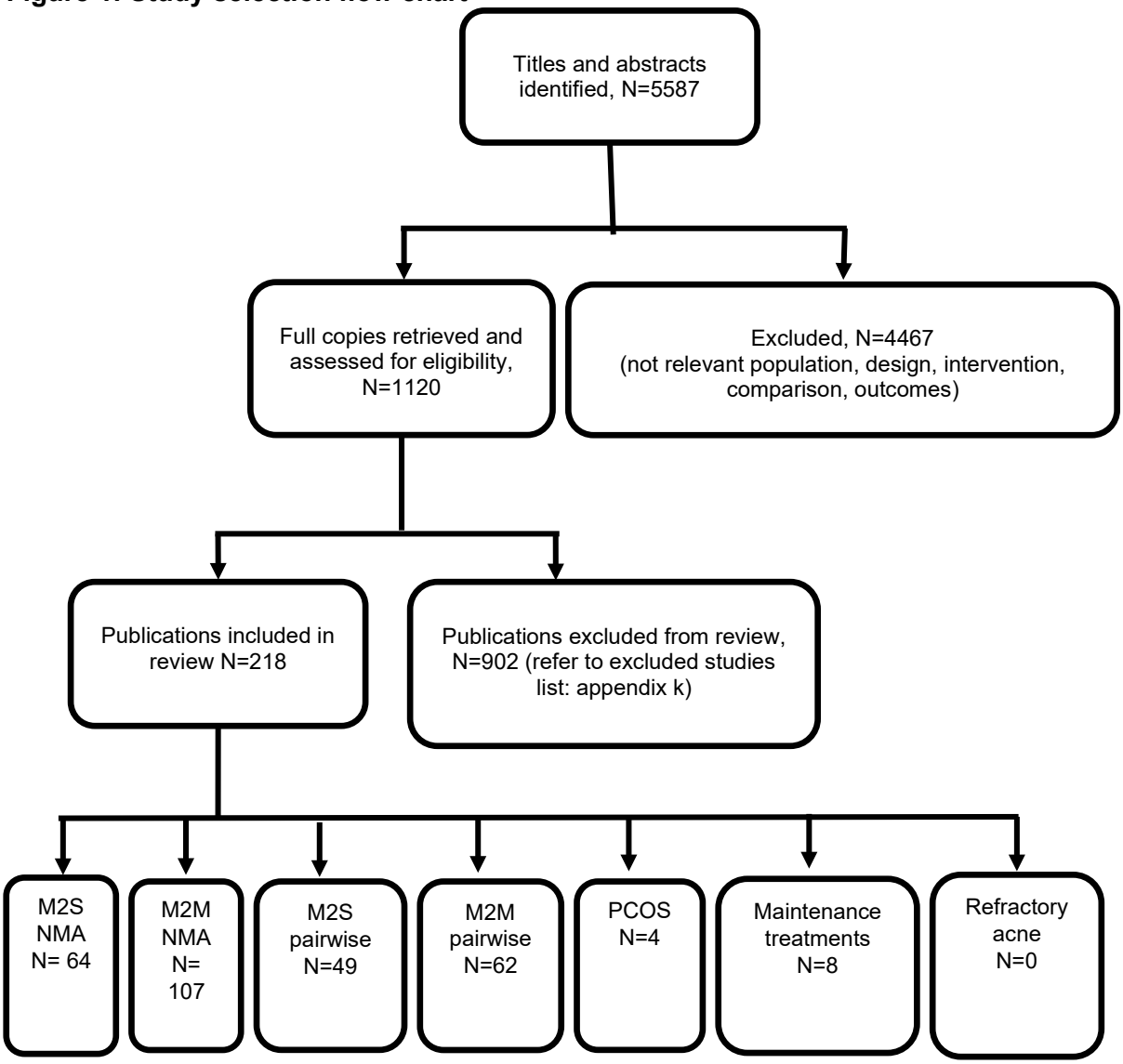
| # | Searches |
|---|---|
| | impacted or deteriorat*)).ab. |
| 26 | Cost-Benefit Analysis/ use ppez and cost-effectiveness ratio*.tw. and (cost-effectiveness ratio* and (perspective* or life expectanc*)).tw. |
| 27 | cost benefit analysis/ use emez and cost-effectiveness ratio*.tw. and (cost-effectiveness 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 review question: What is the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris?

One search was conducted for the 9 review questions summarised at the beginning of this review. This covered a number of different group of people with acne, the data related to each were analysed separately (see the final row of the flowchart). These were people with moderate to severe acne (M2S), people with mild to moderate acne (M2M). These groups were analysed using network meta-analysis (NMA) or pairwise meta-analysis (pairwise). Other groups that were also covered by this search were people receiving maintenance treatments or those whose acne failed to respond to previous treatment (refractory acne) and people with polycystic ovary syndrome (PCOS).

**Figure 1: Study selection flow chart**



# Appendix D – Evidence tables

## Evidence tables for review question: What is the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris?

**Table 4: Evidence table**

| Study details | Participants | Interventions | Results | Risk of bias |
|---|---|---|---|---|
| **Study ID**<br><br>**Full citation**<br><br>Kawashima M., Miyachi Y., Efficacy of BPO 2.5% Gel in the Acute and Maintenance Periods for Moderate or Severe Facial Acne Vulgaris, J Dermatol Dis, 5, 273, 2018<br><br>**Country/ies where the study was carried out**<br><br>Japan<br><br>**RCT type (parallel or split face)**<br>Randomised, parallel-group maintenance phase.<br><br>**Study dates** | N=92<br><br>**Sex (Male, female or mixed)**<br><br>Female (%): 77<br><br>**Age details**<br>Mean age (years): 23.5<br><br>**Acne scale used for inclusion**<br><br>No scale reported. Reduction of inflammatory eruptions to ≤ 5 or fewer on the entire face with ≤ 3 on one side of the face within 12 weeks after treatment initiation in the first stage<br><br>**Other inclusion criteria**<br>Inclusion criteria for inflammatory phase:<br>• Moderate to severe acne vulgaris (6-30 inflammatory eruptions on one side of the face)<br>• Written consent provided after receiving an explanation of the study content<br>• Age ≥ 16 years at the time of obtaining consent. For patients <20 years old, consent was also obtained from a legal representative (such as the patient's parents) | **Treatment duration (weeks)**<br><br>12<br><br>**Info about intensity of physical treatments**<br>Not applicable.<br><br>**Number of treatment arms**<br><br>2<br><br>**Interventions**<br>Intervention 1 (n=47): 0.1% adapalene gel each evening after washing face.<br><br>Intervention 2 (n=45): 2.5% benzoyl peroxide gel each evening after washing face. | Relapse/aggravation of symptoms- Number (%)<br>Intervention 1: 26/47 (55.3)<br>Intervention 2: 27/45 (60)<br><br>Adverse events- Erythema- Number (%)<br>Intervention 1: 1/47 (2.1)<br>Intervention 2: 0/45 (0)<br><br>Adverse events- Dryness- Number (%)<br>Intervention 1: 1/47 (2.1)<br>Intervention 2: 1/45 (2.2) | **Methodological limitations assessed using the Cochrane risk of bias tool for randomised trials (RoB2)**<br><br>**Risk of bias arising from the randomisation process:** Some concerns (adaptive randomisation, minimisation methods used. No details on allocation concealment).<br><br>**Risk of bias due to deviations from the intended interventions:** Some concerns (no blinding reported).<br><br>**Risk of bias due to missing outcome data:** Low risk (6% attrition, n=1 lost from intervention 1 and n=5 lost from intervention 2).<br><br>**Risk of bias in measurement of the outcome:** Some concerns (same measurement methods and thresholds used at comparable timepoints to measure outcomes; no report of participants/outcome assessors being blinded to intervention).<br><br>**Risk of bias in selection of the reported result:** Low risk (trial protocol reported)<br><br>**Overall risk of bias judgement:** study is |

| Study details | Participants | Interventions | Results | Risk of bias |
|---|---|---|---|---|
| **Source of funding** | Inclusion criteria for the maintenance phase:<br>• Written consent provided after a re-explanantion of the study content of the maintenance phase.<br><br>**Exclusion criteria**<br>Exclusion criteria for inflammatory phase:<br>• Treated for acne vulgaris within one month before the study<br>• Contraindicated for the investigational drugs<br>• Continuous use of non-steroidal anti-inflammatory drugs<br>• Pregnant or possibly pregnant women, lactating women, and women who wanted to become pregnant during the study period<br>• Judged as ineligible by the physician directing the study<br>• Participation in another clinical study or post-marketing surveillance of other drugs for acne vulgaris within six months before the study<br><br>Exclusion criteria for the maintenance phase:<br>• Judged as ineligible by the physician directing the study | | | judged to have some concerns some concerns for multiple domains. |
| **Study ID**<br>869180<br>**Full citation** | N=110<br>**Sex (Male, female or mixed)**<br>Female (%): 55 | **Treatment duration (weeks)**<br>12<br>**Info about intensity of physical** | Percentage change in non-inflammatory lesion count after 12 weeks maintenance - mean (±SD)<br>Intervention 1 (n=35): -60.0 (22.9)<br>Intervention 2 (n=37): -52.0 (30.4)<br>Intervention 3 (n=35): -64.0 | **Methodological limitations assessed using the Cochrane risk of bias tool for randomised trials (RoB2)**<br><br>**Risk of bias arising from the randomisation process:** low risk |

| Study details | Participants | Interventions | Results | Risk of bias |
|---|---|---|---|---|
| Leyden, J., Thiboutot, D. M., Shalita, A. R., Webster, G., Washenik, K., Strober, B. E., Shupack, J., Comparison of tazarotene and minocycline maintenance therapies in acne vulgaris: a multicenter, double-blind, randomized, parallel-group study, Archives of Dermatology, 142, 605-12, 2006<br><br>**Country/ies where the study was carried out**<br><br>US<br><br>**RCT type (parallel or split face)**<br>Double-blind, randomised, parallel-group maintenance phase.<br><br>**Study dates**<br>Not reported.<br><br>**Source of funding**<br>Allergan Inc. | **Age details**<br>Mean age (years): 22<br><br>**Acne scale used for inclusion**<br><br>Global response.<br><br>**Other inclusion criteria**<br>• Participants aged at least 17 years of age.<br>• Moderately severe to severe facial acne vulgaris.<br>• 10 to 100 facial non-inflammatory acne lesions.<br>• 25 to 60 facial inflammatory acne lesions.<br>• No more than 2 facial nodular cystic lesions.<br>• 75% or greater global improvement at the end of the initial open-label treatment phase.<br>• Informed consent provided by participants or guardians.<br>• Washout periods required: 14 days for topical acne medications; 30 days for oral antibiotics and investigational treatments; 12 weeks for oestrogens or birth control pills if they had been used for <12 weeks; 2 years for oral retinoids.<br><br>**Exclusion criteria**<br>• Participants with acne vulgaris resistant to oral antibiotics.<br>• Pregnancy, breastfeeding, or planning a pregnancy.<br>• Uncontrolled systemic disease.<br>• Participation in another study in the | **treatments**<br>Not applicable.<br><br>**Number of treatment arms**<br><br>3<br><br>**Interventions**<br>Intervention 1 (n=36): 0.1% tazarotene gel each evening plus placebo capsule twice daily.<br><br>Intervention 2 (n=37): vehicle gel each evening plus a 100 mg minocycline hydrochloride capsule twice daily.<br><br>Intervention 3 (n=37): 0.1% tazarotene gel each evening plus a 100 mg minocycline capsule twice daily.<br>Tazarotene gel was applied to the face as a pea-sized amount in a thin film 15 to 20 minutes after washing with a mild non-medicated cleanser and drying with a soft towel.<br><br>All participants were provided with a non-comedogenic moisturiser to use for facial dryness. No other lotions, creams, medicated powders, or solutions were permitted on the treatment area. | (42.1); p=NS<br><br>Percentage change in inflammatory lesion count after 12 weeks maintenance - mean (±SD)<br>Intervention 1 (n=35): -54.0 (25.1)<br>Intervention 2 (n=37): -66.0 (29.4)<br>Intervention 3 (n=36): -66.0 (27.2); p=NS<br><br>Participants maintaining ≥70% of the reduction in non-inflammatory lesion count achieved in the initial treatment phase, after 12 weeks maintenance - % (n/N)<br>Intervention 1: 81 (22/27) (relapse 5/27)<br>Intervention 2: 71 (22/31) (relapse 9/31)<br>Intervention 3: 90 (27/30) (relapse 3/30)<br><br>Participants maintaining ≥70% of the reduction in inflammatory lesion count achieved in the initial treatment phase, after 12 weeks maintenance - % (n/N)<br>Intervention 1: 67 (18/27) (relapse 9/27)<br>Intervention 2: 84 (26/31) (relapse 5/31)<br>Intervention 3: 77 (24/31) (relapse 7/31)<br><br>Acceptability (treatment discontinuation for any reason) after 12 weeks maintenance - n/N<br>Intervention 1: 8/36<br>Intervention 2: 6/37<br>Intervention 3: 6/37<br><br>Tolerability (treatment | (participants assigned a unique number using computer-generated randomisation schedule; labels on medication containers concealed; demographics similar across treatment groups).<br><br>**Risk of bias due to deviations from the intended interventions:** low risk (double-blind trial - labels on medication containers were concealed and participants received a gel and capsule).<br><br>**Risk of bias due to missing outcome data:** some concerns (data were available for different numbers of participants for different outcomes, the reasons for which were unclear; high attrition rates - intervention 1 (22%), intervention 2 (16%), intervention 3 (16%); no details provided on analysis methods to correct for bias and sensitivity analysis not performed).<br><br>**Risk of bias in measurement of the outcome:** low risk (same measurement methods and thresholds used at comparable timepoints to measure outcomes; participants/outcome assessors blinded to intervention).<br><br>**Risk of bias in selection of the reported result:** some concerns (limited details provided on pre-specified analysis plan, but different outcomes mentioned in the statistical analysis section have data reported and reported results for outcome measures appear to correspond to all intended analyses).<br><br>**Overall risk of bias judgement:** study is judged to have some concerns some concerns for multiple domains. |

| Study details | Participants | Interventions | Results | Risk of bias |
|---|---|---|---|---|
| | preceding 30 days. | | discontinuation due to side effects) after 12 weeks maintenance - n/N<br>Intervention 1: 0/36<br>Intervention 2: 1/37<br>Intervention 3: 1/37<br><br>No adverse events were reported during the maintenance phase that were considered probably related to treatment. | **Other information**<br>Setting: ambulatory participants in research or referral centres.<br>Number of participants in maintenance phase: N=110/189<br>Number of participants completing study: N=90<br>Previous treatment: 0.1% tazarotene gel each evening, plus 1 x 100 mg minocycline capsule orally, twice daily. |
| **Study ID**<br><br>869990<br><br>**Full citation**<br><br>Poulin, Y., Sanchez, N. P., Bucko, A., Fowler, J., Jarratt, M., Kempers, S., Kerrouche, N., Dhuin, J. C., Kunynetz, R., A 6-month maintenance therapy with adapalene-benzoyl peroxide gel prevents relapse and continuously improves efficacy among patients with severe acne vulgaris: results of a randomized controlled trial, Br J Dermatol, 164, 1376-82, 2011<br><br>**Country/ies where the study was carried out** | N=243<br><br>**Sex (Male, female or mixed)**<br><br>Male - n: Adapalene-BPO: 65; Vehicle: 67<br><br>**Age details**<br>Age (years) - mean (±SD)<br>Adapalene-BPO: 19.1 (5.89)<br>Vehicle: 18.2 (5.23)<br><br>**Acne scale used for inclusion**<br><br>Investigator's Global Assessment (IGA)<br><br>**Other inclusion criteria**<br>• Participants with severe acne vulgaris.<br>• Participants who had shown at least 50% global improvement with previous treatment (doxycycline and adapalene-BPO or its vehicle gel for 12 weeks).<br><br>**Exclusion criteria**<br>• Women who were pregnant, nursing or planning a pregnancy. | **Treatment duration (weeks)**<br><br>24<br><br>**Info about intensity of physical treatments**<br>Not applicable.<br><br>**Number of treatment arms**<br><br>2<br><br>**Interventions**<br>Adapalene-BPO (n=123): fixed dose combination gel 0.1% adapalene plus 2.5% benzoyl peroxide (adapalene-BPO) once daily in the evening.<br><br>Vehicle (n=120): vehicle gel once daily in the evening.<br>Participants were encouraged to use sun protection factor 15 daily facial moisturiser and a gentle skin cleanser. | Percentage change in lesion count from baseline to 24 weeks<br>Adapalene-BPO: -26.0%<br>Vehicle: +46.3%; p<0.01<br><br>IGA success rate (% of participants rated 'clear' or 'almost clear')<br>Adapalene-BPO: Baseline (26.8%); 24 weeks (47.5%)<br>Vehicle: Baseline (37.5%); 24 weeks (25.6%); p<0.01<br><br>Participants having at least 50% improvement from baseline to 24 weeks (total lesions)<br>Adapalene-BPO: 78.9% (relapse 21.1%)<br>Vehicle: 45.8% (relapse 54.2%); p<0.001<br><br>Treatment-related adverse effects from baseline to week 24- n (%)<br>Adapalene-BPO: 5 (4.1)<br>Vehicle: 1 (0.8)<br>Irritation from baseline to week 24 - %<br>Adapalene-BPO: erythema (76.7); scaling (70.8); dryness (73.3); stinging/burning (78.3) | **Methodological limitations assessed using the Cochrane risk of bias tool for randomised trials (RoB2)**<br><br>**Risk of bias arising from the randomisation process:** low risk (randomisation using a central telephone/web system; demographics comparable across treatment groups).<br><br>**Risk of bias due to deviations from the intended interventions:** low risk (double-blind trial - vehicle gel used as control).<br><br>**Risk of bias due to missing outcome data:** high risk (high attrition rates - Adapalene-BPO (14.6%), Vehicle (65%); missing data considered as failure except where values of both previous and following visits successful; missingness in outcome may depend on the true value).<br><br>**Risk of bias in measurement of the outcome:** low risk (same measurement methods and thresholds used at comparable timepoints to measure outcomes; participants/outcome assessors blinded to intervention). |

| Study details | Participants | Interventions | Results | Risk of bias |
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| US, Canada, Puerto Rico<br><br>**RCT type (parallel or split face)**<br>Multicentre, double-blind, randomised, vehicle-controlled trial (parallel assignment).<br><br>**Study dates**<br>Not reported.<br><br>**Source of funding**<br>Galderma Research & Development, France. | • Men with facial hair that would interfere with the assessments. | | Vehicle: erythema (83.5); scaling (92.2); dryness (88.7); stinging/burning (92.2)<br><br>Acceptability (treatment discontinuation for any reason) from baseline to week 24 - n/N<br>Adapalene-BPO: 18/123<br>Vehicle: 42/120<br><br>Tolerability (treatment discontinuation due to side effects) from baseline to week 24 - n/N<br>Adapalene-BPO: 0/123<br>Vehicle: 0/120 | **Risk of bias in selection of the reported result:** low risk (limited details provided on pre-specified analysis plan, but different outcomes mentioned in the statistical analysis section have data reported and reported results for outcome measures appear to correspond to all intended analyses).<br><br>**Overall risk of bias judgement:** the study is judged to be at high risk of bias (high risk in one domain and some concerns in one domain).<br><br>**Other information**<br>Number of participants: N=243.<br>Number of participants completing study: n=183.<br>Previous treatment: 100 mg doxycycline daily and adapalene-BPO or its vehicle for 12 weeks.<br>Unclear whether there was a washout period. |
| **Study ID**<br><br>870417<br><br>**Full citation**<br><br>Thiboutot, D. M., Shalita, A. R., Yamauchi, P. S., Dawson, C., Kerrouche, N., Arsonnaud, S., Kang, S., Adapalene gel, 0.1%, as maintenance therapy for acne vulgaris: a randomized, controlled, | N=253<br><br>**Sex (Male, female or mixed)**<br><br>Male - n: Adapalene: 65; Vehicle: 73<br><br>**Age details**<br>Age (years) - mean (±SD) (range)<br>Adapalene: 18.1 (4.2) (12 to 30)<br>Vehicle: 17.8 (3.9) (12 to 32)<br><br>**Acne scale used for inclusion**<br><br>Not reported (participants required to have at least moderate improvement (50%) from baseline.<br><br>**Other inclusion criteria** | **Treatment duration (weeks)**<br><br>16<br><br>**Info about intensity of physical treatments**<br>Not applicable.<br><br>**Number of treatment arms**<br><br>2<br><br>**Interventions**<br>Adapalene (n=126): 0.1% adapalene gel once daily in the evening.<br><br>Vehicle (N=127): gel vehicle once | Percentage of participants maintaining at least 50% improvement after 16 weeks maintenance (total lesions)<br>Adapalene: 75% (relapse 25%)<br>Vehicle: 54% (relapse 46%); p<0.001<br><br>Treatment-related adverse effects after 16 weeks maintenance - n (%)<br>Adapalene: 3 (2.4)<br>Vehicle: 1 (0.8)<br><br>Acceptability (treatment discontinuation for any reason) after 16 weeks maintenance - n/N<br>Adapalene-BPO: 14/126 | **Methodological limitations assessed using the Cochrane risk of bias tool for randomised trials (RoB2)**<br><br>**Risk of bias arising from the randomisation process:** low risk (randomisation using a central telephone system; demographics and dermatological scores comparable across treatment groups).<br><br>**Risk of bias due to deviations from the intended interventions:** some concerns (investigator-blind trial, those involved in the clinical conduct of the study remained blinded to the randomisation schedule and packaging of medication was concealed through use of identical tubes |

| Study details | Participants | Interventions | Results | Risk of bias |
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| investigator-blind follow-up of a recent combination study, Archives of DermatologyArch Dermatol, 142, 597-602, 2006<br><br>**Country/ies where the study was carried out**<br><br>US<br><br>**RCT type (parallel or split face)**<br>Multicentre, randomised, vehicle-controlled, investigator-blind, parallel group trial.<br><br>**Study dates**<br>November 2003 to May 2004.<br><br>**Source of funding**<br>Galderma Research & Development, US. | • Participants with severe acne, aged 12 to 30 years.<br>• Participants showed at least moderate improvement from baseline (50% improvement) to after treatment with either adapalene plus doxycycline, 100 mg once daily, or doxycycline, 100 mg once daily, plus gel vehicle in a previous 12-week study.<br><br>**Exclusion criteria**<br>• Participants with acne requiring treatment with isotretinoin or other dermatologic conditions requirement interfering treatment.<br>• Women who were pregnant, nursing, or planning a pregnancy.<br>• Men with facial hair that would interfere with the assessments. | daily in the evening.<br>Participants were provided with a daily facial moisturiser with sun protection factor 15 to use as needed for the symptomatic relief of skin dryness or irritation. | Vehicle: 20/127<br><br>Tolerability (treatment discontinuation due to side effects) after 16 weeks maintenance - n/N<br>Adapalene-BPO: 0/126<br>Vehicle: 0/127 | and a third party dispensing the medication; no information for participants; however, the author stated that there was a potential risk that patients previously treated with the vehicle and then adapalene may have caused local irritation, which could influence the investigator to be blinded).<br><br>**Risk of bias due to missing outcome data:** some concerns (high attrition rates - Adapalene (11.1% discontinued), Vehicle (15.8% discontinued); efficacy data analysed using ITT and PP population, last observation carried forward used for the ITT population analysis for lesion count to account for missing data or for data from patients who withdrew from the study; missingness in outcome may depend on the true value).<br><br>**Risk of bias in measurement of the outcome:** some concerns (same measurement methods and thresholds used at comparable timepoints to measure outcomes; unclear whether participants blinded to intervention, participant reported outcomes therefore unclear).<br><br>**Risk of bias in selection of the reported result:** high risk (limited details provided on pre-specified analysis plan, but different outcomes mentioned in the statistical analysis section have data reported; post hoc analysis performed for maintaining at least 50% improvement).<br><br>**Overall risk of bias judgement:** this study is judged to be at high risk of bias (high risk in one domain and some |

| Study details | Participants | Interventions | Results | Risk of bias |
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| | | | | concerns in multiple domains).<br><br>**Other information**<br>Number of participants: N=253.<br>Number of participants completing study: n=219.<br>Previous treatment: adapalene plus doxycycline 100 mg once daily or doxycycline 100 mg once daily plus gel vehicle for 12 weeks.<br>Unclear whether there was a washout period. |
| **Study ID**<br><br>870421<br><br>**Full citation**<br><br>Thielitz, A., Sidou, F., Gollnick, H., Control of microcomedone formation throughout a maintenance treatment with adapalene gel, 0.1%, J Eur Acad Dermatol Venereol, 21, 747-53, 2007<br><br>**Country/ies where the study was carried out**<br><br>Germany<br><br>**RCT type (parallel or split face)**<br>Randomised, investigator-blinded, vehicle controlled trial (parallel). | N=49<br><br>**Sex (Male, female or mixed)**<br><br>Male: n=29 (59.2%); female: n=20 (40.8%)<br><br>**Age details**<br>Age (years) - mean (±SD)<br>Intervention 1: 18.33 (5.0)<br>Intervention 2: 16.47 (2.4)<br>Intervention 3: 19.58 (5.4)<br><br>**Acne scale used for inclusion**<br><br>Global severity score.<br><br>**Other inclusion criteria**<br>• Participants with mild to moderate acne vulgaris (defined as global severity grade 2 to 7 according to the Leeds Revised Acne Grading System).<br>• Presence of at least 250 microcomedones per $cm^2$ on the forehead at screening (counted via cyanoacrylate strips).<br><br>**Exclusion criteria** | **Treatment duration (weeks)**<br><br>12<br><br>**Info about intensity of physical treatments**<br>Not applicable.<br><br>**Number of treatment arms**<br><br>3<br><br>**Interventions**<br>Intervention 1 (n=16): 0.1% adapalene gel once daily applied to the face.<br><br>Intervention 2 (n=16): 0.1% adapalene gel alternately with vehicle once daily every other day applied to the face.<br><br>Intervention 3 (n=17): Vehicle once daily applied to the face.<br>Participants applied the same skin cleanser and moisturiser immediately before treatments and were advised to avoid excessive exposure to sunlight. | Percentage change in microcomedone count after 12 weeks maintenance (total lesions) - mean (±SD)<br>Intervention 1: 14.8 (38.9); p (vs vehicle) = 0.056<br>Intervention 2: 18.2 (81.4); p (vs vehicle) = 0.034<br>Intervention 3: 66.2 (83.3)<br><br>There were no treatment-related adverse events during maintenance treatment and no treatment discontinuations. | **Methodological limitations assessed using the Cochrane risk of bias tool (RoB2)**<br><br>**Risk of bias arising from the randomisation process:** some concerns (participants randomly assigned in an equal ratio to treatments, no further details; between-group differences were not significant and participants started maintenance phase with same disease severity).<br><br>**Risk of bias due to deviations from the intended interventions:** some concerns (investigator-blind trial, participants asked not to discuss treatment with investigators; no deviations reported, but authors state that safety population excludes participants who never applied the treatments with certainty).<br><br>**Risk of bias due to missing outcome data:** low risk (no discontinuations).<br><br>**Risk of bias in measurement of the outcome:** some concerns (same measurement methods and thresholds used at comparable timepoints to |

| Study details | Participants | Interventions | Results | Risk of bias |
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| **Study dates**<br>Not reported.<br><br>**Source of funding**<br>Galderma Research & Development, France. | Not reported. | | | measure outcomes; patient-reported outcomes may have been influenced because participants not blind to treatment).<br><br>**Risk of bias in selection of the reported result:** some concerns (limited information provided).<br><br>**Overall risk of bias judgement:** this study is judged to have some concerns in multiple domains.<br><br>**Other information**<br>Number of participants: N=49.<br>Number of participants completing study: n=49.<br>Previous treatment: 0.1% adapalene gel in the morning plus benzoyl peroxide gel 2.5% at bedtime for 8 weeks.<br>Unclear whether there was a washout period. |
| **Study ID**<br><br>870420<br><br>**Full citation**<br><br>Thielitz, A., Lux, A., Wiede, A., Kropf, S., Papakonstantinou, E., Gollnick, H., A randomized investigator-blind parallel-group study to assess efficacy and safety of azelaic acid 15% gel vs. adapalene 0.1% gel in the treatment and maintenance | N=36<br><br>**Sex (Male, female or mixed)**<br><br>Female: 100%<br><br>**Age details**<br>Age (years) - mean (±SD)<br>Azelaic acid: 30.58 (9.28)<br>Observation: 28.14 (4.56)<br><br>**Acne scale used for inclusion**<br><br>ISGA and LRAGS.<br><br>**Other inclusion criteria**<br>• Adult female participants with mild to moderate acne (according to modified Investigator's Static Global | **Treatment duration (weeks)**<br><br>24<br><br>**Info about intensity of physical treatments**<br>Not applicable.<br><br>**Number of treatment arms**<br><br>2<br><br>**Interventions**<br>Azelaic acid (n=17): 15% azelaic acid gel twice daily for 9 months (6 months maintenance).<br><br>Observation (n=19): 6 month observation following 3 months | Relative change in total lesions after 24 weeks maintenance - mean (±SD)<br>Azelaic acid: -9.79 (38.12)<br>Observation: 29.97 (71.27)<br>Difference (95% CI): -30.8 (-61.5 to 0.0); p=0.038<br><br>Absolute change after 24 weeks maintenance in ISGA - mean (±SD)<br>Azelaic acid: -0.24 (0.44)<br>Observation: -0.16 (0.37)<br>Difference (95% CI): 0 (0 to 0); p=0.434<br><br>Absolute change after 24 weeks maintenance in LRAGS - mean (±SD) | **Methodological limitations assessed using the Cochrane risk of bias tool (RoB2)**<br><br>**Risk of bias arising from the randomisation process:** some concerns (randomisation using software RITA on 1:1:1 ratio using minimisation method of Pocock and Simon and stratification for age and severity classification at study entry; unclear whether allocation sequence concealed).<br><br>**Risk of bias due to deviations from the intended interventions:** some concerns (investigator-blind trial, participants (who were not blind to treatment) were requested not to discuss treatment or side-effects with investigators; |

| Study details | Participants | Interventions | Results | Risk of bias |
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| treatment of female adult acne, J Eur Acad Dermatol Venereol, 29, 789-96, 2015<br><br>**Country/ies where the study was carried out**<br><br>Germany<br><br>**RCT type (parallel or split face)**<br>Randomised, investigator-blind, parallel group trial.<br><br>**Study dates**<br><br>**Source of funding**<br>Intendis GmbH, Germany. | Assessment (ISGA) and Leeds Revised Acne Grading Scale (LRAGS), and including 'late-type acne'.<br><br>**Exclusion criteria**<br>• Participants with more than one nodule.<br>• Pregnancy, planned pregnancy or breastfeeding women.<br>• Known hypersensitivity to any study products or medication with a systemic retinoid within the past 6 months before study inclusion.<br>• Participants who had taken any other topical or systemic anti-acne medication including systemic oral corticosteroids in the preceding 2 weeks. | 15% azelaic acid gel twice daily.<br><br>Participants were not permitted to take any other topical or systemic anti-acne medication including systemic oral corticosteroids during the study period. | Azelaic acid: -0.53 (1.01)<br>Observation: -0.37 (0.50)<br>Difference (95% CI): 0 (0 to 0); p=0.464<br><br>Subjects' Global Change Assessment (SGCA) after 24 weeks maintenance<br>Difference (95% CI): -1.0 (-3.0 to 0); p=0.013<br><br>Relapse during 24 weeks maintenance - n/N<br>Azelaic acid: 11/17<br>Observation: 15/19; p=0.163<br>Acceptability (treatment discontinuation for any reason - treatment and maintenance phase) - n/N<br>Azelaic acid: 6/17<br>Observation: 3/19<br><br>Tolerability (treatment discontinuation due to side effects during 24 weeks maintenance phase) - n/N<br>Azelaic acid: 0/17<br>Observation: 0/19 | appropriate analyses used).<br><br>**Risk of bias due to missing outcome data:** low risk (data available for all or nearly all participants during maintenance treatment).<br><br>**Risk of bias in measurement of the outcome:** some concerns (same measurement methods and thresholds used at comparable timepoints to measure outcomes; participants not blind to intervention, therefore participant-reported outcomes may have been influenced).<br><br>**Risk of bias in selection of the reported result:** some concern (limited details provided on pre-specified analysis plan, but different outcomes mentioned in the statistical analysis section have data reported, although a number of outcomes at different timepoints only presented graphically).<br><br>**Overall risk of bias judgement:** this study is judged to have some concerns in multiple domains.<br><br>**Other information**<br>Number of participants: N=36 for the 2 relevant treatment arms.<br>Number of participants completing study: n=27 for the 2 relevant treatment arms.<br>Women of childbearing potential using effective contraceptive methods must have been taking the same birth control for at least 6 months prior to study inclusion and were not permitted to change birth control during the study.<br>A third treatment arm was included in the study (adapalene gel 0.1% for 9 months) |

| Study details | Participants | Interventions | Results | Risk of bias |
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| | | | | but was not relevant to this review question.<br>No washout period for observation arm (3 months azelaic acid then 6 months observation) |
| **Study ID**<br><br>870446<br><br>**Full citation**<br><br>Truchuelo, M. T., Jimenez, N., Mavura, D., Jaen, P., Assessment of the efficacy and safety of a combination of 2 topical retinoids (RetinSphere) in maintaining post-treatment response of acne to oral isotretinoin, Actas Dermo-Sifiliograficas, 106, 126-32, 2015<br><br>**Country/ies where the study was carried out**<br><br>Spain<br><br>**RCT type (parallel or split face)**<br>Prospective, randomised, double-blind, placebo-controlled (vehicle) split face trial.<br><br>**Study dates** | N=30<br><br>**Sex (Male, female or mixed)**<br><br>Male: 40.6%; Female: 59.4%<br><br>**Age details**<br>Age (years) - mean (±SD)<br>Male: 18.4 (5.2)<br>Female: 23.5 (5.6)<br><br>**Acne scale used for inclusion**<br><br>Not reported.<br><br>**Other inclusion criteria**<br>• Participants aged over 14 years of age.<br>• Completed treatment with oral isotretinoin (including participants who had or had not reached the conventional target dose of 120 to 150 mg/kg) in the previous 6 months.<br><br>**Exclusion criteria**<br>• Participants aged <14 years of age.<br>• Participants with other concomitant dermatoses or sensitisation to any of the components of the product.<br>• Women not using a contraceptive method. | **Treatment duration (weeks)**<br><br>12<br><br>**Info about intensity of physical treatments**<br>Not applicable.<br><br>**Number of treatment arms**<br><br>2<br><br>**Interventions**<br>Retinoid combination (retinol encapsulated in glycospheres and hydroxypinacolone retinoate): applied to one side of the face at night for 3 months.<br><br>Vehicle: applied to the other side of the face at night for 3 months. | **Results**<br>Relapse (global count) after 3 months maintenance - n (%)<br>Retinoid combination: 5 (16.7)<br>Vehicle: 13 (43.3)<br><br>Number of total lesions - mean (±SD)<br>Retinoid combination: Baseline: 14 (36.80); 3 months: 8 (19.31); p=0.002<br>Vehicle: Baseline: 13 (36.12); 3 months: 11 (28.93); p=0.08<br><br>Global lesions after 3 months maintenance - mean (±SD)<br>Retinoid combination: 4.1 (3.4)<br>Vehicle: 5.6 (3.8); p=0.05<br><br>Investigator-reported improvement (IGA) - mean<br>Retinoid combination: Baseline: 2.2 (mild severity); 3 months: 1.4 (almost clear); p<0.01<br>Vehicle: Baseline: 2.2 (mild severity); 3 months: 2 (mild); p=0.106<br><br>No adverse events were reported.<br><br>2 participants discontinued due to work commitments. | **Risk of bias**<br>**Methodological limitations assessed using the Cochrane risk of bias tool (RoB2)**<br><br>**Risk of bias arising from the randomisation process:** low risk (randomisation performed by an independent statistician using the Random Function of standard computer software; the code establishing which side of the face to apply the 2 treatments was kept in a sealed envelope until the end of the study).<br><br>**Risk of bias due to deviations from the intended interventions:** low risk (participants and investigators were not informed of the composition of the 2 creams, which were similar in texture and odour and only distinguishable by packaging colouring; 2 participants discontinued treatment and were excluded from analysis).<br><br>**Risk of bias due to missing outcome data:** low risk (data available for nearly all participants).<br><br>**Risk of bias in measurement of the outcome:** low risk (same measurement methods used; split face trial).<br><br>**Risk of bias in selection of the reported result:** some concerns (limited |

| Study details | Participants | Interventions | Results | Risk of bias |
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| Not reported.<br><br>**Source of funding**<br>Industrial Farmaceutica Cantabria, Spain. | | | | information provided).<br><br>**Overall risk of bias judgement:** this study is judged to have some concerns in one domain.<br><br>**Other information**<br>All participants had mild acne at baseline.<br>Number of participants: N=32.<br>Number of participants completing study: n=30.<br>Previous treatment: isotretinoin (majority of participants had not reached total cumulative target dose of 120 to 150 mg/kg).<br>Mean period from discontinuation of isotretinoin treatment until study initiation: 2 months (range 2 weeks to 6 months). |
| **Study ID**<br><br>1048731<br><br>**Full citation**<br><br>Vender, R., Double-blinded, vehicle-controlled proof of concept study to investigate the recurrence of inflammatory and noninflammatory acne lesions using tretinoin gel (Microsphere) 0.04% in male patients after oral isotretinoin use, Dermatology Research and Practice, 2012 (no pagination), 2012 | N=20<br><br>**Sex (Male, female or mixed)**<br><br>Male: 100%<br><br>**Age details**<br>Age (years) - mean (range)<br>Tretinoin: 21 (18 to 29)<br>Vehicle: 22.4 (18 to 42)<br><br>**Acne scale used for inclusion**<br><br>Not reported.<br><br>**Other inclusion criteria**<br>• Males aged between 18 and 45 years.<br>• Successful completion of acne treatment with isotretinoin (minimum 4 months/maximum 6 months with an average of 5 months and a total of 120 to 150 mg/kg/course). | **Treatment duration (weeks)**<br><br>24<br><br>**Info about intensity of physical treatments**<br>Not applicable.<br><br>**Number of treatment arms**<br><br>2<br><br>**Interventions**<br>Tretinoin (n=10): 0.04% gel (microsphere) applied once daily to the whole face (and left on for a minimum of 8 hours) for 24 weeks.<br><br>Vehicle (n=10): applied once daily to the whole face (and left on for a minimum of 8 hours) for 24 weeks. | Lesion counts - mean (95% CI)<br>Tretinoin: Baseline: 0 (0 to 0.369); week 24: 1.2 (0.003 to 0.557)<br>Vehicle: Baseline: 0 (0 to 0.369); week 24: 3.1 (0.062 to 0.877)<br><br>Investigator's Static Global Assessment - mean (range)<br>Tretinoin: Baseline: 0 (0); week 24: 0.33 (0 to 1)<br>Vehicle: Baseline: 0 (0); week 24: 0.33 (0 to 1)<br><br>Subject's Global Assessment - mean (range)<br>Tretinoin: Baseline: 0 (0); week 24: 0.13 (0 to 1)<br>Vehicle: Baseline: 0.13 (0 to 1); week 24: 0.33 (0 to 1)<br><br>Acceptability (treatment discontinuation for any reason) at week 24 - n/N | **Methodological limitations assessed using the Cochrane risk of bias tool (RoB2)**<br><br>**Risk of bias arising from the randomisation process:** some concerns (randomisation on 1:1 ratio; assignment performed by unblinded dispenser; between-group differences were not significant).<br><br>**Risk of bias due to deviations from the intended interventions:** low risk (double-blind trial; treatments provided in unlabelled grey plastic 50 g pump dispensers; ITT analyses).<br><br>**Risk of bias due to missing outcome data:** some concerns (data not available for all participants - high attrition rates - tretinoin (30%); vehicle (20%); last-observation-carried forward for missing data). |

| Study details | Participants | Interventions | Results | Risk of bias |
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| **Country/ies where the study was carried out**<br><br>Canada<br><br>**RCT type (parallel or split face)**<br>Randomised, double-blind, vehicle controlled proof of concept study.<br><br>**Study dates**<br>Not reported.<br><br>**Source of funding**<br>Johnson and Johnson Inc., Canada. | • Able to attend follow-up visits at the outpatient dermatology clinic.<br>• Consent for participation and agreed to comply with treatment and follow-up procedures.<br>• Participants planning to use multi-vitamins (without vitamin A), iron supplements, and folate were acceptable.<br><br>**Exclusion criteria**<br>• Participants who received isotretinoin for conditions other than acne.<br>• No treatment with isotretinoin for less than 30 days or more than 90 days at the time of study enrolment.<br>• Participants who had used prescription topical acne treatment (tretinoin, benzoyl peroxide, topical antibiotics, or any combination treatment) between the end of isotretinoin treatment and within 2 weeks of study enrolment, or oral antibiotics of any type between the end of isotretinoin treatment and within 4 weeks of study enrolment and throughout the study.<br>• Participants who had previously been diagnosed with an endocrinologic disorder likely to cause acne (such as genital/adrenal hyperplasia, adrenal tumours, or any other hypoandrogenic condition.<br>• Participants who used any systemic medications likely to cause or abate acne (such as oral phenytoin or any other epileptic, finasteride, spironolactone, or flutamide, testosterone, or dietary body- | Participants were instructed to wash their face first and allow the areas to fully dry for approximately 20 to 30 minutes before applying treatment in a sufficient amount to cover the entire face. Treatments were to be applied consistently either in the morning or in the evening throughout the study duration.<br><br>Participants were permitted to use moisturiser and cleanser on the face provided. | Tretinoin: 3/10<br>Vehicle: 2/10<br><br>No serious adverse event or adverse events were reported.<br><br>Treatments were well tolerated and no treatment was interrupted due to any local tolerability complaints or local side effects. | **Risk of bias in measurement of the outcome:** low risk (same measurement methods used; investigators and participants were not aware of treatment allocation).<br><br>**Risk of bias in selection of the reported result:** some concerns (limited information provided).<br><br>**Overall risk of bias judgement:** this study is judged to have some concerns in multiple domains.<br><br>**Other information**<br>Participants had previously been treated for moderate to severe acne.<br>Number of participants: N=20.<br>Number of participants completing study: n=15.<br>Previous treatment: isotretinoin. |

| Study details | Participants | Interventions | Results | Risk of bias |
|---|---|---|---|---|
| | building protein powders).<br>• Participants who used topical corticosteroids on the face or systemic corticosteroids within the past 4 weeks.<br>• Participants who inhaled, intra-articular, or intra-lesional steroids other than for facial acne.<br>• Participants who were using any medication that in the opinion of the investigator could influence the action or evaluation of the study product or place the participant at undue risk.<br>• Use of abradants, facials, and peels containing glycolic or other acids; masks, washes or soaps containing BPO, salicylic acid or sulfacetamide sodium; non-mild facial abradants, facials, peels containing glycolic or other acids; masks washes, or soaps containing BPO, salicylic acid or sulfacetamide sodium; non-mild facial cleansers; and moisturisers containing retinol, salicylic acid or α- or β-hydroxy acids within the past 2 weeks of randomisation and throughout the study duration.<br>• Planned use of medications reported to exacerbate acne (for example, megadoses of certain vitamins), haloperidol, halogens, lithium, hydantoin, and phenobarbital.<br>• Participants who had undergone a facial procedure (such as chemical or laser, peel) by an aesthetician, beautician, physician, nurse or other practitioner within the past 4 weeks or planned to undergo such a | | | |

| Study details | Participants | Interventions | Results | Risk of bias |
|---|---|---|---|---|
| | procedure during the study.<br>• Participants with a known hypersensitivity or previous allergic reaction to any of the active components of excipients of the study product, used any investigational treatment within 4 weeks of randomisation, or were currently participating in another clinical trial, currently abusing drugs or alcohol, had a significant medical history of being immunocompromised, had other conditions that, in the opinion of the investigator, would put them at undue risk.<br>• Participants with any major illness within 30 days before screening.<br>• Current employees of the investigator or sponsor involved in the study.<br>• Immediate family members of an employee involved in the study. | | | |
| **Study ID**<br><br>1220444<br><br>**Full citation**<br><br>Zhang, J., Li, L. F., Tu, Y. T., Zheng, J., A successful maintenance approach in inflammatory acne with adapalene gel 0.1% after an initial treatment in combination with | **Sex (Male, female or mixed)**<br><br>Not reported for maintenance phase.<br><br>**Age details**<br>Not reported for maintenance phase.<br><br>**Acne scale used for inclusion**<br><br>Modified International Acne Grading System.<br><br>**Other inclusion criteria**<br>• Males and females with moderate to moderately severe acne vulgaris.<br>• Aged between 12 and 35 years. | **Treatment duration (weeks)**<br><br>12<br><br>**Info about intensity of physical treatments**<br>Not applicable.<br><br>**Number of treatment arms**<br><br>2<br><br>**Interventions**<br>Adapalene (n=122): 0.1% adapalene gel once daily in the evening after gentle cleaning of the face. | Mean percentage reduction after maintenance phase (total lesions)<br>Adapalene: -41.6%<br>No treatment: +92.1%; p<0.01<br><br>Global assessment of change (further improved and much improved/clear) at the end of maintenance phase - %<br>Adapalene: 67.2%<br>No treatment: 4.2%<br>No adverse events were reported. | **Methodological limitations assessed using the Cochrane risk of bias tool (RoB2)**<br><br>**Risk of bias arising from the randomisation process:** high risk (open-label trial; between-group differences were not significant).<br><br>**Risk of bias due to deviations from the intended interventions:** some concerns (open-label trial; ITT analyses).<br><br>**Risk of bias due to missing outcome data:** low risk (data available for participants - no discontinuations reported during the maintenance phase). |

| Study details | Participants | Interventions | Results | Risk of bias |
|---|---|---|---|---|
| clindamycin topical solution 1% or after monotherapy with clindamycin topical solution 1%, Journal of Dermatological Treatment, 15, 372-378, 2004<br><br>**Country/ies where the study was carried out**<br><br>China<br><br>**RCT type (parallel or split face)**<br>Open-labelled, controlled trial.<br><br>**Study dates**<br>Not reported.<br><br>**Source of funding**<br>Not reported. | • Global severity grade ranging from II to III according to the Modified International Acne Grading System.<br>• 10 to 50 inflammatory facial lesions (no more than 3 nodules and/or cysts) and 20 to 150 non-inflammatory facial lesions.<br>• Achieved at least moderate improvement in initial treatment phase.<br>• Participants taking certain topical and systemic treatments were required to complete specified washout periods before they could enter the study.<br><br>**Exclusion criteria**<br>• Participants with acne conglobata, acne fulminans, secondary acne, severe acne or other dermatological conditions requiring systemic treatment.<br>• Women who were pregnant, planning a pregnancy or nursing.<br>• Men with beards if these were likely to interfere with study assessments. | No treatment (n=119): Simple and gentle washing of the face. | | **Risk of bias in measurement of the outcome:** high risk (same measurement methods and thresholds used at comparable timepoints; open-label trial).<br><br>**Risk of bias in selection of the reported result:** some concerns (limited information provided; reported results for the outcome measurements appear to correspond to all intended analyses, although a number only presented graphically at different timepoints).<br><br>**Overall risk of bias judgement:** this study is judged to be at high risk of bias (high risk and some concerns in multiple domains).<br><br>**Other information**<br>Participants had previously been treated for moderate to moderately severe acne.<br>Number of participants: N=241.<br>Number of participants completing study: n=241.<br>Previous treatment: adapalene gel 01% plus clindamycin topical solution 1% or clindamycin topical solution 1% alone. |

*BPO: Benzoyl Peroxide; CI: confidence interval; IGA: Investigator's Global Assessment; ISGA: Investigator's Static Global Assessment; ITT: intention-to-treat; LRAGS: Leeds Revised Acne Grading Scale; N: number; SD: standard deviation; RoB2: risk of bias version 2.*

# Appendix E – Forest plots

## Forest plots for review question: What is the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris?

Figure 2: Forest plot for comparison Adapalene regimens versus vehicle, no treatment or observation for acne vulgaris: Relapse

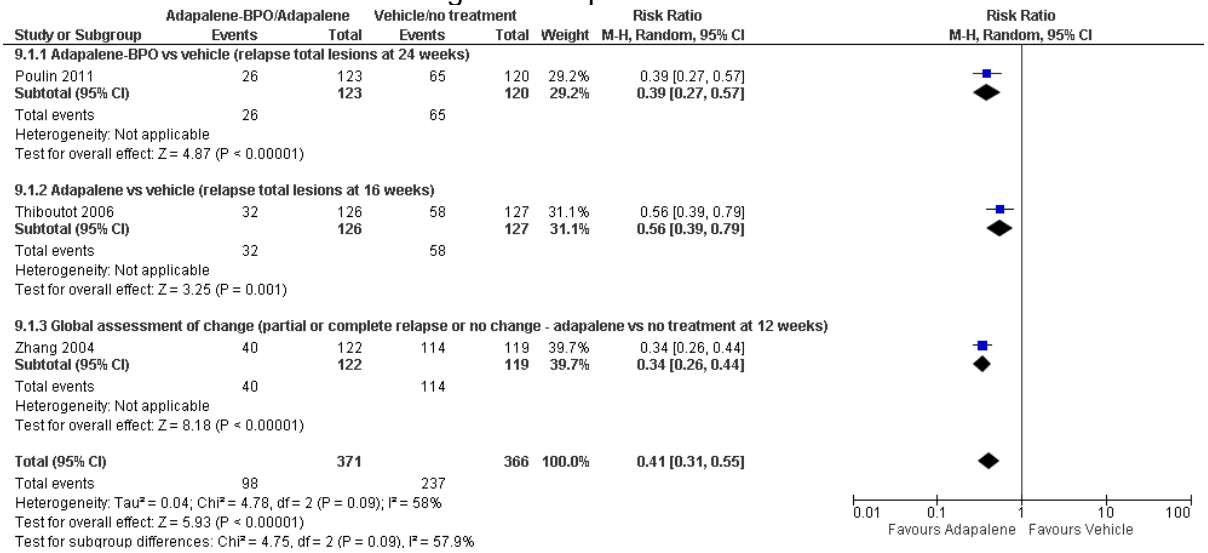
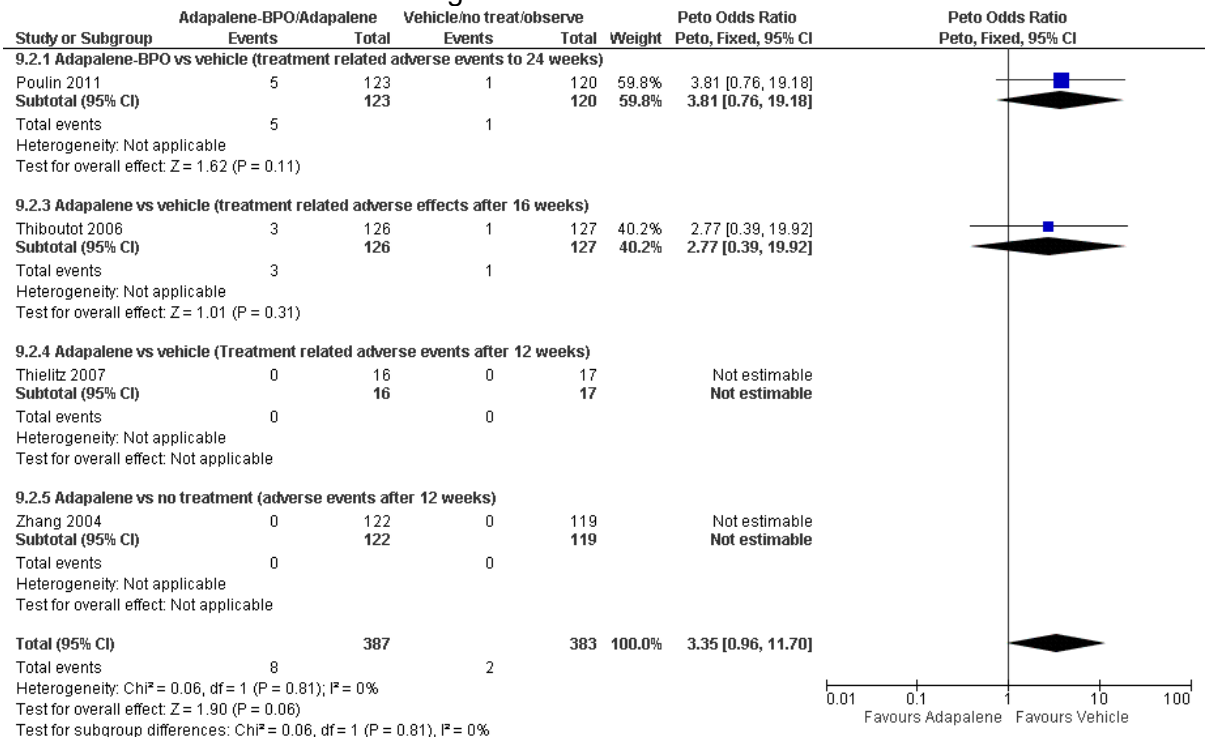
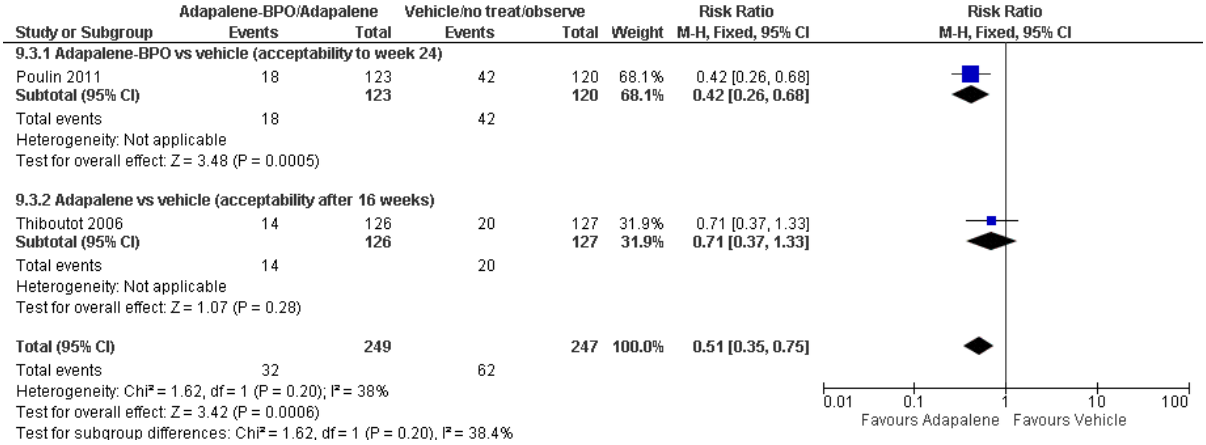



Figure 3: Forest plot for comparison Adapalene regimens versus vehicle, no treatment or observation for acne vulgaris: Adverse events



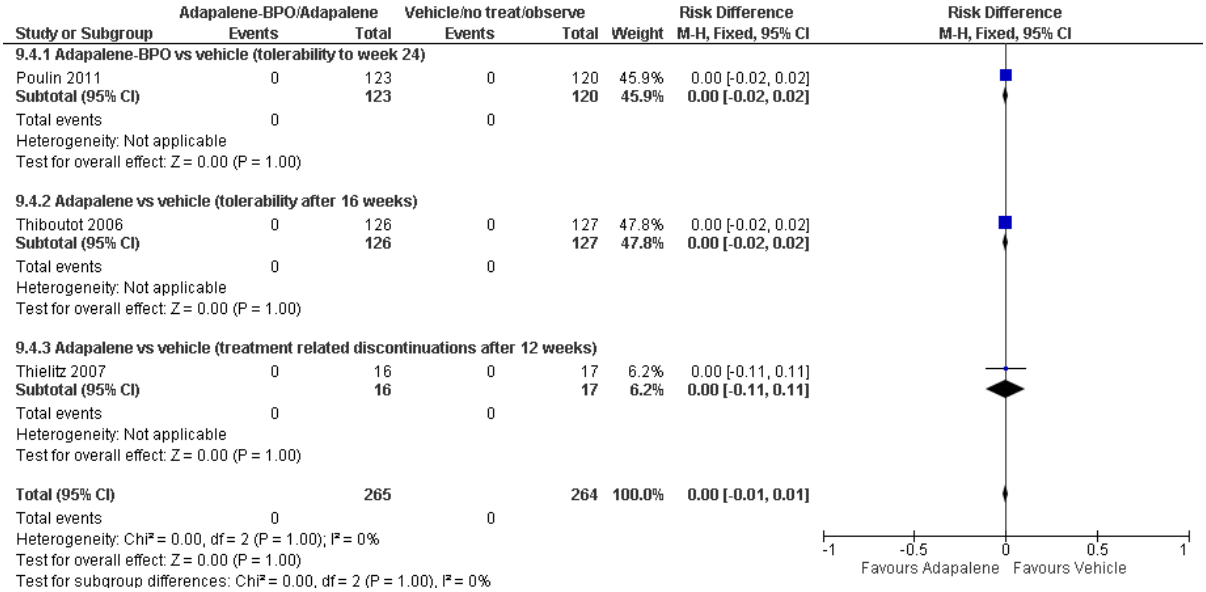

*BPO: benzoyl peroxide*

Figure 4: Forest plot for comparison Adapalene regimens versus vehicle, no treatment or observation for acne vulgaris: Acceptability - Treatment discontinuation for any reason




*BPO: benzoyl peroxide*

Figure 5: Forest plot for comparison Adapalene regimens versus vehicle, no treatment or observation for acne vulgaris: Tolerability - Treatment discontinuation due to side effects




*BPO: benzoyl peroxide*

# Appendix F – GRADE tables

## GRADE tables for review question: What is the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris?

### Table 5: Clinical evidence profile for Tazarotene gel + placebo versus vehicle gel + minocycline maintenance therapy for acne vulgaris

| Quality assessment | | | | | | | No of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Tazarotene gel + placebo | Vehicle gel + minocycline | Relative (95% CI) | Absolute | | |
| **% change in non-inflammatory lesion count after 12 weeks (follow-up 12 weeks; measured with: Lesion count; Better indicated by higher values)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | serious[3] | none | 35 | 37 | - | MD 8 lower (20.39 lower to 4.39 higher) | ⊕⊕OO LOW | CRITICAL |
| **% change in inflammatory lesion count after 12 weeks (follow-up 12 weeks; measured with: Lesion count; Better indicated by higher values)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | serious[4] | none | 35 | 37 | - | MD 12 higher (0.61 lower to 24.61 higher) | ⊕⊕OO LOW | CRITICAL |
| **Participants relapsing after 12 weeks (follow-up 12 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | very serious[5] | none | 9/27 (33.3%) | 5/31 (16.1%) | RR 2.07 (0.79 to 5.42) | 173 more per 1000 (from 34 fewer to 713 more) | ⊕OOO VERY LOW | IMPORTANT |
| **Acceptability (treatment discontinuation for any reason) after 12 weeks (follow-up 12 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | very serious[5] | none | 8/36 (22.2%) | 6/37 (16.2%) | RR 1.37 (0.53 to 3.56) | 60 more per 1000 (from 76 fewer to 415 more) | ⊕OOO VERY LOW | IMPORTANT |
| **Tolerability (treatment discontinuation due to side effects) after 12 weeks (follow-up 12 weeks)** | | | | | | | | | | | | |

| Quality assessment | | | | | | | No of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Tazarotene gel + placebo | Vehicle gel + minocycline | Relative (95% CI) | Absolute | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | very serious[5] | none | 0/36 (0%) | 1/37 (2.7%) | RR 0.34 (0.01 to 8.14) | 18 fewer per 1000 (from 27 fewer to 193 more) | ⊕OOO VERY LOW | IMPORTANT |

*CI: confidence interval; MD: mean difference; MID: minimally important difference; RR: risk ratio*
*[1] Leyden 2006*
*[2] Overall risk of bias judgement: some concerns due to missing outcome data and selection bias.*
*[3] Evidence downgraded by 1 level due to risk of serious imprecision as 95% CI crosses 1 MID. MID calculated as +/-15.2.*
*[4] Evidence downgraded by 1 level due to risk of serious imprecision as 95% CI crosses 1 MID. MID calculated as +/- 14.7.*
*[5] Evidence downgraded by 2 levels due risk of serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.*

**Table 6: Clinical evidence profile for Tazarotene gel + placebo versus tazarotene gel + minocycline maintenance therapy for acne vulgaris**

| Quality assessment | | | | | | | No of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Tazarotene gel + Placebo | Tazarotene gel + minocycline | Relative (95% CI) | Absolute | | |
| **% change in non-inflammatory lesion count after 12 weeks (follow-up 12 weeks; measured with: Lesion count; Better indicated by higher values)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | serious[3] | none | 35 | 35 | - | MD 4 higher (11.88 lower to 19.88 higher) | ⊕⊕OO LOW | CRITICAL |
| **% change in inflammatory lesion count after 12 weeks (follow-up 12 weeks; measured with: Lesion count; Better indicated by higher values)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | serious[4] | none | 35 | 36 | - | MD 12 higher (0.17 lower to 24.17 higher) | ⊕⊕OO LOW | CRITICAL |
| **Participants relapsing after 12 weeks (follow-up 12 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised | serious[2] | no serious | no serious | very | none | 9/27 | 7/31 | RR 1.48 | 108 more per 1000 (from 81 fewer to 549 | ⊕OOO VERY | IMPORTANT |

| Quality assessment | | | | | | | No of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Tazarotene gel + Placebo | Tazarotene gel + minocycline | Relative (95% CI) | Absolute | | |
| | trials | | inconsistency | indirectness | serious[5] | | (33.3%) | (22.6%) | (0.64 to 3.43) | more) | LOW | |
| **Acceptability (treatment discontinuation for any reason) after 12 weeks (follow-up 12 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | very serious[5] | none | 8/36 (22.2%) | 6/37 (16.2%) | RR 1.37 (0.53 to 3.56) | 60 more per 1000 (from 76 fewer to 415 more) | ⊕OOO VERY LOW | IMPORTANT |
| **Tolerability (treatment discontinuation due to side effects) after 12 weeks (follow-up 12 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | very serious[5] | none | 0/36 (0%) | 1/37 (2.7%) | RR 0.34 (0.01 to 8.14) | 18 fewer per 1000 (from 27 fewer to 193 more) | ⊕OOO VERY LOW | IMPORTANT |

*CI: confidence interval; MD: mean difference; MID: minimally important difference; RR: risk ratio*
*[1] Leyden 2006*
*[2] Overall risk of bias judgement: some concerns due to missing outcome data and selection bias.*
*[3] Evidence downgraded by 1 level due to risk of serious imprecision as 95% CI crosses 1 MID. MID calculated as +/-15.2.*
*[4] Evidence downgraded by 1 level due to risk of serious imprecision as 95% CI crosses 1 MID. MID calculated as +/- 13.6.*
*[5] Evidence downgraded by 2 levels due risk of serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.*

### Table 7: Clinical evidence profile for Tazarotene gel + minocycline versus vehicle gel + minocycline maintenance therapy for acne vulgaris

| Quality assessment | | | | | | | No of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Tazarotene gel + minocycline | Vehicle gel + minocycline | Relative (95% CI) | Absolute | | |
| **% change in non-inflammatory lesion count after 12 weeks (follow-up 12 weeks; measured with: Lesion count; Better indicated by higher values)** | | | | | | | | | | | | |
| 1[1] | randomised | serious[2] | no serious | no serious | no serious | none | 35 | 37 | - | MD 12 lower (29.04 | ⊕⊕⊕O | CRITICAL |

| Quality assessment | | | | | | | No of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Tazarotene gel + minocycline | Vehicle gel + minocycline | Relative (95% CI) | Absolute | | |
| | trials | | inconsistency | indirectness | imprecision | | | | | lower to 5.04 higher) | MODERATE | |
| **% change in inflammatory lesion count after 12 weeks (follow-up 12 weeks; measured with: Lesion count; Better indicated by higher values)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | no serious imprecision | none | 36 | 37 | - | MD 0 higher (12.99 lower to 12.99 higher) | ⊕⊕⊕O MODERATE | CRITICAL |
| **Participants relapsing after 12 weeks (follow-up 12 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | very serious[3] | none | 7/31 (22.6%) | 5/31 (16.1%) | RR 1.4 (0.5 to 3.94) | 65 more per 1000 (from 81 fewer to 474 more) | ⊕OOO VERY LOW | IMPORTANT |
| **Acceptability (treatment discontinuation for any reason) after 12 weeks (follow-up 12 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | very serious[3] | none | 6/37 (16.2%) | 6/37 (16.2%) | RR 1 (0.35 to 2.82) | 0 fewer per 1000 (from 105 fewer to 295 more) | ⊕OOO VERY LOW | IMPORTANT |
| **Tolerability (treatment discontinuation due to side effects) after 12 weeks (follow-up 12 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | very serious[3] | none | 1/37 (2.7%) | 1/37 (2.7%) | RR 1 (0.06 to 15.4) | 0 fewer per 1000 (from 25 fewer to 389 more) | ⊕OOO VERY LOW | IMPORTANT |

*CI: confidence interval; MD: mean difference; MID: minimally important difference; RR: risk ratio*

*[1] Leyden 2006*

*[2] Overall risk of bias judgement: some concerns due to missing outcome data and selection bias.*

*[3] Evidence downgraded by 2 levels due risk of serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.*

**Table 8: Clinical evidence profile for adapalene/BPO versus vehicle for acne vulgaris**

| Quality assessment | | | | | | | No of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Adapalene/BPO | Vehicle | Relative (95% CI) | Absolute | | |
| **IGA success rate (% participants rated worse from baseline (follow-up 24 weeks; assessed with: Investigator's Global Assessment score)** | | | | | | | | | | | | |
| 1[1] | randomised trials | very serious[2] | no serious inconsistency | no serious indirectness | no serious imprecision | none | 36/123 (29.3%) | 79/120 (65.8%) | RR 0.44 (0.33 to 0.6) | 369 fewer per 1000 (from 263 fewer to 441 fewer) | ⊕⊕OO LOW | CRITICAL |
| **Irritation from baseline to week 24 - erythema (follow-up 24 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised trials | very serious[2] | no serious inconsistency | no serious indirectness | no serious imprecision | none | 94/123 (76.4%) | 100/120 (83.3%) | RR 0.92 (0.81 to 1.04) | 67 fewer per 1000 (from 158 fewer to 33 more) | ⊕⊕OO LOW | IMPORTANT |
| **Irritation from baseline to week 24 - scaling (follow-up 24 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised trials | very serious[2] | no serious inconsistency | no serious indirectness | serious[3] | none | 87/123 (70.7%) | 111/120 (92.5%) | RR 0.76 (0.68 to 0.87) | 222 fewer per 1000 (from 120 fewer to 296 fewer) | ⊕OOO VERY LOW | IMPORTANT |
| **Irritation from baseline to week 24 - dryness (follow-up 24 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised trials | very serious[2] | no serious inconsistency | no serious indirectness | serious[3] | none | 90/123 (73.2%) | 106/120 (88.3%) | RR 0.83 (0.73 to 0.94) | 150 fewer per 1000 (from 53 fewer to 239 fewer) | ⊕OOO VERY LOW | IMPORTANT |
| **Irritation from baseline to week 24 - stinging/burning (follow-up 24 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised trials | very serious[2] | no serious inconsistency | no serious indirectness | serious[3] | none | 96/123 (78%) | 111/120 (92.5%) | RR 0.84 (0.76 to 0.94) | 148 fewer per 1000 (from 56 fewer to 222 fewer) | ⊕OOO VERY LOW | IMPORTANT |

*BPO: benzoyl peroxide; CI: confidence interval; IGA: investigator's global assessment score; MID: minimally important difference; RR: risk ratio*
*[1] Poulin 2011*
*[2] Overall risk of bias: high risk due to missing outcome data.*
*[3] Evidence downgraded by 1 level due risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes.*

**Table 9: Clinical evidence profile for adapalene gel versus adapalene/vehicle for acne vulgaris**

| Quality assessment | | | | | | | No of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Adapalene gel | Adapalene/vehicle | Relative (95% CI) | Absolute | | |
| **% change in microcomedone count after 12 weeks (follow-up 12 weeks; Better indicated by higher values)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | very serious[3] | none | 16 | 16 | - | MD 3.4 lower (47.61 lower to 40.81 higher) | ⊕OOO VERY LOW | CRITICAL |
| **Treatment related adverse events after 12 weeks (follow-up 12 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | very serious[4] | none | 0/16 (0%) | 0/16 (0%) | RD 0 (-0.11 to 0.11) | - | ⊕OOO VERY LOW | IMPORTANT |
| **Treatment discontinuations after 12 weeks (follow-up 12 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | very serious[4] | none | 0/16 (0%) | 0/16 (0%) | RD 0 (-0.11 to 0.11) | - | ⊕OOO VERY LOW | IMPORTANT |

*CI: confidence interval; MD: mean difference; MID: minimally important difference; RD: risk difference*

[2] Overall risk of bias judgement: some concerns due to limited information on the randomisation process, deviations from intended interventions, measurement of the outcome, and measurement of the outcome.

[3] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% CIs cross both MIDs. MID calculated as +/- 40.7.

[4] Evidence downgraded by 2 levels due to risk of very serious imprecision due to a small number of events.

**Table 10: Clinical evidence profile for adapalene gel versus vehicle for acne vulgaris**

| Quality assessment | | | | | | | No of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Adapalene gel | Vehicle | Relative (95% CI) | Absolute | | |
| **% change in microcomedone count after 12 weeks (follow-up 12 weeks; Better indicated by higher values)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | serious[3] | none | 16 | 17 | - | MD 51.4 lower (95.35 to 7.45 lower) | ⊕⊕OO LOW | CRITICAL |

*CI: confidence interval; MD: mean difference; MID: minimally important difference; RD: risk difference*
*[1] Thielitz 2007*
*[2] Overall risk of bias judgement: some concerns due to limited information on the randomisation process, deviations from intended interventions, measurement of the outcome, and measurement of the outcome.*
*[3] Evidence downgraded by 1 level due to risk of serious imprecision as 95% CI crosses 1 MID. MID calculated as +/- 41.65.*

**Table 11: Clinical evidence profile for adapalene gel versus vehicle for acne vulgaris**

| Quality assessment | | | | | | | No of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Adapalene gel | Vehicle | Relative (95% CI) | Absolute | | |
| **% change in microcomedone count after 12 weeks (follow-up 12 weeks; Better indicated by higher values)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | serious[3] | none | 16 | 17 | - | MD 48 lower (104.2 lower to 8.2 higher) | ⊕⊕OO LOW | CRITICAL |
| **Treatment related adverse events after 12 weeks (follow-up 12 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | very serious[4] | none | 0/16 (0%) | 0/17 (0%) | RD 0 (-0.11 to 0.11) | - | ⊕OOO VERY LOW | IMPORTANT |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Treatment discontinuations after 12 weeks (follow-up 12 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | very serious[4] | none | 0/16 (0%) | 0/17 (0%) | RD 0 (-0.11 to 0.11) | - | ⊕OOO VERY LOW | IMPORTANT |

*CI: confidence interval; MD: mean difference; MID: minimally important difference; RD: risk difference*
*[1] Thielitz 2007*
*[2] Overall risk of bias judgement: some concerns due to limited information on the randomisation process, deviations from intended interventions, measurement of the outcome, and measurement of the outcome.*
*[3] Evidence downgraded by 1 level due to risk of serious imprecision as 95% CI crosses 1 MID. MID calculated as +/- 41.65.*
*[4] Evidence downgraded by 2 levels due to risk of very serious imprecision due to a small number of events.*

### Table 12: Clinical evidence profile for adapalene gel versus BPO gel for acne vulgaris

| Quality assessment | | | | | | | No of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **No of studies** | **Design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Adapalene gel** | **BPO gel** | **Relative (95% CI)** | **Absolute** | | |
| **Relapse/aggravation of symptoms after 12 weeks (follow-up 12 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | very serious[3] | none | 25/47 (53.2%) | 27/45 (60%) | RR 0.89 (0.62 to 1.27) | 66 fewer per 1000 (from 228 fewer to 162 more) | ⊕OOO VERY LOW | CRITICAL |
| **Adverse events after 12 weeks - Erythema (follow-up 12 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | very serious[3] | none | 1/47 (2.1%) | 0/45 (0%) | POR 7.08 (0.14 to 357.20) | - | ⊕OOO VERY LOW | IMPORTANT |
| **Adverse events after 12 weeks - Dryness (follow-up 12 weeks)** | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | very serious[3] | none | 1/45 (2.2%) | 1/47 (2.1%) | RR 0.96 (0.06 to 14.85) | 1 fewer per 1000 (from 20 fewer to 295 more) | ⊕OOO VERY LOW | IMPORTANT |

*BPO: benzoyl peroxide; CI: confidence interval; MID: minimally important difference; POR: peto odds ratio; RR: risk ratio*
*[1] Kawashima 2018*
*[2] Overall risk of bias judgment: some concerns as no information provided on allocation concealment and blinding.*
*[3] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.*

**Table 13: Clinical evidence profile for retinoid combinations versus vehicle for acne vulgaris**

| Quality assessment | | | | | | | No of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Retinoid combination | Vehicle | Relative (95% CI) | Absolute | | |
| **Relapse (global count) after 12 weeks (follow-up 3 months; assessed with: Global count)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | serious[3] | none | 5/30 (16.7%) | 13/30 (43.3%) | RR 0.38 (0.16 to 0.94) | 269 fewer per 1000 (from 26 fewer to 364 fewer) | ⊕⊕OO LOW | IMPORTANT |
| **Number of total lesions after 12 weeks (follow-up 3 months; Better indicated by lower values)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | serious[4] | none | 30 | 30 | - | MD 3 lower (15.45 lower to 9.45 higher) | ⊕⊕OO LOW | CRITICAL |
| **Global lesions after 12 weeks (follow-up 3 months; Better indicated by lower values)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | serious[5] | none | 30 | 30 | - | MD 1.5 lower (3.32 lower to 0.32 higher) | ⊕⊕OO LOW | CRITICAL |
| **Change score - Investigator reported improvement (follow-up 3 months; measured with: Investigator's Global Assessment; Better indicated by lower values)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | no serious imprecision[6] | none | 30 | 30 | - | MD 0 higher (0 to 0 higher) | ⊕⊕⊕O MODERATE | CRITICAL |
| **Adverse events after 12 weeks (follow-up 3 months)** | | | | | | | | | | | | |
| 1[1] | randomised | serious[2] | no serious | no serious | very serious[7] | none | 0/30 | 0/30 | RD 0.00 (- | - | ⊕OOO | IMPORTANT |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | trials | | inconsistency | indirectness | | | (0%) | (0%) | 0.06 to 0.06) | | VERY LOW | |

*CI: confidence interval; MD: mean difference; MID: minimally important difference; RD: risk difference; RR: risk ratio*
*[1] Truchuelo 2015*
*[2] Overall risk of bias judgement: some concerns due to limited information on selection of reported result.*
*[3] Evidence downgraded by 1 level due to risk of serious imprecision as 95% CI crosses 1 default MID for dichotomous outcomes.*
*[4] Evidence downgraded by 1 level due to risk of serious imprecision as 95% CI crosses 1 MID. MID calculated as +/- 14.465.*
*[5] Evidence downgraded by 1 level due to risk of serious imprecision as 95% CI crosses 1 MID. MID calculated as +/- 1.9.*
*[6] MD and 95% CI not estimable.*
*[7] Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events.*

### Table 14: Clinical evidence profile for tretinoin versus vehicle for acne vulgaris

| Quality assessment | | | | | | | No of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **No of studies** | **Design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Tretinoin** | **Vehicle** | **Relative (95% CI)** | **Absolute** | | |
| **Lesion counts after 24 weeks (follow-up 24 weeks; Better indicated by lower values)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | no serious imprecision | none | 10 | 10 | - | MD 1.9 lower (2.4 to 1.4 lower) | ⊕⊕⊕O MODERATE | CRITICAL |
| **Acceptability (treatment discontinuation for any reason) at week 24 (follow-up 24 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | very serious[3] | none | 3/10 (30%) | 2/10 (20%) | RR 1.5 (0.32 to 7.14) | 100 more per 1000 (from 136 fewer to 1000 more) | ⊕OOO VERY LOW | IMPORTANT |
| **Serious or adverse events (follow-up 24 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | very serious[4] | none | 0/10 (0%) | 0/10 (0%) | RD 0.00 (-0.17 to 0.17) | - | ⊕OOO VERY LOW | IMPORTANT |
| **Tolerability (treatment discontinuation due to local tolerability complaints or side effects) (follow-up 24 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | very serious[4] | none | 0/10 (0%) | 0/10 (0%) | RD 0.00 (-0.17 to 0.17) | - | ⊕OOO VERY LOW | IMPORTANT |

*CI: confidence interval; MD: mean difference; MID: minimally important difference; RD: risk difference; RR: risk ratio*
*[1] Vender 2012*
*[2] Overall risk of bias judgement: some concerns due to issues with multiple domains (randomisation process, missing outcome data, and selection of reported result).*

*[3] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% CI crosses 2 default MIDs for dichotomous outcomes.*
*[4] Evidence downgraded by 2 levels due to risk of very serious imprecision due to a small number of events.*

### Table 15: Clinical evidence profile for adapalene versus no treatment for acne vulgaris

| Quality assessment | | | | | | | No of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Adapalene | No treatment | Relative (95% CI) | Absolute | | |
| **Mean % reduction after 12 weeks (total lesions) (follow-up 12 weeks; Better indicated by lower values)** | | | | | | | | | | | | |
| 1[1] | randomised trials | very serious[2] | no serious inconsistency | no serious indirectness | serious[3] | none | 122 | 119 | - | MD 133.7 lower (187.86 to 79.54 lower) | ⊕OOO VERY LOW | CRITICAL |

*CI: confidence interval; MD: mean difference; MID: minimally important difference*
*[1] Zhang 2004*
*[2] Overall risk of bias: high risk due to concerns in multiple domains (randomisation process, deviations from intended interventions, measurement of outcome, and selection of reported result).*
*[3] Evidence downgraded by 1 level due to risk of serious imprecision as 95% CI crosses 1 MID. MID calculated as +/137.6502.*

### Table 16: Clinical evidence profile for azelaic acid versus observation for acne vulgaris

| Quality assessment | | | | | | | No of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Azelaic acid | Observation | Relative (95% CI) | Absolute | | |
| **Relative change in total lesions after 24 weeks (follow-up 24 weeks; Better indicated by lower values)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | serious[3] | none | 17 | 19 | - | MD 39.76 lower (76.57 to 2.95 lower) | ⊕⊕OO LOW | CRITICAL |
| **Absolute change after 24 weeks maintenance in ISGA (follow-up 24 weeks; measured with: Investigator's Static Global Assessment; Better indicated by lower values)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | no serious imprecision | none | 17 | 19 | - | MD 0.08 lower (0.35 lower to 0.19 higher) | ⊕⊕⊕O MODERATE | CRITICAL |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Absolute change after 24 weeks maintenance in LRAGS (follow-up 24 weeks; measured with: Leeds Revised Acne Grading Scale; Better indicated by lower values)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | no serious imprecision | none | 17 | 19 | - | MD 0.16 lower (0.69 lower to 0.37 higher) | ⊕⊕⊕O MODERATE | CRITICAL |
| **Relapse during 24 weeks maintenance (follow-up 24 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | no serious imprecision | none | 11/17 (64.7%) | 15/19 (78.9%) | RR 0.82 (0.54 to 1.25) | 142 fewer per 1000 (from 363 fewer to 197 more) | ⊕⊕⊕O MODERATE | IMPORTANT |
| **Acceptability (treatment discontinuation for any reason - treatment & maintenance phase) (follow-up 24 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | very serious[4] | none | 6/17 (35.3%) | 3/19 (15.8%) | RR 2.24 (0.66 to 7.58) | 196 more per 1000 (from 54 fewer to 1000 more) | ⊕OOO VERY LOW | IMPORTANT |
| **Tolerability (treatment discontinuation due to side effects during 24 weeks maintenance) (follow-up 24 weeks)** | | | | | | | | | | | | |
| 1[1] | randomised trials | serious[2] | no serious inconsistency | no serious indirectness | very serious[5] | none | 0/17 (0%) | 0/19 (0%) | RD 0.00 (-0.10 to 0.10) | - | ⊕OOO VERY LOW | IMPORTANT |

*CI: confidence interval; ISGA: Investigator's Static Global Assessment; MD: mean difference; MID: minimally important difference; RD: risk difference; RR: risk ratio*
*[1] Thielitz 2015*
*[2] Overall risk of bias judgement: some concerns in multiple domains (randomisation process, deviations form intended interventions, measurement of the outcome, and selection of reported result).*
*[3] Evidence downgraded by 1 level due to risk of serious imprecision as 95% CI crosses 1 MID. MID calculated as +/- 35.635.*
*[4] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% CI crosses 2 default MIDs for dichotomous outcomes.*
*[5] Evidence downgraded by 2 levels due to risk of very serious imprecision due to a small number of events.*

### Table 17: Clinical evidence profile for adapalene regimens versus vehicle, no treatment, or observation for acne vulgaris

| Quality assessment | | | | | | | No of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **No of studies** | **Design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Adapalene regimens** | **Vehicle, no treatment or observation** | **Relative (95% CI)** | **Absolute** | | |
| **Relapse from baseline (total lesions) (follow-up 12 to 24 weeks)** | | | | | | | | | | | | |
| 3[1] | randomised | very | serious[3] | no serious | no serious | none | 98/371 | 237/366 | RR 0.41 | 382 fewer per 1000 | ⊕OOO | IMPORTANT |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | trials | serious[2] | | indirectness | imprecision | | (26.4%) | (64.8%) | (0.31 to 0.55) | (from 291 fewer to 447 fewer) | VERY LOW | |
| **Adverse events (follow-up 12 to 24 weeks)** | | | | | | | | | | | | |
| 4[4] | randomised trials | very serious[5] | no serious inconsistency | no serious indirectness | very serious[6] | none | 8/387 (2.1%) | 2/383 (0.52%) | POR 3.35 (0.96 to 11.7) | 12 more per 1000 (from 0 fewer to 53 more) | ⊕OOO VERY LOW | IMPORTANT |
| **Acceptability (follow-up 16 to 24 weeks)** | | | | | | | | | | | | |
| 2[7] | randomised trials | very serious[8] | no serious inconsistency [9] | no serious indirectness | no serious imprecision | none | 32/249 (12.9%) | 62/247 (25.1%) | RR 0.51 (0.35 to 0.75) | 123 fewer per 1000 (from 63 fewer to 163 fewer) | ⊕⊕OO LOW | IMPORTANT |
| **Tolerability (follow-up 12 to 24 weeks)** | | | | | | | | | | | | |
| 3[10] | randomised trials | very serious[11] | no serious inconsistency | no serious indirectness | serious[12] | none | 0/265 (0%) | 0/264 (0%) | RD 0.00 (-0.01 to 0.01) | - | ⊕OOO VERY LOW | IMPORTANT |

*CI: confidence interval; MID: minimally important difference; POR: peto odds ratio; RD: risk difference; RR: risk ratio*

*[1] Poulin 2011, Thiboutot 2006, Zhang 2004*

*[2] Overall risk of bias judgement: high risk due to various concerns (Poulin 2011 at high risk for missing outcome data; Thiboutot 2006 at high risk for selection of reported result, some concerns for deviations from intended intervention, missing outcome data, and measure of result; Zhang 2004 at high risk for randomisation process and measurement of outcome, and some concerns for deviations from intended intervention and selection of reported result).*

*[3] Evidence downgraded by 1 level because there is moderate to substantial heterogeneity across trial (i2=58%) but all trials show efficacy of effect in the same direction (favouring Adapalene-BPO/Adapalene).*

*[4] Poulin 2011, Thiboutot 2006, Thielitz 2007, Zhang 2004*

*[5] Overall risk of bias judgement: high risk due to concerns with all studies (Poulin 2011 at high risk for missing outcome data; Thiboutot 2006 at high risk for selection of reported result, some concerns for deviations from intended intervention, missing outcome data, and measure of result; Zhang 2004 at high risk for randomisation process and measurement of outcome, and some concerns for deviations from intended intervention and selection of reported result); and 1 trial judged to have some concerns in multiple domains (Thielitz 2007: some concerns arising from randomisation process, deviations from the intended interventions, measurement of the outcome, and selection of the reported result).*

*[6] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% CI crosses 2 default MIDs for dichotomous outcomes.*

*[7] Poulin 2011, Thiboutot 2006*

*[8] Overall risk of bias judgement: high risk because Poulin 2011 at high risk for missing outcome data; Thiboutot 2006 at high risk for selection of reported result, some concerns for deviations from intended intervention, missing outcome data, and measure of result.*

*[9] There is moderate heterogeneity across the trials (i2= 38%) which may be explained by subgroup analysis for different duration of follow-up and use of different interventions: 1 trial assesses adapalene-BPO versus vehicle at 24 weeks and the second trial adapalene alone versus vehicle at 16 weeks. One trial favours adapalene-BPO, the second trial crosses the line of no effect.*

*[10] Poulin 2011, Thiboutot 2006, Thielitz 2007*

*[11] Overall risk of bias judgement: high risk because Poulin 2011 at high risk for missing outcome data; Thiboutot 2006 at high risk for selection of reported result, some concerns for deviations from intended intervention, missing outcome data, and measure of result; and 1 trial judged to have some concerns in multiple domains (Thielitz 2007: some concerns arising from randomisation process, deviations from the intended interventions, measurement of the outcome, and selection of the reported result).*

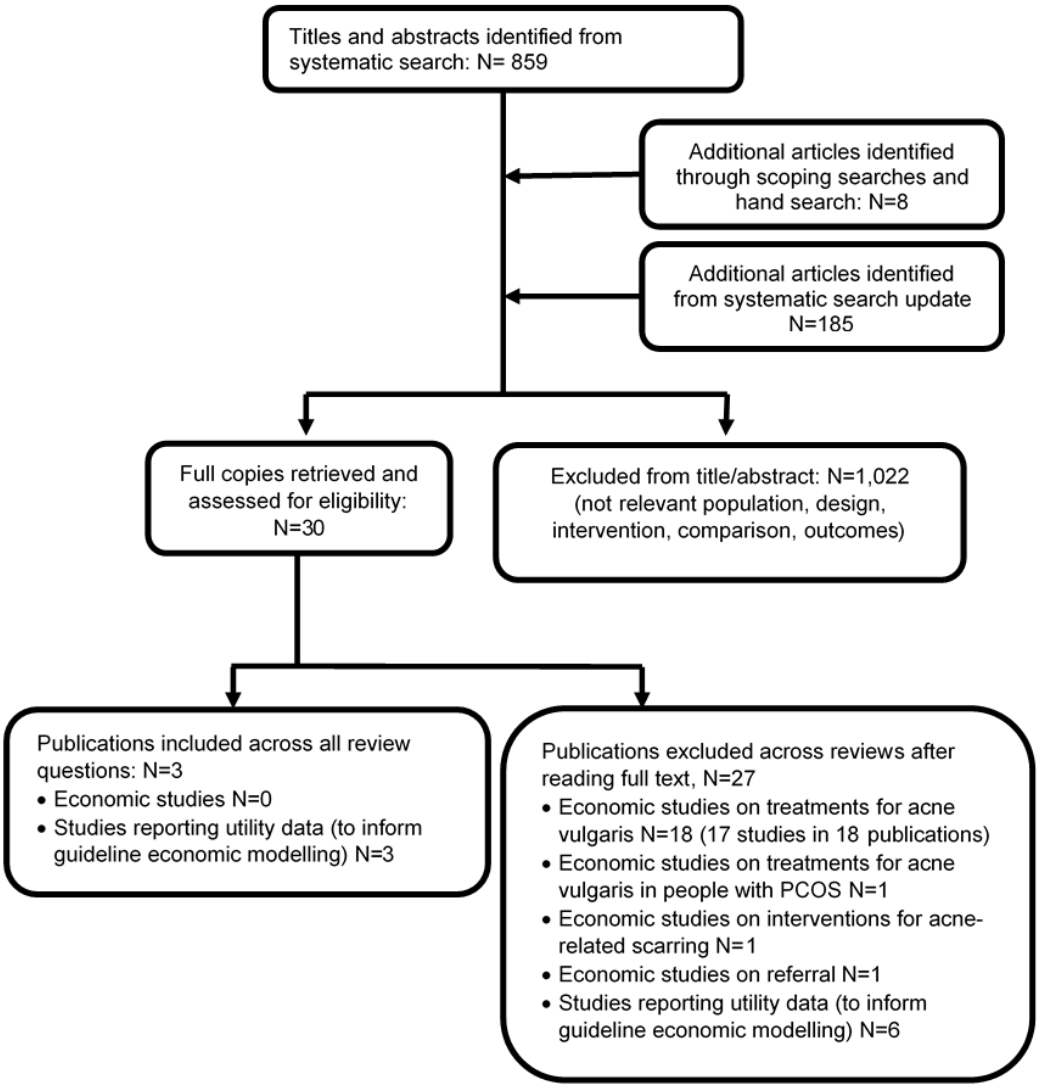
[12] *Evidence downgraded by 1 level due to risk of serious imprecision due to small number of events*

# Appendix G - Economic evidence study selection

## Economic evidence study selection for review question: What is the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris?

A global health economics search was undertaken for all areas covered in the guideline. Figure 6 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 6. 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 is the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris?

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

# Appendix I – Economic evidence profiles

### Economic evidence profiles for review question: What is the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris?

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

# Appendix J – Economic analysis

## Economic analysis for review question: What is the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris?

No economic analysis was conducted for this review question.

# Appendix K – Excluded studies

## Excluded clinical and economic studies for review question: What is the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris?

### Clinical studies

The excluded studies list below relates to all evidence reviews that used the same search output and these are studies that are excluded from all of them: mild-to-moderate NMA, moderate-to-severe NMA, mild-to-moderate pairwise and moderate-to-severe pairwise reports, as well as from refractory acne, maintenance of acne and polycystic ovary syndrome.

**Table 18: Excluded studies and reasons for their exclusion**

| Reference | Reason for exclusion |
|---|---|
| Abbasi, M. A. K., A., Aziz ur, Rehman, Saleem, H.,Jahangir, S. M.,Siddiqui, S. Z.,Ahmad, V. U.Preparation of new formulations of anti-acne creams and their efficacy. 2010. African Journal of Pharmacy and Pharmacology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Abdel Hay, R. H., R.,Abdel Hady, M.,Saleh, N.Clinical and dermoscopic evaluation of combined (salicylic acid 20% and azelaic acid 20%) versus trichloroacetic acid 25% chemical peel in acne: an RCT. 2019. Journal of Dermatological Treatment | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Abdel Meguid, A. M. A. E. A. A., D.,Omar, H.Trichloroacetic acid versus salicylic acid in the treatment of acne vulgaris in dark-skinned patients. 2015. Dermatologic Surgery | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatmentsanalysis |
| Abdel-Naser, M. B. Z., C. C . Clindamycin phosphate/tretinoin gel formulation in the treatment of acne vulgaris. 2008. Expert Opinion on Pharmacotherapy | No relevant article type - expert opinion on pharmacotherapy |
| Abels, C. Glycolic acid: the effect is also now proven in acne. 2011a. Haut | Not in English language |
| Abramovits, W. G., A. Differin (adapalene) Gel, 0.3%. 2007. SKINmed | No relevant study design - not RCT |
| Abramovits, W. O., M., Gupta, A. K.Veltin gel (clindamycin phosphate 1.2% and tretinoin 0.025%). 2011. SKINmed | No relevant article type - non-systematic review |
| Adalatkhah, H. P., F., Sadeghi-Bazargani, H. Flutamide versus a cyproterone acetate-ethinyl estradiol combination in moderate acne: a | Moderate acne - no information on lesion |

| Reference | Reason for exclusion |
|---|---|
| pilot randomized clinical trial. 2011. Clinical, Cosmetic and Investigational Dermatology CCID | counts at baseline and study is not relevant for PCOS, maintenance or refractory treatments |
| Adams, J. T., P. Topical fusidic acid versus peroral doxycycline in the treatment of patients with acne vulgaris of the face. 1991. Current Therapeutic Research - Clinical and Experimental | No relevant intervention - suboptimal dose of doxycycline |
| Adams, R. M. B., K. H. An antiandrogen delta 1 chlormadinone acetate in acne: lack of effect topically. 1970a. Acta Dermato-Venereologica | Duplicate record |
| Adams, U. M. B., K. H. An antiandrogen delta 1 chlormadinone acetate in acne: lack of effect topically. 1970b. Acta Dermatologica | No relevant study population -insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Afzali, B. M. Y., E., Yaghoobi, R., Bagherani, N.,Dabbagh, M. A. Comparison of the efficacy of 5% topical spironolactone gel and placebo in the treatment of mild and moderate acne vulgaris: A randomized controlled trial. 2012. Journal of Dermatological Treatment | No relevant intervention - intervention & class not available in the UK |
| Agarwal, U. S. B., R. K., Bhola, K. Oral isotretinoin in different dose regimens for acne vulgaris: A randomized comparative trial. 2011. Indian Journal of Dermatology, Venereology and Leprology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Agren, U. M. A., M., Maenpaa-Liukko, K., Rantala, M. L.,Rautiainen, H.,Sommer, W. F.,Mommers, E.Effects of a monophasic combined oral contraceptive containing nomegestrol acetate and 17beta-oestradiol compared with one containing levonorgestrel and ethinylestradiol on haemostasis, lipids and carbohydrate metabolism. 2011a. European Journal of Contraception and Reproductive Health Care | No relevant study population - participants did not have acne |
| Agren, U. M. A., M., Maenpaa-Liukko, K., Rantala, M. L.,Rautiainen, H.,Sommer, W. F.,Mommers, E.Effects of a monophasic combined oral contraceptive containing nomegestrol acetate and 17beta-oestradiol in comparison to one containing levonorgestrel and ethinylestradiol on markers of endocrine function. 2011b. European Journal of Contraception and Reproductive Health Care | No relevant study population - participants did not have acne |
| Ahmad, H. M. Analysis of clinical efficacy, side effects, and laboratory changes among patients with acne vulgaris receiving single versus twice daily dose of oral isotretinoin. 2015. Dermatologic Therapy | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Ahmadvand, A. Y., A., Yasrebifar, F., Mohammadi, Y.,Mahjub, R.,Mehrpooya, M.Evaluating the effects of oral and topical simvastatin in the treatment of acne vulgaris: A double-blind, randomized, placebo-controlled clinical trial. 2018. Current Clinical Pharmacology | Intervention not relevant I Simvastatin |
| Ahmed, I. S., M. Topical adapalene cream 0.1% v/s isotretinoin 0.05% in the treatment of acne vulgaris: A randomized open-label clinical trial. 2009. Journal of Pakistan Association of Dermatologists | No relevant outcomes reported |
| Ahn, G. R., Kim, J. M., Park, S. J., Li, K., Kim, B. J. Selective | Reported outcomes |

| Reference | Reason for exclusion |
|---|---|
| Sebaceous Gland Electrothermolysis Using a Single Microneedle Radiofrequency Device for Acne Patients: A Prospective Randomized Controlled Study. 2019. Lasers in Surgery and Medicine. | relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Akamatsu, H. O., M., Nishijima, S., Asada, Y.,Takahashi, M.,Ushijima, T.,Niwa, Y.The inhibition of free radical generation by human neutrophils through the synergistic effects of metronidazole with palmitoleic acid: a possible mechanism of action of metronidazole in rosacea and acne. 1990. Archives of Dermatological Research | No relevant data reported - pharmokinetic study |
| Akaraphanth, R. K., W., Gritiyarangsan, P. Efficacy of ALA-PDT vs blue light in the treatment of acne. 2007. Photodermatology, Photoimmunology & Photomedicine | No relevant study design - not RCT |
| Akerlund, M.Clinical experience of a combined oral contraceptive with very low dose ethinyl estradiol. 1997. Acta Obstetricia et Gynecologica Scandinavica, Supplement | No relevant outcomes reported |
| Aksakal, A. B. K., M.,Onder, M.,Oztas, M. O.,Gurer, M. A.A comparative study of metronidazole 1% cream versus azelaic acid 20% cream in the treatment of acne. 1997. Gazi Medical Journal | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Albuquerque, R. G. d. R., M. A.,Hirotsu, C.,Hachul, H.,Bagatin, E.,Tufik, S.,Andersen, M. L.A randomized comparative trial of a combined oral contraceptive and azelaic acid to assess their effect on sleep quality in adult female acne patients. 2015. Archives of Dermatological Research | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Alexis, A. D. R., J. Q.,Desai, S. R.,Downie, J. B.,Draelos, Z. D.,Feser, C.,Forconi, R.,Fowler, J. F., Jr.,Gold, M.,Kaufman-Janette, J.,Lain, E.,Lee, M.,Ling, M.,Shamban, A. T.,Werschler, W. P.,Daniels, A.BPX-01 Minocycline Topical Gel Shows Promise for the Treatment of Moderate-to-severe Inflammatory Acne Vulgaris. 2018. The Journal of Clinical & Aesthetic Dermatology | No relevant intervention - intervention & class not available in the UK |
| Alexis, A. F. C.-B., F. E.,York, J. P.Adapalene/benzoyl peroxide gel 0.3%/2.5%: A safe and effective acne therapy in all skin phototypes. 2017. Journal of Drugs in Dermatology | No relevant data reported - post hock analysis according to Fitzpatrick skin type of Stein Gold 2016 |
| Alexis, A. F. J., L. A.,Kerrouche, N.,Callender, V. D.A subgroup analysis to evaluate the efficacy and safety of adapalene-benzoyl peroxide topical gel in black subjects with moderate acne. 2014. Journal of Drugs in Dermatology | No relevant data reported - subgroup analysis of Thiboutot 2007, Gollnick 2009, Gold 2009 |
| Alexis, A. F., Cook-Bolden, F., & Lin, T. Treatment of moderate-to-severe acne vulgaris in a hispanic population: a post-hoc analysis of the efficacy and tolerability of clindamycin 1.2%/benzoyl peroxide 3.75% gel. 2017. Journal of clinical and aesthetic dermatology | No relevant data reported - post hoc subgroup analysis for Hispanic population of Pariser 2014 |
| Alirezai, M. M., J.,Jablonska, S.,Czernielewski, J.,Verschoore, | Not in English language |

| Reference | Reason for exclusion |
|---|---|
| M.Comparative study of the efficacy and tolerability of 0.1 and 0.03 p.100 adapalene gel and 0.025 p.100 tretinoin gel in the treatment of acne. 1996. Annales de dermatologie ET de venereologie | |
| Alirezai, M. V., K.,Humbert, P.,Valensi, P.,Cambon, L.,Dupuy, P.A low-salt medical water reduces irritancy of retinoic acid in facial acne. 2000. European Journal of Dermatology | Intervention not targeted at acne but at treatment side effects |
| Allen, H.F., Mazzoni, C., Heptulla, R.A., Murray, M.A., Miller, N., Koenigs, L., Reiter, E.O. Randomized controlled trial evaluating response to metformin versus standard therapy in the treatment of adolescents with polycystic ovary syndrome. 2005. Journal of Pediatric Endocrinology and Metabolism | Not clear what proportion of participants had acne at baseline |
| Al-Mishari, M. A. Clinical and bacteriological evaluation of tetracycline and erythromycin in acne vulgaris. 1987. Clinical Therapeutics | Unclear if RCT |
| Amer, S. S., Nasr, M., Abdel-Aziz, R. T. A., Moftah, N. H., El Shaer, A., Polycarpou, E., Mamdouh, W., Sammour, O. Cosm-nutraceutical nanovesicles for acne treatment: Physicochemical characterization and exploratory clinical experimentation. 2020. International Journal of PharmaceuticsInt J Pharm | No relevant study design - not RCT |
| Amiri, M., Nahidi, F., Bidhendi-Yarandi, R., Khalili, D., Tohidi, M., Ramezani Tehrani, F.A comparison of the effects of oral contraceptives on the clinical and biochemical manifestations of polycystic ovary syndrome: A crossover randomized controlled trial. 2020. Human Reproduction | No relevant outcomes reported |
| An, W. X. Z., Z. H. Curative observation on herbal tea combined with ear acupoint in treating 120 middle school students with acne. 2016. Western journal of traditional chinese medicine[xi bu zhong yi yao] | Not in English language |
| Anadolu, R. Y. S., T.,Tarimci, N.,Birol, A.,Erdem, C.Improved efficacy and tolerability of retinoic acid in acne vulgaris: A new topical formulation with cyclodextrin complex PSI. 2004. Journal of the European Academy of Dermatology and Venereology | Insufficient information about severity of acne at baseline and study is not relevant for PCOS, maintenance or refractory treatments |
| Anonymous, Management of acne vulgaris. 1966. Drug & Therapeutics Bulletin | Duplicate record |
| Anonymous, Pharmacokinetic profile, safety, and tolerability of clascoterone topical cream 1% in subjects with moderate-to-severe acne vulgaris: an open-label phase IIa study. 2019. Journal of the American Academy of Dermatology | No relevant article type - conference abstract |
| Anonymous, Phase III Clinical Study of Clindamycin Phosphate Topical Gel (CLDM-T) in the Treatment of Acne Vulgaris: randomized Comparatie Study with Nadifloxacin Cream as a Control Drug. 1999b. Rinsho iyaku (journal of clinical therapeutics and medicines) | Not in English language |
| Anonymous, Retinoic acid in the treatment of acne. A report from the General Practitioner Research Group. 1974. Practitioner | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Anonymous, The Clinical Phase II Study of CLDM-T Gel in the Treatment of Acne Vulgaris: double-Blind Comparative Study, Evaluation of Efficacy, Safety and Optimal Concentration of CLDM-T Gel in the Treatment of Acne Vulgaris. 1999a. Rinsho iyaku (journal of clinical therapeutics and medicines) | Not in English language |

| Reference | Reason for exclusion |
|---|---|
| Anonymous, Treatment of moderate-to-severe facial acne vulgaris with the use of a solid-state fractional 589/1,319-nm laser. 2018. Journal of the American Academy of Dermatology | No relevant article type - conference abstract |
| Ansarin, H. S., S.,Behzadi, A. H.,Sadigh, N.,Hasanloo, J.Doxycycline plus levamisole: combination treatment for severe nodulocystic acne. 2008. Journal of drugs in dermatology : JDD | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Anstee, P. K., G. T.A prospective randomized study comparing the clinical effects of a norethisterone and a levonorgestrel containing low dose oestrogen oral contraceptive pills. 1993. Australian and New Zealand Journal of Obstetrics and Gynaecology | No relevant study population - participants did not have acne |
| Antoniou, C. D., C.,Sotiriadis, D.,Kalokasidis, K.,Kontochristopoulos, G.,Petridis, A.,Rigopoulos, D.,Vezina, D.,Nikolis, A.A multicenter, randomized, split-face clinical trial evaluating the efficacy and safety of chromophore gel-assisted blue light phototherapy for the treatment of acne. 2016. International Journal of Dermatology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Anyachukwu, C. C. O., O. K. K. Efficacy of adjunct (laser) therapy to topical agents among Southern Nigerian acne vulgaris patients. 2014. Acupuncture and Related Therapies | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Ash, C. H., A.,Drew, S.,Whittall, R.A randomized controlled study for the treatment of acne vulgaris using high-intensity 414 nm solid state diode arrays. 2015. Journal of cosmetic and laser therapy | Unclear what treatment the control group received (over the counter products) |
| Aydin, F. C., T.,Senturk, N.,Yasar Turanli, A.Comparison of clinical efficacy of tretinoin 0.025% gel and adapalene 0.1% gel in the treatment of acne vulgaris. 2002. Ondokuz mayis universitesi tip dergisi | Not in English language |
| Aydinlik, S. L.-F., U.,Lehnert, J.Reduced estrogen ovulation inhibitor in acne therapy. Double-blind study comparing Diane-35 to Diane. 1986. Fortschritte der medizin | Not in English language |
| Aziz-Jalali, M. H. T., S. M.,Djavid, G. E.Comparison of red and infrared low-level laser therapy in the treatment of acne vulgaris. 2012. Indian Journal of Dermatology | No relevant study design as the study does not appear to be randomised - the same treatment was always applied to a give side of the face |
| Babaeinejad, S. K., E.,Fouladi, R. F.Comparison of therapeutic effects of oral doxycycline and azithromycin in patients with moderate acne vulgaris: What is the role of age?. 2011. Journal of Dermatological Treatment | No relevant study population - sample includes people with moderate acne but baseline severity not |

| Reference | Reason for exclusion |
|---|---|
| | reported according to lesion counts and study is not relevant for PCOS, maintenance or refractory treatments |
| Bae, B. G. P., C. O.,Shin, H.,Lee, S. H.,Lee, Y. S.,Lee, S. J.,Chung, K. Y.,Lee, K. H.,Lee, J. H.Salicylic acid peels versus Jessner's solution for acne vulgaris: a comparative study. 2013. Dermatologic surgery | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Barak-Shinar, D. D., Z. D.A randomized controlled study of a novel botanical acne spot treatment. 2017. Journal of Drugs in Dermatology | No relevant intervention - study product was based on 10% herbal botanical ingredients with anti-inflammatory and anti-bacterial activity |
| Barranco, V. P.Effect of androgen-dominant and estrogen-dominant oral contraceptives on acne. 1974. Cutis; cutaneous medicine for the practitioner | No relevant study population - no information on the baseline severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Bassett, I. B. P., D. L.,Barnetson, R. S.A comparative study of tea-tree oil versus benzoylperoxide in the treatment of acne. 1990. Medical Journal of Australia | No relevant intervention - tea-tree oil |
| Baugh, W. P. K., W. D.Nonablative phototherapy for acne vulgaris using the KTP 532 nm laser. 2005. Dermatologic Surgery | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Baumann, L. S. O., 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. 2013. Journal of drugs in dermatology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Behrangi, E. A., E.,Tavakoli, T.,Mehran, G.,Atefi, N.,Esmaeeli, S.,Azizian, Z.Comparing efficacy of montelukast versus doxycycline in treatment of moderate acne. 2015. Journal of Research in Medical Sciences | No relevant intervention - montelukast |
| Behrangi, E., Sadeghi, S., Sadeghzadeh-Bazargan, A., Goodarzi, A., Ghassemi, M., Sepasgozar, S., Rohaninasab, M. The effect of metformin in the treatment of intractable and late onset acne: A | No relevant data reported - reports combined results for those with treatment- |

| Reference | Reason for exclusion |
|---|---|
| comparison with oral isotretinoin. 2019. Iranian Journal of Dermatology | resistant acne and those with severe acne with late onset acne; no subgroups reported and study is not relevant for PCOS, maintenance or refractory treatments |
| Belknap, B. S.Treatment of acne with 5% benzoyl peroxide gel or 0.05% retinoic acid cream. 1979. Cutis | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Belum, V. R. M., M. A.,Dusza, S. W.,Cercek, A.,Kemeny, N. E.,Lacouture, M. E.A prospective, randomized, double-blinded, split-face/chest study of prophylactic topical dapsone 5% gel versus moisturizer for the prevention of cetuximab-induced acneiform rash. 2017. Journal of the American Academy of Dermatology | No relevant study population - sample includes people with metastatic colorectal cancer or head and neck squamous cell carcinoma |
| Bernstein, E. F.A pilot investigation comparing low-energy, double pass 1,450 nm laser treatment of acne to conventional single-pass, high-energy treatment. 2007. Lasers in Surgery and Medicine | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Bernstein, J. E. S., A. R.Topically applied erythromycin in inflammatory acne vulgaris. 1980. Journal of the American Academy of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Bershad, S. K. S., G.,Parente, J. E.,Tan, M. H.,Sherer, D. W.,Persaud, A. N.,Lebwohl, M.Successful treatment of acne vulgaris using a new method: results of a randomized vehicle-controlled trial of short-contact therapy with 0.1% tazarotene gel. 2002. Archives of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Bettoli, V. B., A.,Zauli, S.,Toni, G.,Ricci, M.,Giari, S.,Virgili, A.Maintenance therapy for acne vulgaris: efficacy of a 12-month treatment with adapalene-benzoyl peroxide after oral isotretinoin and a review of the literature. 2013. Dermatology | Duplicate record |
| Bhatia, N. P., R.Randomized, observer-blind, split-face compatibility study with clindamycin phosphate 1.2%/benzoyl peroxide 3.75% gel and facial foundation makeup. 2015. Journal of Clinical and Aesthetic Dermatology | No relevant comparison - split face 6-hour RCT that examines cosmetic compatibility of make up with topical clindamycin and BPO gel |
| Bhavsar, B. C., B.,Sanmukhani, J.,Dogra, A.,Haq, R.,Mehta, S.,Mukherjee, S.,Subramanian, V.,Sheikh, S.,Mittal, R.Clindamycin 1% Nano-emulsion Gel Formulation for the Treatment of Acne Vulgaris: Results of a Randomized, Active Controlled, Multicentre, | No relevant study population - sample includes people with mild to severe acne and study |

| Reference | Reason for exclusion |
|---|---|
| Phase IV Clinical Trial. 2014. Journal of Clinical and Diagnostic Research JCDR | is not relevant for PCOS, maintenance or refractory treatments |
| Bissonnette, R. B., 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. 2009. Journal of Cosmetic Dermatology | No relevant intervention - intervention & class not available in the UK |
| Bissonnette, R. M., C., Nigen, S.,Provost, N.,Bolduc, C.Photodynamic therapy with methylaminolevulinate 80 mg/g without occlusion improves acne vulgaris. 2010. Journal of Drugs in Dermatology | No relevant comparison - photodynamic therapy with methylaminolevulinate with occlusion vs without occlusion |
| Bissonnette, R. P., Y., Drew, J.,Hofland, H.,Tan, J.Olumacostat glasaretil, a novel topical sebum inhibitor, in the treatment of acne vulgaris: A phase IIa, multicenter, randomized, vehicle-controlled study. 2017. Journal of the American Academy of Dermatology | No relevant intervention - intervention not licensed in the UK |
| Biswas, S. M., K. K., Dutta, R. N.,Sarkar, D. K.Comparative evaluation of the efficacy of four topical medications individually or in combination to treat grade I acne vulgaris. 2009. Journal of the Indian Medical Association | No relevant outcomes reported |
| Biyun, C.The clinical observation of treating acne vulgaris with "xiao cuo fang". 2004. Zhong yao cai = Zhongyaocai [Journal of Chinese medicinal materials] | Not in English language |
| Bladon, P. T. B., B. M., Cunliffe, W. J.Topical azelaic acid and the treatment of acne: A clinical and laboratory comparison with oral tetracycline. 1986. British Journal of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Blaney, D. J. C., C. H. Topical use of tetracycline in the treatment of acne. A double blind study comparing topical and oral tetracycline therapy and placebo. 1976. Archives of Dermatology | No relevant intervention - intervention & class not available in the UK |
| Bleeker, J. H., L.,Vincent, J.Effect of systemic erythromycin stearate on the inflammatory lesions and skin surface fatty acids in acne vulgaris. 1981. Dermatologica | No relevant study population - sample includes people with mild to severe acne |
| Bodokh, I. J., Y., Lacour, J. Ph,Ortonne, J. P.Minocycline induces an increase in the number of excreting pilosebaceous follicles in acne vulgaris. A randomised study. 1997. Acta Dermato-Venereologica | No relevant data reported - pharmokinetic study |
| Bojar, R. A. E., E. A., Jones, C. E.,Cunliffe, W. J.,Holland, K. T.Inhibition of erythromycin-resistant propionibacteria on the skin of acne patients by topical erythromycin with and without zinc. 1994. British Journal of Dermatology | Efficacy outcomes reported in figures only |
| Borglund, E. H., O., Nord, C. E.Impact of topical clindamycin and systemic tetracycline on the skin and colon microflora in patients with acne vulgaris. 1984. Scandinavian Journal of Infectious Diseases | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Borglund, E. K., B., Larsson-Stymne, B.,Strand, A.,Veien, N. K.,Jakobsen, H. B.Topical meclocycline sulfosalicylate, benzoyl peroxide, and a combination of the two in the treatment of acne vulgaris. 1991. Acta Dermato-Venereologica | No relevant study population - sample includes people with mild to severe acne and study |

| Reference | Reason for exclusion |
|---|---|
| | is not relevant for PCOS, maintenance or refractory treatments |
| Borhan, W. H. H., H. A.,Aboelnour, N. H.Efficacy of pulsed dye laser on acne vulgaris. 2014. Journal of american science | Insufficient information about treatment (unspecified topical antibiotic) |
| Botsali, A. K., P.,Uran, P.The effects of isotretinoin on affective and cognitive functions are disparate in adolescent acne vulgaris patients. 2019. Journal of Dermatological Treatment. | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Bouloc, A. R., E.,Imko-Walczuk, B.,Moga, A.,Chadoutaud, B.,Dreno, B.A skincare combined with combination of adapalene and benzoyl peroxide provides a significant adjunctive efficacy and local tolerance benefit in adult women with mild acne. 2017. Journal of the European Academy of Dermatology and Venereology | No relevant intervention - compares emolients |
| Bourne, M. S.Comparison of two lotions for acne vulgaris. 1979. Practitioner | No relevant intervention - intervention & class not available in the UK |
| Bowman, S. G., M.,Nasir, A.,Vamvakias, G.Comparison of clindamycin/benzoyl peroxide, tretinoin plus clindamycin, and the combination of clindamycin/benzoyl peroxide and tretinoin plus clindamycin in the treatment of acne vulgaris: a randomized, blinded study. 2005. Journal of drugs in dermatology : JDD | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Bradford, L. G. M., L. F.Topical application of vitamin A acid in acne vulgaris. 1974. Southern Medical Journal | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Bran, E. L. R. A., A. Therapeutic effectiveness of clindamycin phosphate (1% solution) compared with tetracycline (solution) administered topically in the treatment of acne vulgaris. 1986. Medicina cutanea ibero-latino-americana | Not in English language |
| Brand, B. G., R.,Baker, M. D.,Poncet, M.,Greenspan, A.,Georgeian, K.,Soloff, A. M.Cumulative irritancy comparison of adapalene gel 0.1% versus other retinoid products when applied in combination with topical antimicrobial agents. 2003a. Journal of the American Academy of Dermatology | No relevant study population - participants did not have acne |
| Brand, B. G., R.,Baker, M. D.,Poncet, M.,Greenspan, A.,Georgeian, K.,Soto, P.,Arsonnaud, S.Cumulative Irritancy Potential of Adapalene Cream 0.1% Compared with Adapalene Gel 0.1% and Several Tretinoin Formulations. 2003b. Cutis | No relevant study population - participants did not have acne |
| Brand, E. L. R., A. Study of the therapeutic effectiveness of clindamycin phosphate (1% solution) versus tetracycline (solution) administered topically in the treatment of acne vulgaris. 1986. | Not in English language |

| Reference | Reason for exclusion |
|---|---|
| Medicina cutÃ¡nea ibero-latino-americana | |
| Brandt, H. A., P.,Ahokas, T.,Forstrom, L.,Jarvinen, T.,Keskitalo, R.,Lehtonen, L.,Plosila, M.,Rita, H.,Suramo, M. L.Erythromycin acistrate - An alternative oral treatment for acne. 1994. Journal of Dermatological Treatment | No relevant comparison - suboptimal dose |
| Breneman, D. L. A., M. C. Successful treatment of acne vulgaris in women with a new topical sodium sulfacetamide/sulfur lotion. 1993. International Journal of Dermatology | No relevant study design - not RCT |
| Breno, B. K., A.,Richard, A.,Rougier, A.Interest of a new salicylic acid derivative in the prevention of acne relapses. 2002. European journal of dermatology : EJD | No relevant article type - conference abstract |
| Brickman, S. S. L., W. D.,Gareau, J. Y.A double-blind evaluation of a topical antibiotic preparation in acne. 1980. Current Therapeutic Research - Clinical and Experimental | No relevant intervention - intervention & class not available in the UK |
| Brodell, R. T. S., B. J.,Rafal, E.,Toth, D.,Tyring, S.,Wertheimer, A.,Kerrouche, N.,Bucher, D.A fixed-dose combination of adapalene 0.1%BPO 2.5% allows an early and sustained improvement in quality of life and patient treatment satisfaction in severe acne. 2012. Journal of Dermatological Treatment | No relevant outcomes reported |
| Brogden, R. N. S., T. M.,Avery, G. S.Benzoyl peroxide acne lotions : an independent report. 1974. Drugs | No relevant article type - expert review |
| Brookes, D. B. M., R. M.,Sheil, L. P.,Flowers, I. M.,Poulter, G. A. Comparison of Tretinoin and a composite formulation in the treatment of acne. 1978. British Journal of Clinical Practice | No relevant study population - insufficient details reported to determine acne severity and study is not relevant for PCOS, maintenance or refractory treatments |
| Bubna, A. K.Metformin - For the dermatologist. 2016. Indian Journal of Pharmacology | Duplicate record |
| Bucknall, J. H. M., P. N. Comparison of tretinoin solution and benzoyl peroxide lotion in the treatment of acne vulgaris. 1977. Current Medical Research & Opinion | Not obtainable |
| Budden, M. G. Topical and oral tetracycline in the treatment of acne vulgaris. 1988. Practitioner | No relevant intervention - intervention & class not available in the UK |
| Burke, B. E., E. A.,Cunliffe, W. J.Benzoylperoxide versus topical erythromycin in the treatment of acne vulgaris. 1983. British Journal of Dermatology | No relevant study design - not RCT |
| Burkhart, C. G. B., C. N.Treatment of acne vulgaris without antibiotics: tertiary amine-benzoyl peroxide combination vs. benzoyl peroxide alone (Proactiv Solution). 2007. International Journal of Dermatology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Burton, J. E., G.A placebo-controlled study to evaluate the efficacy of topical tetracycline and oral tetracycline in the treatment of mild to moderate acne. 1990. Journal of International Medical Research | No relevant intervention - intervention & class not available in the UK |
| Burton, J. L. P., R. J.,Harris, J. I.Effect of 1% cyproterone acetate in Cetomacrogol cream BPC (formula A) on sebum excretion rate in patients with acne. 1976. British Journal of Dermatology | No relevant data reported - pharmokinetic study |

| Reference | Reason for exclusion |
|---|---|
| Callender, V. D.Fitzpatrick skin types and clindamycin phosphate 1.2%/benzoyl peroxide gel: Efficacy and tolerability of treatment in moderate to severe acne. 2012a. Journal of Drugs in Dermatology | No relevant data reported - post hoc analysis reporting results for people receiving clindamycin 2.1%/BPO 2.5% gel |
| Cambazard, F.Clinical efficacy of Velac, a new tretinoin and clindamycin phosphate gel in acne vulgaris. 1998. Journal of the European Academy of Dermatology & Venereology | No relevant study design - non-systematic review of tretinoin treatment |
| Cannizzaro, M. V. D., A.,Garofalo, V.,Del Duca, E.,Bianchi, L.Reducing the oral Isotretinoin skin side effects: Efficacy of 8% omega-ceramides, hydrophilic sugars, 5% niacinamide cream Compound in acne patients. 2018. Giornale Italiano di Dermatologia e Venereologia | Not in English language |
| Cao, J., Yang, G., Wang, Y., Liu, J. Acupoint Stimulation for Acne: A Systematic Review of Randomized Controlled Trials. 2013. Med Acupunct. 2013 | No relevant intervention - systematic review about acupoint stimulation techniques used to treat acne |
| Cao, J., Yang, G., Wang, Y., Ping Liu, J., Smith, C.A., Luo, H., Liu. Y. Complementary therapies for acne vulgaris. 2015. Cochrane Database Syst Rev | Not relevant intervention - systematic review about complementary and alternative medicine for acne |
| Cao, T. T., E. S.,Chan, Y. H.,Yosipovitch, G.,Tey, H. L.Anti-pruritic efficacies of doxycycline and erythromycin in the treatment of acne vulgaris: a randomized single-blinded pilot study. 2018. Indian journal of dermatology, venereology and leprology | No relevant study design - not RCT |
| Carlborg, L. Cyproterone acetate versus Levonorgestrel combined with ethinyl estradiol in the treatment of acne. Results of a multicenter study. 1986. Acta Obstetricia et Gynecologica Scandinavica | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Carlborg, L. Cyproterone acetate versus levonorgestrel combined with ethinylestradiol in the treatment of acne. Results of a multicenter study. 1987. Contraception fertilite sexualite | Duplicate record |
| Carmina, E. L., R. A.A comparison of the relative efficacy of antiandrogens for the treatment of acne in hyperandrogenic women. 2002. Clinical Endocrinology | Duplicate record |
| Caron, D. S., V.,Clucas, A.,Verschoore, M.Skin tolerance of adapalene 0.1% gel in combination with other topical antiacne treatments. 1997a. Journal of the American Academy of Dermatology | No relevant study population - participants did not have acne |
| Caron, D. S., V.,Kerrouche, N.,Clucas, A.Split-face comparison of adapalene 0. 1% gel and tretinoin 0.025% gel in acne patients. 1997b. Journal of the American Academy of Dermatology | No relevant outcomes reported |
| Cavicchini, S. C., R.Long-term treatment of acne with 20% azelaic acid cream. 1989. Acta Dermato-Venereologica, Supplement | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Cestone, E. M., 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- | Efficacy outcomes reported in figures only |

| Reference | Reason for exclusion |
|---|---|
| controlled clinical study. 2017. Journal of Cosmetic Dermatology | |
| Chalker, D. K. S., A.,Smith, J. G., Jr.,Swann, R. W.A double-blind study of the effectiveness of a 3% erythromycin and 5% benzoyl peroxide combination in the treatment of acne vulgaris. 1983. Journal of the American Academy of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Chan, H. C., G.,Santos, J.,Dee, K.,Co, J. K.A randomized, double-blind, placebo-controlled trial to determine the efficacy and safety of lactoferrin with vitamin E and zinc as an oral therapy for mild to moderate acne vulgaris. 2017. International Journal of Dermatology | No relevant intervention - Lactoferrin + Vitamin E + Zinc |
| Chandrashekha, B. S. A., M.,Ruparelia, M.,Vaidya, P.,Aamir, R.,Shah, S.,Thilak, S.,Aurangabadkar, S.,Pal, S.,Saraswat, A.,et al.,Tretinoin nanogel 0.025% versus conventional gel 0.025% in patients with acne vulgaris: a randomized, active controlled, multicentre, parallel group, phase iv clinical trial. 2015. Journal of clinical and diagnostic research | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Chang, S. E. A., S. J.,Rhee, D. Y.,Choi, J. H.,Moon, K. C.,Suh, H. S.,Soyun, ChoTreatment of facial acne papules and pustules in Korean patients using an intense pulsed light device equipped with a 530- to 750-nm filter. 2007. Dermatologic Surgery | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Chantalat, J., Liu, J. C. Six-week safety and efficacy evaluation of a synergistic microgel complex versus 10% benzoyl peroxide in the treatment of mild to moderate acne. Abstract P101. American Academy of Dermatology 64th Annual Meeting March 3-7, 2006. 2006. NA | No relevant article type - conference abstract |
| Charoenvisal, C. T., Y. Effects on acne of two oral contraceptives containing desogestrel and cyproterone acetate. 1996. International Journal of Fertility and Menopausal Studies | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Chi, C. I. Effects of Salvia miltiorrhiza extract on the improvement and prognosis of acne vulgaris. 2016. Http://www.who.int/trialsearch/trial2.aspx? Trialid=chictr-iir-16010104 | No relevant intervention - Salvia miltiorrhiza extract |
| Chiou, W. L. Low intrinsic drug activity and dominant vehicle (placebo) effect in the topical treatment of acne vulgaris. 2012. International Journal of Clinical Pharmacology and Therapeutics | No relevant study design - not RCT |
| Chlebus, E., Serafin, M., Chlebus, M. Is maintenance treatment in adult acne important? Benefits from maintenance therapy with adapalene, and low doses of alpha and beta hydroxy acids. 2019. Journal of Dermatological Treatment | No relevant study design - the randomized comparison is of skin care regimen rather than maintenance treatment (adapalene in both groups) |
| Cho, S. B. L., J. H.,Choi, M. J.,Lee, K. Y.,Oh, S. H.Efficacy of the fractional photothermolysis system with dynamic operating mode on acne scars and enlarged facial pores. 2009. Dermatologic Surgery | Duplicate record |
| Choudhury, S. C., S.,Sarkar, D. K.,Dutta, R. N.Efficacy and safety of | No relevant intervention - |

| Reference | Reason for exclusion |
|---|---|
| topical nadifloxacin and benzoyl peroxide versus clindamycin and benzoyl peroxide in acne vulgaris: A randomized controlled trial. 2011. Indian Journal of Pharmacology | intervention & class not available in the UK |
| Christian, G. L. K., G. G. Clindamycin vs placebo as adjunctive therapy in moderately severe acne. 1975. Archives of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Christiansen, J. H., P.,Reymann, F.The retinoic acid derivative Ro 11 1430 in Acne vulgaris. A controlled multicenter trial against retinoic acid. 1977. Dermatologica | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Christiansen, J. H., P.,Reymann, F.Treatment of acne vulgaris with the retinoic acid derivative Ro 11-1430. A controlled clinical trial against retinoic acid. 1976. Dermatologica | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Christiansen, J. V. G., E.,Ludvigsen, K.,Konstman Meier, C. H.,Norholm, A.,Osmundsen, P. E.,Pedersen, D.,Rasmussen, K. A.,Reiter, H.,Reymann, F.,et al.,Topical vitamin A acid (Airol) and systemic oxytetracycline in the treatment of acne vulgaris. A controlled clinical trial. 1974a. Dermatologica | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Christiansen, J. V. G., E.,Ludvigsen, K.,Meier, C. H.,Norholm, A.,Pedersen, D.,Rasmussen, K. A.,Reiter, H.,Reymann, F.,Sylvest, B.,et al.,Topical tretinoin, vitamin A acid (Airol) in acne vulgaris. A controlled clinical trial. 1974b. Dermatologica | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Chu, A. H., 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. 1997. British Journal of Dermatology | No relevant study population - sample includes people with too narrow range of acne severity criteria and study is not relevant for PCOS, maintenance or refractory treatments |
| Chularojanamontri, L. T., P.,Kulthanan, K.,Varothai, S.,Winayanuwattikun, W.A double-blinded, randomized, vehicle-controlled study to access skin tolerability and efficacy of an anti-inflammatory moisturizer in treatment of acne with 0.1% adapalene gel. 2016. Journal of Dermatological Treatment | No relevant intervention - Adaplene with or without Eucerin mositurizer |
| Clucas, A. V., M.,Sorba, V.,Poncet, M.,Baker, M.,Czernielewski, J.Adapalene 0.1% gel is better tolerated than tretinoin 0.025% gel in acne patients. 1997. Journal of the American Academy of Dermatology | Duplicate publication from Cunliffe 1997 trial |
| Cochran, R. J. T., S. B.,Flannigan, S. A.Topical zinc therapy for acne vulgaris. 1985. International Journal of Dermatology | No relevant study design - not RCT |

| Reference | Reason for exclusion |
|---|---|
| Colver, G. B. M., P. S.,Dawber, R. P.Cyproterone acetate and two doses of oestrogen in female acne; a double-blind comparison. 1988. British Journal of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Coman, G. C. H., A. C.,Mazloom, S. E.,Chavan, R. N.,Kolodney, M. S.A randomized, split-face, controlled, double-blind, single-centre clinical study: transient addition of a topical corticosteroid to a topical retinoid in patients with acne to reduce initial irritation. 2017. British Journal of Dermatology | No relevant article type - letter to editor |
| Cook-Bolden, F. E. Efficacy and tolerability of a fixed combination of clindamycin phosphate (1.2%) and benzoyl peroxide (3.75%) aqueous gel in moderate or severe adolescent acne vulgaris. 2015. Journal of Clinical and Aesthetic Dermatology | No relevant data reported - post hoc age analysis of Pariser 2014 |
| Cook-Bolden, F. E. Treatment of moderate to severe acne vulgaris in a Hispanic population: A post-hoc analysis of efficacy and tolerability of clindamycin phosphate 1.2%/benzoyl peroxide 2.5% gel. 2012. Journal of Drugs in Dermatology | No relevant data reported - post hoc subgroup analysis by ethnicity of Thiboutot 2008 |
| Cook-Bolden, F. E. W., S. H.,Guenin, E.,Bhatt, V.Novel Tretinoin 0.05% Lotion for Once-Daily Treatment of Moderate-to-Severe Acne Vulgaris in a Hispanic Population. 2019. Journal of drugs in dermatology : JDD | No relevant data reported - post hoc subgroup analysis of Hispanic participants in Tyring 2018 |
| Cook-Bolden, F. E., Gold, M. H., Guenin, E. Tazarotene 0.045% Lotion for the Once-Daily Treatment of Moderate-to-Severe Acne Vulgaris in Adult Males. 2020. Journal of drugs in dermatology : JDD | Not obtainable |
| Corlin, R. M., B.,Mack, H. A. Oral administration of low doses of 13-cis-retinoic acid in acne papulopustulosa. Results of a multicenter study. 1984. Der hautarzt; zeitschrift fur dermatologie, venerologie, und verwandte gebiete | Not in English language |
| Cotterill, J. A.Benzoyl peroxide. 1980. Acta Dermato-Venereologica. Supplementum | Duplicate record |
| Coughlin, C. C. S., S. M.,Horwinski, J.,Sfyroera, G.,Bugayev, J.,Grice, E. A.,Yan, A. C.The preadolescent acne microbiome: A prospective, randomized, pilot study investigating characterization and effects of acne therapy. 2017. Pediatric Dermatology | No relevant data reported - microbiome study |
| Cremoncini, C. V., E.,Libroia, A. Treatment of hirsutism and acne in women with two combinations of cyproterone acetate and ethinylestradiol. 1976. Acta Europaea Fertilitatis | No relevant study design - not RCT |
| Cullberg, G. H., L.,Mattsson, L. A.,Mobacken, H.,Samsioe, G. Effects of a low-dose desogestrel-ethinylestradiol combination on hirsutism, androgens and sex hormone binding globulin in women with a polycystic ovary syndrome. 1985. Acta Obstetricia et Gynecologica Scandinavica | No relevant study population – study focuses on women with PCOS and hirsuitism rather than acne and study is not relevant for other evidence reviews |
| Cunliffe, W. J. B., B.,Dodman, B.,Gould, D. J.A double-blind trial of a zinc sulphate/citrate complex and tetracycline in the treatment of acne vulgaris. 1979. British Journal of Dermatology | No relevant study population - insufficient information reported about acne severity and study is not relevant for PCOS, maintenance or refractory treatments |
| Cunliffe, W. J. C., J. A. Clindamycin as an alternative to tetracycline in severe acne vulgaris. 1973. Practitioner | No relevant study design - not RCT |
| Cunliffe, W. J. C., J. A.,Williamson, B. The effect of a medicated wash | No relevant article type - |

| Reference | Reason for exclusion |
|---|---|
| on acne, sebum excretion rate and skin surface lipid composition. 1972. British Journal of Dermatology | letter to editor |
| Cunliffe, W. J. C., R.,Dreno, B.,Forstrom, L.,Heenen, M.,Orfanos, C. E.,Privat, Y.,Aguilar, A. R.,Meynadier, J.,Alirezai, M.,Jablonska, S.,Shalita, A.,Weiss, J. S.,Chalker, D. K.,Ellis, C. N.,Greenspan, A.,Katz, H. I.,Kantor, I.,Millikan, L. E.,Swinehart, J. M.,Swinyer, L.,Whitmore, C.,Czernielewski, J.,Verschoore, M.Clinical efficacy and safety comparison of adapalene gel and tretinoin gel in the treatment of acne vulgaris: Europe and U.S. multicenter trials. 1997a. Journal of the American Academy of Dermatology | No relevant study design - combined publication of Cunliffe 1997 & US trial |
| Cunliffe, W. J. C., R.,Dreno, B.,Forstrom, L.,Heenen, M.,Orfanos, C. E.,Privat, Y.,Robledo Aguilar, A.,Poncet, M.,Verschoore, M.Efficacy and safety comparison of adapalene (CD271) gel and tretinoin gel in the topical treatment of acne vulgaris. A European multicentre trial. 1997b. Journal of Dermatological Treatment | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Cunliffe, W. J. D., F. W.,Dunlap, F.,Gold, M. H.,Gratton, D.,Greenspan, A.Randomised, controlled trial of the efficacy and safety of adapalene gel 0.1% and tretinoin cream 0.05% in patients with acne vulgaris. 2002. European Journal of Dermatology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Cunliffe, W. J. F., R. A.,Greenwood, N. D.,Hetherington, C.,Holland, K. T.,Holmes, R. L.,Khan, S.,Roberts, C. D.,Williams, M.,Williamson, B.Tetracycline and acne vulgaris: a clinical and laboratory investigation. 1973. British Medical Journal | No relevant study population - insufficient details about acne severity reported and study is not relevant for PCOS, maintenance or refractory treatments |
| Cunliffe, W. J. G., D.,Goode, K.,Stables, G. I.,Boorman, G. C.A double-blind investigation of the potential systemic absorption of isotretinoin, when combined with chemical sunscreens, following topical application to patients with widespread acne of the face and trunk. 2001. Acta Dermato-Venereologica | No relevant data reported - pharmokinetic study |
| Cunliffe, W. J. G., E.,Belaich, S.,Meynadier, J.,Alirezai, M.,Thomas, L.A comparison of the efficacy and safety of lymecycline and minocycline in patients with moderately severe acne vulgaris. 1998. European Journal of Dermatology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Cunliffe, W. J. H., K. T.Clinical and laboratory studies on treatment with 20% azelaic acid cream for acne. 1989. Acta Dermato-Venereologica, Supplement | No relevant study design - not RCT |
| Cunliffe, W. J. S., C.,Forster, R. A. Topical benzoyl peroxide increases the sebum excretion rate in patients with acne. 1983. British Journal of | No relevant data reported - pharmokinetic study |

| Reference | Reason for exclusion |
|---|---|
| Dermatology | |
| Cunliffe, W. J.A new topical retinoid--why a new topical acne therapy?. 1998. British Journal of Dermatology | No relevant article type - commentary |
| Dainichi, T. K., A.,Ueda, S.,Tajiri, R.,Fumimori, T.,Kakuma, T.,Hashimoto, T.Skin tightening effect using fractional laser treatment: I. A randomized half-side pilot study on faces of patients with acne. 2010. Dermatologic Surgery | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Damkerngsuntorn, W., Rerknimitr, P., Panchaprateep, R., Tangkijngamvong, N., Kumtornrut, C., Kerr, S. J., Asawanonda, P., Tantisira, M. H., Khemawoot, P. The Effects of a Standardized Extract of Centella asiatica on Postlaser Resurfacing Wound Healing on the Face: A Split-Face, Double-Blind, Randomized, Placebo-Controlled Trial. 2020. Journal of Alternative & Complementary MedicineJ Altern Complement Med | No relevant intervention - laser with extract of Centella asiatica |
| Danto, J. L. M., W. S.,Stewart, W. D.,Nelson, A. J.A controlled trial of benzoyl peroxide and precipitated sulfur cream in acne vulgaris. 1966. Applied Therapeutics | No relevantstudy population - insufficient information to determine acne severity and study is not relevant for PCOS, maintenance or refractory treatments |
| Darley, C. R. M., J. W.,Besser, G. M.,Munro, D. D.,Kirby, J. D.Low dose prednisolone or oestrogen in the treatment of women with late onset or persistent acne vulgaris. 1983. British Journal of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Darne, S. H., E. L.,Seukeran, D. C.Evaluation of the clinical efficacy of the 1450 nm laser in acne vulgaris: A randomized split-face, investigator-blinded clinical trial. 2011. British Journal of Dermatology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Darne, S. H., E.,Seukeran, D. C.Treatment of inflammatory acne with a 1450-nm smoothbeam diode laser: A split-face randomized single-blinded controlled trial. 2009. British Journal of Dermatology | No relevant article type - conference abstract |
| Dayal, S., Kalra, K. D., Sahu, P. Comparative study of efficacy and safety of 45% mandelic acid versus 30% salicylic acid peels in mild-to-moderate acne vulgaris. 2019. Journal of Cosmetic DermatologyJ | Duplicate of Dayal 2020 first published online 2019 |
| de Arruda, L. H. K., V.,Bastos Filho, A.,Mazzaro, C. B.A prospective, randomized, open and comparative study to evaluate the safety and efficacy of blue light treatment versus a topical benzoyl peroxide 5% formulation in patients with acne grade II and III. 2009. Anais brasileiros de dermatologia | Not in English language |
| De Leeuw, J. V. D. B., N.,Bjerring, P.,Martino Neumann, H. A. Photodynamic therapy of acne vulgaris using 5-aminolevulinic acid 0.5% liposomal spray and intense pulsed light in combination with topical keratolytic agents. 2010. Journal of the European Academy of Dermatology and Venereology | No relevant data reported - article reports that study is RCT but does not report comparative data |

| Reference | Reason for exclusion |
|---|---|
| Degreef, H. V. B., G. Double-blind evaluation of a miconazole - benzoyl peroxide combination for the topical treatment of acne vulgaris. 1982a. Dermatologica | Duplicate record |
| Del Rosso JQ, Kircik L, Gallagher CJ.Comparative efficacy and tolerability of dapsone 5% gel in adult versus adolescent females with acne vulgaris. https://www.ncbi.nlm.nih.gov/pubmed/25610522 | Posthoc analysis of Draelos 2007 |
| Del Rosso, J. Q. Clindamycin phosphate 1.2%/tretinoin 0.025% gel for the treatment of acne vulgaris: Which patients are most likely to benefit the most?. 2015. Journal of Clinical and Aesthetic Dermatology | Duplicate record |
| Del Rosso, J. Q. K., L.,Gallagher, C. J.Comparative efficacy and tolerability of dapsone 5% gel in adult versus adolescent females with acne vulgaris. 2015. Journal of Clinical and Aesthetic Dermatology | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Del Rosso, J. Q. Study results of benzoyl peroxide 5%/clindamycin 1% topical gel, adapalene 0.1% gel, and use in combination for acne vulgaris. 2007. Journal of drugs in dermatology : JDD | No relevant study population - no details of inclusion criteria reported and study is not relevant for PCOS, maintenance or refractory treatments |
| Del Rosso, J. Q. The use of topical azelaic acid for common skin disorders other than inflammatory rosacea. 2006. Cutis | Duplicate record |
| Deshmukh, S. N. B., V. A.,Mahajan, M. M.,Sujata Dudhgaonkar, D.,Mishra, D.Comparison of efficacy and safety of topical 1% nadifloxacin and tretinoin 0.025% combination therapy with 1% clindamycin and tretinoin 0.025% combination therapy in patients of mild-to-moderate acne. 2018. Perspectives in Clinical Research | No relevant intervention - intervention & class not available in the UK |
| DeVillez, R. L.Clinical comparison of the safety and efficacy of Brevoxyl gel and Benzamycin gel. 1992. Drug Investigation | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Dhawan, S. S. Comparison of 2 clindamycin 1%-benzoyl peroxide 5% topical gels used once daily in the management of acne vulgaris. 2009. Cutis; cutaneous medicine for the practitioner | No relevant comparison - clindamycin/BPO topical gel with the hydrating excipients dimethicone and glycerin vs without hydrating excipients |
| Dieben Th, O. M. V., L.,Theeuwes, A.,Coelingh Bennink, H. J. T.The effects of CTR-24, a biphasic oral contraceptive combination, compared to Diane-35 in women with acne. 1994. Contraception | No relevant study population - insufficient details about types of lesions to determine severity of participants |
| Divers, L. S.A new preparation for the topical treatment of acne vulgaris. Report of a year's study. 1966. Journal of the College of General Practitioners | No relevant study design - not RCT |
| Do Nascimento, L. V. G., A. C. M.,Magalhaes, G. M.,De Faria, F. | No relevant study |

| Reference | Reason for exclusion |
|---|---|
| A.,Guerra, R. M.,Almeida, F. D. C.Single-blind and comparative clinical study of the efficacy and safety of benzoyl peroxide 4% gel (BID) and adapalene 0.1% Gel (QD) in the treatment of acne vulgaris for 11 weeks. 2003. Journal of Dermatological Treatment | population - sample includes people with mild to severe acne |
| Dogra, A. S., V. K.,Minocha, Y. C.Comparative evaluation of retinoic acid, benzoyl peroxide and erythromycin lotion in acne vulgaris. 1993. Indian journal of dermatology, venerology and leprology | No relevant study population - sample includes people with mild to severe acne |
| Dominguez, J. H., M. T.,Celayo, J. L.,Dominguez-Soto, L.,Teixeira, F.Topical isotretinoin vs. topical retinoic acid in the treatment of acne vulgaris. 1998. International Journal of Dermatology | No relevant data - insufficient data reported |
| Donadini, A.Is topical antibiotic therapy associated with the same oral treatment useful in patients with acne?. 1989. Ann ital dermatol clin sper | Not in English language and also no relevant study design - not RCT |
| Dosik, J. E., H.,Stuart, I.Topical minocycline foam 4%: Results of four phase 1 studies evaluating the potential for phototoxicity, photoallergy, sensitization, and cumulative irritation. 2019. Journal of immunotoxicology | No relevant study population - participants did not have acne |
| Dosik, J. S. G., R. D.,Arsonnaud, S.Cumulative irritancy comparison of topical retinoid and antimicrobial combination therapies. 2006. Skinmed | No relevant study population - participants did not have acne |
| Dosik, J. S. H., K.,Arsonnaud, S.Cumulative irritation potential of adapalene 0.1% cream and gel compared with tazarotene cream 0.05% and 0.1%. 2005b. Cutis | No relevant study population - participants did not have acne |
| Dosik, J. S. H., K.,Arsonnaud, S.Cumulative irritation potential of adapalene 0.1% cream and gel compared with tretinoin microsphere 0.04% and 0.1%. 2005a. Cutis | No relevant study population - participants did not have acne |
| Draelos, Z. D. Assessing the value of botanical anti-inflammatory agents in an OTC acne treatment regimen. 2015. Journal of Drugs in Dermatology | No relevant comparison/intervention - compares over-the-counter skin care regimens with/without added botanicals |
| Draelos, Z. D. C., E.,Maloney, J. M.,Elewski, B.,Poulin, Y.,Lynde, C.,Garrett, S.Two randomized studies demonstrate the efficacy and safety of dapsone gel, 5% for the treatment of acne vulgaris. 2007. Journal of the American Academy of Dermatology | No relevant data reported - reports pooled results from 2 trials combined |
| Draelos, Z. D. C., V.,Young, C.,Dhawan, S. S.The effect of vehicle formulation on acne medication tolerability. 2008. Cutis | No relevant outcomes reported |
| Draelos, Z. D. E., K.,Rom, D.Five-day study to judge the short-term effect of a benzoyl peroxide 3% gel on acne lesions. 2016. Journal of cosmetic dermatology | No relevant outcomes reported |
| Draelos, Z. D. M., A.,Smiles, K.The effect of 2% niacinamide on facial sebum production. 2006. Journal of Cosmetic and Laser Therapy | No relevant study population - participants did not have acne |
| Draelos, Z. D. P., A.,Alio Saenz, A. B.Randomized tolerability analysis of clindamycin phosphate 1.2%-tretinoin 0.025% gel used with benzoyl peroxide wash 4% for acne vulgaris. 2010. Cutis | No relevant intervention - queous-based gel (clindamycin phosphate 1.2%-tretinoin 0.025%) when used in conjunction with a BPO wash 4% |
| Draelos, Z. D. R., D. A.,Kempers, S. E.,Bruce, S.,Peredo, M. I.,Downie, J.,Chang-Lin, J. E.,Berk, D. R.,Ruan, S.,Kaoukhov, A.Treatment response with once-daily topical dapsone gel, 7.5% for acne vulgaris: Subgroup analysis of pooled data from two randomized, double-blind stu. 2017. Journal of Drugs in Dermatology | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to- |

| Reference | Reason for exclusion |
|---|---|
| | severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Draelos, Z. D. S., A. R.,Thiboutot, D.,Oresajo, C.,Yatskayer, M.,Raab, S.A multicenter, double-blind study to evaluate the efficacy and safety of 2 treatments in participants with mild to moderate acne vulgaris. 2012. Cutis; cutaneous medicine for the practitioner | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Drake, L. Comparative efficacy and tolerance of Cleocin T topical gel (clindamycin phosphate topical gel) versus oral minocycline in the treatment of acne vulgaris. 1990. Data on file (technical report from pharmacia and upjohn ltd) | No relevant article type - not published in peer reviewed journal |
| Dreno, B. B., V.,Ochsendorf, F.,Layton, A. M.,Perez, M.,Dakovic, R.,Gollnick, H.Efficacy and safety of clindamycin phosphate 1.2%/tretinoin 0.025% formulation for the treatment of acne vulgaris: Pooled analysis of data from three randomised, double-blind, parallel-group, phase III studies. 2014. European Journal of Dermatology | No relevant data reported - pooled analysis of 3 studies combined, 2 of which include people with mild to severe acne. Data for third study reported in Schleslinger 2009 |
| Dreno, B. M., D.,Alirezai, M.,Amblard, P.,Auffret, N.,Beylot, C.,Bodokh, I.,Chivot, M.,Daniel, F.,Humbert, P.,Meynadier, J.,Poli, F.Multicenter randomized comparative double-blind controlled clinical trial of the safety and efficacy of zinc gluconate versus minocycline hydrochloride in the treatment of inflammatory acne vulgaris. 2001. Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Dreno, B. T., J.,Rivier, M.,Martel, P.,Bissonnette, R.Adapalene 0.1%/benzoyl peroxide 2.5% gel reduces the risk of atrophic scar formation in moderate inflammatory acne: a split-face randomized controlled trial. 2016. Journal of the european academy of dermatology and venereology : JEADV | Duplicate record |
| Dreno, B. T., J.,Rivier, M.,Martel, P.,Bissonnette, R.Adapalene 0.1%/benzoyl peroxide 2.5% gel reduces the risk of atrophic scar formation in moderate inflammatory acne: a split-face randomized controlled trial. 2017. Journal of the European Academy of Dermatology and Venereology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Dudhia, S. S., R. B.,Agrawal, P.,Shah, A.,Date, S.Efficacy and safety of clindamycin gel plus either benzoyl peroxide gel or adapalene gel in the treatment of acne: a randomized open-label study. 2015. Drugs and Therapy Perspectives | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Dunlap, F. E. B., M. D.,Plott, R. T.,Verschoore, M.Adapalene 0.1% gel | No relevant comparison - |

| Reference | Reason for exclusion |
|---|---|
| has low skin irritation potential even when applied immediately after washing. 1998a. British Journal of Dermatology, Supplement | compares adapalene 0.1% gel application immediately after washing to a delayed application |
| Dunlop, K. J. B., R. S.A comparative study of isolutrol versus benzoyl peroxide in the treatment of acne. 1995. The Australasian journal of dermatology | No relevant intervention - Isolutrol |
| Eady, E. A. B., B. M.,Pulling, K.,Cunliffe, W. J.The benefit of 2% salicylic acid lotion in acne - A placebo-controlled study. 1996a. Journal of dermatological treatment | No relevant data reported - for example, not possible to extract the number of participants in each treatment group |
| Eady, E. A. B., R. A.,Jones, C. E.,Cove, J. H.,Holland, K. T.,Cunliffe, W. J.The effects of acne treatment with a combination of benzoyl peroxide and erythromycin on skin carriage of erythromycin-resistant propionibacteria. 1996b. British Journal of Dermatology | No relevant outcomes reported |
| Eady, E. A. B., R. A.,Jones, C. E.,Cove, K. T.,Cunliffe, W. J.The effects of acne therapy with a combination of benzoyl peroxide and erythromycin on carriage of eryhtromycin resistant cutaneous propionobacteria. 1994. British journal of dermatology | No relevant article type - conference abstract |
| Ede, M.A double blind, comparative study of benzoyl peroxide, benzoyl peroxide chlorhydroxyquinoline, benzoyl peroxide chlorhydroxyquinoline hydrocortisone, and placebo lotions in acne. 1973. Current Therapeutic Research - Clinical and Experimental | No relevant intervention |
| Egan, N. L., M. C.,Baker, M. M.Randomized, controlled, bilateral (split-face) comparison trial of the tolerability and patient preference of adapalene gel 0.1% and tretinoin microsphere gel 0.1% for the treatment of acne vulgaris. 2001. Cutis; cutaneous medicine for the practitioner | No relevant study population - sample includes people with mild, moderate and severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Eichenfield, L. E. J., J. L.,Dirschka, T.,Taub, A. F.,Lynde, C.,Graeber, M.,Kerrouche, N.Treatment of 2,453 acne vulgaris patients aged 12-17 years with the fixed-dose adapalene-benzoyl peroxide combination topical gel: efficacy and safety. 2010a. Journal of Drugs in Dermatology: JDD | Subgroup analysis of Stein Gold 2016 |
| Eichenfield, L. F. A. S., A. B.Safety and efficacy of clindamycin phosphate 1.2%-benzoyl peroxide 3% fixed-dose combination gel for the treatment of acne vulgaris: a phase 3, multicenter, randomized, double-blind, active- and vehicle-controlled study. 2011. Journal of Drugs in Dermatology: JDD | No relevant study population - sample includes people with mild to severe acne acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Eichenfield, L. F. D., Z.,Lucky, A. W.,Herbert, A. A.,Sugarman, J.,Gold, S.,Rudisill, D.Treatment of acne in children 9-11 with a fixed dose combination. 2013b. Pediatric Dermatology | No relevant article type - conference abstract |
| Eichenfield, L. F. H., A. A.,Schachner, L.,Paller, A. S.,Rossi, A. B.,Lucky, A. W.Tretinoin microsphere gel 0.04% pump for treating acne vulgaris in preadolescents: A randomized, controlled study. 2012a. Pediatric Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Eichenfield, L. F. K., A. C.Moderate to severe acne in adolescents with skin of color: Benefits of a fixed combination clindamycin phosphate 1.2% and benzoyl peroxide 2.5% aqueous gel. 2012b. | No relevant data reported - subgroup analysis of Thiboutot 2008 |

| Reference | Reason for exclusion |
|---|---|
| Journal of Drugs in Dermatology | |
| Eichenfield, L. F. S., 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. 2019. Pediatric Dermatology | No relevant data reported - post hock analysis of Tyring 2018 |
| Eichenfield, L. F. T., D.,Shalita, A.,Swinyert, L.,Tanghetti, E.,Tschen, E.,Parr, L.A three-step acne system containing solubilized benzoyl peroxide versus benzoyl peroxide/clindamycin in pediatric patients with acne. 2009a. Journal of clinical and aesthetic dermatology | No relevant data reported - subgroup analysis of Thiboutout 2009 |
| Eichenfield, L. F. W., M.A novel gel formulation of 0.25% tretinoin and 1.2% clindamycin phosphate: Efficacy in acne vulgaris patients aged 12 to 18 years. 2009b. Pediatric Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Eichenfield, L. F., Sugarman, J. L., Guenin, E., Bhatt, V. Novel tretinoin 0.05% lotion for the once-daily treatment of moderate-to-severe acne vulgaris in a preadolescent population. 2019. Journal of Clinical and Aesthetic Dermatology | No relevant article type - conference abstract |
| El Aziz Ragab, M. A. O., S. S.,Collier, A.,El-Wafa, Raha,Gomaa, N.The effect of continuous high versus low dose oral isotretinoin regimens on dermcidin expression in patients with moderate to severe acne vulgaris. 2018. Dermatologic Therapy | No relevant article type - letter to editor |
| Elbaum, D. J.Comparison of the stability of topical isotretinoin and topical tretinoin and their efficacy in acne. 1988. Journal of the American Academy of Dermatology | No relevant study population - insuficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| El-Fakahany, H. M., W.,Abdallah, F.,Abdel-Raouf, H.,Abdelhakeem, M.Fractional microneedling: A novel method for enhancement of topical anesthesia before skin aesthetic procedures. 2016. Dermatologic Surgery | No relevant intervention - skin microneedling for treatment of atrophic scars |
| El-Latif, A. A. H., F. A.,Elshahed, A. R.,Mohamed, A. G.,Elsaie, M. L.Intense pulsed light versus benzoyl peroxide 5% gel in treatment of acne vulgaris. 2014. Lasers in Medical Science | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Ellis, C. N. G., W. R.,Stone, D. Z.,Heezen-Wehner, J. L.A comparison of cleocin T solution cleocin T gel, and placebo in the treatment of acne vulgaris. 1988. Cutis | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Ellis, C. N. L., J.,Katz, H. I.,Goldfarb, M. T.,Hickman, J.,Jones, T. M.,Tschen, E.Therapeutic studies with a new combination benzoyl peroxide/clindamycin topical gel in acne vulgaris. 2001b. Cutis | No relevant data - reports 3 trials but full article is not available; no information about number of participants assigned to each group in trials reported |
| Ellis, C. N. L., J.,Katz, H. I.,Goldfarb, M. T.,Hickman, J.,Jones, T. M.Therapeutic studies with a new combination benzoyl | Duplicate record |

| Reference | Reason for exclusion |
|---|---|
| peroxide/clindamycin topical gel in acne vulgaris.(erratum appears in Cutis 2001 Mar;67(3): 257). 2001a. Cutis; cutaneous medicine for the practitioner | |
| Ellis, C. N. M., L. E.,Smith, E. B.,Chalker, D. M.,Swinyer, L. J.,Katz, I. H.,Berger, R. S.,Mills, O. H.,Baker, M.,Verschoore, M.,et al.,Comparison of adapalene 0.1% solution and tretinoin 0.025% gel in the topical treatment of acne vulgaris. 1998. British journal of dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Elman, M. S., M.,Harth, Y.The effective treatment of acne vulgaris by a high-intensity, narrow band 405-420 nm light source. 2003. Journal of Cosmetic and Laser Therapy | No relevant data - reoprts data from 3 trials. No relevant population - sample includes people with mild to severe acne in first 2 trials, and insufficient details about types of lesions to determine severity of participants in one trial and study is not relevant for PCOS, maintenance or refractory treatments |
| ElRefaei, A. M. A. S., H. A.,Sorour, N. E.Salicylic-mandelic acid versus glycolic acid peels in Egyptian patients with acne vulgaris. 2015. Journal of the egyptian women's dermatologic society | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Enshaieh,The efficacy of 5% topical tea tree oil gel in mild to moderate acne vulgaris: a randomized, double-blind placebo-controlled study. 2007. NA | No relevant intervention - tea tree oil gel |
| Ereaux, L. P.A new lotion for the treatment of acne vulgaris. 1965. Canadian Medical Association journal | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Ergin, S. E., C.,Baysal, V.,Yayli, G.An acne study focused on erythromycin: Benzoyl peroxide alone or with topical erythromycin against Propionibacterium acnes in acne vulgaris. 2001. Gazi Medical Journal | Outcomes reported in figures only |
| Erkkola, R. H., E.,Luikku, J.,Lumme, R.,Mannikko, H.,Aydinlik, S.Ovulation inhibitors containing cyproterone acetate or desogestrel in the treatment of hyperandrogenic symptoms. 1990. Acta Obstetricia et Gynecologica Scandinavica | No relevant study population - participants did not have acne |
| Ernst, E., Huntley, A. Tea tree oil: a systematic review of randomized clinical trials. 2000. Forsch Komplementarmed Klass Naturheilkd | No relevtan intervention - systematic review about tea tree oil for various dermatological conditions |
| Ersoy, L. K., A.,Kilic, I.,Koc, K.,Sen, S.Topical spironolactone in acne vulgaris. 1996. Nouvelles dermatologiques | Not in English language |
| Euctr, C. Z. Assessment of efficacy and safety of a new gel with 10 | No relevant study design - |

| Reference | Reason for exclusion |
|---|---|
| mg/g clindamycin and 30 mg/g benzoyl peroxide in comparison with the approved preparation DUACÃ‚Â® 10 mg/g + 30 mg/g Gel and the underlying vehicle in patients with mild to moderate acne. 2018. http://www.who.int/trialsearch/Trial2.aspx?TrialID=EUCTR2017-000521-13-CZ | not RCT |
| Euctr, F. R. Randomized double-blind study on the benefit of spironolactone for treating acne of adult woman. 2017. http://www.who.int/trialsearch/Trial2.aspx?TrialID=EUCTR2017-001392-22-FR | No relevant study design - not RCT |
| Exner, J. H. C., H.,Dahod, S.,Pochi, P. E.Topical erythromycin/zinc effect on acne and sebum secretion. 1983. Current Therapeutic Research - Clinical and Experimental | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Fabbrocini, G. I., R.,Faggiano, A.,Del Prete, M.,Donnarumma, M.,Marasca, C.,Marciello, F.,Savastano, R.,Monfrecola, G.,Colao, A.Low glycaemic diet and metformin therapy: A new approach in male subjects with acne resistant to common treatments. 2016. Clinical and Experimental Dermatology | No relevant intervention - metformin plus a hypocaloric diet |
| Fabbrocini, G. R., A. B.,Thouvenin, M. D.,Peraud, C.,Mengeaud, V.,Bacquey, A.,Saint Aroman, M.Fragility of epidermis: acne and post-procedure lesional skin. 2017. Journal of the European Academy of Dermatology and Venereology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Faghihi, G. J., K.,Tajmirriahi, N.,Abtahi-Naeini, B.,Nilforoshzadeh, M.,Radan, M.,Hosseini, S. M.The efficacy of oral isotretinoin versus cyproterone compound in female patients with acne and the triad of cutaneous hyperandrogenism: A randomized clinical trial. 2014. Advanced Biomedical Research | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Faghihi, G. K.-I., A.,Hosseini, S. M.,Radan, M. R.,Nilforoushzadeh, M. A. Efficacy of intense pulsed light combined with topical erythromycin solution 2% versus topical erythromycin solution 2% alone in the treatment of persistent facial erythematous acne macules. 2015. Journal of isfahan medical school | No relevant study design - not RCT |
| Faghihi, G. R., M.,Abtahi-Naeini, B.,Nilforoushzadeh, M. A.The efficacy of 5% dapsone gel plus oral isotretinoin versus oral isotretinoin alone in acne vulgaris: A randomized double-blind study. 2014. Advanced Biomedical Research | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Faghihi, G. V., A.,Asilian, A.,Radan, M. R.,Esteki, H.,Elahidoost, M.Comparative efficacy of filtered blue light (emitted from sunlight) | No relevant study design - not RCT (split face study |

| Reference | Reason for exclusion |
|---|---|
| and topical erythromycin solution in acne treatment: A randomized controlled clinical trial. 2011. Journal of Pakistan Association of Dermatologists | but same treatments always applied to left & right) |
| Faloia, E. F., S.,Mancini, V.,Morosini, P.,De Pirro, R.Treatment with a gonadotropin-releasing hormone agonist in acne or idiopathic hirsutism. 1993. Journal of Endocrinological Investigation | No relevant study design - not RCT |
| Falsetti, L. Acne treatment with a new estroprogestinic biphasic combination containing desogestrel. 1991. Acta Europaea Fertilitatis | Not obtainable |
| Fan, L. H., Xu, C. R.A randomised controlled trial of Bimaisen (Compound Erythromycin and Benzoyl Peroxide) versus metronidazole in the treatment of acne (Chinese). 1998. Journal of clinical dermatology | Not in English language |
| Fanta, D. S., N.Miconazole-benzoyl peroxide: a new combination for extending the topical therapy of acne. 1984. Zeitschrift fur hautkrankheiten | Not in English language |
| Farina, M. C., L.,Palumbo, M.,De Leo, V.,Morgante, G.,Cianci, A.Effectiveness of an oral contraceptive containing ethinyl-estradiol combined with drospirenone in the treatment of symptomatic hyperandrogenism. 2006. Italian journal of gynaecology and obstetrics | No relevant study popualtion - article reports 2 trials, both of which are in people with hyperandrogenism and study is not relevant for PCOS, maintenance or refractory treatments |
| Farrell, L. N. S., J. S.,Stranieri, A. M.The treatment of severe cystic acne with 13-cis-retinoic acid. Evaluation of sebum production and the clinical response in a multiple-dose trial. 1980. Journal of the American Academy of Dermatology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Fatemi, F. N., J.,Nasab, S. S.,Nilforoushzadeh, M. A. Treatment of acne vulgaris using the combination of topical erythromycin and Miconazole. 2014. Journal of Skin and Stem Cell | Insufficent detail in reporting - unclear how many participants received each treatment |
| Fatum, B. H., H. H. V.,Mortensen, E.Topical treatment of acne vulgaris with the vitamin A acid derivate motretinide (Tasmaderm), tretinoin (Airol) and a placebo cream. 1980. Ugeskrift for laeger | Not in English language |
| Feldman, S. R. T., J.,Poulin, Y.,Dirschka, T.,Kerrouche, N.,Manna, V.The efficacy of adapalene-benzoyl peroxide combination increases with number of acne lesions. 2011. Journal of the American Academy of Dermatology | No relevant data reported - meta-analysis of Thiboutot 2007, Gollnick 2009, and Stein Gold 2009 |
| Fenske, N. A. M., J. L. Cutaneous pigmentation due to minocycline hydrochloride. 1980. Journal of the American Academy of Dermatology | No relevant study design - not RCT |
| Ferahbas, A. U., S.,Aykol, D.,Borlu, M.,Uksal, U.Clinical Evaluation of Roxithromycin: A Double-Blind, Placebo-Controlled and Crossover Trial in Patients with Acne Vulgaris. 2004. Journal of Dermatology | No relevant study population - insufficient information reported about acne severity and study is not relevant for PCOS, maintenance or refractory treatments |
| Fernandez, J. R. R., K.,Voronkov, M.,Feng, X.,Stock, J. B.,Stock, M.,Gordon, J. S.,Shroot, B.,Christensen, M. S.,Perez, E.SIG1273: a | No relevant intervention - Disodium |

| Reference | Reason for exclusion |
|---|---|
| new cosmetic functional ingredient to reduce blemishes and Propionibacterium acnes in acne prone skin. 2012. Journal of Cosmetic Dermatology | Tetramethylhexadecenyl succinyl Cysteine |
| Feucht, C. L. A., B. S.,Chalker, D. K.,Smith, J. G., Jr.Topical erythromycin with zinc in acne. A double-blind controlled study. 1980. Journal of the American Academy of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Fisher, A. A.Erythromycin "free base" -a nonsensitizing topical antibiotic for infected dermatoses and acne vulgaris. 1977. Cutis | No relevant article type - non-systematic review |
| Fisk, W.A., Lev-Tov, H.A., Sivamani, R.K. Botanical and phytochemical therapy of acne: a systematic review. 2014. Phytother Res | No relevant intervention - systematic review about the use of botanical agents in the treatment of acne |
| Fleischer, A. B. S., A.,Eichenfield, L. F.,Abramovits, W.,Lucky, A.,Garrett, S.Dapsone gel 5% in combination with adapalene gel 0.1%, benzoyl peroxide gel 4% or moisturizer for the treatment of acne vulgaris: a 12-week, randomized, double-blind study. 2010. Journal of drugs in dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Fluhr, J. W. B., B.,Gloor, M.,Hoffler, U.In-vitro and in-vivo efficacy of zinc acetate against Propionibacteria alone and in combination with erythromycin. 1999. Zentralblatt fur Bakteriologie | No relevant study population - sample includes people with mild to severe acne |
| Fonseca, E. F., C.,Camarasa, J. G.,Olmos, L.,Del Pinos, J.,Rodriguez, T.,San Martin, J. C.,Roman, P.,Asin, M.,Sambricio, F.,et al.,Erythromycin lauryl sulphate in combination with tretinoin in the topical treatment of acne vulgaris. A multicentre double-blind clinical trial. 1995b. Journal of dermatological treatment | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Fonseca, E. F., C.,Camarasa, J. G.Erythromycin lauryl sulphate in combination with tretinoin in the topical treatment of acne vulgaris. A multicentrie double-blind clinical trial. 1995a. Indian journal of dermatology, venerology and leprology | Duplicate record |
| Forbat, E. A.-N., F.Nonvascular uses of pulsed dye laser in clinical dermatology. 2019. Journal of Cosmetic Dermatology. | Duplicate record |
| Francomano, M. G., 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. 2000. Giornale italiano di dermatologia e venereologia | Not in English language |
| Frank, S. B. Topical treatment of acne with a tetracycline preparations: results of a multi-group study. 1976. Cutis | No relevant study design - not RCT |
| Franz, E. R., B.,Weidner-Strahl, S.The effectiveness of topical antibacterials in acne: a double-blind clinical study. 1978. Journal of International Medical Research | Not obtainable |
| Fraser, N. B. M., R. A.,Stewart, T. W.,Thornton, E. J.Treatment of acne vulgaris comparing two similar lotion formulations, one with ('Actinac') and one without chloramphenicol. 1980. Current Medical Research & Opinion | No relevant comparison - Actinac with/without chloramphenicol |
| Fried, R. N., M.Acne quality of life and patient satisfaction following treatment with tretinoin pump. 2009. Journal of Drugs in Dermatology: JDD | No relevant study design - not RCT |

| Reference | Reason for exclusion |
|---|---|
| Fu, W. W., Fang, L., Gu, J., Shun, J. F. Clinical efficacy and safety of 5% benzoyl peroxide gel combined with 0.1% adapalene gel in the treatment of acne vulgaris: a multicenter, randomized study. 2003. Chinese journal of dermatology | Not in English language |
| Fulton, J. E., Jr.,Pablo, G.Topical antibacterial therapy for acne. Study of the family of erythromycins. 1974. Archives of Dermatology | No relevant data reported |
| Fyrand, O. J., H. B. Water-based versus alcohol-based benzoyl peroxide preparations in the treatment of acne vulgaris. 1986. Dermatologica | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Galvin, S. A. G., R.,Baker, M.,Guibal, F.,Tuley, M. R.Comparative tolerance of adapalene 0.1% gel and six different tretinoin formulations. 1998. British Journal of Dermatology, Supplement | No relevant study population - participants did not have acne |
| Gammon, W. R. M., C.,Lantis, S.Comparative efficacy of oral erythromycin versus oral tetracycline in the treatment of acne vulgaris. A double-blind study. 1986. Journal of the American Academy of Dermatology | Dosage of erythromycin lower than BNF value |
| Gandola, M. A., G.,Barba, C.,Bassi, R.,Binazzi, M.,Landi, G.,Levi, L.,Randazzo, D.,Serri, F.,Villano, A. P.Topical vitamin A acid in the treatment of acne vulgaris (a controlled multicenter trial). 1976. Archives for dermatological research = archiv fur dermatologische forschung | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Gans, E. H. K., A. M. Comparative efficacy of clindamycin and benzoyl peroxide for in vivo suppression of Propionibacterium acnes. 2002. Journal of Dermatological Treatment | No relevant data reported - pharmokinetic study |
| Garg, V. K. S., S.,Sarkar, R.Glycolic acid peels versus salicylic-mandelic acid peels in active acne vulgaris and post-acne scarring and hyperpigmentation: a comparative study. 2009. Dermatologic Surgery | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Geiger, J. M. H., L.,Harms, M.,Saurat, J. H.Oral 13-cis retinoic acid is superior to 9-cis retinoic acid in sebosuppression in human beings. 1996. Journal of the American Academy of Dermatology | No relevant study population - participants did not have acne |
| Genina, E. A. B., A. N.,Simonenko, G. V.,Odoevskaya, O. D.,Tuchin, V. V.,Altshuler, G. B.Low-intensity indocyanine-green laser phototherapy of acne vulgaris: pilot study. 2004. Journal of biomedical optics | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Ghovvati, M., Kord Afshari, G., Ahmad Nasrollahi, S., Firooz, A., Samadi, A., Karimi, M., Talebi, Z., Kolahdooz, S., Vazirian, M. Efficacy of topical cinnamon gel for the treatment of facial acne vulgaris: A preliminary study. 2019. Biomedical Research and Therapy | No relevant study design - not RCT |
| Gibson, J. R. D., C. R.,Harvey, S. G.,Barth, J.Oral trimethoprim versus oxytetracycline in the treatment of inflammatory acne vulgaris. 1982. British Journal of Dermatology | No relevant study population - insufficient information reported about acne severity and study is not relevant for PCOS, |

| Reference | Reason for exclusion |
|---|---|
| | maintenance or refractory treatments |
| Gibson, J. R.Azelaic acid 20% cream (AZELEX) and the medical management of acne vulgaris. 1997. Dermatology Nursing | No relevant article type - expert review |
| Gloor, M. H., A.,Friederich, H. C.Trial of benzoyl peroxide treatment of acne vulgaris. EXPERIMENTELLE UNTERSUCHUNGEN ZUR BENZOYLPEROXYDTHERAPIE DER ACNE VULGARIS. 1975. ZHAUTKR | Not in English language |
| Goforoushan, F. A., H.,Goldust, M.Efficacy of vitamin E to prevent dermal complications of isotretinoin. 2013. Pakistan Journal of Biological Sciences | No relevant comparison - compares efficacy of treatment to alleviate isotretinoin dermal complications |
| Goh, C. L. T., M. B.,Briantais, P.,Kaoukhov, A.,Soto, P.Adapalene gel 0.1% is better tolerated than tretinoin gel 0.025% among healthy volunteers of various ethnic origins. 2009. Journal of Dermatological Treatment | No relevant study population - participants did not have acne |
| Gold, L. S. B., H.,Rueda, M. J.,Kerrouche, N.,Dreno, B.Adapalene-benzoyl peroxide gel is efficacious and safe in adult female acne, with a profile comparable to that seen in teen-aged females. 2016. Journal of Clinical and Aesthetic Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Gold, L. S., Dhawan, S., Weiss, J., Draelos, Z. D., Ellman, H., Stuart, I.Open-label extension study evaluating long-term safety and efficacy of FMX101 4% minocycline foam for moderate-to-severe acne vulgaris. 2019. Journal of Clinical and Aesthetic Dermatology | No relevant data reported - reported reports results on open-label part of trial only |
| Gold, M. H. B., V. L.,Boring, M. M.,Bridges, T. M.,Biron, J. A.,Carter, L. N.The use of a novel intense pulsed light and heat source and ALA-PDT in the treatment of moderate to severe inflammatory acne vulgaris. 2004. Journal of Drugs in Dermatology: JDD | No relevant study design - not RCT |
| Gold, M. H. R., J.,Goldman, M. P.,Bridges, T. M.,Bradshaw, V. L.,Boring, M. M.,Guider, A. N.A multicenter clinical evaluation of the treatment of mild to moderate inflammatory acne vulgaris of the face with visible blue light in comparison to topical 1% clindamycin antibiotic solution. 2005. Journal of drugs in dermatology : JDD | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Gold, M. H. S., N. S.,Bradshaw, V. L.,Boring, M. M.A randomized, controlled, double-blind study of localized low-heat treatment of acne lesions. 2007. Cosmetic Dermatology | No relevant data reported - response study |
| Gold, M. H. S., W.,Biron, J. A.Clinical efficacy of home-use blue-light therapy for mild-to moderate acne. 2011. Journal of Cosmetic and Laser Therapy | No relevant intervention - only 2 individual lesions treated per patient |
| Gold, M. H., Korotkor., A.Sub-group analyses from a trial of a fixed combination of clindamycin phosphate 1.2% and benzoyl peroxide 3.75% gel for the treatment of moderate-to-severe acne vulgaris. 2015. Journal of Clinical and Aesthetic Dermatology | No relevant article type - non-systematic review |
| Gold, M. R. M., A. P.A randomised, double-blind, multicentre, multinational comparison of 2% fusidic acid lotion and 1% clindamycin lotion in patients with acne vulgaris on the face. 1996. European journal of clinical research | Not obtainable |

| Reference | Reason for exclusion |
|---|---|
| Goldman, M. P. B., S. M.A single-center study of aminolevulinic acid and 417 NM photodynamic therapy in the treatment of moderate to severe acne vulgaris. 2003. Journal of Drugs in Dermatology: JDD | No relevant study design - not RCT |
| Goldstein, J. A. S.-S., A.,Thomsen, R. J.,Pochi, P. E.,Shalita, A. R.,Strauss, J. S.Comparative effect of isotretinoin and etretinate on acne and sebaceous gland secretion. 1982. Journal of the American Academy of Dermatology | No relevant comparison - isotretinoin vs etretinate |
| Gollnick, H. G., K.Azelaic acid for the treatment of acne: Comparative trials. 1989. Journal of Dermatological Treatment | No relevant article type - expert review |
| Gollnick, H. P. G., K.,Zaumseil, R. P.Azelaic acid 15% gel in the treatment of acne vulgaris. Combined results of two double-blind clinical comparative studies. 2004. Journal der Deutschen Dermatologischen Gesellschaft [Journal of the German Society of Dermatology] | Not in English language |
| Gollnick, H. P. M. V., K.,Hermann, J.,Blume, U.,Hahn, H.,Haustein, U. F.,Orfanos, C. E.Topical quinolone OPC-7251: A clinical and microbiological study in acne. 1994. European Journal of Dermatology | No information on the baseline severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Goltz, R. W. C., G. M.,Schnieders, J. R.,Neidert, G. L.A comparison of Cleocin T 1 percent solution and Cleocin T 1 percent lotion in the treatment of acne vulgaris. 1985. Cutis | No relevant data - insufficient data reported |
| Goltz, R. W. K., S.Oral tetracycline treatment on bacterial flora in acne vulgaris. 1966. Archives of Dermatology | No relevant data reported - bacterial flora study |
| Gonzalez, P. V., R.,Cirigliano, M.The tolerability profile of clindamycin 1%/benzoyl peroxide 5% gel vs. adapalene 0.1%/benzoyl peroxide 2.5% gel for facial acne: Results of a randomized, single-blind, split-face study. 2012. Journal of Cosmetic Dermatology | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Goodfellow, A. A.-Z., J.,Carter, G.Oral spironolactone improves acne vulgaris and reduces sebum excretion. 1984. British Journal of Dermatology | No relevant outcomes reported |
| Goreshi, R. S., A.,Ehst, B. D.A double-blind, randomized, bilateral comparison of skin irritancy following application of the combination acne products clindamycin/tretinoin and benzoyl peroxide/adapalene. 2012. Journal of Drugs in Dermatology | No relevant outcomes reported |
| Goswami, B. C. B., B.,Barua, A. B.,Olson, J. A. Topical retinoyl beta-glucuronide is an effective treatment of mild to moderate acne vulgaris in Asian-Indian patients. 1999. Skin Pharmacology & Applied Skin Physiology | No relevant intervention - retinoyl beta-glucuronide |
| Goujon, C. G., P.,Violin, L.,Larnier, C.Biometric and clinical comparative assay of Roaccutane gel (0.05% isotretinoin) versus Retacnyl cream (0.05% tretinoin) in the treatment of moderate retentional acne on the face. 1995. Nouvelles Dermatologiques | Not in English language |
| Gould, D. J. E., R.,Cunliffe, W. J.Oral tetracycline and retinoic acid gel in acne. 1978. Practitioner | No relevant study design - unclear if RCT |
| Graupe, K. C., W. J.,Gollnick, H. P.,Zaumseil, R. P.Efficacy and safety of topical azelaic acid (20 percent cream): an overview of results from European clinical trials and experimental reports. 1996. Cutis | No relevant study design - not RCT |
| Green, L. C., M.,Gwazdauskas, J. A.,Gonzalez, P.The tolerability profile of clindamycin 1%/benzoyl peroxide 5% gel vs. adapalene | No relevant data reported - reports pooled results from |

| Reference | Reason for exclusion |
|---|---|
| 0.1%/benzoyl peroxide 2.5% gel for facial acne: Results of two randomized, single-blind, split-face studies. 2012. Journal of Clinical and Aesthetic Dermatology | 2 trials combined |
| Green, L. J. D. R., J. Q.Efficacy and Tolerability of a Three-Step Acne System Containing a Solubilized Benzoyl Peroxide Lotion versus a Benzoyl Peroxide/Clindamycin Combination Product: An Investigator-Blind, Randomized, Parallel-Group Study. 2008. The Journal of Clinical & Aesthetic Dermatology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Green, L. K., L. H.,Gwazdauskas, J.Randomized, controlled, evaluator-blinded studies conducted to compare the efficacy and tolerability of 3 over-the-counter acne regimens in subjects with mild or moderate acne. 2013. Journal of drugs in dermatology | No relevant comparison - compares over-the-counter 3-part skin care regimens inclunding BPO, SAL etc which have been discontinued (MaxClarity, Proactiv, Murad) |
| Greenwood, R. B., B.,Cunliffe, W. J.Evaluation of a therapeutic strategy for the treatment of acne vulgaris with conventional therapy. 1986. British Journal of Dermatology | No relevant study design - not RCT |
| Gregory, A. N. T., C. R.,Leibowitz, K. R.,Lane, M.A study on the use of a novel light and heat energy system to treat acne vulgaris. 2004. Cosmetic Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Griffiths, C. E. E., J. T.,Bernard, B. A.,Rossio, P.,Cromie, M. A.,Finkel, L. J.,Shroot, B.,Voorhees, J. J.Comparison of CD271 (adapalene) and all-trans retinoic acid in human skin: dissociation of epidermal effects and CRABP-II mRNA expression. 1993. Journal of Investigative Dermatology | No relevant study population - participants did not have acne |
| Grimes, P. C., V.Tazarotene cream for postinflammatory hyperpigmentation and acne vulgaris in darker skin: A double-blind, randomized, vehicle-controlled study. 2006. Cutis | No relevant study population - sample includes people with post-inflammatory hyperpigmentation and acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Grosshans, E. F., A.,Guibaud, B.Clinical evaluation of a topical ethyl lactate treatment of acne vulgaris (author's transl). 1978. Annales de dermatologie ET de venereologie | Not English language |
| Grosshans, E. M., R.,Mascaro, J. M.,Torras, H.,Meynadier, J.,Alirezai, M.,Finlay, A. Y.,Soto, P.,Poncet, M.,Verschoore, M.,Clucas, A.Evaluation of clinical efficacy and safety of adapalene 0.1% gel versus tretinoin 0.025% gel in the treatment of acne vulgaris, with particular reference to the onset of action and impact on quality of life. 1998. British Journal of Dermatology, Supplement | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |

| Reference | Reason for exclusion |
|---|---|
| Grove, G. Z., C.,Gwazdauskas, J.Tolerability and irritation potential of four topical acne regimens in healthy subjects. 2013. Journal of Drugs in Dermatology | No relevant study population - participants did not have acne |
| Gruber, F. G.-G., H.,Kastelan, M.,Brajac, I.,Lenkovic, M.,Zamolo, G.Azithromycin compared with minocycline in the treatment of acne comedonica and papulo-pustulosa. 1998b. Journal of Chemotherapy | No relevant study design - not RCT |
| Gu, W. Z., X. Q.,Wu, J. D.Cuochuang Heji and acupuncture and cupping treatment on acne vulgaris. 2016b. Liaoning journal of traditional chinese medicine [liaoning zhong yi za zhi] | No relevant intervention - Cuochuang Heji and acupuncture |
| Gu,Cuochuang Heji and acupuncture and cupping treatment on acne vulgaris. 2016a. NA | Duplicate record |
| Guerrier, C. J. W. T., E. J.Double-blind comparison of two similar lotion formulations, one without and the other with hydrocortisone acetate ('Actinac') in the treatment of acne vulgaris. 1980. Current Medical Research and Opinion | No relevant comparison - Actinac with/without chloramphenicol |
| Guin, J. D.Topical clindamycin: A double-blind study comparing clindamycin phosphate with clindamycin hydrochloride. 1979. International Journal of Dermatology | No relevant study population - insufficient information to determine acne severity |
| Guin, J. D.Treatment of acne vulgaris with topical clindamycin phosphate: a double-blind study. 1981. International Journal of Dermatology | No relevant study population - insufficient information to determine acne severity |
| Gunning, D. B. B., A. B.,Lloyd, R. A.,Olson, J. A.Retinoyl beta-glucuronide: A nontoxic retinoid for the topical treatment of acne. 1994. Journal of Dermatological Treatment | No relevant intervention - retinoyl beta-glucuronide |
| Gupta, A. K. G., M. D.,Abramovits, W.Ziana (clindamycin phosphate 1.2% and tretinoin 0.025%)gel. 2007. SKINmed | No relevant study design - not RCT |
| Gwiezdzinski, Z. U., S.,Szelemej, R.2.5% Solution of flutamide (a nonsteroidal antiandrogen) in the topical treatment of acne vulgaris. A double-blind randomized study. 1997. Journal of Dermatological Treatment | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Habbema, L. K., B.,Menke, H. E.,Doornweerd, S.,De Boulle, K.A 4% erythromycin and zinc combination (Zineryt) versus 2% erythromycin (Eryderm) in acne vulgaris: A randomized, double-blind comparative study. 1989a. British Journal of Dermatology | No relevant data reported - study does not report number of participants randomised or who completed in each group |
| Habbema, L. K., B.,Menke, H. E.,Doornweerd, S.,De, B. K.A 4% erythromycin and zinc combination (Zineryt (R)) versus 2% erythromycin (Eryderm (R)) in acne vulgaris: a randomized, double-blind comparative study. 1989b. British journal of dermatology | Duplicate record |
| Haedersdal, M. T.-B., K.,Wiegell, S. R.,Wulf, H. C.Long-pulsed dye laser versus long-pulsed dye laser-assisted photodynamic therapy for acne vulgaris: A randomized controlled trial. 2008. Journal of the American Academy of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Hajheydari, Z. S., M.,Morteza-Semnani, K.,Soltani, A.Effect of Aloe vera topical gel combined with tretinoin in treatment of mild and moderate acne vulgaris: A randomized, double-blind, prospective trial. 2014. Journal of Dermatological Treatment | No relevant intervention - aloe vera |

| Reference | Reason for exclusion |
|---|---|
| Halbe, H. W. d. M., N. R.,Bahamondes, L.,Petracco, A.,Lemgruber, M.,de Andrade, R. P.,da Cunha, D. C.,Guazelli, C. A.,Baracat, E. C.Efficacy and acceptability of two monophasic oral contraceptives containing ethinylestradiol and either desogestrel or gestodene. 1998. The European journal of contraception & reproductive health care : the official journal of the European Society of Contraception | No relevant study population - participants did not have acne |
| Hammerstein, J. M., J.,Leo-Rossberg, I.,Moltz, L.,Zielske, F.Use of cyproterone acetate (CPA) in the treatment of acne, hirsutism and virilism. 1975. Journal of Steroid Biochemistry | No relevant study design - not RCT |
| Han, G., Armstrong, A. W., Desai, S. R., Guenin, E.Novel Tretinoin 0.05% Lotion for the Once-Daily Treatment of Moderate-to-Severe Acne Vulgaris in an Asian Population. 2019. Journal of drugs in dermatology : JDD | Not obtainable |
| Handojo, I.Retinoic acid cream (Airol cream) and benzoyl-peroxide in the treatment of acne vulgaris. 1979b. Southeast Asian Journal of Tropical Medicine & Public Health | No relevant study population - insufficient information to determine acne severity and study is not relevant for PCOS, maintenance or refractory treatments |
| Handojo, I.The combined use of topical benzoyl peroxide and tretinoin in the treatment of acne vulgaris. 1979a. International Journal of Dermatology | No relevant study population - insufficient information to determine acne severity and study is not relevant for PCOS, maintenance or refractory treatments |
| Harcup, J. W. C., J.The treatment of acne vulgaris in general practice. A double-blind assessment of co-trimoxazole and tetracycline. 1980. Practitioner | No relevant study population - insufficient information to determine acne severity and study is not relevant for PCOS, maintenance or refractory treatments |
| Hare, P. J.Benzoyl peroxide gel compared with retinoic acid in acne vulgaris. 1975. British Journal of Clinical Practice | No relevant study design - not RCT |
| Harms, M. P., I.,Ceyrac, D.,Saurat, J. H.Isotretinoin ineffective topically. 1985. Lancet (london, england) | No relevant study design - not RCT |
| Harper, J. C. R., W. E.,Zeichner, J. A.,Guenin, E.,Bhatt, V.,Pillai, R.Novel tretinoin 0.05% lotion for the once-daily treatment of moderate-to-severe acne vulgaris: assessment of safety and tolerability in subgroups. 2019. Journal of Dermatological Treatment. | No relevant data reported - post hoc subgroup analyis by ethncity and sex of Tyring 2019 |
| Harper, J. C., Baldwin, H., Stein Gold, L., Guenin, E.Efficacy and Tolerability of a Novel Tretinoin 0.05% Lotion for the Once-Daily Treatment of Moderate or Severe Acne Vulgaris in Adult Females. 2019. Journal of drugs in dermatology : JDD | Not obtainable |
| Harper, J. C., Roberts, W. E., Zeichner, J. A., Guenin, E., Bhatt, V., Pillai, R.Novel tretinoin 0.05% lotion for the once-daily treatment of moderate-to-severe acne vulgaris: assessment of safety and tolerability in subgroups. 2020. Journal of Dermatological Treatment | No relevan data reported - reports post hoc analysis of Tyring 2018 |
| Harper, J. C.Gender as a clinically relevant outcome variable in acne: benefits of a fixed combination clindamycin phosphate (1.2%) and benzoyl peroxide (2.5%) aqueous gel. 2012. Journal of Drugs in Dermatology: JDD | No relevant data reported - post hoc subgroup analysis presenting data for male and female groups straitified by age |
| Harper, J. C.The efficacy and tolerability of a fixed combination | No relevant data reported - |

| Reference | Reason for exclusion |
|---|---|
| clindamycin (1.2%) and benzoyl peroxide (3.75%) aqueous gel in patients with facial acne vulgaris: Gender as a clinically relevant outcome variable. 2015. Journal of Drugs in Dermatology | post hoc subgroup analysis by gender of Pariser 2014 |
| Hashimoto, Y. S., Y.,Mizuno, Y.,Hasegawa, T.,Matsuba, S.,Ikeda, S.,Monma, T.,Ueda, S.Salicylic acid peels in polyethylene glycol vehicle for the treatment of comedogenic acne in Japanese patients. 2008. Dermatologic Surgery | No relevant study design - not RCT |
| Hatwal, A. B., R. P.,Agrawal, J. K.,Singh, G.,Bajpai, H. S.Spironolactone and cimetidine in treatment of acne. 1988. Acta Dermato-Venereologica | No relevant intervention - h2-receptor antagonist - cimetidine |
| Hayashi, N. K., E.,Nogita, T.,Fujiyama, M.,Kawashima, M.A randomized placebo-controlled investigator-blinded face split study of 20% azelaic acid cream to evaluate the efficacy and safety in Japanese patients with acne vulgaris. 2012. Journal of Dermatology | No relevant article type - conference abstract |
| Hayashi, N. K., I.,Siakpere, O.,Endo, A.,Hatanaka, T.,Yamada, M.,Kawashima, M.Clindamycin phosphate 1.2%/benzoyl peroxide 3% fixed-dose combination gel versus topical combination therapy of adapalene 0.1% gel and clindamycin phosphate 1.2% gel in the treatment of acne vulgaris in Japanese patients: A multicenter, randomized, investigator-blind, parallel-group study. 2018. Journal of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Hayashi, N. K., M. Multicenter randomized controlled trial on combination therapy with 0.1% adapalene gel and oral antibiotics for acne vulgaris: Comparison of the efficacy of adapalene gel alone and in combination with oral faropenem. 2012. Journal of Dermatology | No relevant intervention - intervention & class not available in the UK |
| Hayashi, N. K., M. Study of the usefulness of moisturizers on adherence of acne patients treated with adapalene. 2014. Journal of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Hayashi, N. K., M.Efficacy of oral antibiotics on acne vulgaris and their effects on quality of life: a multicenter randomized controlled trial using minocycline, roxithromycin and faropenem. 2011. Journal of Dermatology | No relevant intervention - intervention & class not available in the UK |
| Hebert, A., Thiboutot, D., Stein Gold, L., Cartwright, M., Gerloni, M., Fragasso, E., Mazzetti, A. Efficacy and Safety of Topical Clascoterone Cream, 1%, for Treatment in Patients with Facial Acne: Two Phase 3 Randomized Clinical Trials. 2020. JAMA Dermatology. | No relevant intervention - scoterone cream in the UK |
| Hellgren, L. V., J. Changes of skin surface lipids in acne vulgaris after treatment with trimethoprim-sulphamethoxazole. 1976. Dermatologische Monatsschrift | Not in English language |
| Hellgren, L. V., J.Topical erythromycin for acne vulgaris. 1980. Dermatologica | No relevant data reported - participants received intervention for between 4 and 8 weeks |
| Herndon, J. H., Jr.,Stephens, T. J.,Trookman, N. S.,Rizer, R. L.,Preston, N.,Caveney, S.,Gottschalk, R. W.A comparison of the tolerability of adapalene 0.1% cream and adapalene 0.1% lotion in healthy individuals. 2012. SKINmed | No relevant study population - participants did not have acne |
| Hersle, K. G., H.Minocycline in acne vulgaris: a double blind study. 1976. Current Therapeutic Research - Clinical and Experimental | No relevant study population - insufficient information to determine acne severity and study is not relevant for PCOS, |

| Reference | Reason for exclusion |
|---|---|
| | maintenance or refractory treatments |
| Heymann, W. R.Hyperandrogenism and the skin. 2004. Journal of the American Academy of Dermatology | No relevant study design - not RCT |
| Hjorth, N. G., K.Azelaic acid for the treatment of acne. A clinical comparison with oral tetracycline. 1989. Acta Dermato-Venereologica. Supplementum | No relevant data - insufficient data reported |
| Hjorth, N. S., D.,Dela, K.Topical anhydrous aluminum chloride formulation in the treatment of acne vulgaris: A double-blind study. 1985. Cutis | No relevant study population - insufficient information reported about acne severity and study is not relevant for PCOS, maintenance or refractory treatments |
| Hjorth, N. S., H.,Thomsen, K.,Dela, K.Meclosorb(), a new topical antibiotic agent in the treatment of acne vulgaris: A double-blind clinical study. 1984. Acta Dermato-Venereologica | No relevant study population - insufficient information reported about acne severity and study is not relevant for PCOS, maintenance or refractory treatments |
| Ho, S. G. Y., C. K.,Chan, N. P.,Shek, S. Y.,Kono, T.,Chan, H. H.A retrospective analysis of the management of acne post-inflammatory hyperpigmentation using topical treatment, laser treatment, or combination topical and laser treatments in oriental patients. 2011. Lasers in Surgery & Medicine | Duplicate record |
| Hong, S. B. L., M. H.Topical aminolevulinic acid-photodynamic therapy for the treatment of acne vulgaris. 2005. Photodermatology, Photoimmunology & Photomedicine | No relevant study design - not RCT |
| Hongcharu, W. T., C. R.,Chang, Y.,Aghassi, D.,Suthamjariya, K.,Anderson, R. R.Topical ALA-photodynamic therapy for the treatment of acne vulgaris. 2000. Journal of Investigative Dermatology | Efficacy outcomes reported in figures only |
| Honorato, J. A., J. R.,Sandoval, C. A.,Quintanilla, E.Double-blind, randomized and controlled clinical trial on the efficacy of topical clindamycin in the treatment of acne. 1988. Revista de farmacologia clinica y experimental | Not in English language |
| Horfelt, C. S., B.,Larko, O.,Faergemann, J.,Wennberg, A. M.Photodynamic therapy for acne vulgaris: a pilot study of the dose-response and mechanism of action. 2007. Acta Dermato-Venereologica | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Hubbell, C. G. H., E. R.,Rist, T.,White Jr, J. W.Efficacy of minocycline compared with tetracycline in treatment of acne vulgaris. 1982. Archives of Dermatology | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Hughes, B. R.A double blind evaluation of topical isotretinoin, benzoyl peroxide and placebo in patients with acne. Abstract. 1989. British journal of dermatology | No relevant article type - conference abstract |
| Hurwitz, S.The combined effect of vitamin A acid and benzoyl | No relevant study |

| Reference | Reason for exclusion |
|---|---|
| peroxide in the treatment of acne. 1976. Cutis | population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Ianosi, S. N., D.,Branisteanu, D. E.,Popescu, M.,Calina, D.,Zlatian, O.,Docea, A. O.,Marinas, M. C.,Iordache, A. M.,MitruÈ›, P.,et al.,Comparative efficacy of oral contraceptive versus local treatment versus intense pulsed light combined with vacuum in endocrine acne in women. 2018. Journal of biological regulators and homeostatic agents | No relevant outcomes reported |
| Ibbotson, S. H.Topical 5-aminolaevulinic acid photodynamic therapy for the treatment of skin conditions other than non-melanoma skin cancer. 2002. British Journal of Dermatology | Duplicate record |
| Iglesias, L.Everyday doxycycline (oral) for 16 weeks vs everyday doxycycline (oral ) for the first 4 weeks and on alternate days for the next 12 weeks in the treatment of acne vulgaris. (Spanish). 1992. Actas dermo-sifiliograficas | Not in English language |
| Ikeno, H. O., K.Open study comparing sodium L-ascorbyl-2-phosphate 5% lotion versus adapalene 0.1% gel for acne vulgaris. 2007. Cosmetic Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Ilknur, T. D., M.,Bicak, M. U.,Ozkan, S.Glycolic acid peels versus amino fruit acid peels for acne. 2010. Journal of Cosmetic and Laser Therapy | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| In Jae, J. D. J., H.,Dong Hyun, K.,Yoon, M. S.,Lee, H. J.Comparative study of buffered 50% glycolic acid (pH 3.0) + 0.5% salicylic acid solution vs Jessner's solution in patients with acne vulgaris. 2018. Journal of cosmetic dermatology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Inman, P. G., B.,McNay, R. A.Acne and the pill. 1971. Newcjiedj | Not obtainable |
| Iraji, F. M., 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. 2006. Dermatology Online Journal | No relevant intervention - topical cyproterone acetate alcohol lotion |
| Ito, K. M., S.,Hamada, M.,Tokunaga, T.,Kokuba, H.,Tashiro, K.,Yano, I.,Yasumoto, S.,Imafuku, S.Efficacy and Safety of the Traditional Japanese Medicine Keigairengyoto in the Treatment of Acne Vulgaris. 2018b. Dermatology Research and Practice | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory |

| Reference | Reason for exclusion |
|---|---|
| | treatments |
| Ito,Efficacy and Safety of the Traditional Japanese Medicine Keigairengyoto in the Treatment of Acne Vulgaris. 2018a. NA | Duplicate record |
| Jaffary, F. F., G.,Saraeian, S.,Hosseini, S. M.Comparison the effectiveness of pyruvic acid 50% and salicylic acid 30% in the treatment of acne. 2016. Journal of research in medical sciences | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Jaffary, F. N., M. A.,Koupaiee, H. S.,Faghihi, G.,Hosseini, S. M.,Sokhanvari, F.,Ansari, N.,Sadeghian, G.Omeprazole versus doxycycline combination therapy with topical erythromycin the treatment of acne vulgaris: a randomized clinical trial. 2017. Tehran university medical journal | Not in English language |
| Jaffe, G. V. G., J. J.,Constad, D.Benzoyl peroxide in the treatment of acne vulgaris: a double-blind, multi-centre comparative study of 'Quinoderm' cream and 'Quinoderm' cream with hydrocortisone versus their base vehicle alone and a benzoyl peroxide only gel preparation. 1989. Current Medical Research and Opinion | No relevant study design - not RCT |
| Jang, M. S. D., K. S.,Kang, J. S.,Jeon, Y. S.,Suh, K. S.,Kim, S. T.A comparative split-face study of photodynamic therapy with indocyanine green and indole-3-acetic acid for the treatment of acne vulgaris. 2011. British Journal of Dermatology | No relevant study design - not RCT |
| Jarratt, M. T. B., T.Efficacy and safety of clindamycin-tretinoin gel versus clindamycin or tretinoin alone in acne vulgaris: A randomized, double-blind, vehicle-controlled study. 2012. Journal of Drugs in Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Jarratt, M. T. J., T. M.,Chang-Lin, J. E.,Tong, W.,Berk, D. R.,Lin, V.,Kaoukhov, A.Safety and pharmacokinetics of once-daily dapsone gel, 7.5% in patients with moderate acne vulgaris. 2016. Journal of Drugs in Dermatology | No relevant study population - sample includes mild to severe acne. Participants had 20 to 50 inflammatory lesions (papules and pustules) |
| Jarratt, M. W., C. P.,Alio Saenz, A. B.Tazarotene foam versus tazarotene gel: A randomized relative bioavailability study in acne vulgaris. 2013. Clinical Drug Investigation | No relevant data reported - bioavailability study |
| Jawade, S. A. S., V. A.,Kondalkar, A. R.Efficacy and tolerability of adapalene 0.1%-benzoyl peroxide 2.5% combination gel in treatment of acne vulgaris in indian patients: A randomized investigator-blind controlled trial. 2016. Iranian Journal of Dermatology | No relevant study population - sample includes people mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Jelinek, J. J. Hydrocuorothiazide and the control of premenstrual exacerbation of acne. 1972. Arcilderii | No relevant study population -insuficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |

| Reference | Reason for exclusion |
|---|---|
| Ji, S. Z. T., P.,Li, G. Q.,Liu, L. L.,Chen, X. X.,Zhu, X. J.A comparison of 10% benzoyl peroxide cream and 5% benzoyl peroxide gel in the treatment of acne vulgaris. 2000. The chinese journal of clinical pharmacology | Not in English language |
| Jih, M. H. F., P. M.,Goldberg, L. H.,Robles, M.,Glaich, A. S.,Kimyai-Asadi, A.The 1450-nm diode laser for facial inflammatory acne vulgaris: Dose-response and 12-month follow-up study. 2006. Journal of the American Academy of Dermatology | No relevant intervention - compares 2 fluences of 1450-nm laser |
| Jin, X. Y. D., W.,Hu, X.,Wang, J.,Zou, D. J.Changes of sex hormone levels in male acne patients with normal serum testosterone and effect of antiandrogen therapy. 2009. Academic journal of second military medical university | Not in English language |
| Johnson, K. H.Are oral contraceptives (OCPs) with antiandrogenic progestins preferred over other OCPs in patients with acne?. 2002. Journal of Family Practice | No relevant study design - not RCT |
| Jones, D. H. K., K.,Miller, A. J.,Cunliffe, W. J.A dose-response study of 13-cis-retinoic acid in acne vulgaris. 1983. British Journal of Dermatology | Not possible to extract relevant data |
| Jones, T. M. J., S.,Alio Saenz, A. B.Bioavailability of clindamycin from a new clindamycin phosphate 1.2%-benzoyl peroxide 3% combination gel. 2013. Clinical Pharmacology in Drug Development | No relevant data reported - pharmokinetic study |
| Jorizzo, J. G., R.,Nighland, M.Tretinoin microsphere gel in younger acne patients. 2008. Journal of drugs in dermatology : JDD | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Juhlin, L. M., G.,Ohman, S.Topical triamcinolone acetonide and chlorhydroxyquinoline in acne. 1968. Acta Derm | No relevant study population - insufficient information to determine acne severity and study is not relevant for PCOS, maintenance or refractory treatments |
| Jung, J. Y. H., J. S.,Ahn, C. H.,Yoon, J. Y.,Kwon, H. H.,Suh, D. H.Prospective randomized controlled clinical and histopathological study of acne vulgaris treated with dual mode of quasi-long pulse and Q-switched 1064-nm Nd:YAG laser assisted with a topically applied carbon suspension. 2012. Journal of the American Academy of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Jung, J. Y. K., H. H.,Yeom, K. B.,Yoon, M. Y.,Suh, D. H.Clinical and histological evaluation of 1% nadifloxacin cream in the treatment of acne vulgaris in Korean patients. 2011. International Journal of Dermatology | No relevant intervention - intervention & class not available in the UK |
| Jung, J. Y. L., J. H.,Ryu, D. J.,Lee, S. J.,Bang, D.,Cho, S. B.Lower-fluence, higher-density versus higher-fluence, lower-density treatment with a 10,600-nm carbon dioxide fractional laser system: A split-face, evaluator-blinded study. 2010a. Dermatologic Surgery | Duplicate record |
| Jung, J. Y. Y., M. Y.,Hong, J. S.,Suh, D. H.Treatment of acne vulgaris with a low fluence 1064-nm Nd: YAG laser after applying carbon suspension. 2010b. Journal of Dermatology. Conference: 1st Eastern Asia Dermatology Congress, EADC2010. Fukuoka Japan. Conference | No relevant article type - conference abstract |

| Reference | Reason for exclusion |
|---|---|
| Publication: | |
| Jurairattanaporn, N. C., T.,Ophaswongse, S.,Udompataikul, M.Comparative trial of silver nanoparticle gel and 1% clindamycin gel when use in combination with 2.5% benzoyl peroxide in patients with moderate acne vulgaris. 2017. Journal of the Medical Association of Thailand | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Jurzyk, R. S. S., R. L.,Rose, L. I.Antiandrogens in the treatment of acne and hirsutism. 1992. American Family Physician | No relevant studyd design - not RCT |
| Kabir, M. S., S.,Raza, A.,Kanwal, S.,Tanvir, T.Comparison of efficacy of adapalene (0.1% gel) monotherapy ve adapalene (0.1%) plus benzyl peroxide (2.5%) combination therapy for treatment of mild to moderate acne vulgaris. 2018. Pakistan Journal of Medical and Health Sciences | No relevant data reported |
| Kainz, J. T. B., G.,Auer-Grumbach, P.,Lackner, V.,Perl-Convalexius, S.,Popa, R.,Wolfesberger, B.Azelaic acid 20 % cream: effects on quality of life and disease severity in adult female acne patients. 2016. Journal der Deutschen Dermatologischen Gesellschaft | Duplicate record |
| Kakita, L. Tazarotene versus tretinoin or adapalene in the treatment of acne vulgaris. 2000. Journal of the American Academy of Dermatology | No relevant article type - commentary article |
| Kaminaka, C. U., M.,Matsunaka, H.,Furukawa, F.,Yamomoto, Y.Clinical evaluation of glycolic acid chemical peeling in patients with acne vulgaris: a randomized, double-blind, placebo-controlled, split-face comparative study. 2014. Dermatologic surgery | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Kang, A. L., A.,Herrmann, J.,Moy, R.Treatment of moderate-to-severe facial acne vulgaris with solid-state fractional 589/1,319-nm laser. 2019. Journal of Clinical and Aesthetic Dermatology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Kantikosum, K. C., Y.,Chottawornsak, N.,Asawanonda, P.The efficacy of glycolic acid, salicylic acid, gluconolactone, and licochalcone a combined with 0.1% adapalene vs adapalene monotherapy in mild-to-moderate acne vulgaris: A double-blinded within-person comparative study. 2019. Clinical, Cosmetic and Investigational Dermatology | No relevant study design - not RCT |
| Kantner, V. S., E. Topical effects of oxytetracycline in acne vulgaris. 1970. Ceskoslovenska dermatologie | Not in English language |
| Kar, B. R. T., S.,Panda, M.Comparative study of oral isotretinoin versus oral isotretinoin + 20% salicylic Acid peel in the treatment of active acne. 2013. Journal of Cutaneous & Aestheic Surgery | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for |

| Reference | Reason for exclusion |
|---|---|
| | pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Karoglan, A., Paetzold, B., Pereira de Lima, J., Bruggemann, H., Tuting, T., Schanze, D., Guell, M., Gollnick, H. Safety and Efficacy of Topically Applied Selected Cutibacterium acnes Strains over Five Weeks in Patients with Acne Vulgaris: An Open-label, Pilot Study. 2019. Acta Dermato-Venereologica | No relevant study desgin - the first phase was not randomised and the interventions are not relevant in the second phase |
| Karsai, S. S., L.,Raulin, C.The pulsed-dye laser as an adjuvant treatment modality in acne vulgaris: A randomized controlled single-blinded trial. 2010. British Journal of Dermatology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Katsambas, A. T., A. A.,Stratigos, J.Topical clindamycin phosphate compared with oral tetracycline in the treatment of acne vulgaris. 1987. British Journal of Dermatology | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Katz, H. I. K., S.,Akin, M. D.,Dunlap, F.,Whiting, D.,Norbart, T. C.Effect of a desogestrel-containing oral contraceptive on the skin. 2000. European Journal of Contraception & Reproductive Health Care | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Kawashima, M. H., H.,Alio Saenz, A. B.,Ono, M.,Yamada, M.Clindamycin phosphate 1.2%-benzoyl peroxide 3.0% fixed-dose combination gel has an effective and acceptable safety and tolerability profile for the treatment of acne vulgaris in Japanese patients: A phase III, multicentre, randomised, single-blinded, active-controlled, parallel-group study. 2015. British Journal of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Kawashima, M. H., H.,Alio Saenz, A. B.,Ono, M.,Yamada, M.Is benzoyl peroxide 3% topical gel effective and safe in the treatment of acne vulgaris in Japanese patients? A multicenter, randomized, double-blind, vehicle-controlled, parallel-group study. 2014. Journal of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Kawashima, M. H., S.,Czernielewski, J.,Miyachi, Y.Adapalene gel 0.1% - Topical retinoid-like molecule - For the treatment of Japanese patients with acne vulgaris: A multicenter, randomized, investigator-blinded, dose-ranging study. 2007. Skin Research | No relevant population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Kawashima, M. H., S.,Loesche, C.,Miyachi, Y.Adapalene gel 0.1% is effective and safe for Japanese patients with acne vulgaris: A | No relevant study population - sample |

| Reference | Reason for exclusion |
|---|---|
| randomized, multicenter, investigator-blinded, controlled study. 2008. Journal of Dermatological Science | includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Kawashima, M. N., T.,Katsuramaki, T.Open-label, randomized, multicenter, phase III study to evaluate the safety and efficacy of benzoyl peroxide gel in long-term use in patients with acne vulgaris: A secondary publication. 2017a. Journal of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Kawashima, M. S., S.,Furukawa, F.,Matsunaga, K.,Akamatsu, H.,Igarashi, A.,Tsunemi, Y.,Hayashi, N.,Yamamoto, Y.,Nagare, T.,et al.,Twelve-week, multicenter, placebo-controlled, randomized, double-blind, parallel-group, comparative phase II/III study of benzoyl peroxide gel in patients with acne vulgaris: a secondary publication. 2017b. Journal of dermatology | No relevant study population - includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Kawashima, M. Y., M.,Parish, C.Clindamycin 1%/benzoyl peroxide 3% gel, a new topical combination product, is effective in Japanese patients with acne vulgaris. 2013. Journal of Investigative Dermatology | No relevant article type - conference abstract |
| Kayhan, S. S., I.,Saracoglu, Z. N.,Aksu, A. E. K.,Tozun, M.Comparison of safety and efficacy of oral azithromycin-topical adapalene versus oral doxycycline-topical adapalene in the treatment of acne vulgaris and determination of the effects of these treatments on patients' quality of life. 2012. Turkderm deri hastaliklari ve frengi arsivi | Not in English language |
| Kaymak, Y. T., E.,Taner, Y.Comparison of depression, anxiety and life quality in acne vulgaris patients who were treated with either isotretinoin or topical agents. 2009. International Journal of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Kelidari, H. R. S., M.,Hajheydari, Z.,Akbari, J.,Morteza-Semnani, K.,Akhtari, J.,Valizadeh, H.,Asare-Addo, K.,Nokhodchi, A.Spironolactone loaded nanostructured lipid carrier gel for effective treatment of mild and moderate acne vulgaris: A randomized, double-blind, prospective trial. 2016. Colloids and Surfaces B: Biointerfaces | No relevant intervention - intervention & class not available in the UK |
| Kelly, S. D., E.,Fearns, S.,McKinnon, C.,Carter, R.,Gerlinger, C.,Smithers, A.Effects of oral contraceptives containing ethinylestradiol with either drospirenone or levonorgestrel on various parameters associated with well-being in healthy women: a randomized, single-blind, parallel-group, multicentre study. 2010. Clinical drug investigation | No relevant study population - participants did not have acne |
| Kerscher, M. R., T.,Bayrhammer, J.,Schramm, G.Effects of an oral contraceptive containing chlormadinone and ethinylestradiol on acne-prone skin of women of different age groups: an open-label, single-centre, phase IV study. 2008. Clinical Drug Investigation | No relevant study deisgn - not RCT |
| Kessler, E. F., K.,Chia, C.,Rogers, C.,Anna Glaser, D.Comparison of alpha- and beta-hydroxy acid chemical peels in the treatment of mild to moderately severe facial acne vulgaris. 2008. Dermatologic Surgery | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for |

| Reference | Reason for exclusion |
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| | pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Khaki, I., Valiani, M., Mohammadbeigi, A.Evaluation the effect of auriculotherapy on the clinical signs of single girls with polycystic ovary syndrome: A single-blinded clinical trial. 2019. Clinical Cancer Investigation Journal | No relevant intervention - acupuncture |
| Khan, M. K., N. U.,Anwar, M. I.,Noor, S. M.A comparison of the efficacy of topical adapalene gel 0.1% with tretinoin gel 0.025% in mild acne vulgaris. 2017. Journal of Pakistan Association of Dermatologists | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Kharfi, M. T., N. B.,Zeglaoui, F.,Ezzine, N.,Mokhtar, I.,Kamoun, F.,Kamoun, M. R.Evaluate the efficacy and safety of topical glycolic acid (Glyco A 12%) and retinoin acid (Kefrane 0'05%) on facial acne lesions. 2001a. Tunisie medicale | Not in English language |
| Kharfi, M. T., N.,Zeglaoui, F.,Ezzine, N.,Mokhtar, I.,Kamoun, F.,Kamoun, M. R.Comparative study of the efficacy and tolerance of 12% glycolic acid cream and 0.05% retinoic acid cream for polymorphic acne. 2001b. Tunisie medicale | Not in English language |
| Khodaeiani, E. F., R. F.,Amirnia, M.,Saeidi, M.,Karimi, E. R.Topical 4% nicotinamide vs. 1% clindamycin in moderate inflammatory acne vulgaris. 2013. International Journal of Dermatology | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Khodaeinai, E. B., S.,Amirnia, M.,Shokry, J.,Karimi, L. R.,Fouladi, D. F.,Sedaghat, K.Efficacy of 10% azelaic acid gel with hydro-alcoholic or alcohol-free bases in mild to moderate acne vulgaris; the first clinical trial. 2014. Journal of Medical Sciences (Faisalabad) | Outcomes reported in figures only |
| Kim, B. J. L., H. G.,Woo, S. M.,Youn, J. I.,Suh, D. H.Pilot study on photodynamic therapy for acne using indocyanine green and diode laser. 2009. Journal of Dermatology | Data reported in figures only |
| Kim, B. K., H.,Kim, J. E.,Lee, S. H.Retinyl retinoate, a retinoid derivative improves acne vulgaris in double-blind, vehicle-controlled clinical Study. 2013. Tissue engineering and regenerative medicine | No relevant study design - not RCT |
| Kim, S. J. B., J. H.,Koh, J. S.,Bae, M. I.,Lee, S. J.,Shin, M. K.The effect of physically applied alpha hydroxyl acids on the skin pore and comedone. 2015. International journal of cosmetic science | No relevant study population - sample includes people with acne-prone skin, no further details reported and study is not relevant for PCOS, maintenance or refractory treatments |
| Kim, S. W. M., S. E.,Kim, J. A.,Eun, H. C.Glycolic acid versus Jessner's solution: which is better for facial acne patients? A randomized prospective clinical trial of split-face model therapy. 1999. Dermatologic surgery | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in |

| Reference | Reason for exclusion |
|---|---|
| | the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Kim, W. J. P., J. M.,Ko, H. C.,Kim, B. S.,Kim, M. B.,Song, M.A split-faced, observer-blinded comparison study of topical adapalene/benzoyl peroxide and adapalene in the treatment of Asian acne patients. 2013. Journal of Drugs in Dermatology: JDD | No relevant article type - letter to editor |
| King, K. J., D. H.,Daltrey, D. C.,Cunliffe, W. J.A double-blind study of the effects of 13-cis-retinoic acid on acne, sebum excretion rate and microbial population. 1982. British Journal of Dermatology | No relevant data reported - sebum excretion study |
| Kircik, L. H. B., V.,Martin, G.,Pillai, R.Randomized, double-blind, split-face study to compare the irritation potential of two topical acne formulations over a 21-day treatment period. 2016. Journal of Drugs in Dermatology | No relevant study population - participants did not have acne |
| Kircik, L. H.Comparative efficacy and safety results of two topical combination acne regimens. 2009b. Journal of Drugs in Dermatology | No relevant data reported - study recruited participants for 4 (n=23) or 12 wk (n=42) trial of BPO/CLIND gel vs solubilized BPO gel but reports data for all participants |
| Kircik, L. H.Fixed Combination of Clindamycin Phosphate 1.2% and Benzoyl Peroxide 3.75% Aqueous Gel: Long-Term Use in Adult Females With Moderate Acne Vulgaris. 2017. Journal of Drugs in Dermatology: JDD | No relevant study design - not RCT |
| Kircik, L. H.Tretinoin microsphere gel pump 0.04% versus tazarotene cream 0.05% in the treatment of mild-to-moderate facial acne vulgaris. 2009. Journal of Drugs in Dermatology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Kligman, A. M. F., J. E., Jr.,Plewig, G.Topical vitamin A acid in acne vulgaris. 1969. Archives of Dermatology | No relevant study design - not RCT |
| Kligman, A. M. P., G.,Mills, O. H., Jr.Topically applied tretinoin for senile (solar) comedones. 1971. Archives of Dermatology | No relevant study design - not RCT |
| Kligman, A. M.Comparison of a topical benzoyl peroxide gel, oral minocycline, oral doxycycline and a combination for suppression of P. acnes in acne patients. 1998. Journal of dermatological treatment | No relevant outcmoes reported - bacterial counts |
| Knutson, D. D. S., L. J.,Smoot, W. H.Meclocycline sulfosalicylate. Topical antibiotic agent for the treatment of acne vulgaris. 1981. Cutis | No relevant article type - non-systematic review |
| Ko, H. C. S., M.,Seo, S. H.,Oh, C. K.,Kwon, K. S.,Kim, M. B.Prospective, open-label, comparative study of clindamycin 1%/benzoyl peroxide 5% gel with adapalene 0.1% gel in Asian acne patients: Efficacy and tolerability. 2009. Journal of the European Academy of Dermatology and Venereology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and |

| Reference | Reason for exclusion |
|---|---|
| | refractory treatments |
| Kobayashi, M. N., T.,Fukamachi, K.,Nakamura, M.,Tokura, Y.Efficacy of combined topical treatment of acne vulgaris with adapalene and nadifloxacin: A randomized study. 2011. Journal of Dermatology | No relevant intervention - intervention & class not available in the UK |
| Koltun, W. L., A. W.,Thiboutot, D.,Niknian, M.,Sampson-Landers, C.,Korner, P.,Marr, J.Efficacy and safety of 3 mg drospirenone/20 mcg ethinylestradiol oral contraceptive administered in 24/4 regimen in the treatment of acne vulgaris: a randomized, double-blind, placebo-controlled trial. 2008. Contraception | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Koltun, W. M., J. M.,Marr, J.,Kunz, M.Treatment of moderate acne vulgaris using a combined oral contraceptive containing ethinylestradiol 20 mug plus drospirenone 3 mg administered in a 24/4 regimen: A pooled analysis. 2011. European Journal of Obstetrics and Gynecology and Reproductive Biology | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Kotrajaras, R.Comparative study in the treatment of acne vulgaris with cyproterone acetate, tetracycline and vitamin A acid. 1982. Journal of the Medical Association of Thailand | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Krausz, A. F., A. J.Cutaneous hyperandrogenism: role of antiandrogen therapy in acne, hirsutism, and androgenetic alopecia. 2013. Journal of Drugs in Dermatology: JDD | No relevant article type - non-systematic review |
| Kriplani, A. T., J.,Agrawal, N.,Kulshrestha, V.,Ammini, A. C.,Kumar, G.A comparative study of Diane-35 plus spironolactone and Diane-35 plus finasteride in cases of hirsutism and acne. 2009. International journal of endocrinology and metabolism | No relevant study population - only 38% of participants have acne |
| Krishnan, G.Comparison of two concentrations of tretinoin solution in the topical treatment of acne vulgaris. 1976. Practitioner | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Kubeyinje, E. P.Topical tretinoin compared with topical clindamycin phosphate in the treatment of acne and acne-associated hyperpigmentation in Arabs. 1997. Journal of dermatological treatment | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Kubota, Y. M., A.,Shirahige, Y.,Nakai, K.,Katsuura, J.,Moriue, T.,Murakami, Y.,Matsunaka, H.,Yoneda, K.Effect of sequential application of topical adapalene and clindamycin phosphate in the treatment of Japanese patients with acne vulgaris. 2012. Journal of Dermatological Treatment | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |

| Reference | Reason for exclusion |
|---|---|
| Kuflik, E. G.Benzoyl peroxide gel in acne therapy. 1976. Cutis | No relevant study design - not RCT |
| Kurokawa, I. A., H.,Nishijima, S.,Asada, Y.,Kawabata, S.Clinical and bacteriologic evaluation of OPC-7251 in patients with acne: A double-blind group comparison study versus cream base. 1991. Journal of the American Academy of Dermatology | Duplicate record |
| Kus, S. Y., D.,Aytug, A.Comparison of efficacy of azithromycin vs. doxycycline in the treatment of acne vulgaris. 2005. Clinical and Experimental Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Kwon, H. H. C., S. C.,Jung, J. Y.,Bae, Y. I.,Park, G. H.Comparison of novel dual mode vs conventional single pass of a 1450-nm diode laser in the treatment of acne vulgaris for Korean patients: A 20-week prospective, randomized, split-face study. 2018. Journal of Cosmetic Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Kwon, H. H. L., J. B.,Yoon, J. Y.,Park, S. Y.,Ryu, H. H.,Park, B. M.,Kim, Y. J.,Suh, D. H.The clinical and histological effect of home-use, combination blue-red LED phototherapy for mild-to-moderate acne vulgaris in Korean patients: A double-blind, randomized controlled trial. 2013. British Journal of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Kwon, H. H. M., K. R.,Park, S. Y.,Yoon, J. Y.,Suh, D. H.,Lee, J. B.Daylight photodynamic therapy with 1.5% 3-butenyl 5-aminolevulinate gel as a convenient, effective and safe therapy in acne treatment: A double-blind randomized controlled trial. 2016. Journal of Dermatology | No relevant study population - sample includes mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Kwon, H. H. P., H. Y.,Choi, S. C.,Bae, Y.,Jung, J. Y.,Park, G. H.Novel device-based acne treatments: comparison of a 1450-nm diode laser and microneedling radiofrequency on mild-to-moderate acne vulgaris and seborrhoea in Korean patients through a 20-week prospective, randomized, split-face study. 2018. Journal of the European Academy of Dermatology and Venereology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Kwon, H. H. P., S. Y.,Yoon, J. Y.,Min, S.,Suh, D. H.Do tutorials on application method enhance adapalene-benzoyl peroxide combination gel tolerability in the treatment of acne?. 2015. Journal of Dermatology | No relevant comparator - compares efficacy of adding training module to intervention |
| Kwon, I. K., S.,Lee, D.Photodynamic therapy using chlorophyll-a in the treatment of acne vulgaris: A randomized, single-blind, split-face study. 2014. Journal of Investigative Dermatology | No relevant article type - conference abstract |
| Kwon,Comparison of clinical and histological effects between lactobacillus-fermented Chamaecyparis obtusa and tea tree oil for the treatment of acne: an eight-week double-blind randomized controlled split-face study. 2014. NA | No relevant intervention and comparison - Lactobacillus-fermented Chamaecyparis obtusa vs tea tree oil |
| L. Ghoshal, S. Banerjee, S. Ghosh, D. Gangopadhyay and S. | No relevant study |

| Reference | Reason for exclusion |
|---|---|
| JanaComparative evaluation of effectiveness of adapalene and azithromycin, alone or in combination, in acne vulgaris. 2007. Indian Journal of Dermatology | population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Lachnit-Fixson, U. K., J.Therapy of androgenization symptoms: double blind study of an antiandrogen preparation (SH B 209 AB) against neogynon (author's transl). 1977. Medizinische klinik | Not in English language |
| Lain, E., Day, D., Harper, J., Guenin, E.Tretinoin 0.05% Lotion for the Once-Daily Treatment of Moderate-to-Severe Acne Vulgaris: Impact of Gender and Race on Efficacy and Safety. 2019. Journal of drugs in dermatology : JDD | Not obtainable |
| Langner, A. B., G. C.,Stapor, V.,Wolska, H.,Fraczykowska, M.Isotretinoin cream 0.05% and 0.1% in the treatment of acne vulgaris. 1994. Journal of Dermatological Treatment | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Laquieze, S. C., J.,Rueda, M. J.Beneficial effect of a moisturizing cream as adjunctive treatment to oral isotretinoin or topical tretinoin in the management of acne. 2006. Journal of drugs in dermatology : JDD | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Lassus, A.Local treatment of acne. A clinical study and evaluation of the effect of different concentrations of benzoyl peroxide gel. 1981. Current Medical Research & Opinion | Not an RCT |
| Lee SH, Huh CH, Park KC, Youn SW.Effects of repetitive superficial chemical peels on facial sebum secretion in acne patients.. 2006. J Eur Acad Dermatol Venereol | No relevant outcomes repoted - sebum levels only |
| Lee, E. J. L., H. K.,Shin, M. K.,Suh, D. H.,Lee, S. J.,Kim, N. I.An open-label, split-face trial evaluating efficacy and safty of photopneumatic therapy for the treatment of acne. 2012. Annals of Dermatology | No relevant study design - not RCT |
| Lee, H. E. K., J. Y.,Kim, Y. H.,Yoo, S. R.,Moon, S. H.,Kim, N. I.,Park, C.,Kim, J. H.,Koh, H. J.,Park, W. S.,Ro, Y. S.A double-blind randomized controlled comparison of apddr-0901, a novel cosmeceutical formulation, and 0.1% adapalene gel in the treatment of mild-to-moderate acne vulgaris. 2011a. European Journal of Dermatology | No relevant intervention - intervention & class not available in the UK |
| Lee, H. J., Kim, J. Y., Park, K. D., Lee, W. J.Randomized controlled double-blind study of a cleanser composed of 5-aminolevulinic acid and peptides on mild and moderate acne vulgaris. 2019a. Journal of Cosmetic Dermatology. | No relevant intervention - cleanser |
| Lee, J. W. Y., K. H.,Park, K. Y.,Han, T. Y.,Li, K.,Seo, S. J.,Hong, C. K.Effectiveness of conventional, low-dose and intermittent oral isotretinoin in the treatment of acne: A randomized, controlled comparative study. 2011b. British Journal of Dermatology | No relevant study population - insufficient details to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Lee, S. Y. C.The efficacy of full-spectrum light generated by electrical | No relevant article type - |

| Reference | Reason for exclusion |
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| discharge between two carbon arc rods for the treatment of acne compared to 1% topical clindamycin. 2010. Lasers in Surgery and Medicine | conference abstract |
| Lee, S. Y., Park, A. Y., Shin, J. Y., Lee, H. J., Kim, J. E., Lee, S. H., Lee, J. S.Comparison of the efficacy of azithromycin versus doxycycline in acne vulgaris. 2019b. Journal of the American Academy of Dermatology | No relevant artcile type - conference abstract |
| Lee, W. J. J., H. J.,Kim, J. Y.,Lee, S. J.,Kim, D. W.Effect of photodynamic therapy on inflammatory acne using 3% liposomal 5-aminolevulinic acid emulsion and intense-pulsed light: A pilot study. 2012. Journal of Dermatology | No relevant article type - letter to editor |
| Lekakh, O. M., A. M.,Novice, K.,Kamalpour, J.,Sadeghian, A.,Mondo, D.,Kalnicky, C.,Guo, R.,Peterson, A.,Tung, R.Treatment of Acne Vulgaris With Salicylic Acid Chemical Peel and Pulsed Dye Laser: A Split Face, Rater-Blinded, Randomized Controlled Trial. 2015. Journal of Lasers in Medical Sciences | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Lekwuttikarn, R. T., T.,Chatproedprai, S.,Wananukul, S.Randomized, controlled trial split-faced study of 595-nm pulsed dye laser in the treatment of acne vulgaris and acne erythema in adolescents and early adulthood. 2017. International Journal of Dermatology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Lemay, A. A., D. F.,Roberts, J. L.,Harrison, D. D.The efficacy of an oral contraceptive containing 20ug ethinyl estradiol and 100ug levonorgestrel for the treatment of moderate acne. 2000. Gynecological endocrinology | No relevant article type - conference abstract |
| Lesher, J. L., Jr.,Chalker, D. K.,Smith, J. G., Jr.,Guenther, L. C.,Ellis, C. N.,Voorhees, J. J.,Shalita, A. R.,Klauda, H. C.An evaluation of a 2% erythromycin ointment in the topical therapy of acne vulgaris. 1985. Journal of the American Academy of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Lester, R. S. S., G. D.,Light, M. J.Isotretinoin and tetracycline in the management of severe nodulocystic acne. 1985. International Journal of Dermatology | Dosage of tetracycline lower than BNF value |
| Leu, F. S., U.,Fournet, M.,Truffat, C.Random sample study of the effect of two concentrations of retinoic acid on acne vulgaris. 1974. Medecine ET hygiene | Not in English language |
| Levesque, A. H., I.,Seite, S.,Rougier, A.,Bissonnette, R.Randomized trial comparing a chemical peel containing a lipophilic hydroxy acid derivative of salicylic acid with a salicylic acid peel in subjects with comedonal acne. 2011. Journal of cosmetic dermatology | No relevant intervention - lipohydroxy acid |
| Lew-Kaya, D. A. R., L. L.,Sefton, J.,Stern, K.Once-daily erythromycin 2% gel in the treatment of acne vulgaris: Two double-blind comparisons with tretinoin 0.01% gel. 1992. Advances in Therapy | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes |

| Reference | Reason for exclusion |
|---|---|
| | were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Leyden, J. G., G. L.Randomized facial tolerability studies comparing gel formulations of retinoids used to treat acne vulgaris. 2001. Cutis; cutaneous medicine for the practitioner | No relevant study population - participants did not have acne |
| Leyden, J. J. B., R. S.,Dunlap, F. E.,Ellis, C. N.,Connolly, M. A.,Levy, S. F.Comparison of the efficacy and safety of a combination topical gel formulation of benzoyl peroxide and clindamycin with benzoyl peroxide, clindamycin and vehicle gel in the treatments of acne vulgaris. 2001. American Journal of Clinical Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Leyden, J. J. G., E. H.Evaluation of the antimicrobial effects in vivo of Triaz Gel (benzoyl peroxide special gel), Cleocin-T Lotion (clindamycin phosphate lotion), and Azelex Cream (azelaic acid cream) in humans. 1997. Journal of Dermatological Treatment | No relevant outcomes reported - bacterial counts |
| Leyden, J. J. G., R.,Nighland, M.Cumulative irritation potential of topical retinoid formulations. 2008. Journal of drugs in dermatology : JDD | No relevant study population - participants did not have acne |
| Leyden, J. J. H., J. G.,Jarratt, M. T.,Stewart, D. M.,Levy, S. F.The efficacy and safety of a combination benzoyl peroxide/clindamycin topical gel compared with benzoyl peroxide alone and a benzoyl peroxide/erythromycin combination product. 2001. Journal of Cutaneous Medicine and Surgery | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Leyden, J. J. K., L.,Yaroshinsky, A.Two randomized, double-blind, controlled trials of 2219 subjects to compare the combination clindamycin/tretinoin hydrogel with each agent alone and vehicle for the treatment of acne vulgaris. 2006. Journal of the American Academy of Dermatology | No relevant data reported - study reports combined results of 2 RCTs |
| Leyden, J. J. N., M.,Rossi, A. B.,Ramaswamy, R.Irritation potential of tretinoin gel microsphere pump versus adapalene plus benzoyl peroxide gel. 2010. Journal of Drugs in Dermatology | No relevant study population - participants did not have acne |
| Leyden, J. J. T., E. A.,Miller, B.,Ung, M.,Berson, D.,Lee, J.Once-daily tazarotene 0.1 % gel versus once-daily tretinoin 0.1 % microsponge gel for the treatment of facial acne vulgaris: a double-blind randomized trial. 2002. Cutis; cutaneous medicine for the practitioner | Not obtainable |
| Leyden, J. J. W., M.A novel gel formulation of clindamycin phosphate-tretinoin is not associated with acne flaring. 2008. Cutis | No relevant outcomes reported - reports 2-wk treatment-related flaring outcomes of 12-week RCT reported in Schlessinger 2007 |
| Leyden, J. J.Topical treatment for the inflamed lesion in acne, rosacea, and pseudofolliculitis barbae. 2004. Cutis | No relevant article type - introduction to supplement |
| Leyden, J. W., M.,Baldwin, E. K.Tolerability of clindamycin/tretinoin gel vs. tretinoin microsphere gel and adapalene gel. 2009. Journal of Drugs in Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |

| Reference | Reason for exclusion |
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| Leyden, J., Levy, S.The development of antibiotic resistance in Propionibacterium acnes. 2001. Cutis | Not reported how many people were randomised in each arm; no tables available; also the outcome is bacteria counts which is not relevant |
| Li,Effects of Qingfei Liangxue Fa on sebum excretion rate and free fatty acid of patients with acne vulgaris. 2004. NA | No relevant intervention - complementary therapy |
| Liani, L. P., J. S.Evaluation of topical erythromycin and topical lactate with or without systemic ketoconazole in acne vulgaris. 1992. Indian journal of dermatology, venereology and leprology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Liddell, K.Benzoyl peroxide gel in the treatment of acne vulgaris. 1974. British Journal of Clinical Practice | Not obtainable |
| Lihong, S.He-Ne laser auricular irradiation plus body acupuncture for treatment of acne vulgaris in 36 cases. 2006. Journal of Traditional Chinese Medicine | No relevant intervention - laser plus acupuncture |
| Lim, C. C. P., D. G. C.,Adamson, J.A sustained release tetracycline preparation in acne vulgaris. 1974. Practitioner | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Lim, S. K. H., J. M.,Lee, Y. H.,Lee, Y.,Seo, Y. J.,Kim, C. D.,Lee, J. H.,Im, M.Comparison of Vitamin D Levels in Patients with and without Acne: a Case-Control Study Combined with a Randomized Controlled Trial. 2016. PloS one | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Lin, Z. R. Z., W.,You, S. F.,Xiao, Y.Clinical observation on pricking blood and acupoint injection in treating acne. 2016. Western journal of traditional chinese medicine [xi bu zhong yi yao za zhi] | Not in English language |
| Liu, H., Yu, H., Xia, J., Liu, L., Liu, G. J., Sang, H., Peinemann, F.Topical azelaic acid, salicylic acid, nicotinamide, sulphur, zinc and fruit acid (alphaÃ¢Â€Â□hydroxy acid) for acne. 2020. Cochrane Database of Systematic Reviews | Systematic review - references were checked for relevance |
| Liu, L. H. F., X.,An, Y. X.,Zhang, J.,Wang, C. M.,Yang, R. Y.Randomized trial of three phototherapy methods for the treatment of acne vulgaris in chinese patients. 2014. Photodermatology Photoimmunology and Photomedicine | No relevant outcome data reported - interventions provided until >90% improvement observed in participants |
| Lookingbill, D. P. A., B. B.,Ellis, C. N.,Jegasothy, B. V.,Lucky, A. W.,Ortiz- Ferrer, L. C.,Savin, R. C.,Shupack, J. L.,Stiller, M. J.,Zone, J. J.,Landis, J. R.,Ramaswamy, R.,Cherill, R. J.,Pochi, P. E.Inocoterone and acne: The effect of a topical antiandrogen: Results of a multicenter clinical trial. 1992. Archives of Dermatology | No relevant intervention - never marketed |
| Lookingbill, D. P. C., D. K.,Lindholm, J. S.,Katz, H. I.,Kempers, S. E.,Huerter, C. J.,Swinehart, J. M.,Schelling, D. J.,Klauda, H. C.Treatment of acne with a combination clindamycin/benzoyl peroxide gel compared with clindamycin gel, benzoyl peroxide gel and vehicle gel: Combined results of two double-blind investigations. 1997. | No relevant intervention - never marketed |

| Reference | Reason for exclusion |
|---|---|
| Journal of the American Academy of Dermatology | |
| Lu, J. L., Z.Acupuncture combined with cupping and circling moxibustion for 40 cases of acne. 2018. World Journal of Acupuncture - Moxibustion | No relevant intervention - acupuncture-cupping |
| Lubtikulthum, P. K., N.,Udompataikul, M.A comparative study on the effectiveness of herbal extracts vs 2.5% benzoyl peroxide in the treatment of mild to moderate acne vulgaris. 2019. Journal of Cosmetic Dermatology. | No relevant intervention - topical herbal extract |
| Lucky, A. W. C., S. I.,Funicella, T.,Jarratt, M. T.,Jones, T.,Reddick, M. E.Double-blind, vehicle-controlled, multicenter comparison of two 0.025% tretinoin creams in patients with acne vulgaris. 1998a. Journal of the American Academy of Dermatology | Outcomes reported in figures only |
| Lucky, A. W. C., S. I.,Jarratt, M. T.,Quigley, J. W.Comparative efficacy and safety of two 0.025% tretinoin gels: Results from a multicenter, double-blind, parallel study. 1998b. Journal of the American Academy of Dermatology | Outcomes reported in figures only |
| Lucky, A. W. H., T. A.,Olson, W. H.,Robisch, D. M.,Lebwohl, M.,Swinyer, L. J.Effectiveness of norgestimate and ethinyl estradiol in treating moderate acne vulgaris. 1997. Journal of the American Academy of Dermatology | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Lucky, A. W. K., W.,Thiboutot, D.,Niknian, M.,Sampson-Landers, C.,Korner, P.,Marr, J.A combined oral contraceptive containing 3-mg drospirenone/20-mug ethinyl estradiol in the treatment of acne vulgaris: A randomized, double-blind, placebo-controlled study evaluating lesion counts and participant self-assessment. 2008. Cutis | Outcomes reported in figures only |
| Lucky, A. W. M., J. M.,Roberts, J.,Taylor, S.,Jones, T.,Ling, M.,Garrett, S.Dapsone gel 5% for the treatment of acne vulgaris: safety and efficacy of long-term (1 year) treatment. 2007. Journal of drugs in dermatology : JDD | No relevant study design - not RCT |
| Lucky, A. W. S., J.Comparison of micronized tretinoin gel 0.05% and tretinoin gel microsphere 0.1% in young adolescents with acne: A post hoc analysis of efficacy and tolerability data. 2011. Cutis | Outcomes reported in figures only |
| Lueangarun, S. S., K.,Tempark, T.,Managit, C.,Sithisarn, P.Clinical efficacy of 0.5% topical mangosteen extract in nanoparticle loaded gel in treatment of mild-to-moderate acne vulgaris: A 12-week, split-face, double-blinded, randomized, controlled trial. 2019. Journal of Cosmetic Dermatology. | Non relevant intervention – alpha-mangostin |
| Lyons, R. E.Comparative effectiveness of benzoyl peroxide and tretinoin in acne vulgaris. 1978. International Journal of Dermatology | No relevant study population - insufficient details reported to determine severity of acne |
| Ma, L. X., L. H.,Yu, B.,Yin, R.,Chen, L.,Wu, Y.,Tan, Z. J.,Liu, Y. B.,Tian, H. Q.,Li, H. Z.,Lin, T.,Wang, X. L.,Li, Y. H.,Wang, W. Z.,Yang, H. L.,Lai, W.Low-dose topical 5-aminolevulinic acid photodynamic therapy in the treatment of different severity of acne vulgaris. 2013. Photodiagnosis and Photodynamic Therapy | No relevant study design - not RCT |
| Ma, X. H. Z., S. L.,Zhou, G. M.Clinical observation on treatment of female delayed acne vulgaris with qingre cuochuang tablet. 2004. Zhongguo zhong xi yi jie he za zhi zhongguo zhongxiyi jiehe zazhi = chinese journal of integrated traditional and western medicine | Not in English language |
| Ma, Y. L., Y.,Wang, Q.,Ren, J.,Xiang, L.Prospective study of topical 5- | No relevant study deisgn - |

| Reference | Reason for exclusion |
|---|---|
| aminolevulinic acid photodynamic therapy for the treatment of severe adolescent acne in Chinese patients. 2015. Journal of Dermatology | not RCT |
| MacDonald, R. H. M., H.,Ray, S. K.Clinical trial of Actinac in acne. 1976. British Journal of Clinical Practice | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Mackey, J. P.A small double-blind trial of an anovulant agent in acne vulgaris. 1975. Irish Medical Journal | No relevant study design - not RCT |
| Magin,Topical and oral CAM in acne: A review of the empirical evidence and a consideration of its context. 2006. NA | No relevant intervention - systematic review about complementary and alternative medicines for acne |
| Mahran, H. G., Drbala, K. M.Efficacy of twelve sessions of 905nm infrared laser on acne vulgaris. 2019. Annals of Clinical and Analytical Medicine | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Maiti, R. S., C. S.,Ashique Rahman, M. A.,Srinivasan, A.,Parida, S.,Hota, D.Efficacy and Safety of Tazarotene 0.1% Plus Clindamycin 1% Gel Versus Adapalene 0.1% Plus Clindamycin 1% Gel in Facial Acne Vulgaris: A Randomized, Controlled Clinical Trial. 2017. Clinical Drug Investigation | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Maloney, J. M. A., D. I.,Flack, M.,McLaughlin-Miley, C.,Sevilla, C.,Derman, R.Use of a low-dose oral contraceptive containing norethindrone acetate and ethinyl estradiol in the treatment of moderate acne vulgaris. 2001. Clinical journal of women's health | Not obtainable |
| Maloney, J. M. D. J., P.,Watson, D.,Niknian, M.,Lee-Rugh, S.,Sampson-Landers, C.,Korner, P.A randomized controlled trial of a low-dose combined oral contraceptive containing 3 mg drospirenone plus 20 mug ethinylestradiol in the treatment of acne vulgaris: Lesion counts, investigator ratings and subject self-assessment. 2009a. Journal of Drugs in Dermatology | Duplicate record |
| Maloney, J. M. D., P., Jr.,Watson, D.,Niknian, M.,Lee-Rugh, S.,Sampson-Landers, C.,Korner, P.A randomized controlled trial of a low-dose combined oral contraceptive containing 3 mg drospirenone plus 20 microg ethinylestradiol in the treatment of acne vulgaris: lesion counts, investigator ratings and subject self-assessment. 2009b. Journal of Drugs in Dermatology: JDD | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Maloney, J. M. D., P.,Watson, D.,Niknian, M.,Lee-Rugh, S.,Sampson-Landers, C.,Korner, P.Treatment of acne using A 3-milligram drospirenone/20-microgram ethinyl estradiol oral contraceptive administered in a 24/4 regimen: A randomized controlled trial. 2008. Obstetrics and Gynecology | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to- |

| Reference | Reason for exclusion |
|---|---|
| | severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Mandekou-Lefaki, I. D., F.,Teknetzis, A.,Euthimiadou, R.,Karakatsanis, G.Low-dose schema of isotretinoin in acne vulgaris. 2003. International Journal of Clinical Pharmacology Research | No relevant study design - not RCT |
| Mandy, S.A.A comparison of the efficacy and safety of tretinoin cream 0.025% and 0.05%. 1990. Advances in Therapy | No relevant data reported - post hoc analysis of non-randomised comparison of 2 RCTs |
| Mandy, S.Tretinoin in acne vulgaris. 1975. Modern Problems in Paediatrics | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Mango, D. R., S.,Manna, P.,Miggiano, G. A.,Serra, G. B.Clinical and hormonal effects of ethinylestradiol combined with gestodene and desogestrel in young women with acne vulgaris. 1996. Contraception | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Mansour, D. V., C.,Sommer, W.,Weisberg, E.,Taneepanichskul, S.,Melis, G. B.,SundstrÃ¶m-Poromaa, I.,Korver, T.Efficacy and tolerability of a monophasic combined oral contraceptive containing nomegestrol acetate and 17Î²-oestradiol in a 24/4 regimen, in comparison to an oral contraceptive containing ethinylestradiol and drospirenone in a 21/7 regimen. 2011b. European journal of contraception & reproductive health care | Duplicate record |
| Mansour, D. V., C.,Sommer, W.,Weisberg, E.,Taneepanichskul, S.,Melis, G. B.,Sundstrom-Poromaa, I.,Korver, T.Efficacy and tolerability of a monophasic combined oral contraceptive containing nomegestrol acetate and 17beta-oestradiol in a 24/4 regimen, in comparison to an oral contraceptive containing ethinylestradiol and drospirenone in a 21/7 regimen. 2011a. European Journal of Contraception and Reproductive Health Care | No relevant study population - participants did not have acne |
| Mansurul, A. M. I., A. Z. M.Effect of spironolactone on acne vulgaris - A double blind study. 2000. Bangladesh Journal of Dermatology, Venereology and Leprology | Not obtainable |
| Marazzi, P. B., G.,Donald, A.,Davies, H.Clinical evaluation of Double Strength IsotrexinTM versus Benzamycin in the topical treatment of mild to moderate acne vulgaris. 2002b. Journal of Dermatological Treatment | Duplicate record |
| Marcinkiewicz, J. W.-P., A.,Walczewska, M.,Lipko-Godlewska, S.,Jachowicz, R.,Maciejewska, A.,Bialecka, A.,Kasprowicz, A.Topical taurine bromamine, a new candidate in the treatment of moderate inflammatory acne vulgaris: a pilot study. 2008. European Journal of Dermatology | No relevant intervention - taurine bromaminenot available in the UK |
| Marcinkiewicz, J.Taurine bromamine: a new therapeutic option in inflammatory skin diseases. 2009. Polskie Archiwum Medycyny Wewnetrznej | No relevant study design - not RCT |
| Marczyk, B. M., P.,Budzisz, E.,Rotsztejn, H.Comparative study of the effect of 50% pyruvic and 30% salicylic peels on the skin lipid film in | No relevant data reported - sebum secretion study |

| Reference | Reason for exclusion |
|---|---|
| patients with acne vulgaris. 2014. Journal of Cosmetic Dermatology | |
| Mareledwane, N. G.A randomized, open-label, comparative study of oral doxycycline 100 mg vs. 5% topical benzoyl peroxide in the treatment of mild to moderate acne vulgaris. 2006. International Journal of Dermatology | No relevant data reported |
| Marous, Mr.R., Flaten, H.K., Sledge, B., Rietcheck, H.R., Dellavalle, R., Suneja, T., Dunnick, C.Complementary and Alternative Methods for Treatment of Acne Vulgaris: a Systematic Review. 2018. Current Dermatology Reports | No relevant intervention - systematic review about complementary and alternative medicines for acne |
| Marron, S. E. T.-A., L.,Boira, S. Anxiety, depression, quality of life and patient satisfaction in acne patients treated with oral isotretinoin. 2013. Acta Dermato-Venereologica | No relevant study design - not RCT |
| Marsden, J. R. L., M. F.,Ford, G. P.,Shuster, S.Effect of low dose cyproterone acetate on the response of acne to isotretinoin. 1984. British Journal of Dermatology | No relevant study design - not RCT |
| Matsunaga, K. L., Y. H.,Chan, R.,Kerrouche, N.,Paliargues, F.Adjunctive usage of a non-comedogenic moisturizer with adapalene gel 0.1% improves local tolerance: A randomized, investigator-blinded, split-face study in healthy Asian subjects. 2013. Journal of Dermatological Treatment | No relevant study population – participants did not have acne |
| Mazzarello, V. D., M. G.,Ferrari, M.,Piga, G.,Usai, D.,Zanetti, S.,Sotgiu, M. A.Treatment of acne with a combination of propolis, tea tree oil, and aloe vera compared to erythromycin cream: Two double-blind investigations. 2018. Clinical Pharmacology: Advances and Applications | No relevant intervention - a cream based on three natural extracts vs 3% erythromycin cream vs placebo cream but no useful data for comparison of erythromycin cream and placebo reported |
| Mazzarello, V., Gavini, E., Rassu, G., Donadu, M. G., Usai, D., Piu, G., Pomponi, V., Sucato, F., Zanetti, S., Montesu, M. A. Clinical Assessment of New Topical Cream Containing Two Essential Oils Combined with Tretinoin in the Treatment of Acne. 2020. Clinical, Cosmetic and Investigational Dermatology CCIDClin Cosmet Investig Dermatol | No relevant intervention - a galenic compound containing 2 essential oils (Myrtus communis L. and Origanum vulgare) |
| Mazzetti, A. M., L.,Gerloni, M.,Cartwright, M.A Phase 2b, Randomized, Double-Blind Vehicle Controlled, Dose Escalation Study Evaluating Clascoterone 0.1%, 0.5%, and 1% Topical Cream in Subjects With Facial Acne. 2019. Journal of drugs in dermatology : JDD | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Mazzetti, A., Moro, L., Gerloni, M., Cartwright, M.Pharmacokinetic Profile, Safety, and Tolerability of Clascoterone (Cortexolone 17-alpha propionate, CB-03-01) Topical Cream, 1% in Subjects With Acne Vulgaris: An Open-Label Phase 2a Study. 2019. Journal of Drugs in Dermatology: JDDJ Drugs Dermatol | Not obtainable |
| McGillis, T. J. R., M. J.,Reisner, R. M.,Sternberg, T. H.,Stirling, N. C.,Winer, L. H.Topical Vitamin A Acid in the Management of Comedo Acne. 1971. Cutis; cutaneous medicine for the practitioner | Not obtainable |
| McHugh, R. C. R., A.,Sangha, N. D.,McCarty, M. A.,Utterback, R.,Rohrback, J. M.,Osborne, B. E.,Fleischer, A. B., Jr.,Feldman, S. R.A topical azithromycin preparation for the treatment of acne vulgaris and rosacea. 2004. Journal of Dermatological Treatment | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory |

| Reference | Reason for exclusion |
|---|---|
| | treatments |
| McKenzie, M. W. B., D. C.,Popovich, N. G.Topical clindamycin formulations for the treatment of acne vulgaris. An evaluation. 1981. Archives of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Mehran, G., Sepasgozar, S., Rohaninasab, M., Goodarzi, A., Ghassemi, M., Fotooei, M., Behrangi, E.Comparison between the therapeutic effect of microneedling versus tretinoin in patients with comedonal acne: A randomized clinical trial. 2019. Iranian Journal of Dermatology | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Meigel, W. G., H.,Wokalek, H.Oral treatment of acne conglobata with isotretinoin. Results of the German Multicenter Study. 1983. Der hautarzt; zeitschrift fur dermatologie, venerologie, und verwandte gebiete | Not in English language |
| Merkviladze, N. G., T.,Tushurashvili, P.,Ekaladze, E.,Jojua, N.The efficacy of topical drugs in treatment of noninflammatory acne vulgaris. 2010. Georgian Medical News | No relevant study design - not RCT |
| Merritt, B. B., C. N.,Morrell, D. S.Use of isotretinoin for acne vulgaris. 2009. Pediatric Annals | No relevant study design - not RCT |
| Michaelsson, G. J., L.,Ljunghall, K.A double-blind study of the effect of zinc and oxytetracycline in acne vulgaris. 1977a. British Journal of Dermatology | No relevant comparison - compares oral zinc and tetracyclines |
| Michaelsson, G. J., L.,Vahlquist, A.Effects of oral zinc and vitamin A in acne. 1977b. Archives of Dermatology | No relevant comparison - compares oral zinc sulfate alone and in combination with vitamin A |
| Michaelsson, G.Oral zinc in acne. 1980. Acta dermato-venereologica | No relevant article type - non-systematic review |
| Mikhael, E. M. M., M. Y. Evaluation of the effect of topical atorvastatin solution for the treatment of papulopustular acne. 2013. International Journal of Current Pharmaceutical Research | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Milikan, L. E.A double-blind study of Betadine skin cleanser in acne vulgaris. 1976. Cutis | No relevant intervention - Betadine skin cleanser |
| Miller, J. A. J., H. S.T reatment of hirsutism and acne with cyproterone acetate. 1986a. Clinics in Endocrinology & Metabolism | No relevant article type - non-systematic review |
| Miller, S. T. S., J. J.Low-dose doxycycline moderately effective for acne. 2003. Journal of Family Practice | No relevant study design - not RCT |
| Millikan, L. E. A., R.Use of Buf-Puf and benzoyl peroxide in the treatment of acne. 1981. Cutis | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Mills Jr, O. H. M., R. R.,Kligman, A. M.Acne vulgaris. Oral therapy with tetracycline and topical therapy with vitamin A. 1972. Archives of dermatology | No relevant data - insufficient data reported |

| Reference | Reason for exclusion |
|---|---|
| Mills Jr, O. T., C.,Cardin, C. W.,Smiles, K. A.,Leyden, J. J.Bacterial resistance and therapeutic outcome following three months of topical acne therapy with 2% erythromycin gel versus its vehicle. 2002. Acta Dermato-Venereologica | Outcomes reported in figures only |
| Mills, O. H., Jr.,Kligman, A. M.Treatment of acne vulgaris with topically applied erythromycin and tretinoin. 1978. Acta Dermato-Venereologica | No relevant study design - not RCT |
| Min, S. P., S. Y.,Yoon, J. Y.,Suh, D. H.Comparison of fractional microneedling radiofrequency and bipolar radiofrequency on acne and acne scar and investigation of mechanism: comparative randomized controlled clinical trial. 2015. Archives of Dermatological Research | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Mirnezami, M. R., H.Is Oral Omega-3 Effective in Reducing Mucocutaneous Side Effects of Isotretinoin in Patients with Acne Vulgaris?. 2018. Dermatology Research and Practice | No relevant intervention - oral omega-3 |
| Mitra, A. S., G. I.Topical photodynamic therapy for non-cancerous skin conditions. 2006. Photodiagnosis and Photodynamic Therapy | Duplicate record |
| Miyachi, Y. M., F.,Mita, T.,Bai, L.,Ikoma, A.Efficacy and safety of a fixed dose combination gel of adapalene 0.1% and benzoyl peroxide 2.5% in Japanese patients with acne vulgaris-a multicenter, randomzed, double-blinded, active-controlled, parallel group phase III study. 2016. Skin research | Not English language |
| Mobacken, H. H., K.Topical treatment of acne vulgaris with clindamycin. 1985. Lakartidningen | Not in English language |
| Moftah, N. H. I., S. M.,Wahba, N. H.Intense pulsed light versus photodynamic therapy using liposomal methylene blue gel for the treatment of truncal acne vulgaris: a comparative randomized split body study. 2016. Archives of Dermatological Research | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Mohammadi, S. F., S.,Pardakhty, A.,Khalili, M.,Mohebbi, A.,Yousefian, M. R.,Aflatoonian, M.A survey to compare the efficacy of niosomal erythromycin alone versus combination of erythromycin and zinc acetate in the treatment of acne vulgaris. 2017. Journal of Kerman University of Medical Sciences | Outcomes reported in figures only |
| Mohan Kumar, P., Savitha, A. K., Suthanthira Kannan, S. To compare the side effect profile of azithromycin pulse therapy with doxycycline in acne vulgaris treatment: An open labelled, randomised, parallel group, hospital based study. 2019. Indian Journal of Public Health Research and Development | No relevant study population - sample includes participants with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Mokhtari, F. F., G.,Basiri, A.,Farhadi, S.,Nilforoushzadeh, M.,Behfar, S.Comparison effect of azithromycin gel 2% with clindamycin gel 1% in patients with acne. 2016. Advanced Biomedical Research | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and |

| Reference | Reason for exclusion |
|---|---|
| | refractory treatments |
| Mokhtari, F., Shajari, A., Iraji, F., Faghihi, G., Siadat, A. H., Sadeghian, G., Adibi, N.The effectiveness of adapalene 0.1% with intense pulsed light versus benzoyl peroxide 5% with intense pulsed light in the treatment of acne vulgaris: A comparative study. 2019. Journal of Research in Medical SciencesJ | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Moltz, L. K., E.Medium dose oral cyproterone acetate therapy in women with moderate hyperandrogenism. 1984. Geburtshilfe und frauenheilkunde | Not in English language |
| Moneib, H. T., A. A.,Youssef, S. S.,Fawzy, M. M.Randomized split-face controlled study to evaluate 1550-nm fractionated erbium glass laser for treatment of acne vulgaris-an image analysis evaluation. 2014. Dermatologic Surgery | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Monib, K. M. E. D., Hussein, M. S.Nd:YAG laser vs IPL in inflammatory and noninflammatory acne lesion treatment. 2019. Journal of Cosmetic Dermatology. | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Monk, B. E. A., J. A.,Caldwell, I. W.,Green, B.,Pelta, D.,Leonard, J.,Du Vivier, A.,Johnson, K.,Tolowinska, I.Efficacy of low-dose cyproterone acetate compared with minocycline in the treatment of acne vulgaris. 1987. Clinical & Experimental Dermatology | No relevant intervention - suboptimal dose of minocycline only taken for 21 days each month |
| Montes, L. F.Acne vulgaris: treatment with topical benzoyl peroxide acetone gel. 1977. Cutis | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Moore, C. L., C.,Moltz, L.,Oettel, M.,Klinger, G.,Schreiber, G.Antiandrogenic properties of the dienogest-containing oral contraceptive Valette. 1999. Drugs of Today | Not obtainable |
| Moravvej, H. H., A. M.,Yousefi, M.,Givrad, S.Efficacy of doxycycline versus azithromycin in the treatment of moderate facial acne vulgaris. 2012. Iranian Journal of Dermatology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Morel, P. V., M. P.,Beylot, C.,Bonerandi, J. J.,Dreno, B.,Lehucher-Ceyrac, D.,Slimani, S.,Dupuy, P.Clinical efficacy and safety of a | No relevant intervention - topical retinaldehyde gel |

| Reference | Reason for exclusion |
|---|---|
| topical combination of retinaldehyde 0.1% with erythromycin 4% in acne vulgaris. 1999. Clinical and Experimental Dermatology | |
| Morganti, P. B., E.,Guarneri, B.,Guarneri, F.,Fabrizi, G.,Palombo, P.,Palombo, M.Topical clindamycin 1% vs. linoleic acid-rich phosphatidylcholine and nicotinamide 4% in the treatment of acne: A multicentre-randomized trial. 2011. International Journal of Cosmetic Science | No relevant data reported |
| Morganti, P. R., S. D.,Bruno, C.,Cardillo, A.Ethyl lactate and benzoyl peroxide in acne vulgaris. 1988. Journal of Applied Cosmetology | No relevant study population - insufficient details to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Mugglestone, C. J. R., E. L.The treatment of acne with an anti-androgen/oestrogen combination. 1982. Clinical & Experimental Dermatology | Dosage of tetracycline lower than BNF value |
| Muhlemann, M. F. C., G. D.,Cream, J. J.,Wise, P.Oral spironolactone: An effective treatment for acne vulgaris in women. 1986. British Journal of Dermatology | No relevant data reported - randomised cross-over trial, data for first phase not reported separately from data from second phase |
| Murff, H. J.Combination therapies are more effective than monotherapy for mild to moderate acne. 2008. Journal of Clinical Outcomes Management | No relevant article type - commentary on an RCT |
| Naieni, F. F. A., H.Comparison of three different regimens of oral azithromycin in the treatment of acne vulgaris. 2012. Journal of isfahan medical school | Not in English language |
| Nandimath, M. K. R., N. B.Comparision of clinical efficacy of topical clindamycin with adapalene and adapalene alone in treatment of mild to moderate facial acne vulgaris. 2013. International Journal of Pharma and Bio Sciences | Not obtainable |
| Narurkar, V. A. B., K. R.,Cohen, J. L.An open-label trial examining the efficacy and safety of a pre- and postprocedure topical five-product system (Clinique Medical Optimizing Regimen) specifically formulated to complement laser/light-based facial cosmetic procedures. 2010. Journal of Cosmetic & Laser Therapy | No relevant study population - participants scheduled to undergo facial physical treatment cosmetic procedure |
| Nelson, R. M. R., A. E.Hirsutism and acne treated by an androgen antagonist. 1970. Obstetrics & Gynecology | No relevant study design - not RCT |
| Ng, C. H. T., M. M.,Celi, E.,Tate, B.,Schweitzer, I.Prospective study of depressive symptoms and quality of life in acne vulgaris patients treated with isotretinoin compared to antibiotic and topical therapy. 2002. Australasian Journal of Dermatology | No relevant study design - not RCT |
| Ng, P. P. G., C. L.Treatment outcome of acne vulgaris with oral isotretinoin in 89 patients. 1999. International Journal of Dermatology | No relevant study design - not RCT |
| Niazi, S. S., A.Comparison of efficacy of fixed low-dose regimens (daily vs alternate day) of oral isotretinoin in mild to moderate acne vulgaris. 2015. Journal of Pakistan Association of Dermatologists | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |

| Reference | Reason for exclusion |
|---|---|
| Nicklas, C. R., R.,Cardenas, C.,Hasson, A.Comparison of efficacy of aminolaevulinic acid photodynamic therapy vs. adapalene gel plus oral doxycycline for treatment of moderate acne vulgaris-A simple, blind, randomized, and controlled trial. 2018. Photodermatology photoimmunology and photomedicine | Duplicate record |
| Nielsen, P. G.Treatment of female acne vulgaris with a cream containing the antiandrogen canrenone. 1983. Dermatologica | No relevant article type - letter to editor |
| Nighland, M. G., R.Tretinoin microsphere gel in facial acne vulgaris: a meta-analysis. 2008. Journal of drugs in dermatology : JDD | No relevant data reported - reports pooled results from 3 trials combined |
| NilFroushzadeh, M. A. S., 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. 2009. Indian journal of dermatology, venereology and leprology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Niren, N. M. T., H. M.The Nicomide Improvement in Clinical Outcomes Study (NICOS): results of an 8-week trial. 2006. Cutis | No relevant study design - not RCT |
| Nitzan, Y. B. C., A. D.Zinc in skin pathology and care. 2006. Journal of Dermatological Treatment | Duplicate record |
| Nofal, E. N., A.,Gharib, K.,Nasr, M.,Abdelshafy, A.,Elsaid, E.Combination chemical peels are more effective than single chemical peel in treatment of mild-to-moderate acne vulgaris: A split face comparative clinical trial. 2018. Journal of Cosmetic Dermatology | No relevant study design - not RCT |
| Nordin, K. F., T.,Rylander, C.Ro 11-1430, a new retinoic acid derivative for the topical treatment of acne. 1981. Dermatologica | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Norris, J. F. H., B. R.,Basey, A. J.,Cunliffe, W. J.A comparison of the effectiveness of topical tetracycline, benzoyl-peroxide gel and oral oxytetracycline in the treatment of acne. 1991. Clinical & Experimental Dermatology | No relevant intervention - topical tetracycline and 250 mg of oral oxytetracycline |
| Nyirady, J. G., R. M.,Nighland, M.,Berger, R. S.,Jorizzo, J. L.,Kim, Y. H.,Martin, A. G.,Pandya, A. G.,Schulz, K. K.,Strauss, J. S.A comparative trial of two retinoids commonly used in the treatment of acne vulgaris. 2001. Journal of Dermatological Treatment | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Nyirady, J. N., M.,Payonk, G.,Pote, J.,Phillips, S.,Grossman, R.A comparative evaluation of tretinoin gel microsphere, 0.1%, versus tretinoin cream, 0.025%, in reducing facial shine. 2000. Cutis; cutaneous medicine for the practitioner | No relevant study population - sample includes people with facial oiliness |
| Ochsendorf, F.Clindamycin phosphate 1.2% / tretinoin 0.025%: a novel fixed-dose combination treatment for acne vulgaris. 2015. Journal of the European Academy of Dermatology & Venereology | No relevant study design - not RCT |
| Oh, S. H. R., D. J.,Han, E. C.,Lee, K. H.,Lee, J. H.A comparative study of topical 5-aminolevulinic acid incubation times in photodynamic therapy with intense pulsed light for the treatment of | Split face study - but randomised treatments not compared directly in the |

| Reference | Reason for exclusion |
|---|---|
| inflammatory acne. 2009. Dermatologic Surgery | same participants. |
| Olafsson, J. H. G., J.,Eggertsdottir, G. E.,Kristjansson, F.Doxycycline versus minocycline in the treatment of acne vulgaris: A double-blind study. 1989. Journal of Dermatological Treatment | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Olivier, S. D., A.,Bierschwale, H.,Archer, D.Efficacy of a low-dose oral contraceptive (20mcg ethinyl estradiol/100 mcg levonorgestrel) for the treatment of moderate acne. 2003. International journal of obstetrics & gynecology | No relevant article type - conference abstract |
| Olson, W. H. L., J. S.,Robisch, D. M.The duration of response to norgestimate and ethinyl estradiol in the treatment of acne vulgaris. 1998. International Journal of Fertility and Women's Medicine | No relevant data reported - reports combined results from Redmond 1997 and Lucky 1997 trials |
| Oprica, C. E., L.,Hagstromer, L.,Nord, C. E.Clinical and microbiological comparisons of isotretinoin vs. tetracycline in acne vulgaris. 2007. Acta Dermato-Venereologica | No relevant data - insufficient data reported |
| Orafidiya, L. O. A., E. O.,Oyedele, A. O.,Babalola, O. O.,Onayemi, O.Preliminary clinical tests on topical preparations of Ocimum gratissimum linn leaf essential oil for the treatment of acne vulgaris. 2002. Clinical Drug Investigation | No relevant study population - no information about severity of acne reported and study is not relevant for PCOS, maintenance or refractory treatments |
| Orafidiya,The effect of aloe vera gel on the anti-acne properties of the essential oil of Ocimum gratissimum Linn leaf - A preliminary clinical investigation. 2004. NA | No relevant intervention - Ocimum oil lotion and aloe gel |
| Orringer, J. S. K., S.,Hamilton, T.,Schumacher, W.,Cho, S.,Hammerberg, C.,Fisher, G. J.,Karimipour, D. J.,Johnson, T. M.,Voorhees, J. J.Treatment of acne vulgaris with a pulsed dye laser: A randomized controlled trial. 2004. Journal of the American Medical Association | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Orringer, J. S. K., S.,Maier, L.,Johnson, T. M.,Sachs, D. L.,Karimipour, D. J.,Helfrich, Y. R.,Hamilton, T.,Voorhees, J. J.A randomized, controlled, split-face clinical trial of 1320-nm Nd:YAG laser therapy in the treatment of acne vulgaris. 2007. Journal of the American Academy of Dermatology | No relevant study population - sample includes people mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Orringer, J. S. S., D. L.,Bailey, E.,Kang, S.,Hamilton, T.,Voorhees, J. J.Photodynamic therapy for acne vulgaris: A randomized, controlled, split-face clinical trial of topical aminolevulinic acid and pulsed dye laser therapy. 2010. Journal of Cosmetic Dermatology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Owens, D. W.Clinical evaluation of topical vitamin A acid in therapy of | No relevant study |

| Reference | Reason for exclusion |
|---|---|
| acne vulgaris. 1973. Texas Medicine | population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Ozgen, Z. Y. G., 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. 2013. Marmara Medical Journal | No relevant intervention - nadifloxacin 1% cream not available in the UK |
| Ozkan, M. D., G.,Sabuncu, I.,Saracoglu, N.,Akgun, Y.,Urer, S. M.Clinical efficacy of topical clindamycin phosphate and azelaic acid on acne vulgaris and emergence of resistant coagulase-negative staphylococci. 2000. Turkish Journal of Medical Sciences | Duplicate record |
| Ozolins, M. E., E. A.,Avery, A.,Cunliffe, W. J.,O'Neill, C.,Simpson, N. B.,Williams, H. C.Randomised controlled multiple treatment comparison to provide a cost-effectiveness rationale for the selection of antimicrobial therapy in acne. 2005. Health technology assessment (Winchester, England) | No relevant article type - executive summary of Ozolins 2004 trial |
| PÃ©rez LÃ³pez, M. M. V., J. M.A new salt of erythromycin (A-137 or erythromycin lauryl sulfate) in the topical treatment of acne. 1982. Medicina cutanea ibero-latino-americana | Not in English language |
| Packman, A. M. B., R. H.,Dunlap, F. E.,Kraus, S. J.,Webster, G. F.Treatment of acne vulgaris: Combination of 3% erythromycin and 5% benzoyl peroxide in a gel compared to clindamycin phosphate lotion. 1996. International Journal of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Padilla, R. S. M., J. M.,Becker, L. E.Topical tetracycline hydrochloride vs. topical clindamycin phosphate in the treatment of acne: a comparative study. 1981. International Journal of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Pai, I. F. W., Y. C.,Lu, Y. C.Clinical trial of cyproterone acetate-ethinyl oestradiol compound on androgen dependent skin disorders. 1982. Taiwan i Hsueh Hui Tsa Chih - Journal of the Formosan Medical Association | Not in English language |
| Palacios, S. W., L.,Parke, S.,Machlitt, A.,Romer, T.,Bitzer, J.Efficacy and safety of a novel oral contraceptive based on oestradiol (oestradiol valerate/dienogest): A Phase III trial. 2010. European Journal of Obstetrics and Gynecology and Reproductive Biology | No relevant study population - participants did not have acne |
| Palatsi, R. H., E.,Liukko, P.,Malmiharju, T.,Mattila, L.,Riihiluoma, P.,Ylostalo, P.Serum total and unbound testosterone and sex hormone binding globulin (SHBG) in female acne patients treated with two different oral contraceptives. 1984. Acta Dermato-Venereologica | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Palatsi, R. R., M.,Kivinen, S.Pituitary function and DHEA-S in male acne and DHEA-S, prolactin and cortisol before and after oral contraceptive treatment in female acne. 1986. Acta Dermato-Venereologica | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory |

| Reference | Reason for exclusion |
|---|---|
| | treatments |
| Pandey, D. A., S.Efficacy of isotretinoin and antihistamine versus isotretinoin alone in the treatment of moderate to severe acne: A randomised control trial. 2019. Kathmandu University Medical Journal | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Panzer, J. D. P., W.,Meek, T. J.,Derbes, V. J.,Atkinson, W.Acne treatment: A comparative efficacy trial of clindamycin and tetracycline. 1977. Cutis | No relevant data - insufficient data reported |
| Pariser, D. B., A.,Fried, R.,Jarratt, M. T.,Kempers, S.,Kircik, L.,Lucky, A. W.,Rafal, E.,Rendon, M.,Weiss, J.,et al.,Tretinoin gel microsphere pump 0.04% plus 5% benzoyl peroxide wash for treatment of acne vulgaris: morning/morning regimen is as effective and safe as morning/evening regimen. 2010. Journal of drugs in dermatology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Pariser, D. C., L. E.,Johnson, L. A.,Gottschalk, R. W.Adapalene 0.1% gel compared to tazarotene 0.1% cream in the treatment of acne vulgaris. 2008. Journal of drugs in dermatology : JDD | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Pariser, D. M., Green, L. J., Lain, E. L., Schmitz, C., Chinigo, A. S., McNamee, B., Berk, D. R.Safety and tolerability of sarecycline for the treatment of acne vulgaris: results from a phase III, multicenter, open-label study and a phase I phototoxicity study. 2019. Journal of Clinical and Aesthetic Dermatology | No relevant study design - participants were not randomised on entry to the study and study is not relevant for PCOS, maintenance or refractory treatments |
| Park, K. Y. K., E. J.,Seo, S. J.,Hong, C. K.Comparison of fractional, nonablative, 1550-nm laser and 595-nm pulsed dye laser for the treatment of facial erythema resulting from acne: A split-face, evaluator-blinded, randomized pilot study. 2014. Journal of Cosmetic and Laser Therapy | No relevant study population - sample includes people with acne erythema |
| Parker, F.A comparison of clindamycin 1% solution versus clindamycin 1% gel in the treatment of acne vulgaris. 1987. International Journal of Dermatology | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Pastrana-Ruiz, M. E. V.-M., M. E.,Hojyo-Tomoka, M. T.,Dom inguez-Soto, L.Antibiotics for the treatment of acne. Double-blind comparative study with a 1% solution of clindamycin phosphate versus 500 mg oral tetracycline in patients with moderate acne. 1989. Dermatologia revista mexicana | Not in English language |
| Patel, V. B. M., A. N.,Marfatia, Y. S.Preparation and comparative clinical evaluation of liposomal gel of benzoyl peroxide for acne. | No relevant study design - not RCT |

| Reference | Reason for exclusion |
|---|---|
| 2001a. Drug Development and Industrial Pharmacy | |
| Patel, V. B. M., A.,Marfatia, Y. S.Clinical assessment of the combination therapy with liposomal gels of tretinoin and benzoyl peroxide in acne. 2001b. AAPS PharmSciTech | No relevant study design - not RCT |
| Paver, K.Complications from combined oral tetracycline and oral corticoid therapy in acne vulgaris. 1970. Medical Journal of Australia | Not obtainable |
| Pavithra, G. U., G. M.,Rukmini, M. S.A randomized controlled trial of topical benzoyl peroxide 2.5% gel with a low glycemic load diet versus topical benzoyl peroxide 2.5% gel with a normal diet in acne (grades 1-3). 2018. Indian Journal of Dermatology, Venereology & Leprology | No relevant study population - insufficient details reported to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Peachey, R. D. C., B. L.Topical retinoic acid in the treatment of acne vulgaris. 1971. British Journal of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Peck, G. L. O., T. G.,Butkus, D.,Pandya, M.,Arnaud-Battandier, J.,Gross, E. G.,Windhorst, D. B.,Cheripko, J.Isotretinoin versus placebo in the treatment of cystic acne. A randomized double-blind study. 1982b. Journal of the American Academy of Dermatology | No relevant data - insufficient data reported |
| Peck, G. L. O., T. G.,Butkus, D.Isotretinoin versus placebo in the treatment of cystic acne. 1982a. Journal of the American Academy of Dermatology | Duplicate record |
| Pedace, F. J. S., R.Topical retinoic acid in acne vulgaris. 1971. The British journal of dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Peereboom-Wynia, J. D. R. C., P. J. G.,Bernsen, R.A new alcohol-free preparation of benzoyl peroxide gel (Basiron) for acne vulgaris. A double blind trial. 1984. TGO - Tijdschrift voor Therapie Geneesmiddel en Onderzoek | Not in English language |
| Peker, M. T., H. B.,Arca, E.,Erbil, A. H.,Gur, A. R.Efficacy of topical erythromycin, tetracycline and clindamycin in the treatment of acne vulgaris. 2004. Deri hastaliklari ve frengi arsivi | Not in English language |
| Perez, M. A., F.,De Moragas, J. M.A double blind study comparing clindamycin-phosphate versus oral tetracycline in acne treatment. 1987b. Medicina cutanea ibero-latino-americana | Not in English language |
| Perez, M. A., F.,De Moragas, J. M.Comparative double-blind study of topical clindamycin phosphate and oral tetracycline in the treatment of acne. 1987a. Medicina cutanea ibero-latino-americana | Not in English language |
| Petit, L. P.-F., C.,Uhoda, E.,Vroome, V.,Cauwenbergh, G.,Pierard, G. E.Coping with mild inflammatory catamenial acne: a clinical and bioinstrumental split-face assessment. 2004. Skin Research & Technology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and |

| Reference | Reason for exclusion |
|---|---|
| | refractory treatments |
| Pierard-Franchimont, C. G., V.,Arrese, J. E.,Martalo, O.,Braham, C.,Slachmuylders, P.,Pierard, G. E.Lymecycline and minocycline in inflammatory acne: A randomized, double-blind intent-to-treat study on clinical and in vivo antibacterial efficacy. 2002. Skin Pharmacology and Applied Skin Physiology | Antibiotic dosages lower than BNF values |
| Pierard-Franchimont, C. H., F.,Fraiture, A. L.,Fumal, I.,Pierard, G. E.Split-face clinical and bio-instrumental comparison of 0.1% adapalene and 0.05% tretinoin in facial acne. 1999. Dermatology | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Pinto, C. S., F.,Orellana, J. J.,Gonzalez, S.,Hasson, A.Efficacy of red light alone and methyl-aminolaevulinate-photodynamic therapy for the treatment of mild and moderate facial acne. 2013. Indian Journal of Dermatology, Venereology & Leprology | No relevant study design - not RCT |
| Pisani, M. G., V.,Grimaldi, F. F.Treatment of acne vulgaris with an ointment containing azelaic acid (12%), L-carnitine (2%), enoxolone (1%): double-blind study versus placebo. TRATTAMENTO DELL'ACNE VOLGARE CON UNA CREMA A BASE DI ACIDO AZELAICO (12%), L-CZRNITINA (2%), ENOXOLONE (1%): STUDIO IN DOPPIO CIECO VERSUS PLACEBO. 1991. Chron dermatol | Not in English language |
| Plewig, G. D., H.,Pfleger, M.,Michelsen, S.,Kligman, A. M.Low dose isotretinoin combined with tretinoin is effective to correct abnormalities of acne. 2004. Journal der Deutschen Dermatologischen Gesellschaft | Not in English language |
| Plewig, G. H., K. T.,Nenoff, P.Clinical and bacteriological evaluation of nadifloxacin 1% cream in patients with acne vulgaris: A double-blind, phase III comparison study versus erythromycin 2% cream. 2006. European Journal of Dermatology | No relevant intervention - nadifloxacin 1% cream not available in the UK |
| Plewig, G.Dermabrasion for nodular cutaneous elastosis with cysts and comedones. 1972. Archives of Dermatology | Not obtainable |
| Plewig, G.Vitamin A acid. Topical treatment in acne vulgaris. 1969. Pennsylvania Medicine | No relevant population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Pochi, P. E. B., F. K.,Ellis, C. N.,Stoughton, R. B.,Whitmore, C. G.,Saatjian, G. D.,Sefton, J.Erythromycin 2 percent gel in the treatment of acne vulgaris. 1988. Cutis | Not obtainable |
| Podfigurna, 2019Clinical, hormonal and metabolic parameters in women with PCOS with different combined oral contraceptives (containing chlormadinone acetate versus drospirenone). 2019. Journal of Endocrinological Investigation | Duplicate of Podfigurna 2020 |
| Polakova, K. F., A.,Sayag, M.,Jourdan, E.Adermocosmetic containing bakuchiol, Ginkgo biloba extract and mannitol improves the efficacy of adapalene in patients with acne vulgaris: Result from a controlled randomized trial. 2015. Clinical, Cosmetic and Investigational Dermatology | No relevant intervention - bakuchiol, Ginkgo biloba extract, and mannitol complex |
| Pollock, B. T., D.,Stringer, M. R.,Bojar, R. A.,Goulden, V.,Stables, G. I.,Cunliffe, W. J.Topical aminolaevulinic acid-photodynamic therapy for the treatment of acne vulgaris: A study of clinical efficacy and mechanism of action. 2004. British Journal of Dermatology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in |

| Reference | Reason for exclusion |
|---|---|
| | the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Ponzio, H. A. B., R. T.,Bozko, M. P.Clinical evaluation of a line of products for the control of acne in teenagers. 1994. Anais brasileiros de dermatologia | Not in English language |
| Poulos, E. T. T., F. J.Acne vulgaris. Double blind trial comparing tetracycline and clindamycin. 1976. Archives of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Prasad, S. M., A.,Kubavat, A.,Kelkar, A.,Modi, A.,Swarnkar, B.,Bajaj, B.,Vedamurthy, M.,Sheikh, S.,Mittal, R.Efficacy and safety of a nano-emulsion gel formulation of adapalene 0.1% and clindamycin 1% combination in acne vulgaris: A randomized, open label, active-controlled, multicentric, phase IV clinical trial. 2012. Indian Journal of Dermatology, Venereology and Leprology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Prendiville, J. S. L., R. A.,Russell-Jones, R.A comparison of dapsone with 13-cis retinoic acid in the treatment of nodular cystic acne. 1988. Clinical and Experimental Dermatology | No relevant data reported - group numbers not reported |
| Pria, S. D. G., R. B.,Mahesh, V. B.An antiandrogen in acne and idiopathic hirsutism. 1969. Journal of Investigative Dermatology | No relevant study design - not RCT |
| Priano, L. B., S.,Isola, V.,Grazioli, I.,Melzi, G.,Massone, L.Topical spironolactone 5% versus benzoylperoxide 5% + miconazole 2% in the therapy of acne: double-blind, controlled study to evaluate the efficacy and the eventual systemic absorption. 1993. Giornale italiano di dermatologia e venereologia | Not in English language |
| Prince, R. A. B., D. A.,Hepler, C. D.,Feldick, H. G.Clinical trial of topical erythromycin in inflammatory acne. 1981. Drug Intelligence & Clinical Pharmacy | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Prince, R. A. H., J. M.,Maroc, J. A.Comparative trial of benzoyl peroxide versus benzoyl peroxide with urea in inflammatory acne. 1982. Cutis | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Privitera, G. B., S.,Del Mastro, S.Clinical and pharmacokinetic evaluation of josamycin in the treatment of inflammatory acne. 1989. Journal of Chemotherapy | No relevant study deisgn - not RCT |
| Rafanelli, A. G., I.,Melzi, G.A controlled study spironolactone vs progesterone in the topical treatment of acne. 1993. Giornale italiano di dermatologia e venereologia | Not in English language |
| Rafiei R, Yaghoobi RAzithromycin versus tetracycline in the treatment | No relevant intervention - |

| Reference | Reason for exclusion |
|---|---|
| of acne vulgaris.. 2006. J Dermatolog Treat | suboptimal dose of tetracycline |
| Raimer, S. M., J. M.,Bourcier, M.,Wilson, D.,Papp, K.,Siegfried, E.,Garrett, S.Efficacy and safety of dapsone gel 5% for the treatment of acne vulgaris in adolescents. 2008. Cutis | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Rajka, G.On therapeutic approaches to some special types of acne. 1985. Acta Dermato-Venereologica. Supplementum | No relevant study deisgn - not RCT |
| Raoof, J., Hooper, D., Moore, A., Zaiac, M., Sullivan, T., Kircik, L., Lain, E., Jankicevic, J., Stuart, I.FMX101 4% topical minocycline foam for the treatment of moderate-to-severe acne vulgaris: efficacy and safety from a Phase III randomized, doubleblind, vehicle-controlled study. 2019. Journal of Clinical and Aesthetic Dermatology | No relevant article type - conference abstract |
| Raoof, T. J. H., D.,Moore, A.,Zaiac, M.,Sullivan, T.,Kircik, L.,Lain, E.,Jankicevic, J.,Stuart, I.Efficacy and Safety of a Novel Topical Minocycline Foam for the Treatment of Moderate-to-Severe Acne Vulgaris: A Phase 3 Study. 2019. Journal of the American Academy of Dermatology. | No relevant intervention - FMX101 4% topical minocycline foam not available in the UK |
| Raoof, T. J., Hooper, D., Moore, A., Zaiac, M., Sullivan, T., Kircik, L., Lain, E., Jankicevic, J., Stuart, I.Efficacy and safety of a novel topical minocycline foam for the treatment of moderate to severe acne vulgaris: A phase 3 study. 2020. Journal of the American Academy of Dermatology | No relevant intervention - FMX101 4% topical minocycline foam not available in the UK |
| Rapaport, M. P., S. M.,Reisner, R. M.Evaluation of topical erythromycin and oral tetracycline in acne vulgaris. 1982. Cutis; cutaneous medicine for the practitioner | No relevant intervention - suboptimal dose of tetracycline |
| Rassai, S. R., E.,Ramirez-Fort, M. K.,Feily, A.Adjuvant Narrow Band UVB Improves the Efficacy of Oral Azithromycin for the Treatment of Moderate to Severe Inflammatory Facial Acne Vulgaris. 2014. Journal of Cutaneous & Aestheic Surgery | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Rea, S. T., S.,Frittelli, V.,Gunnarsson, R.A feasibility study for a triple-blind randomized controlled trial investigating the effects of oral isotretinoin on mood and quality of life in patients with acne vulgaris. 2017. Clinical and experimental dermatology | No releavant study design - not RCT |
| Rea, S. T., S.,Frittelli, V.,Gunnarsson, R.A feasibility study for a triple-blind randomized controlled trial investigating the effects of oral isotretinoin on mood and quality of life in patients with acne vulgaris. 2018. Clinical and Experimental Dermatology | Duplicate record |
| Rebillo, T. H., J. L.Skin surface glycerol levels in acne vulgaris. 1978. Journal of Investigative Dermatology | No relevant study design - not RCT |
| Redmond, G. P. G., G. P.,Gupta, M. K.,Bedocs, N. M.,Parker, R.,Skibinski, C.,Bergfeld, W.Treatment of androgenic disorders with dexamethasone: dose-response relationship for suppression of dehydroepiandrosterone sulfate. 1990. Journal of the American Academy of Dermatology | No relevant study population - sample includes people with hirsuitism or alopecia, only 11% participants with acne |
| Reinel, D. B., H.A new drug combination for the topical treatment of acne. Miconazole 2% + benzoyl peroxide 5% versus benzoyl peroxide | Not in English language |

| Reference | Reason for exclusion |
|---|---|
| 5%--a double-blind study. 1985. Zeitschrift fur hautkrankheiten | |
| Richter, C. T., C.,Hillmann, K.,Dobos, G.,Stroux, A.,Kottner, J.,Blume-Peytavi, U.Reduction of Inflammatory and Noninflammatory Lesions with Topical Tyrothricin 0.1% in the Treatment of Mild to Severe Acne Papulopustulosa: A Randomized Controlled Clinical Trial. 2016. Skin Pharmacology and Physiology | No relevant intervention - topical Tyrothricin;nNo relevant study population - sample includes people with mild to severe acne |
| Richter, J. R. F., L. R.,Kiistala, U. O.,Jung, E. G.Efficacy of the fixed 1.2% clindamycin phosphate, 0.025% tretinoin gel formulation (Velac) and a proprietary 0.025% tretinoin gel formulation (Aberela) in the topical control of facial acne. 1998b. Journal of the European Academy of Dermatology and Venereology | Duplicate record |
| Rietschel, R. L. D., S. H.Benzoyl peroxide reactions in an acne study group. 1982. Contact Dermatitis | No relevant data reported - pharmokinetic study |
| Rietschel, R. L. D., S. H.Clindamycin phosphate used in combination with tretinoin in the treatment of acne. 1983. International Journal of Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Rist, T. D., M. W.Study design and selection criteria in the BEST study. 2003. Cutis | No relevant data reported |
| Rivkin, L. R., M.Clinical evaluation of a new erythromycin solution for acne vulgaris. 1980. Cutis | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Riyanto, P. S., P.,Lelyana, R.Advantage of soybean isoflavone as antiandrogen on acne vulgaris. 2015. Dermato-Endocrinology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Robinson, S. K., Z.,Tang, M. M.Metformin as an adjunct therapy for the treatment of moderate to severe acne vulgaris: A randomized open-labeled study. 2019. Dermatologic Therapy | Dosage of tetracycline lower than BNF value |
| Robledo Aguilar, A. L. B., E.,del Pino Gamboa, J.,Sambricio Guiu, F.,Rodriguez Pichardo, A.,Sotillo Gago, I.,Chaparro Martinez, A.,Garcia Aparicio, P. G.Multicentric comparative study of the efficacy and tolerance of clindamycin phosphate 1% topical solution and tetracycline topical solution for the treatment of acne vulgaris. 1988. Current therapeutic research - clinical and experimental | No relevant intervention - tetracycline topical solutio not available in the UK |
| Rocha, M. A. D. G., L. R. S.,Sanudo, A.,Bagatin, E.Modulation of Toll Like Receptor-2 on sebaceous gland by the treatment of adult female acne. 2017a. Dermato-endocrinology | No relevant study design - not RCT |
| Rocha, M. C., K. H. M.,Carvalho, V. M.,Bagatin, E.ADT-G as a promising biomarker for peripheral hyperandrogenism in adult female acne. 2017b. Dermato-endocrinology | No relevant data reported - pharmokinetic study |
| Rocha, M. S., A.,Bagatin, E.The effect on acne quality of life of topical azelaic acid 15% gel versus a combined oral contraceptive in adult female acne: A randomized trial. 2017c. Dermato-endocrinology | No relevant data reported - quality of life data only |
| Rojanamatin, J. C., P.Treatment of inflammatory facial acne vulgaris with intense pulsed light and short contact of topical 5-aminolevulinic | No relevant study population - sample |

| Reference | Reason for exclusion |
|---|---|
| acid: a pilot study. 2006. Dermatologic Surgery | includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Romiti, N.Use of the aromatic retinoid Ro-11-1430 for acne therapy. 1978. Pharmatherapeutica | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Ruamrak, C. L., N.,Natakankitkul, S.Comparison of clinical efficacies of sodium ascorbyl phosphate, retinol and their combination in acne treatment. 2009. International Journal of Cosmetic Science | No relevant study population - sample includes people with mild to severe acne; No relevant intervention - topical sodium ascorbyl phosphate |
| Ruxton,A novel topical ingredient derived from seaweed significantly reduces symptoms of acne vulgaris: a general literature review. 2013. NA | No relevant intervention - marine-derived ingredients for acne |
| Ryou, J. H. L., S. J.,Park, Y. M.,Kim, H. O.,Kim, H. S.Acne-photodynamic therapy with intra-lesional injection of 5-aminolevulinic acid. 2009. Photodermatology, Photoimmunology & Photomedicine | No relevant study design - not RCT |
| Sadick, N. S. L., Z.,Laver, L.Treatment of mild-to-moderate acne vulgaris using a combined light and heat energy device: Home-use clinical study. 2010c. Journal of Cosmetic and Laser Therapy | No relevant article type - conference abstract |
| Sadick, N., Edison, B. L., John, G., Bohnert, K. L., Green, B.An Advanced, Physician-Strength Retinol Peel Improves Signs of Aging and Acne Across a Range of Skin Types Including Melasma and Skin of Color. 2019. Journal of Drugs in Dermatology: JDDJ Drugs Dermatol | Not obtainable |
| Sadick, N.An open-label, split-face study comparing the safety and efficacy of levulan kerastick (aminolevulonic acid) plus a 532 nm KTP laser to a 532 nm KTP laser alone for the treatment of moderate facial acne. 2010a. Journal of Drugs in Dermatology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Saihan, E. M. B., J. L.,Meyrick, G.,Speller, D. C.,Thornton, E.,Chestney, V.The effect of a topical antibiotic preparation in acne vulgaris--a controlled clinical and laboratory study. 1981. British Journal of Clinical Practice | No relevant intervention - actinac discontinued in the UK |
| Salagnac, V. L., F.,De, L. O.,Le, C. Y.,Kalis, B.Topical treatment of actinic ageing with vitamin A acid at various concentrations. TRAITEMENT DU VIEILLISSEMENT ACTINIQUE PAR LA VITAMINE A ACIDE TOPIQUE A DIFFERENTES CONCENTRATIONS. 1991. REV. FR. GYNECOL. OBSTET. | Not in English language |
| Sampaio, S. A. P. M., H. C. B.,Freitas, T. H. P.,Totoli, Sasm,Martins, MrfcA multicenter trial comparing the efficacy and tolerance of isotretinoin gel 0,05% and tretinoin cream 0.05% in the treatment of acne vulgaris. 1997. Revista brasileira de medicina | Not in English language |
| Sanam, M. Z., O.Desogestrel+ethinylestradiol versus levonorgestrel | No relevant study |

| Reference | Reason for exclusion |
|---|---|
| +ethinylestradiol: Which one has better affect on acne, hirsutism, and weight change. 2011. Saudi Medical Journal | population - participants did not have acne |
| Santos, M. A. B., V. G.,Santos, G.Effectiveness of photodynamic therapy with topical 5-aminolevulinic acid and intense pulsed light versus intense pulsed light alone in the treatment of acne vulgaris: comparative study. 2005. Dermatologic Surgery | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Santos-Caetano, J. P. C., M. R.A Randomized Controlled Tolerability Study to Evaluate Reformulated Benzoyl Peroxide Face Washes for Acne Vulgaris. 2019. Journal of drugs in dermatology : JDD | No relevant intervention - intervention is washed off the face |
| Sardesai Vkambli, V.Comparison of efficacy of topical clindamycin and nicotinamide combination with plain clindamycin for the treatment of acne vulgaris and acne resistant to topical antibiotics. 2003. Indian journal of dermatology, venereology and leprology | No relevant study design - not RCT |
| Sauer, G. C.Prospective study on the safety of long-term tetracycline therapy for acne. 1981. Cutis | No relevant study design - not RCT |
| Sayyafan, M. S. R., M.,Salmanpour, R.Clinical assessment of topical erythromycin gel with and without zinc acetate for treating mild-to-moderate acne vulgaris. 2019. Journal of Dermatological Treatment. | No relevant study design - not RCT |
| Sayyafran, 2019 Clinical assessment of topical erythromycin gel with and without zinc acetate for treating mild-to-moderate acne vulgaris. 2019. Journal of Dermatological Treatment | Duplication of Sayyafan 2019 |
| Schachner, L. E., W.,Kittles, C.,Mertz, P.Topical erythromycin and zinc therapy for acne. 1990a. Journal of the American Academy of Dermatology | No relevant data - insufficient data reported |
| Schachner, L. P., A.,Kittles, C.A clinical trial comparing the safety and efficacy of a topical erythromycin-zinc formulation with a topical clindamycin formulation. 1990b. Journal of the American Academy of Dermatology | No relevant data - insufficient data reported |
| Scheinfeld, N.ABSORICA (isotretinoin): a new form. 2013. SKINmed | No relevant study design - not RCT |
| Schlessinger, J. M., A.,Gold, M.,Leonardi, C.,Eichenfield, L.,Plott, R. T.,Leyden, J.,Wortzman, M.Clinical safety and efficacy studies of a novel formulation combining 1.2% clindamycin phosphate and 0.025% tretinoin for the treatment of acne vulgaris. 2007. Journal of drugs in dermatology : JDD | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Schutte, H. C., W. J.,Forster, R. A.The short-term effects of benzoyl peroxide lotion on the resolution of inflamed acne lesions. 1982. British Journal of Dermatology | No relevant study population - sample includes people with mild to severe acne |
| Schwanitz, H. J. M., E.Internal versus topical tetracycline therapy of acne. 1984. Zeitschrift fur hautkrankheiten | Not in English language |
| Scott, A. M., Stehlik, P., Clark, J., Zhang, D., Yang, Z., Hoffmann, T., Mar, C. D., Glasziou, P.Blue-Light Therapy for Acne Vulgaris: A Systematic Review and Meta-Analysis. 2019. Annals of Family Medicine | Systematic review - references were checked for relevance |
| Semprini, A., Braithwaite, B., Corin, A., Sheahan, D., Tofield, C., Helm, C., Montgomery, B., Fingleton, J., Weatherall, M., Beasley, R. Randomised controlled trial of topical kanuka honey for the treatment of acne. 2016. BMJ Open | No relevant intervention - compairson of addition of topical 90% medicalgrade kanuka honey and 10% glycerine to standard antibacterial soap wash |

| Reference | Reason for exclusion |
|---|---|
| | with antibacterial soap wash alone |
| Sen, A. K., S.,Chatterjee, R. N.,Sarkar, M.,Bhattacharjee, S.,Ram, A. K.Acomparativestudyof efficacy and safetyoftopical clindamycingelversus combination of clindamycingeland benzoylperoxidecreamin patients ofmildtomoderateacnevulgaris. 2013. Indian Journal of Pharmacology | No relevant article type - conference abstract |
| Shafiq, Y. N., B. S.,Rizwani, G. H.,Usman, M.,Shah, B. A.,Aslam, M.,Hina, B.Anti-acne activity of Casuarina equisetifolia bark extract: a randomized clinical trial. 2014. Bangladesh journal of pharmacology | No relevant intervention - Casuarina equisetifolia bark extract (5% cream) |
| Shaheen, J. A. K., M.,Kareem, A.,Ahmad, M.,Ansari, N. U. H.,Ahmad, I.Clinical evaluation of roxithromyin in acne vulgaris: Comparison of daily versus alternate day regimen. 2005. Journal of Pakistan Association of Dermatologists | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Shahid, J. K., T.Tretinoin cream versus benzoyl peroxide(10%) gel in the tropical treatment of mild acne vulgaris. 1996. Biomedica | Not obtainable |
| Shahlita, A. R. S., E. B.,Bauer, E.Topical erythromycin v clindamycin therapy for acne. A multicenter, double-blind comparison. 1984. Archives of Dermatology | No relevant study population - insufficient information to determine severity of acne |
| Shahmoradi, Z. I., F.,Siadat, A. H.,Ghorbaini, A.,Nilforoushzadeh, M. A.Comparison of topical 5% nicotinamid and 2% clindamycin gels in the treatment of the mild to moderate acne vulgaris: a double-blinded randomized clinical trial. 2015. Journal of isfahan medical school | Not in English language |
| Shahmoradi, Z. I., F.,Siadat, A. H.,Ghorbaini, A.Comparison of topical 5% nicotinamid gel versus 2% clindamycin gel in the treatment of the mild-moderate acne vulgaris: A double-blinded randomized clinical trial. 2013. Journal of Research in Medical Sciences | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Shalita, A. M., B.,Menter, A.,Abramovits, W.,Loven, K.,Kakita, L.Tazarotene cream versus adapalene cream in the treatment of facial acne vulgaris: a multicenter, double-blind, randomized, parallel-group study. 2005. Journal of drugs in dermatology : JDD | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Shalita, A. R. B., D. S.,Thiboutot, D. M.,Leyden, J. J.,Parizadeh, D.,Sefton, J.,Walker, P. S.,Gibson, J. R.Effects of tazarotene 0.1% cream in the treatment of facial acne vulgaris: Pooled results from two multicenter, double-blind, randomized, vehicle-controlled, parallel-group trials. 2004. Clinical Therapeutics | No relevant data reported - reports pooled result from 2 trials combined |
| Shalita, A. R. C., D. K.,Parish, L. C.,Bernstein, J. E.,Evans, C. S.The effects of topical nicotinamide on acne vulgaris. 1992. Journal of investigative dermatology | No relevant article type - conference abstract |
| Shalita, A. R. R., 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. 2003. Cutis | No relevantinternvention - facial cleanser; No relevant study population - insufficient information to determine seveirty of acne |

| Reference | Reason for exclusion |
|---|---|
| | and study is not relevant for PCOS, maintenance or refractory treatments |
| Shalita, A. R.Comparison of a salicylic acid cleanser and a benzoyl peroxide wash in the treatment of acne vulgaris. 1989. Clinical therapeutics | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Shalita, A. R.Comparison of a salicylic acid cleanser and a benzoyl peroxide wash in the treatment of acne vulgaris: COMPARACAO ENTRE SISTEMA DE LIMPEZA COM ACIDO SALICILICO E SOLUCAO DE PEROXIDO DE BENZOILA NO TRATAMENTO DO ACNE VULGARIS. 1998. Revista brasileira de medicina | Not in English language |
| Shalita, A. W., J. S.,Chalker, D. K.,Ellis, C. N.,Greenspan, A.,Katz, H. I.,Kantor, I.,Millikan, L. E.,Swinehart, T.,Swinyer, L.,et al.,A comparison of the efficacy and safety of adapalene gel 0.1% and tretinoin gel 0.025% in the treatment of acne vulgaris: a multicenter trial. 1996. Journal of the American Academy of Dermatology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Sharma, A. D. G., P. D.,Sundaram, M.,Janaki, V. R.,Rege, V. L.,Bilimoria, F. E.,Arora, J.Topical lincomycin gel in acne vulgaris: A multicentric placebo controlled study. 2003. Indian Journal of Dermatology, Venereology and Leprology | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Sharquie,Treatment of acne vulgaris with 2% topical tea lotion. 2006. NA | No relevant intervention - 2% tea lotion |
| Sheehan-Dare, R. A. P.-S., J. W.,Cunliffe, W. J.A comparative study between topical clindamycin and oral minocycline in the treatment of acne vulgaris. 1989. Round table series - royal society of medicine | Duplicate record |
| Sheehan-Dare, R. A. P.-S., J.,Cunliffe, W. J.A double-blind comparison of topical clindamycin and oral minocycline in the treatment of acne vulgaris. 1990. Acta Dermato-Venereologica | No relevant data - insufficient data reported |
| Shen, W. T., Wu, Y., He, H. Q., Yu, Y., Qin, H. H., Fei, J. B., Wang, G. J.Efficacy and safety of artemether emulsion for the treatment of mild-to-moderate acne vulgaris: a randomized pilot study. 2020. Journal of Dermatological Treatment | No relevant intervention - artemether |
| Shetti, S. A. N., H. N.,Hanumantharaya, N.A randomized, open-label, comparative study of efficacy of low-dose continuous versus low-dose intermittent oral isotretinoin therapy in moderate-to-severe acne vulgaris. 2017. National Journal of Physiology, Pharmacy and Pharmacology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, |

| Reference | Reason for exclusion |
|---|---|
| | maintenance and refractory treatments |
| Shie Morteza, M., Hayati, Z., Namazi, N., Abdollahimajd, F.Efficacy and safety of oral silymarin in comparison with oral doxycycline and their combination therapy in the treatment of acne vulgaris. 2019. Dermatologic Therapy | No relevant intervention - silymarin |
| Shin JU, Lee SH, Jung JY, Lee JH.A split-face comparison of a fractional microneedle radiofrequency device and fractional carbon dioxide laser therapy in acne patients.. 2012. J Cosmet Laser Ther | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Shwetha, H. G., A.A comparative study of efficacy and safety of combination of topical 1% clindamycin and 0.1% adapalene with 1% clindamycin and 2.5% benzoyl peroxide in mild to moderate acne in a tertiary care hospital. 2013. Indian Journal of Pharmacology | No relevant article type - conference abstract |
| Sidgiddi, 2019Efficacy of oral isotretinoin in combination with desloratadine in the treatment of common vulgaris acne in Vietnamese Patients. 2019. Open Access Macedonian Journal of Medical Sciences | Duplication of Van 2019 |
| Sidgiddi, S., Allenby, K., Okumu, F., Gautam, A.Bioavailability, Pharmacokinetics, and Transepidermal Water Loss of Short Contact Tazarotene Lotion 0.1% Versus Tazarotene (Tazorac<sup> R</sup>) Cream 0.1. 2019. The Journal of Clinical & Aesthetic DermatologyJ Clin Aesthet Dermatol | The paper reports 2 studies, both do not meet inclusion criteria: the first one describes a non-relevant comparison and the second one does not reported severity of acne |
| Simpson, N. B. B., P. E.,Forster, R. A.,Cunliffe, W. J.The effect of topically applied progesterone on sebum excretion rate. 1979. British Journal of Dermatology | No relevant data reported - pharmokinetic study |
| Simpson, N. B. M., K. A.5% Aluminium chloride hexahydrate and sebum excretion rate. 1982. Acta Dermato-Venereologica | Duplicate record |
| Singhi, M. G. B. R.Comparison of oral azithromycin pulse with daily doxycycline in the treatment of acne vulgaris. 2003. Indian journal of dermatology, venereology and leprology | No relevant study design - not RCT |
| Skidmore, R. K., R.,Walker, C.,Thomas, J.,Bradshaw, M.,Leyden, J.,Powala, C.,Ashley, R.Effects of subantimicrobial-dose doxycycline in the treatment of moderate acne. 2003. Archives of Dermatology | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Smit, F.Minocycline versus doxycycline in the treatment of acne vulgaris. A double-blind study. 1978. Dermatologica | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and |

| Reference | Reason for exclusion |
|---|---|
| | refractory treatments |
| Smith, E. B. P., R. S.,McCabe, J. M.,Becker, L. E.Benzoyl peroxide lotion (20%) in acne. 1980a. Cutis | Duplicate record |
| Smith, J. G., Jr.,Chalker, D. K.,Wehr, R. F.The effectiveness of topical and oral tetracycline for acne. 1976. Southern Medical Journal | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Smith, M. A., Waterworth, P. M., & Curwen, M. P.A controlled trial of oral antibiotics in the treatment of acne vulgaris. 1962. British journal of dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Soldo-Belic, A. C., V.,Vujic-Podlipec, D.,Oremovic, L.,Sviben-Radovcic, Z.,Kostovic, K.,Nola, I.,Mateljic, V.Advantages of liposome-encapsulated 1% clindamycin solution versus 1% clindamycin solution in the therapy of acne vulgaris. 1999. Acta Dermatovenerologica Croatica | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Spellman, M. C. P., S. H.Efficacy and safety of azelaic acid and glycolic acid combination therapy compared with tretinoin therapy for acne. 1998. Clinical therapeutics | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| St Surin-Lord, S., Schlesinger, T. E., Guenin, E.Novel tretinoin 0.05% lotion for the oncedaily treatment of moderatetosevere acne vulgaris in a preadolescent and adolescent population. 2019. Journal of Clinical and Aesthetic Dermatology | No relevant data reported - reports pooled data of 2 trials combined |
| Stainforth, J. M.-H., S.,Papworth-Smith, J. W.,Eady, E. A.,Cunliffe, W. J.,Norris, J. F. B.,Simpson, N. B.,Cork, M. J.A single-blind comparison of topical erythromycin/zinc lotion and oral minocycline in the treatment of acne vulgaris. 1993. Journal of Dermatological Treatment | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Stankler, L.Pustular acne vulgaris. Rotational oral antibacterial therapy for 1 year. 1979. British Journal of Clinical Practice | No relevant study design - not RCT |
| Stein Gold, L., D., S.,Weiss, J.,Draelos, Z. D.,Ellman, H.,Stuart, I. A.A novel topical minocycline foam for the treatment of moderate-to-severe acne vulgaris: Results of 2 randomized, double-blind, phase 3 studies. 2019. Journal of the American Academy of Dermatology | No relevant intervention - FMX101 4% is a topical minocycline foam not available in the UK |
| Stein Gold, L., Pariser, D. M., Guenin, E.Tretinoin 0.05% Lotion for the Once-Daily Treatment of Moderate and Severe Acne Vulgaris in Females: Effect of Age on Efficacy and Tolerability. 2019. Journal of drugs in dermatology : JDD | Not obtainable |
| Stein Gold, L., T., J.,Cruz-Santana, A.,Papp, K.,Poulin, Y.,Schlessinger, J.,Gidner, J.,Liu, Y.,Graeber, M.A North American | No relevant data reported - a repeat publication of |

| Reference | Reason for exclusion |
|---|---|
| study of adapalene-benzoyl peroxide combination gel in the treatment of acne. 2009. Cutis | Gollnick 2009 |
| Stein Gold, L..,Werschler, W. P., & Mohawk, J.Â Adapalene/benzoyl peroxide gel 0.3%/2.5%: effective acne therapy regardless of age or gender. 2017. Journal of drugs in dermatology | No relevant data reported - post hoc analysis by gender and age of Stein Gold & Weiss 2016. |
| Stein Gold, L.Efficacy and tolerability of a fixed combination of clindamycin phosphate (1.2%) and benzoyl peroxide (3.75%) aqueous gel in moderate and severe acne vulgaris subpopulations. 2015. Journal of Drugs in Dermatology | No relevant data reported - post hoc analysis by acne severity of Pariser 2014 |
| Stein Gold, L.Efficacy and tolerability of fixed-combination acne treatment in adolescents. 2013. Cutis | No relevant data reported - publication from Thiboutot 2008 |
| Stinco, G. P., F.,Valent, F.,Errichetti, E.,Di Meo, N.,Trevisan, G.,Patrone, P.Efficacy, tolerability, impact on quality of life and sebostatic activity of three topical preparations for the treatment of mild to moderate facial acne vulgaris. 2016. Giornale italiano di dermatologia e venereologia | Not in English language |
| Stoughton, R. B. C., R. C.,Gange, R. W.,Walter, J. F.Double-blind comparison of topical 1 percent clindamycin phosphate (Cleocin T) and oral tetracycline 500 mg/day in the treatment of acne vulgaris. 1980. Cutis | No relevant study design - not RCT |
| Stoughton, R. B. R., W.Topical clindamycin in the control of acne vulgaris. 1976. Cutis | No relevant article type - non-systematic review |
| Strauss, J. S. G., A. B.,Jones, T.,Koo, J. Y.,Leyden, J. J.,Lucky, A.,Pappas, A. A.,McLane, J.,Leach, E. E.Concomitant administration of vitamin E does not change the side effects of isotretinoin as used in acne vulgaris: a randomized trial. 2000. Journal of the American Academy of Dermatology | No relevant intervention - isotretinoin with vitamin E |
| Strauss, J. S., Leyden, J. J., Lucky, A. W., Lookingbill, D. P., Drake, L. A., Hanifin, J. M., Lowe, N. J., Jones, T. M., Stewart, D. M., Jarratt, M. T., Katz, I., Pariser, D. M., Pariser, R. J., Tschen, E., Chalker, D. K., Rafal, E. S., Savin, R. P., Roth, H. L., Chang, L. K., Baginski, D. J., Kempers, S., McLane, J., Eberhardt, D., Leach, E. E., Bryce, G., Hong, J.A randomized trial of the efficacy of a new micronized formulation versus a standard formulation of isotretinoin in patients with severe recalcitrant nodular acne. 2001. Journal of the American Academy of DermatologyJ Am Acad Dermatol | No relevant comparison - micronized isotretinoin vs standard isotretinoin |
| Stuttgen, G. I., H.,Mahrle, G.Oral vitamin A acid in treatment of dermatoses with pathologic keratinization. 1977. International Journal of Dermatology | No relevant study design - not RCT |
| Stuttgen, G.Oral vitamin A acid therapy. 1975. Acta Dermato-Venereologica. Supplementum | No relevant study design - not RCT |
| Sun, X., Qian, F., He, Y., Gu, X., Di, W.Safety and Efficacy of Combined Oral Contraceptive Ethinyl Estradiol/Drospirenone (YAZ) in Chinese Women: A Single-Arm, Open-Label, Multicenter, Post-Authorization Study. 2020. Advances in Therapy | No relevant study design - not a RCT |
| Sutono, T.Efficacy of Garcinia mangostana L. (mangosteen rind extract) to reduce acne severity. 2013. Medical Journal of Indonesia | No relevant intervention - extract of mangosteen rind |
| Swinyer, L. J. S., T. A.,Britt, M. R.Topical agents alone in acne. A blind assessment study. 1980. JAMA | No relevant intervention - suboptimal doses |
| Taaffe, A. C., W. J.,Cove, J.Topical erythromycin in acne - a double-blind study. 1981. British Journal of Dermatology | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, |

| Reference | Reason for exclusion |
|---|---|
| | maintenance or refractory treatments |
| Tabasum, H. A., T.,Anjum, F.,Rehman, H.The effect of Unani antiacne formulation (Zimade Muhasa) on acne vulgaris: A singleblind, randomized, controlled clinical trial. 2014. Journal of Pakistan Association of Dermatologists | No relevantstudy population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Takigawa, M. T., Y.,Shimada, S.,Furukawa, F.,Noguchi, N.,Ito, T.Clinical and bacteriological evaluation of adapalene 0.1% gel plus nadifloxacin 1% cream versus adapalene 0.1% gel in patients with acne vulgaris. 2013. Journal of Dermatology | No relevant intervention - adapalene 0.1% gel plus nadifloxacin 1% cream not available in the UK |
| Tan, J. G., H. P. M.,Loesche, C.,Ma, Y. M.,Gold, L. S.Synergistic efficacy of adapalene 0.1%-benzoyl peroxide 2.5% in the treatment of 3855 acne vulgaris patients. 2011. Journal of Dermatological Treatment | No relevant data reported - pooled analysis of Thiboutout 2007, Stein Gold 2009, and Gollnick 2009 |
| Tan, J. G., L. S.,Schlessinger, J.,Brodell, R.,Jones, T.,Cruz, A.,Kerrouche, N.,Jarratt, M.Short-term combination therapy and long-term relapse prevention in the treatment of severe acne vulgaris. 2012a. Journal of Drugs in Dermatology | Study design does not meet protocol eligibility criteria - combines individual patient data from 2 RCTs |
| Tan, J. G., L. S.,Schlessinger, J.,Brodell, R.,Jones, T.,Dhuin, J. C.,Jarratt, M.Combination of adapalene-benzoyl peroxide and oral doxycycline is efficacious in short-term therapy: Maintenance with adapalene-benzoyl peroxide prevents relapse in treatment of severe acne vulgaris. 2012b. Pediatric Dermatology | No relevant article type - conference abstract |
| Tang, X., Li, C., Ge, S., Chen, Z., Lu, L.Efficacy of photodynamic therapy for the treatment of inflammatory acne vulgaris: A systematic review and meta-analysis. 2020. Journal of Cosmetic DermatologyJ | Systematic review - references were checked for relevance |
| Tanghetti, E. A., Werschler, W. P., Lain, T., Guenin, E., Martin, G., Pillai, R.Tazarotene 0.045% Lotion for Once-Daily Treatment of Moderate-to-Severe Acne Vulgaris: Results from Two Phase 3 Trials. 2020. Journal of drugs in dermatology : JDD | Not obtainable |
| Tanghetti, E. D., S.,Green, L.,Del Rosso, J.,Draelos, Z.,Leyden, J.,Shalita, A.,Glaser, D. A.,Grimes, P.,Webster, G.,Barnett, P.,Le Gall, N.Randomized comparison of the safety and efficacy of tazarotene 0.1% cream and adapalene 0.3% gel in the treatment of patients with at least moderate facial acne vulgaris. 2010. Journal of Drugs in Dermatology | No relevant data reported - subgroup analysis by sex of Draelos 2007 |
| Tanghetti, E. H., J. C.,Oefelein, M. G.The efficacy and tolerability of dapsone 5% gel in female vs male patients with facial acne vulgaris: Gender as a clinically relevant outcome variable. 2012. Journal of Drugs in Dermatology | No relevant data reported - subgroup analysis by sex of Draelos 2007 |
| Tanghetti, E. H., J.,Baldwin, H.,Kircik, L.,Bai, Z.,Alvandi, N.Once-Daily Topical Dapsone Gel, 7.5%: Effective for Acne Vulgaris Regardless of Baseline Lesion Count, With Superior Efficacy in Females. 2018. Journal of drugs in dermatology : JDD | No relevant data reported - post hoc analysis by sex of Stein Gold 2016 |
| Tangjaturonrusamee, C. R., P.,Ditre, C. M.Comparison of pneumatic broadband light plus adapalene gel 0.3% versus adapalene gel 0.3% monotherapy in the treatment of mild to moderate acne. 2016. Cutis | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, |

| Reference | Reason for exclusion |
|---|---|
| | maintenance and refractory treatments |
| Tanzi, E. L. A., T. S.Comparison of a 1450-nm Diode Laser and a 1320-nm Nd:YAG Laser in the Treatment of Atrophic Facial Scars: A Prospective Clinical and Histologic Study. 2004. Dermatologic Surgery | Duplicate record |
| Tao, S. Q. X., R. S.,Li, F.,Cao, L.,Fan, H.,Fan, Y.,Yang, L. J.Efficacy of 3.6% topical ALA-PDT for the treatment of severe acne vulgaris. 2016. European Review for Medical & Pharmacological Sciences | No relevant study design - not RCT |
| Taub, A. F.A comparison of intense pulsed light, combination radiofrequency and intense pulsed light, and blue light in photodynamic therapy for acne vulgaris. 2007. Journal of drugs in dermatology : JDD | No relevant data reported - number of participants assigned to each group not reported |
| Tay, C. H.Treatment of acne vulgaris with topical vitamin A acid. 1978. Singapore Medical Journal | No relevant study design - not RCT |
| Taylor, S. C. C.-B., F. E.,McMichael, A.,Downie, J. B.,Rodriguez, D. A.,Alexis, A. F.,Callender, V. D.,Alvandi, N.Efficacy, safety, and tolerability of topical dapsone gel, 7.5% for treatment of acne vulgaris by Fitzpatrick skin phototype. 2018. Journal of Drugs in Dermatology | No relevant data reported - post-hoc analysis of Eichenfeld 2016 & Stein Gold 2016 trials |
| Taylor, S. C.Utilizing combination therapy for ethnic skin. 2007. Cutis | No relevant data reported - subgroup analysis by skin type of Kircik 2007 |
| Thappa, D. M. D., J.Nodulocystic acne: Oral gugulipid versus tetracycline. 1994. Journal of Dermatology | No relevant intervention - Guggulsterone |
| Thiboutot, D. A., D. F.,Lemay, A.,Washenik, K.,Roberts, J.,Harrison, D. D.A randomized, controlled trial of a low-dose contraceptive containing 20 mug of ethinyl estradiol and 100 mug of levonorgestrel for acne treatment. 2001. Fertility and Sterility | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Thiboutot, D. A., S.,Soto, P.Efficacy and tolerability of adapalene 0.3% gel compared to tazarotene 0.1% gel in the treatment of acne vulgaris. 2008. Journal of drugs in dermatology : JDD | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Thiboutot, D. M. K., L.,McMichael, A.,Cook-Bolden, F. E.,Tyring, S. K.,Berk, D. R.,Chang-Lin, J. E.,Lin, V.,Kaoukhov, A.Efficacy, safety, and dermal tolerability of dapsone gel, 7.5% in patients with moderate acne vulgaris: A pooled analysis of two phase 3 trials. 2016. Journal of Clinical and Aesthetic Dermatology | No relevant population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Thomas, D. R. R., S.,Smith, E. B.Comparison of topical erythromycin 1.5 percent solution versus topical clindamycin phosphate 1.0 percent solution in the treatment of acne vulgaris. 1982. Cutis | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - |

| Reference | Reason for exclusion |
|---|---|
| | including PCOS, maintenance and refractory treatments |
| Thomsen, R. J. S., A.,Knutson, D.,Strauss, J. S.Topical clindamycin treatment of acne. Clinical, surface lipid composition, and quantitative surface microbiology response. 1980. Archives of Dermatology | No relevant intervention - topical 1% clindamycin hydrochloride hydrate not licensed in the UK |
| Thorneycroft, I. H. S., F. Z.,Bradshaw, K. D.,Ballagh, S. A.,Nichols, M.,Weber, M. E.Effect of low-dose oral contraceptives on androgenic markers and acne. 1999. Contraception | No relevant study population - sample includes women with and without acne, no further details reported |
| Thuangtong, R. T., C.,Rattanaumpawan, P.,Ditre, C. M.Comparison of salicylic acid 30% peel and pneumatic broadband light in the treatment of mild to moderately severe facial acne vulgaris. 2017. Cutis; cutaneous medicine for the practitioner | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Ting, W.Randomized, observer-blind, split-face study to compare the irritation potential of 2 topical acne formulations over a 14-day treatment period. 2012. Cutis; cutaneous medicine for the practitioner | No relevant study population - insufficient information to determine severity of acne |
| Toossi, P. F., M.,Malekzad, F.,Mohtasham, N.,Kimyai-Asadi, A.Subantimicrobial-dose doxycycline in the treatment of moderate facial acne. 2008. Journal of drugs in dermatology : JDD | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Trice, E. R.Treatment of acne vulgaris with Secomat -S lotion. 1966. Virginia Medical Monthly | No relevant study design - not RCT |
| Tschen, E. H. K., H. I.,Jones, T. M.,Monroe, E. W.,Kraus, S. J.,Connolly, M. A.,Levy, S. F.A combination benzoyl peroxide and clindamycin topical gel compared with benzoyl peroxide, clindamycin phosphate, and vehicle in the treatment of acne vulgaris. 2001. Cutis; cutaneous medicine for the practitioner | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Tuchin, V. V. G., E. A.,Bashkatov, A. N.,Simonenko, G. V.,Odoevskaya, O. D.,Altshuler, G. B.A Pilot Study of ICG Laser Therapy of Acne Vulgaris: Photodynamic and Photothermolysis Treatment. 2003. Lasers in Surgery and Medicine | No relevant data reported - sebum excretion data |
| Tucker, S. B. T., R.,Cochran, R.,Flannigan, S. A.Comparison of topical clindamycin phosphate, benzoyl peroxide, and a combination of the two for the treatment of acne vulgaris. 1984. British Journal of Dermatology | No relevant data - insufficient data reported |
| Tucker, S. B. T., T.,Cochran, R.Comparison of topical clindamycin phosphate, benzoyl peroxide and a combination of the two, for the treatment of acne vulgaris. 1990. Indian journal of dermatology, venerology and leprology | Duplicate record |
| Tunca, M. A., A.,Ozmen, I.,Erbil, H.Topical nadifloxacin 1% cream vs. topical erythromycin 4% gel in the treatment of mild to moderate acne. | No relevant intervention - topical nadifloxacin 1% cream not available in the |

| Reference | Reason for exclusion |
|---|---|
| 2010. International Journal of Dermatology | UK |
| Turan, A. S., H.,Baskan, E. B.,Turan, H.,Aydogan, K.Efficacy of topical sodium sulfacetamide in the treatment of mild and moderate acne vulgaris: a randomized, comparative study. 2012. Turkderm deri hastaliklari ve frengi arsivi | Not in English language |
| Tye, M. J. L., E.Acne treated with wet compresses followed by corticosteroid cream. 1968. Arizona Medicine | No relevant study design - not RCT |
| Tzung, T. Y. W., K. H.,Huang, M. L.Blue light phototherapy in the treatment of acne. 2004. Photodermatology Photoimmunology and Photomedicine | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Uebelhoer, N. S. B., M. A.,Dover, J. S.,Arndt, K. A.,Rohrer, T. E.Comparison of stacked pulses versus double-pass treatments of facial acne with a 1,450-nm laser. 2007. Dermatologic Surgery | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Uede, M. K., C.,Yonei, N.,Furukawa, F.,Yamamoto, Y.Persistent effects of adapalene gel after chemical peeling with glycolic acid in patients with acne vulgaris. 2013. Open dermatology journal | Participants were not selected on their complete/partial response to the first treatment |
| Ullah, G. N., S. M.,Bhatti, Z.,Ahmad, M.,Bangash, A. R.Comparison of oral azithromycin with oral doxycycline in the treatment of acne vulgaris. 2014. Journal of Ayub Medical College, Abbottabad : JAMC | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Ustuner, P. G., A. T.,Demirbilek, M.Clinical and bacteriological evaluation of nadifloxacin 1% cream versus erythromycin 4% gel in the treatment of mild-to-moderate facial acne vulgaris: a randomized study. 2015. Turkiye klinikleri journal of medical sciences | No relevant intervention - nadifloxacin 1% cream not available in the UK |
| Vali, A. F., G.,Zaghian, N.,Koosha, M.The efficacy of topical solution of 0.3% ciprofloxacin in treatment of mild to moderate acne vulgaris. 2009. Iranian Red Crescent Medical Journal | No relevant intervention - topical ciprofloxacin cream |
| Van der Meeren, H. L. M. V. d. S., J. G.,Stijnen, T.Dose-response relationship in isotretinoin therapy for conglobate acne. 1983. Dermatologica | Relevant outcomes only reported graphically - cannot extract useful data |
| Van Neste, D. T., D.,Decroix, J.Imidazoles and benzoyl peroxide: A comparative trial of two treatment schedules. 1986. Dermatologica | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| van Wayjen, R. G. v. d. E., A.Experience in the long-term treatment of patients with hirsutism and/or acne with cyproterone acetate-containing preparations: efficacy, metabolic and endocrine effects. 1995. Experimental & Clinical Endocrinology & Diabetes | No relevant study design - not RCT |
| Van, d. V., dMHLM,Stijnen, T.The treatment of acne conglobata with | Not in English language |

| Reference | Reason for exclusion |
|---|---|
| 13-cis retinoic acid (isotretinoin). 1983. Nederlands tijdschrift voor geneeskunde | |
| Van, T. N. D. T., L.,Nguyen Trong, H.,Chau Van, T.,Trinh Minh, T.,Thi Minh, P. P.,Dinh Huu, N.,Tran Cam, V.,Le Huyen, M.,Tran Hau, K.,Gandolfi, M.,Satolli, F.,Feliciani, C.,Tirant, M.,Vojvodic, A.,Lotti, T.Efficacy of oral isotretinoin in combination with desloratadine in the treatment of common vulgaris acne in Vietnamese Patients. 2019. Open Access Macedonian Journal of Medical Sciences | No relevant internvention - oral Desloratadine; also no relevant study population - insufficient information to determine severity of acne |
| Vartiainen, M. d. G., H.,Broekmeulen, C. J.Comparison of the effect on acne with a combiphasic desogestrel-containing oral contraceptive and a preparation containing cyproterone acetate. 2001. European Journal of Contraception & Reproductive Health Care | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Vasarinsh, P.Benzoyl Peroxide- Sulfur Lotions in Acne Vulgaris- A Controlled Study. 1969. Cutis; cutaneous medicine for the practitioner | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Vaswani, N. P., R. K.,Bhutani, L. K.,Ramachandran, K.Topical therapy of acne vulgaris with retinoic acid and erythromycin lotion. 1989. Indian journal of dermatology, venerology and leprology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Vaswani, N. P., R. K.Treatment of acne vulgaris with anti-androgens. 1990. Indian journal of dermatology, venerology and leprology | No relevant intervention - cimetidine |
| Vatanchi, M. F., G.,Siegel, D.Updates on novel research in laser and photodynamic therapy for treatment of acne vulgaris. 2017. Journal of the american academy of dermatology | Duplicate record |
| Venier, A. C., P.,Salvatori, S.,Varricchio, M. C.Topical treatment of acne vulgaris with clindamycin phosphate solution (double blind clinical trial). 1985. Chronica dermatologica | Not in English language |
| Verma, K. C. S., A. S.,Dhamija, S. K.Oral zinc sulphate therapy in acne vulgaris: a double-blind trial. 1980. Acta Dermato-Venereologica | No relevant study population - insufficient details to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Vermeulen, A. R., R.Effects of cyproterone acetate plus ethinylestradiol low dose on plasma androgens and lipids in mildly hirsute or acneic young women. 1988. Contraception | No relevant study population - sample includes people with hirsuitism or acne but no details of acne participants provided and study is not relevant for PCOS, maintenance or refractory treatments |
| Verschoore, M. L., A.,Wolska, H.,Jablonska, S.,Czernielewski, J.,Schaefer, H.Efficacy and safety of CD 271 alcoholic gels in the topical treatment of acne vulgaris. 1991. British Journal of Dermatology | No relevant intervention - CD 271 alcoholic gel |

| Reference | Reason for exclusion |
|---|---|
| Verschoore, M. P., M.,Czernielewski, J.,Sorba, V.,Clucas, A.Adapalene 0.1% gel has low skin-irritation potential. 1997. Journal of the American Academy of Dermatology | No relevant study population - participants did not have acne |
| Voravutinon, N. R., J.,Sadhwani, D.,Iyengar, S.,Alam, M.A comparative split-face study using different mild purpuric and subpurpuric fluence level of 595-nm pulsed-dye laser for treatment of moderate to severe acne vulgaris. 2016. Dermatologic Surgery | No relevant study design - not RCT |
| Wahab, M. A. R., M. H.,Monamie, N. S.,Jamaluddin, M.,Khondker, L.,Afroz, W.Isotretinoin versus weekly pulse dose azithromycin in the treatment of acne- A comparative study. 2008. Journal of Pakistan Association of Dermatologists | No relevant comparison - azithromycin |
| Walton, S. C., W. J.,Lookingbill, P.,Keczkes, K.Lack of effect of topical spironolactone on sebum excretion. 1986. British Journal of Dermatology | No relevant article type - letter to editor |
| Wang, A. P., Tu, P., Ji, S. Z., Wu, Y., Shen, Y., Zhu, X. J.Clinical efficacy of benzoyl peroxide gel with different concentrations in acne vulgaris. 2003. Chinese journal of dermatology | Not in English language |
| Wang, H. W. L., T.,Zhang, L. L.,Guo, M. X.,Stepp, H.,Yang, K.,Huang, Z.,Wang, X. L.Prospective study of topical 5-aminolevulinic acid photodynamic therapy for the treatment of moderate to severe acne vulgaris in Chinese patients. 2012. Journal of Cutaneous Medicine & Surgery | No relevant study design - not RCT |
| Wang, J. H. W., B.,Zheng, R. D.Effective observation on external using tretinoin cream treating common acne (Chinese). 2001. China journal of leprosy & skin diseases | Not in English language |
| Wang, Q. Y., D.,Liu, W.,Chen, J.,Lin, X.,Cheng, S.,Li, F.,Duan, X.Use of optical fiber imported intra-tissue photodynamic therapy for treatment of moderate to severe acne vulgaris. 2016. Medical Science Monitor | No relevant data - insufficient data reported |
| Wang, S. Q. C., J. T.,Flor, M. E.,Zelickson, B. D.Treatment of inflammatory facial acne with the 1,450 nm diode laser alone versus microdermabrasion plus the 1,450 nm laser: A randomized, split-face trial. 2006. Dermatologic Surgery | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Wangsuwan, S., Meephansan, J.Comparative study of photodynamic therapy with riboflavin-tryptophan gel and 13% 5-aminolevulinic acid in the treatment of mild to moderate acne vulgaris. 2019. Clinical, Cosmetic and Investigational Dermatology | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Wanitphakdeedecha, R. I., T.,Phothong, W.,Eimpunth, S.,Manuskiatti, W.Local and systemic effects of low-level light therapy with light-emitting diodes to improve erythema after fractional ablative skin resurfacing: a controlled study. 2019. Lasers in Medical Science | Duplicate record |
| Wanitphakdeedecha, R., Tavechodperathum, N., Tantrapornpong, P., Suphatsathienkul, P., Techapichetvanich, T., Eimpunth, S., Manuskiatti, W.Acne treatment efficacy of intense pulsed light | No relevant study population - sample includes people with mild |

| Reference | Reason for exclusion |
|---|---|
| photodynamic therapy with topical licochalcone A, l-carnitine, and decanediol: A spilt-face, double-blind, randomized controlled trial. 2020. Journal of Cosmetic DermatologyJ | to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Waranuch, N. P., P.,Yakaew, S.,Nakyai, W.,Grandmottet, F.,Onlom, C.,Srivilai, J.,Viyoch, J.Antiacne and antiblotch activities of a formulated combination of Aloe barbadensis leaf powder, Garcinia mangostana peel extract, and Camellia sinensis leaf extract. 2019. Clinical, Cosmetic and Investigational Dermatology CCID | No relevant intervention - a combination of Aloe barbadensis leaf extract, Garcinia mangostana peel extract, and Camellia sinensis leaf extract |
| Warren, M. R., J.,Arbit, D.,Sevilla, C.,Flack, M.The effects on weight of a low-dose oral contraceptive in the treatment of women with moderate acne vulgaris. 2001. Fertility and sterility | No relevant article type - conference abstract |
| Webster, G. C., D. I.,Quiring, J.,Vogelson, C. T.,Slade, H. B.A combined analysis of 2 randomized clinical studies of tretinoin gel 0.05% for the treatment of acne. 2009. Cutis; cutaneous medicine for the practitioner | No relevant dat reported - reports pooled results of 2 trials combined |
| Webster, G. F. G., L.,Poulin, Y. P.,Solomon, B. A.,Loven, K.,Lee, J.A multicenter, double-blind, randomized comparison study of the efficacy and tolerability of once-daily tazarotene 0.1% gel and adapalene 0.1% gel for the treatment of facial acne vulgaris. 2002. Cutis; cutaneous medicine for the practitioner | Not obtainable |
| Webster, G. F.Safety and efficacy of Tretin-X compared with Retin-A in patients with mild-to-severe acne vulgaris. 2006. Skinmed | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Webster, G. R., P.,Gold, M. H.,Mraz, S.,Calvarese, B.,Chen, D.Efficacy and tolerability of a fixed combination of clindamycin phosphate (1.2%) and low concentration benzoyl peroxide (2.5%) aqueous gel in moderate or severe acne subpopulations. 2009. Journal of Drugs in Dermatology | No relevant data reported - pblication from Thiboutot 2008 |
| Webster, G. T., D. M.,Chen, D. M.,Merikle, E.Impact of a fixed combination of clindamycin phosphate 1.2%-benzoyl peroxide 2.5% aqueous gel on health-related quality of life in moderate to severe acne vulgaris. 2010. Cutis | No relevant data reported - reports quality of life outcomes |
| Weiss, J. G., L. S.,Leoni, M.,Rueda, M. J.,Liu, H.,Tanghetti, E.Customized single-agent therapy management of severe inflammatory acne: A randomized, double-blind, parallel-Group, controlled study of a new treatment - Adapalene 0.3%-benzoyl peroxide 2.5% gel. 2015. Journal of Drugs in Dermatology | No relevant data reported - subgroup analysis of people with severe acne participating in Stein Gold 2016 |
| Weiss, J. S. G., L.,Leoni, M.,Rueda, M. J.,Liu, H.,Tanghetti, E.Customized Single-agent Therapy Management of Severe Inflammatory Acne: A Randomized, Double-blind, Parallel-group, Controlled Study of a New Treatment--Adapalene 0.3%-Benzoyl Peroxide 2.5% Gel. 2015. Journal of Drugs in Dermatology: JDD | Duplicate record |
| Weissmann, A. W., A.,Plewig, G.Reduction of bacterial skin flora during oral treatment of severe acne with 13-cis retinoic acid. 1981. Archives of Dermatological Research | No relevant study design - not RCT |
| Weltert, Y. C., S.,Gibaud, C.,Courau, S.,Pechenart, P.,Sirvent, A.,Girard, F.Double-blind clinical assessment of the efficacy of a 4% nicotinamide gel (Exfoliac NC Gel) versus a 4% erythromycin gel in the treatment of moderate acne with a predominant inflammatory component. [French, English]. 2004. Nouvelles Dermatologiques | Not in English language |

| Reference | Reason for exclusion |
|---|---|
| Wen, X. L., Y.,Hamblin, M. R.Photodynamic therapy in dermatology beyond non-melanoma cancer: An update. 2017. Photodiagnosis and Photodynamic Therapy | Duplicate record |
| Wexler, L.Two controlled studies of a topical steroid preparation in the treatment of acne vulgaris. 1968. Applied Therapeutics | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Wiegell, S. R. W., H. C.Photodynamic therapy of acne vulgaris using 5-aminolevulinic acid versus methyl aminolevulinate. 2006a. Journal of the American Academy of Dermatology | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Wilhelm, K. P. W., D.,Neumeister, C.,Zsolt, I.,Schwantes, U.Lack of irritative potential of nadifloxacin 1% when combined with other topical anti-acne agents. 2012. Clinical and Experimental Dermatology | No relevant study population - participants did not have acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Wilkinson, R. D. A., J. E.,Murray, J. J.,Craig, G. E.Benzoyl peroxide and sulfur: foundation for acne management. 1966. Canadian Medical Association Journal | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Winkler, U. H. F., H.,Mulders, J. A.Cycle control, quality of life and acne with two low-dose oral contraceptives containing 20 microg ethinylestradiol. 2004a. Contraception | Duplicate record |
| Winkler, U. H. F., H.,Mulders, JapaCycle control, quality of life and acne with two low-dose oral contraceptives containing 20 mug ethinylestradiol. 2004b. Contraception | No relevant study population - participants did not have acne |
| Wishart, J. M.An open study of Triphasil and Diane 50 in the treatment of acne. 1991. The Australasian journal of dermatology | No relevant population - insufficient information reported about acne severity and study is not relevant for PCOS, maintenance or refractory treatments |
| Witkowski, J. A. P., L. C.Chlorhydroxyquin-Benzoyl Peroxide Lotion in the Treatment of Acne - An Objective Evaluation. 1969. Cutis; cutaneous medicine for the practitioner | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Wolf, J. E., Jr.Safety and tolerability in the MORE trial. 2006. Cutis | No relevant study design - not RCT |
| Wong, R. C. K., S.,Heezen, J. L.Oral ibuprofen and tetracycline for the treatment of acne vulgaris. 1984. Journal of the American Academy of Dermatology | No relevant comparison |
| Woolery-Lloyd, H. B., L.,Ikeno, H.Sodium L-ascorbyl-2-phosphate 5% | No relevant study |

| Reference | Reason for exclusion |
|---|---|
| lotion for the treatment of acne vulgaris: a randomized, double-blind, controlled trial. 2010. NA | population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Worret, I. A., W.,Zahradnik, H. P.,Andreas, J. O.,Binder, N.Acne resolution rates: Results of a single-blind, randomized, controlled, parallel phase III trial with EE/CMA (Belara) and EE/LNG (Microgynon). 2001. Dermatology | No relevant data reported |
| Xia, J. H., G.,Hu, D.,Geng, S.,Zeng, W.Concomitant use of 1,550-nm nonablative fractional laser with low-dose isotretinoin for the treatment of acne vulgaris in asian patients: A randomized split-face controlled study. 2018. Dermatologic Surgery | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Xing,Fire needle therapy for moderate-severe acne: A PRISMA systematic review and meta-analysis of randomized controlled trials. 2019. NA | No relevant intervention - systematic review about fire needle therapy |
| Xu, H. L.Supplemented Raising and Sinking powder for treating ninety cases with acne due to blood heat stagnation. 2015b. Henan traditional chinese medicine [henan zhong yi] | No relevant intervention - supplemented raising and sinking powder combined with isotretinoin erythromycin gel |
| Xu,Supplemented Raising and Sinking powder for treating ninety cases with acne due to blood heat stagnation. 2015a. NA | Duplicate record |
| Yang, G. L. Z., M.,Wang, J. M.,He, C. F.,Luo, Y.,Liu, H. Y.,Gao, J.,Long, C. Q.,Bai, J. R.Short-term clinical effects of photodynamic therapy with topical 5-aminolevulinic acid for facial acne conglobata: an open, prospective, parallel-arm trial. 2013. Photodermatology, Photoimmunology & Photomedicine | No relevant study design - not RCT |
| Yang, Z., Zhang, Y., Lazic Mosler, E., Hu, J., Li, H., Zhang, Y., Liu, J., Zhang, Q.Topical benzoyl peroxide for acne. 2020. Cochrane Database of Systematic Reviews | Systematic review - references were checked for relevance |
| Yeung, C. K. S., S. Y.,Bjerring, P.,Yu, C. S.,Kono, T.,Chan, H. H.A comparative study of intense pulsed light alone and its combination with photodynamic therapy for the treatment of facial acne in Asian skin. 2007. Lasers in Surgery and Medicine | No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Yilmaz, O. S., N.,Yuksel, E. P.,Aydin, F.,Ozden, M. G.,Canturk, T.,Turanli, A.Evaluation of 532-nm KTP laser treatment efficacy on acne vulgaris with once and twice weekly applications. 2011. Journal of Cosmetic & Laser Therapy | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Yong, C. C.Benzoyl peroxide gel therapy in acne in Singapore. 1979. International Journal of Dermatology | No relevant study population - sample |

| Reference | Reason for exclusion |
|---|---|
| | includes 11% people with 11% acne |
| Yoon, J. H. P., E. J.,Kwon, I. H.,Kim, C. W.,Lee, G. S.,Hann, S. K.,Kim, K. H.,Kim, K. J.Concomitant use of an infrared fractional laser with low-dose isotretinoin for the treatment of acne and acne scars. 2014. Journal of dermatological treatment | No relevant intervention - laser treatment for acne scarring |
| Yoon, J. Y. K., H. H.,Min, S. U.,Thiboutot, D. M.,Suh, D. H.Epigallocatechin-3-gallate improves acne in humans by modulating intracellular molecular targets and inhibiting P. acnes. 2013. Journal of Investigative Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Yu, Z. S., J.,Lew-Kaya, D.,Walker, P.,Yu, D.,Tang-Liu, D. D.Pharmacokinetics of tazarotene cream 0.1% after a single dose and after repeat topical applications at clinical or exaggerated application rates in patients with acne vulgaris or photodamaged skin. 2003. Clinical Pharmacokinetics | No relevant study population - sample includes people with acne or photodamage - relevant outcomes not reported separately |
| Zachariae, H.Topical vitamin-A-acid in acne. 1980. Acta dermato-venereologica | No relevant study design - not RCT |
| Zander, E. W., S.Treatment of acne vulgaris with salicylic acid pads. 1992. Clinical Therapeutics | Duplicate record |
| Zarate, A. M., V. B.,Greenblatt, R. B.Effect of an antiandrogen, 17-alpha-methyl-B-nortestosterone, on acne and hirsutism. 1966. Journal of Clinical Endocrinology & Metabolism | No relevant study design - not RCT |
| Zeichner, J. A. H., M.,Linkner, R. V.,Wong, V.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. 2013. Journal of Drugs in Dermatology | No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments |
| Zeichner, J. A. P., R. V.,Haddican, M.,Wong, V.Efficacy and safety of a ceramide containing moisturizer followed by fixed-dose clindamycin phosphate 1.2%/benzoyl peroxide 2.5% gel in the morning in combination with a ceramide containing moisturizer followed by tretinoin 0.05% gel in the evening for the treatment of facial acne vulgaris. 2012. Journal of Drugs in Dermatology: JDD | No relevant study design - not RCT |
| Zeichner, J. A., Harper, J. C., Roberts, W. E., Guenin, E., Bhatt, V., Pillai, R.Novel tretinoin 0.05% lotion for the once-daily treatment of moderate-to-severe acne vulgaris: assessment of safety and tolerability in subgroups. 2019. Journal of Clinical and Aesthetic Dermatology | Not obtainable |
| Zeichner, J. A.The Efficacy and Tolerability of a Fixed Combination Clindamycin (1.2%) and Benzoyl Peroxide (3.75%) Aqueous Gel in Adult Female Patients with Facial Acne Vulgaris. 2015. The Journal of Clinical & Aesthetic Dermatology | Reports post hoc analysis of >=25 years old for Pariser 2014 |
| Zeichner, J.Strategies to minimize irritation and potential iatrogenic post-inflammatory pigmentation when treating acne patients with skin of color. 2011. Journal of Drugs in Dermatology: JDD | Duplicate record |
| Zeng, R., Liu, Y., Zhao, W., Yang, Y., Wu, Q., Li, M., Lin, T.A split-face comparison of a fractional microneedle radiofrequency device and fractional radiofrequency therapy for moderate-to-severe acne vulgaris. 2020. Journal of Cosmetic Dermatology. | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes |

| Reference | Reason for exclusion |
|---|---|
| | were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Zeng, X. L., W. L.,Zhao, T.Effects of Chinese medical facial mask comprehensive therapy in treating acne vulgaris. 2012b. Zhongguo zhong xi yi jie he za zhi zhongguo zhongxiyi jiehe zazhi = chinese journal of integrated traditional and western medicine | Duplicate record |
| Zeng,Effects of Chinese medical facial mask comprehensive therapy in treating acne vulgaris. 2012a. NA | Not in English language |
| Zhang, J., Zhang, X., He, Y., Wu, X., Huang, J., Huang, H., Lu, C.Photodynamic therapy for severe facial acne vulgaris with 5% 5-aminolevulinic acid vs 10% 5-aminolevulinic acid: A split-face randomized controlled study. 2020. Journal of Cosmetic DermatologyJ | Duplicate publication |
| Zhang, X. M.Clinical observations on the efficacy of autohemotherapy plus pricking-cupping bloodletting in treating common acne. 2015. Shanghai journal of acupuncture and moxibustion [shang hai zhen jiu za zhi] | Not in English language |
| Zhou, B. R. Z., T.,Bin Jameel, A. A.,Xu, Y.,Guo, S. L.,Wang, Y.,Permatasari, F.,Luo, D.The efficacy of conditioned media of adipose-derived stem cells combined with ablative carbon dioxide fractional resurfacing for atrophic acne scars and skin rejuvenation. 2016b. Journal of Cosmetic and Laser Therapy | No relevant study population - sample includes people with acne scars |
| Zhou, L.Pipa Qingfei Decoction combined with External Application of Acne Tincture in Treating Acne for 120 Cases. 2016c. Chinese medicine modern distance education of china [zhong guo zhong yi yao xian dai yuan cheng jiao yu] | Duplicate record |
| Zhou, Y. Q. Y., R. J.The Curative Effect Observation of Tretinoin Capsule Combined with Tretinoin Cream in Treating Acne Vulgaris (Chinese). 2000. Chinese journal of dermatovenereology | Not in English language |
| Zhou,Pipa Qingfei Decoction combined with External Application of Acne Tincture in Treating Acne for 120 Cases. 2016a. NA | Not obtainable |
| Zhu, X. J. T., P.,Zhen, J.,Duan, Y. Q.Adapalene gel 0.1%: effective and well tolerated in the topical treatment of acne vulgaris in Chinese patients. 2001. Cutis; cutaneous medicine for the practitioner | Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments |
| Zouboulis, C. C. F., T. C.,Wohlrab, J.,Barnard, J.,Alio, A. B.Study of the efficacy, tolerability, and safety of 2 fixed-dose combination gels in the management of acne Vulgaris. 2009. Cutis | No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments |

*PCOS: polycystic ovary syndrome; RCT: randomised controlled trial*

## Economic studies

No economic evidence was identified for this review.

# Appendix L – Research recommendations

### Research recommendations for review question: What is the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris?

No research recommendations were made for this review question.