

## Acne vulgaris: management

### [I] Maintenance treatments for acne vulgaris

*NICE guideline number tbc*

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

*December 2020*

*Draft for Consultation*

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



## **Disclaimer**

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

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

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the [Welsh Government](#), [Scottish Government](#), and [Northern Ireland Executive](#). All NICE guidance is subject to regular review and may be updated or withdrawn.

## **Copyright**

© NICE 2020. All rights reserved. Subject to [Notice of rights](#).

ISBN:

## Contents

<b>Maintenance treatment for acne vulgaris .....</b>	<b>6</b>
Review question .....	6
Summary of the protocol .....	6
Methods and process .....	7
Clinical evidence .....	7
Summary of clinical studies included in the evidence review .....	8
Quality assessment of clinical studies included in the evidence review .....	12
Economic evidence .....	13
Economic model.....	13
The committee’s discussion of the evidence.....	13
Recommendations supported by this evidence review .....	15
References.....	15
<b>Appendices.....</b>	<b>17</b>
Appendix A – Review protocol.....	17
Review protocol for review question: What is the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris?.....	17
Appendix B – Literature search strategies .....	24
Literature search strategies for review question: What is the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris?.....	24
Clinical search.....	24
Economic search.....	36
Appendix C – Clinical evidence study selection .....	39
Clinical study selection for review question: What is the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris?.....	39
Appendix D – Evidence tables.....	40
Evidence tables for review question: What is the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris?.....	40
Appendix E – Forest plots.....	55
Forest plots for review question: What is the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris?.....	55
Appendix F – GRADE tables .....	57
GRADE tables for review question: What is the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris?.....	57
Appendix G - Economic evidence study selection .....	71
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?.....	71

Appendix H– Economic evidence tables .....	72
Economic evidence tables for review question: What is the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris?.....	72
Appendix I – Economic evidence profiles .....	73
Economic evidence profiles for review question: What is the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris?.....	73
Appendix J – Economic analysis .....	74
Economic analysis for review question: What is the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris?.....	74
Appendix K – Excluded studies .....	75
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? .....	75
Clinical studies .....	75
Economic studies .....	157
Appendix L – Research recommendations .....	158
Research recommendations for review question: What is the effectiveness of topical or oral pharmacological and physical interventions as maintenance treatment for acne vulgaris?.....	158

# 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**

<b>Population</b>	People of all ages whose acne is 'in remission', have had their acne treated successfully, or whose acne has responded to treatment.
<b>Intervention</b>	<ul style="list-style-type: none"><li>• Topical treatments including abrasive/cleaning agents, anthelmintics, antibacterials, antibiotics, antiseptics, dicarboxylic acids, vitamin B3, retinoids or retinoid-like agents, or any combination of these.</li><li>• Oral antibiotics including, for example, carbapenems, cephamycins/cephalosporins, sulphones, fucidic acid, lincosamides, macrolides, monobactams, penicillins, or any combination of these.</li><li>• Oral isotretinoin.</li><li>• Hormonal treatments including (monophasic and phasic) progestogen-only contraceptives, co-cyprindiol, and combined oral contraceptives.</li><li>• Hormone-modifying agents including, for example, aldosterone antagonists (for example, spironolactone), class 5<math>\alpha</math>-reductase inhibitor (for example, dutasteride), other non-steroidal anti-androgens (for example, flutamide), and metformin.</li><li>• 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).</li></ul>
<b>Comparison</b>	<ul style="list-style-type: none"><li>• Any other active acne treatment</li><li>• No treatment</li><li>• Placebo (for example, vehicle capsule, gel, solution, tablet)</li><li>• Sham physical treatment</li><li>• Waiting list</li></ul>
<b>Outcomes</b>	<b>Critical</b> <ul style="list-style-type: none"><li>• Clinician-rated improvement at treatment endpoint:<ul style="list-style-type: none"><li>○ Percentage change in acne lesion count</li><li>○ Change from baseline or final score on a validated acne severity scale.</li></ul></li><li>• Prevention of scarring at any follow-up:<ul style="list-style-type: none"><li>○ Change from baseline or final number of scars</li></ul></li></ul>

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

1 For further details see the review protocol in appendix A.

## 2 **Methods and process**

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

7 Declarations of interest were recorded according to [NICE's conflicts of interest policy](#).

## 8 **Clinical evidence**

### 9 **Included studies**

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

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

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

19 One RCT (Truchuelo 2015) was a split-face study comparing retinoid combination versus  
20 vehicle in participants who had previously been treated with isotretinoin. One RCT (Vender  
21 2012) compared tretinoin versus vehicle in participants who had also previously been treated  
22 with isotretinoin. One RCT (Thielitz 2015) compared azelaic acid versus observation; this  
23 study included a third treatment arm that was not included in the review because participants  
24 received adapalene gel for 9 months, which did not meet protocol eligibility criteria for  
25 treatment duration. Evidence from these 3 studies was analysed separately.

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

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

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

11 The included studies are summarised in Table 2.

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

### 13 Excluded studies

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

### 16 Summary of clinical studies included in the evidence review

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

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

Study	Population	Intervention	Comparison	Outcomes
Kawashima 2018 RCT Japan	N=92 randomised to: <ul style="list-style-type: none"> <li>Adapalene gel (n=47)</li> <li>Benzoyl peroxide gel (n=45)</li> </ul> <p>Participants with moderate to severe facial acne vulgaris who had less than mild (<math>\leq 5</math> inflammatory eruptions on the entire face with <math>\leq 3</math> on one side of the face)</p> <p>Mean age (years): NR for maintenance phase Sex (male): NR for maintenance phase</p>	<ul style="list-style-type: none"> <li>0.1% adapalene gel applied once a day</li> </ul> <p>Applied after washing face before sleep</p>	<ul style="list-style-type: none"> <li>2.5% benzoyl peroxide applied once a day</li> </ul> <p>Applied after washing face before sleep</p>	<ul style="list-style-type: none"> <li>Relapse/aggravation of symptoms after 12 weeks</li> <li>Adverse events- Erythema</li> <li>Adverse events- Dryness</li> </ul>
Leyden 2006 RCT US	N=110 randomised to: <ul style="list-style-type: none"> <li>Tazarotene gel plus placebo capsule (n=36)</li> <li>Vehicle gel plus minocycline hydrochloride capsule (n=37)</li> <li>Tazarotene gel plus minocycline capsule (n=37)</li> </ul>	<ul style="list-style-type: none"> <li>0.1% tazarotene gel each evening plus placebo capsule twice daily</li> <li>0.1% tazarotene gel each evening plus a 100 mg minocycline capsule twice</li> </ul>	<ul style="list-style-type: none"> <li>Vehicle gel each evening plus a 100 mg minocycline hydrochloride capsule twice daily</li> </ul>	<ul style="list-style-type: none"> <li>Percentage change in inflammatory and non-inflammatory lesion count after 12 weeks</li> <li>Participants maintaining <math>\geq 70\%</math> reduction in inflammatory and non-inflammatory lesion count</li> </ul>



Study	Population	Intervention	Comparison	Outcomes
	<p>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</p> <p>Mean age (years): 22 Sex (female): 55%</p>	<p>daily</p> <p>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.</p>		<p>achieved in the initial treatment phase, after 12 weeks (relapse rate calculated)</p> <ul style="list-style-type: none"> <li>• Acceptability (treatment discontinuation for any reason) after 12 weeks</li> <li>• Tolerability (treatment discontinuation due to side effects) after 12 weeks</li> </ul>
<p>Poulin 2011</p> <p>RCT</p> <p>US, Canada, Puerto Rico</p>	<p>N=243 randomised to:</p> <ul style="list-style-type: none"> <li>• Adapalene plus BPO (n=123)</li> <li>• Vehicle gel (n=120)</li> </ul> <p>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).</p> <p>Mean (<math>\pm</math> SD) age (years): Adapalene-BPO: 19.1 (5.89) Vehicle: 18.2 (5.23) Sex (male): Adapalene-BPO: n=65 Vehicle: n=67</p>	<ul style="list-style-type: none"> <li>• Fixed dose combination gel 0.1% adapalene plus 2.5% benzoyl peroxide (adapalene-BPO) once daily in the evening</li> </ul> <p>Participants were encouraged to use sun protection factor 15 daily facial moisturiser and a gentle skin cleanser</p>	<ul style="list-style-type: none"> <li>• Vehicle gel once daily in the evening</li> </ul> <p>Participants were encouraged to use sun protection factor 15 daily facial moisturiser and a gentle skin cleanser</p>	<ul style="list-style-type: none"> <li>• Percentage change in lesion count from baseline to 24 weeks</li> <li>• IGA success rate (% of participants rated better or same as baseline) at 24 weeks</li> <li>• Participants having at least 50% improvement from at 24 weeks in total lesions</li> <li>• Treatment-related adverse effects at 24 weeks</li> <li>• Irritation at 24 weeks (including erythema, scaling, dryness, stinging/burning)</li> <li>• Acceptability (treatment discontinuation for any reason) at 24 weeks</li> <li>• Tolerability (treatment discontinuation due to side effects) at 24 weeks</li> </ul>
<p>Thiboutot 2006</p> <p>RCT</p> <p>US</p>	<p>N=253 randomised to:</p> <ul style="list-style-type: none"> <li>• Adapalene (n=126)</li> <li>• Vehicle gel (n=127)</li> </ul> <p>Participants with severe acne and who showed at least moderate improvement from baseline (50%)</p>	<ul style="list-style-type: none"> <li>• 0.1% adapalene gel once daily in the evening</li> </ul> <p>Participants were provided with a daily facial moisturiser with sun protection factor 15 to use as</p>	<ul style="list-style-type: none"> <li>• Vehicle gel once daily in the evening</li> </ul> <p>Participants were provided with a daily facial moisturiser with sun protection</p>	<ul style="list-style-type: none"> <li>• Percentage of participants maintaining at least 50% improvement after 16 weeks (total lesions)</li> <li>• Treatment-related adverse effects after 16 weeks</li> <li>• Acceptability</li> </ul>

Study	Population	Intervention	Comparison	Outcomes
	<p>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</p> <p>Mean (<math>\pm</math> SD) age (years): Adapalene: 18.1 (4.2) Vehicle: 17.8 (3.9) Sex (male): Adapalene: n=65 Vehicle: n=73</p>	<p>needed for the symptomatic relief of skin dryness or irritation</p>	<p>factor 15 to use as needed for the symptomatic relief of skin dryness or irritation</p>	<p>(treatment discontinuation for any reason) after 16 weeks</p> <ul style="list-style-type: none"> <li>• Tolerability (treatment discontinuation due to side effects) after 16 weeks</li> </ul>
<p>Thielitz 2007</p> <p>RCT</p> <p>Germany</p>	<p>N=49 randomised to:</p> <ul style="list-style-type: none"> <li>• Adapalene (n=16)</li> <li>• Adapalene alternately with vehicle (n=16)</li> <li>• Vehicle gel (n=17)</li> </ul> <p>Participants with mild to moderate acne and with a presence of at least 250 microcomedones per cm<sup>2</sup> on the forehead at screening (counted via cyanoacrylate strips)</p> <p>Mean (<math>\pm</math> SD) age (years): Adapalene: 18.33 (5.0) Adapalene alternately with vehicle: 16.47 (2.4) Vehicle: 19.58 (5.4) Sex (male): 59.2%</p>	<ul style="list-style-type: none"> <li>• 0.1% adapalene gel once daily applied to the face</li> <li>• 0.1% adapalene gel alternately with vehicle once daily every other day applied to the face</li> </ul> <p>Participants applied the same skin cleanser and moisturiser immediately before treatments and were advised to avoid excessive exposure to sunlight</p>	<ul style="list-style-type: none"> <li>• Vehicle once daily applied to the face</li> </ul> <p>Participants applied the same skin cleanser and moisturiser immediately before treatments and were advised to avoid excessive exposure to sunlight</p>	<ul style="list-style-type: none"> <li>• Percentage change in microcomedone count after 12 weeks (total lesions)</li> <li>• Treatment-related adverse events</li> <li>• Treatment discontinuations</li> </ul>
<p>Thielitz 2015</p> <p>RCT</p> <p>Germany</p>	<p>N=36 randomised to:</p> <ul style="list-style-type: none"> <li>• Azelaic acid (n=17)</li> <li>• Observation (n=19)</li> </ul> <p>Participants with mild to moderate acne including those with 'late-type acne'</p> <p>Mean (<math>\pm</math> SD) age (years): Azelaic acid: 30.58 (9.28)</p>	<ul style="list-style-type: none"> <li>• 15% azelaic acid gel twice daily for 9 months (6 months maintenance)</li> </ul> <p>Participants were not permitted to take any other topical or systemic anti-acne medication including systemic oral</p>	<ul style="list-style-type: none"> <li>• 6 months observation following 3 months 15% azelaic acid gel twice daily</li> </ul> <p>Participants were not permitted to take any other topical or systemic anti-acne medication</p>	<ul style="list-style-type: none"> <li>• Relative change in total lesions after 24 weeks</li> <li>• Absolute change after 24 weeks maintenance in ISGA</li> <li>• Absolute change after 24 weeks maintenance in LRAGS</li> <li>• SGCA after 24 weeks</li> <li>• Relapse during 24</li> </ul>

Study	Population	Intervention	Comparison	Outcomes
	Observation: 28.14 (4.56) Sex (female): 100%	corticosteroids during the study period	including systemic oral corticosteroids during the study period	weeks <ul style="list-style-type: none"> <li>Acceptability (treatment discontinuation for any reason - treatment and maintenance phase)</li> <li>Tolerability (treatment discontinuation due to side effects during 24 weeks)</li> </ul>
Truchuelo 2015  RCT (Split face)  Spain	N=30 – sides of the face randomised to: <ul style="list-style-type: none"> <li>Retinoid combination</li> <li>Vehicle</li> </ul> <p>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</p> <p>Mean (± SD) age (years): Male: 18.4 (5.2) Female: 23.5 (5.6) Sex (male): 40.6%</p>	<ul style="list-style-type: none"> <li>Retinoid combination (retinol encapsulated in glycospheres and hydroxypinacolone retinoate) applied to one side of the face at night</li> </ul>	<ul style="list-style-type: none"> <li>Vehicle applied to the other side of the face at night</li> </ul>	<ul style="list-style-type: none"> <li>Relapse (global count) after 3 months</li> <li>Number of total lesions after 3 months</li> <li>Global lesions after 3 months</li> <li>IGA after 3 months</li> <li>Adverse events</li> <li>Discontinuations</li> </ul>
Vender 2012  RCT  Canada	N=20 randomised to: <ul style="list-style-type: none"> <li>Tretinoin (n=10)</li> <li>Vehicle (n=10)</li> </ul> <p>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)</p> <p>Mean age (years): Tretinoin: 21 Vehicle: 22.4 Sex (male): 100%</p>	<ul style="list-style-type: none"> <li>0.04% Tretinoin gel (microsphere) applied once daily to the whole face (and left on for a minimum of 8 hours)</li> </ul> <p>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</p>	<ul style="list-style-type: none"> <li>Vehicle applied once daily to the whole face (and left on for a minimum of 8 hours)</li> </ul> <p>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.</p>	<ul style="list-style-type: none"> <li>Lesion count at 24 weeks</li> <li>ISGA at 24 weeks</li> <li>SGCA at 24 weeks</li> <li>Acceptability (treatment discontinuation for any reason) at week 24</li> <li>Serious adverse events or adverse events</li> <li>Tolerability</li> </ul>

Study	Population	Intervention	Comparison	Outcomes
		in the morning or in the evening throughout the study duration.  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.  Participants were permitted to use moisturiser and cleanser on the face provided	
Zhang 2004  Open-labelled controlled trial  China	N=241 randomised to: • Adapalene (n=122) • No treatment (n=119)  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.  Mean age (years): NR for maintenance phase 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)	<ul style="list-style-type: none"> <li>• Mean percentage reduction after 12 weeks maintenance phase (total lesions)</li> <li>• Global assessment of change (further improved and much improved/clear) at the end of 12 weeks maintenance phase</li> <li>• Adverse events</li> </ul>

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

4 See the full evidence table in appendix D and forest plots in appendix E.

## 5 Quality assessment of clinical studies included in the evidence review

6 See the evidence profiles in appendix F.

1 **Economic evidence**

2 **Included studies**

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

7 **Excluded studies**

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

9 **Economic model**

10 No economic modelling was conducted for this review question, because the committee  
11 agreed that other topics were higher priorities for economic evaluation.

12 **The committee's discussion of the evidence**

13 ***Interpreting the evidence***

14 ***The outcomes that matter most***

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

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

22 ***The quality of the evidence***

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

29 ***Benefits and harms***

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

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

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

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

4 Based on evidence from 2 studies where acne had improved rather than cleared and  
5 treatment was effectively maintaining this improvement, the committee decided that people  
6 with incomplete response to acne treatment would be likely to benefit from maintenance  
7 treatment. They noted that a maintenance treatment may also reduce the acne further. They  
8 also agreed that it could be appropriate for people where acne frequently relapses after  
9 treatment because a maintenance treatment could also reduce the likelihood of acne  
10 recurring.

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

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

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

### 38 **Cost effectiveness and resource use**

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

1 **Other factors the committee took into account**

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

9 **Recommendations supported by this evidence review**

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

11 **References**

12 **Kawashima 2018**

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

15 **Leyden 2006**

16 Leyden, J., Thiboutot, D. M., Shalita, A. R., Webster, G., Washenik, K., Strober, B. E.,  
17 Shupack, J., Comparison of tazarotene and minocycline maintenance therapies in acne  
18 vulgaris: a multicenter, double-blind, randomized, parallel-group study, Arch Dermatol, 142,  
19 605-12, 2006

20 **Poulin 2011**

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

25 **Thiboutot 2006**

26 Thiboutot, D. M., Shalita, A. R., Yamauchi, P. S., Dawson, C., Kerrouche, N., Arsonnaud, S.,  
27 Kang, S., Adapalene gel, 0.1%, as maintenance therapy for acne vulgaris: a randomized,  
28 controlled, investigator-blind follow-up of a recent combination study, Arch Dermatol, 142,  
29 597-602, 2006

30 **Thielitz 2007**

31 Thielitz, A., Sidou, F., Gollnick, H., Control of microcomedone formation throughout a  
32 maintenance treatment with adapalene gel, 0.1%, J Eur Acad Dermatol Venereol, 21, 747-  
33 53, 2007

34 **Thielitz 2015**

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

39 **Truchuelo 2015**

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

1     **Vender 2012**

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

6     **Zhang 2004**

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



# 1 Appendices

## 2 Appendix A – Review protocol

### 3 Review protocol for review question: What is the effectiveness of topical 4 or oral pharmacological and physical interventions as maintenance 5 treatment for acne vulgaris?

6 **Table 3: Review protocol for topical or oral pharmacological and physical**  
7 **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	<p>The following databases will be searched:</p> <ul style="list-style-type: none"> <li>• Cochrane Central Register of Controlled Trials (CENTRAL)</li> <li>• Cochrane Database of Systematic Reviews (CDSR)</li> <li>• Embase</li> <li>• MEDLINE</li> </ul> <p>Searches will be restricted by:</p> <ul style="list-style-type: none"> <li>• Date: No restriction.</li> <li>• Language of publication: English language only.</li> <li>• 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.</li> <li>• Standard exclusions filter (animal studies/low level publication types) will be applied .</li> <li>• 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.</li> <li>• Other search methods will involve scanning the reference lists of all eligible systematic reviews for published studies meeting inclusion criteria.</li> </ul>
Condition or domain being studied	<ul style="list-style-type: none"> <li>• Acne vulgaris</li> </ul>
Population	<p>Inclusion:</p> <ul style="list-style-type: none"> <li>• People of all ages whose acne is ‘in remission’, have had their acne treated successfully, or whose acne has responded to treatment.</li> </ul> <p>All settings (community, primary, secondary, and tertiary healthcare) will be considered.</p> <p>Exclusion:</p> <ul style="list-style-type: none"> <li>• Neonatal acne</li> </ul>

Field	Content
	<ul style="list-style-type: none"> <li>• People with post-inflammatory dyspigmentation</li> <li>• Trials in people with PCOS.</li> </ul>
Intervention	<ul style="list-style-type: none"> <li>• Topical treatments including abrasive/cleaning agents, anthelmintics, antibacterials, antibiotics, antiseptics, dicarboxylic acids, vitamin B3, retinoids or retinoid-like agents, or any combination of these.</li> <li>• Oral antibiotics including, for example, carbapenems, cephamycins/cephalosporins, sulphones, fucidic acid, lincosamides, macrolides, monobactams, penicillins, or any combination of these.</li> <li>• Oral isotretinoin.</li> <li>• Hormonal treatments including (monophasic and phasic) progestogen-only contraceptives, co-cyprindiol, and combined oral contraceptives.</li> <li>• Hormone-modifying agents including, for example, aldosterone antagonists (for example spironolactone), class 5<math>\alpha</math>- reductase inhibitor (for example dutasteride), other non-steroidal anti-androgens (for example flutamide), and metformin.</li> <li>• 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).</li> <li>•</li> </ul>
Comparator	<p>Comparisons include:</p> <ul style="list-style-type: none"> <li>• Any other active acne treatment</li> <li>• No treatment</li> <li>• Placebo (for example vehicle capsule, gel, solution, tablet)</li> <li>• Sham physical treatment</li> <li>• Waiting list</li> </ul>
Types of study to be included	<p>Included study designs:</p> <ul style="list-style-type: none"> <li>• Systematic reviews/meta-analyses of randomised controlled trials (RCTs).</li> <li>• RCTs (individual or cluster parallel group, or split-face/-body trials).</li> </ul> <p>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.</p> <p>Excluded study designs:</p> <ul style="list-style-type: none"> <li>• Quasi-randomised or non-randomised controlled trials</li> <li>• Case-control studies</li> <li>• Cohort studies</li> <li>• Cross-sectional studies</li> <li>• Epidemiological reviews or reviews on associations</li> <li>• Non-comparative studies</li> </ul> <p>Note: For further details, see the algorithm in appendix H, <a href="#">Developing NICE guidelines: the manual</a>.</p>
Other exclusion criteria	<ul style="list-style-type: none"> <li>• 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.</li> <li>• Trials with &lt;50% completion data.</li> <li>• Trials that do not report the level of acne severity in the study sample, or they include all ranges of severity.</li> </ul>

Field	Content
	<ul style="list-style-type: none"> <li>• 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 &lt;66% of the relevant population will be excluded, unless subgroup analysis for acne vulgaris is reported.</li> </ul>
Context	<p>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.</p> <p>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.</p> <p>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 (<a href="https://www.gov.uk/drug-safety-update">https://www.gov.uk/drug-safety-update</a>) and Summary of Product characteristics (<a href="https://www.medicines.org.uk/emc">https://www.medicines.org.uk/emc</a>), and the principle that the use of antibiotics should be limited or optimised where possible.</p>
Primary outcomes (critical outcomes)	<p><b>Critical outcomes</b></p> <p>Efficacy:</p> <p>Efficacy of acne treatments will be assessed by the following three outcomes:</p> <ul style="list-style-type: none"> <li>• Clinician-rated improvement at treatment endpoint <ul style="list-style-type: none"> <li>○ Percentage change in acne lesion count</li> <li>○ Change from baseline or final score on a validated acne severity scale</li> </ul> </li> <li>• Prevention of scarring at any follow up <ul style="list-style-type: none"> <li>○ Change from baseline or final number of scars</li> <li>○ Incidence of scarring</li> </ul> </li> <li>• Participant-reported improvement <ul style="list-style-type: none"> <li>○ Change in acne severity or symptoms (for example assessed using global acne score)</li> </ul> </li> </ul> <p>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.</p>
Secondary outcomes (important outcomes)	<p><b>Important outcomes</b></p> <ul style="list-style-type: none"> <li>• Relapse <ul style="list-style-type: none"> <li>○ Relapse during or after maintenance treatment</li> </ul> </li> <li>• Acceptability <ul style="list-style-type: none"> <li>○ Treatment discontinuation for any reason</li> </ul> </li> </ul>

Field	Content
	<ul style="list-style-type: none"> <li>• Tolerability               <ul style="list-style-type: none"> <li>○ Treatment discontinuation due to side effects</li> </ul> </li> <li>• Side effects</li> </ul> <p>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):</p> <ul style="list-style-type: none"> <li>○ Topical treatments, oral antibiotics or combination treatments: skin irritation (for example burning or tingling, dryness/irritation, swelling).</li> <li>○ Topical retinoids: sensitivity to light.</li> <li>○ Oral antibiotics: gastrointestinal side effects; thrush candidiasis.</li> <li>○ Hormonal contraceptives and hormone-modifying agents: breast tenderness; neurological side effects (headache/migraine, mood disturbance, nausea); sexual dysfunction.</li> <li>○ Hormonal contraceptives: breakthrough bleeding; mood disturbance.</li> <li>○ Hormone-modifying agents: hepatobiliary side effects. For aldosterone receptor antagonists: renal side effects.</li> <li>○ Metformin: gastrointestinal side effects.</li> <li>○ 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.</li> <li>○ Physical treatments: persistent skin redness of 'treated' area; changes in pigmentation (for example hypopigmentation).</li> <li>○ Chemical peels: heart, kidney or liver damage; infection of 'treated' area.</li> <li>○ Comedone extraction: infection of 'treated' area; pain of 'treated' area.</li> <li>○ Energy-based devices: skin irritation.</li> </ul> <p>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.</p>
Data extraction (selection and coding)	<ul style="list-style-type: none"> <li>• 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.</li> <li>• Dual sifting will be performed on at least 10% of records; 90% agreement is required.</li> <li>• Disagreements will be resolved via discussion between the 2 reviewers, and consultation with senior staff if necessary.</li> <li>• 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</li> </ul>

Field	Content														
	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 <a href="#">Developing NICE guidelines: the manual</a> .														
Strategy for data synthesis	<ul style="list-style-type: none"> <li>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.</li> <li>Heterogeneity in the effect estimates of the individual studies will be assessed using the I<sup>2</sup> statistic. I<sup>2</sup> 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.</li> <li>Default MIDs will be used for risk ratios and continuous outcomes only, unless the committee pre-specifies published or other MIDs for specific outcomes <ul style="list-style-type: none"> <li>For risk ratios: 0.8 and 1.25.</li> <li>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.</li> </ul> </li> <li>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: <a href="http://www.gradeworkinggroup.org/">http://www.gradeworkinggroup.org/</a>.</li> </ul>														
Analysis of sub-groups	<p>Stratified analysis will be conducted for the following groups:</p> <ul style="list-style-type: none"> <li>Severity of acne <ul style="list-style-type: none"> <li>Mild to moderate</li> <li>Moderate to severe</li> </ul> </li> </ul>														
Type and method of review	<table border="0"> <tr> <td><input checked="" type="checkbox"/></td> <td>Intervention</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Diagnostic</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Prognostic</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Qualitative</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Epidemiologic</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Service Delivery</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Other (please specify)</td> </tr> </table>	<input checked="" type="checkbox"/>	Intervention	<input type="checkbox"/>	Diagnostic	<input type="checkbox"/>	Prognostic	<input type="checkbox"/>	Qualitative	<input type="checkbox"/>	Epidemiologic	<input type="checkbox"/>	Service Delivery	<input type="checkbox"/>	Other (please specify)
<input checked="" type="checkbox"/>	Intervention														
<input type="checkbox"/>	Diagnostic														
<input type="checkbox"/>	Prognostic														
<input type="checkbox"/>	Qualitative														
<input type="checkbox"/>	Epidemiologic														
<input type="checkbox"/>	Service Delivery														
<input type="checkbox"/>	Other (please specify)														
Language	English														
Country	England														
Anticipated or actual start date	20 October 2019														
Anticipated completion date	13 January 2021														
Stage of review	<table border="0"> <tr> <td>Review stage</td> <td>Started</td> <td>Completed</td> </tr> </table>	Review stage	Started	Completed											
Review stage	Started	Completed													

Field	Content
at time of this submission	Preliminary searches <input checked="" type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/>
	Piloting of the study selection process <input checked="" type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/>
	Formal screening of search results against eligibility criteria <input checked="" type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/>
	Data extraction <input checked="" type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/>
	Risk of bias (quality) assessment <input checked="" type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/>
	Data analysis <input checked="" type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/>
Named contact	5a. Named contact National Guideline Alliance (NGA) 5b Named contact e-mail AcneManagement@nice.org.uk 5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and National Guideline Alliance: <a href="http://www.nice.org.uk">www.nice.org.uk</a> ; <a href="http://www.rcog.org.uk/en/about-us/nga/">www.rcog.org.uk/en/about-us/nga/</a> .
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 <a href="#">Developing NICE guidelines: the manual</a> . Members of the guideline committee are available on the NICE website: <a href="https://www.nice.org.uk/guidance/gid-ng10109/documents/committee-member-list">https://www.nice.org.uk/guidance/gid-ng10109/documents/committee-member-list</a>
Other registration details	Not applicable
Reference/URL for published protocol	<a href="https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=165925">https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=165925</a>
Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: <ul style="list-style-type: none"> <li>• notifying registered stakeholders of publication</li> <li>• publicising the guideline through NICE's newsletter and alerts</li> <li>• 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.</li> </ul>

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	<input checked="" type="checkbox"/> Ongoing
	<input type="checkbox"/> Completed but not published
	<input type="checkbox"/> Completed and published
	<input type="checkbox"/> Completed, published and being updated
	<input type="checkbox"/> Discontinued
Additional information	
Details of final publication	<a href="http://www.nice.org.uk">www.nice.org.uk</a>

1 *GRADE: Grading of Recommendations Assessment, Development and Evaluation; MID: minimally*  
2 *important difference; NHS: National health service; NICE: National Institute for Health and Care*  
3 *Excellence; NGA: National Guidelines Alliance; PCOS: polycystic ovary syndrome; RCT: randomised*  
4 *controlled trial; SD: standard deviation*

5  
6

## 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?* or anti-helmint?* or antiparasit* or anti-parasit* or vermifug*).tw.
14	adapalene/
15	aluminum oxide/ use emczd
16	amoxicillin/
17	ampicillin/
18	ivermectin/ 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	Floxacin/ 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 azelaic acid or benzylpenicillin or benzyl penicillin or benzoyl peroxide or cefaclor or cefadroxil or cefalexin or cephalixin or cefixime or cefotaxime or cefradine or ceftaroline or ceftazidime or ceftriaxone or cefuroxime or cephalixin 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 isotretinoin* or ivermectin or lincosamide* or lymecycline or macrolide* or metronidazole or minocycline or nadifloxacin or niacinamide or nicotinamide or nitroimidazole or ozenoxacin or oxytetracycline 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 retinoin* 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 antihelminthi* or anti-helminthi* or anti-helminthi* 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: [Ticarillin] 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 azelaic acid or azelaic acid or benzylpenicillin or benzyl penicillin or benzoyl peroxide or cefaclor or cefadroxil or cefalexin or cephalaxin 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 oxytetracycline 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 ceftazopran or cefpiramide or cepirome or cefpodoxime or cefprozil or cefquinome or cefradine or cefroxadine or cefsulodin or ceftaroline fosamile or ceftazidime or ceftazidime or cefteteram or ceftazole or ceftibiprole or ceftibuten or ceftiolene or ceftolozane or ceftolozane or ceftaroline or ceftioxone or cefuroxime or cefuzonam or cephamycin or depfimizole or flomoxef or latamoxef or oxacephem).tw.
32	dapsone.tw.
33	(isotretinoi* or iso tretinoin or isotretinoin 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 ciprofloxacin 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 rifloxacin or sitafloxacin or sparfloxacin or temafloxacin or tosufloxacin).tw.
39	(tetracycline* 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 cephalixin or cefixime or cefotaxime or cephotaxim* or cefradine or cephradine or ceftaroline or ceftazidime or ceftriaxone or cefuroxime or chlortetracycline 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 colflumactone 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 cocypriindiol or co-cypriindiol 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 norgestrol 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 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 trichloroacetic 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	(multiattribute* 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
<p><b>Study ID</b></p> <p><b>Full citation</b></p> <p>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</p> <p><b>Country/ies where the study was carried out</b></p> <p>Japan</p> <p><b>RCT type (parallel or split face)</b></p> <p>Randomised, parallel-group maintenance phase.</p> <p><b>Study dates</b></p>	<p>N=92</p> <p><b>Sex (Male, female or mixed)</b></p> <p>Female (%): 77</p> <p><b>Age details</b></p> <p>Mean age (years): 23.5</p> <p><b>Acne scale used for inclusion</b></p> <p>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</p> <p><b>Other inclusion criteria</b></p> <p><u>Inclusion criteria for inflammatory phase:</u></p> <ul style="list-style-type: none"> <li>Moderate to severe acne vulgaris (6-30 inflammatory eruptions on one side of the face)</li> <li>Written consent provided after receiving an explanation of the study content</li> <li>Age ≥ 16 years at the time of obtaining consent. For patients &lt;20 years old, consent was also obtained from a legal representative</li> </ul>	<p><b>Treatment duration (weeks)</b></p> <p>12</p> <p><b>Info about intensity of physical treatments</b></p> <p>Not applicable.</p> <p><b>Number of treatment arms</b></p> <p>2</p> <p><b>Interventions</b></p> <p>Intervention 1 (n=47): 0.1% adapalene gel each evening after washing face.</p> <p>Intervention 2 (n=45): 2.5% benzoyl peroxide gel each evening after washing face.</p>	<p><u>Relapse/aggravation of symptoms- Number (%)</u></p> <p>Intervention 1: 26/47 (55.3)</p> <p>Intervention 2: 27/45 (60)</p> <p><u>Adverse events- Erythema- Number (%)</u></p> <p>Intervention 1: 1/47 (2.1)</p> <p>Intervention 2: 0/45 (0)</p> <p><u>Adverse events- Dryness- Number (%)</u></p> <p>Intervention 1: 1/47 (2.1)</p> <p>Intervention 2: 1/45 (2.2)</p>	<p><b>Methodological limitations assessed using the Cochrane risk of bias tool for randomised trials (RoB2)</b></p> <p><b>Risk of bias arising from the randomisation process:</b> Some concerns (adaptive randomisation, minimisation methods used. No details on allocation concealment).</p> <p><b>Risk of bias due to deviations from the intended interventions:</b> Some concerns (no blinding reported).</p> <p><b>Risk of bias due to missing outcome data:</b> Low risk (6% attrition, n=1 lost from intervention 1 and n=5 lost from intervention 2).</p> <p><b>Risk of bias in measurement of the outcome:</b> Some concerns (same measurement methods and thresholds used at comparable timepoints to measure outcomes; no report of participants/outcome assessors being blinded to intervention).</p> <p><b>Risk of bias in selection of the reported result:</b> Low risk (trial protocol reported)</p> <p><b>Overall risk of bias judgement:</b> study is</p>



Study details	Participants	Interventions	Results	Risk of bias
<b>Source of funding</b>	<p>(such as the patient's parents)</p> <p><u>Inclusion criteria for the maintenance phase:</u></p> <ul style="list-style-type: none"> <li>• Written consent provided after a re-explanation of the study content of the maintenance phase.</li> </ul> <p><b>Exclusion criteria</b></p> <p><u>Exclusion criteria for inflammatory phase:</u></p> <ul style="list-style-type: none"> <li>• Treated for acne vulgaris within one month before the study</li> <li>• Contraindicated for the investigational drugs</li> <li>• Continuous use of non-steroidal anti-inflammatory drugs</li> <li>• Pregnant or possibly pregnant women, lactating women, and women who wanted to become pregnant during the study period</li> <li>• Judged as ineligible by the physician directing the study</li> <li>• Participation in another clinical study or post-marketing surveillance of other drugs for acne vulgaris within six months before the study</li> </ul> <p><u>Exclusion criteria for the maintenance phase:</u></p> <ul style="list-style-type: none"> <li>• Judged as ineligible by the physician directing the study</li> </ul>			<p>judged to have some concerns some concerns for multiple domains.</p>
<b>Study ID</b> 869180	<p>N=110</p> <p><b>Sex (Male, female or mixed)</b></p>	<p><b>Treatment duration (weeks)</b></p> <p>12</p>	<p><u>Percentage change in non-inflammatory lesion count after 12 weeks maintenance - mean (<math>\pm</math>SD)</u></p> <p>Intervention 1 (n=35): -60.0 (22.9)</p>	<p><b>Methodological limitations assessed using the Cochrane risk of bias tool for randomised trials (RoB2)</b></p>

Study details	Participants	Interventions	Results	Risk of bias
<p><b>Full citation</b></p> <p>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</p> <p><b>Country/ies where the study was carried out</b></p> <p>US</p> <p><b>RCT type (parallel or split face)</b></p> <p>Double-blind, randomised, parallel-group maintenance phase.</p> <p><b>Study dates</b></p> <p>Not reported.</p> <p><b>Source of funding</b></p> <p>Allergan Inc.</p>	<p>Female (%): 55</p> <p><b>Age details</b></p> <p>Mean age (years): 22</p> <p><b>Acne scale used for inclusion</b></p> <p>Global response.</p> <p><b>Other inclusion criteria</b></p> <ul style="list-style-type: none"> <li>• Participants aged at least 17 years of age.</li> <li>• Moderately severe to severe facial acne vulgaris.</li> <li>• 10 to 100 facial non-inflammatory acne lesions.</li> <li>• 25 to 60 facial inflammatory acne lesions.</li> <li>• No more than 2 facial nodular cystic lesions.</li> <li>• 75% or greater global improvement at the end of the initial open-label treatment phase.</li> <li>• Informed consent provided by participants or guardians.</li> <li>• 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 &lt;12 weeks; 2 years for oral retinoids.</li> </ul> <p><b>Exclusion criteria</b></p> <ul style="list-style-type: none"> <li>• Participants with acne vulgaris resistant to oral antibiotics.</li> <li>• Pregnancy, breastfeeding, or planning a pregnancy.</li> </ul>	<p><b>Info about intensity of physical treatments</b></p> <p>Not applicable.</p> <p><b>Number of treatment arms</b></p> <p>3</p> <p><b>Interventions</b></p> <p>Intervention 1 (n=36): 0.1% tazarotene gel each evening plus placebo capsule twice daily.</p> <p>Intervention 2 (n=37): vehicle gel each evening plus a 100 mg minocycline hydrochloride capsule twice daily.</p> <p>Intervention 3 (n=37): 0.1% tazarotene gel each evening plus a 100 mg minocycline capsule twice daily.</p> <p>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.</p> <p>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.</p>	<p>Intervention 2 (n=37): -52.0 (30.4) Intervention 3 (n=35): -64.0 (42.1); p=NS</p> <p><u>Percentage change in inflammatory lesion count after 12 weeks maintenance - mean (±SD)</u></p> <p>Intervention 1 (n=35): -54.0 (25.1) Intervention 2 (n=37): -66.0 (29.4) Intervention 3 (n=36): -66.0 (27.2); p=NS</p> <p><u>Participants maintaining ≥70% of the reduction in non-inflammatory lesion count achieved in the initial treatment phase, after 12 weeks maintenance - % (n/N)</u></p> <p>Intervention 1: 81 (22/27) (relapse 5/27) Intervention 2: 71 (22/31) (relapse 9/31) Intervention 3: 90 (27/30) (relapse 3/30)</p> <p><u>Participants maintaining ≥70% of the reduction in inflammatory lesion count achieved in the initial treatment phase, after 12 weeks maintenance - % (n/N)</u></p> <p>Intervention 1: 67 (18/27) (relapse 9/27) Intervention 2: 84 (26/31) (relapse 5/31) Intervention 3: 77 (24/31) (relapse 7/31)</p> <p><u>Acceptability (treatment discontinuation for any reason) after 12 weeks maintenance - n/N</u></p> <p>Intervention 1: 8/36 Intervention 2: 6/37 Intervention 3: 6/37</p>	<p><b>Risk of bias arising from the randomisation process:</b> low risk (participants assigned a unique number using computer-generated randomisation schedule; labels on medication containers concealed; demographics similar across treatment groups).</p> <p><b>Risk of bias due to deviations from the intended interventions:</b> low risk (double-blind trial - labels on medication containers were concealed and participants received a gel and capsule).</p> <p><b>Risk of bias due to missing outcome data:</b> 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).</p> <p><b>Risk of bias in measurement of the outcome:</b> low risk (same measurement methods and thresholds used at comparable timepoints to measure outcomes; participants/outcome assessors blinded to intervention).</p> <p><b>Risk of bias in selection of the reported result:</b> 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).</p> <p><b>Overall risk of bias judgement:</b> study is</p>

Study details	Participants	Interventions	Results	Risk of bias
	<ul style="list-style-type: none"> <li>Uncontrolled systemic disease.</li> <li>Participation in another study in the preceding 30 days.</li> </ul>		<p><u>Tolerability (treatment discontinuation due to side effects) after 12 weeks maintenance - n/N</u> Intervention 1: 0/36 Intervention 2: 1/37 Intervention 3: 1/37</p> <p>No adverse events were reported during the maintenance phase that were considered probably related to treatment.</p>	<p>judged to have some concerns some concerns for multiple domains.</p> <p><b>Other information</b> Setting: ambulatory participants in research or referral centres. Number of participants in maintenance phase: N=110/189 Number of participants completing study: N=90 Previous treatment: 0.1% tazarotene gel each evening, plus 1 x 100 mg minocycline capsule orally, twice daily.</p>
<p><b>Study ID</b> 869990</p> <p><b>Full citation</b> 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</p> <p><b>Country/ies where</b></p>	<p>N=243</p> <p><b>Sex (Male, female or mixed)</b></p> <p>Male - n: Adapalene-BPO: 65; Vehicle: 67</p> <p><b>Age details</b> <u>Age (years) - mean (±SD)</u> Adapalene-BPO: 19.1 (5.89) Vehicle: 18.2 (5.23)</p> <p><b>Acne scale used for inclusion</b></p> <p>Investigator's Global Assessment (IGA)</p> <p><b>Other inclusion criteria</b></p> <ul style="list-style-type: none"> <li>Participants with severe acne vulgaris.</li> <li>Participants who had shown at least 50% global improvement with previous treatment (doxycycline and adapalene-BPO or its vehicle gel for 12 weeks).</li> </ul> <p><b>Exclusion criteria</b></p>	<p><b>Treatment duration (weeks)</b> 24</p> <p><b>Info about intensity of physical treatments</b> Not applicable.</p> <p><b>Number of treatment arms</b> 2</p> <p><b>Interventions</b> Adapalene-BPO (n=123): fixed dose combination gel 0.1% adapalene plus 2.5% benzoyl peroxide (adapalene-BPO) once daily in the evening.  Vehicle (n=120): vehicle gel once daily in the evening. Participants were encouraged to use sun protection factor 15 daily facial moisturiser and a gentle skin cleanser.</p>	<p><u>Percentage change in lesion count from baseline to 24 weeks</u> Adapalene-BPO: -26.0% Vehicle: +46.3%; p&lt;0.01</p> <p><u>IGA success rate (% of participants rated 'clear' or 'almost clear')</u> Adapalene-BPO: Baseline (26.8%); 24 weeks (47.5%) Vehicle: Baseline (37.5%); 24 weeks (25.6%); p&lt;0.01</p> <p><u>Participants having at least 50% improvement from baseline to 24 weeks (total lesions)</u> Adapalene-BPO: 78.9% (relapse 21.1%) Vehicle: 45.8% (relapse 54.2%); p&lt;0.001</p> <p><u>Treatment-related adverse effects from baseline to week 24- n (%)</u> Adapalene-BPO: 5 (4.1) Vehicle: 1 (0.8) <u>Irritation from baseline to week 24 - %</u> Adapalene-BPO: erythema (76.7);</p>	<p><b>Methodological limitations assessed using the Cochrane risk of bias tool for randomised trials (RoB2)</b></p> <p><b>Risk of bias arising from the randomisation process:</b> low risk (randomisation using a central telephone/web system; demographics comparable across treatment groups).</p> <p><b>Risk of bias due to deviations from the intended interventions:</b> low risk (double-blind trial - vehicle gel used as control).</p> <p><b>Risk of bias due to missing outcome data:</b> 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).</p> <p><b>Risk of bias in measurement of the outcome:</b> low risk (same measurement methods and thresholds used at comparable timepoints to measure outcomes; participants/outcome</p>

Study details	Participants	Interventions	Results	Risk of bias
<p><b>the study was carried out</b></p> <p>US, Canada, Puerto Rico</p> <p><b>RCT type (parallel or split face)</b> Multicentre, double-blind, randomised, vehicle-controlled trial (parallel assignment).</p> <p><b>Study dates</b> Not reported.</p> <p><b>Source of funding</b> Galderma Research &amp; Development, France.</p>	<ul style="list-style-type: none"> <li>Women who were pregnant, nursing or planning a pregnancy.</li> <li>Men with facial hair that would interfere with the assessments.</li> </ul>		<p>scaling (70.8); dryness (73.3); stinging/burning (78.3) Vehicle: erythema (83.5); scaling (92.2); dryness (88.7); stinging/burning (92.2)</p> <p><u>Acceptability (treatment discontinuation for any reason) from baseline to week 24 - n/N</u> Adapalene-BPO: 18/123 Vehicle: 42/120</p> <p><u>Tolerability (treatment discontinuation due to side effects) from baseline to week 24 - n/N</u> Adapalene-BPO: 0/123 Vehicle: 0/120</p>	<p>assessors blinded to intervention).</p> <p><b>Risk of bias in selection of the reported result:</b> 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).</p> <p><b>Overall risk of bias judgement:</b> the study is judged to be at high risk of bias (high risk in one domain and some concerns in one domain).</p> <p><b>Other information</b> Number of participants: N=243. Number of participants completing study: n=183. Previous treatment: 100 mg doxycycline daily and adapalene-BPO or its vehicle for 12 weeks. Unclear whether there was a washout period.</p>
<p><b>Study ID</b></p> <p>870417</p> <p><b>Full citation</b></p> <p>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</p>	<p>N=253</p> <p><b>Sex (Male, female or mixed)</b></p> <p>Male - n: Adapalene: 65; Vehicle: 73</p> <p><b>Age details</b> <u>Age (years) - mean (±SD) (range)</u> Adapalene: 18.1 (4.2) (12 to 30) Vehicle: 17.8 (3.9) (12 to 32)</p> <p><b>Acne scale used for inclusion</b></p> <p>Not reported (participants required to have at least moderate improvement (50%) from baseline.</p>	<p><b>Treatment duration (weeks)</b></p> <p>16</p> <p><b>Info about intensity of physical treatments</b></p> <p>Not applicable.</p> <p><b>Number of treatment arms</b></p> <p>2</p> <p><b>Interventions</b></p> <p>Adapalene (n=126): 0.1% adapalene gel once daily in the evening.</p>	<p><u>Percentage of participants maintaining at least 50% improvement after 16 weeks maintenance (total lesions)</u> Adapalene: 75% (relapse 25%) Vehicle: 54% (relapse 46%); p&lt;0.001</p> <p><u>Treatment-related adverse effects after 16 weeks maintenance - n (%)</u> Adapalene: 3 (2.4) Vehicle: 1 (0.8)</p> <p><u>Acceptability (treatment discontinuation for any reason)</u></p>	<p><b>Methodological limitations assessed using the Cochrane risk of bias tool for randomised trials (RoB2)</b></p> <p><b>Risk of bias arising from the randomisation process:</b> low risk (randomisation using a central telephone system; demographics and dermatological scores comparable across treatment groups).</p> <p><b>Risk of bias due to deviations from the intended interventions:</b> some concerns (investigator-blind trial, those involved in the clinical conduct of the study remained blinded to the randomisation schedule</p>

Study details	Participants	Interventions	Results	Risk of bias
<p>randomized, controlled, investigator-blind follow-up of a recent combination study, Archives of Dermatology Arch Dermatol, 142, 597-602, 2006</p> <p><b>Country/ies where the study was carried out</b></p> <p>US</p> <p><b>RCT type (parallel or split face)</b></p> <p>Multicentre, randomised, vehicle-controlled, investigator-blind, parallel group trial.</p> <p><b>Study dates</b></p> <p>November 2003 to May 2004.</p> <p><b>Source of funding</b></p> <p>Galderma Research &amp; Development, US.</p>	<p><b>Other inclusion criteria</b></p> <ul style="list-style-type: none"> <li>Participants with severe acne, aged 12 to 30 years.</li> <li>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.</li> </ul> <p><b>Exclusion criteria</b></p> <ul style="list-style-type: none"> <li>Participants with acne requiring treatment with isotretinoin or other dermatologic conditions requirement interfering treatment.</li> <li>Women who were pregnant, nursing, or planning a pregnancy.</li> <li>Men with facial hair that would interfere with the assessments.</li> </ul>	<p>Vehicle (N=127): gel vehicle once daily in the evening.</p> <p>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.</p>	<p><u>after 16 weeks maintenance - n/N</u> Adapalene-BPO: 14/126 Vehicle: 20/127</p> <p><u>Tolerability (treatment discontinuation due to side effects) after 16 weeks maintenance - n/N</u> Adapalene-BPO: 0/126 Vehicle: 0/127</p>	<p>and packaging of medication was concealed through use of identical tubes 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).</p> <p><b>Risk of bias due to missing outcome data:</b> 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).</p> <p><b>Risk of bias in measurement of the outcome:</b> 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).</p> <p><b>Risk of bias in selection of the reported result:</b> 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).</p> <p><b>Overall risk of bias judgement:</b> this</p>

Study details	Participants	Interventions	Results	Risk of bias
				<p>study is judged to be at high risk of bias (high risk in one domain and some concerns in multiple domains).</p> <p><b>Other information</b> Number of participants: N=253. Number of participants completing study: n=219. Previous treatment: adapalene plus doxycycline 100 mg once daily or doxycycline 100 mg once daily plus gel vehicle for 12 weeks. Unclear whether there was a washout period.</p>
<p><b>Study ID</b> 870421</p> <p><b>Full citation</b> 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</p> <p><b>Country/ies where the study was carried out</b> Germany</p> <p><b>RCT type (parallel or split face)</b> Randomised, investigator-blinded,</p>	<p>N=49</p> <p><b>Sex (Male, female or mixed)</b> Male: n=29 (59.2%); female: n=20 (40.8%)</p> <p><b>Age details</b> <u>Age (years) - mean (<math>\pm</math>SD)</u> Intervention 1: 18.33 (5.0) Intervention 2: 16.47 (2.4) Intervention 3: 19.58 (5.4)</p> <p><b>Acne scale used for inclusion</b> Global severity score.</p> <p><b>Other inclusion criteria</b></p> <ul style="list-style-type: none"> <li>Participants with mild to moderate acne vulgaris (defined as global severity grade 2 to 7 according to the Leeds Revised Acne Grading System).</li> <li>Presence of at least 250 microcomedones per cm<sup>2</sup> on the forehead at screening (counted via cyanoacrylate strips).</li> </ul>	<p><b>Treatment duration (weeks)</b> 12</p> <p><b>Info about intensity of physical treatments</b> Not applicable.</p> <p><b>Number of treatment arms</b> 3</p> <p><b>Interventions</b> Intervention 1 (n=16): 0.1% adapalene gel once daily applied to the face.  Intervention 2 (n=16): 0.1% adapalene gel alternately with vehicle once daily every other day applied to the face.  Intervention 3 (n=17): Vehicle once daily applied to the face. Participants applied the same skin cleanser and moisturiser immediately before treatments</p>	<p><u>Percentage change in microcomedone count after 12 weeks maintenance (total lesions) - mean (<math>\pm</math>SD)</u> Intervention 1: 14.8 (38.9); p (vs vehicle) = 0.056 Intervention 2: 18.2 (81.4); p (vs vehicle) = 0.034 Intervention 3: 66.2 (83.3)</p> <p>There were no treatment-related adverse events during maintenance treatment and no treatment discontinuations.</p>	<p><b>Methodological limitations assessed using the Cochrane risk of bias tool (RoB2)</b></p> <p><b>Risk of bias arising from the randomisation process:</b> 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).</p> <p><b>Risk of bias due to deviations from the intended interventions:</b> 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).</p> <p><b>Risk of bias due to missing outcome data:</b> low risk (no discontinuations).</p> <p><b>Risk of bias in measurement of the outcome:</b> some concerns (same</p>

Study details	Participants	Interventions	Results	Risk of bias
<p>vehicle controlled trial (parallel).</p> <p><b>Study dates</b> Not reported.</p> <p><b>Source of funding</b> Galderma Research &amp; Development, France.</p>	<p><b>Exclusion criteria</b> Not reported.</p>	<p>and were advised to avoid excessive exposure to sunlight.</p>		<p>measurement methods and thresholds used at comparable timepoints to measure outcomes; patient-reported outcomes may have been influenced because participants not blind to treatment).</p> <p><b>Risk of bias in selection of the reported result:</b> some concerns (limited information provided).</p> <p><b>Overall risk of bias judgement:</b> this study is judged to have some concerns in multiple domains.</p> <p><b>Other information</b> Number of participants: N=49. Number of participants completing study: n=49. Previous treatment: 0.1% adapalene gel in the morning plus benzoyl peroxide gel 2.5% at bedtime for 8 weeks. Unclear whether there was a washout period.</p>
<p><b>Study ID</b> 870420</p> <p><b>Full citation</b> 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</p>	<p>N=36</p> <p><b>Sex (Male, female or mixed)</b> Female: 100%</p> <p><b>Age details</b> <u>Age (years) - mean (<math>\pm</math>SD)</u> Azelaic acid: 30.58 (9.28) Observation: 28.14 (4.56)</p> <p><b>Acne scale used for inclusion</b> ISGA and LRAGS.</p> <p><b>Other inclusion criteria</b> • Adult female participants with mild</p>	<p><b>Treatment duration (weeks)</b> 24</p> <p><b>Info about intensity of physical treatments</b> Not applicable.</p> <p><b>Number of treatment arms</b> 2</p> <p><b>Interventions</b> Azelaic acid (n=17): 15% azelaic acid gel twice daily for 9 months (6 months maintenance).</p>	<p><u>Relative change in total lesions after 24 weeks maintenance - mean (<math>\pm</math>SD)</u> Azelaic acid: -9.79 (38.12) Observation: 29.97 (71.27) Difference (95% CI): -30.8 (-61.5 to 0.0); p=0.038</p> <p><u>Absolute change after 24 weeks maintenance in ISGA - mean (<math>\pm</math>SD)</u> Azelaic acid: -0.24 (0.44) Observation: -0.16 (0.37) Difference (95% CI): 0 (0 to 0); p=0.434</p> <p><u>Absolute change after 24 weeks</u></p>	<p><b>Methodological limitations assessed using the Cochrane risk of bias tool (RoB2)</b></p> <p><b>Risk of bias arising from the randomisation process:</b> 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).</p> <p><b>Risk of bias due to deviations from the intended interventions:</b> some concerns (investigator-blind trial, participants (who were not blind to treatment) were</p>

Study details	Participants	Interventions	Results	Risk of bias
<p>in the treatment and maintenance treatment of female adult acne, J Eur Acad Dermatol Venereol, 29, 789-96, 2015</p> <p><b>Country/ies where the study was carried out</b></p> <p>Germany</p> <p><b>RCT type (parallel or split face)</b></p> <p>Randomised, investigator-blind, parallel group trial.</p> <p><b>Study dates</b></p> <p><b>Source of funding</b></p> <p>Intendis GmbH, Germany.</p>	<p>to moderate acne (according to modified Investigator's Static Global Assessment (ISGA) and Leeds Revised Acne Grading Scale (LRAGS), and including 'late-type acne'.</p> <p><b>Exclusion criteria</b></p> <ul style="list-style-type: none"> <li>• Participants with more than one nodule.</li> <li>• Pregnancy, planned pregnancy or breastfeeding women.</li> <li>• Known hypersensitivity to any study products or medication with a systemic retinoid within the past 6 months before study inclusion.</li> <li>• Participants who had taken any other topical or systemic anti-acne medication including systemic oral corticosteroids in the preceding 2 weeks.</li> </ul>	<p>Observation (n=19): 6 month observation following 3 months 15% azelaic acid gel twice daily.</p> <p>Participants were not permitted to take any other topical or systemic anti-acne medication including systemic oral corticosteroids during the study period.</p>	<p><u>maintenance in LRAGS - mean (<math>\pm</math>SD)</u> Azelaic acid: -0.53 (1.01) Observation: -0.37 (0.50) Difference (95% CI): 0 (0 to 0); p=0.464</p> <p><u>Subjects' Global Change Assessment (SGCA) after 24 weeks maintenance</u> Difference (95% CI): -1.0 (-3.0 to 0); p=0.013</p> <p><u>Relapse during 24 weeks maintenance - n/N</u> Azelaic acid: 11/17 Observation: 15/19; p=0.163</p> <p><u>Acceptability (treatment discontinuation for any reason - treatment and maintenance phase) - n/N</u> Azelaic acid: 6/17 Observation: 3/19</p> <p><u>Tolerability (treatment discontinuation due to side effects during 24 weeks maintenance phase) - n/N</u> Azelaic acid: 0/17 Observation: 0/19</p>	<p>requested not to discuss treatment or side-effects with investigators; appropriate analyses used).</p> <p><b>Risk of bias due to missing outcome data:</b> low risk (data available for all or nearly all participants during maintenance treatment).</p> <p><b>Risk of bias in measurement of the outcome:</b> 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).</p> <p><b>Risk of bias in selection of the reported result:</b> 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).</p> <p><b>Overall risk of bias judgement:</b> this study is judged to have some concerns in multiple domains.</p> <p><b>Other information</b></p> <p>Number of participants: N=36 for the 2 relevant treatment arms.</p> <p>Number of participants completing study: n=27 for the 2 relevant treatment arms.</p> <p>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.</p>



Study details	Participants	Interventions	Results	Risk of bias
				A third treatment arm was included in the study (adapalene gel 0.1% for 9 months) but was not relevant to this review question. No washout period for observation arm (3 months azelaic acid then 6 months observation)
<p><b>Study ID</b> 870446</p> <p><b>Full citation</b> 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</p> <p><b>Country/ies where the study was carried out</b> Spain</p> <p><b>RCT type (parallel or split face)</b> Prospective, randomised, double-blind, placebo-controlled (vehicle) split face trial.</p>	<p>N=30</p> <p><b>Sex (Male, female or mixed)</b> Male: 40.6%; Female: 59.4%</p> <p><b>Age details</b> <u>Age (years) - mean (±SD)</u> Male: 18.4 (5.2) Female: 23.5 (5.6)</p> <p><b>Acne scale used for inclusion</b> Not reported.</p> <p><b>Other inclusion criteria</b></p> <ul style="list-style-type: none"> <li>Participants aged over 14 years of age.</li> <li>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.</li> </ul> <p><b>Exclusion criteria</b></p> <ul style="list-style-type: none"> <li>Participants aged &lt;14 years of age.</li> <li>Participants with other concomitant dermatoses or sensitisation to any of the components of the product.</li> <li>Women not using a contraceptive method.</li> </ul>	<p><b>Treatment duration (weeks)</b> 12</p> <p><b>Info about intensity of physical treatments</b> Not applicable.</p> <p><b>Number of treatment arms</b> 2</p> <p><b>Interventions</b> Retinoid combination (retinol encapsulated in glycospheres and hydroxypinacolone retinoate): applied to one side of the face at night for 3 months.  Vehicle: applied to the other side of the face at night for 3 months.</p>	<p><b>Results</b> <u>Relapse (global count) after 3 months maintenance - n (%)</u> Retinoid combination: 5 (16.7) Vehicle: 13 (43.3)</p> <p><u>Number of total lesions - mean (±SD)</u> Retinoid combination: Baseline: 14 (36.80); 3 months: 8 (19.31); p=0.002 Vehicle: Baseline: 13 (36.12); 3 months: 11 (28.93); p=0.08</p> <p><u>Global lesions after 3 months maintenance - mean (±SD)</u> Retinoid combination: 4.1 (3.4) Vehicle: 5.6 (3.8); p=0.05</p> <p><u>Investigator-reported improvement (IGA) - mean</u> Retinoid combination: Baseline: 2.2 (mild severity); 3 months: 1.4 (almost clear); p&lt;0.01 Vehicle: Baseline: 2.2 (mild severity); 3 months: 2 (mild); p=0.106</p> <p>No adverse events were reported.</p> <p>2 participants discontinued due to work commitments.</p>	<p><b>Risk of bias</b> <b>Methodological limitations assessed using the Cochrane risk of bias tool (RoB2)</b></p> <p><b>Risk of bias arising from the randomisation process:</b> 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).</p> <p><b>Risk of bias due to deviations from the intended interventions:</b> 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).</p> <p><b>Risk of bias due to missing outcome data:</b> low risk (data available for nearly all participants).</p> <p><b>Risk of bias in measurement of the outcome:</b> low risk (same measurement methods used; split face trial).</p>

Study details	Participants	Interventions	Results	Risk of bias
<p><b>Study dates</b> Not reported.</p> <p><b>Source of funding</b> Industrial Farmaceutica Cantabria, Spain.</p>				<p><b>Risk of bias in selection of the reported result:</b> some concerns (limited information provided).</p> <p><b>Overall risk of bias judgement:</b> this study is judged to have some concerns in one domain.</p> <p><b>Other information</b> All participants had mild acne at baseline. Number of participants: N=32. Number of participants completing study: n=30. Previous treatment: isotretinoin (majority of participants had not reached total cumulative target dose of 120 to 150 mg/kg). Mean period from discontinuation of isotretinoin treatment until study initiation: 2 months (range 2 weeks to 6 months).</p>
<p><b>Study ID</b> 1048731</p> <p><b>Full citation</b> 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</p>	<p>N=20</p> <p><b>Sex (Male, female or mixed)</b> Male: 100%</p> <p><b>Age details</b> <u>Age (years) - mean (range)</u> Tretinoin: 21 (18 to 29) Vehicle: 22.4 (18 to 42)</p> <p><b>Acne scale used for inclusion</b> Not reported.</p> <p><b>Other inclusion criteria</b></p> <ul style="list-style-type: none"> <li>• Males aged between 18 and 45 years.</li> <li>• Successful completion of acne treatment with isotretinoin (minimum 4 months/maximum 6 months with</li> </ul>	<p><b>Treatment duration (weeks)</b> 24</p> <p><b>Info about intensity of physical treatments</b> Not applicable.</p> <p><b>Number of treatment arms</b> 2</p> <p><b>Interventions</b> 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. Vehicle (n=10): applied once daily to the whole face (and left on for a</p>	<p><u>Lesion counts - mean (95% CI)</u> Tretinoin: Baseline: 0 (0 to 0.369); week 24: 1.2 (0.003 to 0.557) Vehicle: Baseline: 0 (0 to 0.369); week 24: 3.1 (0.062 to 0.877)</p> <p><u>Investigator's Static Global Assessment - mean (range)</u> Tretinoin: Baseline: 0 (0); week 24: 0.33 (0 to 1) Vehicle: Baseline: 0 (0); week 24: 0.33 (0 to 1)</p> <p><u>Subject's Global Assessment - mean (range)</u> Tretinoin: Baseline: 0 (0); week 24: 0.13 (0 to 1) Vehicle: Baseline: 0.13 (0 to 1); week 24: 0.33 (0 to 1)</p> <p><u>Acceptability (treatment</u></p>	<p><b>Methodological limitations assessed using the Cochrane risk of bias tool (RoB2)</b></p> <p><b>Risk of bias arising from the randomisation process:</b> some concerns (randomisation on 1:1 ratio; assignment performed by unblinded dispenser; between-group differences were not significant).</p> <p><b>Risk of bias due to deviations from the intended interventions:</b> low risk (double-blind trial; treatments provided in unlabelled grey plastic 50 g pump dispensers; ITT analyses).</p> <p><b>Risk of bias due to missing outcome data:</b> some concerns (data not available for all participants - high attrition rates - tretinoin (30%); vehicle (20%); last-</p>

Study details	Participants	Interventions	Results	Risk of bias
<p>Practice, 2012 (no pagination), 2012</p> <p><b>Country/ies where the study was carried out</b></p> <p>Canada</p> <p><b>RCT type (parallel or split face)</b></p> <p>Randomised, double-blind, vehicle controlled proof of concept study.</p> <p><b>Study dates</b></p> <p>Not reported.</p> <p><b>Source of funding</b></p> <p>Johnson and Johnson Inc., Canada.</p>	<p>an average of 5 months and a total of 120 to 150 mg/kg/course).</p> <ul style="list-style-type: none"> <li>• Able to attend follow-up visits at the outpatient dermatology clinic.</li> <li>• Consent for participation and agreed to comply with treatment and follow-up procedures.</li> <li>• Participants planning to use multi-vitamins (without vitamin A), iron supplements, and folate were acceptable.</li> </ul> <p><b>Exclusion criteria</b></p> <ul style="list-style-type: none"> <li>• Participants who received isotretinoin for conditions other than acne.</li> <li>• No treatment with isotretinoin for less than 30 days or more than 90 days at the time of study enrolment.</li> <li>• 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.</li> <li>• 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).</li> <li>• Participants who used any systemic medications likely to cause or abate acne (such as oral phenytoin or any other epileptic, finasteride,</li> </ul>	<p>minimum of 8 hours) for 24 weeks.</p> <p>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.</p> <p>Participants were permitted to use moisturiser and cleanser on the face provided.</p>	<p><u>discontinuation for any reason) at week 24 - n/N</u></p> <p>Tretinoin: 3/10 Vehicle: 2/10</p> <p>No serious adverse event or adverse events were reported.</p> <p>Treatments were well tolerated and no treatment was interrupted due to any local tolerability complaints or local side effects.</p>	<p>observation-carried forward for missing data).</p> <p><b>Risk of bias in measurement of the outcome:</b> low risk (same measurement methods used; investigators and participants were not aware of treatment allocation).</p> <p><b>Risk of bias in selection of the reported result:</b> some concerns (limited information provided).</p> <p><b>Overall risk of bias judgement:</b> this study is judged to have some concerns in multiple domains.</p> <p><b>Other information</b></p> <p>Participants had previously been treated for moderate to severe acne. Number of participants: N=20. Number of participants completing study: n=15. Previous treatment: isotretinoin.</p>

Study details	Participants	Interventions	Results	Risk of bias
	<p>spironolactone, or flutamide, testosterone, or dietary body-building protein powders).</p> <ul style="list-style-type: none"> <li>• Participants who used topical corticosteroids on the face or systemic corticosteroids within the past 4 weeks.</li> <li>• Participants who inhaled, intra-articular, or intra-lesional steroids other than for facial acne.</li> <li>• 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.</li> <li>• Use of abrasives, facials, and peels containing glycolic or other acids; masks, washes or soaps containing BPO, salicylic acid or sulfacetamide sodium; non-mild facial abrasives, 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 <math>\alpha</math>- or <math>\beta</math>-hydroxy acids within the past 2 weeks of randomisation and throughout the study duration.</li> <li>• Planned use of medications reported to exacerbate acne (for example, megadoses of certain vitamins), haloperidol, halogens, lithium, hydantoin, and phenobarbital.</li> <li>• Participants who had undergone a facial procedure (such as chemical or laser, peel) by an aesthetician, beautician, physician, nurse or other</li> </ul>			

Study details	Participants	Interventions	Results	Risk of bias
	<p>practitioner within the past 4 weeks or planned to undergo such a procedure during the study.</p> <ul style="list-style-type: none"> <li>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.</li> <li>Participants with any major illness within 30 days before screening.</li> <li>Current employees of the investigator or sponsor involved in the study.</li> <li>Immediate family members of an employee involved in the study.</li> </ul>			
<p><b>Study ID</b> 1220444</p> <p><b>Full citation</b> 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</p>	<p><b>Sex (Male, female or mixed)</b> Not reported for maintenance phase.</p> <p><b>Age details</b> Not reported for maintenance phase.</p> <p><b>Acne scale used for inclusion</b> Modified International Acne Grading System.</p> <p><b>Other inclusion criteria</b></p> <ul style="list-style-type: none"> <li>Males and females with moderate to</li> </ul>	<p><b>Treatment duration (weeks)</b> 12</p> <p><b>Info about intensity of physical treatments</b> Not applicable.</p> <p><b>Number of treatment arms</b> 2</p> <p><b>Interventions</b> Adapalene (n=122): 0.1% adapalene gel once daily in the</p>	<p><u>Mean percentage reduction after maintenance phase (total lesions)</u> Adapalene: -41.6% No treatment: +92.1%; p&lt;0.01</p> <p><u>Global assessment of change (further improved and much improved/clear) at the end of maintenance phase - %</u> Adapalene: 67.2% No treatment: 4.2% No adverse events were reported.</p>	<p><b>Methodological limitations assessed using the Cochrane risk of bias tool (RoB2)</b></p> <p><b>Risk of bias arising from the randomisation process:</b> high risk (open-label trial; between-group differences were not significant).</p> <p><b>Risk of bias due to deviations from the intended interventions:</b> some concerns (open-label trial; ITT analyses).</p> <p><b>Risk of bias due to missing outcome data:</b> low risk (data available for</p>

Study details	Participants	Interventions	Results	Risk of bias
<p>treatment in combination with clindamycin topical solution 1% or after monotherapy with clindamycin topical solution 1%, Journal of Dermatological Treatment, 15, 372-378, 2004</p> <p><b>Country/ies where the study was carried out</b></p> <p>China</p> <p><b>RCT type (parallel or split face)</b></p> <p>Open-labelled, controlled trial.</p> <p><b>Study dates</b></p> <p>Not reported.</p> <p><b>Source of funding</b></p> <p>Not reported.</p>	<p>moderately severe acne vulgaris.</p> <ul style="list-style-type: none"> <li>• Aged between 12 and 35 years.</li> <li>• Global severity grade ranging from II to III according to the Modified International Acne Grading System.</li> <li>• 10 to 50 inflammatory facial lesions (no more than 3 nodules and/or cysts) and 20 to 150 non-inflammatory facial lesions.</li> <li>• Achieved at least moderate improvement in initial treatment phase.</li> <li>• Participants taking certain topical and systemic treatments were required to complete specified washout periods before they could enter the study.</li> </ul> <p><b>Exclusion criteria</b></p> <ul style="list-style-type: none"> <li>• Participants with acne conglobata, acne fulminans, secondary acne, severe acne or other dermatological conditions requiring systemic treatment.</li> <li>• Women who were pregnant, planning a pregnancy or nursing.</li> <li>• Men with beards if these were likely to interfere with study assessments.</li> </ul>	<p>evening after gentle cleaning of the face.</p> <p>No treatment (n=119): Simple and gentle washing of the face.</p>		<p>participants - no discontinuations reported during the maintenance phase).</p> <p><b>Risk of bias in measurement of the outcome:</b> high risk (same measurement methods and thresholds used at comparable timepoints; open-label trial).</p> <p><b>Risk of bias in selection of the reported result:</b> 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).</p> <p><b>Overall risk of bias judgement:</b> this study is judged to be at high risk of bias (high risk and some concerns in multiple domains).</p> <p><b>Other information</b></p> <p>Participants had previously been treated for moderate to moderately severe acne. Number of participants: N=241. Number of participants completing study: n=241. Previous treatment: adapalene gel 01% plus clindamycin topical solution 1% or clindamycin topical solution 1% alone.</p>

*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

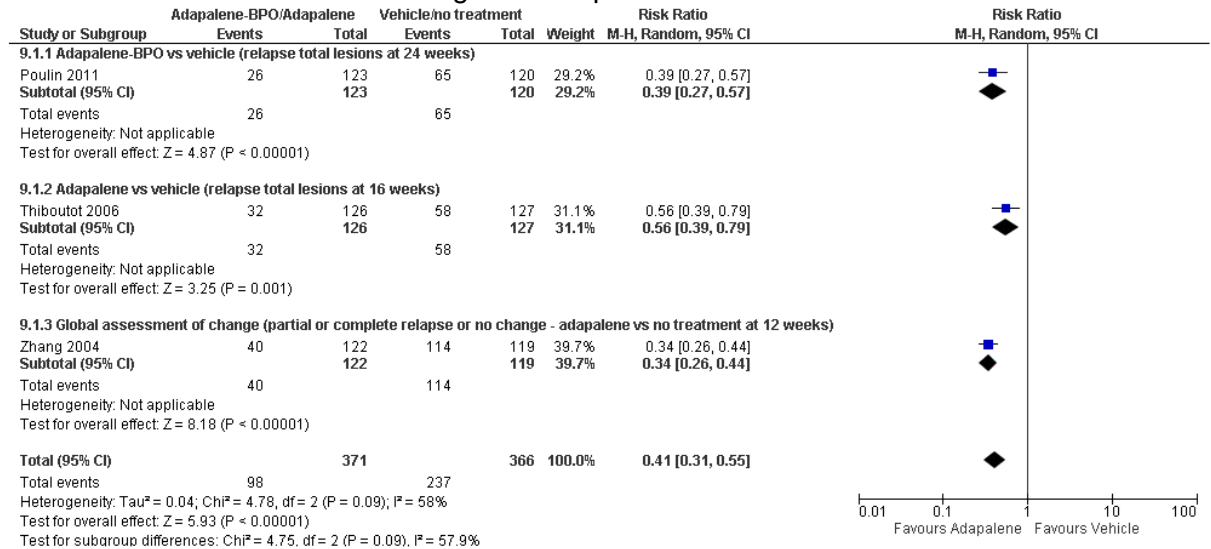
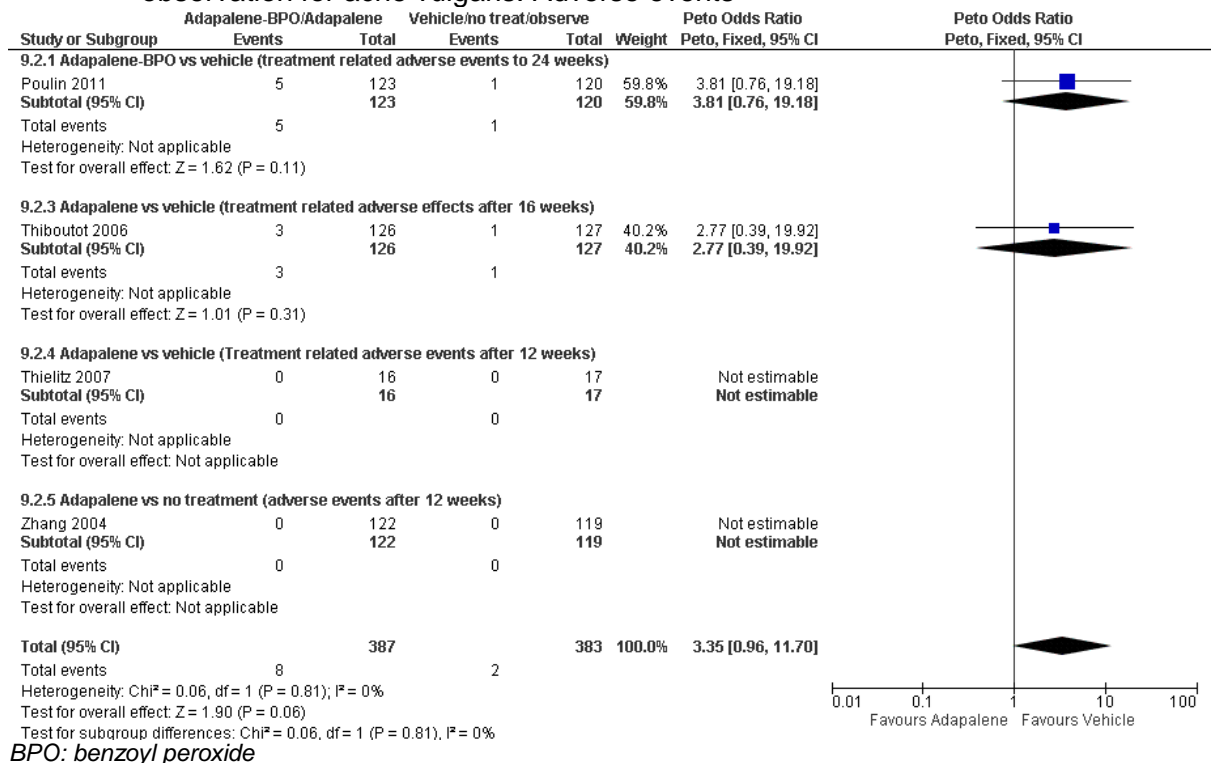


Figure 3: Forest plot for comparison Adapalene regimens versus vehicle, no treatment or observation for acne vulgaris: Adverse events



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

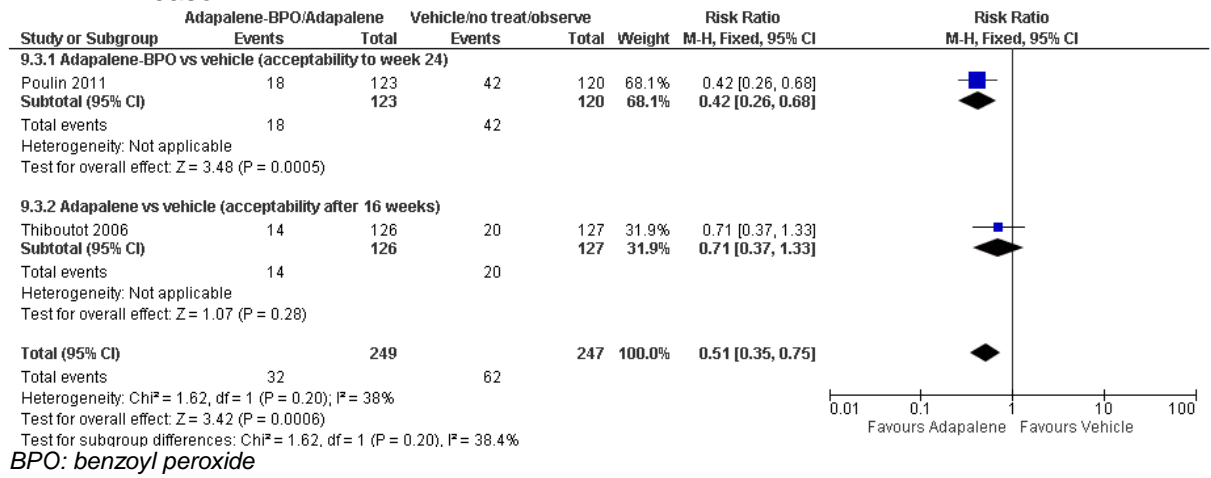
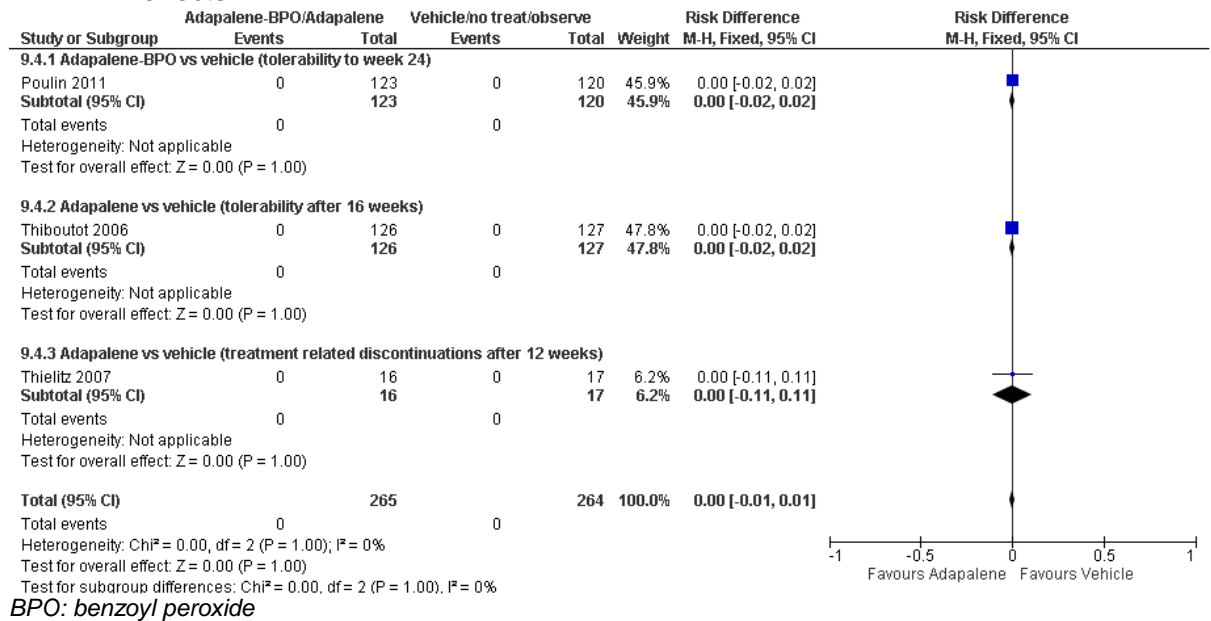


Figure 5: Forest plot for comparison Adapalene regimens versus vehicle, no treatment or observation for acne vulgaris: Tolerability - Treatment discontinuation due to side effects





## 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		
<b>% change in non-inflammatory lesion count after 12 weeks (follow-up 12 weeks; measured with: Lesion count; Better indicated by higher values)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	35	37	-	MD 8 lower (20.39 lower to 4.39 higher)	⊕⊕⊕⊕ LOW	CRITICAL
<b>% change in inflammatory lesion count after 12 weeks (follow-up 12 weeks; measured with: Lesion count; Better indicated by higher values)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	35	37	-	MD 12 higher (0.61 lower to 24.61 higher)	⊕⊕⊕⊕ LOW	CRITICAL
<b>Participants relapsing after 12 weeks (follow-up 12 weeks)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	very serious <sup>5</sup>	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)	⊕⊕⊕⊕ VERY LOW	IMPORTANT
<b>Acceptability (treatment discontinuation for any reason) after 12 weeks (follow-up 12 weeks)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	very serious <sup>5</sup>	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)	⊕⊕⊕⊕ VERY LOW	IMPORTANT
<b>Tolerability (treatment discontinuation due to side effects) after 12 weeks (follow-up 12 weeks)</b>												

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 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	very serious <sup>5</sup>	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)	⊕○○○ VERY LOW	IMPORTANT

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

<sup>1</sup> Leyden 2006

<sup>2</sup> Overall risk of bias judgement: some concerns due to missing outcome data and selection bias.

<sup>3</sup> Evidence downgraded by 1 level due to risk of serious imprecision as 95% CI crosses 1 MID. MID calculated as +/-15.2.

<sup>4</sup> Evidence downgraded by 1 level due to risk of serious imprecision as 95% CI crosses 1 MID. MID calculated as +/- 14.7.

<sup>5</sup> 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		
<b>% change in non-inflammatory lesion count after 12 weeks (follow-up 12 weeks; measured with: Lesion count; Better indicated by higher values)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	35	35	-	MD 4 higher (11.88 lower to 19.88 higher)	⊕⊕○○ LOW	CRITICAL
<b>% change in inflammatory lesion count after 12 weeks (follow-up 12 weeks; measured with: Lesion count; Better indicated by higher values)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	35	36	-	MD 12 higher (0.17 lower to 24.17 higher)	⊕⊕○○ LOW	CRITICAL
<b>Participants relapsing after 12 weeks (follow-up 12 weeks)</b>												
1 <sup>1</sup>	randomised	serious <sup>2</sup>	no serious	no serious	very	none	9/27	7/31	RR 1.48	108 more per 1000 (from 81 fewer to 549)	⊕○○○ 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 <sup>5</sup>		(33.3%)	(22.6%)	(0.64 to 3.43)	more)	LOW	
<b>Acceptability (treatment discontinuation for any reason) after 12 weeks (follow-up 12 weeks)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	very serious <sup>5</sup>	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)	⊕○○○ VERY LOW	IMPORTANT
<b>Tolerability (treatment discontinuation due to side effects) after 12 weeks (follow-up 12 weeks)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	very serious <sup>5</sup>	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)	⊕○○○ VERY LOW	IMPORTANT

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

<sup>1</sup> Leyden 2006

<sup>2</sup> Overall risk of bias judgement: some concerns due to missing outcome data and selection bias.

<sup>3</sup> Evidence downgraded by 1 level due to risk of serious imprecision as 95% CI crosses 1 MID. MID calculated as +/-15.2.

<sup>4</sup> Evidence downgraded by 1 level due to risk of serious imprecision as 95% CI crosses 1 MID. MID calculated as +/- 13.6.

<sup>5</sup> 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		
<b>% change in non-inflammatory lesion count after 12 weeks (follow-up 12 weeks; measured with: Lesion count; Better indicated by higher values)</b>												
1 <sup>1</sup>	randomised	serious <sup>2</sup>	no serious	no serious	no serious	none	35	37	-	MD 12 lower (29.04)	⊕⊕⊕○	CRITICAL

DRAFT FOR CONSULTATION  
Maintenance treatment 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		
	trials		inconsistency	indirectness	imprecision					lower to 5.04 higher)	MODERATE	
<b>% change in inflammatory lesion count after 12 weeks (follow-up 12 weeks; measured with: Lesion count; Better indicated by higher values)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	no serious imprecision	none	36	37	-	MD 0 higher (12.99 lower to 12.99 higher)	⊕⊕⊕○ MODERATE	CRITICAL
<b>Participants relapsing after 12 weeks (follow-up 12 weeks)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	very serious <sup>3</sup>	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)	⊕○○○ VERY LOW	IMPORTANT
<b>Acceptability (treatment discontinuation for any reason) after 12 weeks (follow-up 12 weeks)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	very serious <sup>3</sup>	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)	⊕○○○ VERY LOW	IMPORTANT
<b>Tolerability (treatment discontinuation due to side effects) after 12 weeks (follow-up 12 weeks)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	very serious <sup>3</sup>	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)	⊕○○○ VERY LOW	IMPORTANT

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

<sup>1</sup> Leyden 2006

<sup>2</sup> Overall risk of bias judgement: some concerns due to missing outcome data and selection bias.

<sup>3</sup> 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		
<b>IGA success rate (% participants rated worse from baseline (follow-up 24 weeks; assessed with: Investigator's Global Assessment score))</b>												
1 <sup>1</sup>	randomised trials	very serious <sup>2</sup>	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)	⊕⊕○○ LOW	CRITICAL
<b>Irritation from baseline to week 24 - erythema (follow-up 24 weeks)</b>												
1 <sup>1</sup>	randomised trials	very serious <sup>2</sup>	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)	⊕⊕○○ LOW	IMPORTANT
<b>Irritation from baseline to week 24 - scaling (follow-up 24 weeks)</b>												
1 <sup>1</sup>	randomised trials	very serious <sup>2</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	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)	⊕○○○ VERY LOW	IMPORTANT
<b>Irritation from baseline to week 24 - dryness (follow-up 24 weeks)</b>												
1 <sup>1</sup>	randomised trials	very serious <sup>2</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	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)	⊕○○○ VERY LOW	IMPORTANT
<b>Irritation from baseline to week 24 - stinging/burning (follow-up 24 weeks)</b>												
1 <sup>1</sup>	randomised trials	very serious <sup>2</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	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)	⊕○○○ VERY LOW	IMPORTANT

BPO: benzoyl peroxide; CI: confidence interval; IGA: investigator's global assessment score; MID: minimally important difference; RR: risk ratio

<sup>1</sup> Poulin 2011

<sup>2</sup> Overall risk of bias: high risk due to missing outcome data.

<sup>3</sup> 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		
<b>% change in microcomedone count after 12 weeks (follow-up 12 weeks; Better indicated by higher values)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	very serious <sup>3</sup>	none	16	16	-	MD 3.4 lower (47.61 lower to 40.81 higher)	⊕000 VERY LOW	CRITICAL
<b>Treatment related adverse events after 12 weeks (follow-up 12 weeks)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	very serious <sup>4</sup>	none	0/16 (0%)	0/16 (0%)	RD 0 (-0.11 to 0.11)	-	⊕000 VERY LOW	IMPORTANT
<b>Treatment discontinuations after 12 weeks (follow-up 12 weeks)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	very serious <sup>4</sup>	none	0/16 (0%)	0/16 (0%)	RD 0 (-0.11 to 0.11)	-	⊕000 VERY LOW	IMPORTANT

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

<sup>2</sup> 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.

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

<sup>4</sup> 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		
<b>% change in microcomedone count after 12 weeks (follow-up 12 weeks; Better indicated by higher values)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	16	17	-	MD 51.4 lower (95.35 to 7.45 lower)	⊕⊕○○ LOW	CRITICAL

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

<sup>1</sup> Thielitz 2007

<sup>2</sup> 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.

<sup>3</sup> 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		
<b>% change in microcomedone count after 12 weeks (follow-up 12 weeks; Better indicated by higher values)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	16	17	-	MD 48 lower (104.2 lower to 8.2 higher)	⊕⊕○○ LOW	CRITICAL
<b>Treatment related adverse events after 12 weeks (follow-up 12 weeks)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	very serious <sup>4</sup>	none	0/16 (0%)	0/17 (0%)	RD 0 (-0.11 to 0.11)	-	⊕○○○ VERY LOW	IMPORTANT

Treatment discontinuations after 12 weeks (follow-up 12 weeks)												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	very serious <sup>4</sup>	none	0/16 (0%)	0/17 (0%)	RD 0 (-0.11 to 0.11)	-	⊕○○○ VERY LOW	IMPORTANT

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

<sup>1</sup> Thielitz 2007

<sup>2</sup> 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.

<sup>3</sup> Evidence downgraded by 1 level due to risk of serious imprecision as 95% CI crosses 1 MID. MID calculated as +/- 41.65.

<sup>4</sup> 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		
<b>Relapse/aggravation of symptoms after 12 weeks (follow-up 12 weeks)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	very serious <sup>3</sup>	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)	⊕○○○ VERY LOW	CRITICAL
<b>Adverse events after 12 weeks - Erythema (follow-up 12 weeks)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	very serious <sup>3</sup>	none	1/47 (2.1%)	0/45 (0%)	POR 7.08 (0.14 to 357.20)	-	⊕○○○ VERY LOW	IMPORTANT
<b>Adverse events after 12 weeks - Dryness (follow-up 12 weeks)</b>												



1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	very serious <sup>3</sup>	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)	⊕○○○ VERY LOW	IMPORTANT
----------------	-------------------	----------------------	--------------------------	-------------------------	---------------------------	------	-------------	-------------	-------------------------	--	---------------	-----------

BPO: benzoyl peroxide; CI: confidence interval; MID: minimally important difference; POR: peto odds ratio; RR: risk ratio

<sup>1</sup> Kawashima 2018

<sup>2</sup> Overall risk of bias judgment: some concerns as no information provided on allocation concealment and blinding.

<sup>3</sup> 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		
<b>Relapse (global count) after 12 weeks (follow-up 3 months; assessed with: Global count)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	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)	⊕⊕○○ LOW	IMPORTANT
<b>Number of total lesions after 12 weeks (follow-up 3 months; Better indicated by lower values)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	30	30	-	MD 3 lower (15.45 lower to 9.45 higher)	⊕⊕○○ LOW	CRITICAL
<b>Global lesions after 12 weeks (follow-up 3 months; Better indicated by lower values)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	none	30	30	-	MD 1.5 lower (3.32 lower to 0.32 higher)	⊕⊕○○ LOW	CRITICAL
<b>Change score - Investigator reported improvement (follow-up 3 months; measured with: Investigator's Global Assessment; Better indicated by lower values)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	no serious imprecision <sup>6</sup>	none	30	30	-	MD 0 higher (0 to 0 higher)	⊕⊕⊕○ MODERATE	CRITICAL
<b>Adverse events after 12 weeks (follow-up 3 months)</b>												
1 <sup>1</sup>	randomised	serious <sup>2</sup>	no serious	no serious	very serious <sup>7</sup>	none	0/30	0/30	RD 0.00 (-	-	⊕○○○	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

<sup>1</sup> Truchuelo 2015

<sup>2</sup> Overall risk of bias judgement: some concerns due to limited information on selection of reported result.

<sup>3</sup> Evidence downgraded by 1 level due to risk of serious imprecision as 95% CI crosses 1 default MID for dichotomous outcomes.

<sup>4</sup> Evidence downgraded by 1 level due to risk of serious imprecision as 95% CI crosses 1 MID. MID calculated as +/- 14.465.

<sup>5</sup> Evidence downgraded by 1 level due to risk of serious imprecision as 95% CI crosses 1 MID. MID calculated as +/- 1.9.

<sup>6</sup> MD and 95% CI not estimable.

<sup>7</sup> 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		
<b>Lesion counts after 24 weeks (follow-up 24 weeks; Better indicated by lower values)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	no serious imprecision	none	10	10	-	MD 1.9 lower (2.4 to 1.4 lower)	⊕⊕⊕○ MODERATE	CRITICAL
<b>Acceptability (treatment discontinuation for any reason) at week 24 (follow-up 24 weeks)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	very serious <sup>3</sup>	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)	⊕○○○ VERY LOW	IMPORTANT
<b>Serious or adverse events (follow-up 24 weeks)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	very serious <sup>4</sup>	none	0/10 (0%)	0/10 (0%)	RD 0.00 (-0.17 to 0.17)	-	⊕○○○ VERY LOW	IMPORTANT
<b>Tolerability (treatment discontinuation due to local tolerability complaints or side effects) (follow-up 24 weeks)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	very serious <sup>4</sup>	none	0/10 (0%)	0/10 (0%)	RD 0.00 (-0.17 to 0.17)	-	⊕○○○ VERY LOW	IMPORTANT

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

<sup>1</sup> Vender 2012

<sup>2</sup> Overall risk of bias judgement: some concerns due to issues with multiple domains (randomisation process, missing outcome data, and selection of reported result).

<sup>3</sup> Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% CI crosses 2 default MIDs for dichotomous outcomes.

<sup>4</sup> 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		
<b>Mean % reduction after 12 weeks (total lesions) (follow-up 12 weeks; Better indicated by lower values)</b>												
1 <sup>1</sup>	randomised trials	very serious <sup>2</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	122	119	-	MD 133.7 lower (187.86 to 79.54 lower)	⊕○○○ VERY LOW	CRITICAL

CI: confidence interval; MD: mean difference; MID: minimally important difference

<sup>1</sup> Zhang 2004

<sup>2</sup> 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).

<sup>3</sup> 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		
<b>Relative change in total lesions after 24 weeks (follow-up 24 weeks; Better indicated by lower values)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	17	19	-	MD 39.76 lower (76.57 to 2.95 lower)	⊕⊕○○ LOW	CRITICAL
<b>Absolute change after 24 weeks maintenance in ISGA (follow-up 24 weeks; measured with: Investigator's Static Global Assessment; Better indicated by lower values)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	no serious imprecision	none	17	19	-	MD 0.08 lower (0.35 lower to 0.19 higher)	⊕⊕⊕○ 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 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	no serious imprecision	none	17	19	-	MD 0.16 lower (0.69 lower to 0.37 higher)	⊕⊕⊕○ MODERATE	CRITICAL
Relapse during 24 weeks maintenance (follow-up 24 weeks)												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	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)	⊕⊕⊕○ MODERATE	IMPORTANT
Acceptability (treatment discontinuation for any reason - treatment & maintenance phase) (follow-up 24 weeks)												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	very serious <sup>4</sup>	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)	⊕○○○ VERY LOW	IMPORTANT
Tolerability (treatment discontinuation due to side effects during 24 weeks maintenance) (follow-up 24 weeks)												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	very serious <sup>5</sup>	none	0/17 (0%)	0/19 (0%)	RD 0.00 (-0.10 to 0.10)	-	⊕○○○ 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

<sup>1</sup> Thielitz 2015

<sup>2</sup> Overall risk of bias judgement: some concerns in multiple domains (randomisation process, deviations from intended interventions, measurement of the outcome, and selection of reported result).

<sup>3</sup> Evidence downgraded by 1 level due to risk of serious imprecision as 95% CI crosses 1 MID. MID calculated as +/- 35.635.

<sup>4</sup> Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% CI crosses 2 default MIDs for dichotomous outcomes.

<sup>5</sup> 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 <sup>1</sup>	randomised	very	serious <sup>3</sup>	no serious	no serious	none	98/371	237/366	RR 0.41	382 fewer per 1000	⊕○○○	IMPORTANT

DRAFT FOR CONSULTATION  
Maintenance treatment for acne vulgaris

	trials	serious <sup>2</sup>		indirectness	imprecision		(26.4%)	(64.8%)	(0.31 to 0.55)	(from 291 fewer to 447 fewer)	VERY LOW	
<b>Adverse events (follow-up 12 to 24 weeks)</b>												
4 <sup>4</sup>	randomised trials	very serious <sup>5</sup>	no serious inconsistency	no serious indirectness	very serious <sup>6</sup>	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)	⊕○○○ VERY LOW	IMPORTANT
<b>Acceptability (follow-up 16 to 24 weeks)</b>												
2 <sup>7</sup>	randomised trials	very serious <sup>8</sup>	no serious inconsistency <sup>9</sup>	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)	⊕⊕○○ LOW	IMPORTANT
<b>Tolerability (follow-up 12 to 24 weeks)</b>												
3 <sup>10</sup>	randomised trials	very serious <sup>11</sup>	no serious inconsistency	no serious indirectness	serious <sup>12</sup>	none	0/265 (0%)	0/264 (0%)	RD 0.00 (-0.01 to 0.01)	-	⊕○○○ VERY LOW	IMPORTANT

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

<sup>1</sup> Poulin 2011, Thiboutot 2006, Zhang 2004

<sup>2</sup> 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).

<sup>3</sup> Evidence downgraded by 1 level because there is moderate to substantial heterogeneity across trial ( $i^2=58%$ ) but all trials show efficacy of effect in the same direction (favouring Adapalene-BPO/Adapalene).

<sup>4</sup> Poulin 2011, Thiboutot 2006, Thielitz 2007, Zhang 2004

<sup>5</sup> 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).

<sup>6</sup> Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% CI crosses 2 default MIDs for dichotomous outcomes.

<sup>7</sup> Poulin 2011, Thiboutot 2006

<sup>8</sup> 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.

<sup>9</sup> There is moderate heterogeneity across the trials ( $i^2=38%$ ) 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.

<sup>10</sup> Poulin 2011, Thiboutot 2006, Thielitz 2007

<sup>11</sup> 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).

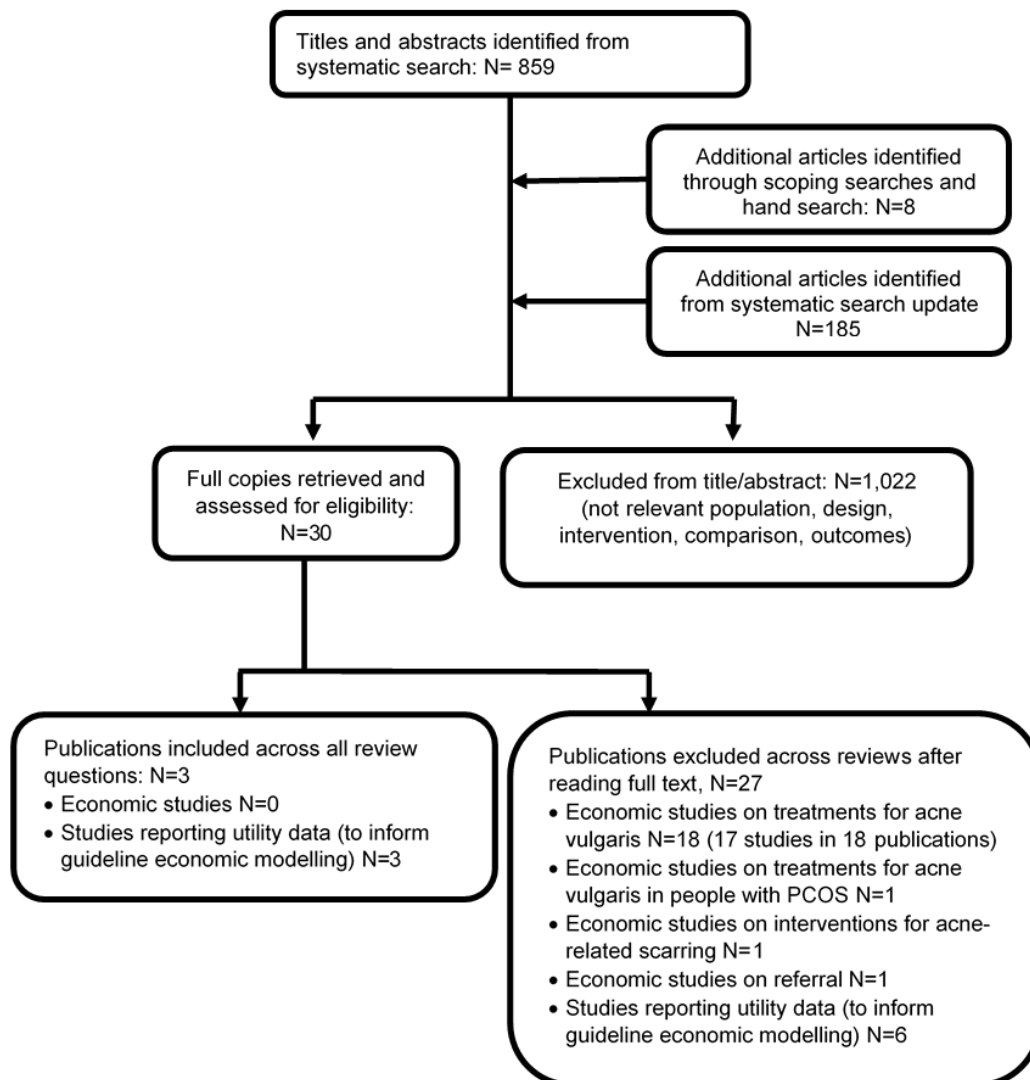
<sup>12</sup> *Evidence downgraded by 1 level due to risk of serious imprecision due to small number of events*

## 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
Adalatkah, 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 norgestrel 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 norgestrel 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 - pharmacokinetic study
Akaraphanth, R. K., W., Gritiyarangsana, 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 Obstetrica 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 hoc 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.,Biol, 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 Comparative 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 lipophilic 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 = Zhongyao cai [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 - pharmacokinetic 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 emollients
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 cutánea 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., Tying, 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 - pharmacokinetic 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. <i>Journal of Drugs in Dermatology</i>	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. <i>Journal of the European Academy of Dermatology &amp; Venereology</i>	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. <i>Giornale Italiano di Dermatologia e Venereologia</i>	Not in English language
Cao, J., Yang, G., Wang, Y., Liu, J. Acupoint Stimulation for Acne: A Systematic Review of Randomized Controlled Trials. 2013. <i>Med Acupunct</i> . 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. <i>Cochrane Database Syst Rev</i>	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. <i>Indian journal of dermatology, venereology and leprology</i>	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. <i>Acta Obstetricia et Gynecologica Scandinavica</i>	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. <i>Contraception fertilitate sexualite</i>	Duplicate record
Carmina, E. L., R. A. A comparison of the relative efficacy of antiandrogens for the treatment of acne in hyperandrogenic women. 2002. <i>Clinical Endocrinology</i>	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. <i>Journal of the American Academy of Dermatology</i>	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. <i>Journal of the American Academy of Dermatology</i>	No relevant outcomes reported
Cavicchini, S. C., R. Long-term treatment of acne with 20% azelaic acid cream. 1989. <i>Acta Dermato-Venereologica, Supplement</i>	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. 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. <a href="http://www.who.int/trialssearch/trial2.aspx? Trialid=chictr-iir-16010104">http://www.who.int/trialssearch/trial2.aspx? Trialid=chictr-iir-16010104</a>	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 (Aiol) 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 (Aiol) 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 assess 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 Obstetrica et Gynecologica Scandinavica	No relevant study population – study focuses on women with PCOS and hirsutism 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 - pharmacokinetic 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 - pharmacokinetic 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 Medicine J 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 relevant study 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 Dermatology J	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. <a href="https://www.ncbi.nlm.nih.gov/pubmed/25610522">https://www.ncbi.nlm.nih.gov/pubmed/25610522</a>	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
DeViliez, 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. <i>Cutis; cutaneous medicine for the practitioner</i>	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. <i>European Journal of Dermatology</i>	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 Schlesinger 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. <i>Dermatology</i>	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. <i>Journal of the european academy of dermatology and venereology : JEADV</i>	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. <i>Journal of the European Academy of Dermatology and Venereology</i>	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. <i>Drugs and Therapy Perspectives</i>	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 isotretinoin versus benzoyl peroxide in the treatment of acne. 1995. The Australasian journal of dermatology	No relevant intervention - Isotretinoin
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 erythromycin resistant cutaneous propionibacteria. 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 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 hoc analysis of Tying 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 - insufficient 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
Ereux, 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 relevant 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 DUACÂ,Â® 10 mg/g + 30 mg/g Gel and the underlying vehicle in patients with mild to moderate acne. 2018. <a href="http://www.who.int/trialsearch/Trial2.aspx?TrialID=EUCTR2017-000521-13-CZ">http://www.who.int/trialsearch/Trial2.aspx?TrialID=EUCTR2017-000521-13-CZ</a>	not RCT
Euctr, F. R. Randomized double-blind study on the benefit of spironolactone for treating acne of adult woman. 2017. <a href="http://www.who.int/trialsearch/Trial2.aspx?TrialID=EUCTR2017-001392-22-FR">http://www.who.int/trialsearch/Trial2.aspx?TrialID=EUCTR2017-001392-22-FR</a>	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.,Nilfroushzadeh, 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.,Nilfroushzadeh, 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 population - 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	Insufficient 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 tretinoin (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 multicentric 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 - pharmacokinetic 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. <i>Dermatology Nursing</i>	No relevant article type - expert review
Gloor, M. H., A., Friederich, H. C. Trial of benzoyl peroxide treatment of acne vulgaris. EXPERIMENTELLE UNTERSUCHUNGEN ZUR BENZOYLPEROXYD THERAPIE DER ACNE VULGARIS. 1975. <i>ZHAUTKR</i>	Not in English language
Goforoushan, F. A., H., Goldust, M. Efficacy of vitamin E to prevent dermal complications of isotretinoin. 2013. <i>Pakistan Journal of Biological Sciences</i>	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. <i>Journal of Dermatological Treatment</i>	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. <i>Journal of Clinical and Aesthetic Dermatology</i>	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. <i>Journal of Clinical and Aesthetic Dermatology</i>	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. <i>Journal of Drugs in Dermatology: JDD</i>	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. <i>Journal of drugs in dermatology : JDD</i>	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. <i>Cosmetic Dermatology</i>	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. <i>Journal of Cosmetic and Laser Therapy</i>	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. <i>Journal of Clinical and Aesthetic Dermatology</i>	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. <i>European journal of clinical research</i>	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 including 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 venerologie	Not English language
Grosshans, E. M., R., Mascaró, 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
Gwiedzinski, 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 Boule, 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 (Ainol 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 analysis by ethnicity and sex of Tying 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 relevant data reported - reports post hoc analysis of Tying 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 stratified 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. <i>Journal of the American Academy of Dermatology</i>	No relevant study design - not RCT
Hjorth, N. G., K. Azelaic acid for the treatment of acne. A clinical comparison with oral tetracycline. 1989. <i>Acta Dermato-Venereologica. Supplementum</i>	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. <i>Cutis</i>	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. <i>Acta Dermato-Venereologica</i>	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. <i>Lasers in Surgery &amp; Medicine</i>	Duplicate record
Hong, S. B. L., M. H. Topical aminolevulinic acid-photodynamic therapy for the treatment of acne vulgaris. 2005. <i>Photodermatology, Photoimmunology &amp; Photomedicine</i>	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. <i>Journal of Investigative Dermatology</i>	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. <i>Revista de farmacologia clinica y experimental</i>	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. <i>Acta Dermato-Venereologica</i>	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. <i>Archives of Dermatology</i>	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. <i>British journal of dermatology</i>	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
Ianosı, S. N., D.,Branısteanu, D. E.,Popescu, M.,Calina, D.,Zlatian, O.,Docea, A. O.,Marinas, M. C.,Iordache, A. M.,MitruÈş, 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. Hydrocortisone and the control of premenstrual exacerbation of acne. 1972. Arcilderii	No relevant study population - insufficient 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 - pharmacokinetic 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 study design - not RCT
Kabir, M. S., S., Raza, A., Kanwal, S., Tanvir, T. Comparison of efficacy of adapalene (0.1% gel) monotherapy vs 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-Convaletius, 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., Yamamoto, 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 & Aesthetic 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 design - 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.Spirolactone 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.,Fearn, 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
Kersch, 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 design - 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
	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. 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 outcomes 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. <i>Cutis</i>	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. <i>Journal of the American Academy of Dermatology</i>	Duplicate record
Kus, S. Y., D., Aytug, A. Comparison of efficacy of azithromycin vs. doxycycline in the treatment of acne vulgaris. 2005. <i>Clinical and Experimental Dermatology</i>	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. <i>Journal of Cosmetic Dermatology</i>	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. <i>British Journal of Dermatology</i>	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. <i>Journal of Dermatology</i>	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. <i>Journal of the European Academy of Dermatology and Venereology</i>	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. <i>Journal of Dermatology</i>	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. <i>Journal of Investigative Dermatology</i>	No relevant article type - conference abstract
Kwon, Comparison of clinical and histological effects between lactobacillus-fermented <i>Chamaecyparis obtusa</i> 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 <i>Chamaecyparis obtusa</i> 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 reported - 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 safety 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
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 article 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
Leshner, 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. <i>Cutis; cutaneous medicine for the practitioner</i>	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. <i>American Journal of Clinical Dermatology</i>	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. <i>Journal of Dermatological Treatment</i>	No relevant outcomes reported - bacterial counts
Leyden, J. J. G., R., Nighland, M. Cumulative irritation potential of topical retinoid formulations. 2008. <i>Journal of drugs in dermatology : JDD</i>	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. <i>Journal of Cutaneous Medicine and Surgery</i>	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. <i>Journal of the American Academy of Dermatology</i>	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. <i>Journal of Drugs in Dermatology</i>	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 % microsphere gel for the treatment of facial acne vulgaris: a double-blind randomized trial. 2002. <i>Cutis; cutaneous medicine for the practitioner</i>	Not obtainable
Leyden, J. J. W., M. A novel gel formulation of clindamycin phosphate-tretinoin is not associated with acne flaring. 2008. <i>Cutis</i>	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. <i>Cutis</i>	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. <i>Journal of Drugs in Dermatology</i>	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
Leyden, J., Levy, S. The development of antibiotic resistance in <i>Propionibacterium acnes</i> . 2001. <i>Cutis</i>	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. <i>Indian journal of dermatology, venereology and leprology</i>	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. <i>British Journal of Clinical Practice</i>	Not obtainable
Lihong, S. He-Ne laser auricular irradiation plus body acupuncture for treatment of acne vulgaris in 36 cases. 2006. <i>Journal of Traditional Chinese Medicine</i>	No relevant intervention - laser plus acupuncture
Lim, C. C. P., D. G. C., Adamson, J. A sustained release tetracycline preparation in acne vulgaris. 1974. <i>Practitioner</i>	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. <i>PloS one</i>	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. <i>Western journal of traditional chinese medicine [xi bu zhong yi yao za zhi]</i>	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 (alpha-hydroxy acid) for acne. 2020. <i>Cochrane Database of Systematic Reviews</i>	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. <i>Photodermatology Photoimmunology and Photomedicine</i>	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. <i>Archives of Dermatology</i>	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 design -

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., Sundström-Poromaa, I., Korver, T. Efficacy and tolerability of a monophasic combined oral contraceptive containing norgestrel acetate and 17β-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., Sundström-Poromaa, I., Korver, T. Efficacy and tolerability of a monophasic combined oral contraceptive containing norgestrel acetate and 17β-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 Isotretinoin 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., Kasproicz, 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 bromamine not available in the UK
Marcinkiewicz, J. Taurine bromamine: a new therapeutic option in inflammatory skin diseases. 2009. Polskie Archiwum Medycyny Wewnętrznej	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. <i>Journal of Cosmetic Dermatology</i>	
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. <i>International Journal of Dermatology</i>	No relevant data reported
Marous, Mr.R., Flaten, H.K., Sledge, B., Rietcheck, H.R., Dellavalle, R., Suneja, T., Dunnick, C. <i>Complementary and Alternative Methods for Treatment of Acne Vulgaris: a Systematic Review</i> . 2018. <i>Current Dermatology Reports</i>	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. <i>Acta Dermato-Venereologica</i>	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. <i>British Journal of Dermatology</i>	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. <i>Journal of Dermatological Treatment</i>	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. <i>Clinical Pharmacology: Advances and Applications</i>	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. <i>Clinical, Cosmetic and Investigational Dermatology CCIDClin Cosmet Investig Dermatol</i>	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. <i>Journal of drugs in dermatology : JDD</i>	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. <i>Journal of Drugs in Dermatology: JDDJ Drugs Dermatol</i>	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. <i>Cutis; cutaneous medicine for the practitioner</i>	Not obtainable
McHugh, R. C. R., A., Sangha, N. D., McCarty, M. A., Utterback, R., Rohrbach, 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. <i>Journal of Dermatological Treatment</i>	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. Treatment 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, randomized, 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., Iraj, 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 Nicamide 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 LÃ©pez, 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., Pflieger, 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, 2019 Clinical, 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 design - 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 R. Azithromycin 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
Raooof, 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
Raooof, 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
Raooof, 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 hirsutism 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; No 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 - pharmacokinetic 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 solution 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 - pharmacokinetic 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 (aminolevulinic 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 Vkampli, 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
Sayyafan, 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 - comparison of addition of topical 90% medical grade 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. A comparative study of efficacy and safety of topical clindamycin gel versus combination of clindamycin gel and benzoyl peroxide cream in patients of mild to moderate acne vulgaris. 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 roxithromycin 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 relevant intervention - facial cleanser; No relevant study population - insufficient information to determine severity 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, 2019 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	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 Dermatology J 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 - pharmacokinetic 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-Radovic, Z.,Kostovic, K.,Nola, I.,Mateljc, 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. <i>Cutis</i>	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. <i>Journal of drugs in dermatology</i>	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. <i>Journal of Drugs in Dermatology</i>	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. <i>Cutis</i>	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. <i>Giornale italiano di dermatologia e venereologia</i>	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. <i>Cutis</i>	No relevant study design - not RCT
Stoughton, R. B. R., W. Topical clindamycin in the control of acne vulgaris. 1976. <i>Cutis</i>	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. <i>Journal of the American Academy of Dermatology</i>	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. <i>Journal of the American Academy of Dermatology</i> <i>J Am Acad Dermatol</i>	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. <i>International Journal of Dermatology</i>	No relevant study design - not RCT
Stuttgen, G. Oral vitamin A acid therapy. 1975. <i>Acta Dermato-Venereologica. Supplementum</i>	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. <i>Advances in Therapy</i>	No relevant study design - not a RCT
Sutono, T. Efficacy of <i>Garcinia mangostana</i> L. (mangosteen rind extract) to reduce acne severity. 2013. <i>Medical Journal of Indonesia</i>	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. <i>JAMA</i>	No relevant intervention - suboptimal doses
Taaffe, A. C., W. J., Cove, J. Topical erythromycin in acne - a double-blind study. 1981. <i>British Journal of Dermatology</i>	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 dapsons 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 intervention - 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 combiphase 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 hirsutism 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., Meephanan, 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 split-face, double-blind, randomized controlled trial. 2020. <i>Journal of Cosmetic Dermatology</i>	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. <i>Clinical, Cosmetic and Investigational Dermatology CCID</i>	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. <i>Fertility and sterility</i>	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. <i>Cutis; cutaneous medicine for the practitioner</i>	No relevant data 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. <i>Cutis; cutaneous medicine for the practitioner</i>	Not obtainable
Webster, G. F. Safety and efficacy of Tretin-X compared with Retin-A in patients with mild-to-severe acne vulgaris. 2006. <i>Skinmed</i>	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. <i>Journal of Drugs in Dermatology</i>	No relevant data reported - publication 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. <i>Cutis</i>	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. <i>Journal of Drugs in Dermatology</i>	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. <i>Journal of Drugs in Dermatology: JDD</i>	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. <i>Archives of Dermatological Research</i>	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. <i>Nouvelles Dermatologiques</i>	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, J. A. Cycle 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 dermatovenereologica	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 Dermatology	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.