

## Acne vulgaris: management

[G] Management options for people with acne vulgaris and polycystic ovary syndrome

NG198

*Evidence review underpinning recommendations 1.5.28 and 1.5.29 and research recommendation 2 in the NICE guideline  
June 2021*

*Final*

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



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# 1 Management options for people with acne 2 vulgaris and polycystic ovary syndrome

## 3 Review question

4 What is an effective management option for people with acne vulgaris and polycystic ovary  
5 syndrome (PCOS)?

## 6 Introduction

7 Acne in people with confirmed polycystic ovarian syndrome may be exacerbated by  
8 hyperandrogenism potentially resulting in persistent or recurrent acne. This review therefore  
9 explores treatment options for this group of people separately as certain therapies, for  
10 example anti-androgens, may be more relevant compared to people without polycystic  
11 ovarian syndrome (who are covered in evidence reviews E1/E2 and F1/F2).

## 12 Summary of the protocol

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

### 15 Table 1: Summary of the protocol

<b>Population</b>	People with acne vulgaris and polycystic ovarian syndrome, of all ages and levels of acne severity
<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 intervention</li> <li>• No treatment</li> <li>• Placebo</li> <li>• Sham physical treatment</li> <li>• Waiting list</li> </ul>

Outcome	
	<p><b>Critical</b></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 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 rated improvement <ul style="list-style-type: none"> <li>○ Change in acne severity or symptoms (e.g. assessed using global acne score)</li> </ul> </li> </ul> <p><b>Important</b></p> <ul style="list-style-type: none"> <li>• Acceptability <ul style="list-style-type: none"> <li>○ Treatment discontinuation for any reason.</li> </ul> </li> <li>• Tolerability <ul style="list-style-type: none"> <li>○ Treatment discontinuation due to side effects.</li> </ul> </li> <li>• Relapse <ul style="list-style-type: none"> <li>○ Relapse after treatment at follow-up.</li> </ul> </li> <li>• Side effects</li> </ul> <p>Specific short-term side effects for comparisons of treatments within the same class or those that involve an inactive arm (for example, placebo, no or sham treatment).</p>

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 4 randomised controlled trials (RCTs) were included for this review (Colonna 2012,  
11 Hagag 2014, Leelaphiwat 2015, and Podfigurna 2020).

12 The included studies are summarised in Table 2.

13 Two studies compared ethinylestradiol and drospirenone to ethinylestradiol and  
14 chlormadinone (Colonna 2012, Podfigurna 2020); 1 study conducted a 3 arm trial which  
15 compared norgestimate, ethinylestradiol, and spironolactone, to cyproterone acetate and  
16 ethinylestradiol, and to norgestimate and ethinylestradiol (Hagag 2014); and 1 study  
17 compared ethinylestradiol, desogestrel, and spironolactone to ethinylestradiol and  
18 cyproterone acetate (Leelaphiwat 2015).

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

### 20 Excluded studies

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

## 1 Summary of studies included in the evidence review

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

### 3 Table 2: Summary of included studies

Study	Population	Intervention	Comparison	Outcomes
Colonna 2012 RCT Italy	N=59  Mean age: 25.5 years  Baseline acne score on Pillsbury Scale: Group A: 2.77±0.53 Group B: 2.70±0.55	Group A Ethinylestradiol 30 microgram + drospirenone 3mg	Group B Ethinylestradiol 30 microgram + chlormadinone acetate 2mg	<ul style="list-style-type: none"> <li>Clinician-rated improvement at treatment endpoint (6 months, measured by Pillsbury Acne Scale)</li> </ul>
Hagag 2014 RCT Israel	N=175  Overall age- (mean (±SD)): 21.6 ±0.7 years  Baseline acne score on Leeds Acne Scale: Group A: 2.8±0.15 Group B: 3.2±1.44 Group C: 3.1±0.75	Group A Norgestimate 250 microgram + ethinylestradiol 35 microgram + spironolactone 100mg  Group B Cyproterone acetate 2mg + ethinylestradiol 35microgram	Group C Norgestimate 250microgram + ethinylestradiol 35microgram	<ul style="list-style-type: none"> <li>Clinician-rated improvement at treatment endpoint (12 months, measured by Leeds Acne Scale)</li> <li>Participant rated improvement</li> </ul>
Leelaphiwat 2015 RCT Thailand	N=36  Mean (±SD) age: 26.72±6.01  Baseline acne score on Global Acne Grading System: Group A: 14.12±5.82 Group B: 13.31±6.19	Group A Ethinylestradiol 30microgram + desogestrel 150microgram + spironolactone 25mg	Group B Ethinylestradiol 35microgram + cyproterone acetate 2 mg	<ul style="list-style-type: none"> <li>Clinician-rated improvement at treatment endpoint (3 months, Global Acne Grading Scale)</li> </ul>
Podfigurna 2020 RCT Poland	N=120  Mean (±SD) age: 26.92±4.72 years  Baseline acne score (on scale from 0-3): Group A:	Group A Ethinylestradiol 30 microgram + drospirenone 3mg	Group B Ethinylestradiol 30 microgram + chlormadinone acetate 2mg	<ul style="list-style-type: none"> <li>Clinician-rated improvement at treatment endpoint (6 months, measured by 0-3 scale)</li> </ul>



Study	Population	Intervention	Comparison	Outcomes
	2.32±0.89 Group B: 2.32±0.89			

1 *RCT: randomised controlled trial; SD: standard deviation.*

2 See the full evidence tables in appendix D and the forest plots in appendix E.

### 3 **Quality assessment of studies included in the evidence review**

4 See the evidence profiles in appendix F.

### 5 **Economic evidence**

#### 6 **Included studies**

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

#### 11 **Excluded studies**

12 Economic studies not included in this review are listed, and reasons for their exclusion are  
13 provided, in appendix K.

#### 14 **Economic model**

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

### 17 **The committee's discussion of the evidence**

#### 18 **Interpreting the evidence**

##### 19 ***The outcomes that matter most***

20 Clinician rated and participant rated improvement of acne were prioritised by the committee  
21 as critical outcomes because they indicate the effectiveness of any treatment option.  
22 Prevention of scarring was another critical outcome due to its lasting negative impact on self-  
23 esteem and psychological wellbeing. Discontinuation of treatment and discontinuation due to  
24 side effects as well as individual side effects (within each class) were important outcomes  
25 because they indicate how well a treatment is tolerated. Relapse was also an important  
26 outcome because it indicates how long a treatment may be effective.

##### 27 ***The quality of the evidence***

28 There was only evidence about hormonal treatments – none of the other interventions of  
29 interest were reported in the subgroup of people with polycystic ovary syndrome and acne.  
30 Of the outcomes of interest, only clinician-rated improvement was reported.

31 The quality of the evidence as assessed by GRADE ranged from low to very low quality.  
32 Evidence about clinician-rated improvement was downgraded due to risk of bias and  
33 imprecision around the effect estimate.

## 1 **Benefits and harms**

2 There was insufficient evidence to identify the most effective treatment for acne vulgaris in  
3 people with polycystic ovary syndrome. This was due to the limited number of studies as well  
4 as the limited number of treatment options that were investigated in the identified evidence.  
5 So the committee based their recommendations on knowledge and experience. They agreed  
6 that standard first line care options are appropriate in the first instance. The committee  
7 thought it was important that people with polycystic ovary syndrome were not treated  
8 differently to other people in initial care, where there is evidence of effective first line care  
9 options. This would also enable treatment for acne to be started without any delays  
10 associated with the diagnosis of polycystic ovary syndrome.

11 If standard first line options do not work, the committee agreed, based on their knowledge  
12 and experience that adding one of the 2 hormonal treatments such as ethinylestradiol with  
13 cyproterone (co-cyprindiol) or an alternative combined oral contraceptive pill could be used  
14 due to their known effectiveness in treating hyperandrogenism which is the defining feature  
15 in people with polycystic ovary syndrome. The committee agreed that co-cyprindiol is a  
16 hormonal treatment option because it has a different mechanism of action to alternative  
17 combined oral contraceptives and, based on the committee's knowledge, is also known to be  
18 effective in the treatment of hyperandrogenism. The committee agreed the combined oral  
19 contraceptive pill is an established and widely available hormonal treatment that is used to  
20 treat symptoms of polycystic ovary syndrome. While there was some evidence comparing  
21 different hormonal treatments against each other, the committee agreed that the choice of  
22 combined oral contraceptive pill should be based on a discussion of benefits and harms of  
23 the various combined hormonal contraceptive pill options available.

24 The committee thought that a 6-month review for those using co-cyprindiol would be needed  
25 to decide whether treatment needs to be changed, to avoid prolonging ineffective treatment  
26 and to avoid side-effects associated with its long-term use. It was discussed based on  
27 expertise that people requiring co-cyprindiol may have an inherently increased risk of  
28 cardiovascular disease and that longer term use should therefore be considered with  
29 caution.

30 The committee agreed that the standard first line treatment options as well as the combined  
31 contraceptive pill and co-cyprindiol could be delivered in primary care but some people with  
32 acne vulgaris and polycystic ovary syndrome who have additional features of  
33 hyperandrogenism (for example a high degree of hirsutism) which can cause significant  
34 psychological distress, would require more specialist treatment and would benefit from  
35 referral to a specialist, such a reproductive endocrinologist.

36 Due to the small number of studies identified, the committee prioritised this topic for further  
37 research to increase the evidence base to inform future updates (see appendix L).

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

39 No economic evidence on the cost effectiveness of management options for people with  
40 polycystic ovary syndrome and acne vulgaris was identified. The recommendation to treat  
41 acne in this population using first line care options in the first instance, which were shown to  
42 be clinically and cost-effective in people with acne vulgaris according to the guideline  
43 network meta-analysis and economic analysis, likely comprises efficient use of resources,  
44 although it was acknowledged that the available clinical and economic evidence was not  
45 specific to people with polycystic ovary syndrome and acne vulgaris. The committee  
46 expressed the opinion that adding the combined oral contraceptive pill to first line treatment,  
47 if the latter is not effective, may result in health benefits relating to the management of both  
48 acne and polycystic ovary syndrome symptoms, and has small resource implications as the  
49 drug acquisition and the extra monitoring costs of the combined oral contraceptive pill are  
50 rather low. The same opinion regarding benefits and costs was expressed about the use of  
51 cyproterone acetate with ethinylestradiol, in case treatment with the combined oral

1 contraceptive pill is not desired or is ineffective. The committee agreed that reviewing  
2 treatment after 6 months in order to decide whether to continue or change treatment ensured  
3 efficient use of resources, as it avoided prolonging use of ineffective treatment. They also  
4 agreed that for some people with acne vulgaris and polycystic ovary syndrome who have  
5 features of hyperandrogenism, referral to appropriate specialist care may be beneficial. The  
6 committee was aware that referral to specialist care requires use of additional healthcare  
7 resources at extra cost, but decided to make a 'consider' recommendation based on their  
8 expertise because they expressed the view that benefits of referral to specialist care are  
9 likely to outweigh future costs incurred by more resource intensive management of  
10 symptoms further down the care pathway, that may be needed if people are not referred to a  
11 specialist.

## 12 Other factors the committee took into account

13 The committee were aware that sexual health advisory groups like the Faculty of  
14 Reproductive and Sexual Health offer [guidance](#) on contraindications, benefits and harms of  
15 various hormonal contraceptive pills which would inform shared decision making on the  
16 choice of these treatments.

## 17 Recommendations supported by this evidence review

18 This evidence review supports recommendations 1.5.28 and 1.5.29 and research  
19 recommendation 2 on treatment options for people with polycystic ovary syndrome.

## 20 References

### 21 Colonna 2012

22 Colonnao, L., Pacifico, V., Lello, S., Sorge, R., Raskovic, D., Primavera, G., Skin  
23 improvement with two different oestrogestins in patients affected by acne and polycystic  
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27 Hagag, P., Steinschneider, M., Weiss, M., Role of the combination spironolactone-  
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### 30 Leelaphiwat 2015

31 Leelaphiwat, S., Jongwutiwes, T., Lertvikool, S., Tabcharoen, C., Sukprasert, M., Rattanasiri,  
32 S., Weerakiet, S., Comparison of desogestrel/ethinylestradiol plus spironolactone versus  
33 cyproterone acetate/ethinylestradiol in the treatment of polycystic ovary syndrome: A  
34 randomised controlled trial, The Journal of Obstetrics and Gynaecology Research, 41, 402-  
35 410, 2015

### 36 Podfigurna 2020

37 Podfigurna, A., Meczekalski, B., Petraglia, F., Luisi, S., Clinical, hormonal and metabolic  
38 parameters in women with PCOS with different combined oral contraceptives (containing  
39 chlormadinone acetate versus drospirenone), Journal of Endocrinological Investigation, 43,  
40 483-492, 2020

# 1 Appendices

## 2 Appendix A – Review protocol

### 3 Review protocol for review question: What is an effective management option for 4 people with acne vulgaris and polycystic ovary syndrome (PCOS)?

5 **Table 3: Review protocol**

Field	Content
PROSPERO registration number	CRD42020165916
Review title	Effectiveness of topical or oral pharmacological and physical interventions in the treatment of acne vulgaris in people with polycystic ovary syndrome
Review questions	- What is an effective management option for people with acne vulgaris and polycystic ovary syndrome (PCOS)?
Objective	The objective of this review is to establish which pharmacological and physical interventions are effective, acceptable and tolerable in the treatment of acne vulgaris in people with polycystic ovary syndrome.
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	Treatment and management of acne vulgaris in people with people with polycystic ovary syndrome
Population	<p><b>Inclusion</b></p> <ul style="list-style-type: none"> <li>• People with acne vulgaris and polycystic ovary syndrome (PCOS), of all ages and levels of acne severity</li> </ul> <p>All settings (community, primary, secondary, and tertiary health care) will be considered.</p> <p><b>Exclusion</b></p> <ul style="list-style-type: none"> <li>• Neonatal acne</li> <li>• People with post-inflammatory dyspigmentation</li> <li>• Trials in people with PCOS without acne vulgaris</li> <li>• Trials of maintenance treatment ('relapse prevention' trials), which recruit people currently in remission or people who have responded to treatment or who have</li> </ul>

Field	Content
	<p>had successful treatment or who are reported to have received primary or 'acute' treatment immediately prior to randomisation to maintenance treatment.</p> <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> </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,</li> <li>• Combination of topical treatments with an oral antibiotic</li> <li>• Oral hormonal contraceptives (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>• Oral isotretinoin</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> <p>Studies will be categorised according to duration of treatment as follows:</p> <ul style="list-style-type: none"> <li>- 0 to &lt;6 weeks</li> <li>- <math>\geq 6</math> to &lt;12 weeks</li> <li>- <math>\geq 12</math> to &lt;24 weeks</li> <li>- <math>\geq 24</math> weeks</li> </ul>
Comparator/Reference standard/Confounding factors	<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 <a href="#">appendix H, Developing NICE guidelines: the manual</a>.</p>
Other exclusion criteria	NA

Field	Content
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 setting (for example community, primary care, secondary care, 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 of acne treatments will be assessed by the following three outcomes:</p> <p>(1) Clinician-rated improvement at treatment endpoint</p> <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> <p>(2) Prevention of scarring at any follow up</p> <ul style="list-style-type: none"> <li>• Change from baseline or final number of scars</li> <li>• Incidence of scarring</li> </ul> <p>(3) Participant-reported improvement</p> <ul style="list-style-type: none"> <li>• -Change in acne severity or symptoms (for example assessed using global acne score)</li> </ul>
Secondary outcomes (important outcomes)	<p><b>Important outcomes</b></p> <p>Acceptability</p> <ul style="list-style-type: none"> <li>• Treatment discontinuation for any reason</li> </ul> <p>Tolerability</p> <ul style="list-style-type: none"> <li>• Treatment discontinuation due to side effects</li> </ul> <p>Other outcomes</p> <p>Relapse</p> <ul style="list-style-type: none"> <li>• Relapse after treatment at follow-up</li> </ul> <p>Side effects</p> <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</p>

Field	Content
	<p>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>
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 two 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 assessed by a senior reviewer.</li> </ul>
Risk of bias (quality) assessment	<p>Risk of bias of individual studies will be assessed using the relevant version of the Cochrane RoB tool, v2. checklist (that is for parallel group or individually-randomised cross-over trials) as described in Developing NICE guidelines: the manual.</p>
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</li> </ul>



Field	Content		
	<p>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.</p> <ul style="list-style-type: none"> <li>• Default minimum important differences (MIDs) will be used for risk ratios and continuous outcomes only, unless the committee pre-specifies published or other MIDs for specific outcomes. For risk ratios: 0.8 and 1.25. For continuous outcomes: +/-0.5 times the baseline SD of the control arm. If there are 2 studies, the MID is calculated as +/- 0.5 times the mean of the SDs of the control arms at baseline. If there are 3 or more studies, the MID is calculated as +/- 0.5 times the median of the SDs of the control arms at baseline. If baseline SD is not available, then SD at follow up will be used.</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>For all outcomes, separate analyses will be conducted for</p> <ul style="list-style-type: none"> <li>• Mild-to-moderate acne vulgaris</li> <li>• Moderate-to-severe acne vulgaris.</li> </ul> <p>Studies will be categorised according to level of severity as defined in each study. If a study reports only moderate acne or it is unclear, the committee will be consulted to classify the study to the appropriate analysis.</p>		
Type and method of review	<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	20/10/2019		
Anticipated completion date	13/01/2021		
Stage of review at time of this submission	Review stage	Started	Completed
	Preliminary searches	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
	Piloting of the study selection process	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
	Formal screening of search results against eligibility criteria	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
	Data extraction	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
	Risk of bias (quality) assessment	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
	Data analysis	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Named contact	<p>5a. Named contact National Guideline Alliance 5b Named contact e-mail AcneManagement@nice.org.uk</p>		



Field	Content	
	5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and National Guideline Alliance	
Review team members	National Guideline Alliance	
Funding sources/sponsor	This systematic review is being completed by the National Guideline Alliance, which is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists. NICE funds the National Guideline Alliance to develop guidelines for those working in the NHS, public health, and social care in England.	
Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.	
Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of <a href="#">Developing NICE guidelines: the manual</a> . Members of the guideline committee are available on the NICE website: <a href="http://www.nice.org.uk/guidance/NG198/history">http://www.nice.org.uk/guidance/NG198/history</a>	
Other registration details	Not applicable	
Reference/URL for published protocol	<a href="https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020165916">https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020165916</a>	
Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: notifying registered stakeholders of publication publicising the guideline through NICE's newsletter and alerts issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.	
Keywords	polycystic ovary syndrome; acne; acne severity; chemical peels; energy-based devices; hormone therapy; laser therapy; light therapy; management; meta-analysis; oral antibiotics; oral isotretinoin; physical; systematic review; topical antibiotics; topical retinoids; treatment.	
Details of existing review of same topic by same authors	Not applicable	
Current review status	<input checked="" type="checkbox"/>	Ongoing
	<input checked="" 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	NA	
Details of final publication	<a href="http://www.nice.org.uk">www.nice.org.uk</a>	

- 1 *CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; DARE:*
- 2 *Database of Abstracts of Reviews of Effects; GRADE: Grading of Recommendations Assessment, Development and*
- 3 *Evaluation; HTA: Health Technology Assessment; MID: minimally important difference; NA: not applicable; NGA:*
- 4 *National Guideline Alliance; NHS: National health service; NICE: National Institute for Health and Care Excellence;*
- 5 *PCOS: polycystic ovary syndrome; RCT: randomised controlled trial; RoB: risk of bias; SD: standard deviation*
- 6

## 1 Appendix B – Literature search strategies

### 2 Literature search strategies for review question: What is an effective management option for people with acne vulgaris and polycystic ovary syndrome (PCOS)?

#### 4 Clinical search

#### 5 Topical interventions (including topical retinoids)

6 Date of initial search: 07/08/2019

7 Additional terms added and searched: 10/09/2019

8 Last searched: 07/05/2020

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

11 Multifile database codes: emczd = Embase Classic+Embase; ppez= MEDLINE(R) and Epub Ahead of  
12 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 antihelmin* or anti-helmin* 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
44	fusidic acid/

#	Searches
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
105	randomized controlled trial/ use ppez

#	Searches
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

- 1 Database(s): The Cochrane Library: Cochrane Database of Systematic Reviews, Issue 5 of  
2 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}
#12	MeSH descriptor: [Anti-Bacterial Agents] explode all trees

#	Searches
#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: [Flxacillin] this term only
#36	MeSH descriptor: [Fusidic Acid] this term only
#37	MeSH descriptor: [Isotretinoin] this term only
#38	MeSH descriptor: [Ivermectin] this term only
#39	MeSH descriptor: [Lymecycline] this term only
#40	MeSH descriptor: [Minocycline] this term only
#41	MeSH descriptor: [Mupirocin] this term only
#42	MeSH descriptor: [Niacinamide] this term only
#43	MeSH descriptor: [Oxytetracycline] this term only
#44	MeSH descriptor: [Penicillin G] this term only
#45	MeSH descriptor: [Penicillin V] this term only
#46	MeSH descriptor: [Phenol] this term only
#47	MeSH descriptor: [Piperacillin] this term only
#48	MeSH descriptor: [Praziquantel] this term only
#49	MeSH descriptor: [Vitamin A] this term only
#50	MeSH descriptor: [Tetracycline] this term only
#51	MeSH descriptor: [Ticarcillin] this term only
#52	MeSH descriptor: [Tretinoin] this term only
#53	MeSH descriptor: [Trimethoprim] this term only
#54	MeSH descriptor: [Zinc Acetate] this term only
#55	(adapalene or aluminum oxide or ampicillin or amoxicillin or avermectin or azaelaic acid or azelaic acid or benzylpenicillin or benzyl penicillin or benzoyl peroxide or cefaclor or cefadroxil or cefalexin or cephalixin or cephalosporin* or cephamycin* or cefixime or cefotaxime or cefradine or ceftaroline or ceftazidime or ceftriaxone or cefuroxime or cephalixin 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

## 1 Oral antibiotics and oral isotretinoin

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

4 Multifile database codes: emczd = Embase Classic+Embase; ppez= MEDLINE(R) and Epub Ahead of  
5 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 antibiotic agent/ use emczd

#	Searches
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 cefdaloixime 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 cefpirome 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 ceftioleone 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	(isotretinoin* or iso tretinoin or isotretinoin or isotren or isotrex* or accutane or roaccutan* or roaccuttan* or roaccuttan* 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 rufloxacin or sitafloxacin or sparfloxacin or temafoxacin 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
57	Case Report/ use ppez

#	Searches
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

- 1 Database(s): The Cochrane Library: Cochrane Database of Systematic Reviews, Issue 5 of  
2 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
#8	MeSH descriptor: [Azithromycin] this term only



#	Searches
#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: [Ticarillin] 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 ticarillin 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
#69	#67 or #68

#	Searches
#70	#66 and #69

## 1 Hormonal interventions

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

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

#	Searches
1	exp Acne Vulgaris/ use ppez
2	exp acne/ use emczd
3	acne.tw.
4	or/1-3
5	exp aldosterone antagonist/ use emczd
6	exp Mineralocorticoid Receptor Antagonists/ use ppez
7	spironolactone/
8	hydroflumethiazide plus spironolactone/ use emczd
9	canrenone/
10	eplerenone/
11	furosemide plus spironolactone/ use emczd
12	(aldactone or spironolactone or canrenone or co-flumactone or coflumactone or eplerenon* or furosemide).tw.
13	or/5-12
14	exp alpha adrenergic receptor blocking agent/ use emczd
15	exp Adrenergic alpha-Antagonists/ use ppez
16	alfuzosin/ use emczd
17	doxazosin/
18	indoramin/
19	prazosin/
20	tamsulosin/
21	dutasteride plus tamsulosin/ use emczd
22	solifenacin plus tamsulosin/ use emczd
23	terazosin/ use emczd
24	(alfuzosin or doxazosin or uroprost or indoramin or prazosin or tamsulosin or terazosin).tw.
25	or/14-24
26	exp steroid 5alpha reductase inhibitor/ use emczd
27	exp 5-alpha Reductase Inhibitors/ use ppez
28	dutasteride/
29	finasteride/
30	(5a reductase inhibitor* or 5-alpha reductase inhibitor* or dutastaride or finasteride).tw.
31	or/26-30
32	exp antiandrogen/ use emczd
33	exp Androgen Antagonists/ use ppez
34	metformin/
35	abiraterone acetate/
36	apalutamide/ use emczd
37	bicalutamide/ use emczd
38	cyproterone acetate plus ethinylestradiol/ use emczd
39	cyproterone acetate/
40	enzalutamide/ use emczd
41	flutamide/
42	(antiandrogen* or anti-androgen* or androgen antagonist* or abiraterone acetate or apalutamide or bicalutamide or cocyprindiol or co-cyprindiol or cyproterone acetate or enzalutamide or flutamide or metformin).tw.
43	or/32-42
44	exp oral contraceptive agent/ use emczd
45	exp Contraceptives, Oral, Combined/ use ppez
46	exp gestagen/ use emczd
47	exp Progestins/ use ppez
48	(chlormadinone acetate plus ethinylestradiol/ or desogestrel plus ethinylestradiol/ or dienogest plus ethinylestradiol/ or drospirenone plus ethinylestradiol/ or dydrogesterone plus estradiol/ or estradiol plus levonorgestrel/ or estradiol plus nomegestrol acetate/ or estradiol plus norethisterone acetate/ or ethinylestradiol plus etonogestrel/ or ethinylestradiol plus gestodene/ or ethinylestradiol plus levonorgestrel/ or ethinylestradiol plus norelgestromin/ or ethinylestradiol plus norethisterone/ or ethinylestradiol plus norgestimate/) use emczd
49	Ethinyl Estradiol-Norgestrel Combination/ use ppez
50	(Ethinyl Estradiol/ use ppez and (Chlormadinone Acetate/ or Desogestrel/ or Levonorgestrel/ or Norethindrone/ or Norgestrel/)) use ppez
51	(Mestranol/ and (Norethindrone/ or Norethynodrel/)) use ppez
52	(Estradiol/ and (Dydrogesterone/ or Levonorgestrel/ or Medroxyprogesterone Acetate/ or Norethindrone/)) use ppez
53	((oral* adj contracept*) or progest?gen* or gestagen* or progestin*).tw.

#	Searches
54	((ethinyl?estradiol or ethinyl estradiol or ethinyl oestradiol) adj3 (chlormadinone acetate or desogestrel or dienogest or drospirenone or etonogestrel or gestodene or levonorgestrel or nomogestrol or norelgestromin* or norethindrone or norethisterone or norgestimate or norgestrel)).tw.
55	(mestranol adj3 (norethindrone or norethisterone or noretynodrel or norethynodrel)).tw.
56	((estradiol or oestradiol) adj3 (dienogest or dydrogesterone or levonorgestrel or medroxyprogesterone acetate or nomegestrol or norethindrone or norethisterone)).tw.
57	or/44-56
58	or/13,25,31,43,57
59	4 and 58
60	limit 59 to english language
61	Letter/ use ppez
62	letter.pt. or letter/ use emczd
63	note.pt.
64	editorial.pt.
65	Editorial/ use ppez
66	News/ use ppez
67	exp Historical Article/ use ppez
68	Anecdotes as Topic/ use ppez
69	Comment/ use ppez
70	Case Report/ use ppez
71	case report/ or case study/ use emczd
72	(letter or comment*).ti.
73	or/61-72
74	randomized controlled trial/ use ppez
75	randomized controlled trial/ use emczd
76	random*.ti,ab.
77	or/74-76
78	73 not 77
79	animals/ not humans/ use ppez
80	animal/ not human/ use emczd
81	nonhuman/ use emczd
82	exp Animals, Laboratory/ use ppez
83	exp Animal Experimentation/ use ppez
84	exp Animal Experiment/ use emczd
85	exp Experimental Animal/ use emczd
86	exp Models, Animal/ use ppez
87	animal model/ use emczd
88	exp Rodentia/ use ppez
89	exp Rodent/ use emczd
90	(rat or rats or mouse or mice).ti.
91	or/78-90
92	60 not 91
93	clinical Trials as topic.sh. or (controlled clinical trial or pragmatic clinical trial or randomized controlled trial).pt. or (placebo or randomi#ed or randomly).ab. or trial.ti.
94	93 use ppez
95	(controlled clinical trial or pragmatic clinical trial or randomized controlled trial).pt. or drug therapy.fs. or (groups or placebo or randomi#ed or randomly or trial).ab.
96	95 use ppez
97	crossover procedure/ or double blind procedure/ or randomized controlled trial/ or single blind procedure/ or (assign* or allocat* or crossover* or cross over* or ((doubl* or singl*) adj blind*) or factorial* or placebo* or random* or volunteer*).ti,ab.
98	97 use emczd
99	94 or 96
100	98 or 99
101	Meta-Analysis/
102	exp Meta-Analysis as Topic/
103	systematic review/
104	meta-analysis/
105	(meta analy* or metanaly* or metaanaly*).ti,ab.
106	((systematic or evidence) adj2 (review* or overview*)).ti,ab.
107	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
108	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
109	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
110	(search* adj4 literature).ab.
111	(medline or pubmed or cochrane or embase or psychlit or psychlit 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
116	or/114-115

#	Searches
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

1 Database(s): The Cochrane Library: Cochrane Database of Systematic Reviews, Issue 5 of  
2 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

3

#### 4 Physical interventions

5 Database(s): Embase Classic+Embase 1947 to 2019 August 12, Ovid MEDLINE(R) and  
6 Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to May 06,  
7 2020

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

#	Searches
1	exp Acne Vulgaris/ use ppez

#	Searches
2	exp acne/ use emezd
3	acne.tw.
4	or/1-3
5	chemexfoliation/
6	(amino acid/ or 2 hydroxyacid/) use emezd
7	(Amino Acids/ or Hydroxy Acids/) use ppez
8	glycolic acid/ use emezd
9	Glycolates/ use ppez
10	lactic acid/
11	mandelic acid/ use emezd
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 emezd
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 emezd
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 microneed* or micro need* 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 emezd
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
64	case report/ or case study/ use emezd

#	Searches
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 psychlit 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

- 1 Database(s): The Cochrane Library: Cochrane Database of Systematic Reviews, Issue 5 of  
 2 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
#9	MeSH descriptor: [Mandelic Acids] this term only

#	Searches
#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

## 1 Economic search

2 Date of initial search: 12/12/2018

3 Date of updated search: 06/05/2020

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

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

#	Searches
1	exp Acne Vulgaris/ use ppez
2	exp acne/ use emez
3	acne.tw.
4	or/1-3
5	Economics/
6	Value of life/
7	exp "Costs and Cost Analysis"/
8	exp Economics, Hospital/
9	exp Economics, Medical/
10	Economics, Nursing/
11	Economics, Pharmaceutical/
12	exp "Fees and Charges"/
13	exp Budgets/
14	(or/5-13) use ppez
15	health economics/
16	exp economic evaluation/
17	exp health care cost/
18	exp fee/
19	budget/



#	Searches
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

1 Date of initial search: 12/12/2018

2 Date of updated search: 06/05/2020

3 Databases(s): NIHR Centre for Reviews and Dissemination: Health Technology Assessment  
4 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

5 **Search for health utility values**

6 Date of initial search: 29/01/2019

7 Date of updated search: 06/05/2020

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

10 Multifile database codes: emez = Embase; ppez = MEDLINE(R) and Epub Ahead of Print, In-Process  
11 & 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 impacted or deteriorat*)).ab.



#	Searches
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

1

2

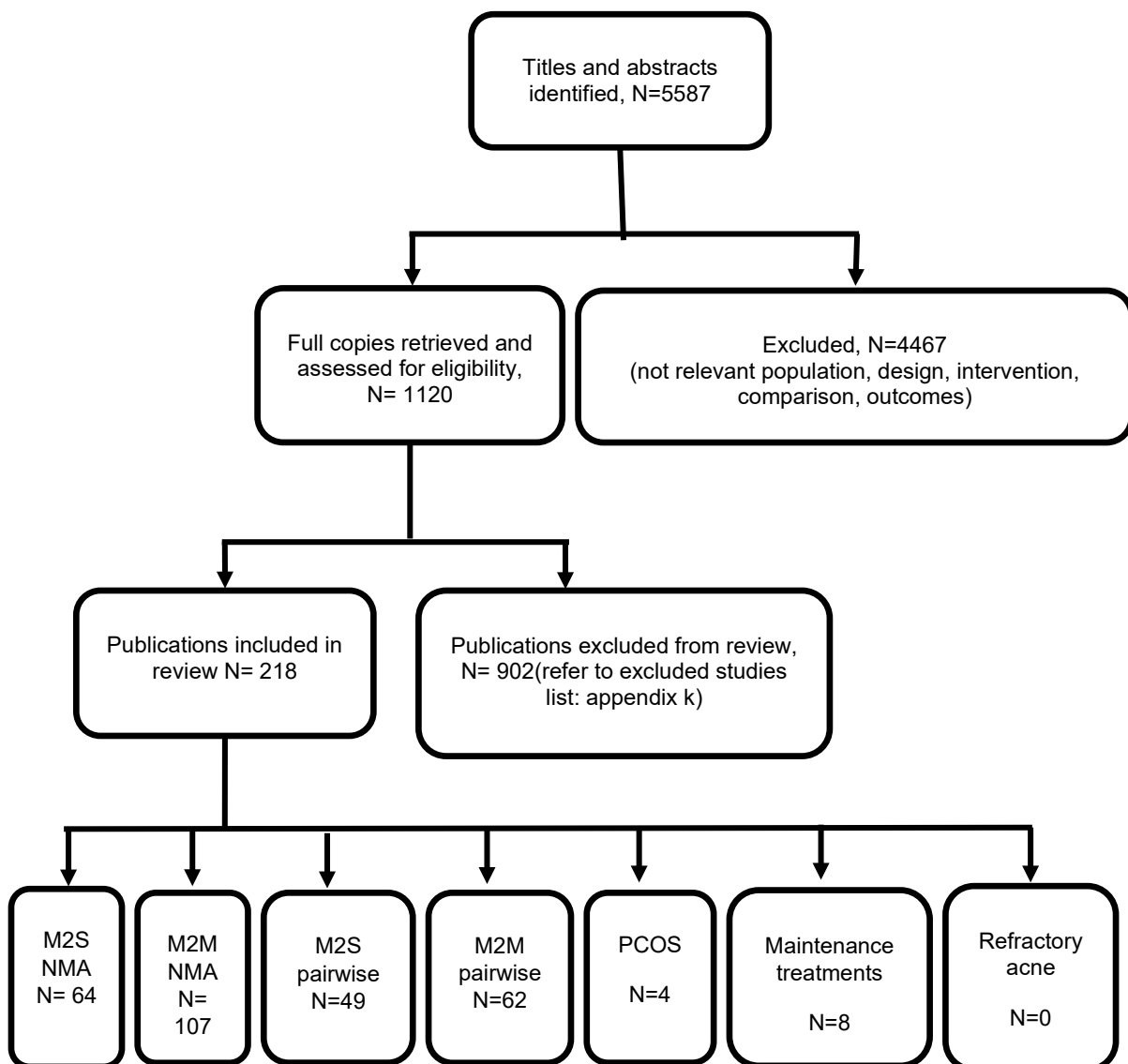
3

## 1 Appendix C – Clinical evidence study selection

### 2 Study selection for: What is an effective management option for people with acne vulgaris and polycystic ovary syndrome (PCOS)?

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

12 **Figure 1: Study selection flow chart**



## 1 Appendix D – Evidence tables

### 2 Evidence tables for review question: What is an effective management option for people with acne vulgaris and polycystic ovary syndrome (PCOS)?

#### 4 Table 4: Evidence table

Study details	Participants	Interventions	Results	Risk of bias
<p><b>Study ID</b> 868256</p> <p><u>Full citation</u> Colonna, L., Pacifico, V., Lello, S., Sorge, R., Raskovic, D., Primavera, G., Skin improvement with two different oestroprogestins in patients affected by acne and polycystic ovary syndrome: clinical and instrumental evaluation, Journal of the European Academy of Dermatology &amp; Venereology/J Eur Acad Dermatol Venereol, 26, 1364-71, 2012</p> <p><u>Country/ies where the study was carried out</u> Italy</p> <p><u>RCT type (parallel or split face)</u> Parallel randomised controlled trial</p>	<p>N=59</p> <p><u>Sex (Male, female or mixed)</u> Female</p> <p><u>Age details</u> Mean: 25.55 years Range: 18-29 years</p> <p><u>Baseline acne score on Pillsbury Scale- Mean±SD:</u> Group A: 2.77±0.53 Group B: 2.70±0.55</p> <p><u>Acne scale used for inclusion</u> Pillsbury</p> <p><u>Other inclusion criteria</u> Inclusion/exclusion criteria were those followed for estroprogestins administration.</p> <p><u>Exclusion criteria</u> Inclusion/exclusion criteria were those followed for estroprogestins administration.</p>	<p><u>Treatment duration (weeks)</u> 24 weeks</p> <p><u>Info about intensity of physical treatments</u> N/A</p> <p><u>Number of treatment arms</u> 2</p> <p><u>Interventions</u> <b>Intervention (group A):</b> Ethinyl-estradiol 30 micrograms+ drospirenone 3mg <b>Control (group B):</b> Ethinyl-estradiol 30 micrograms + chlormadinone acetate 2mg</p>	<p><b>Results</b> <b><u>Clinician-rated improvement at treatment endpoint (Pillsbury Acne Scale):</u></b> <u>Acne score at 6 months (measured by Pillsbury Acne Scale):</u> EE/DRSP: 0.80+/-0.58 EE/CMA: 0.95+/-0.60</p>	<p><b>Risk of bias</b> <b><u>Cochrane RoB Tool v2.0</u></b> <u>Selection bias:</u> some concerns (no sufficient information provided about the randomisation and allocation concealment) <u>Performance bias:</u> some concerns (outcome assessment by investigator blinded to treatment) <u>Attrition bias:</u> low risk of bias (no reported exclusions) <u>Detection bias:</u> low risk of bias <u>Reporting bias:</u> some concerns (no study protocol reported) <u>Other bias:</u> low risk of bias <u>Overall risk of bias:</u> some concerns</p>

Study details	Participants	Interventions	Results	Risk of bias
<u>Study dates</u> Not mentioned.				<u>Other information</u> None
<u>Source of funding</u> Not mentioned.				
<b>Study ID</b> 1170391  <u>Full citation</u> Hagag, P., Steinschneider, M., Weiss, M., Role of the combination spironolactone-norgestimate-estrogen in hirsute women with polycystic ovary syndrome, Journal of Reproductive Medicine, 59, 455-463, 2014  <u>Country/ies where the study was carried out</u> Israel  <u>RCT type (parallel or split face)</u> Parallel randomised controlled trial  <u>Study dates</u> January 2005 to January 2010  <u>Source of funding</u> Not mentioned.	N=175  <u>Sex (Male, female or mixed)</u> Female  <u>Age details</u> <b>Age (years)- Mean (SD):</b> Group A: 22±0.4 Group B: 21±0.3 Group C: 22±0.7  Overall age (mean (±SD)): 21.6 ±0.7 years  <u>Baseline acne score on Leeds Acne Scale:</u> Group A: 2.8±0.15 Group B: 3.2±1.44 Group C: 3.1±0.75  <u>Acne scale used for inclusion</u> Leeds Acne Scale  <u>Other inclusion criteria</u> Not mentioned.  <u>Exclusion criteria</u> Not mentioned.	<u>Treatment duration (weeks)</u> 52 weeks  <u>Info about intensity of physical treatments</u> N/A  <u>Number of treatment arms</u> 3  <u>Interventions</u> Group A: Norgestimate 250micrograms + ethinylestradiol 35micrograms + spironolactone 100milligrams  Group B: Cyproterone acetate 2milligrams + ethinylestradiol 35micrograms  <i>During 21-day intervention, 10milligrams CPA added in all group B participants</i>  Group C: Norgestimate 250micrograms + ethinylestradiol 35micrograms	<b>Results</b> <b><u>Clinician-rated improvement at treatment endpoint (Leeds Acne Scale)</u></b> <u>Number of participants with Leeds acne score of &gt;0.25- investigator assessed at 12 months</u> Group A: N=41/66 Group B: N=38/65 Group C: N=11/24  <u>Leeds Acne Scale Score- percent change from baseline- investigator assessed (mean +/- SE)</u> Group A: -78% +/- 1.6 Group B: -70% +/- 4.9 Group C: -68% +/- 5.2  <b>Participant rated improvement</b> <u>Number of participants with Leeds acne score of &gt;0.25- participant assessed at 12 months</u> Group A: 43/66 Group B: 41/65 Group C: 12/24	<b>Risk of bias</b> <b><u>Cochrane RoB Tool v2.0</u></b> <u>Selection bias:</u> some concerns (no sufficient information provided about allocation concealment) <u>Performance bias:</u> some concerns (no details given) <u>Attrition bias:</u> low risk of bias (less than 5% lost to follow up) <u>Detection bias:</u> some concerns (no details provided) <u>Reporting bias:</u> some concerns (no study protocol reported) <u>Other bias:</u> low risk of bias <u>Overall risk of bias:</u> some concerns  <u>Other information</u> Withdrawals: Group A: -Nausea n=2 -Vomiting n=1 Group B:

Study details	Participants	Interventions	Results	Risk of bias
				-Amenorrhoea n=3 -Nausea n=1 - Lost to follow-up n=1
<p><b>Study ID</b> 869134</p> <p><u>Full citation</u> Leelaphiwat, S., Jongwutiwes, T., Lertvikool, S., Tabcharoen, C., Sukprasert, M., Rattanasiri, S., Weerakiet, S., Comparison of desogestrel/ethinyl estradiol plus spironolactone versus cyproterone acetate/ethinyl estradiol in the treatment of polycystic ovary syndrome: a randomized controlled trial, Journal of Obstetrics &amp; Gynaecology Research, 41, 402-10, 2015</p> <p><u>Country/ies where the study was carried out</u> Thailand</p> <p><u>RCT type (parallel or split face)</u> Parallel randomised controlled trial</p> <p><u>Study dates</u> Not mentioned</p>	<p>N=36</p> <p><u>Sex (Male, female or mixed)</u> Female</p> <p><u>Age details</u> Mean age (years)- Mean±SD: Group A: 26.29±4.04 Group B: 26.94±6.87</p> <p>Overall mean age- Mean±SD: 26.72±6.01</p> <p><u>Baseline acne score on Global Acne Grading System- Mean±SD:</u> Group A: 14.12±5.82 Group B: 13.31±6.19</p> <p><u>Acne scale used for inclusion</u> Global acne grading system</p> <p><u>Other inclusion criteria</u></p> <ul style="list-style-type: none"> <li>○ Aged 20-35 years;</li> <li>○ Having all three presentations comprising oligo-amenorrhoea, clinical signs of hyperandrogenism and polycystic ovaries according to the Rotterdam</li> </ul>	<p><u>Treatment duration (weeks)</u> 12</p> <p><u>Info about intensity of physical treatments</u> N/A</p> <p><u>Number of treatment arms</u> 2</p> <p><u>Interventions</u> Intervention (Group A): Ethinyl-estradiol 30 micrograms + desogestrel 150 micrograms + spironolactone 25milligrams</p> <p>*Spironolactone added continuously daily for 12 weeks</p> <p>Control (Group B): Ethinyl-estradiol 35 micrograms + cyproterone acetate 2 milligrams</p>	<p><b>Results</b> <b><u>Clinician-rated improvement at treatment endpoint</u></b> <u>Global acne score on GAGS at the end of treatment (3 months):</u> Group A: 6.94 +/- 3.47 Group B: 8.13 +/- 6.09</p>	<p><u>Risk of bias</u> <b><u>Cochrane RoB Tool v2.0</u></b> <u>Selection bias:</u> low risk <u>Performance bias:</u> some concerns (no details given) <u>Attrition bias:</u> some concerns (8% lost to follow up) <u>Detection bias:</u> some concerns (no details provided) <u>Reporting bias:</u> some concerns (no study protocol reported) <u>Other bias:</u> low risk <u>Overall risk of bias:</u> some concerns</p> <p><u>Other information</u> Three participants excluded from study: -Group A: emergency appendectomy N=1 -Group B: severe headache during treatment N=1, lost to follow-up N=1</p>

Study details	Participants	Interventions	Results	Risk of bias
<p><u>Source of funding</u> Research Grant from the Faculty of Medicine Ramathibodi Hospital, Mahidol University.</p>	<p>criteria.</p> <p><u>Exclusion criteria</u></p> <ul style="list-style-type: none"> <li>○ Having previous ovarian surgery;</li> <li>○ Having taken any hormonal medications such as OCP during the last 3 months.</li> </ul>			
<p><b>Study ID</b> 1251019</p> <p><u>Full citation</u> Podfigurna, A., Meczekalski, B., Petraglia, F., Luisi, S., Clinical, hormonal and metabolic parameters in women with PCOS with different combined oral contraceptives (containing chlormadinone acetate versus drospirenone), Journal of Endocrinological Investigation, 43, 483-492, 2020</p> <p><u>Country/ies where the study was carried out</u> Poland</p> <p><u>RCT type (parallel or split face)</u> Parallel randomised controlled trial</p> <p><u>Study dates</u></p>	<p>N=120</p> <p><u>Sex (Male, female or mixed)</u> Female</p> <p><u>Age details</u> <u>Mean age (years)- Mean±SD:</u> 26.92 ± 4.72 years</p> <p><u>Baseline acne score (on scale from 0-3)- Mean±SD:</u> Group A: 2.32±0.89 Group B: 2.32±0.89</p> <p><u>Acne scale used for inclusion</u> Subjective scale from 0 to 3</p> <p><u>Other inclusion criteria</u> Not mentioned.</p> <p><u>Exclusion criteria</u></p> <ul style="list-style-type: none"> <li>○ People receiving hormonal therapy (including oral contraceptives);</li> <li>○ People who have undergone</li> </ul>	<p><u>Treatment duration (weeks)</u> 24 weeks</p> <p><u>Info about intensity of physical treatments</u> N/A</p> <p><u>Number of treatment arms</u> 2</p> <p><u>Interventions</u> Intervention: Ethinylestradiol 30 micrograms+ drospirenone 3mg Control: Ethinylestradiol 30 micrograms + chlormadinone acetate 2mg</p>	<p><b>Results</b> <b><u>Clinician-rated improvement at treatment endpoint</u></b> <u>Acne score at 6 months (measured on a scale from 0-3):</u> EE/DRSP: 0.31+/-0.78 EE/CMA: 0.45+/-0.98</p>	<p><b>Risk of bias</b> <b><u>Cochrane RoB Tool v2.0</u></b> <u>Selection bias:</u> some concerns (insufficient information provided allocation concealment) <u>Performance bias:</u> some concerns (no details provided) <u>Attrition bias:</u> low risk of bias (no reported exclusions) <u>Detection bias:</u> some concerns (double-blinded but no details provided) <u>Reporting bias:</u> some concerns (no study protocol reported) <u>Other bias:</u> low risk of bias <u>Overall risk of bias:</u> high risk</p> <p><u>Other information</u></p>

Study details	Participants	Interventions	Results	Risk of bias
Not mentioned	hormonal therapy in the previous 6 months;			None
<u>Source of funding</u> This research received no external funding.	<ul style="list-style-type: none"> <li>○ People reporting any chronic illness</li> </ul>			

1 CMA: chlormadinone acetate; CPA: cyproterone acetate; DRSP: drospirenone; EE: ethinylestradiol; GAGS: global acne grading scale; OCP: oral contraceptive pill; RoB: risk of  
2 bias; SD: standard deviation

3

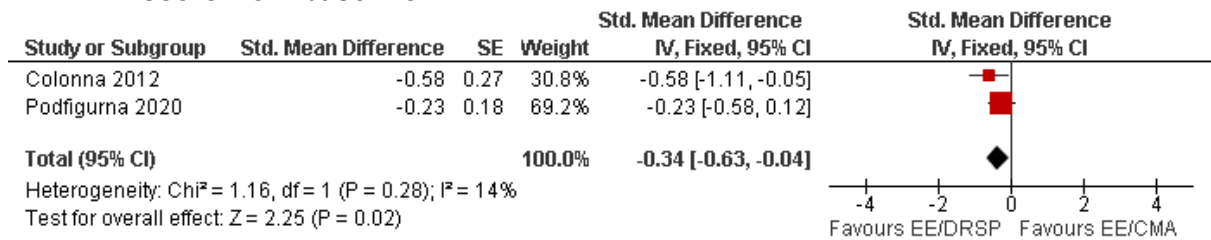
4

## 5 Appendix E – Forest plots

### 6 Forest plots for review question: What is an effective management option for 7 people with acne vulgaris and polycystic ovary syndrome (PCOS)?

8

**Figure 2: Ethinyl-estradiol + chlormadinone acetate versus ethinyl-estradiol + drospirenone; Clinician-rated improvement at treatment endpoint - change score from baseline**



EE/CMA: Ethinyl-estradiol + chlormadinone acetate; EE/DRSP: Ethinyl-estradiol + drospirenone



## 1 Appendix F – GRADE tables

### 2 GRADE tables for review question: What is an effective management option for people with acne vulgaris and polycystic ovary syndrome (PCOS)?

4 Table 5: EE/DRSP vs EE/CMA for acne vulgaris in PCOS sub-population

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EE/DRSP	EE/CMA	Relative (95% CI)	Absolute		
Clinician-rated improvement at treatment endpoint- Change score from baseline (follow-up mean 6 months; measured with two scales: Pillsbury Acne Scale and 0-3 scale; Better indicated by higher values)												
2 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	92	87	-	SMD 0.34 lower (0.63 to 0.04 lower)	⊕⊕⊕⊕ LOW	CRITICAL

5 CI: confidence interval; EE/CMA: ethinylestradiol/chlormadinone; EE/DRSP: ethinylestradiol/ drospirenone; SMD: standard mean difference; PCOS: polycystic ovarian  
6 syndrome

7 <sup>1</sup> Colonna 2012, Podfigurna 2020

8 <sup>2</sup> Evidence downgraded 1 level due to some concerns with selection, performance, detection, and reporting bias

9 <sup>3</sup> Evidence downgraded 1 level as 95% CI crosses 1 MID (MID +/-0.50 as outcome is SMD)

10

11 Table 6: NOR/EE/SPIR vs CPA/EE for acne vulgaris in PCOS sub-population

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NOR/EE/SPIR	CPA/EE	Relative (95% CI)	Absolute		
Clinician-rated improvement at treatment endpoint- Percentage change score from baseline (follow-up mean 12 months; measured with: Leeds Acne Scale; Better indicated by higher values)												
1 <sup>1</sup>	randomised	serious <sup>2</sup>	no serious	no serious	very	none	75	75	-	MD 8 lower (18.1 lower to	⊕⊕⊕⊕	CRITICAL

	trials		inconsistency	indirectness	serious <sup>3</sup>					2.1 higher)	VERY LOW	
<b>Participant-rated improvement at treatment endpoint (follow-up mean 12 months; assessed with: Leeds Acne Scale)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	very serious <sup>4</sup>	none	43/66 (65.2%)	41/65 (63.1%)	RR 1.03 (0.80 to 1.33)	19 more per 1000 (from 126 fewer to 208 more)	⊕○○○ VERY LOW	CRITICAL

- 1 *CI: confidence interval; CPA/EE: cyproterone acetate/ethinylestradiol; MD: mean difference; NOR/EE/SPIR: norgestimate/ethinylestradiol/spironolactone; PCOS: polycystic ovarian syndrome*
- 2
- 3 <sup>1</sup> Hagag 2014
- 4 <sup>2</sup> Evidence downgraded by 1 level due to some concerns with selection, performance, detection, and reporting bias.
- 5 <sup>3</sup> Evidence downgraded 2 levels as 95% CI crosses 2 MIDs. MID calculated as +/-0.15.
- 6 <sup>4</sup> Evidence downgraded by 2 levels as 95% CI crosses 2 default MIDs for dichotomous outcomes.

7

8 **Table 7: NOR/EE/SPIR vs NOR/EE for acne vulgaris in PCOS sub-population**

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NOR/EE/SPIR	NOR/EE	Relative (95% CI)	Absolute		
<b>Clinician-rated improvement at treatment endpoint- Percentage change score from baseline (follow-up mean 12 months; measured with: Leeds Acne Scale; 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	75	25	-	MD 10 lower (20.66 lower to 0.66 higher)	⊕○○○ VERY LOW	CRITICAL
<b>Participant-rated improvement at treatment endpoint (follow-up mean 12 months; assessed with: Leeds Acne Scale)</b>												
1 <sup>1</sup>	randomised trials	serious <sup>4</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	none	43/66 (65.2%)	12/24 (50%)	RR 1.30 (0.84 to 2.02)	150 more per 1000 (from 80 fewer to 510 more)	⊕⊕○○ LOW	CRITICAL

- 9 *CI: confidence interval; MD: mean difference; NOR/EE: norgestimate/ethinylestradiol; NOR/EE/SPIR: norgestimate/ethinylestradiol/spironolactone; PCOS: polycystic ovarian syndrome*
- 10
- 11 <sup>1</sup> Hagag 2014
- 12 <sup>2</sup> Evidence downgraded due to some concerns with selection, performance, detection, and reporting bias.
- 13 <sup>3</sup> Evidence downgraded 2 levels as 95% CI crosses 2 MIDs. MID calculated as +/-0.375.

1 <sup>4</sup> Evidence downgraded by 1 level due to some concerns with selection, performance, detection, and reporting bias.

2 <sup>5</sup> Evidence downgraded by 1 level as 95% CI crosses 1 default MID for dichotomous outcomes.

3 **Table 8: CPA/EE vs NOR/EE for acne vulgaris in PCOS sub-population**

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CPA/EE	NOR/EE	Relative (95% CI)	Absolute		
Clinician-rated improvement at treatment endpoint- Percentage change score from baseline (follow-up mean 12 months; measured with: Leeds Acne Scale; Better indicated by higher values)												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	very serious <sup>3</sup>	none	75	25	-	MD 2 lower (16 lower to 12 higher)	⊕○○○ VERY LOW	CRITICAL
Participant-rated improvement at treatment endpoint (follow-up mean 12 months; assessed with: Leeds Acne Scale)												
1 <sup>1</sup>	randomised trials	serious <sup>4</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	none	41/65 (63.1%)	12/24 (50%)	RR 1.26 (0.81 to 1.96)	130 more per 1000 (from 95 fewer to 480 more)	⊕⊕○○ LOW	CRITICAL

4 CI: confidence interval; CPA/EE: cyproterone acetate/ethinylestradiol; MD: mean difference; NOR/EE: norgestimate/ethinylestradiol; PCOS: polycystic ovarian syndrome

5 <sup>1</sup> Hagag 2014

6 <sup>2</sup> Evidence downgraded due to some concerns with selection, performance, detection, and reporting bias.

7 <sup>3</sup> Evidence downgraded 2 levels as 95% CI crosses 2 MIDs. MID calculated as +/-0.375.

8 <sup>4</sup> Evidence downgraded by 1 level due to some concerns with selection, performance, detection, and reporting bias.

9 <sup>5</sup> Evidence downgraded by 1 level as 95% CI crosses 1 default MID for dichotomous outcomes.

10

11 **Table 9: EE/DSG/SPIR vs EE/CPA for acne vulgaris in PCOS sub-population**

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EE/DSG/SPIR	EE/CPA	Relative (95% CI)	Absolute		

Clinician-rated improvement at treatment endpoint- Change score from baseline (follow-up mean 3 months; measured with: Global Acne Grading System; Better indicated by higher values)												
1 <sup>1</sup>	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	16	16	-	MD 2 lower (4.95 lower to 0.95 higher)	⊕⊕⊕⊕ LOW	CRITICAL

1 *CI: confidence interval; EE/CPA: ethinylestradiol/cyproterone acetate; EE/DSG/SPIR: ethinylestradiol/desogestrel/spironolactone; MD: mean difference; PCOS: polycystic ovarian syndrome*

3 <sup>1</sup> Leelaphiwat 2015

4 <sup>2</sup> Evidence downgraded due to some concerns with performance, attrition, detection, and reporting bias

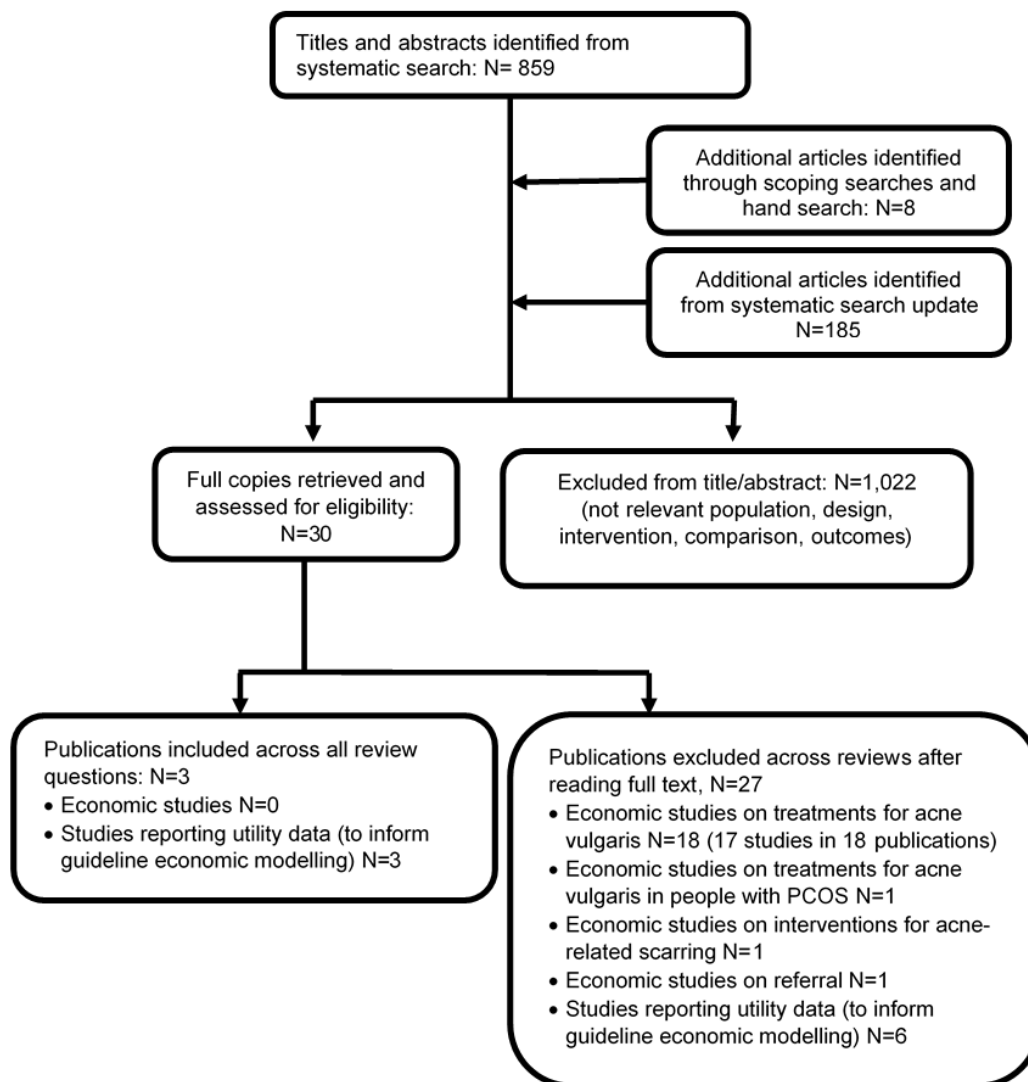
5 <sup>3</sup> Evidence downgraded 1 level as 95% CI crosses 1 MID. MID calculated as +/-3.095

## 1 Appendix G – Economic evidence study selection

### 2 Economic evidence study selection for review question: What is an effective 3 management option for people with acne vulgaris and polycystic ovary 4 syndrome (PCOS)?

5 A global health economics search was undertaken for all areas covered in the guideline.  
6 Figure 3 shows the flow diagram of the selection process for economic evaluations of  
7 interventions and strategies associated with the care of people with acne vulgaris and  
8 studies reporting acne vulgaris-related health state utility data.

9 **Figure 3. 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**  
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## 1 **Appendix H – Economic evidence tables**

### 2 **Economic evidence tables for review question: What is an effective management option for people with acne vulgaris and polycystic ovary syndrome (PCOS)?**

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

5

6

1 **Appendix I – Economic evidence profiles**

2 **Economic evidence profiles for review question: What is an effective management**  
3 **option for people with acne vulgaris and polycystic ovary syndrome (PCOS)?**

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

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## 1 **Appendix J – Economic analysis**

2 **Economic evidence analysis for review question: What is an effective**  
3 **management option for people with acne vulgaris and polycystic ovary**  
4 **syndrome (PCOS)?**

5 No economic analysis was conducted for this review question.

6



## 1 Appendix K – Excluded studies

### 2 Excluded studies for review question: What is an effective management option 3 for people with acne vulgaris and polycystic ovary syndrome (PCOS)?

#### 4 Clinical studies

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

#### 10 Table 10: 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 pilot randomized clinical trial. 2011. Clinical, Cosmetic and	Moderate acne - no information on lesion counts at baseline and

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

Reference	Reason for exclusion
Radiofrequency Device for Acne Patients: A Prospective Randomized Controlled Study. 2019. Lasers in Surgery and Medicine.	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, M. Comparative study of the efficacy and tolerability of 0.1 and 0.03	Not in English language

Reference	Reason for exclusion
p.100 adapalene gel and 0.025 p.100 tretinoin gel in the treatment of acne. 1996. Annales de dermatologie ET de venerologie	
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.,Biro, 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
Anonymous, Treatment of moderate-to-severe facial acne vulgaris	No relevant article type -

Reference	Reason for exclusion
with the use of a solid-state fractional 589/1,319-nm laser. 2018. Journal of the American Academy of Dermatology	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 reported according to

Reference	Reason for exclusion
	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 comparison with oral isotretinoin. 2019. Iranian Journal of	No relevant data reported - reports combined results for those with treatment-resistant acne and those



Reference	Reason for exclusion
Dermatology	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. <i>Cutis</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
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. <i>Journal of the American Academy of Dermatology</i>	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. <i>Lasers in Surgery and Medicine</i>	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. <i>Journal of the American Academy 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
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. <i>Archives 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
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. <i>Dermatology</i>	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. <i>Journal of Clinical and Aesthetic Dermatology</i>	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, Phase IV Clinical Trial. 2014. <i>Journal of Clinical and Diagnostic</i>	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS,

Reference	Reason for exclusion
Research JCDR	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. <i>Journal of Cosmetic Dermatology</i>	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. <i>Journal of Drugs in Dermatology</i>	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. <i>Journal of the American Academy of Dermatology</i>	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. <i>Journal of the Indian Medical Association</i>	No relevant outcomes reported
Biyun, C. The clinical observation of treating acne vulgaris with "xiao cuo fang". 2004. <i>Zhong yao cai = Zhongyaocai [Journal of Chinese medicinal materials]</i>	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. <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
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. <i>Archives of Dermatology</i>	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. <i>Dermatologica</i>	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. <i>Acta Dermato-Venereologica</i>	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. <i>British Journal of Dermatology</i>	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. <i>Scandinavian Journal of Infectious Diseases</i>	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. <i>Acta Dermato-Venereologica</i>	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS,



Reference	Reason for exclusion
	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. Medicina cutanea ibero-latino-americana	Not in English language

Reference	Reason for exclusion
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
Callender, V. D. Fitzpatrick skin types and clindamycin phosphate	No relevant data reported -

Reference	Reason for exclusion
1.2%/benzoyl peroxide gel: Efficacy and tolerability of treatment in moderate to severe acne. 2012a. Journal of Drugs in Dermatology	post hoc analysis reporting results for people receiving clindamycin 2.1%/BPO 2.5% gel
Cambazard, F. Clinical efficacy of Velac, a new tretinoin and clindamycin phosphate gel in acne vulgaris. 1998. Journal of the European Academy of Dermatology & Venereology	No relevant study design - non-systematic review of tretinoin treatment
Cannizzaro, M. V. D., A., Garofalo, V., Del Duca, E., Bianchi, L. Reducing the oral Isotretinoin skin side effects: Efficacy of 8% omega-ceramides, hydrophilic sugars, 5% niacinamide cream Compound in acne patients. 2018. Giornale Italiano di Dermatologia e Venereologia	Not in English language
Cao, J., Yang, G., Wang, Y., Liu, J. Acupoint Stimulation for Acne: A Systematic Review of Randomized Controlled Trials. 2013. Med Acupunct. 2013	No relevant intervention - systematic review about acupoint stimulation techniques used to treat acne
Cao, J., Yang, G., Wang, Y., Ping Liu, J., Smith, C.A., Luo, H., Liu. Y. Complementary therapies for acne vulgaris. 2015. Cochrane Database Syst Rev	Not relevant intervention - systematic review about complementary and alternative medicine for acne
Cao, T. T., E. S., Chan, Y. H., Yosipovitch, G., Tey, H. L. Anti-pruritic efficacies of doxycycline and erythromycin in the treatment of acne vulgaris: a randomized single-blinded pilot study. 2018. Indian journal of dermatology, venereology and leprology	No relevant study design - not RCT
Carlborg, L. Cyproterone acetate versus Levonorgestrel combined with ethinyl estradiol in the treatment of acne. Results of a multicenter study. 1986. Acta Obstetrica et Gynecologica Scandinavica	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Carlborg, L. Cyproterone acetate versus levonorgestrel combined with ethinylestradiol in the treatment of acne. Results of a multicenter study. 1987. Contraception fertilitate sexualite	Duplicate record
Carmina, E. L., R. A. A comparison of the relative efficacy of antiandrogens for the treatment of acne in hyperandrogenic women. 2002. Clinical Endocrinology	Duplicate record
Caron, D. S., V., Clucas, A., Verschoore, M. Skin tolerance of adapalene 0.1% gel in combination with other topical antiacne treatments. 1997a. Journal of the American Academy of Dermatology	No relevant study population - participants did not have acne
Caron, D. S., V., Kerrouche, N., Clucas, A. Split-face comparison of adapalene 0.1% gel and tretinoin 0.025% gel in acne patients. 1997b. Journal of the American Academy of Dermatology	No relevant outcomes reported
Cavicchini, S. C., R. Long-term treatment of acne with 20% azelaic acid cream. 1989. Acta Dermato-Venereologica, Supplement	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Cestone, E. M., A., Zanoletti, V., Zanardi, A., Mantegazza, R., Dossena, M. Acne RA-1,2, a novel UV-selective face cream for patients with acne: Efficacy and tolerability results of a randomized, placebo-controlled clinical study. 2017. Journal of Cosmetic Dermatology	Efficacy outcomes reported in figures only

Reference	Reason for exclusion
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, Cho Treatment of facial acne papules and pustules in Korean patients using an intense pulsed light device equipped with a 530- to 750-nm filter. 2007. Dermatologic Surgery	Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments
Chantalat, J., Liu, J. C. Six-week safety and efficacy evaluation of a synergistic microgel complex versus 10% benzoyl peroxide in the treatment of mild to moderate acne. Abstract P101. American Academy of Dermatology 64th Annual Meeting March 3-7, 2006. 2006. NA	No relevant article type - conference abstract
Charoenvisal, C. T., Y. Effects on acne of two oral contraceptives containing desogestrel and cyproterone acetate. 1996. International Journal of Fertility and Menopausal Studies	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Chi, C. I. Effects of Salvia miltiorrhiza extract on the improvement and prognosis of acne vulgaris. 2016. <a href="http://www.who.int/trialsearch/trial2.aspx?Trialid=chictr-iir-16010104">http://www.who.int/trialsearch/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 topical nadifloxacin and benzoyl peroxide versus clindamycin and	No relevant intervention - intervention & class not

Reference	Reason for exclusion
benzoyl peroxide in acne vulgaris: A randomized controlled trial. 2011. Indian Journal of Pharmacology	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 (Ainol) 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 (Ainol) 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 - Adapalene with or without Eucerin moisturizer
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
Colver, G. B. M., P. S.,Dawber, R. P.Cyproterone acetate and two	No relevant study



Reference	Reason for exclusion
doses of oestrogen in female acne; a double-blind comparison. 1988. British Journal of Dermatology	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 Tying 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 on acne, sebum excretion rate and skin surface lipid composition.	No relevant article type - letter to editor

Reference	Reason for exclusion
1972. British Journal of Dermatology	
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 Dermatology	No relevant data reported - pharmacokinetic study

Reference	Reason for exclusion
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., Kumtorrut, 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
Degreef, H. V. B., G. Double-blind evaluation of a miconazole -	Duplicate record



Reference	Reason for exclusion
benzoyl peroxide combination for the topical treatment of acne vulgaris. 1982a. Dermatologica	
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
DeVillez, R. L. Clinical comparison of the safety and efficacy of Brevoxyl gel and Benzamycin gel. 1992. Drug Investigation	No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Dhawan, S. S. Comparison of 2 clindamycin 1%-benzoyl peroxide 5% topical gels used once daily in the management of acne vulgaris. 2009. Cutis; cutaneous medicine for the practitioner	No relevant comparison - clindamycin/BPO topical gel with the hydrating excipients dimethicone and glycerin vs without hydrating excipients
Dieben Th, O. M. V., L., Theeuwes, A., Coelingh Bennink, H. J. T. The effects of CTR-24, a biphasic oral contraceptive combination, compared to Diane-35 in women with acne. 1994. Contraception	No relevant study population - insufficient details about types of lesions to determine severity of participants
Divers, L. S. A new preparation for the topical treatment of acne vulgaris. Report of a year's study. 1966. Journal of the College of General Practitioners	No relevant study design - not RCT
Do Nascimento, L. V. G., A. C. M., Magalhaes, G. M., De Faria, F. A., Guerra, R. M., Almeida, F. D. C. Single-blind and comparative clinical study of the efficacy and safety of benzoyl peroxide 4% gel	No relevant study population - sample includes people with mild

Reference	Reason for exclusion
(BID) and adapalene 0.1% Gel (QD) in the treatment of acne vulgaris for 11 weeks. 2003. Journal of Dermatological Treatment	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 microspheres 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 - aqueous-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-severe acne and study is not relevant for PCOS,

Reference	Reason for exclusion
	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 has low skin irritation potential even when applied immediately after	No relevant comparison - compares adapalene 0.1% gel application immediately

Reference	Reason for exclusion
washing. 1998a. British Journal of Dermatology, Supplement	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. Journal of Drugs in Dermatology	No relevant data reported - subgroup analysis of Thiboutot 2008
Eichenfield, L. F. S., J. L., Guenin, E., Harris, S., Bhatt, V. Novel tretinoin	No relevant data reported -

Reference	Reason for exclusion
0.05% lotion for the once-daily treatment of moderate-to-severe acne vulgaris in a preadolescent population. 2019. <i>Pediatric Dermatology</i>	post hoc analysis of Tying 2018
Eichenfield, L. F. T., D., Shalita, A., Swinyert, L., Tanghetti, E., Tschen, E., Parr, L. A. A three-step acne system containing solubilized benzoyl peroxide versus benzoyl peroxide/clindamycin in pediatric patients with acne. 2009a. <i>Journal of clinical and aesthetic dermatology</i>	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. <i>Pediatric 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
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. <i>Journal of Clinical and Aesthetic Dermatology</i>	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. <i>Dermatologic Therapy</i>	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. <i>Journal of the American Academy of Dermatology</i>	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. <i>Dermatologic Surgery</i>	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. <i>Lasers in Medical Science</i>	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. <i>Cutis</i>	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. <i>Cutis</i>	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 peroxide/clindamycin topical gel in acne vulgaris. (erratum appears in <i>Cutis</i> 2001 Mar;67(3): 257). 2001a. <i>Cutis; cutaneous medicine for the</i>	Duplicate record



Reference	Reason for exclusion
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 - reports data from 3 trials. No relevant population - sample includes people with mild to severe acne in first 2 trials, and insufficient details about types of lesions to determine severity of participants in one trial and study is not relevant for PCOS, maintenance or refractory treatments
ElRefaei, A. M. A. S., H. A., Sorour, N. E. Salicylic-mandelic acid versus glycolic acid peels in Egyptian patients with acne vulgaris. 2015. Journal of the Egyptian women's dermatologic society	No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Enshaieh, The efficacy of 5% topical tea tree oil gel in mild to moderate acne vulgaris: a randomized, double-blind placebo-controlled study. 2007. NA	No relevant intervention - tea tree oil gel
Ereaux, L. P. A new lotion for the treatment of acne vulgaris. 1965. Canadian Medical Association journal	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Ergin, S. E., C., Baysal, V., Yayli, G. An acne study focused on erythromycin: Benzoyl peroxide alone or with topical erythromycin against Propionibacterium acnes in acne vulgaris. 2001. Gazi Medical Journal	Outcomes reported in figures only
Erkkola, R. H., E., Luikku, J., Lumme, R., Mannikko, H., Aydinlik, S. Ovulation inhibitors containing cyproterone acetate or desogestrel in the treatment of hyperandrogenic symptoms. 1990. Acta Obstetrica 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 mg/g clindamycin and 30 mg/g benzoyl peroxide in comparison with the approved preparation DUACÁ, Á® 10 mg/g + 30 mg/g Gel and the	No relevant study design - not RCT

Reference	Reason for exclusion
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>	
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., Nilforoushzadeh, M. A. Efficacy of intense pulsed light combined with topical erythromycin solution 2% versus topical erythromycin solution 2% alone in the treatment of persistent facial erythematous acne macules. 2015. Journal of isfahan medical school	No relevant study design - not RCT
Faghihi, G. R., M., Abtahi-Naeini, B., Nilforoushzadeh, M. A. The efficacy of 5% dapsone gel plus oral isotretinoin versus oral isotretinoin alone in acne vulgaris: A randomized double-blind study. 2014. Advanced Biomedical Research	Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments
Faghihi, G. V., A., Asilian, A., Radan, M. R., Esteki, H., Elahidoost, M. Comparative efficacy of filtered blue light (emitted from sunlight) and topical erythromycin solution in acne treatment: A randomized controlled clinical trial. 2011. Journal of Pakistan Association of	No relevant study design - not RCT (split face study but same treatments always applied to left &

Reference	Reason for exclusion
Dermatologists	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 (Aiol) 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 new cosmetic functional ingredient to reduce blemishes and Propionibacterium acnes in acne prone skin. 2012. Journal of	No relevant intervention - Disodium Tetramethylhexadecenyl succinyl Cysteine



Reference	Reason for exclusion
Cosmetic Dermatology	
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 venerologia	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
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	Not in English language

Reference	Reason for exclusion
treatment of acne vulgaris: a multicenter, randomized study. 2003. Chinese journal of dermatology	
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, maintenance or refractory treatments

Reference	Reason for exclusion
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. ZHAUTKR	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
Goldman, M. P. B., S. M. A single-center study of aminolevulinic acid and 417 NM photodynamic therapy in the treatment of moderate to	No relevant study design - not RCT

Reference	Reason for exclusion
severe acne vulgaris. 2003. Journal of Drugs in Dermatology: JDD	
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 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	No relevant data reported - reports pooled results from 2 trials combined

Reference	Reason for exclusion
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. <i>The Journal of Clinical &amp; Aesthetic Dermatology</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
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. <i>Journal of drugs in dermatology</i>	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. <i>British Journal of Dermatology</i>	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. <i>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
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. <i>Journal of Investigative Dermatology</i>	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. <i>Cutis</i>	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. <i>Annales de dermatologie ET de venerologie</i>	Not English language
Grosshans, E. M., R., Mascaro, J. M., Torras, H., Meynadier, J., Alirezai, M., Finlay, A. Y., Soto, P., Poncet, M., Verschoore, M., Clucas, A. Evaluation of clinical efficacy and safety of adapalene 0.1% gel versus tretinoin 0.025% gel in the treatment of acne vulgaris, with particular reference to the onset of action and impact on quality of life. 1998. <i>British Journal of Dermatology, Supplement</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
Grove, G. Z., C., Gwazdauskas, J. Tolerability and irritation potential of four topical acne regimens in healthy subjects. 2013. <i>Journal of Drugs in Dermatology</i>	No relevant study population - participants did not have acne



Reference	Reason for exclusion
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 Boulle, K.A 4% erythromycin and zinc combination (Zineryt) versus 2% erythromycin (Eryderm) in acne vulgaris: A randomized, double-blind comparative study. 1989a. British Journal of Dermatology	No relevant data reported - study does not report number of participants randomised or who completed in each group
Habbema, L. K., B.,Menke, H. E.,Doornweerd, S.,De, B. K.A 4% erythromycin and zinc combination (Zineryt (R)) versus 2% erythromycin (Eryderm (R)) in acne vulgaris: a randomized, double-blind comparative study. 1989b. British journal of dermatology	Duplicate record
Haedersdal, M. T.-B., K.,Wiegell, S. R.,Wulf, H. C.Long-pulsed dye laser versus long-pulsed dye laser-assisted photodynamic therapy for acne vulgaris: A randomized controlled trial. 2008. Journal of the American Academy of Dermatology	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Hajheydari, Z. S., M.,Morteza-Semnani, K.,Soltani, A.Effect of Aloe vera topical gel combined with tretinoin in treatment of mild and moderate acne vulgaris: A randomized, double-blind, prospective trial. 2014. Journal of Dermatological Treatment	No relevant intervention - aloe vera
Halbe, H. W. d. M., N. R.,Bahamondes, L.,Petraacco, 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.	No relevant study population - participants did not have acne

Reference	Reason for exclusion
The European journal of contraception & reproductive health care : the official journal of the European Society of Contraception	
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 (Aiol 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 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	No relevant data reported - post hoc subgroup analysis by gender of Pariser 2014
Hashimoto, Y. S., Y.,Mizuno, Y.,Hasegawa, T.,Matsuba, S.,Ikeda,	No relevant study design -

Reference	Reason for exclusion
S., Monma, T., Ueda, S. Salicylic acid peels in polyethylene glycol vehicle for the treatment of comedogenic acne in Japanese patients. 2008. <i>Dermatologic Surgery</i>	not RCT
Hatwal, A. B., R. P., Agrawal, J. K., Singh, G., Bajpai, H. S. Spironolactone and cimetidine in treatment of acne. 1988. <i>Acta Dermato-Venereologica</i>	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. <i>Journal of Dermatology</i>	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. <i>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
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. <i>Journal of Dermatology</i>	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. <i>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
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. <i>Journal of Dermatology</i>	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. <i>JAMA Dermatology</i> .	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. <i>Dermatologische Monatsschrift</i>	Not in English language
Hellgren, L. V., J. Topical erythromycin for acne vulgaris. 1980. <i>Dermatologica</i>	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. <i>SKINmed</i>	No relevant study population - participants did not have acne
Hersle, K. G., H. Minocycline in acne vulgaris: a double blind study. 1976. <i>Current Therapeutic Research - Clinical and Experimental</i>	No relevant study population - insufficient information to determine acne severity and study is not relevant for PCOS, 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



Reference	Reason for exclusion
Hjorth, N. G., K. Azelaic acid for the treatment of acne. A clinical comparison with oral tetracycline. 1989. Acta Dermato-Venereologica. Supplementum	No relevant data - insufficient data reported
Hjorth, N. S., D., Dela, K. Topical anhydrous aluminum chloride formulation in the treatment of acne vulgaris: A double-blind study. 1985. Cutis	No relevant study population - insufficient information reported about acne severity and study is not relevant for PCOS, maintenance or refractory treatments
Hjorth, N. S., H., Thomsen, K., Dela, K. Meclosorb(), a new topical antibiotic agent in the treatment of acne vulgaris: A double-blind clinical study. 1984. Acta Dermato-Venereologica	No relevant study population - insufficient information reported about acne severity and study is not relevant for PCOS, maintenance or refractory treatments
Ho, S. G. Y., C. K., Chan, N. P., Shek, S. Y., Kono, T., Chan, H. H. A retrospective analysis of the management of acne post-inflammatory hyperpigmentation using topical treatment, laser treatment, or combination topical and laser treatments in oriental patients. 2011. Lasers in Surgery & Medicine	Duplicate record
Hong, S. B. L., M. H. Topical aminolevulinic acid-photodynamic therapy for the treatment of acne vulgaris. 2005. Photodermatology, Photoimmunology & Photomedicine	No relevant study design - not RCT
Hongcharu, W. T., C. R., Chang, Y., Aghassi, D., Suthamjariya, K., Anderson, R. R. Topical ALA-photodynamic therapy for the treatment of acne vulgaris. 2000. Journal of Investigative Dermatology	Efficacy outcomes reported in figures only
Honorato, J. A., J. R., Sandoval, C. A., Quintanilla, E. Double-blind, randomized and controlled clinical trial on the efficacy of topical clindamycin in the treatment of acne. 1988. Revista de farmacologia clinica y experimental	Not in English language
Horfelt, C. S., B., Larko, O., Faergemann, J., Wennberg, A. M. Photodynamic therapy for acne vulgaris: a pilot study of the dose-response and mechanism of action. 2007. Acta Dermato-Venereologica	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Hubbell, C. G. H., E. R., Rist, T., White Jr, J. W. Efficacy of minocycline compared with tetracycline in treatment of acne vulgaris. 1982. Archives of Dermatology	No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Hughes, B. R. A double blind evaluation of topical isotretinoin, benzoyl peroxide and placebo in patients with acne. Abstract. 1989. British journal of dermatology	No relevant article type - conference abstract
Hurwitz, S. The combined effect of vitamin A acid and benzoyl peroxide in the treatment of acne. 1976. Cutis	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
	treatments
Ianos, S. N., D., Branisteanu, D. E., Popescu, M., Calina, D., Zlatian, O., Docea, A. O., Marinas, M. C., Iordache, A. M., Mitru, 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-sifilograficas	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. Newcjidj	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 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	Reported outcomes relevant for the network

Reference	Reason for exclusion
treatment of acne. 2016. Journal of research in medical sciences	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
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-	No relevant intervention -

Reference	Reason for exclusion
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	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 Publication:	No relevant article type - conference abstract
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	No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-

Reference	Reason for exclusion
Thailand	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-Convaexius, 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 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	No relevant study design - the first phase was not

Reference	Reason for exclusion
Topically Applied Selected Cutibacterium acnes Strains over Five Weeks in Patients with Acne Vulgaris: An Open-label, Pilot Study. 2019. Acta Dermato-Venereologica	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 randomized, multicenter, investigator-blinded, controlled study. 2008. Journal of Dermatological Science	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. N., T.,Katsuramaki, T.Open-label, randomized,	No relevant study



Reference	Reason for exclusion
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	population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Kawashima, M. S., S., Furukawa, F., Matsunaga, K., Akamatsu, H., Igarashi, A., Tsunemi, Y., Hayashi, N., Yamamoto, Y., Nagare, T., et al., Twelve-week, multicenter, placebo-controlled, randomized, double-blind, parallel-group, comparative phase II/III study of benzoyl peroxide gel in patients with acne vulgaris: a secondary publication. 2017b. Journal of dermatology	No relevant study population - includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Kawashima, M. Y., M., Parish, C. Clindamycin 1%/benzoyl peroxide 3% gel, a new topical combination product, is effective in Japanese patients with acne vulgaris. 2013. Journal of Investigative Dermatology	No relevant article type - conference abstract
Kayhan, S. S., I., Saracoglu, Z. N., Aksu, A. E. K., Tozun, M. Comparison of safety and efficacy of oral azithromycin-topical adapalene versus oral doxycycline-topical adapalene in the treatment of acne vulgaris and determination of the effects of these treatments on patients' quality of life. 2012. Turkderm deri hastaliklari ve frengi arsivi	Not in English language
Kaymak, Y. T., E., Taner, Y. Comparison of depression, anxiety and life quality in acne vulgaris patients who were treated with either isotretinoin or topical agents. 2009. International Journal of Dermatology	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Kelidari, H. R. S., M., Hajheydari, Z., Akbari, J., Morteza-Semnani, K., Akhtari, J., Valizadeh, H., Asare-Addo, K., Nokhodchi, A. Spironolactone loaded nanostructured lipid carrier gel for effective treatment of mild and moderate acne vulgaris: A randomized, double-blind, prospective trial. 2016. Colloids and Surfaces B: Biointerfaces	No relevant intervention - intervention & class not available in the UK
Kelly, S. D., E., 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
Kerscher, M. R., T., Bayrhammer, J., Schramm, G. Effects of an oral contraceptive containing chlormadinone and ethinylestradiol on acne-prone skin of women of different age groups: an open-label, single-centre, phase IV study. 2008. Clinical Drug Investigation	No relevant study 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 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	No relevant intervention - acupuncture

Reference	Reason for exclusion
ovary syndrome: A single-blinded clinical trial. 2019. Clinical Cancer Investigation Journal	
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 the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments



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

Reference	Reason for exclusion
ethinylestradiol oral contraceptive administered in 24/4 regimen in the treatment of acne vulgaris: a randomized, double-blind, placebo-controlled trial. 2008. Contraception	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
Kuflik, E. G. Benzoyl peroxide gel in acne therapy. 1976. Cutis	No relevant study design - not RCT
Kurokawa, I. A., H., Nishijima, S., Asada, Y., Kawabata, S. Clinical and bacteriologic evaluation of OPC-7251 in patients with acne: A double-blind group comparison study versus cream base. 1991. Journal of the American Academy of Dermatology	Duplicate record

Reference	Reason for exclusion
Kus, S. Y., D.,Aytug, A.Comparison of efficacy of azithromycin vs. doxycycline in the treatment of acne vulgaris. 2005. Clinical and Experimental Dermatology	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Kwon, H. H. C., S. C.,Jung, J. Y.,Bae, Y. I.,Park, G. H.Comparison of novel dual mode vs conventional single pass of a 1450-nm diode laser in the treatment of acne vulgaris for Korean patients: A 20-week prospective, randomized, split-face study. 2018. Journal of Cosmetic Dermatology	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Kwon, H. H. L., J. B.,Yoon, J. Y.,Park, S. Y.,Ryu, H. H.,Park, B. M.,Kim, Y. J.,Suh, D. H.The clinical and histological effect of home-use, combination blue-red LED phototherapy for mild-to-moderate acne vulgaris in Korean patients: A double-blind, randomized controlled trial. 2013. British Journal of Dermatology	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Kwon, H. H. M., K. R.,Park, S. Y.,Yoon, J. Y.,Suh, D. H.,Lee, J. B.Daylight photodynamic therapy with 1.5% 3-butenyl 5-aminolevulinate gel as a convenient, effective and safe therapy in acne treatment: A double-blind randomized controlled trial. 2016. Journal of Dermatology	No relevant study population - sample includes mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Kwon, H. H. P., H. Y.,Choi, S. C.,Bae, Y.,Jung, J. Y.,Park, G. H.Novel device-based acne treatments: comparison of a 1450-nm diode laser and microneedling radiofrequency on mild-to-moderate acne vulgaris and seborrhoea in Korean patients through a 20-week prospective, randomized, split-face study. 2018. Journal of the European Academy of Dermatology and Venereology	Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments
Kwon, H. H. P., S. Y.,Yoon, J. Y.,Min, S.,Suh, D. H.Do tutorials on application method enhance adapalene-benzoyl peroxide combination gel tolerability in the treatment of acne?. 2015. Journal of Dermatology	No relevant comparator - compares efficacy of adding training module to intervention
Kwon, I. K., S.,Lee, D.Photodynamic therapy using chlorophyll-a in the treatment of acne vulgaris: A randomized, single-blind, split-face study. 2014. Journal of Investigative Dermatology	No relevant article type - conference abstract
Kwon,Comparison of clinical and histological effects between lactobacillus-fermented Chamaecyparis obtusa and tea tree oil for the treatment of acne: an eight-week double-blind randomized controlled split-face study. 2014. NA	No relevant intervention and comparison - Lactobacillus-fermented Chamaecyparis obtusa vs tea tree oil
L. Ghoshal, S. Banerjee, S. Ghosh, D. Gangopadhyay and S. JanaComparative evaluation of effectiveness of adapalene and azithromycin, alone or in combination, in acne vulgaris. 2007. Indian 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

Reference	Reason for exclusion
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 discharge between two carbon arc rods for the treatment of acne compared to 1% topical clindamycin. 2010. Lasers in Surgery and Medicine	No relevant article type - 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	No relevant article type - conference abstract

Reference	Reason for exclusion
doxycycline in acne vulgaris. 2019b. Journal of the American Academy of Dermatology	
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 were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments



Reference	Reason for exclusion
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
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

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

Reference	Reason for exclusion
effectiveness of herbal extracts vs 2.5% benzoyl peroxide in the treatment of mild to moderate acne vulgaris. 2019. Journal of Cosmetic Dermatology.	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-aminolevulinic acid photodynamic therapy for the treatment of severe adolescent acne in Chinese patients. 2015. Journal of Dermatology	No relevant study design - 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



Reference	Reason for exclusion
	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-severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Mandekou-Lefaki, I. D., F., Teknetzis, A., Euthimiadou,	No relevant study design -

Reference	Reason for exclusion
R.,Karakatsanis, G.Low-dose schema of isotretinoin in acne vulgaris. 2003. International Journal of Clinical Pharmacology Research	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.,Sundstrom-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 Isotrexin™ versus Benzamycin in the topical treatment of mild to moderate acne vulgaris. 2002b. Journal of Dermatological Treatment	Duplicate record
Marcinkiewicz, J. W.-P., A.,Walczewska, M.,Lipko-Godlewska, S.,Jachowicz, R.,Maciejewska, A.,Bialecka, A.,Kasprowicz, A.Topical taurine bromamine, a new candidate in the treatment of moderate inflammatory acne vulgaris: a pilot study. 2008. European Journal of Dermatology	No relevant intervention - taurine 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.,Rotsztein, H.Comparative study of the effect of 50% pyruvic and 30% salicylic peels on the skin lipid film in patients with acne vulgaris. 2014. Journal of Cosmetic Dermatology	No relevant data reported - sebum secretion study
Mareledwane, N. G.A randomized, open-label, comparative study of oral doxycycline 100 mg vs. 5% topical benzoyl peroxide in the treatment of mild to moderate acne vulgaris. 2006. International Journal of Dermatology	No relevant data reported

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

Reference	Reason for exclusion
	maintenance or refractory treatments
Mehran, G., Sepasgozar, S., Rohaninasab, M., Goodarzi, A., Ghassemi, M., Fotooei, M., Behrangi, E. Comparison between the therapeutic effect of microneedling versus tretinoin in patients with comedonal acne: A randomized clinical trial. 2019. Iranian Journal of Dermatology	No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments
Meigel, W. G., H., Wokalek, H. Oral treatment of acne conglobata with isotretinoin. Results of the German Multicenter Study. 1983. Der hautarzt; zeitschrift fur dermatologie, venerologie, und verwandte gebiete	Not in English language
Merkviladze, N. G., T., Tushurashvili, P., Ekaladze, E., Jojua, N. The efficacy of topical drugs in treatment of noninflammatory acne vulgaris. 2010. Georgian Medical News	No relevant study design - not RCT
Merritt, B. B., C. N., Morrell, D. S. Use of isotretinoin for acne vulgaris. 2009. Pediatric Annals	No relevant study design - not RCT
Michaelsson, G. J., L., Ljunghall, K. A double-blind study of the effect of zinc and oxytetracycline in acne vulgaris. 1977a. British Journal of Dermatology	No relevant comparison - compares oral zinc and tetracyclines
Michaelsson, G. J., L., Vahlquist, A. Effects of oral zinc and vitamin A in acne. 1977b. Archives of Dermatology	No relevant comparison - compares oral zinc sulfate alone and in combination with vitamin A
Michaelsson, G. Oral zinc in acne. 1980. Acta dermato-venereologica	No relevant article type - non-systematic review
Mikhael, E. M. M., M. Y. Evaluation of the effect of topical atorvastatin solution for the treatment of papulopustular acne. 2013. International Journal of Current Pharmaceutical Research	No relevant study population - insufficient information to determine severity of acne and study is not relevant for PCOS, maintenance or refractory treatments
Milikan, L. E. A double-blind study of Betadine skin cleanser in acne vulgaris. 1976. Cutis	No relevant intervention - Betadine skin cleanser
Miller, J. A. J., H. S. T 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
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	No relevant study design -

Reference	Reason for exclusion
applied erythromycin and tretinoin. 1978. Acta Dermato-Venereologica	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 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.	Reported outcomes relevant for the network meta-analysis but not in enough detail to include in

Reference	Reason for exclusion
Journal of Research in Medical SciencesJ	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 topical combination of retinaldehyde 0.1% with erythromycin 4% in acne vulgaris. 1999. Clinical and Experimental Dermatology	No relevant intervention - topical retinaldehyde gel
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	No relevant data reported



Reference	Reason for exclusion
multicentre-randomized trial. 2011. International Journal of Cosmetic Science	
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. Comparison 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 post-procedure 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
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



Reference	Reason for exclusion
Nielsen, P. G. Treatment of female acne vulgaris with a cream containing the antiandrogen canrenone. 1983. <i>Dermatologica</i>	No relevant article type - letter to editor
Nighland, M. G., R. Tretinoin microsphere gel in facial acne vulgaris: a meta-analysis. 2008. <i>Journal of drugs in dermatology : JDD</i>	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. <i>Indian journal of dermatology, venereology and leprology</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
Niren, N. M. T., H. M. The Nicamide Improvement in Clinical Outcomes Study (NICOS): results of an 8-week trial. 2006. <i>Cutis</i>	No relevant study design - not RCT
Nitzan, Y. B. C., A. D. Zinc in skin pathology and care. 2006. <i>Journal of Dermatological Treatment</i>	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. <i>Journal of Cosmetic Dermatology</i>	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. <i>Dermatologica</i>	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. <i>Clinical &amp; Experimental Dermatology</i>	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. <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 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. <i>Cutis; cutaneous medicine for the practitioner</i>	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. <i>Journal of the European Academy of Dermatology &amp; Venereology</i>	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 inflammatory acne. 2009. <i>Dermatologic Surgery</i>	Split face study - but randomised treatments not compared directly in the 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. <i>Journal of Dermatological Treatment</i>	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
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 acne vulgaris. 1973. Texas Medicine	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
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 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

Reference	Reason for exclusion
	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. <i>Cutis</i>	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. <i>Journal of drugs in dermatology</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
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. <i>Journal of drugs in dermatology : JDD</i>	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. <i>Journal of Clinical and Aesthetic Dermatology</i>	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. <i>Journal of Cosmetic and Laser Therapy</i>	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. <i>International Journal of Dermatology</i>	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., Dominguez-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. <i>Dermatologia revista mexicana</i>	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. 2001a. <i>Drug Development and Industrial Pharmacy</i>	No relevant study design - not RCT
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. <i>AAPS PharmSciTech</i>	No relevant study design - not RCT
Paver, K. Complications from combined oral tetracycline and oral	Not obtainable

Reference	Reason for exclusion
corticoid therapy in acne vulgaris. 1970. Medical Journal of Australia	
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 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	Antibiotic dosages lower than BNF values



Reference	Reason for exclusion
and Applied Skin Physiology	
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. <i>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
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. <i>Indian Journal of Dermatology, Venereology &amp; Leprology</i>	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. <i>Chron dermatol</i>	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. <i>Journal der Deutschen Dermatologischen Gesellschaft</i>	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. <i>European Journal of Dermatology</i>	No relevant intervention - nadifloxacin 1% cream not available in the UK
Plewig, G. Dermabrasion for nodular cutaneous elastosis with cysts and comedones. 1972. <i>Archives of Dermatology</i>	Not obtainable
Plewig, G. Vitamin A acid. Topical treatment in acne vulgaris. 1969. <i>Pennsylvania Medicine</i>	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. <i>Cutis</i>	Not obtainable
Podfigurna, 2019 Clinical, hormonal and metabolic parameters in women with PCOS with different combined oral contraceptives (containing chlormadinone acetate versus drospirenone). 2019. <i>Journal of Endocrinological Investigation</i>	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. <i>Clinical, Cosmetic and Investigational Dermatology</i>	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. <i>British Journal of Dermatology</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

Reference	Reason for exclusion
	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 of acne vulgaris. 2006. J Dermatolog Treat	No relevant intervention - 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	No relevant study population - sample



Reference	Reason for exclusion
of acne vulgaris in adolescents. 2008. <i>Cutis</i>	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. <i>Acta Dermato-Venereologica. Supplementum</i>	No relevant study design - not RCT
Raouf, 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, double-blind, vehicle-controlled study. 2019. <i>Journal of Clinical and Aesthetic Dermatology</i>	No relevant article type - conference abstract
Raouf, 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. <i>Journal of the American Academy of Dermatology</i> .	No relevant intervention - FMX101 4% topical minocycline foam not available in the UK
Raouf, 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. <i>Journal of the American Academy of Dermatology</i>	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. <i>Cutis; cutaneous medicine for the practitioner</i>	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. <i>Journal of Cutaneous &amp; Aesthetic Surgery</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
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. <i>Clinical and experimental dermatology</i>	No relevant 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. <i>Clinical and Experimental Dermatology</i>	Duplicate record
Rebillo, T. H., J. L. Skin surface glycerol levels in acne vulgaris. 1978. <i>Journal of Investigative Dermatology</i>	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. <i>Journal of the American Academy of Dermatology</i>	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 5%--a double-blind study. 1985. <i>Zeitschrift fur hautkrankheiten</i>	Not in English language
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	No relevant intervention - topical Tyrothricin; No relevant study population -

Reference	Reason for exclusion
Papulopustulosa: A Randomized Controlled Clinical Trial. 2016. Skin Pharmacology and Physiology	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 acid: a pilot study. 2006. Dermatologic Surgery	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
Romiti, N. Use of the aromatic retinoid Ro-11-1430 for acne therapy. 1978. <i>Pharmatherapeutica</i>	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. <i>International Journal of Cosmetic Science</i>	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. <i>Photodermatology, Photoimmunology &amp; Photomedicine</i>	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. <i>Journal of Cosmetic and Laser Therapy</i>	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. <i>Journal of Drugs in Dermatology: JDDJ Drugs Dermatol</i>	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. <i>Journal of Drugs in Dermatology</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
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. <i>British Journal of Clinical Practice</i>	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. <i>REV. FR. GYNECOL. OBSTET.</i>	Not in English language
Sampaio, S. A. P. M., H. C. B., Freitas, T. H. P., Totoli, Sasm, Martins, M. A. A multicenter trial comparing the efficacy and tolerance of isotretinoin gel 0.05% and tretinoin cream 0.05% in the treatment of acne vulgaris. 1997. <i>Revista brasileira de medicina</i>	Not in English language
Sanam, M. Z., O. Desogestrel+ethinylestradiol versus levonorgestrel +ethinylestradiol: Which one has better affect on acne, hirsutism, and weight change. 2011. <i>Saudi Medical Journal</i>	No relevant study population - participants did not have acne
Santos, M. A. B., V. G., Santos, G. Effectiveness of photodynamic	No relevant study

Reference	Reason for exclusion
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	population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Santos-Caetano, J. P. C., M. R.A Randomized Controlled Tolerability Study to Evaluate Reformulated Benzoyl Peroxide Face Washes for Acne Vulgaris. 2019. Journal of drugs in dermatology : JDD	No relevant intervention - intervention is washed off the face
Sardesai Vkambli, V.Comparison of efficacy of topical clindamycin and nicotinamide combination with plain clindamycin for the treatment of acne vulgaris and acne resistant to topical antibiotics. 2003. Indian journal of dermatology, venereology and leprology	No relevant study design - not RCT
Sauer, G. C.Prospective study on the safety of long-term tetracycline therapy for acne. 1981. Cutis	No relevant study design - not RCT
Sayyafan, M. S. R., M.,Salmanpour, R.Clinical assessment of topical erythromycin gel with and without zinc acetate for treating mild-to-moderate acne vulgaris. 2019. Journal of Dermatological Treatment.	No relevant study design - not RCT
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% medicalgrade kanuka honey and 10% glycerine to standard antibacterial soap wash with antibacterial soap wash alone
Sen, A. K., S.,Chatterjee, R. N.,Sarkar, M.,Bhattacharjee, S.,Ram, A.	No relevant article type -

Reference	Reason for exclusion
K.Acomparativestudyof efficacy and safetyoftopical clindamycingelversus combination of clindamycingeland benzoylperoxidecreamin patients ofmildtomoderateacnevulgaris. 2013. Indian Journal of Pharmacology	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 roxithromylin 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 relevantintervention - facial cleanser; 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
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, maintenance and refractory treatments
Shie Morteza, M., Hayati, Z., Namazi, N., Abdollahimajd, F. Efficacy	No relevant intervention -

Reference	Reason for exclusion
and safety of oral silymarin in comparison with oral doxycycline and their combination therapy in the treatment of acne vulgaris. 2019. Dermatologic Therapy	silymarin
Shin JU, Lee SH, Jung JY, Lee JH.A split-face comparison of a fractional microneedle radiofrequency device and fractional carbon dioxide laser therapy in acne patients.. 2012. J Cosmet Laser Ther	Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments
Shwetha, H. G., A.A comparative study of efficacy and safety of combination of topical 1% clindamycin and 0.1% adapalene with 1% clindamycin and 2.5% benzoyl peroxide in mild to moderate acne in a tertiary care hospital. 2013. Indian Journal of Pharmacology	No relevant article type - conference abstract
Sidgiddi, 2019Efficacy of oral isotretinoin in combination with desloratadine in the treatment of common vulgaris acne in Vietnamese Patients. 2019. Open Access Macedonian Journal of Medical Sciences	Duplication of Van 2019
Sidgiddi, S., Allenby, K., Okumu, F., Gautam, A.Bioavailability, Pharmacokinetics, and Transepidermal Water Loss of Short Contact Tazarotene Lotion 0.1% Versus Tazarotene (Tazorac<sup> R</sup> Cream 0.1. 2019. The Journal of Clinical & Aesthetic DermatologyJ Clin Aesthet Dermatol	The paper reports 2 studies, both do not meet inclusion criteria: the first one describes a non-relevant comparison and the second one does not reported severity of acne
Simpson, N. B. B., P. E.,Forster, R. A.,Cunliffe, W. J.The effect of topically applied progesterone on sebum excretion rate. 1979. British Journal of Dermatology	No relevant data reported - 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 refractory treatments
Smith, E. B. P., R. S.,McCabe, J. M.,Becker, L. E.Benzoyl peroxide lotion (20%) in acne. 1980a. Cutis	Duplicate record



Reference	Reason for exclusion
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 study of adapalene-benzoyl peroxide combination gel in the treatment of acne. 2009. Cutis	No relevant data reported - a repeat publication of Gollnick 2009
Stein Gold, L., Werschler, W. P., & Mohawk, J. A. Adapalene/benzoyl	No relevant data reported -

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

Reference	Reason for exclusion
formulation (Zimade Muhasa) on acne vulgaris: A singleblind, randomized, controlled clinical trial. 2014. Journal of Pakistan Association of Dermatologists	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., Dhain, 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 Dermatology J	Systematic review - references were checked for relevance
Tanghetti, E. A., Werschler, W. P., Lain, T., Guenin, E., Martin, G., Pillai, R. Tazarotene 0.045% Lotion for Once-Daily Treatment of Moderate-to-Severe Acne Vulgaris: Results from Two Phase 3 Trials. 2020. Journal of drugs in dermatology : JDD	Not obtainable
Tanghetti, E. D., S., Green, L., Del Rosso, J., Draelos, Z., Leyden, J., Shalita, A., Glaser, D. A., Grimes, P., Webster, G., Barnett, P., Le Gall, N. Randomized comparison of the safety and efficacy of tazarotene 0.1% cream and adapalene 0.3% gel in the treatment of patients with at least moderate facial acne vulgaris. 2010. Journal of Drugs in Dermatology	No relevant data reported - subgroup analysis by sex of Draelos 2007
Tanghetti, E. H., J. C., Oefelein, M. G. The efficacy and tolerability of dapsone 5% gel in female vs male patients with facial acne vulgaris: Gender as a clinically relevant outcome variable. 2012. Journal of Drugs in Dermatology	No relevant data reported - subgroup analysis by sex of Draelos 2007
Tanghetti, E. H., J., Baldwin, H., Kircik, L., Bai, Z., Alvandi, N. Once-Daily Topical Dapsone Gel, 7.5%: Effective for Acne Vulgaris Regardless of Baseline Lesion Count, With Superior Efficacy in Females. 2018. Journal of drugs in dermatology : JDD	No relevant data reported - post hoc analysis by sex of Stein Gold 2016
Tangjaturonrusamee, C. R., P., Ditre, C. M. Comparison of pneumatic broadband light plus adapalene gel 0.3% versus adapalene gel 0.3% monotherapy in the treatment of mild to moderate acne. 2016. Cutis	Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments

Reference	Reason for exclusion
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 - including PCOS, maintenance and

Reference	Reason for exclusion
	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. 2010. International Journal of Dermatology	No relevant intervention - topical nadifloxacin 1% cream not available in the UK



Reference	Reason for exclusion
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 13-cis retinoic acid (isotretinoin). 1983. Nederlands tijdschrift voor	Not in English language

Reference	Reason for exclusion
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
Verschoore, M. P., M., Czernielewski, J., Sorba, V., Clucas,	No relevant study



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

Reference	Reason for exclusion
2020. Journal of Cosmetic DermatologyJ	maintenance or refractory treatments
Waranuch, N. P., P.,Yakaew, S.,Nakyai, W.,Grandmottet, F.,Onlom, C.,Srivilai, J.,Viyoch, J.Antiacne and antiblotch activities of a formulated combination of Aloe barbadensis leaf powder, Garcinia mangostana peel extract, and Camellia sinensis leaf extract. 2019. Clinical, Cosmetic and Investigational Dermatology CCID	No relevant intervention - a combination of Aloe barbadensis leaf extract, Garcinia mangostana peel extract, and Camellia sinensis leaf extract
Warren, M. R., J.,Arbit, D.,Sevilla, C.,Flack, M.The effects on weight of a low-dose oral contraceptive in the treatment of women with moderate acne vulgaris. 2001. Fertility and sterility	No relevant article type - conference abstract
Webster, G. C., D. I.,Quiring, J.,Vogelson, C. T.,Slade, H. B.A combined analysis of 2 randomized clinical studies of tretinoin gel 0.05% for the treatment of acne. 2009. Cutis; cutaneous medicine for the practitioner	No relevant 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. Cutis; cutaneous medicine for the practitioner	Not obtainable
Webster, G. F.Safety and efficacy of Tretin-X compared with Retin-A in patients with mild-to-severe acne vulgaris. 2006. Skinmed	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Webster, G. R., P.,Gold, M. H.,Mraz, S.,Calvarese, B.,Chen, D.Efficacy and tolerability of a fixed combination of clindamycin phosphate (1.2%) and low concentration benzoyl peroxide (2.5%) aqueous gel in moderate or severe acne subpopulations. 2009. Journal of Drugs in Dermatology	No relevant data reported - 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. Cutis	No relevant data reported - reports quality of life outcomes
Weiss, J. G., L. S.,Leoni, M.,Rueda, M. J.,Liu, H.,Tanghetti, E.Customized single-agent therapy management of severe inflammatory acne: A randomized, double-blind, parallel-Group, controlled study of a new treatment - Adapalene 0.3%-benzoyl peroxide 2.5% gel. 2015. Journal of Drugs in Dermatology	No relevant data reported - subgroup analysis of people with severe acne participating in Stein Gold 2016
Weiss, J. S. G., L.,Leoni, M.,Rueda, M. J.,Liu, H.,Tanghetti, E.Customized Single-agent Therapy Management of Severe Inflammatory Acne: A Randomized, Double-blind, Parallel-group, Controlled Study of a New Treatment--Adapalene 0.3%-Benzoyl Peroxide 2.5% Gel. 2015. Journal of Drugs in Dermatology: JDD	Duplicate record
Weissmann, A. W., A.,Plewig, G.Reduction of bacterial skin flora during oral treatment of severe acne with 13-cis retinoic acid. 1981. Archives of Dermatological Research	No relevant study design - not RCT
Weltert, Y. C., S.,Gibaud, C.,Courau, S.,Pechenart, P.,Sirvent, A.,Girard, F.Double-blind clinical assessment of the efficacy of a 4% nicotinamide gel (Exfoliac NC Gel) versus a 4% erythromycin gel in the treatment of moderate acne with a predominant inflammatory component. [French, English]. 2004. Nouvelles Dermatologiques	Not in English language
Wen, X. L., Y.,Hamblin, M. R.Photodynamic therapy in dermatology beyond non-melanoma cancer: An update. 2017. Photodiagnosis and	Duplicate record

Reference	Reason for exclusion
Photodynamic Therapy	
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% lotion for the treatment of acne vulgaris: a randomized, double-blind, controlled trial. 2010. NA	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
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 includes 11% people with 11% acne
Yoon, J. H. P., E. J.,Kwon, I. H.,Kim, C. W.,Lee, G. S.,Hann, S.	No relevant intervention -

Reference	Reason for exclusion
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	laser treatment for acne scarring
Yoon, J. Y. K., H. H.,Min, S. U.,Thiboutot, D. M.,Suh, D. H.Epigallocatechin-3-gallate improves acne in humans by modulating intracellular molecular targets and inhibiting P. acnes. 2013. Journal of Investigative Dermatology	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Yu, Z. S., J.,Lew-Kaya, D.,Walker, P.,Yu, D.,Tang-Liu, D. D.Pharmacokinetics of tazarotene cream 0.1% after a single dose and after repeat topical applications at clinical or exaggerated application rates in patients with acne vulgaris or photodamaged skin. 2003. Clinical Pharmacokinetics	No relevant study population - sample includes people with acne or photodamage - relevant outcomes not reported separately
Zachariae, H.Topical vitamin-A-acid in acne. 1980. Acta dermato-venereologica	No relevant study design - not RCT
Zander, E. W., S.Treatment of acne vulgaris with salicylic acid pads. 1992. Clinical Therapeutics	Duplicate record
Zarate, A. M., V. B.,Greenblatt, R. B.Effect of an antiandrogen, 17-alpha-methyl-B-nortestosterone, on acne and hirsutism. 1966. Journal of Clinical Endocrinology & Metabolism	No relevant study design - not RCT
Zeichner, J. A. H., M.,Linkner, R. V.,Wong, V.Efficacy and safety of tretinoin 0.025%/clindamycin phosphate 1.2% gel in combination with benzoyl peroxide 6% cleansing cloths for the treatment of facial acne vulgaris. 2013. Journal of Drugs in Dermatology	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Zeichner, J. A. P., R. V.,Haddican, M.,Wong, V.Efficacy and safety of a ceramide containing moisturizer followed by fixed-dose clindamycin phosphate 1.2%/benzoyl peroxide 2.5% gel in the morning in combination with a ceramide containing moisturizer followed by tretinoin 0.05% gel in the evening for the treatment of facial acne vulgaris. 2012. Journal of Drugs in Dermatology: JDD	No relevant study design - not RCT
Zeichner, J. A., Harper, J. C., Roberts, W. E., Guenin, E., Bhatt, V., Pillai, R.Novel tretinoin 0.05% lotion for the once-daily treatment of moderate-to-severe acne vulgaris: assessment of safety and tolerability in subgroups. 2019. Journal of Clinical and Aesthetic Dermatology	Not obtainable
Zeichner, J. A.The Efficacy and Tolerability of a Fixed Combination Clindamycin (1.2%) and Benzoyl Peroxide (3.75%) Aqueous Gel in Adult Female Patients with Facial Acne Vulgaris. 2015. The Journal of Clinical & Aesthetic Dermatology	Reports post hoc analysis of $\geq 25$ 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 were not relevant for pairwise comparisons - including PCOS, maintenance and



Reference	Reason for exclusion
	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

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

2

### 3 Economic studies

Study	Reason for exclusion
Dizon MP, Schmidt TH, Shinkai K. High-value, cost-conscious evaluation for PCOS: which tests	Intervention outside scope (laboratory testing for PCOS in women with acne)



Study	Reason for exclusion
should be routinely ordered in acne patients? Cutis. 2016; 98(1):11-3.	

1

## 1 Appendix L – Research recommendations

### 2 Research recommendations for review question: What is an effective 3 management option for people with acne vulgaris and polycystic ovary 4 syndrome (PCOS)?

#### 5 Research question

6 What is the most effective first-line treatment option for any severity of acne vulgaris for  
7 people with polycystic ovary syndrome?

#### 8 Why this is important

9 Polycystic ovary syndrome (PCOS) is associated with increased androgen concentrations  
10 that may cause or exacerbate acne vulgaris. Using hormonal methods to suppress ovarian  
11 androgen production, and block the effect of androgens on the skin, is a therapeutically  
12 plausible treatment. However, in people without PCOS standard first-line treatment for acne  
13 rather than hormonal treatments should be used. There is no evidence in women with PCOS  
14 about the optimal initial treatment for acne vulgaris. Further research would provide greater  
15 clarity about the role of hormonal manipulation in the treatment of acne in PCOS.

#### 16 Table 11: Research recommendation rationale

Research question	What is the most effective first-line treatment option for any severity of acne vulgaris for people with polycystic ovary syndrome?
<b>Why is this needed</b>	
<b>Importance to 'patients' or the population</b>	Hormonal manipulation has beneficial effects for menstrual regulation in people with PCOS. However, there are no trials that show that it is beneficial for the treatment of acne. In people without PCOS the first-line treatment should not be hormonal manipulation but one of the recommended acne treatments. The common use of hormonal manipulation in PCOS might impact on those with PCOS getting effective acne treatment. It is not known if the effect of hormonal manipulation is equal to recommended acne treatments PCOS or if the effect of hormonal manipulation is additive to recommended treatments. This is an area that required further research.
<b>Relevance to NICE guidance</b>	There was insufficient evidence to recommend any treatment for acne vulgaris in people with PCOS. The recommendations of effective treatments are assumed to be the same as people without PCOS, although these studies were not conducted in people with PCOS. The discussion of management in PCOS was theoretical rather than evidence-based. As hormonal manipulation has a different mechanism of action from recommended acne treatments, it is not known if it would be additive in treatment efficacy. There are no studies that have addressed the adjunct use of hormonal manipulation. Further research would clarify the role for hormonal manipulation in the

<b>Research question</b>	<b>What is the most effective first-line treatment option for any severity of acne vulgaris for people with polycystic ovary syndrome?</b>
	management of acne vulgaris in PCOS.
<b>Relevance to the NHS</b>	Acne vulgaris is the most common skin condition affecting the young adults of reproductive age in Western Industrialised countries. PCOS is the commonest endocrine condition affecting 7-8% and it is associated with increased androgens that can promote acne. Efficient first-line interventions could reduce return appointments and referral to secondary care.
<b>National priorities</b>	This links to the improvement young people's mental health and sits within precision medicine and the personalisation of care. Improving the mental health of young people is a national priority. Rates of depression, poor body image and reduced self-esteem are increasing in young people. Those with acne and PCOS have increased risk of poor mental health and reduced self-esteem. This aligns with a need to understand support required for young people with acne vulgaris.
<b>Current evidence base</b>	The evidence base identified in the review was very small and did not have and place trials and it was therefore difficult to base recommendations on limited evidence.
<b>Equality</b>	PCOS is more common in the South Asian population and in those with obesity.
<b>Feasibility</b>	The use of hormonal manipulation is common in PCOS and the use of oral contraception is common in young people. Not all young people wish oral contraception. Contraception is important to consider in studies that have some interventions that are contraceptive.
<b>Other comments</b>	PCOS is defined by at least two out of three criteria: a polycystic ovary morphology on pelvic ultrasound scan, biochemical and/or clinical evidence of hyperandrogenism, and anovulation. As acne would be considered clinical evidence of hyperandrogenism infrequent menses in the presence of acne would be sufficient to make a presumed diagnosis of PCOS without a pelvic scan.

1 PCOS: *polycystic ovary syndrome*

2 **Table 12: Research recommendation modified PICO table**

<b>Criterion</b>	<b>Explanation</b>
<b>Population</b>	People with PCOS and acne vulgaris who are not using hormonal contraception or other acne treatments.
<b>Intervention</b>	Non-inferiority comparison of co-cyprindiol with a standard first-line acne treatment
<b>Comparator</b>	<ul style="list-style-type: none"> <li>• Defined standard first-line acne treatment</li> <li>• Placebo first-line acne treatment</li> <li>• Placebo first-line acne treatment + co-cyprindiol</li> </ul>

Criterion	Explanation
	<ul style="list-style-type: none"> <li>• First line standard acne treatment + co-cyprindiol</li> </ul>
<b>Outcomes</b>	<ul style="list-style-type: none"> <li>• Change in severity of acne using a validated scoring system.</li> </ul>
<b>Study design</b>	Randomised controlled trial
<b>Timeframe</b>	<ul style="list-style-type: none"> <li>• 3-6 months (intervention)</li> <li>• 6 month (follow-up)</li> </ul>
<b>Additional information</b>	As hormonal manipulation is associated with a regular cycle there are challenges blinding the subjects to hormonal treatment and as such using a placebo of co-cyprindiol is not possible. With four arms the trial will be large and the no treatment arm might be challenging, although unlike those without PCOS there is no placebo controlled comparison with hormonal treatment.

1 PCOS: polycystic ovary syndrome