National Institute for Health and Care Excellence

Draft for consultation

Acne vulgaris: management

[F2] Management options for moderate to severe acne – pairwise comparisons

NICE guideline number tbc

Evidence review underpinning recommendations 1.5.1, 1.5.2 and 1.5.4 to 1.5.12, 1.5.15 to 1.5.21 as well as 1.5.24 and 3 research recommendations in the NICE guideline (see evidence review F1 for the committee's discussion of the evidence)

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Draft for consultation

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

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Summary of review questions covered in this report

A single review protocol and literature search was used to identify randomised trials of treatments for acne vulgaris to address 9 review questions covering topical or oral pharmacological treatments and physical treatments, shown below. Outcomes were prioritised for either pairwise or network meta-analysis (NMA) and the evidence was divided according to the severity of acne into mild to moderate and moderate to severe categories. NMA was employed to assess comparative efficacy, acceptability and tolerability of treatments, which are outcomes commonly reported in the literature for the majority of treatments. Pairwise meta-analysis was used to synthesise outcomes for which evidence was more limited across treatments or was treatment-specific. The evidence was then summarised in four separate reviews covering the treatment of:

- mild to moderate acne (NMA)
- mild to moderate acne (pairwise meta-analysis)
- moderate to severe acne (NMA)
- moderate to severe acne (pairwise meta-analysis)

This evidence review contains information on the pairwise meta-analyses conducted to assess treatments for people with moderate to severe acne vulgaris. NMA has been the main method of analysis to inform these questions (see evidence review F1). This review reports the associated pairwise meta-analysis for outcomes not covered in the NMA. Information on the NMAs and pairwise meta-analyses conducted to assess treatments for people with mild to moderate acne vulgaris are contained in the evidence reports E1 and E2, respectively.

1. What is the effectiveness of topical treatments individually or in combination in the treatment of acne vulgaris, for example:

- benzoyl peroxide
- antibiotics
- antiseptics
- retinoids and retinoid-like agents (for example, tretinoin, adapalene)
- azelaic acid
- nicotinamide
- combination of antibiotic and retinoid or retinoid-like agent
- combination of benzoyl peroxide and retinoid or retinoid-like agent
- combination of antibiotic and benzoyl peroxide?

2. What is the effectiveness of oral antibiotic treatments individually or in combination in the treatment of acne vulgaris, for example:

- tetracyclines (for example oxytetracycline, doxycycline, minocycline, tetracycline, lymecycline)
- macrolide antibiotics (for example, erythromycin and azithromycin)
- trimethoprim?

3. What is the effectiveness of an oral antibiotic with a topical agent compared to oral antibiotic alone in the treatment of acne vulgaris?

4. What is the optimal duration of antibiotic treatments (topical and systemic) for acne vulgaris?

5. What is the effectiveness of hormonal contraceptives in the treatment of acne vulgaris?

6. What is the effectiveness of spironolactone in the treatment of acne vulgaris?

7. What is the effectiveness of metformin in the treatment of acne vulgaris?

8. What is the effectiveness of oral isotretinoin in the treatment of acne vulgaris?

9. What is the effectiveness of physical treatments for acne vulgaris, for example
- comedone extraction
- chemical peels (for example, glycolic acid, lactic acid, salicylic acid)
- intralesional steroids
- light devices (for example, intense pulsed light, photopneumatic therapy and photodynamic therapy)?

Management options for moderate to severe acne – pairwise comparisons

Review question

What is the effectiveness and acceptability of interventions for the treatment of moderate to severe acne vulgaris (side effects and participant reported improvement)?

Introduction

Moderate to severe acne encompasses a spectrum of inflammatory lesions including nodules and cysts, and in the most severe form, acne conglobata and acne fulminans. Individuals within this group may require differing treatments compared to those with mild to moderate acne. There is also potentially a higher risk of scarring within this group. This evidence review therefore aims to find the most effective treatment option for people with moderate to severe acne.

Summary of the protocol

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

Table 1: Summary of the protocol

Population	People with acne vulgaris, with moderate to severe symptom severity
Intervention	Interventions will be categorised into the following classes (and, if relevant, subclasses): ➢ **TOPICAL TREATMENTS** **Abrasive/cleaning agents** • Aluminium oxide [own class] **Anthelmintics** • Cysticide (praziquantel) [own class] • Class of avermectins: ivermectin **Antibacterials** • Class of triclocarban and triclozan **Antibiotics** • Class of sulphones (dapsone) • Fucidic acid (sodium fusidate) [own class] • Class of lincosamides (for example clindamycin) • Class of macrolides (for example clarithromycin, erythromycin with zinc acetate dihydrate) • Class of nitroimidazoles (metronidazole) • Class of carboxylic acids (mupirocin) • Class of penicillins ○ Sub-class of natural (for example almecillin) ○ Sub-class of aminopenicillins (for example ampicillin) ○ Sub-class of β-lactamase-resistant (for example methicillin) ○ Sub-class of carboxypenicillins (for example ticarcillin) ○ Sub-class of ureidopenicillins (for example azlocillin) ○ Sub-class of other penicillins (mecillinam, pivmecillinam hydrochloride) • Class of pleuromutilins (for example retapamulin) **Antiseptics** • Benzoyl peroxide (trade: Acnecide, Brevoxyl, Panoxyl) [own class] • Chlorhexidine gluconate (trade: Acnemed, Cepton) or digluconate [own class] **Dicarboxylic acids** • Azelaic acid [own class]

Vitamin B3

- Nicotinamide (niacinamide) [own class]

Retinoids or retinoid-like agents

- Class of retinoids or retinoid-like agents (adapalene, isotretinoin, retinol, tazarotene, tretinoin)

Combined interventions

- Benzoyl peroxide & potassium hydroxyguinoline sulfate [own class]
- Class of benzoyl peroxide & retinoid (benzoyl peroxide + adapalene)
- Class of benzoyl peroxide & lincosamide (benzoyl peroxide + clindamycin)
- Class of lincosamides & retinoid (clindamycin + tretinoin)
- Class of macrolides & retinoid (erythomycin + retinoid) [topical]
- Germolene (phenol 1.2% + chlorhexidine diculconate [own class]

➢ **ORAL ANTIBIOTICS**

- Class of carbapenems (for example imipenem, meropenem)
- Class of carbapenems with cilastatin (imipenem with cilastatin)
- Class of carbapenems with b lactamase inhibitor (meropenem with vaborbactam)
- Class of cephamycins/cephalosporins
  - Sub-class of 1st-generation (for example cefadroxil)
  - Sub-class of 2nd-generation (for example cefaclore)
  - Sub-class of 3rd-generation (for example cefdinir)
  - Sub-class of 4th-generation (for example cefozopran)
  - Sub-class of 5th-generation (for example ceftolozane)
- Class of cephamycins/cephalosporins with β-lactamase inhibitor (for example ceftraroline or ceftazidime with avibactam, cefoperazone with sulbactam, ceftolozane with tazobactam)
- Class of sulphones (dapsone)
- Fucidic acid (sodium fusidate) [own class]
- Class of lincosamides (for example clindamycin)
- Class of macrolides (for example clarithromycin, erythromycin)
- Class of monobactams (aztreonam)
- Class of monobactams with β-lactamase inhibitor (aztreonam with avibactam)
- Class of penicillins
  - Sub-class of natural (for example almecillin)
  - Sub-class of aminopenicillins (for example ampicillin)
  - Sub-class of β-lactamase-resistant (for example methicillin)
  - Sub-class of carboxypenicillins (for example ticarcillin)
  - Sub-class of ureidopenicillins (for example azlocillin)
  - Sub-class of other penicillins (mecillinam, pivmecillinam hydrochloride)
- Class of penicillin with β-lactamase inhibitor (for example co-amoxiclav [amoxicillin with clavulanic acid], piperacillin with tazobactam, ticaricillin with clavulanic acid, sultamicillin [ampicillin with sulbactam])
- Class of penicillin with flucloxacilin (co-fluampicil [ampicillin + flucloxacilin])
- Class of pleuromutilins (for example retapamulin)
- Class of quinolones
  - Sub-class of 1st-generation (for example rosoxacin)
  - Sub-class of 2nd-generation (for example ofloxacin)
  - Sub-class of 3rd-generation (for example temafloxacin)
  - Sub-class of 4th-generation (for example sitafloxacin)
- Class of tetracyclines (for example doxycycline, oxytetracycline)
- Trimethoprim [own class]
- Co-trimoxazole (trimethoprim-sulfamethoxazole; TMP-SMX) [own class]

➢ **TOPICAL TREATMENTS COMBINED WITH ORAL ANTIBIOTICS**

➢ **ORAL HORMONAL CONTRACEPTIVES AND HORMONE-MODIFYING AGENTS**

- Co-cyprindiol (ethinylestradiol + cyproterone acetate) [own class of combined oral contraceptive]

- Class of combined oral contraceptives
  - Sub-class of 2nd generation (oestrogen, for example ethinylestradiol or estradiol or mestranol combined with levonorgestrel or norethisterone)
  - Sub-class of 3rd generation (oestrogen, for example ethinylestradiol combined with desogestrel or gestodene or norgestimate)
  - Sub-class of 4th generation (oestrogen, for example ethinylestradiol or estradiol combined with dienogest or drospirenone or nomegestrol acetate)

Monophasic and phasic combined oral contraceptives containing the same hormones will be analysed as separate interventions within their sub-class.

- Class of progestogen-only oral contraceptives
  - Sub-class of 1st generation (for example medroxyprogesterone acetate)
  - Sub-class of 2nd generation (for example levonorgestrel, norethisterone/ norethindrone)
  - Sub-class of 3rd generation (for example desogestrel, norgestimate, gestodene)
  - Sub-class of 4th generation (for example dienogest, drospirenone, nomegestrol acetate)
- Class of selective aldosterone receptor antagonists (for example spironolactone alone or combined with furosemide or hydroflumethiazide [co-flumactone], eplerenone, canrenone)
- Class of 5α-reductase inhibitors (dutasteride, finasteride, tamsulosin with dutasteride)
- Class of other non-steroidal anti-androgens (for example abiraterone acetate, apalutamide, bicalutamide, cyproterone acetate, clormadinone acetate, enzalutamide, flutamide)
- Metformin [own class]

➢ **ORAL ISOTRETINOIN**

- Class of oral retinoid and total cumulative dose ≥ 120mg/kg (single course)
  - Sub-class of daily dosing (dose ≥0.5mg/kg/day or <0.5mg/kg/day)
  - Sub-class of alternate day dosing (dose ≥0.5mg/kg/day or <0.5mg/kg/day)
  - Sub-class of less frequent or other dosing (dose ≥0.5mg/kg/day or <0.5mg/kg/day)
- Class of oral retinoid and total cumulative dose < 120mg/kg (single course)
  - Sub-class of daily dosing (dose ≥0.5mg/kg/day or <0.5mg/kg/day)
  - Sub-class of alternate day dosing (dose ≥0.5mg/kg/day or <0.5mg/kg/day)
  - Sub-class of less frequent or other dosing (dose ≥0.5mg/kg/day or <0.5mg/kg/day)

➢ **PHYSICAL TREATMENTS**

- Class of chemical peels
  - Sub-class of superficial peels
  - Sub-class of moderate peels
  - Sub-class of deep peels

  for example amino fruit acid, glycolic acid, Jessner's peel, lactic acid, salicylic acid, trichloroacetic acid [TCA]; these will be categorised into different sub-classes as reported in the included studies, according to the concentration of their active ingredient and treatment duration.
- Comedone extraction [own class]
- Class of photothermal therapy (for example fractional erbium glass laser)
- Class of photochemical therapy (for example blue or red light and their combination)
- Class of photochemical and photothermal therapy (for example potassium titanyul phosphate laser, Intense Pulsed Light [IPL], Pulsed Dye Laser)
- Class of photodynamic therapy (for example 5-aminolevuliniv acid [ALA], liposomal methylene blue gel, methylaminolevulinate [MAL])
- Smoothbeam™ laser [own class]

	• Photopneumatic therapy (for example intense pulsed light + vacuum) • Radiofrequency (for example fractional microneedling, bipolar)
Comparison	• No treatment • Waiting list • Pill placebo • Other active intervention • Sham physical treatment

Outcomes	**Critical**
	• Prevention of scarring
	
	Important
	• Specific short-term side effects for comparisons of treatments within the same class or those that involve an inactive arm
	  ○ topical non-retinoid treatments:
	  – skin irritation
	  ○ topical retinoid treatments:
	  – skin irritation
	  – light sensitivity
	  ○ oral antibiotics:
	  – skin irritation
	  – gastrointestinal
	  – thrush/candidiasis
	  ○ oral hormonal contraceptives and hormone-modifying agents:
	  – breast tenderness
	  – neurological
	  – sexual dysfunction
	  – hepatobillary effects
	  – mood disturbance
	  – breakthrough bleeding
	  ○ oral isotretinoin:
	  – mucosal / cutaneous changes (for example new chelitis)
	  – change in mood
	  – new psychiatric diagnosis
	  – suicidality
	  ○ physical treatments:
	  – chemical peels:
	  - skin irritation
	  - skin redness (erythema)
	  - changes in pigmentation
	  - infection of treated area
	  – energy based treatments (light/laser):
	  - skin irritation
	  - skin redness (erythema)
	  - changes in pigmentation
	• Participant reported improvement

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

Methods and process

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

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

Clinical evidence

Included studies

Overall 49 studies were included in this pairwise review. These are divided into the following categories of interventions: topical non-retinoids and retinoids, oral antibiotics, topical and oral combinations, oral hormonal contraceptives and hormone-modifying agents, oral isotretinoin and physical treatments.

Topical non-retinoids and retinoids

Six parallel group design RCTs (Dobson 1980, Jones 1981, Jones 2002, Kuhlman 1986, Sklar 1996, Thiboutot 2002) reported on side effects of skin irritation of topical non-retinoid treatment in people with moderate to severe acne vulgaris. All these studies were conducted in the USA.

Twenty parallel group design RCTs (Braathen 1984, Degreef 1982b, Dhawan 2013, Dogra 2020, Feldman 2013 (study 301/Trial 1), Feldman 2013 (study 302/Trial 2), Gratton 1982, Lassus 1984, Pariser 2005, Pariser 2014, Richter 1998a, Schmidt 2011, Stein Gold 2008, Stein Gold 2016, Tanghetti 2006, Tanghetti 2011, Tanghetti 2019, Thiboutot 2008, Tyring 2018, Zouboulis 2000) reported on side effects and participant reported improvement of topical retinoid treatments or combinations thereof, in people with moderate to severe acne vulgaris.

Fifteen studies reported on skin irritation (Dhawan 2013, Dogra 2020, Feldman 2013 (study 301/Trial 1), Feldman 2013 (study 302/Trial 2), Lassus 1984, Pariser 2005, Richter 1998a, Schmidt 2011, Stein Gold 2008, Stein Gold 2016, Tanghetti 2006, Tanghetti 2011, Tanghetti 2019, Tyring 2018, Zouboulis 2000).

Two studies reported on light sensitivity (Feldman 2013 (study 301/Trial 1), Feldman 2013 (study 302/Trial 2)).

Seven studies reported on participant reported improvement of acne vulgaris (Braathen 1984, Degreef 1982, Gratton 1982, Pariser 2014, Stein Gold 2016, Tanghetti 2019, Thiboutot 2008).

Ten studies were conducted in the USA (Dhawan 2013, Pariser 2005, Pariser 2014, Schmidt 2011, Stein Gold 2008, Stein Gold 2016, Tanghetti 2006, Tanghetti 2011, Tanghetti 2019, Thiboutot 2008), 2 studies in North America (Feldman 2013), 1 study in Belgium (Degreef 1982b), Canada (Gratton 1982), Norway (Braathen 1984), Finland (Lassus 1984) and India (Dogra 2020); 2 studies were a collaboration studies from Europe (Richter 1998a, Zouboulis 2000) and 1 study was an international collaboration from Europe/North America (Tyring 2018).

There were also 2 split-face RCTs (Dreno 2017, Dreno 2018, both conducted in France/Canada) reporting prevention of scarring which is a critical but seldom reported outcome, therefore they were included in this pairwise report.

Oral antibiotics

Eight parallel group design RCTs (Bossuyt 2003, Braathen 1984, Dubertret 2003, Khanna 1993, Leyden 2018, Moore 2018 (SC1401/Trial 1), Moore 2018 (SC1402/Trial 2), Stewart 2006) reported on side effects and participant reported improvement of oral antibiotics or combinations thereof, in people with moderate to severe acne vulgaris.

One study reported on skin irritation (Stewart 2006); 6 studies reported on gastrointestinal side effects (Bossuyt 2003, Dubertret 2003, Leyden 2018, Moore 2018 (SC1401/Trial 1), Moore 2018 (SC1402/Trial 2), Stewart 2006); 3 studies reported on thrush/candiasis (Khanna 1993, Moore 2018 (SC1401/Trial 1), Moore 2018 (SC1402/Trial 2)); and 2 studies reported on participant reported improvement of acne vulgaris (Bossuyt 2003, Braathen 1984).

Three studies were conducted in the USA (Leyden 2018, Moore 2018, Stewart 2006), 1 study in India (Khanna 1993) and Norway (Braathen 1984); 2 studies were collaboration studies from Europe (Bossuyt 2003, Dubertret 2003).

Topical and oral combination interventions

Two parallel group design RCTs (Del Rosso 2007, Parsad 2001) reported on side effects of topical and oral combination interventions, in people with moderate to severe acne vulgaris.

Both studies reported on skin irritation (Del Rosso 2007, Parsad 2001) and 1 study reported on gastrointestinal side effects (Del Rosso 2007).

One study was conducted in the USA (Del Rosso 2007) and 1 study in India (Parsad 2001).

Oral hormonal contraceptives and hormone-modifying agents

Two parallel group design RCTs (Fugere 1990, Miller 1986b) reported on side effects of oral hormonal contraceptives or combinations thereof, in people with moderate to severe acne vulgaris.

One study reported on breast tenderness, sexual dysfunction, and mood disturbance (Miller 1986b); and 2 studies reported on breakthrough bleeding (Fugere 1990, Miller 1986b).

One study was conducted in Canada (Fugere 1990) and 1 study in the UK (Miller 1986b).

Oral isotretinoin

Five parallel group design RCTs (Akman 2007, Dhaked 2016, Faghihi 2017, Kapadia 2005, Strauss 1984a) reported on side effects of oral isotretinoin in varying dosages, in people with moderate to severe acne vulgaris.

All five studies reported on mucosal/cutaneous changes (Akman 2007, Dhaked 2016, Faghili 2017, Kapadia 2005, Strauss 1984a); 1 study reported on new psychiatric diagnoses (Faghili 2017); 1 study reported on change in mood (Kapadia 2005); and 3 studies reported on relapse (Akman 2007, Dhaked 2016, Strauss 1984a).

One study was conducted in India (Dhaked 2016), Iran (Faghili 2017), Pakistan (Kapadia 2005), Turkey (Akman 2007) and the USA (Strauss 1984a).

Physical treatments

Five parallel group design RCTs (Chen 2015, Kim 2017, Mei 2013, Pariser 2016, Sami 2008) reported on side effects and participant reported improvement of physical treatments or combinations thereof, in people with moderate to severe acne vulgaris.

Two studies reported on skin irritation (Chen 2015, Mei 2013); 3 studies reported on skin redness (Kim 2017, Mei 2013, Pariser 2016); 3 studies reported on changes in pigmentation (Kim 2017, Pariser 2016, Sami 2008); and 2 studies reported on participant reported improvement of acne vulgaris (Kim 2017, Sami 2008).

Two studies were conducted in China (Chen 2015, Mei 2013), 1 study in Egypt (Sami 2008), Korea (Kim 2017) and the USA (Pariser 2016).

The included studies are summarised in Table 2. See the literature search strategy in appendix B and study selection flow chart in appendix C.

Excluded studies

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

Summary of included studies

Summaries of the studies that were included in this review are presented in Table 2. The evidence table in appendix D lists all relevant outcomes including those extracted for the network meta-analysis (clinician reported improvement, discontinuation due for any reason and discontinuation due to adverse events). Only the relevant outcomes for the pairwise analysis are listed below.

Table 2: Summary of included studies

Study	Population	Interventions	Outcomes
Akman 2007 **Country**: Turkey **Study type**: RCT	N=66 **Sex**: mixed **Number randomised: arm 1**: n=22 **Number randomised: arm 2**: n=22 **Number randomised: arm 3**: n=22 **Inclusion details**: Participants with FDA global grade 2 (moderate) and 3 to 4 (severe) acne who had not responded to conventional antibiotic treatment or had rapidly relapsed after conventional treatment. Participants receiving any conventional treatments underwent an appropriate washout period before study treatment began.	**Intervention: arm 1**: ISO<120.Other=0.5 (first 10 days, every month) **Intervention: arm 2**: ISO<120.Other=0.5 (every day for month 1 then first 10 days of every month) **Intervention: arm 3**: ISO<120.Daily=0.5	• Mucosal or cutaneous changes • Relapse
Bossuyt 2003 **Country**: Europe **Study type**: RCT	N=134 **Sex**: mixed **Number randomised: arm 1**: n=66 **Number randomised: arm 2**: n=68 **Inclusion details**: Males or females aged between 12 and 30 years**.** Participants with at least 15 and at most 120 inflammatory facial lesions (papules,	**Intervention: arm 1**: LYME-oral 300mg **Intervention: arm 2**: MINO-oral 100mg	• GI side effects • Participant reported improvement

Study	Population	Interventions	Outcomes
	pustules, nodules) including at most 2 facial nodules (diameter >1 cm), a maximum of 60 non-inflammatory facial lesions (open and closed comedones) and an acne severity grade between 1 and 5 (Leeds grading scale)**.** Women of childbearing age were required to use contraception during the study and for 1 month after completing the trial. Women on oral contraceptives were to have been using the same method for 3 months prior to enrolment, or for at least 12 months for contraceptive pills constraining cyproterone acetate. Use of cosmetics was permitted during the course of the study, but contraceptives and cosmetics had to be listed as concomitant medication.		
Braathen 1984 **Country**: Norway **Study type**: RCT	N=87 **Sex**: mixed **Number randomised: arm 1**: na, n=29 completed **Number randomised: arm 2**: na, n=29 completed **Number randomised: arm 3**: na, n=29 completed **Inclusion details**: Participants with moderate to severe acne vulgaris.	**Intervention: arm 1**: CLIND-topical 1% + PLC-oral **Intervention: arm 2**: TETRA-oral 500mg bid + Vehicle **Intervention: arm 3**: PLC-oral + Vehicle	• Participant reported improvement
Chen 2015 **Country**: China **Study type**: RCT	N=50 **Sex**: mixed **Number randomised: arm 1**: n=25 **Number randomised: arm 2**: n=25 **Inclusion details**: Participants with moderate (acne with inflammatory papules and pustules) to severe (acne with inflammatory	**Intervention: arm 1**: 5ALA 5% photodynamic therapy **Intervention: arm 2**: Sham treatment	• Skin irritation

Study	Population	Interventions	Outcomes
	papules, nodules, cysts and scars) facial acne vulgaris.		
Degreef 1982b **Country**: Belgium **Study type**: RCT	N=105 **Sex**: mixed **Number randomised: arm 1**: n=52 **Number randomised: arm 2**: n=53 **Inclusion details**: Participants with moderate to severe facial acne.	**Intervention: arm 1**: BPO 5%/MICO 2% cream **Intervention: arm 2**: BPO 5% cream	• Participant reported improvement
Del Rosso 2007 **Country**: United States **Study type**: RCT	N=71 **Sex**: mixed **Number randomised: arm 1**: n=36 **Number randomised: arm 2**: n=35 **Inclusion details**: Participants aged 16 years of age or older**.** Acne vulgaris, truncal involvement on the back with or without chest involvement, truncal inflammatory acne severity graded as moderate or severe**.** Informed consent obtained**.** Undergone a washout period of at least 2 weeks for all previous topical acne treatments (including over-the-counter products), at least 4 weeks for systemic antibiotic treatment, and more than 6 months for oral isotretinoin.	**Intervention: arm 1**: BPO 9% cleanser + CLIND 1% foam + DOXY 100 mg **Intervention: arm 2**: BPO 9% cleanser + DOXY 100 mg	• Skin irritation • GI side effects
Dhaked 2016 **Country**: India **Study type**: RCT	N=240 **Sex**: mixed **Number randomised: arm 1**: n=120 **Number randomised: arm 2**: n=120 **Inclusion details**: Participants with moderate to severe acne vulgaris attending the outpatient clinic in the dermatology department.	**Intervention: arm 1**: ISO<120.Daily<0.5 **Intervention: arm 2**: ISO<120.Alt<0.5	• Mucosal or cutaneous changes • Relapse
Dhawan 2013 **Country**: United States	N=40 **Sex**: mixed **Number randomised:**	**Intervention: arm 1**: BPO 5%/CLIND 1.2% gel + TAZ 0.1% cream **Intervention: arm 2**:	• Skin irritation

Study	Population	Interventions	Outcomes
Study type: RCT	**arm 1**: n=20 **Number randomised: arm 2**: n=20 **Inclusion details**: Males and females aged 12 to 45 years**.** Participants with grade 3 or higher according to the investigator static global assessment (ISGA) (3=moderate; 4=severe; 5=very severe)**.**20 to 50 papules and pustules (inflammatory lesions), 30 to 100 open and closed comedones (non-inflammatory lesions), 1 or fewer small nodular lesions, no facial cystic lesions.	BPO 2.5%/CLIND 1.2% gel + TAZ 0.1% cream	
Dobson 1980 **Country**: United States **Study type**: RCT	N=253 **Sex**: mixed **Number randomised: arm 1**: n=127 **Number randomised: arm 2**: n=126 **Inclusion details**: Participants with moderate to severe acne vulgaris of the face (at least 10 papules or pustules, one or more comedones, and not more than 5 nodulocystic lesions)**.** No concurrent illness and not receiving any anti-acne treatment (topical or systemic) for at least 2 weeks prior to study entry.	**Intervention: arm 1**: ERYTH 1.5% solution **Intervention: arm 2**: Vehicle	• Skin irritation
Dogra 2020 **Country**: India **Study type**: RCT	N=750 **Sex**: mixed **Number randomised: arm 1**: n=300 **Number randomised: arm 2**: n=300 **Number randomised: arm 3**: n=150 **Inclusion details**: Participants aged >/=12 years. Facial acne (inflammatory lesion count [papules, pustules] count between >20 to <50; non-inflammatory lesion count [open or closed comedones]	**Intervention: arm 1**: Fixed dose tretinoin 0.04% (microsphere) + clindamycin 1.0% gel, o.d. **Intervention: arm 2**: Tretinoin gel 0.025%, o.d. **Intervention: arm 3**: Clindamycin gel 1.0%, o.d.	• Skin irritation

Study	Population	Interventions	Outcomes
	between >20 to <100, and nodules [inflammatory lesion 5mm in diameter] 2) and Investigator's Static Global Assessment (ISGA) score of 3 (moderate) or 4 (severe)		
Dreno 2017 **Country:** France/Canada **Study type:** split-face RCT	N=76 **Sex**: mixed **Number randomised: arm 1**: n=38 **Number randomised: arm 2**: n=38 **Inclusion details**: Male and female participants aged 18–35 years with moderate facial acne vulgaris with 20–40 inflammatory lesions (papules and pustules, excluding the nose), no more than 1 acne nodule and a minimum of 10 atrophic acne scars (larger than 1.5mm in diameter, smaller scars could not be accurately differentiated from other lesion types). Participants had no more than twice as many lesions on one half of the face than on the other half.	**Intervention: arm 1**: ADAP 0.1% gel + BPO 2.5% gel **Intervention: arm 2**: Vehicle	• Prevention of scarring
Dreno 2018 **Country:** France/Canada **Study type:** split-face RCT	N=134 **Sex**: mixed **Number randomised: arm 1**: n=67 **Number randomised: arm 2**: n=67 **Inclusion details**: Male or female participants aged 16–35 years with Fitzpatrick skin phototype I–IV and a clinical diagnosis of moderate or severe acne vulgaris on the face. Participants had an Investigator Global Assessment (IGA) score of 3 or 4 on both sides; >=25 inflammatory lesions (papules and pustules) with 10 or more on each side (excluding	**Intervention: arm 1**: ADAP 0.3% gel + BPO 2.5% gel **Intervention: arm 2**: Vehicle	• Prevention of scarring

Study	Population	Interventions	Outcomes
	the nose); up to two acne nodules >=1 cm for whole face; 10 or more atrophic acne scars >2 mm (for whole face excluding the nose); with an approximately symmetric number of inflammatory and non-inflammatory lesions, and atrophic acne scars on the whole face.		
Dubertret 2003 **Country**: Europe **Study type**: RCT	N=271 **Sex**: mixed **Number randomised: arm 1**: n=111 **Number randomised: arm 2**: n=107 **Number randomised: arm 3**: n=53 **Inclusion details**: Males and females aged between 16 and 40 years**.** Acne vulgaris with a minimum of 15 inflammatory facial lesions and a global severity of at least grade 3 on the Leeds Revised Acne Grading System.	**Intervention: arm 1**: LYME-oral 300mg od + PLC-oral **Intervention: arm 2**: LYME-oral 150mg bid **Intervention: arm 3**: PLC-oral bid	• GI side effects
Faghihi 2017 **Country**: Iran **Study type**: RCT	N=66 **Sex**: mixed **Number randomised: arm 1**: n=36 **Number randomised: arm 2**: n=30 **Inclusion details**: Males and females with moderate to severe acne vulgaris referred for treatment to Alzahra Medical and Training Centre, several clinical affiliated to Isfahan University of Medical Sciences and a privately-owned doctor's office**.** Consent to participate in the study**.** No sensitivity to retinoids**.** No pregnancy, not willing to become pregnant, and absence of hormonal disorders.	**Intervention: arm 1**: ISO<120.Daily<0.5 + PRED 0.25 mg wk 1 + AZITH 250 mg wks 1-2 **Intervention: arm 2**: ISO<120.Daily=0.5 + PRED 0.25 mg wk 1 + AZITH 250 mg wks 1-2	• Mucosal or cutaneous changes • New psychiatric diagnosis
Feldman 2013; Trial 1 **Country**: North	N=744 **Sex**: mixed	**Intervention: arm 1**: TAZ 0.1% foam **Intervention: arm 2**:	• Skin irritation • Light sensitivity

Study	Population	Interventions	Outcomes
America **Study type**: RCT	**Number randomised: arm 1**: n=372 **Number randomised: arm 2**: n=372 **Inclusion details**: Males and females aged between 12 and 45 years, in good general health and agreed to use a medically-acceptable form of contraception throughout the study. Moderate to severe acne vulgaris: Investigator's Static Global Assessment (ISGA) score =3 at baseline; lesion counts of 25 to 50 facial inflammatory lesions (papules plus pustules), including nasal lesions, with no more than one facial nodular lesion (<5 mm) and no cystic lesions, and 30 to 125 facial non-inflammatory lesions (open and closed comedones), excluding nasal lesions**.** Provide consent.	Vehicle	
Feldman 2013; Trial 2 **Country**: North America **Study type**: RCT	N=742 **Sex**: mixed **Number randomised: arm 1**: n=373 **Number randomised: arm 2**: n=369 **Inclusion details**: Males and females aged between 12 and 45 years, in good general health and agreed to use a medically-acceptable form of contraception throughout the study. Moderate to severe acne vulgaris: Investigator's Static Global Assessment (ISGA) score =3 at baseline; lesion counts of 25 to 50 facial inflammatory lesions (papules plus pustules), including nasal lesions, with no more than one facial nodular lesion (<5 mm) and no cystic lesions, and 30 to 125 facial non-inflammatory	**Intervention: arm 1**: TAZ 0.1% foam **Intervention: arm 2**: Vehicle	• Skin irritation • Light sensitivity

Study	Population	Interventions	Outcomes
	lesions (open and closed comedones), excluding nasal lesions**.**		
Fugere 1990 **Country**: Canada **Study type**: RCT	N=73 **Sex**: female **Number randomised: arm 1**: n=40 **Number randomised: arm 2**: n=33 **Inclusion details**: Women in good health aged between 18 and 35 years**.** Moderate to severe androgen-dependent acne vulgaris (defined as presence of comedones, papules and macules on at least half of the face**.** Previous treatment withdrawn within 6 weeks of starting study treatments.	**Intervention: arm 1**: CPA 2mg + EE 0.035 mg (Diane-35) **Intervention: arm 2**: CPA 2mg + EE 0.05 mg (Diane-50)	• Breakthrough bleeding
Gratton 1982 **Country**: Canada **Study type**: RCT	N=225 **Sex**: mixed **Number randomised: arm 1**: n=121 **Number randomised: arm 2**: n=124 **Inclusion details**: Participants with moderate to severe acne (defined as presence of a minimum of 12 to 70 inflammatory papules and pustules, and a maximum of 6 nodulocystic lesions on the face above the jawline).	**Intervention: arm 1**: CLIND 1% solution + PLC capsule **Intervention: arm 2**: PLC capsule + PLC solution	• Participant reported improvement
Jones 1981 **Country**: United States **Study type**: RCT	N=175 **Sex**: mixed **Number randomised: arm 1**: n=90 **Number randomised: arm 2**: n=85 **Inclusion details**: Males and females aged 12 years or older, seeking medical care for acne or recruited volunteers, but otherwise in good general health**.** Facial acne grades 2 or 3 on the severity scale (grade 2: a moderate number of comedones, papules, and small cysts,	**Intervention: arm 1**: BPO 5%/ERYTH 3% gel **Intervention: arm 2**: Vehicle	• Skin irritation

Study	Population	Interventions	Outcomes
	occasional pustules, and inflammation; grade 3: a great number of lesions with deeper and larger cysts and minimal scarring). Minimum of 10 papular inflammatory acne lesions in the facial area. Participants could be pregnant or of childbearing age. Unresponsive to treatment with oral tetracycline hydrochloride, topical benzoyl peroxide, and tretinoin.		
Jones 2002 **Country**: United States **Study type**: RCT	N=223 **Sex**: mixed **Number randomised: arm 1**: n=112 **Number randomised: arm 2**: n=111 **Inclusion details**: Males and females aged =13 years. Moderate to moderately severe acne vulgaris (overall acne severity score =1.5 on the Physician's Global Acne Severity Scale, 15 to 80 inflammatory lesions, 20 to 140 comedones, and =2 nodules or cysts measuring greater than 5mm. The comedone count did not include the nasal and nasolabial fold area). Treatment with systemic antibiotics known to affect acne and systemic corticosteroids should be discontinued 4 weeks prior to study commencement, and 6 months for oral retinoids. A 2-week washout period was required for topical antibiotics and/or anti-acne medication, topical corticosteroids, and topical retinoids.	**Intervention: arm 1**: BPO 5%/ERYTH 3% gel (dual pouch pack) **Intervention: arm 2**: Vehicle	• Skin irritation • Participant reported improvement
Kapadia 2005 **Country**: Pakistan **Study type**: RCT	N=60 **Sex**: mixed **Number randomised: arm 1**: n=30 **Number randomised:**	**Intervention: arm 1**: ISO<120.Daily<0.5 (20mg) **Intervention: arm 2**: ISO<120.Daily=0.5	• Mucosal or cutaneous changes • Change in mood

Study	Population	Interventions	Outcomes
	arm 2: n=30 **Inclusion details**: Participants with moderate to severe acne vulgaris (graded using the Global Acne Grading System (GAGS)) attending an outpatient clinical in Karachi.	(40mg)	
Khanna 1993 **Country**: India **Study type**: RCT	N=44 **Sex**: mixed **Number randomised: arm 1**: n=21 **Number randomised: arm 2**: n=23 **Inclusion details**: Males and females with moderately severe acne (defined when acne lesion score (ALS) was 30 to 70) and severe acne (defined as ALS score of more than 70)**.** Participants who had taken oral antibiotics were included in the study after 1 month discontinuation of the antibiotics.	**Intervention: arm 1**: TETRA 500 mg po bid **Intervention: arm 2**: MINO 50 mg po bid	• Thrush/candidiasis
Kim 2017 **Country**: Korea **Study type**: RCT	N=32 **Sex**: mixed **Number randomised: arm 1**: n=16 **Number randomised: arm 2**: n=16 **Inclusion details**: Participants aged between 19 and 45 years**.** Active acne lesions and Fitzpatrick skin phototypes III to IV; acne severity grade 3 or 4 according to the IGA.	**Intervention: arm 1**: MAL 16%-DL PDT **Intervention: arm 2**: NAFL + MAL 16%-DL PDT	• Skin redness • Pigment changes • Participant reported improvement
Kuhlman 1986 **Country**: United States **Study type**: RCT	N=35 **Sex**: mixed **Number randomised: arm 1**: na, n=21 completed **Number randomised: arm 2**: na, n=14 completed **Inclusion details**: Men and women aged 12 to 30 years**.** Moderate to severe acne vulgaris defined as 12 to 70 inflammatory papules	**Intervention: arm 1**: CLIND 1% lotion **Intervention: arm 2**: Vehicle	• Skin irritation

Study	Population	Interventions	Outcomes
	and no more than 6 cystic lesions on the face above the jawline.		
Lassus 1984 **Country**: Finland **Study type**: RCT	N=30 **Sex**: mixed **Number randomised: arm 1**: n=15 **Number randomised: arm 2**: n=15 **Inclusion details**: Participants diagnosed with acne vulgaris of the papulopustular type.	**Intervention: arm 1**: motretinide 1% cream **Intervention: arm 2**: BPO 5% gel	• Skin irritation
Leyden 2018 **Country**: United States **Study type**: RCT	N=285 **Sex**: mixed **Number randomised: arm 1**: n=76 **Number randomised: arm 2**: n=70 **Number randomised: arm 3**: n=66 **Number randomised: arm 4**: n=73 **Inclusion details**: Males and females aged 12 to 45 years**.** Moderate to severe facial acne vulgaris characterised by 20 to 50 inflammatory lesions, 30 to 100 non-inflammatory lesions, and no more than 2 facial nodules. IGA baseline score of 3 ('moderate') or 4 ('severe')**.** Body weight between 52 kg and 88 kg at screening**.** Participants receiving prohibited medications entered an appropriate washout period prior to screening procedures**.** Females of childbearing potential had to have a negative urine pregnancy test and use of an effective method of contraception.	**Intervention: arm 1**: SAR 0.75 mg/kg **Intervention: arm 2**: SAR 1.5 mg/kg **Intervention: arm 3**: SAR 3.0 mg/kg **Intervention: arm 4**: PL	• GI side effects
Mei 2013 **Country**: China **Study type**: RCT	N=41 **Sex**: mixed **Number randomised: arm 1**: n=21 **Number randomised: arm 2**: n=20 **Inclusion details**: Chinese patients aged over 18 years**.** Participants with II–IV	**Intervention: arm 1**: 5ALA 10%-IPL-PDT **Intervention: arm 2**: IPL-PT + Vehicle	• Skin redness • Skin irritation

Study	Population	Interventions	Outcomes
	facial acne according to Pillsbury grade and Fitzpatrick skin type II–IV.		
Miller 1986b **Country**: United Kingdom **Study type**: RCT	N=90 **Sex**: female **Number randomised: arm 1**: n=28 **Number randomised: arm 2**: n=32 **Number randomised: arm 3**: n=30 **Inclusion details**: Women aged between 16 and 36 years**.** Moderate to severe acne (graded according to Burke & Cunliffe, 1984)**.** Any acne medication (other than contraceptive pill) stopped 6 weeks prior to study participation. Oral contraception was continued until the commencement of the trial.	**Intervention: arm 1**: CPA 2mg/EE 0.05 mg (days 5-25) + PL (days 5-14) **Intervention: arm 2**: NOR 1mg/EE 0.05mg (days 5-25) + PL (days 5-14) **Intervention: arm 3**: CPA 50mg (days 5-14), then EE 0.05 mg (days 5-25)	• Breast tenderness • Sexual dysfunction • Change in mood • Breakthrough bleeding
Moore 2018; Trial 1 **Country**: United States **Study type**: RCT	N=968 **Sex**: mixed **Number randomised: arm 1**: n=483 **Number randomised: arm 2**: n=485 **Inclusion details**: Participants aged 9 to 45 years, weighing 33 to 136 kg**.** Score of 3 (moderate) or 4 (severe) on the IGA scale for inflammatory lesions of acne; 20 to 50 inflammatory and =100 non-inflammatory lesions, and =2 nodules.	**Intervention: arm 1**: SAR 1.5 mg/kg **Intervention: arm 2**: PL	• GI side effects • Thrush/candidiasis
Moore 2018; Trial 2 **Country**: United States **Study type**: RCT	N=1034 **Sex**: mixed **Number randomised: arm 1**: n=519 **Number randomised: arm 2**: n=515 **Inclusion details**: Participants aged 9 to 45 years, weighing 33 to 136 kg**.** Score of 3 (moderate) or 4 (severe) on the IGA scale for inflammatory lesions of acne; 20 to 50 inflammatory and =100 non-inflammatory lesions, and =2 nodules.	**Intervention: arm 1**: SAR 1.5 mg/kg **Intervention: arm 2**: PL	• GI side effects • Thrush/candidiasis

Study	Population	Interventions	Outcomes
Pariser 2005 **Country**: United States **Study type**: RCT	N=214 **Sex**: mixed **Number randomised: arm 1**: n=70 **Number randomised: arm 2**: n=70 **Number randomised: arm 3**: n=74 **Inclusion details**: Participants aged 12 to 40 years**.** Moderate to moderately severe acne vulgaris; minimum of 20 inflammatory facial lesions (not >2 nodules/cysts), 20 non-inflammatory facial lesions; global facial severity grade 4 to 10 according to the Leeds Revised Acne Grading System**.** Washout periods for certain topical and systemic treatments were required**.** Negative urine pregnancy test results required at screening and at the final visit for women of childbearing potential.	**Intervention: arm 1**: ADAP 0.3% gel **Intervention: arm 2**: ADAP 0.1% gel **Intervention: arm 3**: Vehicle	• Skin irritation
Pariser 2014 **Country**: United States **Study type**: RCT	N=498 **Sex**: mixed **Number randomised: arm 1**: n=253 **Number randomised: arm 2**: n=245 **Inclusion details**: Males and females of any race and ethnicity, aged 12 to 40 years**.** Moderate to severe acne vulgaris (a score of 3 or 4 on the Global Severity Score (EGSS), presenting with 20 to 40 inflammatory lesions (papules, pustules, and nodules), 20 to 100 non-inflammatory lesions (open and closed comedones), and =2 nodules**.** Women of childbearing age were required to have a negative urine pregnancy test and to agree to use an effective form of contraception during the	**Intervention: arm 1**: BPO 3.75%/CLIND 1.2% gel **Intervention: arm 2**: Vehicle	• Participant reported improvement

Study	Population	Interventions	Outcomes
	study period**.** A washout period of up to 1 month was required for participants who used previous prescription and over-the-counter acne treatments (including, topical (face) and systemic treatments: topical astringents and abrasives (1 week); topical anti-acne products, including soaps containing antimicrobials, and known comedogenic products (2 weeks); topical retinoids, retinol, and systemic acne treatments (4 weeks); and systemic retinoids (6 months).		
Pariser 2016 **Country**: United States **Study type**: RCT	N=153 **Sex**: mixed **Number randomised: arm 1**: n=100 **Number randomised: arm 2**: n=53 **Inclusion details**: Males and females aged 12 to 35 years**.** Severe facial acne vulgaris (defined by an IGA rating score of 4); 27 to 75 inflammatory lesions (papules, pustules and no more than 3 nodules) and 20 to 100 non-inflammatory lesions (open and closed comedones) on the face; Fitzpatrick skin types I to VI. Confirmed using standardised clinical photographs**.** Females of childbearing potential were required to use appropriate contraception (same product and dose if using an oral contraceptive) for at least 14 days before the first treatment and during the study.	**Intervention: arm 1**: MAL 8%-RED-PDT **Intervention: arm 2**: Vehicle-RED-PDT	• Skin redness • Pigment changes
Parsad 2001 **Country**: India **Study type**: RCT	N=60 **Sex**: mixed **Number randomised: arm 1**: n=30 **Number randomised:**	**Intervention: arm 1**: DOXY 100mg + TRET 0.05% cream **Intervention: arm 2**: AZITH 500 mg + TRET	• Skin irritation

Study	Population	Interventions	Outcomes
	arm 2: n=30 **Inclusion details**: Participants with moderate to severe acne (grade 2 to 8) on the Burke & Cunliffe scale.	0.05% cream	
Richter 1998a **Country**: Europe **Study type**: RCT	N=161 **Sex**: mixed **Number randomised: arm 1**: n=81 **Number randomised: arm 2**: n=80 **Inclusion details**: Outpatients aged 14 to 26 years**.** Facial acne (severity grades of 3 and higher according to the modified scoring scale of Cook).	**Intervention: arm 1**: CLIND 1.2%/TRET 0.025% gel **Intervention: arm 2**: TRET 0.025% gel	• Skin irritation
Sami 2008 **Country**: Egypt **Study type**: RCT	N=45 **Sex**: mixed **Number randomised: arm 1**: n=15 **Number randomised: arm 2**: n=15 **Number randomised: arm 3**: n=15 **Inclusion details**: Males and females with moderate to severe facial acne according to Burton classification.	**Intervention: arm 1**: 595 nm PDL PT **Intervention: arm 2**: 550 nm-1200 nm IPL PT **Intervention: arm 3**: BR-LED PT	• Pigment changes • Participant reported improvement
Schmidt 2011 **Country**: United States **Study type**: RCT	N=2010 **Sex**: mixed **Number randomised: arm 1**: n=1008 **Number randomised: arm 2**: n=1002 **Inclusion details**: Males and females aged over 12 years**.** Facial acne vulgaris with 20 to 50 inflammatory lesions (papules and pustules), 20 to 100 non-inflammatory lesions (open and closed comedones), and not more than 2 nodules; Evaluators Global Severity Score (EGSS) of moderate or severe**.** Willing to undergo the specified washout periods for topical antibiotics and other topical antibacterial drugs	**Intervention: arm 1**: CLIND 1.2%/TRET 0.025% gel **Intervention: arm 2**: CLIND 1.2% gel	• Skin irritation

Study	Population	Interventions	Outcomes
	(2 weeks); facial anti-inflammatory agents and corticosteroids (4 weeks); retinoids, including retinol (4 weeks). Had undergone the specified washout periods of systemic treatments including corticosteroids and intramuscular injections (4 weeks); antibiotics (4 weeks); other systemic acne treatments (4 weeks); systemic retinoids (6 months).		
Sklar 1996 **Country**: United States **Study type**: RCT	N=94 **Sex**: mixed **Number randomised: arm 1**: n=30 **Number randomised: arm 2**: n=32 **Number randomised: arm 3**: n=32 **Inclusion details**: Males and females aged 16 to 30 years. Moderate to moderately severe, papular-pustular, facial acne vulgaris with a minimum number of inflamed lesions. Willingness to co-operate and adhere to study criteria. Absence of interfering medical and dermatological conditions and medications. Absence of pregnancy and avoidance of interference from oral contraceptives.	**Intervention: arm 1**: BPO-topical 5%/ ERYTH-topical 3% **Intervention: arm 2**: BPO-topical 10% **Intervention: arm 3**: Vehicle	• Skin irritation
Stein Gold 2008 **Country**: United States **Study type**: RCT	N=201 **Sex**: mixed **Number randomised: arm 1**: n=101 **Number randomised: arm 2**: n=100 **Inclusion details**: Males and females aged between 12 and 35 years. 15 to 100 non-inflammatory lesions, at least 20 inflammatory lesions, and no more than 3 nodules.	**Intervention: arm 1**: ADAP 0.1% gel **Intervention: arm 2**: ADAP 0.1% gel for 6 weeks then TAZ 0.1% cream for 6 weeks	• Skin irritation
Stein Gold 2016	N=494	**Intervention: arm 1**:	• Skin irritation

Study	Population	Interventions	Outcomes
Country: United States. **Study type**: RCT	**Sex**: mixed **Number randomised: arm 1**: n=213 **Number randomised: arm 2**: n=212 **Number randomised: arm 3**: n=69 **Inclusion details**: Males and females**.** Moderate to severe inflammatory facial acne, that is a score of 3 (moderate) or 4 (severe) on the IGA, the presence of 20 to 100 inflammatory lesions, 30 to 150 non-inflammatory lesions (including the nose), and up to 2 nodules on the face**.** A urine pregnancy test was required for females at baseline and throughout the study.	ADAP 0.3%/BPO 2.5% gel **Intervention: arm 2**: ADAP 0.1%/BPO 2.5% gel **Intervention: arm 3**: Vehicle	• Participant reported improvement
Stewart 2006 **Country**: United States **Study type**: RCT	N=174 **Sex**: mixed **Number randomised: arm 1**: n=59 **Number randomised: arm 2**: n=60 **Number randomised: arm 3**: n=55 **Inclusion details**: Participants aged 12 to 30 years, weighing between 39.1 kg and 102.3 kg (86 to 225 lb)**.** Diagnosed with moderate to severe facial acne vulgaris; at least 20 and no more than 100 inflammatory facial lesions and <5 facial nodules or cysts**.** Females of childbearing potential must have had a negative urine pregnancy test result (25 µg/mL sensitivity), be using contraception and will to continue on contraception during the study**.** Participants or parent/guardian consent provided.	**Intervention: arm 1**: MINO-oral 2mg/kg/day **Intervention: arm 2**: MINO-oral 3mg/kg/day **Intervention: arm 3**: PLC-oral	• Skin irritation • GI side effects
Strauss 1984a **Country**: United States	N=141 **Sex**: mixed **Number randomised:**	**Intervention: arm 1**: ISO<120.Daily<0.5 (0.1 mg/kg daily for 140 days) **Intervention: arm 2**:	• Mucosal or cutaneous changes • Relapse

Study	Population	Interventions	Outcomes
Study type: RCT	**arm 1**: na, n=46 completed **Number randomised: arm 2**: na, n=46 completed **Number randomised: arm 3**: na, n=49 completed **Inclusion details**: Participants with treatment-resistant, severe nodulocystic acne; minimum of 10 inflammatory nodulocystic acne lesions at least 4 mm in diameter on the face, back, or chest**.** Off all treatment for at least 1 month**.** Female participants were required to have negative pregnancy test within 2 weeks prior to starting treatment.	ISO<120.Daily=0.5 (0.5 mg/kg daily for 140 days) **Intervention: arm 3**: ISO=120.Daily=0.5 (1 mg/kg daily for 140 days)	
Tanghetti 2006 **Country**: United States **Study type**: RCT	N=121 **Sex**: mixed **Number randomised: arm 1**: n=61 **Number randomised: arm 2**: n=60 **Inclusion details**: Participants aged at least 12 years of age**.** Stable moderate to severe facial inflammatory acne vulgaris (defined as 15 to 60 papules plus pustules, 10 to 100 comedos, and no more than 2 nodulocystic lesions with a maximum diameter of 5 mm)**.**Washout periods required: 2 weeks for topical acne treatments, 30 days for systemic antibiotics and investigational drugs, 12 weeks for oestrogens/birth control pills if previously used for <12 weeks, and 6 months for oral retinoids.	**Intervention: arm 1**: TAZ 0.1% cream + Vehicle gel **Intervention: arm 2**: BPO 5%/CLIND 1% gel + TAZ 0.1% cream	• Skin irritation
Tanghetti 2011 **Country**: United States **Study type**: RCT	N=171 **Sex**: mixed **Number randomised: arm 1**: n=85 **Number randomised: arm 2**: n=86	**Intervention: arm 1**: TAZ 0.1% cream **Intervention: arm 2**: DAP 5% gel + TAZ 0.1% cream	• Skin irritation

Study	Population	Interventions	Outcomes
	Inclusion details: Males or females aged at least 12 years**.** Stable, non-rapidly progressing facial acne vulgaris characterised by the presence of 50 to 100 inflammatory lesions (papules, pustules), 25 to 100 facial non-inflammatory lesions (open/closed comedones0, no more than 3 facial nodules and/or cysts of diameter =1 cm**.** Females of childbearing potential were required to use reliable methods of birth control.		
Tanghetti 2019 **Country**: United States **Study type**: RCT	N=210 **Sex**: mixed **Number randomised: arm 1**: n=69 **Number randomised: arm 2**: n=72 **Number randomised: arm 3**: n=69 **Inclusion details**: Participants of any gender, race and ethnicity, aged 12 years or older**.** Participants with moderate to severe acne; EGSS score of 3 (moderate) or 4 (severe); 20 to 40 inflammatory lesions (papules, pustules, and nodules), 20 to 100 non-inflammatory lesions (open and closed comedones), and 2 nodules or less**.** Women of childbearing potential were required to have a negative urine pregnancy test at and agree to use a reliable method of contraceptive during the study period**.** Washout period of 1 month required for participants who previously used prescription and over-the-counter acne treatments, and 6 months for systemic retinoids.	**Intervention: arm 1**: TAZ 0.045% lotion **Intervention: arm 2**: TAZ 0.1% cream **Intervention: arm 3**: Lotion vehicle or cream vehicle (arms combined)	• Skin irritation • Participant reported improvement

Study	Population	Interventions	Outcomes
Thiboutot 2002 **Country**: United States **Study type**: RCT	N=327 **Sex**: mixed **Number randomised: arm 1**: n=124 **Number randomised: arm 2**: n=121 **Number randomised: arm 3**: n=42 **Number randomised: arm 4**: n=40 **Inclusion details**: Males and females aged >12 years of age**.** Moderate to moderately severe acne; 15 to 80 facial inflammatory lesions, 20 to 140 facial comedones (not including the nose or nasolabial area), <2 nodules or cysts >5 mm, and a minimum Physician's Global Acne Severity score of 1.5.	**Intervention: arm 1**: BPO 5%/ERYTH 3% gel **Intervention: arm 2**: BPO 5%/ERYTH 3% jar **Intervention: arm 3**: Vehicle gel **Intervention: arm 4**: Vehicle Jar	• Skin irritation
Thiboutot 2008 **Country**: United States **Study type**: RCT	N=2813 **Sex**: mixed **Number randomised: arm 1**: n=797 **Number randomised: arm 2**: n=812 **Number randomised: arm 3**: n=809 **Number randomised: arm 4**: n=395 **Inclusion details**: Males and females of any race and ethnicity, aged 12 years or older**.** Moderate to severe acne vulgaris (a score of 3 or 4 on the EGSS); presenting with 17 to 40 inflammatory lesions (papules, pustules, and nodules), 20 to 100 non-inflammatory lesions (open and closed comedones), and 2 nodules or less**.** Women of childbearing potential were required to have a negative urine pregnancy test and to agree to use an effective form of contraception during the study**.** Washout periods required: 1 month for	**Intervention: arm 1**: CLIND 1.2%/BPO 2.5% gel **Intervention: arm 2**: CLIND 1.2% **Intervention: arm 3**: BPO 2.5% **Intervention: arm 4**: Vehicle	• Participant reported improvement

Study	Population	Interventions	Outcomes
	previous prescription and over-the-counter acne treatments; for topical (face) and systemic treatments: topical astringents and abrasives (1 week); topical antiacne products, including soaps containing antimicrobials, and known comedogenic products (2 weeks); topical retinoids, retinol, and systemic acne treatments (4 weeks); and systemic retinoids (6 months).		
Tyring 2018 **Country**: International study **Study type**: RCT	N=1640 **Sex**: mixed **Number randomised: arm 1**: n=819 **Number randomised: arm 2**: n=821 **Inclusion details**: Males and females of any race and ethnicity, aged 9 years and older**.** Moderate (EGSS score 3) to severe (EGSS score 4) acne presenting with 20 to 40 inflammatory lesions (papules, pustules, and nodules), 20 to 100 non-inflammatory lesions (open and closed comedones), and 2 nodules or less**.** Women of childbearing potential were required to have a negative urine pregnancy test and to agree to use an effective form of contraception during the study**.** Washout periods required: 1 month for previous prescription and over-the-counter acne treatments; for topical and systemic treatments: topical astringents and abrasives (1 week); topical anti-acne products, including soaps containing antimicrobials, and known comedogenic products (2 weeks); topical retinoids, retinol, and systemic acne treatments such as	**Intervention: arm 1**: TRET 0.05% lotion **Intervention: arm 2**: Vehicle	• Skin irritation

Study	Population	Interventions	Outcomes
	hormonal or antibiotic treatments (4 weeks); and systemic retinoids (6 months).		
Zouboulis 2000 **Country**: Europe **Study type**: RCT	N=209 **Sex**: mixed **Number randomised: arm 1**: n=104 **Number randomised: arm 2**: n=105 **Inclusion details**: Participants aged between 14 and 26 years**.** Moderate to severe acne vulgaris; scoring =3 on the Cook acne scale.	**Intervention: arm 1**: CLIND 1%/TRET 0.025% gel **Intervention: arm 2**: CLIND 1% lotion	• Skin irritation

Abbreviations: 1319-LSR: 1319 nm laser phototherapy; 589-LSR: 589 nm laser phototherapy; 5ALA-IPL-PDT: 5-aminolevulinic acid using intense pulsed light; 5ALA-KTP-PDT: 5-aminolevulinic acid using potassium titanyl phosphate laser; 5ALA-RED-PDT: 5-aminolevulinic acid using red light; ADAP + BPO: adapalene + benzoyl peroxide; ADAP: adapalene; AZE: azelaic acid; AZITH: azithromycin ; BiRF: bipolar radiofrequency; BLU-PT: blue light phototherapy; BPO + CLIND: benzoyl peroxide 5%/clindamycin 1%; BPO: benzoyl peroxide; BR-LED: blue + red light light emitting diode; CLIND: clindamycin; CLIND + TRET: clindamycin 1% + tretinoin 0.025%; CLIND: clindamycin; CPA + EE (CO-CYPRINDIOL): ethinylestradiol with cyproterone acetate; CPA: cyproterone acetate; DAPS: dapsone; DEM: demeclocycline; DOXY: doxycycline; EE: ethinyl estradiol; ERYTH + ZINC: erythromycin with zinc acetate dihydrate; ERYTH: erythromycin; GLY: glycolic acid; GOLDMP: gold microparticles; IPL: intense pulsed light; ISO<120.Alt<0.5: isotretinoin ≥0.5mg/kg/every other day total cumulative dose < 120mg/kg; isotretinoin ≥0.5mg/kg/day total cumulative dose < 120mg/kg; ISO<120.Daily≥0.5: isotretinoin <0.5mg/kg/day total cumulative dose < 120mg/kg; ISO<120.Other<0.5: isotretinoin ≥0.5mg/kg/less frequently total cumulative dose < 120mg/kg; ISO<120.Other≥0.5: isotretinoin <0.5mg/kg/less frequently total cumulative dose < 120mg/kg; ISO≥120.Alt<0.5: isotretinoin ≥0.5mg/kg/every other day total cumulative dose >= 120mg/kg; ISO≥120.Alt≥0.5: isotretinoin <0.5mg/kg/every other day total cumulative dose >= 120mg/kg; ISO≥120.Daily<0.5: isotretinoin ≥0.5mg/kg/day total cumulative dose >= 120mg/kg; ISO≥120.Daily≥0.5: isotretinoin <0.5mg/kg/day total cumulative dose >= 120mg/kg; ISO≥120.Other<0.5: isotretinoin ≥0.5mg/kg/less frequently total cumulative dose >= 120mg/kg; ISO≥120.Other≥0.5: isotretinoin <0.5mg/kg/less frequently total cumulative dose >= 120mg/kg; ISO: isotretinoin ; JES: Jessner's peel; KTP: potassium titanyl phosphate laser; LEVA: levamisole; LYME: lymecycline; MAL-DL-PDT: methyl aminolevulinate using daylight; MAL-IPL-PDT: methyl aminolevulinate using IPL; MAL-RED-PDT: methyl aminolevulinate using red light; MD: microdermabrasion; METF: metformin; MET: metronidazole; MICO: miconazole nitrate; MINO: minocycline; MOT: motretinide; n: number of participants randomised/completed to/in each trial arm; NAFL: fractional erbium glass laser; NBUVB: nearband type B ultraviolet light; NICO: nicotinamide (niacinamid); NOR + EE: northisterone + ethinylestradiol; PDL: pulsed dye laser; PLC: pill placebo; PLC-physical: sham physical treatment; PLC: topical placebo; RED: red light; ROXI: roxithromycin; SAL: salicyclic acid; SARE: sarecycline; SPIRO: spironolactone; TAZ: tazarotene; TETRA: tetracycline; TRET: tretinoin (RETIN A, All-trans retinoic acid); TRIF: trifarotene; ZINCG: zinc gluconate

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

Quality assessment of included studies in the evidence review

See the evidence profiles in appendix F.

Economic evidence

Included studies

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

Excluded studies

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

Economic model

The economic model associated with these review questions was based on the NMA results (see evidence report F1).

The committee's discussion of the evidence

The pairwise analysis was supplementary to the network meta-analysis so evidence from both of these were discussed when recommendations were drafted. For the discussion of the evidence that supported the recommendations see evidence report F1.

Recommendations supported by this evidence review

This evidence review supports recommendations 1.5.1, 1.5.2 and 1.5.4 to 1.5.12, 1.5.15 to 1.5.21 as well as 1.5.24 and 3 research recommendations on the effectiveness of a reduced dose of oral isotretinoin, physical modalities and the effectiveness of chemical peels in the NICE guideline. Other evidence supporting these recommendations can be found in the evidence reviews on management of moderate to severe acne (network meta-analysis – evidence report F1).

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Appendices

Appendix A - Review protocol

Review protocol for review question: For people with moderate to severe acne vulgaris what are the best treatment options of those covered in 9 review questions?

A single review protocol and literature search was used to identify randomised trials of treatments for acne. Outcomes were prioritised for either pairwise or network meta-analysis (NMA) and the evidence was divided according to the severity of acne into mild to moderate and moderate to severe categories. The evidence was then summarised in four separate reviews covering the treatment of:

- mild to moderate acne (NMA)
- mild to moderate acne (pairwise meta-analysis)
- moderate to severe acne (NMA)
- moderate to severe acne (pairwise meta-analysis)

Table 3: Review protocol

Field	Content
PROSPERO registration number	CRD42020154100
Review title	Comparative effectiveness, acceptability and tolerability of topical or oral pharmacological and physical interventions in the treatment of acne vulgaris: a systematic review using network and pairwise meta-analysis
Review question	2.1 What is the effectiveness of topical treatments individually or in combination in the treatment of acne vulgaris? 3.1 What is the effectiveness of oral antibiotic treatments in the treatment of acne vulgaris? 4.1 What is the effectiveness of combining an oral antibiotic with a topical agent compared to an oral antibiotic alone in the treatment of acne vulgaris? 5.1 What is the optimal duration of antibiotic treatments (topical and systemic) for acne vulgaris? 6.1 What is the effectiveness of oral hormonal contraceptives in the treatment of acne vulgaris?

Field	Content
	6.2 What is the effectiveness of non- hormonal contraceptive anti-androgens (including spironolactone) in the treatment of acne vulgaris? 6.3 What is the effectiveness of metformin in the treatment of acne vulgaris? 8.1 What is the effectiveness of oral isotretinoin in the treatment of acne vulgaris? 9.1 What is the effectiveness of physical treatments for acne vulgaris?
Objective	The objective of this review is to establish which topical or oral pharmacological and physical interventions are effective, acceptable and tolerable in the treatment of acne vulgaris.
Searches	• The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE Searches will be restricted by: • Date: No restriction • Language of publication: English language only • Publication status: Conference abstracts will be excluded because these do not typically provide sufficient information to fully assess risk of bias. Unpublished data will also be excluded. • Standard exclusions filter (animal studies/low level publication types) will be applied • 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 Other search methods will involve scanning the reference lists of all eligible systematic reviews for published studies meeting inclusion criteria.
Condition or domain being studied	Acne vulgaris

Field	Content
Population	Inclusion: People with acne vulgaris, of all ages and levels of symptom severity. Studies need to provide data specific to people with mild to moderate acne, and/or people with moderate to severe acne. See under 'Analysis of sub-groups' for the approach followed in order to categorise population in the studies into mild to moderate acne or moderate to severe acne. All settings (community, primary, secondary, and tertiary health care) will be considered. Exclusions: • Neonatal acne • People with post-inflammatory dyspigmentation • Trials recruiting specifically people with acne vulgaris and polycystic ovary syndrome (PCOS) • Trials of maintenance treatment ('relapse prevention' trials), which recruit people currently in remission or people who have responded to treatment or who have had successful treatment or who are reported to have received primary or 'acute' treatment immediately prior to randomisation to maintenance treatment. • 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 • Trials that include all ranges of severity • Trials with indirect population: Where studies with a mixed population (i.e. include people with acne vulgaris and another condition, e.g. hirsutism) are identified, those with <66% of the relevant population will be excluded, unless subgroup analysis for acne vulgaris is reported.
Intervention	Interventions will be categorised into the following classes, and, if relevant, subclasses (the list is non-exhaustive): ➢ **TOPICAL TREATMENTS** **Abrasive/cleaning agents** • Aluminium oxide [own class] **Anthelmintics**

Field	Content
	• Cysticide (praziquantel) [own class] • Class of avermectins: ivermectin **Antibacterials** • Class of triclocarban and triclozan **Antibiotics** • Class of sulphones (dapsone) • Fusidic acid (sodium fusidate) [own class] • Class of lincosamides (for example clindamycin) • Class of macrolides (for example clarithromycin, erythromycin with zinc acetate dihydrate) • Class of nitroimidazoles (metronidazole) • Class of carboxylic acids (mupirocin) • Class of penicillins ○ Sub-class of natural (for example almecillin) ○ Sub-class of aminopenicillins (for example ampicillin) ○ Sub-class of β-lactamase-resistant (for example methicillin) ○ Sub-class of carboxypenicillins (for example ticarcillin) ○ Sub-class of ureidopenicillins (for example azlocillin) ○ Sub-class of other penicillins (mecillinam, pivmecillinam hydrochloride) • Class of pleuromutilins (for example retapamulin) **Antiseptics** • Benzoyl peroxide (trade: Acnecide, Brevoxyl, Panoxyl) [own class] • Chlorhexidine gluconate (trade: Acnemed, Cepton) or digluconate [own class]

Field	Content
	Dicarboxylic acids • Azelaic acid [own class] **Vitamin B3** • Nicotinamide (niacinamide) [own class] **Retinoids or retinoid-like agents** • Class of retinoids or retinoid-like agents (adapalene, isotretinoin, retinol, tazarotene, tretinoin) **Combined interventions** • Benzoyl peroxide & potassium hydroxyguinoline sulfate [own class] • Class of benzoyl peroxide & retinoid (benzoyl peroxide + adapalene) • Class of benzoyl peroxide & lincosamide (benzoyl peroxide + clindamycin) • Class of lincosamides & retinoid (clindamycin + tretinoin) • Class of macrolides & retinoid (erythomycin + retinoid) [topical] • Germolene (phenol 1.2% + chlorhexidine diculconate [own class] ➢ **ORAL ANTIBIOTICS** • Class of carbapenems (for example imipenem, meropenem) • Class of carbapenems with cilastatin (imipenem with cilastatin) • Class of carbapenems with b lactamase inhibitor (meropenem with vaborbactam) • Class of cephamycins/cephalosporins ○ Sub-class of 1st-generation (for example cefadroxil) ○ Sub-class of 2nd-generation (for example cefaclore) ○ Sub-class of 3rd-generation (for example cefdinir)

Field	Content
	○ Sub-class of 4th-generation (for example cefozopran) ○ Sub-class of 5th-generation (for example ceftolozane) • Class of cephamycins/cephalosporins with β-lactamase inhibitor (for example ceftraroline or ceftazidime with avibactam, cefoperazone with sulbactam, ceftolozane with tazobactam) • Class of sulphones (dapsone) • Fusidic acid (sodium fusidate) [own class] • Class of lincosamides (for example clindamycin) • Class of macrolides (for example clarithromycin, erythromycin) • Class of monobactams (aztreonam) • Class of monobactams with β-lactamase inhibitor (aztreonam with avibactam) • Class of penicillins ○ Sub-class of natural (for example almecillin) ○ Sub-class of aminopenicillins (for example ampicillin) ○ Sub-class of β-lactamase-resistant (for example methicillin) ○ Sub-class of carboxypenicillins (for example ticarcillin) ○ Sub-class of ureidopenicillins (for example azlocillin) ○ Sub-class of other penicillins (mecillinam, pivmecillinam hydrochloride) • Class of penicillin with β-lactamase inhibitor (for example co-amoxiclav [amoxicillin with clavulanic acid], piperacillin with tazobactam, ticaricillin with clavulanic acid, sultamicillin [ampicillin with sulbactam]) • Class of penicillin with flucloxacilin (co-fluampicil [ampicillin + flucloxacilin]) • Class of pleuromutilins (for example retapamulin) • Class of quinolones

Field	Content
	○ Sub-class of 1st-generation (for example rosoxacin) ○ Sub-class of 2nd-generation (for example ofloxacin) ○ Sub-class of 3rd-generation (for example temafloxacin) ○ Sub-class of 4th-generation (for example sitafloxacin) • Class of tetracyclines (for example doxycycline, oxytetracycline) • Trimethoprim [own class] • Co-trimoxazole (trimethoprim-sulfamethoxazole; TMP-SMX) [own class] ➢ **TOPICAL TREATMENTS COMBINED WITH ORAL ANTIBIOTICS** ➢ **ORAL HORMONAL CONTRACEPTIVES AND HORMONE-MODIFYING AGENTS** • Co-cyprindiol (ethinylestradiol + cyproterone acetate) [own class of combined oral contraceptive] • Class of combined oral contraceptives ○ Sub-class of 2nd generation (oestrogen, for example ethinylestradiol or estradiol or mestranol combined with levonorgestrel or norethisterone) ○ Sub-class of 3rd generation (oestrogen, for example ethinylestradiol combined with desogestrel or gestodene or norgestimate) ○ Sub-class of 4th generation (oestrogen, for example ethinylestradiol or estradiol combined with dienogest or drospirenone or nomegestrol acetate) Monophasic and phasic combined oral contraceptives containing the same hormones will be analysed as separate interventions within their sub-class. • Class of progestogen-only oral contraceptives ○ Sub-class of 1st generation (for example medroxyprogesterone acetate)

Field	Content
	○ Sub-class of 2nd generation (for example levonorgestrel, norethisterone/ norethindrone) ○ Sub-class of 3rd generation (for example desogestrel, norgestimate, gestodene) ○ Sub-class of 4th generation (for example dienogest, drospirenone, nomegestrol acetate) • Class of selective aldosterone receptor antagonists (for example spironolactone alone or combined with furosemide or hydroflumethiazide [co-flumactone], eplerenone, canrenone) • Class of 5α-reductase inhibitors (dutasteride, finasteride, tamsulosin with dutasteride) • Class of other non-steroidal anti-androgens (for example abiraterone acetate, apalutamide, bicalutamide, cyproterone acetate, clormadinone acetate, enzalutamide, flutamide) • Metformin [own class] ➢ **ORAL ISOTRETINOIN** • Class of oral retinoid and total cumulative dose ≥ 120mg/kg (single course) ○ Sub-class of daily dosing (dose ≥0.5mg/kg/day or <0.5mg/kg/day) ○ Sub-class of alternate day dosing (dose ≥0.5mg/kg/day or <0.5mg/kg/day) ○ Sub-class of less frequent or other dosing (dose ≥0.5mg/kg/day or <0.5mg/kg/day) • Class of oral retinoid and total cumulative dose < 120mg/kg (single course) ○ Sub-class of daily dosing (dose ≥0.5mg/kg/day or <0.5mg/kg/day) ○ Sub-class of alternate day dosing (dose ≥0.5mg/kg/day or <0.5mg/kg/day) ○ Sub-class of less frequent or other dosing (dose ≥0.5mg/kg/day or <0.5mg/kg/day) ➢ **PHYSICAL TREATMENTS** • Class of chemical peels

Field	Content
	○ Sub-class of superficial peels ○ Sub-class of moderate peels ○ Sub-class of deep peels for example amino fruit acid, glycolic acid, Jessner's peel, lactic acid, salicylic acid, trichloroacetic acid [TCA]; these will be categorised into different sub-classes as reported in the included studies, according to the concentration of their active ingredient and treatment duration. • Comedone extraction [own class] • Class of photothermal therapy (for example fractional erbium glass laser) • Class of photochemical therapy (for example blue or red light and their combination) • Class of photochemical and photothermal therapy (for example potassium titanyul phosphate laser, Intense Pulsed Light [IPL], Pulsed Dye Laser) • Class of photodynamic therapy (for example 5-aminolevuliniv acid [ALA], liposomal methylene blue gel, methylaminolevulinate [MAL]) • Smoothbeam™ laser [own class] • Photopneumatic therapy (for example intense pulsed light + vacuum) • Radiofrequency (for example fractional microneedling, bipolar) Combined interventions within and across classes will be considered. Only drug classes available in the UK will be considered. To estimate class effects, we will consider any intervention belonging to a class, irrespective of its availability in the UK. However, we will only report individual drug effects for interventions that are currently (or soon expected to be) available in the UK. These may include pharmacological interventions that are (or soon expected to be) licensed in the UK for the treatment of acne or another condition. If existing evidence is not adequate to allow estimation of individual drug effects within each class, we will exclude drugs that are not available in the UK. We will include pharmacological interventions listed above, alone or in combinations, 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.

Field	Content
	Trial arms evaluating a class or sub-class of pharmacological interventions that is of interest, as determined above (for example a mixture of oral macrolides, a mixture of COC), rather than an individual drug, will be included as separate nodes within the class. However, trial arms evaluating broad types of interventions that are wider than classes as defined above (for example oral antibiotics) will be excluded from consideration. We will consider substantially different durations of treatment within the same class/drug as different interventions, that is as different network nodes, as duration of treatment may impact on its effects. We will consider the following durations of treatment: 0 to <6 weeks; ≥6 to <12 weeks, ≥12 to <24 weeks, ≥24 weeks. We will not consider in the NMA interventions that do not meet inclusion criteria, unless they act as the sole connectors of the interventions of interest in the network. In this case, interventions not meeting inclusion criteria will be included in the NMA but will not form part of the decision problem. A network diagram for all outcomes of interest will be constructed to explore whether all interventions are connected to the network. If more than one networks are formed, then separate NMAs will be conducted for each network, as long as the network contains at least 3 interventions that are part of the decision problem. If pairs of interventions are not connected to a network, they will be analysed in pairwise meta-analysis. We assume that any individual that meets all inclusion criteria is, in principle, equally likely to be randomized to any of the interventions in the synthesis comparator set.
Comparator	• No treatment • Waiting list • Pill placebo • Other active intervention • Sham physical treatment
Types of study to be included	Included study designs: • Systematic reviews/meta-analyses of randomised controlled trials (RCTs) • RCTs (individual or cluster); this includes RCTs of topical or physical treatments that randomise different parts of body (for example left-right side of face/body) in each participant Excluded study designs:

Field	Content
	• Quasi-randomised or non-randomised controlled trials • Case-control studies • Cohort studies • Cross-sectional studies • Epidemiological reviews or reviews on associations • Non-comparative studies Note: For further details, see the algorithm in appendix H, Developing NICE guidelines: the manual.
Other exclusion criteria	• Trials with <50% completion data (drop-out of ≥ 50%)
Context	Recommendations will apply to those receiving care in any healthcare setting (for example community, primary care, secondary care, tertiary care). For antibiotics, the committee will consider the evidence in conjunction with considerations regarding antimicrobial resistance patterns (for example ESPAUR report), the safety of the specific antibiotic as determined by any relevant MHRA Drug Safety Update (https://www.gov.uk/drug-safety-update) and Summary of Product characteristics (https://www.medicines.org.uk/emc), and the principle that the use of antibiotics should be limited or optimised where possible. Only the short-term safety of interventions in the treatment of acne vulgaris will be covered. For the long-term safety of interventions, see BNF and MHRA. Relevant legislation and national policy will also inform the guideline [see 'Developing NICE guidelines: the manual' (p. 102)].

Primary outcomes (critical outcomes)	**Critical outcomes**
	Efficacy
	• Clinician-rated improvement at treatment endpoint
	  ○ % change in acne lesion count
	  ○ change or final score on a validated acne severity scale
	We will prioritise for extraction and analysis the mean of the % change in acne lesion count, where reported together with a standard error (or a standard error can be derived). If this is not reported, mean change in lesion counts from baseline will be prioritised, as long as it is reported with a standard error and also mean and standard error of counts at baseline. If this is not reported, the mean counts and standard error at baseline and treatment endpoint will be prioritised, accounting for correlations

Field	Content
	between baseline and final counts, exploring such correlations from studies reporting change, baseline and final scores. In studies where such data on lesion counts are not reported, we will extract data on validated acne severity scale scores, if the latter are available. We will prioritise mean % change in scale if it is reported with a standard error, followed by mean change from baseline if it is reported with a standard error, and baseline mean score and standard error are available. If neither of these are reported we will extract mean scores at baseline and treatment endpoint, accounting for correlations between baseline and final scores using a correlation based on studies that report all of change, baseline and final scores. These two types of data will be synthesised, where appropriate (as explained below), to jointly estimate treatment effects on the two outcomes, to estimate a single clinician-rated measure of outcome, expressing mean % of improvement of acne symptoms. <u>Regarding mean % change in acne lesion count:</u> If summaries for total lesion count are reported, these will be extracted and used in the analysis. In studies that do not report total lesion count, but do report count of different types of lesions, we will estimate the change in total lesion count from reported data, where this is possible. If this is not possible, we will extract the change in lesion count for the following types of lesions in this hierarchy, as a proxy for total lesion count: • All inflammatory lesions (pustules, papules, nodules, cysts) • Sum of any of the types of inflammatory lesions, according to data availability • Pustules • Papules • Nodules • Cysts • Non-inflammatory lesions (comedones) <u>Regarding data on validated acne severity scale scores:</u> We will compare the relative effects on mean % change in acne scale scores and mean % change in acne lesion score in studies that report both. This will be achieved by visual inspection of a scatter plot of relative effect on the scale vs count, by scale, and also by weighted linear regression. Only scales with a sufficiently good visual fit and model fit in the regression will be included. For scales where these relative effects are found to be sufficiently linearly related, we will include the respective extracted scale

Field	Content

	score data in the NMA from studies reporting only this type of outcome, using a bivariate NMA model.
	
	For scales where relative effects measured using the two types of outcomes are not sufficiently linearly related, the extracted data will not be considered in the NMA and studies reporting only symptom scale scores on those scales (and not acne lesion count) will be excluded from the analysis.
	
	Only one acne symptom scale will be used per study. If a study reports data on more than one scale, we will prioritise data from scales according to the extent of the strength of the linear relationship between their relative effects and the relative effects obtained from change in acne lesion count.
	
	Correlations between counts of different types of acne lesions and between acne lesions and acne symptom scales will also be sought in published literature (for example Allen & Smith, 1982).
	
	• Participant-reported improvement at treatment endpoint
	  ○ Change in acne severity or symptoms (e.g. assessed using global acne score)
	
	• Prevention of scarring at any follow-up
	  ○ Final / change in number of scars from baseline
	  ○ Incidence of scarring
	
	Reference:
	Allen BS, Smith JG Jr. Various parameters for grading acne vulgaris. Archives of Dermatology 1982; 118(1): 23-5.

Secondary outcomes (important outcomes)	**Important outcomes** ***Acceptability*** • Treatment discontinuation for any reason (numbers of trial participants "leaving the study early", "leaving the study before treatment completion" or "loss to follow-up") by treatment endpoint ***Tolerability*** • Treatment discontinuation due to side effects by treatment endpoint

Field	Content
	Relapse • Relapse after treatment at follow-up ***Side effects*** 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 (e.g. placebo, no or sham treatment): - Topical treatments, oral antibiotics or combination treatments: skin irritation (e.g. burning or tingling, dryness/irritation, swelling) - Topical retinoids: sensitivity to light - Oral antibiotics: gastrointestinal side effects; thrush candidiasis - Hormonal contraceptives and hormone-modifying agents: breast tenderness; neurological side effects (headache/migraine, mood disturbance, nausea); sexual dysfunction - Hormonal contraceptives: breakthrough bleeding; mood disturbance - Hormone-modifying agents: hepatobiliary side effects. For aldosterone receptor antagonists: renal side effects - Metformin: gastrointestinal side effects - Oral isotretinoin: change in mucosal and/or cutaneous condition (e.g. new chelitis); change in participant's mood (as assessed by score on validated scale); diagnosis of any psychiatric disorder (e.g. depressive disorder); suicidality - Physical treatments: persistent skin redness of 'treated' area; changes in pigmentation (e.g. hypopigmentation) - Chemical peels: heart, kidney or liver damage; infection of 'treated' area - Comedone extraction: infection of 'treated' area; pain of 'treated' area - Energy-based devices: skin irritation
Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into STAR and de-duplicated. As the review question was selected as high priority for health economic analysis, it will be subject to dual weeding and study selection; any discrepancies above 10% of the dual weeded resources will be resolved through discussion between the first and second reviewers or by reference to a third person. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). All data extraction will quality assured by a senior reviewer. Draft excluded studies and evidence tables will be circulated to the Topic Group for their comments. Resolution of disputes will be by discussion between the senior reviewer, Topic Advisor and Chair. An intention-to-treat (ITT) approach will be taken and where possible ITT data will be extracted; if both ITT and completer data

Field	Content
	are reported, the former will be preferred; completer data will be used only if ITT data are not reported**.**
Risk of bias (quality) assessment	Risk of bias of individual studies will be assessed using the relevant version of the Cochrane RoB tool, v2. checklist (i.e. for parallel group or individually-randomised cross-over trials), as described in Developing NICE guidelines: the manual.
Strategy for data synthesis	**Method of analysis** Network meta-analysis Network meta-analysis (NMAs) will be used to synthesise clinician-rated improvement, prevention of scarring, acceptability and tolerability for all eligible interventions that are connected to one or more networks of at least 3 interventions. NMA will be conducted within a Bayesian framework using Markov Chain Monte Carlo simulation techniques implemented in WinBUGS 1.4.3 (Lunn 2000; Spiegelhalter 2003). Non-informative priors will be initially used, but if the data are sparse or there are convergence problems, then we will use evidence-based priors for the between studies standard deviation (Turner 2015, Rhodes 2015). To test whether prior estimates have an impact on the results, two chains with different initial values will be run simultaneously for each analysis. Convergence will be assessed by visually inspecting the mixing of the two chains in the history plots and the Brooks Gelman-Rubin diagram in WinBUGS (Brooks 1998). For the synthesis of dichotomous outcomes (discontinuation due to any reason; discontinuation due to side effects) a binomial likelihood and logit link model will be used (Dias 2013a). The output of this analysis will be expressed as log-odds ratios (LORs) with 95% credible intervals (95% CrI) between all pairs of treatments assessed. For the synthesis of rate data (incidence of scarring) a Poisson likelihood and log link will be used. The output of this analysis will be expressed as log-rate ratios (LRRs) with 95% CrIs between all pairs of treatments assessed. For the synthesis of continuous data (mean of the % change in the total lesion count) a normal likelihood will be used with an identity link for the proportionate reduction in counts at treatment endpoint relative to baseline. The output of this analysis will be expressed, for each treatment relative to the reference treatment, as the difference in the mean percentage reduction in total lesions between baseline and treatment endpoint. If some studies do not report data on total lesion counts, a bivariate NMA model will be fitted which relates the treatment effects on a clinician-related acne symptom scale to treatment effects on the mean proportionate reduction from baseline. We will also evaluate the ranking of each treatment and 95% CrI in each analysis, where a rank of 1 indicates best treatment. The goodness of fit of each model will be tested by comparing the posterior mean of the residual deviance, which measures the magnitude of the differences between the observed data and the model predictions of the data, with the number of data points in the model (Dempster 1997). Smaller values of the residual deviance are preferred, and in a well-fitting model the posterior mean

Field	Content
	residual deviance should be close to the number of data points in the analysis (each study arm contributes one data point) (Spiegelhalter 2002). Models will also be compared using the deviance information criterion (DIC), a measure of model fit that is equal to the sum of the posterior mean deviance and the effective number of parameters, thus penalising model fit for model complexity; lower values are preferred and typically differences of at least 3 points are considered meaningful (Dias 2013a; Spiegelhalter 2002). The posterior median between-study standard deviation, which measures the heterogeneity of treatment effects estimated by trials within contrasts, will also be used to compare models. Inconsistency between direct and indirect evidence will be explored by comparing the fit of a model assuming consistency with a model which allowed for inconsistency (also known as an unrelated mean effects model (Dias 2013b). Deviance plots, in which the posterior mean deviance of the individual data points in the inconsistency model are plotted against their posterior mean deviance in the consistency model, will be inspected in order to identify studies which may have contributed to loops of evidence where inconsistency may be present. If these analyses identify potential inconsistency, further checks will be conducted using a node-split approach implemented in R using the gemtc package in R. This method permits the direct and indirect evidence contributing to an estimate of a relative effect to be split and compared (Dias 2013b; van Valkenhoef & Kuiper, 2016). If we find evidence of inconsistency, studies contributing to loops of evidence where there may be inconsistency will be checked for data accuracy and assessment of study inclusion will be revisited against inclusion/exclusion criteria. Baseline characteristics will be checked to identify any differences in effect modifiers across studies in loops identified as potentially inconsistent. Analyses will be repeated if corrections in the data extraction or study inclusion are made. If an important effect modifier is identified, then this may be explored in subgroup analyses if sufficient evidence is available. However, if evidence of inconsistency is still present following data corrections, revisiting inclusion criteria, exploring effect modification, no further studies will be excluded from the analysis, as their results cannot be considered as less valid than those of other studies solely because of the inconsistency findings. The presence of inconsistency in the NMA will be highlighted and results will be interpreted accordingly. Sensitivity analysis: If there is sufficient evidence, we will explore bias adjustment models, where evidence from studies at high or unclear risk of bias will be down-weighted (Dias 2010; Welton 2009). Appraisal of methodological quality of the NMA: To test the robustness of the treatment recommendations based on the NMA to potential biases or sampling variation in the included evidence, we will undertake threshold analyses (Phillippo 2019). These will be carried out at two levels: (i) at a study level, assessing the influence of individual study estimates on the conclusion of the analysis and (ii) at a contrast level, where the influence of the combined evidence on each treatment contrast is considered (Caldwell 2016; Phillippo 2018; Phillippo 2019).

Field	Content
	Pairwise meta-analysis Pairwise meta-analysis will be used for all outcomes not included in NMA, i.e. participant-reported improvement, relapse and side effects. 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. Heterogeneity in the effect estimates of the individual studies will be assessed using the I2 statistic. I2 values of greater than 50% and 80% will be considered as significant and very significant heterogeneity, respectively. Heterogeneity will be explored as appropriate using sensitivity analyses and pre-specified subgroup analyses. If heterogeneity cannot be explained through subgroup analysis then a random effects model will be used for meta-analysis, or the data will not be pooled. 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: http://www.gradeworkinggroup.org/ **References** Brooks SP, Gelman A (1998) Alternative methods for monitoring convergence of iterative simulations. Journal of Computational and Graphical Statistics, 7, 434-455. Caldwell DM, Ades AE, Dias S, Watkins S, Li T, Taske N, Naidoo B, Welton NJ (2016) A threshold analysis assessed the credibility of conclusions from network meta-analysis. Journal of Clinical Epidemiology, 80, 68-76. Dempster A (1997) The direct use of likelihood for significance testing. Statistics and Computing, 7, 247-252. Dias S, Welton NJ, Marinho VCC, Salanti G, Higgins JPT, Ades AE (2010) Estimation and adjustment of bias in randomised evidence by using Mixed Treatment Comparison Meta-analysis. Journal of the Royal Statistical Society (A), 173(3), 613-629. Dias S, Sutton AJ, Ades AE, Welton NJ (2013a) Evidence synthesis for decision making 2: a generalized linear modeling framework for pairwise and network meta-analysis of randomized controlled trials. Medical Decision Making, 33, 607-617. Dias S, Welton NJ, Sutton AJ, Caldwell DM, Lu G, Ades AE (2013b) Evidence synthesis for decision making 4: inconsistency in

Field	Content
	networks of evidence based on randomized controlled trials. Medical Decision Making, 33, 641-656. Lunn DJ, Thomas A, Best N, Spiegelhalter D (2000) WinBUGS-A Bayesian modelling framework: Concepts, structure, and extensibility. Statistics and Computing, 10, 325-337. Phillippo DM, Dias S, Ades AE, Didelez V, Welton NJ (2018) Sensitivity of treatment recommendations to bias in network meta-analysis. Journal of the Royal Statistical Society: Series A, 181, 843-867. Phillippo DM, Dias S, Welton NJ, Caldwell DM, Taske N, Ades AE (2019) Threshold Analysis as an Alternative to GRADE for Assessing Confidence in Guideline Recommendations Based on Network Meta-analyses. Annals of Internal Medicine, 170, 538-546. Rhodes KM, Turner RM, Higgins JPT (2015) Predictive distributions were developed for the extent of heterogeneity in meta-analyses of continuous outcome data. Journal of Clinical Epidemiology, 68, 52-60. Spiegelhalter DJ, Best NG, Carlin BP, van der Linde A (2002) Bayesian measures of model complexity and fit. Journal of the Royal Statistical Society: Series B, 64, 583-616. Spiegelhalter D, Thomas A, Best N, Lunn DJ (2003) WinBUGS user manual: version 1.4. Cambridge: MRC Biostatistics Unit. Turner RM, Jackson D, Wei Y, Thompson SG, Higgins JPT (2015) Predictive distributions for between-study heterogeneity and simple methods for their application in Bayesian meta-analysis. Statistics in Medicine, 34, 984-998. van Valkenhoef G, Kuiper J (2016) gemtc: Network Meta-Analysis Using Bayesian Methods. R package version 0.8-2. Available from: https://CRAN.R-project.org/package=gemtc Welton NJ, Ades AE, Carlin, JB, Altman DG, Sterne JAC (2009) Models for potentially biased evidence in meta-analysis using empirically based priors. Journal of the Royal Statistical Society (A), 172(1), 119-136.
Analysis of sub-groups	**Severity** For all outcomes, we will conduct separate analyses for people with

Field	Content
	• mild to moderate acne vulgaris • moderate to severe acne vulgaris. We will categorise studies according to level of severity as defined in each study. The committee will be consulted to classify a study to the appropriate network/analysis if acne severity of included participants is described as moderate or it is unclear (for example it includes participants on basis of lesion counts). The committee agreed the following criteria to categorise studies into one of two severity groups, when the study population is described as having moderate acne or if the level of severity is unclear: • If the number of nodules in every study participant is at least 3, the study population will be categorised as having moderate to severe acne. • If study participants have only non-inflammatory lesions (regardless of their number) and no inflammatory lesions, the study population will be categorised as having mild to moderate acne. • If all study participants have fewer than 35 inflammatory lesions each, the study population will be categorised as having mild to moderate acne. • If all study participants have ≥ 35 inflammatory lesions each, the study population will be categorised as having moderate to severe acne. • If the number of inflammatory lesions varies across the study participants, and the mean number of inflammatory lesions at baseline is ○ ≤ 30, the study population will be categorised as having mild to moderate acne ○ ≥40, the study population will be categorised as having moderate to severe acne ○ above 30 but below 40, the study will be excluded as the population is not possible to assign to a mild to moderate or moderate to severe level. • If a study does not report the mean number of inflammatory lesions at baseline, it will be excluded. • If a study includes all ranges of severity, from mild to severe, without providing sub-group analyses by level of acne severity, it will be excluded. **Sex** Separate NMAs will be run for decisions regarding the male and female populations, in accordance with data reported in the included studies, where only appropriate interventions for each sex are included in the network (for example, excluding hormonal contraceptives for males). We assume there is no interaction between sex and treatment effects for interventions that are suitable for both sexes. **Age** If possible, a random effects meta-regression according to age will be conducted for NMA of efficacy (% change in acne lesion

Field	Content	
	count), to specify outcomes for people ≤25 years of age and those >25 years of age. In order to include studies that do not report results by age-group, we will need to estimate proportion of participants below/above 25 years of age in studies of mixed population that don't report results by age. If this is not reported, proportions in age group can be approximated if the study reports age ranges, mean age and standard deviation, median age and quartile range, etc. This requires an assumption as to the distribution of age in the study population, which can be based on inspection of the reported summaries (normal if evidence of symmetry or log-normal if skewed). We will perform this analysis by age only if at least 90% of the studies meeting inclusion criteria provide sufficient information that would allow us to estimate the proportion of participants >25 and ≤25 years of age. If we are able to follow this approach, we will exclude the remaining studies that do not provide this information. If <90% of studies meeting inclusion criteria provide relevant information on age, then we will include all studies, irrespective of the age of their population, in the NMA of efficacy (% change in acne lesion count), but will not perform meta-regression.	
Type and method of review	☒	Intervention
	☐	Diagnostic
	☐	Prognostic
	☐	Qualitative
	☐	Epidemiologic
	☐	Service Delivery
	☐	Other (please specify)
Language	English	
Country	England	
Anticipated or actual start date	20 October 2019	
Anticipated completion	13 January 2021	

Field	Content		
date			
Stage of review at time of this submission	**Review stage**	**Started**	**Completed**
	Preliminary searches	☑	☑
	Piloting of the study selection process	☑	☑
	Formal screening of search results against eligibility criteria	☑	☑
	Data extraction	☑	☑
	Risk of bias (quality) assessment	☑	☑
	Data analysis	☑	☑
Named contact	**5a. Named contact** National Guideline Alliance **5b. Named contact e-mail** AcneManagement@nice.org.uk **5e. Organisational affiliation of the review** National Institute for Health and Care Excellence (NICE) and National Guideline Alliance		
Review team members	National Guideline Alliance		
Funding sources/sponsor	This systematic review is being completed by the National Guideline Alliance, which is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists. NICE funds the National Guideline Alliance to develop guidelines for those working in the NHS, public health, and social care in England.		
Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each		

Field	Content	
	guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.	
Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/gid-ng10109/documents/committee-member-list NICE Guidelines Technical Support Unit: Professor Nicky J Welton, NICE Guidelines Technical Support Unit, Department of Population Health Sciences, Bristol Medical School Miss Caitlin Daly, NICE Guidelines Technical Support Unit, Department of Population Health Sciences, Bristol Medical School	
Other registration details	Not applicable	
Reference/URL for published protocol	https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=154100	
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. • Peer-reviewed publications	
Keywords	Acne; acne severity; chemical peels; energy-based devices; hormone therapy; isotretinoin; laser therapy; light therapy; management; network meta-analysis; oral antibiotics; physical; systematic review; topical antibiotics; topical retinoids; treatment.	
Details of existing review of same topic by same authors	Not applicable	
Current review status	☒	Ongoing

Field	Content	
	☐	Completed but not published
	☐	Completed and published
	☐	Completed, published and being updated
	☐	Discontinued
Additional information	Not applicable	
Details of final publication	www.nice.org.uk	

CrI: credibility interval; NICE: National Institute for Health and Care Excellence; NMA: network meta-analysis; RCT: randomised controlled trial

Appendix B - Literature search strategies

Literature search strategies for review question: What is the effectiveness and acceptability of interventions for the treatment of moderate to severe acne (side effects and participant reported improvement)?

Clinical search

Topical interventions (including topical retinoids)

Date of initial search: 07/08/2019

Additional terms added and searched: 10/09/2019

Last searched: 07/05/2020

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

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

#	Searches
1	exp Acne Vulgaris/ use ppez
2	exp acne/ use emczd
3	acne.tw.
4	or/1-3
5	exp topical antiinfective agent/ use emczd
6	exp Anti-Infective Agents, Local/ use ppez
7	5 or 6
8	exp antibiotic agent/ use emczd
9	exp Anti-Bacterial Agents/ use ppez
10	exp anthelmintic agent/ use emczd
11	exp Anthelmintics/ use ppez
12	(antibiotic* or anti biotic* or anti bacteri* or antibacteri* or bacteriocid*).tw.
13	(anthelminti* or antihelmint?i* or anti-helmint?i* or antiparasit* or anti-parasit* or vermifug*).tw.
14	adapalene/
15	aluminum oxide/ use emczd
16	amoxicillin/
17	ampicillin/
18	avermectin/ use emczd
19	azelaic acid/
20	benzoyl peroxide plus clindamycin/ use emczd
21	benzoyl peroxide/
22	(Benzoyl Peroxide/ and Clindamycin/) use ppez
23	cefaclor/
24	cefadroxil/
25	cefalexin/ use emczd
26	Cephalexin/ use ppez
27	cefixime/
28	cefotaxime/
29	cefradine/ use emczd
30	Cephradine/ use ppez
31	ceftaroline/ use emczd
32	ceftazidime/
33	ceftriaxone/
34	cefuroxime/
35	chlorhexidine gluconate/
36	clarithromycin/
37	clindamycin/
38	dapsone/
39	doxycycline/
40	erythromycin/
41	erythromycin plus isotretinoin/ use emczd
42	flucloxacillin/ use emczd
43	Floxacillin/ use ppez
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 az?laic acid or benzylpenicillin or benzyl penicillin or benzoyl peroxide or cefaclor or cefadroxil or cefalexin or cephalexin or cefixime or cefotaxime or cefradine or ceftaroline or ceftazidime or ceftriaxone or cefuroxime or cephalexin or cephalosporin* or cephamycin* or cephradine or chlorhexidine digluconate or chlorhexidine gluconate or clarithromycin or clindamycin or dapsone or diaminodiphenyl sulfone or doxycyclin* or erythromycin or floxacillin or flucloxacillin or fucidin or fusidic acid or fusidate sodium or sodium fusidate or germolene or isotretinoi* or ivermectin or lincosamide* or lymecycline or macrolide* or metronidazole or minocycline or nadifloxacin or niacinamide or nicotinamide or nitroimidazole or ozenoxacin or oxytetracyline or penicillin* or phenol or phenoxymethylpenicillin or piperacillin or pleuromutilin or praziquantel or cysticide or pseudomonic acid or mupirocin or quinoderm or quinolon* or retapamulin or retinoi* or retinol or tazarotene or temocillin or tetracyclin* or ticarcillin or tretinoin or triclocarban or triclosan or triclozan or trimethoprim or vitamin a or vitamin b3 or zinc acetate).tw.
80	or/7-79
81	(topical or topically or cream? or emulsi* or gel? or foam? or ointment* or solution? or lotion? or pad?).tw.
82	(ointment/ or exp gel/) use emczd
83	(Ointments/ or exp Gels/) use ppez
84	skin cream/
85	(cutaneous drug administration/ or topical drug administration/) use emczd
86	(Administration, Topical/ or Administration, Cutaneous/) use ppez
87	topical drug administration.fs.
88	(cutaneous or dermal or skin or transcutaneous or transdermal or percutaneous).tw.
89	or/81-88
90	4 and 80 and 89
91	limit 90 to english language
92	Letter/ use ppez
93	letter.pt. or letter/ use emczd
94	note.pt.
95	editorial.pt.
96	Editorial/ use ppez
97	News/ use ppez
98	exp Historical Article/ use ppez
99	Anecdotes as Topic/ use ppez
100	Comment/ use ppez
101	Case Report/ use ppez
102	case report/ or case study/ use emczd
103	(letter or comment*).ti.
104	or/92-103
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

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

#	Searches
#1	MeSH descriptor: [Acne Vulgaris] explode all trees
#2	acne:ti,ab
#3	#1 or #2
#4	(topical or topically or cream or creams or emulsi* gel or gels or foam or foams or ointment* or solution or solutions or lotion or lotions or pad or pads):ti,ab
#5	MeSH descriptor: [Ointments] this term only
#6	MeSH descriptor: [Gels] explode all trees
#7	MeSH descriptor: [Skin Cream] this term only
#8	MeSH descriptor: [Administration, Topical] this term only
#9	MeSH descriptor: [Administration, Cutaneous] this term only
#10	(cutaneous or dermal or skin or transcutaneous or transdermal or percutaneous):ti,ab
#11	{or #4-#10}
#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 antithelminti* or anti-helminthi* or anti-helminti* or antiparasit* or anti-parasit* or vermifug*):ti,ab
#16	MeSH descriptor: [Adapalene] this term only
#17	MeSH descriptor: [Aluminum Oxide] this term only
#18	MeSH descriptor: [Amoxicillin] this term only
#19	MeSH descriptor: [Ampicillin] this term only
#20	MeSH descriptor: [Benzoyl Peroxide] this term only
#21	MeSH descriptor: [Cefaclor] this term only
#22	MeSH descriptor: [Cefadroxil] this term only
#23	MeSH descriptor: [Cephalexin] this term only
#24	MeSH descriptor: [Cefixime] this term only
#25	MeSH descriptor: [Cefotaxime] this term only
#26	MeSH descriptor: [Cephradine] this term only
#27	MeSH descriptor: [Ceftazidime] this term only
#28	MeSH descriptor: [Ceftriaxone] this term only
#29	MeSH descriptor: [Cefuroxime] this term only
#30	MeSH descriptor: [Clarithromycin] this term only
#31	MeSH descriptor: [Clindamycin] this term only
#32	MeSH descriptor: [Dapsone] this term only
#33	MeSH descriptor: [Doxycycline] this term only
#34	MeSH descriptor: [Erythromycin] this term only
#35	MeSH descriptor: [Floxacillin] this term only
#36	MeSH descriptor: [Fusidic Acid] this term only
#37	MeSH descriptor: [Isotretinoin] this term only
#38	MeSH descriptor: [Ivermectin] this term only
#39	MeSH descriptor: [Lymecycline] this term only
#40	MeSH descriptor: [Minocycline] this term only
#41	MeSH descriptor: [Mupirocin] this term only
#42	MeSH descriptor: [Niacinamide] this term only
#43	MeSH descriptor: [Oxytetracycline] this term only
#44	MeSH descriptor: [Penicillin G] this term only
#45	MeSH descriptor: [Penicillin V] this term only
#46	MeSH descriptor: [Phenol] this term only
#47	MeSH descriptor: [Piperacillin] this term only
#48	MeSH descriptor: [Praziquantel] this term only
#49	MeSH descriptor: [Vitamin A] this term only
#50	MeSH descriptor: [Tetracycline] this term only
#51	MeSH descriptor: [Ticarcillin] this term only
#52	MeSH descriptor: [Tretinoin] this term only
#53	MeSH descriptor: [Trimethoprim] this term only
#54	MeSH descriptor: [Zinc Acetate] this term only
#55	(adapalene or aluminum oxide or ampicillin or amoxicillin or avermectin or azaelaic acid or azelaic acid or benzylpenicillin or benzyl penicillin or benzoyl peroxide or cefaclor or cefadroxil or cefalexin or cephalexin or cephalosporin* or cephamycin* or cefixime or cefotaxime or cefradine or ceftaroline or ceftazidime or ceftriaxone or cefuroxime or cephalexin or cephradine or chlorhexidine digluconate or chlorhexidine gluconate or clarithromycin or clindamycin or dapsone or diaminodiphenyl sulfone or doxycyclin* or erythromycin or floxacillin or flucloxacillin or fucidin or fusidic acid or fusidate sodium or sodium fusidate or germolene or isotretinoi* or ivermectin or lincosamide* or lymecycline or macrolide* or minocycline or mupirocin or pseudomonic acid or nadifloxacin or niacinamide or nicotinamide or nitroimidazole or ozenoxacin or oxytetracyline or penicillin* or phenol or phenoxymethylpenicillin or piperacillin or pleuromutilin or praziquantel or cysticide or quinoderm or quinolone* or retapamulin or retino* or retinol or temocillin or tetracyclin* or ticarcillin or tretinoin or trimethoprim or vitamin a or zinc acetate):ti,ab
#56	{or #12-#55}
#57	#3 and #11 and #56

Oral antibiotics and oral isotretinoin

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

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

#	Searches
1	exp Acne Vulgaris/ use ppez
2	exp acne/ use emczd
3	acne.tw.
4	or/1-3
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 cefdaloxime or cefdinir or cefditoren or cefepime or cefetamet or cefixime or cefmenoxime or cefmetazole or cefminox or cefodizime or cefonicid or cefoperazone or cefoperazone or ceforanide or cefotaxime or cefotetan or cefotiam or cefozopran or cefpiramide or cefpirome or cefpodoxime or cefprozil or cefquinome or cefradine or cefroxadine or cefsulodin or ceftaroline fosamile or ceftazidime or ceftazidime or cefteram or ceftezole or ceftibiprole or ceftibuten or ceftiolene or ceftolozane or ceftolozane or ceftraroline or ceftriaxone or cefuroxime or cefuzonam or cephamycin or depfimizole or flomoxef or latamoxef or oxacephem).tw.
32	dapsone.tw.
33	(isotretinoi* or iso tretinoin or isoretinoin or isotren or isotrex* or accutane or roaccutan* or roaccuttan* or roacuttan* or roacutan* or retinoic acid).tw.
34	(lincosamide* or clindamycin or lincomycine or linkomycine).tw.
35	(macrolide* or azithromycin or carbomycin a or clarithromycin or erythromycin or fidaxomicin or josamycin or kitasamycin or midecamycin or oleandomycin or roxithromycin or solithromycin or spiramycin or telithromycin or troleandomycin).tw.
36	(monobactam* or mono- bactam* or aztreonam).tw.
37	(penicillin* or almecillin or amoxicillin or ampicillin or azlocillin or bacampicillin or benzathine benzylpenicillin or benzylpenicillin sodium or carbenicillin or carindacillin or cloxacillin or co-amoxiclav or co-fluampicil or co-trimoxazole or dicloxacillin or epicillin or flucloxacillin or hetacillin or mecillinam or metampicillin or methicillin or mezlocillin or nafcillin or oxacillin or phenoxymethylpenicillin or piperacillin or pivampicillin or pivmecillinam hydrochloride or procaine benzylpenicillin or sultamicillin or talampicillin or temocillin or ticarcillin).tw.
38	(quinolone* or balofloxacin or besifloxacin or ciprofloxacine or clinafloxacin or delafloxacin or enoxacin or fleroxacin or gatifloxacin or gemifloxacin or grepafloxacin or levofloxacin or lomefloxacin or moxifloxacin or nadifloxacin or norfloxacin or ofloxacin or oxolinic acid or ozenoxacin or pazufloxacin or pefloxacin or prulifloxacin or rosoxacin or rufloxacin or sitafloxacin or sparfloxacin or temafloxacin or tosufloxacin).tw.
39	(tetracylcline* or chlortetracycline or demeclocycline or doxycycline or eravacycline or lymecycline or methacycline or minocycline or omadacycline or oxytetracycline or rolitetracycline or sarecycline or tetracycline or tigecycline).tw.
40	trimethoprim.tw.
41	or/5-40
42	oral drug administration/ use emczd
43	Administration, Oral/ use ppez
44	oral drug administration.fs.
45	(oral* or per os).tw.
46	or/42-45
47	4 and 41 and 46
48	Letter/ use ppez
49	letter.pt. or letter/ use emczd
50	note.pt.
51	editorial.pt.
52	Editorial/ use ppez
53	News/ use ppez
54	exp Historical Article/ use ppez
55	Anecdotes as Topic/ use ppez
56	Comment/ use ppez
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

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

#	Searches
#1	MeSH descriptor: [Acne Vulgaris] explode all trees
#2	acne:ti,ab
#3	#1 or #2
#4	MeSH descriptor: [Anti-Bacterial Agents] explode all trees
#5	(antibiotic* or "anti biotic*" or "anti bacteri*" or antibacteri* or bacteriocid*):ti,ab
#6	MeSH descriptor: [Amoxicillin] this term only
#7	MeSH descriptor: [Ampicillin] this term only
#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 cephalexin or cefixime or cefotaxime or cephotaxim* or cefradine or cephradine or ceftaroline or ceftazidime or ceftriaxone or cefuroxime or chlortetracyline or clarithromycin or clindamycin or cloxacillin or co amoxiclav or coamoxiclav or co fluampcil or cofluampcil or co trimoxazole or cotrimoxazole):ti,ab
#27	MeSH descriptor: [Demeclocycline] this term only
#28	MeSH descriptor: [Dicloxacillin] this term only
#29	MeSH descriptor: [Doripenem] this term only
#30	MeSH descriptor: [Doxycycline] this term only
#31	MeSH descriptor: [Ertapenem] this term only
#32	MeSH descriptor: [Erythromycin] this term only
#33	MeSH descriptor: [Fidaxomicin] this term only
#34	MeSH descriptor: [Floxacillin] this term only
#35	(demeclocycline or dicloxacillin or doripenem or doxycycline or epicillin or eravacycline or ertapenem or erythromycin or fidaxomicin or floxacillin or flucloxacillin):ti,ab
#36	MeSH descriptor: [Imipenem] this term only
#37	MeSH descriptor: [Cilastatin, Imipenem Drug Combination] this term only
#38	MeSH descriptor: [Josamycin] this term only
#39	MeSH descriptor: [Kitasamycin] this term only
#40	MeSH descriptor: [Lymecycline] this term only
#41	MeSH descriptor: [Meropenem] this term only
#42	MeSH descriptor: [Methacycline] this term only
#43	MeSH descriptor: [Methicillin] this term only
#44	MeSH descriptor: [Mezlocillin] this term only
#45	MeSH descriptor: [Miocamycin] this term only
#46	MeSH descriptor: [Nafcillin] this term only
#47	(hetacillin or imipenem or isotretinoi* or josamycin* or kitasamycin or leucomycin or lymecycline or meropenem or metampicillin or methampicillin or metacycline or methacycline or methicillin or mezlocillin or midecamycin or minocycline or miocamycin* or miokamycin* or nafcillin):ti,ab
#48	MeSH descriptor: [Oleandomycin] this term only
#49	MeSH descriptor: [Oxacillin] this term only
#50	MeSH descriptor: [Oxytetracycline] this term only
#51	MeSH descriptor: [Penicillin V] this term only
#52	MeSH descriptor: [Piperacillin] this term only
#53	MeSH descriptor: [Piperacillin, Tazobactam Drug Combination] this term only
#54	MeSH descriptor: [Amdinocillin Pivoxil] this term only
#55	MeSH descriptor: [Rolitetracycline] this term only
#56	MeSH descriptor: [Roxithromycin] this term only
#57	MeSH descriptor: [Spiramycin] this term only
#58	MeSH descriptor: [Talampicillin] this term only
#59	MeSH descriptor: [Tetracycline] this term only
#60	MeSH descriptor: [Ticarcillin] this term only
#61	MeSH descriptor: [Tigecycline] this term only
#62	MeSH descriptor: [Trimethoprim] this term only
#63	MeSH descriptor: [Troleandomycin] this term only
#64	(oleandomycin or omadacycline or "PTK-0796" or oxacillin* or oxytetracycline or panipenem or betamipron or carbenin or phenoxymethylpenicillin or "penicillin v" or piperacillin or pivmeillinam or amdinocillin pivoxil or retinoi* or rolitetracycline or roxithromycin or sarecycline or solithromycin or spiramycin or talampicillin or tebipenem or telithromycin or temocillin or tetracylin* or ticarcillin or timentin or tigecycline or trimethoprim or troleandomycin):ti,ab
#65	{or #4-#64}
#66	#3 and #65
#67	MeSH descriptor: [Administration, Oral] explode all trees
#68	(oral or per os):ti,ab
#69	#67 or #68

#	Searches
#70	#66 and #69

Hormonal interventions

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

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

#	Searches
1	exp Acne Vulgaris/ use ppez
2	exp acne/ use emczd
3	acne.tw.
4	or/1-3
5	exp aldosterone antagonist/ use emczd
6	exp Mineralocorticoid Receptor Antagonists/ use ppez
7	spironolactone/
8	hydroflumethiazide plus spironolactone/ use emczd
9	canrenone/
10	eplerenone/
11	furosemide plus spironolactone/ use emczd
12	(aldactone or spironolactone or canrenone or co-flumactone or coflumactone or eplerenon* or furosemide).tw.
13	or/5-12
14	exp alpha adrenergic receptor blocking agent/ use emczd
15	exp Adrenergic alpha-Antagonists/ use ppez
16	alfuzosin/ use emczd
17	doxazosin/
18	indoramin/
19	prazosin/
20	tamsulosin/
21	dutasteride plus tamsulosin/ use emczd
22	solifenacin plus tamsulosin/ use emczd
23	terazosin/ use emczd
24	(alfuzosin or doxazosin or uroprost or indoramin or prazosin or tamsulosin or terazosin).tw.
25	or/14-24
26	exp steroid 5alpha reductase inhibitor/ use emczd
27	exp 5-alpha Reductase Inhibitors/ use ppez
28	dutasteride/
29	finasteride/
30	(5a reductase inhibitor* or 5-alpha reductase inhibitor* or dutastaride or finasteride).tw.
31	or/26-30
32	exp antiandrogen/ use emczd
33	exp Androgen Antagonists/ use ppez
34	metformin/
35	abiraterone acetate/
36	apalutamide/ use emczd
37	bicalutamide/ use emczd
38	cyproterone acetate plus ethinylestradiol/ use emczd
39	cyproterone acetate/
40	enzalutamide/ use emczd
41	flutamide/
42	(antiandrogen* or anti-androgen* or androgen antagonist* or abiraterone acetate or apalutamide or bicalutamide or cocyprindiol or co-cyprindiol or cyproterone acetate or enzalutamide or flutamide or metformin).tw.
43	or/32-42
44	exp oral contraceptive agent/ use emczd
45	exp Contraceptives, Oral, Combined/ use ppez
46	exp gestagen/ use emczd
47	exp Progestins/ use ppez
48	(chlormadinone acetate plus ethinylestradiol/ or desogestrel plus ethinylestradiol/ or dienogest plus ethinylestradiol/ or drospirenone plus ethinylestradiol/ or dydrogesterone plus estradiol/ or estradiol plus levonorgestrel/ or estradiol plus nomegestrol acetate/ or estradiol plus norethisterone acetate/ or ethinylestradiol plus etonogestrel/ or ethinylestradiol plus gestodene/ or ethinylestradiol plus levonorgestrel/ or ethinylestradiol plus norelgestromin/ or ethinylestradiol plus norethisterone/ or ethinylestradiol plus norgestimate/) use emczd
49	Ethinyl Estradiol-Norgestrel Combination/ use ppez
50	(Ethinyl Estradiol/ use ppez and (Chlormadinone Acetate/ or Desogestrel/ or Levonorgestrel/ or Norethindrone/ or Norgestrel/)) use ppez
51	(Mestranol/ and (Norethindrone/ or Norethynodrel/)) use ppez
52	(Estradiol/ and (Dydrogesterone/ or Levonorgestrel/ or Medroxyprogesterone Acetate/ or Norethindrone/)) use ppez
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 psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
112	cochrane.jw.
113	((pool* or combined) adj2 (data or trials or studies or results)).ab.
114	(or/101-103,105,107-112) use ppez
115	(or/103-106,108-113) use emczd
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

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

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

Physical interventions

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

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

#	Searches
1	exp Acne Vulgaris/ use ppez

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

#	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 psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
106	cochrane.jw.
107	((pool* or combined) adj2 (data or trials or studies or results)).ab.
108	(or/95-97,99,101-106) use ppez
109	(or/97-100,102-107) use emczd
110	or/108-109
111	network meta-analysis/
112	((network adj (MA or MAs)) or (NMA or NMAs)).tw.
113	((indirect or mixed or multiple or multi-treatment* or simultaneous) adj1 comparison*).tw.
114	or/111-113
115	94 or 110 or 114
116	86 and 115

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

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

Health economics search

Date of initial search: 12/12/2018

Date of updated search: 06/05/2020

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

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

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

#	Searches
16	exp economic evaluation/
17	exp health care cost/
18	exp fee/
19	budget/
20	funding/
21	(or/15-20) use emez
22	budget*.ti,ab.
23	cost*.ti.
24	(economic* or pharmaco?economic*).ti.
25	(price* or pricing*).ti,ab.
26	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
27	(financ* or fee or fees).ti,ab.
28	(value adj2 (money or monetary)).ti,ab.
29	or/22-27
30	14 or 21 or 29
31	4 and 30
32	limit 31 to english language
33	limit 32 to yr="2004 -Current"
34	remove duplicates from 33

Date of initial search: 12/12/2018

Date of updated search: 06/05/2020

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

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

Search for health utility values

Date of initial search: 29/01/2019

Date of updated search: 06/05/2020

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

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

#	Searches
1	exp Acne Vulgaris/ use ppez
2	exp acne/ use emez
3	acne.tw.
4	or/1-3
5	Quality-Adjusted Life Years/ use ppez
6	Sickness Impact Profile/
7	quality adjusted life year/ use emez
8	"quality of life index"/ use emez
9	(quality adjusted or quality adjusted life year*).tw.
10	(qaly* or qal or qald* or qale* or qtime* or qwb* or daly).tw.
11	(illness state* or health state*).tw.
12	(hui or hui2 or hui3).tw.
13	(multiattibute* or multi attribute*).tw.
14	(utilit* adj3 (score*1 or valu* or health* or cost* or measur* or disease* or mean or gain or gains or index*)).tw.
15	utilities.tw.
16	(eq-5d* or eq5d* or eq-5* or eq5* or euroqual* or euro qual* or euroqual 5d* or euro qual 5d* or euro qol* or euroqol*or euro quol* or euroquol* or euro quol5d* or euroquol5d* or eur qol* or eurqol* or eur qol5d* or eurqol5d* or eur?qul* or eur?qul5d* or euro* quality of life or european qol).tw.
17	(euro* adj3 (5 d* or 5d* or 5 dimension* or 5dimension* or 5 domain* or 5domain*)).tw.
18	(sf36 or sf 36 or sf thirty six or sf thirtysix).tw.
19	(time trade off*1 or time tradeoff*1 or tto or timetradeoff*1).tw.
20	Quality of Life/ and ((quality of life or qol) adj (score*1 or measure*1)).tw.
21	Quality of Life/ and ec.fs.
22	Quality of Life/ and (health adj3 status).tw.
23	(quality of life or qol).tw. and Cost-Benefit Analysis/ use ppez

#	Searches
24	(quality of life or qol).tw. and cost benefit analysis/ use emez
25	((qol or hrqol or quality of life).tw. or *quality of life/) and ((qol or hrqol* or quality of life) adj2 (increas* or decreas* or improv* or declin* or reduc* or high* or low* or effect or effects or worse or score or scores or change*1 or impact*1 or impacted or deteriorat*)).ab.
26	Cost-Benefit Analysis/ use ppez and cost-effectiveness ratio*.tw. and (cost-effectiveness ratio* and (perspective* or life expectanc*)).tw.
27	cost benefit analysis/ use emez and cost-effectiveness ratio*.tw. and (cost-effectiveness ratio* and (perspective* or life expectanc*)).tw.
28	*quality of life/ and (quality of life or qol).ti.
29	quality of life/ and ((quality of life or qol) adj3 (improv* or chang*)).tw.
30	quality of life/ and health-related quality of life.tw.
31	Models, Economic/ use ppez
32	economic model/ use emez
33	or/5-32
34	4 and 33
35	limit 34 to english language
36	limit 35 to yr="2004 -Current"
37	remove duplicates from 36

Appendix C – Clinical evidence study selection

Clinical study selection for review question: What is the effectiveness and acceptability of interventions for the treatment of moderate to severe acne (side effects and participant reported improvement)?

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

Figure 1: Study selection flow chart

Appendix D - Evidence tables

Evidence tables for review question: What is the effectiveness and acceptability of interventions for the treatment of moderate to severe acne (side effects and participant reported improvement)?

Table 4: Evidence table

Study details	Participants	Interventions	Outcomes and results	Comments
Study details **Reference** Akman, A. D., C.,Senturk, M.,Koc, C. K.,Soyturk, D.,Alpsoy, E.Treatment of acne with intermittent and conventional isotretinoin: A randomized, controlled multicenter study. 2007. Archives of Dermatological Research **Trial ID** Akman 2007 **Country** Turkey **Study type** RCT **Source of funding** Supported by Akdeni University Scientific Research Projects Unit. ***Analysis method*** **Intention to treat or completers analysis** completers	N=66 ***Characteristics*** **Sex** mixed **age (mean±SD)** 20.97±6.02 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** US FDA **Inclusion details** Participants with FDA global grade 2 (moderate) and 3 to 4 (severe) acne who had not responded to conventional antibiotic treatment or had rapidly relapsed after conventional treatment. Participants receiving any conventional treatments underwent an appropriate washout period before study treatment began. **Exclusion details** Participants who had acne conglobata, acne fulminans or systemic disorders requiring any treatment. ***Number included***	***Interventions*** **Treatment duration (weeks)** 26 **Treatment duration category** 24+ weeks **Number of arms** 3 **Split face design** No **Intervention: arm 1** ISO<120.Other=0.5 (first 10 days, every month) **Intervention: arm 2** ISO<120.Other=0.5 (every day for month 1 then first 10 days of every month) **Intervention: arm 3** ISO<120.Daily=0.5 **Coded intervention: arm 1** ISO<120.Other=0.5-oral **Coded intervention: arm 2** ISO<120.Other=0.5-oral **Coded intervention: arm 3**	***Results*** **Mucosal or cutaneous changes (n/N): arm 1** 16/22 **Mucosal or cutaneous changes (n/N): arm 2** 18/19 **Mucosal or cutaneous changes (n/N): arm 3** 19/19 **Relapse follow up: arm 1** 52 weeks **Relapse follow up: arm 2** 52 weeks **Relapse follow up: arm 3** 52 weeks **Relapse (n/N): arm 1** 3/22 **Relapse (n/N): arm 2** 0/19 **Relapse (n/N): arm 3** 0/19	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information provided **2. Deviation from intervention** Some concerns;no information provided; no ITT was done **3. Missing outcome data (efficacy)** High;10% withdrawals / loss to follow-up - balanced between arms; no ITT; unclear reasons for wihdrawal **4. Outcome measurement (efficacy)** Some concerns;not reported if assessment of outcome was blinded

Study details	Participants	Interventions	Outcomes and results	Comments
	Number randomised: arm 1 22 **Number randomised: arm 2** 22 **Number randomised: arm 3** 22 **Number completed: arm 1** 22 **Number completed: arm 2** 19 **Number completed: arm 3** 19	ISO<120.Daily=0.5-oral **Treatment category** Oral isotretinoin		**5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** High
Study details **Reference** Bossuyt, L. B., J.,Richert, B.,Cromphaut, P.,Mitchell, T.,Al Abadie, M.,Henry, I.,Bewley, A.,Poyner, T.,Mann, N.,Czernielewski, J.Lymecycline in the treatment of acne: An efficacious, safe and cost-effective alternative to minocycline. 2003. European Journal of Dermatology **Trial ID** Bossuyt 2003 **Country** Europe **Study type** RCT **Source of funding** Galderma Belgilux N.V./S.A. and Galderma UK Limited. ***Analysis method*** **Intention to treat or completers analysis**	N=134 ***Characteristics*** **Sex** mixed **age (mean±SD)** 18.6 **age (min/max)** 12/29 **age (other information)** LYME mean age 18.6 (range 13 - 29), MINO mean age 18.6 (range 12 - 29) ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Leeds Grading Scale, Cunliffe **Inclusion details** Males or females aged between 12 and 30 years. Participants with at least 15 and at most 120 inflammatory facial lesions (papules, pustules, nodules) including at most 2 facial nodules (diameter >1 cm), a maximum of 60 non-inflammatory facial lesions (open and	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** LYME-oral 300mg **Intervention: arm 2** MINO-oral 100mg **Coded intervention: arm 1** LYME-oral **Coded intervention: arm 2** MINO-oral **Treatment category** Oral antibiotics	***Results*** **GI side effects (n/N): arm 1** 3/56 **GI side effects (n/N): arm 2** 2/53 **Participant reported improvement (n/N): arm 1** 53/66 **Patient reported improvement (n/N): arm 2** 53/68	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information provided **2. Deviation from intervention** Some concerns;not reported if participants were blinded; ITT analysis was done; 8% protocol deviations in LYME arm vs 1.5% in MINO arm **3. Missing outcome data (efficacy)** Some concerns;22% withdrawals / loss to follow-up -

Study details	Participants	Interventions	Outcomes and results	Comments
ITT **Method of ITT imputation** LOCF	closed comedones) and an acne severity grade between 1 and 5 (Leeds grading scale). Women of childbearing age were required to use contraception during the study and for 1 month after completing the trial. Women on oral contraceptives were to have been using the same method for 3 months prior to enrolment, or for at least 12 months for contraceptive pills constraining cyproterone acetate. Use of cosmetics was permitted during the course of the study, but contraceptives and cosmetics had to be listed as concomitant medication. **Exclusion details** Pregnancy or lactating women..Participants with acne conglobata, acne fulminans or secondary acne..Participants using topical anti-acne or anti-inflammatory drugs or antibiotics, with the exception of short-courses of penicillin during the previous 6 months. ***Number included*** **Number randomised: arm 1** 66 **Number randomised: arm 2** 68 **Number completed: arm 1** 52 **Number completed: arm 2** 52			balanced between arms; 1.5% due to lack of efficacy; ITT used; **4. Outcome measurement (efficacy)** Low;investigator-masked **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** Some concerns
Study details **Reference** Braathen, L. R.Topical clindamycin versus oral tetracycline and placebo in acne vulgaris. 1984. Scandinavian Journal of Infectious Diseases	N=87 ***Characteristics*** **Sex** mixed **age (mean±SD)** 20 **age (min/max)** 16/35	***Interventions*** **Treatment duration (weeks)** 8 **Treatment duration category** 6 to <12 weeks **Number of arms**	***Results*** **Participant reported improvement (n/N): arm 1** 22/29 **Patient reported improvement (n/N): arm 2**	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information provided **2. Deviation from intervention**

Study details	Participants	Interventions	Outcomes and results	Comments
Trial ID Braathen 1984 **Country** Norway **Study type** RCT **Source of funding** Not reported. ***Analysis method*** **Intention to treat or completers analysis** completers	***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** Participants with moderate to severe acne vulgaris. **Exclusion details** Participants with a history of gastrointestinal disease..Participants who had received systemic or topical antibiotics, systemic or topical steroids, or androgenic drugs within 30 days of entering the study. .Females who were pregnant, or had been on oral contraceptives for less than 3 months, or had changed oral contraceptive within the previous 3 months. ***Number included*** **Number randomised: arm 1** na **Number randomised: arm 2** na **Number randomised: arm 3** na **Number completed: arm 1** 29 **Number completed: arm 2** 29 **Number completed: arm 3** 29	3 **Split face design** No **Intervention: arm 1** CLIND-topical 1% + PLC-oral **Intervention: arm 2** TETRA-oral 500mg bid + Vehicle **Intervention: arm 3** PLC-oral + Vehicle **Coded intervention: arm 1** CLIND-topical + PLC-oral **Coded intervention: arm 2** TETRA-oral + Vehicle **Coded intervention: arm 3** PLC-oral + Vehicle **Treatment category** Topical non-retinoids ± other treatment	21/29 **Participant reported improvement (n/N): arm 3** 1/29	Some concerns;double-blinded but not clear who was blinded; no ITT analysis **3. Missing outcome data (efficacy)** High;12% excluded from analysis for unclear reasons - not clear if balanced between arms; no ITT **4. Outcome measurement (efficacy)** Some concerns;not reported if assessment of outcome was blinded **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** High

Study details	Participants	Interventions	Outcomes and results	Comments
Study details **Reference** Chen, X. S., H.,Chen, S.,Zhang, J.,Niu, G.,Liu, X.Clinical efficacy of 5-aminolevulinic acid photodynamic therapy in the treatment of moderate to severe facial acne vulgaris. 2015. Experimental and Therapeutic Medicine **Trial ID** Chen 2015 **Country** China **Study type** RCT **Source of funding** Not reported. ***Analysis method*** **Intention to treat or completers analysis** completers	N=50 ***Characteristics*** **Sex** mixed **age (min/max)** 18/33 **age (other information)** ALA-PDT mean age=23.57; control=24.12 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** Participants with moderate (acne with inflammatory papules and pustules) to severe (acne with inflammatory papules, nodules, cysts and scars) facial acne vulgaris. **Exclusion details** Use of topical antibiotics within 2 weeks of the study or intake of systemic oral antibiotics within 4 weeks of the study.Use of systemic retinoids within 6 months of the study..Porphyria or facial atopic dermatitis..Pregnancy or lactation..History of keloid or photosensitivity disorders..Photosensitive eczema or autoimmune diseases..Use of anti-acne medication such as prophylactics, glucocorticoid and photosensitisers. ***Number included*** **Number randomised: arm 1** 25 **Number randomised: arm 2** 25 **Number completed: arm 1** 24	***Interventions*** **Treatment duration (weeks)** 3 **Treatment duration category** 0 to <6 weeks **Treatment intensity** Total 4 sessions, once every week **Number of arms** 2 **Split face design** No **Intervention: arm 1** 5ALA 5% photodynamic therapy **Intervention: arm 2** Sham treatment **Coded intervention: arm 1** 5ALA-RED-PDT **Coded intervention: arm 2** PLC-physical **Treatment category** Energy based (light / laser)	***Results*** **Skin irritation (n/N): arm 1** 7/24 **Skin irritation (n/N): arm 2** 2/23	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information provided **2. Deviation from intervention** Some concerns;no information provided; not reported if ITT analysis was done **3. Missing outcome data (efficacy)** Low;1 participant withdrew for unreported reason **4. Outcome measurement (efficacy)** Some concerns;not reported if assessment of outcome was blinded **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** Some concerns

Study details	Participants	Interventions	Outcomes and results	Comments
	Number completed: arm 2 23			
Study details **Reference** Degreef, H. V., B. G.Double-blind evaluation of miconazole-benzoyl peroxide combination for the topical treatment of acne vulgaris. 1982b. Dermatologica **Trial ID** Degreef 1982b **Country** Belgium **Study type** RCT **Source of funding** Not reported. ***Analysis method*** **Intention to treat or completers analysis** completers	N=105 ***Characteristics*** **Sex** mixed **age group** =25 years **age (median)** 15 **age (min/max)** 12/24 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Unknown, 5-point scale **Inclusion details** Participants with moderate to severe facial acne. **Exclusion details** Not reported. ***Number included*** **Number randomised: arm 1** 52 **Number randomised: arm 2** 53 **Number completed: arm 1** 51 **Number completed: arm 2** 51	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** BPO 5%/MICO 2% cream **Intervention: arm 2** BPO 5% cream **Coded intervention: arm 1** BPO-topical + MICO-topical **Coded intervention: arm 2** BPO-topical **Treatment category** Topical or combination	***Results*** **Participant reported improvement (n/N): arm 1** 45/51 **Patient reported improvement (n/N): arm 2** 27/51	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information provided **2. Deviation from intervention** Low;double-blinded; it looks like participants were blinded; no ITT analysis **3. Missing outcome data (efficacy)** Low;less than 5% withdrawals - balanced between arms **4. Outcome measurement (efficacy)** Some concerns;not reported if assessment of outcome was blinded **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias**

Study details	Participants	Interventions	Outcomes and results	Comments
				Some concerns
Study details **Reference** Del Rosso, J. Q.Truncal acne vulgaris: the relative roles of topical and systemic antibiotic therapy. 2007. Journal of drugs in dermatology **Trial ID** Del Rosso 2007 **Country** United States **Study type** RCT **Source of funding** Not reported. ***Analysis method*** **Intention to treat or completers analysis** completers	N=71 ***Characteristics*** **Sex** mixed **age (mean±SD)** 18 **age (min/max)** 16/32 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** Participants aged 16 years of age or older..Acne vulgaris, truncal involvement on the back with or without chest involvement, truncal inflammatory acne severity graded as moderate or severe..Informed consent obtained..Undergone a washout period of at least 2 weeks for all previous topical acne treatments (including over-the-counter products), at least 4 weeks for systemic antibiotic treatment, and more than 6 months for oral isotretinoin. **Exclusion details** Participants with concurrent intake or use within 4 weeks of baseline of systemic anti-inflammatory medication that may influence study outcomes (for example, systemic corticosteroids), concurrent application or use within 2 weeks of baseline of topical anti-inflammatory medication (for example, corticosteroids or calcineurin inhibitors)..History of sensitivity or intolerance associated with use of components of	***Interventions*** **Treatment duration (weeks)** 10 **Treatment duration category** 6 to <12 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** BPO 9% cleanser + CLIND 1% foam + DOXY 100 mg **Intervention: arm 2** BPO 9% cleanser + DOXY 100 mg **Coded intervention: arm 1** BPO-topical + CLIND-topical + DOXY-oral **Coded intervention: arm 2** BPO-topical + DOXY-oral	***Results*** **Skin irritation (n/N): arm 1** 3/32 **Skin irritation (n/N): arm 2** 2/28 **GI side effects (n/N): arm 1** 1/33 **GI side effects (n/N): arm 2** 5/33	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information provided **2. Deviation from intervention** Some concerns;no information provided; no ITT analysis **3. Missing outcome data (efficacy)** High;15% withdrawals (half possibly due to inefficiacy) - imbalanced between arms (more in group 2); no ITT **4. Outcome measurement (efficacy)** Low **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** High

Study details	Participants	Interventions	Outcomes and results	Comments
	medications or products used in the study..Presence of a concurrent medical condition that the study investigator deems may potentially interfere with the study outcomes or participant assessments. ***Number included*** **Number randomised: arm 1** 36 **Number randomised: arm 2** 35 **Number completed: arm 1** 32 **Number completed: arm 2** 28			
Study details **Reference** Dhaked, D. R. M., R. S.,Maheshwari, A.,Agarwal, U. S.,Purohit, S.A randomized comparative trial of two low-dose oral isotretinoin regimens in moderate to severe acne vulgaris. 2016. Indian Dermatology Online Journal **Trial ID** Dhaked 2016 **Country** India **Study type** RCT **Source of funding** None (no conflicts of interest). ***Analysis method*** **Intention to treat or completers analysis** completers	N=240 ***Characteristics*** **Sex** mixed **age (mean±SD)** 18.88±2.46 **age (median)** 18.51 **age (min/max)** 15/30 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Pochi **Inclusion details** Participants with moderate to severe acne vulgaris attending the outpatient clinic in the dermatology department.	***Interventions*** **Treatment duration (weeks)** 24 **Treatment duration category** 24+ weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** ISO<120.Daily<0.5 **Intervention: arm 2** ISO<120.Alt<0.5 **Coded intervention: arm 1** ISO<120.Daily<0.5-oral **Coded intervention: arm 2** ISO<120.Alt<0.5-oral **Treatment category**	***Results*** **Mucosal or cutaneous changes (n/N): arm 1** 115/118 **Mucosal or cutaneous changes (n/N): arm 2** 111/116 **Relapse follow up: arm 1** 12 **Relapse follow up: arm 2** 12 **Relapse (n/N): arm 1** 0/118 **Relapse (n/N): arm 2** 0/116	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information provided **2. Deviation from intervention** Some concerns;no information provided; no ITT analysis **3. Missing outcome data (efficacy)** Low;2.5% withdrawals / lost to follow-up - balanced between arms **4. Outcome measurement (efficacy)**

Study details	Participants	Interventions	Outcomes and results	Comments
	Exclusion details Participants with a personal or family history of hyperlipidaemia or diabetes. ***Number included*** **Number randomised: arm 1** 120 **Number randomised: arm 2** 120 **Number completed: arm 1** 118 **Number completed: arm 2** 116	Oral isotretinoin		Some concerns;not reported if assessment of outcome was blinded **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** Some concerns
Study details **Reference** Dhawan, S. S. G., J.Clindamycin phosphate 1.2%-benzoyl peroxide (5% or 2.5%) plus tazarotene cream 0.1% for the treatment of acne. 2013. Cutis **Trial ID** Dhawan 2013 **Country** United States **Study type** RCT **Source of funding** Stiefel, a GlaxoSmithKline company (conflicts of interest reported). ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** not reported	N=40 ***Characteristics*** **Sex** mixed **age (mean±SD)** 21.9±8.34 **age (min/max)** 12.3/45.9 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Investigator's Static Global Assessment (ISGA)/Investigator's global severity Assessment **Inclusion details** Males and females aged 12 to 45 years..Participants with grade 3 or higher according to the investigator static global assessment (ISGA) (3=moderate; 4=severe; 5=very severe)..20 to 50 papules and pustules (inflammatory lesions), 30 to 100 open and closed comedones (non-inflammatory lesions), 1 or fewer small nodular lesions, no facial	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** BPO 5%/CLIND 1.2% gel + TAZ 0.1% cream **Intervention: arm 2** BPO 2.5%/CLIND 1.2% gel + TAZ 0.1% cream **Coded intervention: arm 1** BPO-topical + CLIND-topical + TAZ-topical **Coded intervention: arm 2** BPO-topical + CLIND-	***Results*** **Skin irritation (n/N): arm 1** 1 **Skin irritation (n/N): arm 2** 0 **Skin irritation (n/N): arm 1** 20 **Skin irritation (n/N): arm 2** 20	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;insufficient information provided on allocation concealment **2. Deviation from intervention** Low;likely participants were blinded; ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;12.5% withdrawals/lost to FU unclear reasons - not clear if balanced between arms; ITT

Study details	Participants	Interventions	Outcomes and results	Comments
	cystic lesions. **Exclusion details** ***Number included*** **Number randomised: arm 1** 20 **Number randomised: arm 2** 20 **Number completed: arm 1** na **Number completed: arm 2** na	topical + TAZ-topical **Treatment category** Topical or combination		done **4. Outcome measurement (efficacy)** Some concerns;not reported if assessment of outcome was blinded **5. Selective reporting** Low **6. Overall bias** Some concerns
Study details **Reference** Dobson, R. L. B., B. S.Topical erythromycin solution in acne. Results of a multiclinic trial. 1980. Journal of the American Academy of Dermatology **Trial ID** Dobson 1980 **Country** United States **Study type** RCT **Source of funding** Not reported. ***Analysis method*** **Intention to treat or completers analysis** completers	N=253 ***Characteristics*** **Sex** mixed **age (other information)** no age info reported ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** Participants with moderate to severe acne vulgaris of the face (at least 10 papules or pustules, one or more comedones, and not more than 5 nodulocystic lesions).. .No concurrent illness and not receiving any anti-acne treatment (topical or systemic) for at least 2 weeks prior to study entry. **Exclusion details** Not reported.	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** ERYTH 1.5% solution **Intervention: arm 2** Vehicle **Coded intervention: arm 1** ERYTH-topical **Coded intervention: arm 2** Vehicle **Treatment category** Topical or combination	***Results*** **Skin irritation (n/N): arm 1** 26 **Skin irritation (n/N): arm 2** 26 **Skin irritation (n/N): arm 1** 109 **Skin irritation (n/N): arm 2** 90	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information provided **2. Deviation from intervention** Some concerns;double-blinded but not clear who was blinded; no ITT analysis **3. Missing outcome data (efficacy)** High;21% withdrawals - imbalanced between arms & due to lack of efficacy (2 X more in the vehicle arm);

Study details	Participants	Interventions	Outcomes and results	Comments
	Number included **Number randomised: arm 1** 127 **Number randomised: arm 2** 126 **Number completed: arm 1** 109 **Number completed: arm 2** 90			no ITT **4. Outcome measurement (efficacy)** Some concerns;double-blinded but not clear who was blinded **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** High
Study details **Reference** Dogra, S., Sumathy, T. K., Nayak, C., Ravichandran, G., Vaidya, P. P., Mehta, S., Mittal, R., Mane, A., Charugulla, S. N.Efficacy and safety comparison of combination of 0.04% tretinoin microspheres plus 1% clindamycin versus their monotherapy in patients with acne vulgaris: a phase 3, randomized, double-blind study. 2020. Journal of Dermatological Treatment **Trial ID** Dogra 2020 **Country** India **Study type**	N=750 ***Characteristics*** **Sex** mixed **age (mean±SD)** 21.2 **age (median)** 20 **age (min/max)** 12/48 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Investigator's Static Global Assessment (ISGA)/Investigator's global severity Assessment **Inclusion details** Participants aged >/=12 years.Facial acne (inflammatory lesion count [papulesþpustules]	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 3 **Split face design** No **Intervention: arm 1** Fixed dose tretinoin 0.04% (microsphere) + clindamycin 1.0% gel, o.d. **Intervention: arm 2** Tretinoin gel 0.025%, o.d. **Intervention: arm 3**	***Results*** **Skin irritation (n/N): arm 1** 0 **Skin irritation (n/N): arm 2** 2 **Skin irritation (n/N): arm 3** 0 **Skin irritation (n/N): arm 1** 300 **Skin irritation (n/N): arm 2** 300 **Skin irritation (n/N): arm 3** 150	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;random allocation software used - but no further information given **2. Deviation from intervention** Low;double-blinded but not clear who was blinded; ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;10%

Study details	Participants	Interventions	Outcomes and results	Comments
RCT **Source of funding** Dr. Reddy's Laboratories Ltd, India. ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	count between >20 to <50; non-inflammatory lesion count [openþclosed comedones] between >20 to <100, and nodules [inflammatory lesion 5mm in diameter] 2) and Investigator's Static Global Assessment (ISGA) score of 3 (moderate) or 4 (severe) **Exclusion details** Patients with a known allergy or sensitivity to study drug, or who were concomitantly using any potentially irritating over-the-counter products that contained benzoyl peroxide, a-hydroxy acids, salicylic acid, retinol or glycolic acids, or who required concurrent use of topical (antimicrobials, anti-acne drugs, anti-inflammatory agents, corticosteroids, retinoids) or systemic (corticosteroids, antimicrobials, retinoids) medication and not willing to undergo the specified washout period ***Number included*** **Number randomised: arm 1** 300 **Number randomised: arm 2** 300 **Number randomised: arm 3** 150 **Number completed: arm 1** 277 **Number completed: arm 2** 267 **Number completed: arm 3** 133	Clindamycin gel 1.0%, o.d. **Coded intervention: arm 1** TRET-topical+CLIND-topical **Coded intervention: arm 2** TRET-topical **Coded intervention: arm 3** CLIND-topical **Treatment category** Topical		discontinued in total **4. Outcome measurement (efficacy)** Some concerns;not reported if assessment of outcome was blinded **5. Selective reporting** Low **6. Overall bias** Some concerns
Study details **Reference** Dréno, B., Tan, J., Rivier, M., Martel, P., Bissonnette, R. Adapalene 0.1%/benzoyl peroxide 2.5% gel reduces the	N=76 ***Characteristics*** **Sex** mixed **age (mean±SD)** 23.4 (3.6)	***Interventions*** **Treatment duration (weeks)** 26 **Treatment duration category**	***Results*** **Prevention of scarring reported as a mean % increase from baseline in scars: arm 1** 4.5%	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns; no information provided on

Study details	Participants	Interventions	Outcomes and results	Comments
risk of atrophic scar formation in moderate inflammatory acne: a split-face randomized controlled trial. 2017. Journal of the European Academy of Dermatology and Venereology **Trial ID** Dreno 2017 **Country** France/Canada **Study type** Split-face RCT **Source of funding** Funded by Galderma R&D ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** Not reported	**age (median)** 22 **age (min/max)** 19/32 ***Inclusion/exclusion criteria*** **Used validated acne scale** No **Acne scale** No **Inclusion details** Male and female participants aged 18–35 years with moderate facial acne vulgaris with 20–40 inflammatory lesions (papules and pustules, excluding the nose), no more than 1 acne nodule and a minimum of 10 atrophic acne scars (larger than 1.5mm in diameter, smaller scars could not be accurately differentiated from other lesion types). Participants had no more than twice as many lesions on one half of the face than on the other half. **Exclusion details** Not reported ***Number included*** **Number randomised: arm 1** 38 **Number randomised: arm 2** 38 **Number completed: arm 1** 33 **Number completed: arm 2** 33	24+ weeks **Number of arms** 2 **Split face design** Yes **Intervention: arm 1** ADAP 0.1% gel + BPO 2.5% gel. **Intervention: arm 2** Vehicle **Coded intervention: arm 1** ADAP-topical + BPO-topical **Coded intervention: arm 2** Vehicle **Treatment category** Topical	**Prevention of scarring reported as a mean % increase from baseline in scars: arm 2** 24.8%	allocation concealment **2. Deviation from intervention** Some concerns; participants not blinded; ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns; 13% withdrawals **4. Outcome measurement (efficacy)** Low **5. Selective reporting** Some concerns; additional outcomes were reported which were not in the trial protocol **6. Overall bias** Some concerns
Study details **Reference** Dréno, B., Bissonnette, R., Gagné-Henley., A., Barankin, B., Lynde, C., Kerrouche, N.,	N=134 ***Characteristics*** **Sex** mixed **age (mean±SD)**	***Interventions*** **Treatment duration (weeks)** 24	***Results*** **Prevention of scarring reported as a mean % decrease from baseline in scars: arm 1**	***Cochrane RoB Tool v2.0*** **1. Randomisation** Low **2. Deviation from**

Study details	Participants	Interventions	Outcomes and results	Comments
Tan, J. Prevention and Reduction of Atrophic Acne Scars with Adapalene 0.3%/Benzoyl Peroxide 2.5% Gel in Subjects with Moderate or Severe Facial Acne: Results of a 6-Month Randomized, Vehicle-Controlled Trial Using Intra-Individual Comparison. 2018. American Journal of Clinical Dermatology **Trial ID** Dreno 2018 **Country** France/Canada **Study type** Split-face RCT **Source of funding** Funded by Galderma R&D/Nestle Skin Health ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	21.5 (4.2) ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Investigator Global Assessment (IGA) **Inclusion details** Male or female participants aged 16–35 years with Fitzpatrick skin phototype I–IV and a clinical diagnosis of moderate or severe acne vulgaris on the face. Participants had an Investigator Global Assessment (IGA) score of 3 or 4 on both sides; >=25 inflammatory lesions (papules and pustules) with 10 or more on each side (excluding the nose); up to two acne nodules >=1 cm for whole face; 10 or more atrophic acne scars >2 mm (for whole face excluding the nose); with an approximately symmetric number of inflammatory and non-inflammatory lesions, and atrophic acne scars on the whole face. **Exclusion details** Excluded were those ith acne conglobata, acne fulminans, secondary acne, nodulocystic acne, or acne requiring systemic treatment. ***Number included*** **Number randomised: arm 1** 67 **Number randomised: arm 2** 67 **Number completed: arm 1** 54 **Number completed: arm 2** 54	**Treatment duration category** 24+ weeks ……. **Number of arms** 2 **Split face design** Yes **Intervention: arm 1** ADAP 0.3% gel + BPO 2.5% gel **Intervention: arm 2** Vehicle **Coded intervention: arm 1** ADAP-topical + BPO-topical **Coded intervention: arm 2** Vehicle **Treatment category** Topical	15.5% **Prevention of scarring reported as a mean % increase from baseline in scars: arm 2** 14.4%	**intervention** Some concerns; participants not blinded; ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns; 19% withdrawals **4. Outcome measurement (efficacy)** Low **5. Selective reporting** Some concerns; additional outcomes were reported which were not in the trial protocol **6. Overall bias** Some concerns
Study details **Reference** Dubertret, L. A., M.,Rostain,	N=271 ***Characteristics***	***Interventions*** **Treatment duration (weeks)**	***Results*** **GI side effects (n/N): arm 1**	***Cochrane RoB Tool v2.0*** **1. Randomisation**

Study details	Participants	Interventions	Outcomes and results	Comments
G.,Lahfa, M.,Forsea, D.,Dimitrie Niculae, B.,Simola, M.,Horvath, A.,Mizzi, F.The use of lymecycline in the treatment of moderate to severe acne vulgaris: A comparison of the efficacy and safety of two dosing regimens. 2003. European Journal of Dermatology **Trial ID** Dubertret 2003 **Country** Europe **Study type** RCT **Source of funding** Not reported. ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	**Sex** mixed **age (min/max)** 14/39 **age (other information)** mean age was 20.4, 21.2 & 20.5 yrs for LYME 300mg, LYME 150mg and PLC groups ***Inclusion/exclusion criteria*** **Used validated acne scale** yes **Acne scale** Leeds Revised Grading Scale **Inclusion details** Males and females aged between 16 and 40 years..Acne vulgaris with a minimum of 15 inflammatory facial lesions and a global severity of at least grade 3 on the Leeds Revised Acne Grading System. **Exclusion details** ***Number included*** **Number randomised: arm 1** 111 **Number randomised: arm 2** 107 **Number randomised: arm 3** 53 **Number completed: arm 1** 105 **Number completed: arm 2** 88 **Number completed: arm 3** 45	12 **Treatment duration category** 12 to <24 weeks **Number of arms** 3 **Split face design** No **Intervention: arm 1** LYME-oral 300mg od + PLC-oral **Intervention: arm 2** LYME-oral 150mg bid **Intervention: arm 3** PLC-oral bid **Coded intervention: arm 1** LYME-oral + PLC-oral **Coded intervention: arm 2** LYME-oral **Coded intervention: arm 3** PLC-oral **Treatment category** Oral antibiotics	4/111 **GI side effects (n/N): arm 2** 3/107 **GI side effects (n/N): arm 3** 4/53	Some concerns;no information provided **2. Deviation from intervention** Low;double-blinded; participants likely blinded; ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;12% withdrawals (unclear reasons) - imbalanced between arms (more in lymecycline arm); ITT used **4. Outcome measurement (efficacy)** Some concerns;not reported if assessment of outcome was blinded **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** Some concerns

Study details	Participants	Interventions	Outcomes and results	Comments
Study details **Reference** Faghihi, G. M., F.,Fard, N. M.,Motamedi, N.,Hosseini, S. M.Comparing the efficacy of low dose and conventional dose of oral isotretinoin in treatment of moderate and severe acne vulgaris. 2017. Journal of Research in Pharmacy Practice **Trial ID** Faghihi 2017 **Country** Iran, Islamic Republic of **Study type** RCT **Source of funding** Isfahan University of Medical Sciences (no conflicts of interest). ***Analysis method*** **Intention to treat or completers analysis** completers	N=66 ***Characteristics*** **Sex** mixed **age (mean±SD)** 23±5.54 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Global Acne Grading System (GAGS) **Inclusion details** Males and females with moderate to severe acne vulgaris referred for treatment to Alzahra Medical and Training Centre, several clinical affiliated to Isfahan University of Medical Sciences and a privately-owned doctor's office..Consent to participate in the study..No sensitivity to retinoids..No pregnancy, not willing to become pregnant, and absence of hormonal disorders. **Exclusion details** Failure of participants to attend follow-up visits for any reason..Adoption of other supplementary treatments during the study. ***Number included*** **Number randomised: arm 1** 36 **Number randomised: arm 2** 30 **Number completed: arm 1** 36 **Number completed: arm 2** 30	***Interventions*** **Treatment duration (weeks)** 26 **Treatment duration category** 24+ weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** ISO<120.Daily<0.5 + PRED 0.25 mg wk 1 + AZITH 250 mg wks 1-2 **Intervention: arm 2** ISO<120.Daily=0.5 + PRED 0.25 mg wk 1 + AZITH 250 mg wks 1-2 **Coded intervention: arm 1** ISO<120.Daily<0.5-oral **Coded intervention: arm 2** ISO<120.Daily=0.5-oral **Treatment category** Oral isotretinoin	***Results*** **Mucosal or cutaneous changes (n/N): arm 1** 6/36 **Mucosal or cutaneous changes (n/N): arm 2** 12/30 **New psychiactric diagnosis (n/N): arm 1** 2/36 **New psychiactric diagnosis (n/N): arm 2** 2/30 **Relapse follow up: arm 1** 26 **Relapse follow up: arm 2** 26	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;not clear how allocation sequence and concealment were done **2. Deviation from intervention** Some concerns;not reported if participants were blinded; no ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;not reported how many/if participants withdrew **4. Outcome measurement (efficacy)** Low **5. Selective reporting** Low;looks like trial protocol was registered but not possible to access **6. Overall bias** Some concerns
Study details	N=744	***Interventions***	***Results***	***Cochrane RoB***

Study details	Participants	Interventions	Outcomes and results	Comments
Reference Feldman, S. R. W., C. P.,Alio Saenz, A. B.The efficacy and tolerability of tazarotene foam, 0.1%, in the treatment of acne vulgaris in 2 multicenter, randomized, vehicle-controlled, double-blind studies. 2013. Journal of Drugs in Dermatology: JDD **Trial ID** Feldman 2013;Trial 1 **Country** North America **Study type** RCT **Source of funding** Stiefel, a GlaxoSmithKline company (conflicts of interest were reported). ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	***Characteristics*** **Sex** mixed **age (mean±SD)** 18.400269179004±6.0598000000000001 **age (min/max)** 12/44 **age (other information)** TAZ: 12-17, n=223, 18-25, n=104, 26-35, n=38, 36-45, n=6; VEH: 12-17, n=227, 18-25, n=99, 26-35, n=33, 36-45, n=13 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Investigator's Static Global Assessment (ISGA)/Investigator's global severity Assessment **Inclusion details** Males and females aged between 12 and 45 years, in good general health and agreed to use a medically-acceptable form of contraception throughout the study. Moderate to severe acne vulgaris: Investigator's Static Global Assessment (ISGA) score =3 at baseline; lesion counts of 25 to 50 facial inflammatory lesions (papules plus pustules), including nasal lesions, with no more than one facial nodular lesion (<5 mm) and no cystic lesions, and 30 to 125 facial non-inflammatory lesions (open and closed comedones), excluding nasal lesions..Provide consent. **Exclusion details** History of suspected intolerance to tazarotene or any of the ingredients of the study products..Participants taking certain topical and systemic treatments were required to	**Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** TAZ 0.1% foam **Intervention: arm 2** Vehicle **Coded intervention: arm 1** TAZ-topical **Coded intervention: arm 2** Vehicle **Treatment category** Topical retinoids	**Skin irritation (n/N): arm 1** 66/371 **Skin irritation (n/N): arm 2** 5/372 **Light sensitivity (n/N): arm 1** 2/371 **Light sensitivity (n/N): arm 2** 0/372	***Tool v2.0*** **1. Randomisation** Low **2. Deviation from intervention** Low;double-blinded; study center, study monitors, sponsor personnel were blinded to the treatment assignments. ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;14% discontinued (unclear how many due to inefficacy)-imbalanced between arms (more in tazarotene foam arm) **4. Outcome measurement (efficacy)** Low **5. Selective reporting** Low **6. Overall bias** Some concerns

Study details	Participants	Interventions	Outcomes and results	Comments
	undergo specified washout periods. ***Number included*** **Number randomised: arm 1** 372 **Number randomised: arm 2** 372 **Number completed: arm 1** 307 **Number completed: arm 2** 333			
Study details **Reference** Feldman, S. R. W., C. P.,Alio Saenz, A. B.The efficacy and tolerability of tazarotene foam, 0.1%, in the treatment of acne vulgaris in 2 multicenter, randomized, vehicle-controlled, double-blind studies. 2013. Journal of Drugs in Dermatology: JDD **Trial ID** Feldman 2013;Trial 2 **Country** North America **Study type** RCT **Source of funding** Stiefel, a GlaxoSmithKline company (conflicts of interest were reported). ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	N=742 ***Characteristics*** **Sex** mixed **age (mean±SD)** 19.2±6.6463999999999999 **age (min/max)** 12/45 **age (other information)** TAZ: 12-17, n=205, 18-25, n=117, 26-35, n=35, 36-45, n=16; VEH: 12-17, n=205, 18-25, n=108, 26-35, n=37, 36-45, n=19 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Investigator's Static Global Assessment (ISGA)/Investigator's global severity Assessment **Inclusion details** Males and females aged between 12 and 45 years, in good general health and agreed to use a medically-acceptable form of contraception throughout the study. .Moderate to severe acne vulgaris:	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** TAZ 0.1% foam **Intervention: arm 2** Vehicle **Coded intervention: arm 1** TAZ-topical **Coded intervention: arm 2** Vehicle **Treatment category** Topical retinoids	***Results*** **Skin irritation (n/N): arm 1** 41/373 **Light sensitivity (n/N): arm 1** 1/373	***Cochrane RoB Tool v2.0*** **1. Randomisation** Low **2. Deviation from intervention** Low;double-blinded; study center, study monitors, sponsor personnel were blinded to the treatment assignments. ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;14% discontinued (unclear how many due to inefficacy)-imbalanced between arms

Study details	Participants	Interventions	Outcomes and results	Comments
	Investigator's Static Global Assessment (ISGA) score =3 at baseline; lesion counts of 25 to 50 facial inflammatory lesions (papules plus pustules), including nasal lesions, with no more than one facial nodular lesion (<5 mm) and no cystic lesions, and 30 to 125 facial non-inflammatory lesions (open and closed comedones), excluding nasal lesions..Provide consent. **Exclusion details** History of suspected intolerance to tazarotene or any of the ingredients of the study products..Participants taking certain topical and systemic treatments were required to undergo specified washout periods. ***Number included*** **Number randomised: arm 1** 373 **Number randomised: arm 2** 369 **Number completed: arm 1** 307 **Number completed: arm 2** 334			(more in tazarotene foam arm) **4. Outcome measurement (efficacy)** Low **5. Selective reporting** Low **6. Overall bias** Some concerns
Study details **Reference** Fugere, P. P.-S., R. K.,Lussier-Cacan, S.,Davignon, J.,Farquhar, D.Cyproterone acetate/ethinyl estradiol in the treatment of acne. A comparative dose-response study of the estrogen component. 1990. Contraception **Trial ID** Fugere 1990	N=73 ***Characteristics*** **Sex** female **age (mean±SD)** 22.9260273972603±3.2639999999999998 **age (min/max)** 17/35 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Cook	***Interventions*** **Treatment duration (weeks)** 48 **Treatment duration category** 24+ weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** CPA 2mg + EE 0.035 mg	***Results*** **Breakthrough bleeding (n/N): arm 1** 2/40 **Breakthrough bleeding (n/N): arm 2** 4/33	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information provided **2. Deviation from intervention** Low;double-blinded - clear that participants were blinded; no ITT analysis

Study details	Participants	Interventions	Outcomes and results	Comments
Country Canada **Study type** RCT **Source of funding** Not reported. ***Analysis method*** **Intention to treat or completers analysis** completers	**Inclusion details** Women in good health aged between 18 and 35 years..Moderate to severe androgen-dependent acne vulgaris (defined as presence of comedones, papules and macules on at least half of the face..Previous treatment withdrawn within 6 weeks of starting study treatments. **Exclusion details** Not reported. ***Number included*** **Number randomised: arm 1** 40 **Number randomised: arm 2** 33 **Number completed: arm 1** 37 **Number completed: arm 2** 25	(Diane-35) **Intervention: arm 2** CPA 2mg + EE 0.05 mg (Diane-50) **Coded intervention: arm 1** CPA-oral + EE-oral **Coded intervention: arm 2** CPA-oral + EE-oral **Treatment category** Hormonal contraceptives / Hormone-modifying agents		**3. Missing outcome data (efficacy)** High;23% withdrawals - not clear if balanced between arms; no ITT used **4. Outcome measurement (efficacy)** Some concerns;not reported if assessment of outcome was blinded **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** High
Study details **Reference** Gratton, D. R., G. P.,Guertin-Larochelle, S.,Maddin, S. W.,Leneck, C. M.,Warner, J.,Collins, J. P.,Gaudreau, P.,Bendl, B. J.Topical clindamycin versus systemic tetracycline in the treatment of acne. Results of a multiclinic trial. 1982. Journal of the American Academy of Dermatology **Trial ID**	N=225 ***Characteristics*** **Sex** mixed **age (min/max)** 18/35 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** Participants with moderate to severe acne	***Interventions*** **Treatment duration (weeks)** 8 **Treatment duration category** 6 to <12 weeks **Number of arms** 3 **Split face design** No **Intervention: arm 1** CLIND 1% solution +	***Results*** **Participant reported improvement (n/N): arm 1** 92/105 **Participant reported improvement (n/N): arm 2** 56/97	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information provided **2. Deviation from intervention** Low;double-blinded; likely that participants were blinded; no ITT analysis **3. Missing**

Study details	Participants	Interventions	Outcomes and results	Comments
Gratton 1982 **Country** Canada **Study type** RCT **Source of funding** Not reported. ***Analysis method*** **Intention to treat or completers analysis** completers	(defined as presence of a minimum of 12 to 70 inflammatory papules and pustules, and a maximum of 6 nodulocystic lesions on the face above the jawline). **Exclusion details** Participants with a history of gastrointestinal disease..Participants who had received systemic or topical antibiotics, systemic or topical steroids, or androgenic drugs within 30 days of starting study medication. .Females who had been on oral contraceptives for 3 months, or made a change in oral contraceptives within the previous 3 months; pregnancy. ***Number included*** **Number randomised: arm 1** 121 **Number randomised: arm 2** 124 **Number completed: arm 1** 105 **Number completed: arm 2** 97	PLC capsule **Intervention: arm 2** PLC capsule + PLC solution **Coded intervention: arm 1** CLIND-topical + PLC-oral **Coded intervention: arm 2** PLC-oral + PLC-topical **Treatment category** Topical non-retinoids ± other treatment		**outcome data (efficacy)** High;17% discontinued - imbalanced between arms (more in placebo arm); no ITT **4. Outcome measurement (efficacy)** Some concerns;not reported if assessment of outcome was blinded **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** High
Study details **Reference** Jones, E. L. C., A. F.Topical erythromycin vs blank vehicle in a multiclinic acne study. 1981. Archives of Dermatology **Trial ID** Jones 1981 **Country**	N=175 ***Characteristics*** **Sex** mixed **age (other information)** ERYTH 13-20, n=31; 21-30, n=46; 31-40, n=3; 41+, n=1; not known=0. Vehicle 13-20, n=29; 21-30, n=39; 31-40, n=6;	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2	***Results*** **Skin irritation (n/N): arm 1** 5 **Skin irritation (n/N): arm 2** 9 **Skin irritation (n/N): arm 1**	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information provided **2. Deviation from intervention** Some

Study details	Participants	Interventions	Outcomes and results	Comments
United States **Study type** RCT **Source of funding** Not reported. ***Analysis method*** **Intention to treat or completers analysis** completers	41+, n=0; not known=1. ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Unclear, type of lesion x counts scale **Inclusion details** Males and females aged 12 years or older, seeking medical care for acne or recruited volunteers, but otherwise in good general health..Facial acne grades 2 or 3 on the severity scale (grade 2: a moderate number of comedones, papules, and small cysts, occasional pustules, and inflammation; grade 3: a great number of lesions with deeper and larger cysts and minimal scarring)..Minimum of 10 papular inflammatory acne lesions in the facial area..Participants could be pregnant or of childbearing age..Unresponsive to treatment with oral tetracycline hydrochloride, topical benzoyl peroxide, and tretinoin. **Exclusion details** Children aged <12 years of age..Participants could not be planning to move within 12 weeks..Use of concomitant antibiotics given for systemic effect or another topical acne treatment, unless it was possible to discontinue such treatment 3 weeks before the start of the study. ***Number included*** **Number randomised: arm 1** 90 **Number randomised: arm 2** 85 **Number completed: arm 1** 81 **Number completed: arm 2**	**Split face design** No **Intervention: arm 1** BPO 5%/ERYTH 3% gel **Intervention: arm 2** Vehicle **Coded intervention: arm 1** BPO-topical + ERYTH-topical **Coded intervention: arm 2** Vehicle **Treatment category** Topical or combination	90 **Skin irritation (n/N): arm 2** 85	concerns;double-blinded but not clear who was blinded; not clear if ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;more than 5% withdrawals - balanced between arms **4. Outcome measurement (efficacy)** Some concerns;not clear if blinded **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** High

Study details	Participants	Interventions	Outcomes and results	Comments
	75			
Study details **Reference** Jones, T. M., L.,Monroe, E.,Weiss, J.,Levy, S.A multicentre, double-blind, parallel-group study to evaluate 3% erythromycin/5% benzoyl peroxide dual-pouch pack for acne vulgaris. 2002. Clinical Drug Investigation **Trial ID** Jones 2002 **Country** United States **Study type** RCT **Source of funding** Dermick Laboratories, US. ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** not reported	N=223 ***Characteristics*** **Sex** mixed **age (mean±SD)** 18.5±5.8 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Physician's Global Assessment (PGA)/Physician's Global Acne Severity Score **Inclusion details** Male and females aged =13 years..Moderate to moderately severe acne vulgaris (overall acne severity score =1.5 on the Physician's Global Acne Severity Scale, 15 to 80 inflammatory lesions, 20 to 140 comedones, and =2 nodules or cysts measuring greater than 5mm. The comedo count did not include the nasal and nasolabial fold area). Treatment with systemic antibiotics known to affect acne and systemic corticosteroids should be discontinued 4 weeks prior to study commencement, and 6 months for oral retinoids. A 2-week washout period was required for topical antibiotics and/or anti-acne medication, topical corticosteroids, and topical retinoids. **Exclusion details** Pregnant or lactating women..Participants with beards or long sideburns..Participants with cystic acne or any other diseases affecting their condition or interfering with treatment evaluation. ***Number included***	***Interventions*** **Treatment duration (weeks)** 8 **Treatment duration category** 6 to <12 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** BPO 5%/ERYTH 3% gel (dual pouch pack) **Intervention: arm 2** Vehicle **Coded intervention: arm 1** BPO-topical + ERYTH-topical **Coded intervention: arm 2** Vehicle **Treatment category** Topical or combination	***Results*** **Skin irritation (n/N): arm 1** 14 **Skin irritation (n/N): arm 2** 6 **Skin irritation (n/N): arm 1** 112 **Skin irritation (n/N): arm 2** 111 **Participant reported improvement (n/N): arm 1** 2/112 **Participant reported improvement (n/N): arm 2** 1.6/111	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information provided **2. Deviation from intervention** Low;double-blinded & ITT analysis **3. Missing outcome data (efficacy)** Some concerns;Unclear how many discontinued during the trial **4. Outcome measurement (efficacy)** Low;Assessors blinded **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** Some concerns

Study details	Participants	Interventions	Outcomes and results	Comments
	Number randomised: arm 1 112 **Number randomised: arm 2** 111 **Number completed: arm 1** 112 **Number completed: arm 2** 110			
Study details **Reference** Kapadia, N. F. K., G.,Burhany, T.,Nakhoda, T.Comparative efficacy and safety and efficacy of systemic 13-cis retinoic acid 20mg/day vs. 40mg/day in acne vulgaris. 2005. Journal of Pakistan Association of Dermatologists **Trial ID** Kapadia 2005 **Country** Pakistan **Study type** RCT **Source of funding** Not reported.	N=60 ***Characteristics*** **Sex** mixed **age (other information)** no age or sex data reported ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Global Acne Grading System (GAGS) **Inclusion details** Participants with moderate to severe acne vulgaris (graded using the Global Acne Grading System (GAGS)) attending an outpatient clinical in Karachi. **Exclusion details** Not reported. ***Number included*** **Number randomised: arm 1** 30 **Number randomised: arm 2** 30 **Number completed: arm 1** 30	***Interventions*** **Treatment duration (weeks)** 24 **Treatment duration category** 24+ weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** ISO<120.Daily<0.5 (20mg) **Intervention: arm 2** ISO<120.Daily=0.5 (40mg) **Coded intervention: arm 1** ISO<120.Daily<0.5-oral **Coded intervention: arm 2** ISO<120.Daily=0.5-oral **Treatment category** Oral isotretinoin	***Results*** **Mucosal or cutaneous changes (n/N): arm 1** 30/30 **Mucosal or cutaneous changes (n/N): arm 2** 30/30 **Change in mood (n/N): arm 1** 0/30 **Change in mood (n/N): arm 2** 3/30	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information provided **2. Deviation from intervention** Some concerns;no information provided **3. Missing outcome data (efficacy)** Low **4. Outcome measurement (efficacy)** Some concerns;no information provided **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** Some concerns

Study details	Participants	Interventions	Outcomes and results	Comments
	Number completed: arm 2 30			
Study details **Reference** Khanna, N.Treatment of acne vulgaris with oral tetracylines. 1993. Indian journal of dermatology, venerology and leprology **Trial ID** Khanna 1993 **Country** India **Study type** RCT **Source of funding** None (no conflicts of interest). ***Analysis method*** **Intention to treat or completers analysis** completers **Method of ITT imputation** not reported	N=44 ***Characteristics*** **Sex** mixed **age group** =25 years **age (min/max)** 14/24 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Unclear, type of lesion x counts scale **Inclusion details** Males and females with moderately severe acne (defined when acne lesion score (ALS) was 30 to 70) and severe acne (defined as ALS score of more than 70)..Participants who had taken oral antibiotics were included in the study after 1 month discontinuation of the antibiotics. **Exclusion details** Participants with acne conglobata..Pregnant women or women using oral contraceptives..Participants with obvious endocrinopathy. ***Number included*** **Number randomised: arm 1** 21 **Number randomised: arm 2** 23 **Number completed: arm 1** 15 **Number completed: arm 2**	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** TETRA 500 mg po bid **Intervention: arm 2** MINO 50 mg po bid **Coded intervention: arm 1** TETRA-oral **Coded intervention: arm 2** MINO-oral **Treatment category** Oral antibiotics	***Results*** **Thrush/candidiasis (n/N): arm 1** 1/21 **Thrush/candidiasis (n/N): arm 2** 1/23	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;No detials on methods **2. Deviation from intervention** High;No blinding; no ITT **3. Missing outcome data (efficacy)** High;Withdrawals of 23% - some due to lack of efficacy & imbalanced between groups **4. Outcome measurement (efficacy)** High;not blinded **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** High

Study details	Participants	Interventions	Outcomes and results	Comments
	19			
Study details **Reference** Kim, T. I. A., H. J.,Kang, I. H.,Jeong, K. H.,Kim, N. I.,Shin, M. K.Nonablative fractional laser-assisted daylight photodynamic therapy with topical methyl aminolevulinate for moderate to severe facial acne vulgaris: Results of a randomized and comparative study. 2017. Photodermatology Photoimmunology and Photomedicine **Trial ID** Kim 2017 **Country** Korea, Republic of **Study type** RCT **Source of funding** Galderma Research & Development (no conflicts of interest). ***Analysis method*** **Intention to treat or completers analysis** completers	N=32 ***Characteristics*** **Sex** mixed **age (mean±SD)** 24.75±3.5999999999999996 **age (min/max)** 19/45 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Investigator's Global Assessment scale (IGA) **Inclusion details** Participants aged between 19 and 45 years..Active acne lesions and Fitzpatrick skin phototypes III to IV; acne severity grade 3 or 4 according to the IGA. **Exclusion details** History of photosensitive disorders..Use of medications such as oral isotretinoin for 3 months and oral contraceptives or antibiotics for 4 weeks, topical treatments or facial procedures for 4 weeks..Pregnant or lactating women..Participants were prohibited from using oral or topical medications for treatment of acne during the study. ***Number included*** **Number randomised: arm 1** 16 **Number randomised: arm 2** 16 **Number completed: arm 1** 14 **Number completed: arm 2** 14	***Interventions*** **Treatment duration (weeks)** 16 **Treatment duration category** 12 to <24 weeks **Treatment intensity** Total 2 sessions, once every 2 weeks. FU visits at 2, 6, 10 and 14 wks after last session. **Number of arms** 2 **Split face design** No **Intervention: arm 1** MAL 16%-DL PDT **Intervention: arm 2** NAFL + MAL 16%-DL PDT **Coded intervention: arm 1** MAL-DL-PDT **Coded intervention: arm 2** NAFL + MAL-DL-PDT **Treatment category** Energy based (light / laser)	***Results*** **Skin redness (n/N): arm 1** 2/14 **Skin redness (n/N): arm 2** 0/14 **Pigment changes (n/N): arm 1** 1/14 **Pigment changes (n/N): arm 2** 1/14 **Participant reported improvement (n/N): arm 1** 12/14 **Participant reported improvement (n/N): arm 2** 14/14	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information about allocation concealment provided **2. Deviation from intervention** Some concerns;Not reported if participants were blinded; not reported if ITT analysis was done **3. Missing outcome data (efficacy)** High;more than 5% withdrawals - balanced between arms **4. Outcome measurement (efficacy)** Low **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** High

Study details	Participants	Interventions	Outcomes and results	Comments
Study details **Reference** Kuhlman, D. S. C., J. P.A comparison of clindamycin phosphate 1 percent topical lotion and placebo in the treatment of acne vulgaris. 1986. Cutis **Trial ID** Kuhlman 1986 **Country** United States **Study type** RCT **Source of funding** Not reported. ***Analysis method*** **Intention to treat or completers analysis** completers	N=35 ***Characteristics*** **Sex** mixed **age (min/max)** 12/30 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** Men and women aged 12 to 30 years..Moderate to severe acne vulgaris defined as 12 to 70 inflammatory papules and no more than 6 cystic lesions on the face above the jawline. **Exclusion details** Participants sensitive to clindamycin..Pregnant or nursing women..Participants with chronic bowel disease or frequent periodic diarrhoea..Participants requiring additional acne treatment, those who had received systemic antibiotics, steroids, or androgens within the past 30 days or topical acne medications within the past 14 days, and participants who had started or stopped using oral contraceptives in the past 60 days. ***Number included*** **Number randomised: arm 1** na **Number randomised: arm 2** na **Number completed: arm 1** 21 **Number completed: arm 2** 14	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** CLIND 1% lotion **Intervention: arm 2** Vehicle **Coded intervention: arm 1** CLIND-topical **Coded intervention: arm 2** Vehicle **Treatment category** Topical or combination	***Results*** **Skin irritation (n/N): arm 1** 2 **Skin irritation (n/N): arm 2** 0 **Skin irritation (n/N): arm 1** 21 **Skin irritation (n/N): arm 2** 14	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information provided **2. Deviation from intervention** Some concerns;double-blinded but not clear who was blinded **3. Missing outcome data (efficacy)** High;not reported how many participants were randomised to each arm; not reported how many withdrew **4. Outcome measurement (efficacy)** Some concerns;not reported if assessment of outcome was blinded **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias**

Study details	Participants	Interventions	Outcomes and results	Comments
				High
Study details **Reference** Lassus, A. J., T.,Lauharanta, J.Motretinide versus benzoyl peroxide in the treatment of acne vulgaris. 1984. Dermatologica **Trial ID** Lassus 1984 **Country** Finland **Study type** RCT **Source of funding** Not reported. ***Analysis method*** **Intention to treat or completers analysis** completers	N=30 ***Characteristics*** **Sex** mixed **age (other information)** no age data reported ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** Participants diagnosed with acne vulgaris of the papulopustular type. **Exclusion details** Not reported. ***Number included*** **Number randomised: arm 1** 15 **Number randomised: arm 2** 15 **Number completed: arm 1** 13 **Number completed: arm 2** 13	***Interventions*** **Treatment duration (weeks)** 8 **Treatment duration category** 6 to <12 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** motretinide 1% cream **Intervention: arm 2** BPO 5% gel **Coded intervention: arm 1** MOT-topical **Coded intervention: arm 2** BPO-topical **Treatment category** Topical or combination	***Results*** **Skin irritation (n/N): arm 1** 1 **Skin irritation (n/N): arm 2** 11 **Skin irritation (n/N): arm 1** 15 **Skin irritation (n/N): arm 2** 15	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information provided **2. Deviation from intervention** High;open label; not reported if ITT analysis was done **3. Missing outcome data (efficacy)** High;13% withdrawals - balanced between arms; no ITT **4. Outcome measurement (efficacy)** High;open-labeled **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** High
Study details **Reference** Leyden, J. J. S., V.,Berk, D. R.,Kaoukhov, A.Efficacy and Safety of Sarecycline, a Novel, Once-Daily, Narrow Spectrum	N=285 ***Characteristics*** **Sex** mixed **age (mean±SD)** 20.1676056338028±6.7286646771969361	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category**	***Results*** **GI side effects (n/N): arm 1** 6/76 **GI side effects (n/N): arm 2**	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information provided

Study details	Participants	Interventions	Outcomes and results	Comments
Antibiotic for the Treatment of Moderate to Severe Facial Acne Vulgaris: Results of a Phase 2, Dose-Ranging Study. 2018. Journal of Drugs in Dermatology: JDD **Trial ID** Leyden 2018 **Country** United States **Study type** RCT **Source of funding** Allergan plc, Ireland (conflicts of interest reported). ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF?	**age (other information)** age data reported for 284 participants as 1 person in PL group withdrew consent and did not have post-baseline efficacy assessment ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Investigator's Global Assessment scale (IGA) **Inclusion details** Males and females aged 12 to 45 years..Moderate to severe facial acne vulgaris characterised by 20 to 50 inflammatory lesions, 30 to 100 non-inflammatory lesions, and no more than 2 facial nodules. IGA baseline score of 3 ('moderate') or 4 ('severe')..Body weight between 52 kg and 88 kg at screening..Participants receiving prohibited medications entered an appropriate washout period prior to screening procedures..Females of childbearing potential had to have a negative urine pregnancy test and use of an effective method of contraception. **Exclusion details** Use of other acne treatments, excessive sun exposure, and tanning booths..Participants with dermatologic conditions of the face or facial hair that could interfere with clinical assessments of acne, facial sunburn..Prolonged Fridericia's corrected QT interval (>450 msec) on electrocardiogram..Allergy to tetracycline-class antibiotics or any component in the study drug..Pseudomembranous colitis or an antibiotic-associated colitis, cancer within the previous 6 months, or hepatitis, liver damage, or renal impairment.	12 to <24 weeks **Number of arms** 4 **Split face design** No **Intervention: arm 1** SAR 0.75 mg/kg **Intervention: arm 2** SAR 1.5 mg/kg **Intervention: arm 3** SAR 3.0 mg/kg **Intervention: arm 4** PL **Coded intervention: arm 1** SARE-oral **Coded intervention: arm 2** SARE-oral **Coded intervention: arm 3** SARE-oral **Coded intervention: arm 4** PLC-oral **Treatment category** Oral antibiotics	1/70 **GI side effects (n/N): arm 3** 2/66 **GI side effects (n/N): arm 4** 4/73	**2. Deviation from intervention** Low;double-blinded; likely participant-blinded; a modified ITT was done **3. Missing outcome data (efficacy)** Some concerns;14% discontinued - balanced between arms; ITT used **4. Outcome measurement (efficacy)** Some concerns;not reported if assessment of outcome was blinded **5. Selective reporting** High;Some of the specified outcomes in the protocol not reported **6. Overall bias** High

Study details	Participants	Interventions	Outcomes and results	Comments
	Number included **Number randomised: arm 1** 76 **Number randomised: arm 2** 70 **Number randomised: arm 3** 66 **Number randomised: arm 4** 73 **Number completed: arm 1** 64 **Number completed: arm 2** 60 **Number completed: arm 3** 57 **Number completed: arm 4** 64			
Study details **Reference** Mei, X. S., W.,Piao, Y.Effectiveness of photodynamic therapy with topical 5-aminolevulinic acid and intense pulsed light in Chinese acne vulgaris patients. 2013. Photodermatology Photoimmunology and Photomedicine **Trial ID** Mei 2013 **Country** China **Study type** RCT **Source of funding** Not reported (no conflicts of	N=41 ***Characteristics*** **Sex** mixed **age (mean±SD)** 24 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Global Acne Severity Scale (GEA Scale) **Inclusion details** Chinese patients aged over 18 years..Participants with II–IV facial acne according to Pillsbury grade and Fitzpatrick skin type II–IV. **Exclusion details** Participants exposed to systemic retinoid treatment in the last 6 months, systemic	***Interventions*** **Treatment intensity** Total 4 sessions, once every week. Assessments 1-wk after each session so have assumed endpoint is at 4th treatment (see table1) **Number of arms** 2 **Split face design** No **Intervention: arm 1** 5ALA 10%-IPL-PDT **Intervention: arm 2** IPL-PT + Vehicle **Coded intervention: arm 1**	***Results*** **Skin redness (n/N): arm 1** 3/21 **Skin redness (n/N): arm 2** 0/20 **Skin irritation (n/N): arm 1** 21/21 **Skin irritation (n/N): arm 2** 20/20	***Cochrane RoB Tool v2.0*** **1. Randomisation** High;Allocation not concealed **2. Deviation from intervention** Low;Participants & investigators blinded **3. Missing outcome data (efficacy)** Low;No withrawals / loss to follow-up. **4. Outcome measurement (efficacy)** Low;Assessor blinded

Study details	Participants	Interventions	Outcomes and results	Comments
interest). ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** not reported	antibiotics treatment or contraceptive and photosensitive drugs in the previous month, local acne drug treatment in the last 2 weeks..Participants with a tendency to form keloids or with a history of photosensitivity..Pregnant or breastfeeding women. ***Number included*** **Number randomised: arm 1** 21 **Number randomised: arm 2** 20 **Number completed: arm 1** 21 **Number completed: arm 2** 20	5ALA-IPL-PDT **Coded intervention: arm 2** IPL + Vehicle **Treatment category** Energy based (light / laser)		**5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** High
Study details **Reference** Miller, J. A. W., F. T.,Dowd, P. M.Anti-androgen treatment in women with acne: A controlled trial. 1986b. British Journal of Dermatology **Trial ID** Miller 1986b **Country** United Kingdom **Study type** RCT **Source of funding** Schering Chemicals Ltd. ***Analysis method*** **Intention to treat or completers analysis** completers	N=90 ***Characteristics*** **Sex** female **age (min/max)** 16/36 **age (other information)** CPA/EE mean age=24.2 (range 18-34); NOR/EE mean age 24.2 (range 18-36); CPA mean age=22.8 (range 16-30) ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Leeds Grading Scale, Cunliffe **Inclusion details** Women aged between 16 and 36 years..Moderate to severe acne (graded according to Burke & Cunliffe, 1984)..Any acne medication (other than contraceptive pill) stopped 6 weeks prior to study participation.	***Interventions*** **Treatment duration (weeks)** 26 **Treatment duration category** 24+ weeks **Number of arms** 3 **Split face design** No **Intervention: arm 1** CPA 2mg/EE 0.05 mg (days 5-25) + PL (days 5-14) **Intervention: arm 2** NOR 1mg/EE 0.05mg (days 5-25) + PL (days 5-14) **Intervention: arm 3** CPA 50mg (days 5-14),	***Results*** **Breast tenderness (n/N): arm 1** 5/26 **Breast tenderness (n/N): arm 2** 3/24 **Breast tenderness (n/N): arm 3** 4/26 **Sexual dysfunction (n/N): arm 1** 0/26 **Sexual dysfunction (n/N): arm 2** 1/24 **Sexual dysfunction (n/N): arm 3** 1/26 **Change in mood (n/N): arm 1**	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information provided **2. Deviation from intervention** Some concerns;double-blinded but not clear who was blinded; not reported if ITT analysis was done **3. Missing outcome data (efficacy)** High;Withdrawal imbalanced between groups

Study details	Participants	Interventions	Outcomes and results	Comments
	Oral contraception was continued until the commencement of the trial. **Exclusion details** Participants with medical contraindications to the study treatment..Current smokers (more than 5 cigarettes daily). ***Number included*** **Number randomised: arm 1** 28 **Number randomised: arm 2** 32 **Number randomised: arm 3** 30 **Number completed: arm 1** 24 **Number completed: arm 2** 26 **Number completed: arm 3** 26	then EE 0.05 mg (days 5-25) **Coded intervention: arm 1** CPA-oral + EE-oral + PLC-oral **Coded intervention: arm 2** NOR-oral + EE-oral + PLC-oral **Coded intervention: arm 3** CPA-oral + EE-oral **Treatment category** Hormonal contraceptives / Hormone-modifying agents	3/26 **Change in mood (n/N): arm 2** 3/24 **Change in mood (n/N): arm 3** 3/26 **Breakthrough bleeding (n/N): arm 1** 2/26 **Breakthrough bleeding (n/N): arm 2** 3/24 **Breakthrough bleeding (n/N): arm 3** 4/26	(more in Diane and placebo arm) and more than 5% **4. Outcome measurement (efficacy)** Some concerns;not reported if assessment of outcome was blinded **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** High
Study details **Reference** Moore, A. G., L. J.,Bruce, S.,Sadick, N.,Tschen, E.,Werschler, P.,Cook-Bolden, F. E.,Dhawan, S. S.,Forsha, D.,Gold, M. H.,et al.,Once-Daily Oral Sarecycline 1.5 mg/kg/day Is Effective for Moderate to Severe Acne Vulgaris: results from Two Identically Designed, Phase 3, Randomized, Double-Blind Clinical Trials. 2018. Journal of drugs in dermatology **Trial ID** Moore 2018;Trial 1	N=968 ***Characteristics*** **Sex** mixed **age (other information)** SAR mean age=19.6 (range 10-45); PL mean age=19.8 (range 10-45) ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Investigator's Global Assessment scale (IGA) **Inclusion details** Participants aged 9 to 45 years, weighing 33 to 136 kg..Score of 3 (moderate) or 4 (severe) on the IGA scale for inflammatory lesions of	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** SAR 1.5 mg/kg **Intervention: arm 2** PL **Coded intervention:**	***Results*** **GI side effects (n/N): arm 1** 22/481 **GI side effects (n/N): arm 2** 12/483 **Thrush/candidiasis (n/N): arm 1** 3/481 **Thrush/candidiasis (n/N): arm 2** 0/483	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information provided **2. Deviation from intervention** Low;double-blinded - participants were likely blinded; ITT analysis was done **3. Missing outcome data (efficacy)** Some

Study details	Participants	Interventions	Outcomes and results	Comments
Country United States **Study type** RCT **Source of funding** Allergan plc, Ireland (conflicts of interest reported). ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** MI (no other details reported)	acne; 20 to 50 inflammatory and =100 non-inflammatory lesions, and =2 nodules. **Exclusion details** Dermatologic condition or facial hair, any chronic illness interfering with study assessment, allergy or resistance to tetracyclines, drug-induced acne, hormonal contraceptive initiation, systemic retinoids, systemic corticosteroids, androgens, or anti-androgens within 12 weeks prior to study. ***Number included*** **Number randomised: arm 1** 483 **Number randomised: arm 2** 485 **Number completed: arm 1** 420 **Number completed: arm 2** 405	**arm 1** SARE-oral **Coded intervention: arm 2** PLC-oral **Treatment category** Oral antibiotics		concerns;Discontinuations 15% - balanced between arms; few due inefficacy **4. Outcome measurement (efficacy)** Some concerns;not reported if assessment of outcome was blinded **5. Selective reporting** Some concerns;Some of the specified outcomes in the protocol not reported; report used IGA success for facial acne defined as a =2-point decrease from baseline and a score of 0 (clear) or 1 (almost clear) - differs from the protocol **6. Overall bias** Some concerns
Study details **Reference** Moore, A. G., L. J.,Bruce, S.,Sadick, N.,Tschen, E.,Werschler, P.,Cook-Bolden, F. E.,Dhawan, S. S.,Forsha,	N=1034 ***Characteristics*** **Sex** mixed **age (other information)** SAR mean age=20.4 (range 9-44); PL mean	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category**	***Results*** **GI side effects (n/N): arm 1** 10/513 **GI side effects (n/N): arm 2**	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information provided

Study details	Participants	Interventions	Outcomes and results	Comments
D.,Gold, M. H.,et al.,Once-Daily Oral Sarecycline 1.5 mg/kg/day Is Effective for Moderate to Severe Acne Vulgaris: results from Two Identically Designed, Phase 3, Randomized, Double-Blind Clinical Trials. 2018. Journal of drugs in dermatology **Trial ID** Moore 2018;Trial 2 **Country** United States **Study type** RCT **Source of funding** Allergan plc, Ireland (conflicts of interest reported). ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** MI (no other details reported)	age=19.7 (range 10-44) ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Investigator's Global Assessment scale (IGA) **Inclusion details** Participants aged 9 to 45 years, weighing 33 to 136 kg..Score of 3 (moderate) or 4 (severe) on the IGA scale for inflammatory lesions of acne; 20 to 50 inflammatory and =100 non-inflammatory lesions, and =2 nodules. **Exclusion details** Dermatologic condition or facial hair, any chronic illness interfering with study assessment, allergy or resistance to tetracyclines, drug-induced acne, hormonal contraceptive initiation, systemic retinoids, systemic corticosteroids, androgens, or anti-androgens within 12 weeks prior to study. ***Number included*** **Number randomised: arm 1** 519 **Number randomised: arm 2** 515 **Number completed: arm 1** 433 **Number completed: arm 2** 444	12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** SAR 1.5 mg/kg **Intervention: arm 2** PL **Coded intervention: arm 1** SARE-oral **Coded intervention: arm 2** PLC-oral **Treatment category** Oral antibiotics	5/513 **Thrush/candidiasis (n/N): arm 1** 1/513 **Thrush/candidiasis (n/N): arm 2** 0/513	**2. Deviation from intervention** Low;double-blinded - participants were likely blinded; ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;Discontinuations 15% - balanced between arms; few due inefficacy **4. Outcome measurement (efficacy)** Some concerns;not reported if assessment of outcome was blinded **5. Selective reporting** Some concerns;Some of the specified outcomes in the protocol not reported; report used IGA success for facial acne defined as a =2-point decrease from baseline and a score of 0 (clear)

Study details	Participants	Interventions	Outcomes and results	Comments
				or 1 (almost clear) - differs from the protocol **6. Overall bias** Some concerns
Study details **Reference** Pariser, D. M. T., D. M.,Clark, S. D.,Jones, T. M.,Liu, Y.,Graeber, M.The efficacy and safety of adapalene gel 0.3% in the treatment of acne vulgaris: A randomized, multicenter, investigator-blinded, controlled comparison study versus adapalene gel 0.1% and vehicle. 2005. Cutis **Trial ID** Pariser 2005 **Country** United States **Study type** RCT **Source of funding** Galderma Research & Development (conflicts of interest reported). ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** baseline assigned?	N=214 ***Characteristics*** **Sex** mixed **age (mean±SD)** 17.3±5.07 **age (median)** 16 **age (min/max)** 12/45 ***Inclusion/exclusion criteria*** **Used validated acne scale** yes **Acne scale** Leeds Revised Grading Scale **Inclusion details** Participants aged 12 to 40 years..Moderate to moderately severe acne vulgaris; minimum of 20 inflammatory facial lesions (not >2 nodules/cysts), 20 non-inflammatory facial lesions; global facial severity grade 4 to 10 according to the Leeds Revised Acne Grading System..Washout periods for certain topical and systemic treatments were required..Negative urine pregnancy test results required at screening and at the final visit for women of childbearing potential. **Exclusion details** Not reported. ***Number included*** **Number randomised: arm 1** 70	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 3 **Split face design** No **Intervention: arm 1** ADAP 0.3% gel **Intervention: arm 2** ADAP 0.1% gel **Intervention: arm 3** Vehicle **Coded intervention: arm 1** ADAP-topical **Coded intervention: arm 2** ADAP-topical **Coded intervention: arm 3** Vehicle **Treatment category** Topical retinoids	***Results*** **Skin irritation (n/N): arm 1** 16/70 **Skin irritation (n/N): arm 2** 13/70 **Skin irritation (n/N): arm 3** 0/74	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;reported only that medication was dispensed by a third party to protect blinding **2. Deviation from intervention** Some concerns;not reported if participants were blinded; ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;Withdrawal imbalanced between groups (21% in the adapalene gel 0.3% arm, only 7% in the adapalene 0.1% gel arm) **4. Outcome measurement (efficacy)** Low;investigator-

Study details	Participants	Interventions	Outcomes and results	Comments
	Number randomised: arm 2 70 **Number randomised: arm 3** 74 **Number completed: arm 1** 55 **Number completed: arm 2** 65 **Number completed: arm 3** 62			blinded **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** High
Study details **Reference** Pariser, D. M. R., P.,Cook-Bolden, F. E.,Korotzer, A.An aqueous gel fixed combination of clindamycin phosphate 1.2% and benzoyl peroxide 3.75% for the once-daily treatment of moderate to severe acne vulgaris. 2014. Journal of Drugs in Dermatology **Trial ID** Pariser 2014 **Country** United States **Study type** RCT **Source of funding** Valeant Pharmaceuticals North America LLC. ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** MI MCMC	N=498 ***Characteristics*** **Sex** mixed **age (mean±SD)** 18.7±5.82 **age (median)** 17 **age (min/max)** 12/40 **age (other information)** Sig. diff (p=0.02) between age of groups ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Evaluator's Global Severity Scale (EGSS) **Inclusion details** Males and females of any race and ethnicity, aged 12 to 40 years..Moderate to severe acne vulgaris (a score of 3 or 4 on the Global Severity Score (EGSS), presenting with 20 to 40 inflammatory lesions (papules, pustules, and nodules), 20 to 100 non-inflammatory lesions (open and closed comedones), and =2 nodules..Women of childbearing age were	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** BPO 3.75%/CLIND 1.2% gel **Intervention: arm 2** Vehicle **Coded intervention: arm 1** BPO-topical + CLIND-topical **Coded intervention: arm 2** Vehicle **Treatment category** Topical or combination	***Results*** **Participant reported improvement (n/N): arm 1** 169/253 **Participant reported improvement (n/N): arm 2** 101/245	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;insufficient information provided on allocation concealment **2. Deviation from intervention** Low;double-blinded & ITT analysis **3. Missing outcome data (efficacy)** Some concerns;Withdrawal imbalanced between groups, &>5% **4. Outcome measurement (efficacy)** Low **5. Selective**

Study details	Participants	Interventions	Outcomes and results	Comments
	required to have a negative urine pregnancy test and to agree to use an effective form of contraception during the study period..A washout period of up to 1 month was required for participants who used previous prescription and over-the-counter acne treatments (including, topical (face) and systemic treatments: topical astringents and abrasives (1 week); topical anti-acne products, including soaps containing antimicrobials, and known comedogenic products (2 weeks); topical retinoids, retinol, and systemic acne treatments (4 weeks); and systemic retinoids (6 months). **Exclusion details** Not reported. ***Number included*** **Number randomised: arm 1** 253 **Number randomised: arm 2** 245 **Number completed: arm 1** 234 **Number completed: arm 2** 213			**reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** Some concerns
Study details **Reference** Pariser, D. M. E., L. F.,Bukhalo, M.,Waterman, G.,Jarratt, M.,Bhatia, A.,Greenstein, D.,Hamzavi, F.,Kantor, J.,Speelman, P. N.,Murakawa, G. J.,Tichy, E.,Zaengelin, A.,Frankel, E.,Werschler, W.Photodynamic therapy with methyl aminolaevulinate 80 mg g⁻¹ for severe	N=153 ***Characteristics*** **Sex** mixed **age (min/max)** 12/36 **age (other information)** MAL-PDT median age=17 (range 12-36), <18 years-old, n=59; Vehicle median age=17 (range 12-35), <18 years-old, n=31 ***Inclusion/exclusion criteria*** **Used validated acne scale**	***Interventions*** **Treatment intensity** Total 4 sessions, once every 2 weeks. Endpoint is 6-wks after last treatment. **Number of arms** 2 **Split face design** No **Intervention: arm 1** MAL 8%-RED-PDT	***Results*** **Skin redness (n/N): arm 1** 4/100 **Skin redness (n/N): arm 2** 0/53 **Pigment changes (n/N): arm 1** 2/100 **Pigment changes (n/N): arm 2**	***Cochrane RoB Tool v2.0*** **1. Randomisation** Low **2. Deviation from intervention** Low;double-blinded; according to the study protocol it is quadruple-blinded (participant, care

Study details	Participants	Interventions	Outcomes and results	Comments
facial acne vulgaris: A randomized vehicle-controlled study. 2016. British Journal of Dermatology **Trial ID** Pariser 2016 **Country** United States **Study type** RCT **Source of funding** Photocure ASA, Norway (conflicts of interest reported). ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	no **Acne scale** Investigator's Global Assessment scale (IGA) **Inclusion details** Males and females aged 12 to 35 years..Severe facial acne vulgaris (defined by an IGA rating score of 4); 27 to 75 inflammatory lesions (papules, pustules and no more than 3 nodules) and 20 to 100 non-inflammatory lesions (open and closed comedones) on the face; Fitzpatrick skin types I to VI. Confirmed using standardised clinical photographs. Females of childbearing potential were required to use appropriate contraception (same product and dose if using an oral contraceptive) for at least 14 days before the first treatment and during the study. **Exclusion details** Participants with acne conglobata, acne fulminans, secondary acne, melanoma or dysplastic naevi in the treatment area..Facial har that might interfere with study assessments..Participants with porphyria, cutaneous photosensitivity or known allergy to methyl aminolaevulinate, components of the cream or similar photosensitisers..Participants with moderate-to-very-severe facial acne scarring..Pregnant or nursing females..Systemic acne treatment (oral antibiotics within 1 month or oral isotretinoin within 6 months); topical treatments (other than medicated cleansers) within 14 days; facial procedures (for example, dermabrasion, chemical or laser peels); exposure to ultraviolet radiation (other than sunlight) within 1 month and concomitant hormonal therapy for acne were prohibited. ***Number included***	**Intervention: arm 2** Vehicle-RED-PDT **Coded intervention: arm 1** MAL-RED-PDT **Coded intervention: arm 2** Vehicle + RED **Treatment category** Energy based (light / laser)	0/53	provider, investigator, outcomes assessor); ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;16% withdrawals - imbalanced between arms as 12 out of 17 in the active arm discontinued due to adverse events and none in the other arm **4. Outcome measurement (efficacy)** Low **5. Selective reporting** Low **6. Overall bias** Some concerns

Study details	Participants	Interventions	Outcomes and results	Comments
	Number randomised: arm 1 100 **Number randomised: arm 2** 53 **Number completed: arm 1** 83 **Number completed: arm 2** 46			
Study details **Reference** Parsad, D. P., R.,Nagpal, R.,Negi, K. S.Azithromycin monthly pulse vs daily doxycycline in the treatment of acne vulgaris. 2001. Journal of Dermatology **Trial ID** Parsad 2001 **Country** India **Study type** RCT **Source of funding** Not reported. ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** Unclear	N=60 ***Characteristics*** **Sex** mixed **age (min/max)** 16 **age (other information)** no other data on age reported ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Leeds Grading Scale, Cunliffe **Inclusion details** Participants with moderate to severe acne (grade 2 to 8) on the Burke & Cunliffe scale. **Exclusion details** Participants aged <16 years of age..Participants with sensitivity to any drugs used in the study..Women who were pregnant, planning pregnancy, or nursing a child. ***Number included*** **Number randomised: arm 1** 30 **Number randomised: arm 2**	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** DOXY 100mg + TRET 0.05% cream **Intervention: arm 2** AZITH 500 mg + TRET 0.05% cream **Coded intervention: arm 1** DOXY-oral + TRET-topical **Coded intervention: arm 2** AZITH-oral + TRET-topical	***Results*** **Skin irritation (n/N): arm 1** 3/22 **Skin irritation (n/N): arm 2** 4/28	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information provided **2. Deviation from intervention** Some concerns;not reported if investigators/participants were blinded; ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;17% withdrawals - imbalanced between arms (more in the 100 mg doxycycline + topical 0.05% tretinoin cream arm) **4. Outcome measurement**

Study details	Participants	Interventions	Outcomes and results	Comments
	30 **Number completed: arm 1** 22 **Number completed: arm 2** 28			**(efficacy)** Some concerns;not reported if assessment of outcome was blinded **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** High
Study details **Reference** Richter, J. R. B., M. T.,De Boulle, Klvm,Degreef, H. J.,Poli, F.Efficacy of a fixed clindamycin phosphate 1.2%, tretinoin 0.025% gel formulation (Velac) in the topical control of facial acne lesions. 1998a. Journal of dermatological treatment **Trial ID** Richter 1998a **Country** Europe **Study type** RCT **Source of funding** Not reported. ***Analysis method*** **Intention to treat or completers analysis** ITT	N=161 ***Characteristics*** **Sex** mixed **age (mean±SD)** 19.7±2.9 **age (min/max)** 14/26 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Cook **Inclusion details** Outpatients aged 14 to 26 years..Facial acne (severity grades of 3 and higher according to the modified scoring scale of Cook). **Exclusion details** Use of tretinoin, topical or systemic antibiotics, irritants or hormonal treatments in the 4 weeks prior to study commencement..Skin disorders likely to affect drug absorption or disorders requiring medical treatment within 5 days prior	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** CLIND 1.2%/TRET 0.025% gel **Intervention: arm 2** TRET 0.025% gel **Coded intervention: arm 1** CLIND-topical + TRET-topical **Coded intervention: arm 2** TRET-topical	***Results*** **Skin irritation (n/N): arm 1** 5 **Skin irritation (n/N): arm 2** 3 **Skin irritation (n/N): arm 1** 72 **Skin irritation (n/N): arm 2** 73	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information provided **2. Deviation from intervention** Low;double-blinded - likely that participants were blinded; ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;more than 5% withdrawals in one arm, mainly due to adverse effects **4. Outcome measurement**

Study details	Participants	Interventions	Outcomes and results	Comments
Method of ITT imputation not reported	to study start..Known or suspected hypersensitivity to the agents in CTG or related compounds..History of serious allergic reactions to drug treatment..Pregnancy, lactation and/or use of oral contraceptives with a specific anti-androgenic action or any oral contraceptive treatment started within 3 months prior to study commencement. ***Number included*** **Number randomised: arm 1** 81 **Number randomised: arm 2** 80 **Number completed: arm 1** 69 **Number completed: arm 2** 69	**Treatment category** Topical or combination		**(efficacy)** Some concerns;not reported if assessment of outcome was blinded **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** Some concerns
Study details **Reference** Sami, N. A. A., A. T.,Badawi, A. M.Phototherapy in the treatment of acne vulgaris. 2008. Journal of drugs in dermatology **Trial ID** Sami 2008 **Country** Egypt **Study type** RCT **Source of funding** Not reported. ***Analysis method*** **Intention to treat or completers analysis** ITT	N=45 ***Characteristics*** **Sex** mixed **age (mean±SD)** 29 **age (min/max)** 20/38 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Burton **Inclusion details** Males and females with moderate to severe facial acne according to Burton classification. **Exclusion details** Participants with a history of topical acne treatment or systemic antibiotics within the past 2 weeks, or use of systemic steroids,	***Interventions*** **Treatment duration (weeks)** 4 **Treatment duration category** 0 to <6 weeks **Treatment intensity** Trial continued until 90% lesion clearance observed but 1-mo data available. Total sessions at 1-mo are 4, 4 and 8, respectively, for PDL (1 session, once a week), IPL (1 session, once a week) and BR-LED (2 sessions every week) groups **Number of arms**	***Results*** **Pigment changes (n/N): arm 1** 3/15 **Pigment changes (n/N): arm 2** 0/15 **Pigment changes (n/N): arm 3** 0/15 **Participant reported improvement (n/N): arm 1** 15/15 **Participant reported improvement (n/N): arm 2** 12/15 **Participant reported improvement (n/N): arm**	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;methods not reported **2. Deviation from intervention** Some concerns;Not reported if participants were blinded **3. Missing outcome data (efficacy)** Some concerns;not clear if/how many participants discontinued

Study details	Participants	Interventions	Outcomes and results	Comments
	systemic retinoids, or anti-inflammatory drugs within the past 6 months..History of photosensitivity..Pregnancy. ***Number included*** **Number randomised: arm 1** 15 **Number randomised: arm 2** 15 **Number randomised: arm 3** 15 **Number completed: arm 1** 15 **Number completed: arm 2** 15 **Number completed: arm 3** 15	3 **Split face design** No **Intervention: arm 1** 595 nm PDL PT **Intervention: arm 2** 550 nm-1200 nm IPL PT **Intervention: arm 3** BR-LED PT **Coded intervention: arm 1** PDL **Coded intervention: arm 2** IPL **Coded intervention: arm 3** BR-LED **Treatment category** Energy based (light / laser)	**3** 6/15	**4. Outcome measurement (efficacy)** Low **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** Some concerns
Study details **Reference** Schmidt, N. G., E. H.Clindamycin 1.2% tretinoin 0.025% gel versus clindamycin gel treatment in acne patients: A focus on fitzpatrick skin types. 2011. Journal of Clinical and Aesthetic Dermatology **Trial ID** Schmidt 2011 **Country** United States **Study type** RCT	N=2010 ***Characteristics*** **Sex** mixed **age (mean±SD)** 19.0501492537313±7.2507470119521908 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Evaluator's Global Severity Scale (EGSS) **Inclusion details** Males and females aged over 12 years..Facial acne vulgaris with 20 to 50 inflammatory lesions (papules and pustules), 20 to 100 non-	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** CLIND 1.2%/TRET 0.025% gel **Intervention: arm 2**	***Results*** **Skin irritation (n/N): arm 1** 34 **Skin irritation (n/N): arm 2** 14 **Skin irritation (n/N): arm 1** 1008 **Skin irritation (n/N): arm 2** 1002	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information about allocation concealment provided **2. Deviation from intervention** Some concerns;double-blinded but not clear who was blinded; ITT analysis was done

Study details	Participants	Interventions	Outcomes and results	Comments
Source of funding Not reported (conflicts of interest reported). ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	inflammatory lesions (open and closed comedones), and not more than 2 nodules; Evaluators Global Severity Score (EGSS) of moderate or severe..Willing to undergo the specified washout periods for topical antibiotics and other topical antibacterial drugs (2 weeks); facial anti-inflammatory agents and corticosteroids (4 weeks); retinoids, including retinol (4 weeks)..Had undergone the specified washout periods of systemic treatments including corticosteroids and intramuscular injections (4 weeks); antibiotics (4 weeks); other systemic acne treatments (4 weeks); systemic retinoids (6 months). **Exclusion details** Participated in a similar study within 30 days of enrolment or participating in another study..Facial dermatological conditions that could hinder or obstruct clinical evaluations..Use of other non-acne topical medication that could interfere with study treatment..Pregnant, nursing, planning a pregnancy, or became pregnant during the trial..Non-compliance with washout criteria for topical or systemic treatment. ***Number included*** **Number randomised: arm 1** 1008 **Number randomised: arm 2** 1002 **Number completed: arm 1** 859 **Number completed: arm 2** 838	CLIND 1.2% gel **Coded intervention: arm 1** CLIND-topical + TRET-topical **Coded intervention: arm 2** CLIND-topical **Treatment category** Topical or combination		**3. Missing outcome data (efficacy)** Some concerns;16% withdrawals - balanced between arms (unclear how many due to inefficacy); ITT used **4. Outcome measurement (efficacy)** Some concerns;not reported if assessment of outcome was blinded **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** High
Study details **Reference** Sklar, J. L. J., C.,Rizer, R.,Gans, E. H.Evaluation of	N=94 ***Characteristics*** **Sex**	***Interventions*** **Treatment duration (weeks)** 13	***Results*** **Skin irritation (n/N): arm 1** 13	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no

Study details	Participants	Interventions	Outcomes and results	Comments
Triaz 10% Gel and Benzamycin in acne vulgaris. 1996. Journal of dermatological treatment **Trial ID** Sklar 1996 **Country** United States **Study type** RCT **Source of funding** Not reported. ***Analysis method*** **Intention to treat or completers analysis** completers	mixed **age (min/max)** 16/30 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** Males and females aged 16 to 30 years..Moderate to moderately severe, papular-pustular, facial acne vulgaris with a minimum number of inflamed lesions..Willingness to co-operate and adhere to study criteria..Absence of interfering medical and dermatological conditions and medications..Absence of pregnancy and avoidance of interference from oral contraceptives. **Exclusion details** Not reported. ***Number included*** **Number randomised: arm 1** 30 **Number randomised: arm 2** 32 **Number randomised: arm 3** 32 **Number completed: arm 1** 28 **Number completed: arm 2** 30 **Number completed: arm 3** 28	**Treatment duration category** 12 to <24 weeks **Number of arms** 3 **Split face design** No **Intervention: arm 1** BPO-topical 5%/ ERYTH-topical 3% **Intervention: arm 2** BPO-topical 10% **Intervention: arm 3** Vehicle **Coded intervention: arm 1** BPO-topical + ERYTH-topical **Coded intervention: arm 2** BPO-topical **Coded intervention: arm 3** Vehicle **Treatment category** Topical or combination	**Skin irritation (n/N): arm 2** 4 **Skin irritation (n/N): arm 3** 1 **Skin irritation (n/N): arm 1** 32 **Skin irritation (n/N): arm 2** 30 **Skin irritation (n/N): arm 3** 31	information provided **2. Deviation from intervention** Some concerns;participants not blinded; ITT not used **3. Missing outcome data (efficacy)** Some concerns;5% discontinued **4. Outcome measurement (efficacy)** Low;Investigator blinded **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** Some concerns
Study details	N=201	***Interventions***	***Results***	***Cochrane RoB***

Study details	Participants	Interventions	Outcomes and results	Comments
Reference Stein Gold, L. ,. C., L. E., Johnson, L. A., Gottschalk, R. W.Is switching retinoids a sound strategy for the treatment of acne vulgaris?. 2008. Journal of drugs in dermatology **Trial ID** Stein Gold 2008 **Country** United States **Study type** RCT **Source of funding** Not reported (conflicts of interest reported). ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	***Characteristics*** **Sex** mixed **age (mean±SD)** 19 **age (other information)** ADAP mean age=18.5; ADAP then TAZ, mean age=19.4. ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** Males and females aged between 12 and 35 years. .15 to 100 non-inflammatory lesions, at least 20 inflammatory lesions, and no more than 3 nodules. **Exclusion details** Participants with severe nodulocystic acne..Pregnant, nursing, or planning a pregnancy during the study..Participants with facial hair that would interfere with study assessments..Washout periods <4 weeks for topical acne treatments or <6 months for systemic treatment..Participants with other dermatologic conditions requiring interfering treatment. ***Number included*** **Number randomised: arm 1** 101 **Number randomised: arm 2** 100	**Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** ADAP 0.1% gel **Intervention: arm 2** ADAP 0.1% gel for 6 weeks then TAZ 0.1% cream for 6 weeks **Coded intervention: arm 1** ADAP-topical **Coded intervention: arm 2** ADAP-topical / TAZ-topical **Treatment category** Topical retinoids	**Skin irritation (n/N): arm 1** 6 **Skin irritation (n/N): arm 2** 8 **Skin irritation (n/N): arm 1** 98 **Skin irritation (n/N): arm 2** 100	***Tool v2.0*** **1. Randomisation** Some concerns;no information provided **2. Deviation from intervention** Some concerns;not reported if participants were blinded; ITT analysis was done **3. Missing outcome data (efficacy)** High;more than 5% withdrawals; not clear how balanced between arms; no reasons reported **4. Outcome measurement (efficacy)** Low **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** High
Study details	N=494	***Interventions***	***Results***	***Cochrane RoB***

Study details	Participants	Interventions	Outcomes and results	Comments
Reference Stein Gold, L. F. J., M. T.,Bucko, A. D.,Grekin, S. K.,Berlin, J. M.,Bukhalo, M.,Weiss, J. S.,Berk, D. R.,Chang-Lin, J. E.,Lin, V.,et al.,Efficacy and Safety of Once-Daily Dapsone Gel, 7.5% for Treatment of Adolescents and Adults With Acne Vulgaris: first of Two Identically Designed, Large, Multicenter, Randomized, Vehicle-controlled Trials. 2016. Journal of drugs in dermatology **Trial ID** Stein Gold 2016 **Country** United States. **Study type** RCT.RCT **Source of funding** Industry funded. Galderma Research & Development (conflicts of interest reported). ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOFC	***Characteristics*** **Sex** mixed.mixed **age (mean±SD)** 20±7.47 **age (median)** 17 **age (min/max)** 12/63 **age (other information)** ADAP 0.3%, range 12-57; ADAP 0.1%, range 12-49; Vehicle, range=12-36 ***Inclusion/exclusion criteria*** **Used validated acne scale** no. **Acne scale** Global Acne Assessment Score (GAAS). **Inclusion details** Moderate to severe inflammatory facial acne, that is a score of 3 (moderate) or 4 (severe) on the IGA, the presence of 20 to 100 inflammatory lesions, 30 to 150 non-inflammatory lesions (including the nose), and up to 2 nodules on the face..A urine pregnancy test was required for females at baseline and throughout the study. **Exclusion details** Severe cystic acne, acne conglobata, acne fulminans, or secondary acne (eg, chloracne, drug-induced acne) and having one or more nodule or cyst above the mandibular line. Patients using oral contraceptives solely for acne control were excluded, as were patients planning to use any systemic therapy during the study period that could potentially affect their acne. Additional exclusion criteria included underlying diseases or dermatologic	**Treatment duration (weeks)** 12.12 **Treatment duration category** 12 to <24 weeks.12 to <24 weeks **Number of arms** 3 **Split face design** no **Intervention: arm 1** ADAP 0.3%/BPO 2.5% gel **Intervention: arm 2** ADAP 0.1%/BPO 2.5% gel **Intervention: arm 3** Vehicle **Coded intervention: arm 1** DAPS-topical.ADAP-topical + BPO-topical **Coded intervention: arm 2** ADAP-topical + BPO-topical **Coded intervention: arm 3** Vehicle **Treatment category** Topical non-retinoids ± other treatment.	**Skin irritation (n/N): arm 1** 45/213 **Skin irritation (n/N): arm 2** 34/212 **Skin irritation (n/N): arm 3** 5/68 **Participant reported improvement (n/N): arm 1** 182/204 **Participant reported improvement (n/N): arm 2** na/na **Participant reported improvement (n/N): arm 3** 26/65	***Tool v2.0*** **1. Randomisation** Some concerns;participants randomised on a 1:1 ratio and stratified by sex using an interactive voice/web randomisation system; methods not reported for allocation concealment;Low **2. Deviation from intervention** Some concerns;double-blind (not reported if participants were blinded); ITT analysis was done;Low;double-blinded; ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;9.2% vs 7.8% participants discontinued, mainly because lost to follow-up, personal reasons, or other reasons; a study site (n=51) also discontinued

Study details	Participants	Interventions	Outcomes and results	Comments
	conditions that required the use of topical or systemic therapy, and skin abnormalities or other physical characteristics that could confound study results. Patients undergoing topical procedures, such as phototherapy or use of energy-based devices, or cosmetic procedures within 1 week of screening and those using topical acne treatments, including anti-inflammatory drugs, salicylic acid, corticosteroids, and retinoids, within 2 weeks of screening. Participants with acne conglobata, acne fulminans, nodulocystic acne, or acne requiring systemic treatment. ***Number included*** **Number randomised: arm 1** 213 **Number randomised: arm 2** 212 **Number completed: arm 1** 197 **Number completed: arm 2** 192 **Number randomised: arm 3** 69 **Number completed: arm 3** 61			due to termination (serious non-compliance with Good Clinical Practices);Some concerns;10% withdrawals - balanced between arms; ITT used **4. Outcome measurement (efficacy)** Some concerns;unclear who was blinded;Some concerns;not reported if assessment of outcome was blinded **5. Selective reporting** Some concerns;registered with clinicaltrials.gov; the authors stated that sensitivity analysis was concuted to include participants from the terminated site to evaluate the impact of excluding these participant, but no results appear to have

Study details	Participants	Interventions	Outcomes and results	Comments
				been reported;Low **6. Overall bias** High;Some concerns
Study details **Reference** Stewart, D. M. T., H. M.,Weiss, J. S.,Plott, R. T.Dose-ranging efficacy of new once-daily extended-release minocycline for acne vulgaris. 2006. Cutis; cutaneous medicine for the practitioner **Trial ID** Stewart 2006 **Country** United States **Study type** RCT **Source of funding** Not reported (conflicts of interest reported). ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	N=174 ***Characteristics*** **Sex** mixed **age (mean±SD)** 17.7 **age (min/max)** 17/19 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** Participants aged 12 to 30 years, weighing between 39.1 kg and 102.3 kg (86 to 225 lb)..Diagnosed with moderate to severe facial acne vulgaris; at least 20 and no more than 100 inflammatory facial lesions and <5 facial nodules or cysts..Females of childbearing potential must have had a negative urine pregnancy test result (25 µg/mL sensitivity), be using contraception and will to continue on contraception during the study..Participants or parent/guardian consent provided. **Exclusion details** Participants sensitive to minocycline or any of the components..Pregnancy..Males with facial hair..Use of supplements containing aluminium, calcium, iron, or magnesium, or vitamin A..Prior history of complicating illnesses or medications.	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 3 **Split face design** No **Intervention: arm 1** MINO-oral 2mg/kg/day **Intervention: arm 2** MINO-oral 3mg/kg/day **Intervention: arm 3** PLC-oral **Coded intervention: arm 1** MINO-oral **Coded intervention: arm 2** MINO-oral **Coded intervention: arm 3** PLC-oral **Treatment category** Oral antibiotics	***Results*** **Skin irritation (n/N): arm 1** 3/59 **Skin irritation (n/N): arm 2** 2/60 **Skin irritation (n/N): arm 3** 1/55 **GI side effects (n/N): arm 1** 14/59 **GI side effects (n/N): arm 2** 20/60 **GI side effects (n/N): arm 3** 18/55	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;methods not reported **2. Deviation from intervention** Low;double-blind;ITT **3. Missing outcome data (efficacy)** High;>20% discontinued - unclear how many were due to lack of efficacy - or which arm they were in **4. Outcome measurement (efficacy)** Low;described as double-blind, without further details **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias**

Study details	Participants	Interventions	Outcomes and results	Comments
	Number included **Number randomised: arm 1** 59 **Number randomised: arm 2** 60 **Number randomised: arm 3** 55 **Number completed: arm 1** na **Number completed: arm 2** na **Number completed: arm 3** na			High
Study details **Reference** Strauss, J. S. R., R. P.,Shalita, A. R.,Konecky, E.,Pochi, P. E.,Comite, H.,Exner, J. H.Isotretinoin therapy for acne: Results of a multicenter dose-response study. 1984a. Journal of the American Academy of Dermatology **Trial ID** Strauss 1984a **Country** United States **Study type** RCT **Source of funding** Not reported. ***Analysis method*** **Intention to treat or completers analysis** Completers	N=141 ***Characteristics*** **Sex** mixed **age (other information)** Mean age 23.3,23.1 & 22.2 in the 3 groups (no SDs reported) ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** Participants with treatment-resistant, severe nodulocystic acne; minimum of 10 inflammatory nodulocystic acne lesions at least 4 mm in diameter on the face, back, or chest..Off all treatment for at least 1 month..Female participants were required to have negative pregnancy test within 2 weeks prior to starting treatment. **Exclusion details** Not reported.	***Interventions*** **Treatment duration (weeks)** 20 **Treatment duration category** 12 to <24 weeks **Number of arms** 3 **Split face design** No **Intervention: arm 1** ISO<120.Daily<0.5 (0.1 mg/kg daily for 140 days) **Intervention: arm 2** ISO<120.Daily=0.5 (0.5 mg/kg daily for 140 days) **Intervention: arm 3** ISO=120.Daily=0.5 (1 mg/kg daily for 140 days) **Coded intervention: arm 1** ISO<120.Daily<0.5-oral	***Results*** **Mucosal or cutaneous changes (n/N): arm 1** 35/46 **Mucosal or cutaneous changes (n/N): arm 2** 41/46 **Mucosal or cutaneous changes (n/N): arm 3** 46/49 **Relapse follow up: arm 1** 12 **Relapse follow up: arm 2** 12 **Relapse follow up: arm 3** 12 **Relapse (n/N): arm 1** 19/46 **Relapse (n/N): arm 2** 9/46	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns; no information about allocation concealment provided **2. Deviation from intervention** High; study was double-blinded in the beginning; then "The protocol design allowed participating participants to be retreated with isotretinoin in an open study beginning at least 8 weeks after the completion of the first course of

Study details	Participants	Interventions	Outcomes and results	Comments
	Number included **Number randomised: arm 1** na **Number randomised: arm 2** na **Number randomised: arm 3** na **Number completed: arm 1** 46 **Number completed: arm 2** 46 **Number completed: arm 3** 49	**Coded intervention: arm 2** ISO<120.Daily=0.5-oral **Coded intervention: arm 3** ISO=120.Daily=0.5-oral **Treatment category** Oral isotretinoin	**Relapse (n/N): arm 3** 5/49	therapy if optimal improvement (less than a 95% reduction in lesions) had not been achieved in the first course." No ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;6% withdrawals in 2 out of 3 arms; no reasons provided; no ITT **4. Outcome measurement (efficacy)** Some concerns;not reported if assessment of outcome was blinded **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** High
Study details **Reference** Tanghetti, E. A., W.,Solomon, B.,Loven, K.,Shalita,	N=121 ***Characteristics*** **Sex** mixed	***Interventions*** **Treatment duration (weeks)** 12	***Results*** **Skin irritation (n/N): arm 1** 11/61	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no

Study details	Participants	Interventions	Outcomes and results	Comments
A.Tazarotene versus tazarotene plus clindamycin/benzoyl peroxide in the treatment of acne vulgaris: a multicenter, double-blind, randomized parallel-group trial. 2006. Journal of drugs in dermatology **Trial ID** Tanghetti 2006 **Country** United States **Study type** RCT **Source of funding** Not reported (conflicts of interest reported). ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** not reported	**age (mean±SD)** 20 **age (min/max)** 12 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** Participants aged at least 12 years of age. Stable moderate to severe facial inflammatory acne vulgaris (defined as 15 to 60 papules plus pustules, 10 to 100 comedos, and no more than 2 nodulocystic lesions with a maximum diameter of 5 mm). Washout periods required: 2 weeks for topical acne treatments, 30 days for systemic antibiotics and investigational drugs, 12 weeks for oestrogens/birth control pills if previously used for <12 weeks, and 6 months for oral retinoids. **Exclusion details** Participants with acne known to be resistant to oral antibiotics. Pregnancy, breastfeeding or of childbearing potential and not using reliable contraception. ***Number included*** **Number randomised: arm 1** 61 **Number randomised: arm 2** 60 **Number completed: arm 1** 50 **Number completed: arm 2** 52	**Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** TAZ 0.1% cream + Vehicle gel **Intervention: arm 2** BPO 5%/CLIND 1% gel + TAZ 0.1% cream **Coded intervention: arm 1** TAZ-topical + Vehicle **Coded intervention: arm 2** BPO-topical + CLIND-topical + TAZ **Treatment category** Topical retinoids ± other treatment	**Skin irritation (n/N): arm 2** 6/60	information provided **2. Deviation from intervention** Some concerns;Double blind but not clear if participants were blinded; no ITT **3. Missing outcome data (efficacy)** High;Around 20% discontinued - insufficient information on reasons **4. Outcome measurement (efficacy)** Some concerns;not clear **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** High
Study details **Reference**	N=171 ***Characteristics***	***Interventions*** **Treatment duration**	***Results*** **Skin irritation (n/N):**	***Cochrane RoB Tool v2.0***

Study details	Participants	Interventions	Outcomes and results	Comments
Tanghetti, E. D., S.,Green, L.,Ling, M.,Downie, J.,Germain, M. A.,Kasteler, J. S.,Kircik, L.,Oefelein, M. G.,Draelos, Z.Clinical evidence for the role of a topical anti-inflammatory agent in comedonal acne: Findings from a randomized study of dapsone gel 5% in combination with tazarotene cream 0.1% in patients with acne vulgaris. 2011. Journal of Drugs in Dermatology **Trial ID** Tanghetti 2011 **Country** United States **Study type** RCT **Source of funding** Allergan Inc (conflicts of interest reported). ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	**Sex** mixed **age (mean±SD)** 19.8±6.7 **age (median)** 17.2 **age (min/max)** 12.1/45.7 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** Males or females aged at least 12 years..Stable, non-rapidly progressing facial acne vulgaris characterised by the presence of 50 to 100 inflammatory lesions (papules, pustules), 25 to 100 facial non-inflammatory lesions (open/closed comedones0, no more than 3 facial nodules and/or cysts of diameter =1 cm..Females of childbearing potential were required to use reliable methods of birth control. **Exclusion details** Participants with a skin disease or disorder that might interfere with the diagnosis or assessments of acne vulgaris or who failed to comply with the protocol specified washout periods for prohibited treatments..History of clinically significant anaemia or haemolysis..Evidence of recent alcohol or drug abuse..Participants with a history of poor co-operation or non-compliance with medical treatment or who failed to comply with specified procedures. ***Number included***	**(weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** TAZ 0.1% cream **Intervention: arm 2** DAP 5% gel + TAZ 0.1% cream **Coded intervention: arm 1** TAZ-topical **Coded intervention: arm 2** DAP-topical + TAZ-topical **Treatment category** Topical non-retinoids ± other treatment	**arm 1** 4 **Skin irritation (n/N): arm 2** 2 **Skin irritation (n/N): arm 1** 84 **Skin irritation (n/N): arm 2** 86	**1. Randomisation** Some concerns;no information provided **2. Deviation from intervention** Some concerns;not clear if participants or investigators were blinded (single-blinded study); ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;6% discontinued (1 participant for inefficacy); ITT used; imbalanced between arms **4. Outcome measurement (efficacy)** Low **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** Some concerns

Study details	Participants	Interventions	Outcomes and results	Comments
	Number randomised: arm 1 85 **Number randomised: arm 2** 86 **Number completed: arm 1** 77 **Number completed: arm 2** 83			
Study details **Reference** Tanghetti, E. A. K., L. H.,Green, L. J.,Guenin, E.,Harris, S.,Martin, G.,Pillai, R.A Phase 2, Multicenter, Double-Blind, Randomized, Vehicle-Controlled Clinical Study to Compare the Safety and Efficacy of a Novel Tazarotene 0.045% Lotion and Tazarotene 0.1% Cream in the Treatment of Moderate-to-Severe Acne Vulgaris. 2019. Journal of drugs in dermatology **Trial ID** Tanghetti 2019 **Country** United States **Study type** RCT **Source of funding** Ortho Dermatologics funded Konic Limited's activities relating to the manuscript (conflicts of interest reported). ***Analysis method*** **Intention to treat or**	N=210 ***Characteristics*** **Sex** mixed **age (mean±SD)** 22.1332857142857±9.2005769230769214 **age (min/max)** 12 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Evaluator's Global Severity Scale (EGSS) **Inclusion details** Participants of any gender, race and ethnicity, aged 12 years or older..Participants with moderate to severe acne; EGSS score of 3 (moderate) or 4 (severe); 20 to 40 inflammatory lesions (papules, pustules, and nodules), 20 to 100 non-inflammatory lesions (open and closed comedones), and 2 nodules or less..Women of childbearing potential were required to have a negative urine pregnancy test at and agree to use a reliable method of contraceptive during the study period..Washout period of 1 month required for participants who previously used prescription and over-the-counter acne treatments, and 6 months for systemic retinoids.	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 3 **Split face design** No **Intervention: arm 1** TAZ 0.045% lotion **Intervention: arm 2** TAZ 0.1% cream **Intervention: arm 3** Lotion vehicle or cream vehicle (arms combined) **Coded intervention: arm 1** TAZ-topical **Coded intervention: arm 2** TAZ-topical **Coded intervention: arm 3** Vehicle **Treatment category**	***Results*** **Skin irritation (n/N): arm 1** 0/68 **Skin irritation (n/N): arm 2** 1/71 **Skin irritation (n/N): arm 3** 0/67 **Participant reported improvement (n/N): arm 1** 27/69 **Participant reported improvement (n/N): arm 2** 26/72 **Participant reported improvement (n/N): arm 3** 20/69	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information provided **2. Deviation from intervention** Low;double-blinded; ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;10% withdrawals - imbalanced between arms **4. Outcome measurement (efficacy)** Low;likely blinded **5. Selective reporting** Some concerns;not reported if trial protocol was registered

Study details	Participants	Interventions	Outcomes and results	Comments
completers analysis ITT **Method of ITT imputation** LOCF	**Exclusion details** Not reported. ***Number included*** **Number randomised: arm 1** 69 **Number randomised: arm 2** 72 **Number randomised: arm 3** 69 **Number completed: arm 1** 65 **Number completed: arm 2** 63 **Number completed: arm 3** 61	Topical retinoids		**6. Overall bias** Some concerns
Study details **Reference** Thiboutot, D. J., M.,Rich, P.,Rist, T.,Rodriguez, D.,Levy, S.A randomized, parallel, vehicle-controlled comparison of two erythromycin/benzoyl peroxide preparations for acne vulgaris. 2002. Clinical Therapeutics **Trial ID** Thiboutot 2002 **Country** United States **Study type** RCT **Source of funding** Dermik Laboratories, US. ***Analysis method*** **Intention to treat or completers analysis**	N=327 ***Characteristics*** **Sex** mixed **age (mean±SD)** 19.9 **age (min/max)** 12/46 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Physician's Global Assessment (PGA)/Physician's Global Acne Severity Score **Inclusion details** Males and females aged >12 years of age..Moderate to moderately severe acne; 15 to 80 facial inflammatory lesions, 20 to 140 facial comedones (not including the nose or nasolabial area), <2 nodules or cysts >5 mm, and a minimum Physician's Global Acne	***Interventions*** **Treatment duration (weeks)** 8 **Treatment duration category** 6 to <12 weeks **Number of arms** 4 **Split face design** No **Intervention: arm 1** BPO 5%/ERYTH 3% gel **Intervention: arm 2** BPO 5%/ERYTH 3% jar **Intervention: arm 3** Vehicle gel **Intervention: arm 4** Vehicle Jar **Coded intervention: arm 1**	***Results*** **Skin irritation (n/N): arm 1** 1 **Skin irritation (n/N): arm 2** 3 **Skin irritation (n/N): arm 3** 0 **Skin irritation (n/N): arm 4** 0 **Skin irritation (n/N): arm 1** 124 **Skin irritation (n/N): arm 2** 121 **Skin irritation (n/N): arm 3**	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;insufficient information provided **2. Deviation from intervention** Low;Double blind; ITT **3. Missing outcome data (efficacy)** Low **4. Outcome measurement (efficacy)** Low **5. Selective reporting** Some concerns;not

Study details	Participants	Interventions	Outcomes and results	Comments
ITT **Method of ITT imputation** Unclear	Severity score of 1.5. **Exclusion details** Not reported. ***Number included*** **Number randomised: arm 1** 124 **Number randomised: arm 2** 121 **Number randomised: arm 3** 42 **Number randomised: arm 4** 40 **Number completed: arm 1** 115 **Number completed: arm 2** 110 **Number completed: arm 3** 33 **Number completed: arm 4** 35	BPO-topical + ERYTH-topical **Coded intervention: arm 2** BPO-topical + ERYTH-topical **Coded intervention: arm 3** Vehicle **Coded intervention: arm 4** Vehicle **Treatment category** Topical or combination	42 **Skin irritation (n/N): arm 4** 40	reported if trial protocol was registered **6. Overall bias** Some concerns
Study details **Reference** 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 **Trial ID** Thiboutot 2008 **Country** United States **Study type** RCT	N=2813 ***Characteristics*** **Sex** mixed **age (mean±SD)** 19.3 **age (median)** 16.8 **age (min/max)** 12/70.2 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Evaluator's Global Severity Scale (EGSS)	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 4 **Split face design** No **Intervention: arm 1** CLIND 1.2%/BPO 2.5% gel **Intervention: arm 2**	***Results*** **Participant reported improvement (n/N): arm 1** 284/724 **Participant reported improvement (n/N): arm 2** 215/724 **Participant reported improvement (n/N): arm 3** 211/711 **Participant reported improvement (n/N): arm**	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;insufficient information provided on allocation concealment **2. Deviation from intervention** Low;Double blind; ITT **3. Missing outcome data**

Study details	Participants	Interventions	Outcomes and results	Comments
Source of funding Arcutis Pharmaceuticals (conflicts of interest reported). ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	**Inclusion details** Males and females of any race and ethnicity, aged 12 years or older..Moderate to severe acne vulgaris (a score of 3 or 4 on the EGSS); presenting with 17 to 40 inflammatory lesions (papules, pustules, and nodules), 20 to 100 non-inflammatory lesions (open and closed comedones), and 2 nodules or less..Women of childbearing potential were required to have a negative urine pregnancy test and to agree to use an effective form of contraception during the study..Washout periods required: 1 month for previous prescription and over-the-counter acne treatments; for topical (face) and systemic treatments: topical astringents and abrasives (1 week); topical antiacne products, including soaps containing antimicrobials, and known comedogenic products (2 weeks); topical retinoids, retinol, and systemic acne treatments (4 weeks); and systemic retinoids (6 months). **Exclusion details** Not reported. ***Number included*** **Number randomised: arm 1** 797 **Number randomised: arm 2** 812 **Number randomised: arm 3** 809 **Number randomised: arm 4** 395 **Number completed: arm 1** 724 **Number completed: arm 2**	CLIND 1.2% **Intervention: arm 3** BPO 2.5% **Intervention: arm 4** Vehicle **Coded intervention: arm 1** BPO-topical + CLIND-topical **Coded intervention: arm 2** CLIND-topical **Coded intervention: arm 3** BPO-topical **Coded intervention: arm 4** Vehicle **Treatment category** Topical or combination	**4** 55/333	**(efficacy)** Some concerns;around 10% discontinued **4. Outcome measurement (efficacy)** Low **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** Some concerns

Study details	Participants	Interventions	Outcomes and results	Comments
	724 **Number completed: arm 3** 711 **Number completed: arm 4** 333			
Study details **Reference** Tyring, S. K., Kircik, L. H., Pariser, D. M., Guenin, E., Bhatt, V., & Pillai, R.Novel Tretinoin 0.05% Lotion for the Once-Daily Treatment of Moderate-to-Severe Acne Vulgaris: assessment of Efficacy and Safety in Patients Aged 9 Years and Older. 2018. Journal of drugs in dermatology **Trial ID** Tyring 2018 **Country** International **Study type** RCT **Source of funding** Dow Pharmaceutical Sciences, US; Ortho Dermatologics funded Konic's activities relating to the manuscript (conflicts of interest reported). ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** MI MCMC	N=1640 ***Characteristics*** **Sex** mixed **age (mean±SD)** 20.5±7.31 **age (min/max)** 9/58 ***Inclusion/exclusion criteria*** **Acne scale** None **Inclusion details** Males and females of any race and ethnicity, aged 9 years and older..Moderate (EGSS score 3) to severe (EGSS score 4) acne presenting with 20 to 40 inflammatory lesions (papules, pustules, and nodules), 20 to 100 non-inflammatory lesions (open and closed comedones), and 2 nodules or less..Women of childbearing potential were required to have a negative urine pregnancy test and to agree to use an effective form of contraception during the study..Washout periods required: 1 month for previous prescription and over-the-counter acne treatments; for topical and systemic treatments: topical astringents and abrasives (1 week); topical anti-acne products, including soaps containing antimicrobials, and known comedogenic products (2 weeks); topical retinoids, retinol, and systemic acne treatments such as hormonal or antibiotic treatments (4 weeks); and systemic retinoids	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** TRET 0.05% lotion **Intervention: arm 2** Vehicle **Coded intervention: arm 1** TRET-topical **Coded intervention: arm 2** Vehicle **Treatment category** Topical retinoids	***Results*** **Skin irritation (n/N): arm 1** 28/767 **Skin irritation (n/N): arm 2** 1/783	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;no information provided **2. Deviation from intervention** Low;Double-blinded: ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;more than 5% withdrawals - balanced between arms **4. Outcome measurement (efficacy)** Low **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** Some concerns

Study details	Participants	Interventions	Outcomes and results	Comments
	(6 months). **Exclusion details** Not reported. ***Number included*** **Number randomised: arm 1** 819 **Number randomised: arm 2** 821 **Number completed: arm 1** 680 **Number completed: arm 2** 701			
Study details **Reference** Zouboulis Ch, C. D., L.,Decroix, J.,Maciejewska-Udziela, B.,Cambazard, F.,Stuhlert, A.A multicentre, single-blind, randomized comparison of a fixed clindamycin phosphate/tretinoin gel formulation (Velac) applied once daily and a clindamycin lotion formulation (Dalacin T) applied twice daily in the topical treatment of acne vulgaris. 2000. British Journal of Dermatology **Trial ID** Zouboulis 2000 **Country** Europe **Study type** RCT **Source of funding** Yamanouchi Europe BV, The	N=209 ***Characteristics*** **Sex** mixed **age group** =25 years **age (mean±SD)** 18.6±3.2 **age (median)** 18 **age (min/max)** 14/26 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Cook **Inclusion details** Participants aged between 14 and 26 years..Moderate to severe acne vulgaris; scoring =3 on the Cook acne scale. **Exclusion details** Use of tretinoin or antibiotic treatments for acne during the 4 weeks prior to study; use of	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** CLIND 1%/TRET 0.025% gel **Intervention: arm 2** CLIND 1% lotion **Coded intervention: arm 1** CLIND-topical + TRET-topical **Coded intervention: arm 2** CLIND-topical **Treatment category**	***Results*** **Skin irritation (n/N): arm 1** 7 **Skin irritation (n/N): arm 2** 1 **Skin irritation (n/N): arm 1** 104 **Skin irritation (n/N): arm 2** 105	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;No information provided **2. Deviation from intervention** Low; participants were blinded; ITT used **3. Missing outcome data (efficacy)** Some concerns;Withdrawal imbalanced between groups,(5% vs 13%) - mostly due to patient request. **4. Outcome measurement (efficacy)** Some

Study details	Participants	Interventions	Outcomes and results	Comments
Netherlands. ***Analysis method*** **Intention to treat or completers analysis** completers	irritants such as salicylic acid and benzoyl peroxide during the 2 weeks prior to study; required other medical interventions within 5 days of the study..Participants with skin disorders likely to compromise drug absorption, known or suspected hypersensitivity to lincomycin, clindamycin or vitamin A derivatives..Participants who had changed or started use of contraceptives or use of Diane® within 3 months of the study. Those who had participated in another clinical trial within 3 months of the study. ***Number included*** **Number randomised: arm 1** 104 **Number randomised: arm 2** 105 **Number completed: arm 1** 90 **Number completed: arm 2** 100	Topical or combination		concerns;Investigator not blinded **5. Selective reporting** Some concerns;not reported if trial protocol was registered **6. Overall bias** Some concerns

ADAP: adapalene; ALA-PDT: aminolevulinic acid photodymanic therapy; ALA-RED-PDT: aminolevulinic acid using red light photodymanic therapy; AZITH: azithromycin; BPO: benzoyl peroxide; CLIND: clindomycin; CPA: cyproterone acetate; DAPS: dapsone; DOXY: doxycycline; EE: ethinylestradiol; ERYTH: erythromycin; FU: follow up; ISO: isotretinoin; IPL: intense pulsed light; ITT: intention to treat analysis; LOCF: last observation carried forward; LYME: lymecycline; MAL DL: methyl aminolevulinate using daylight; MICO: miconazole nitrate; MINO: minocycline; MOT: motretinide; NAFL: fractional erbium glass laser; NOR: norfloxacin; PDL: pulsed dye laser; PLC: placebo; PDT: photodynamic; PT: photochemical; RCT: randomised controlled trial; SAR/SARE: sarecycline; SD: standard deviation; TAZ: tazarotene; TETRA: tetracycline; TRET: tretinoin

Appendix E

Appendix E - Forest plots

Forest plots for review question: What is the effectiveness and acceptability of interventions for the treatment of moderate to severe acne (side effects and participant reported improvement)?

This section includes forest plots only for outcomes that are meta-analysed. Outcomes from single studies are not presented here; the quality assessment for such outcomes is provided in the GRADE profiles in appendix F.

Oral antibiotics

Figure 2: Comparison of oral antibiotics with placebo for the outcome of gastrointestinal effects

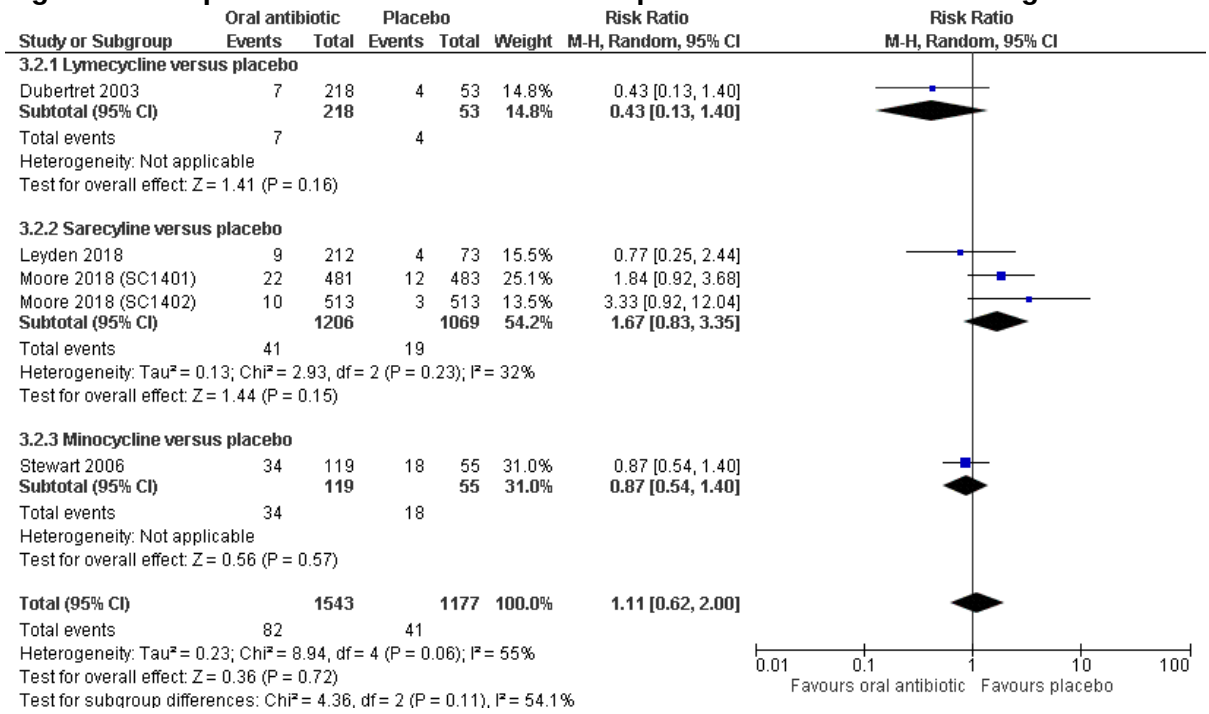
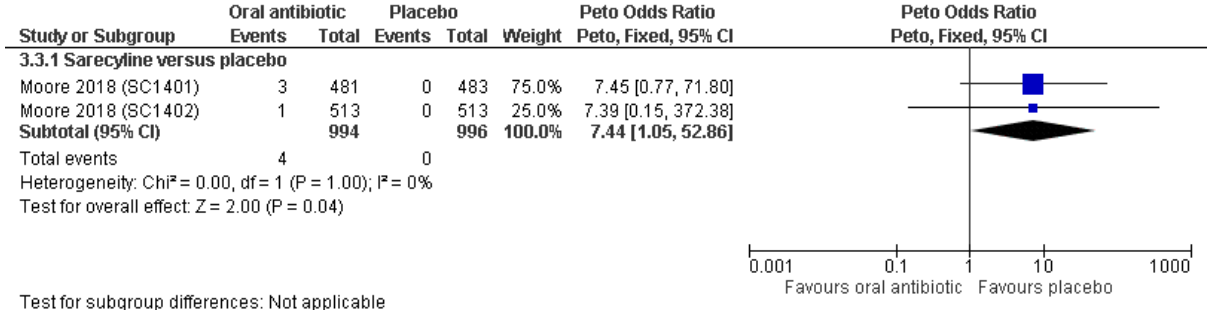


Figure 3: Comparison of oral antibiotics with placebo for the outcome of thrush/candiasis

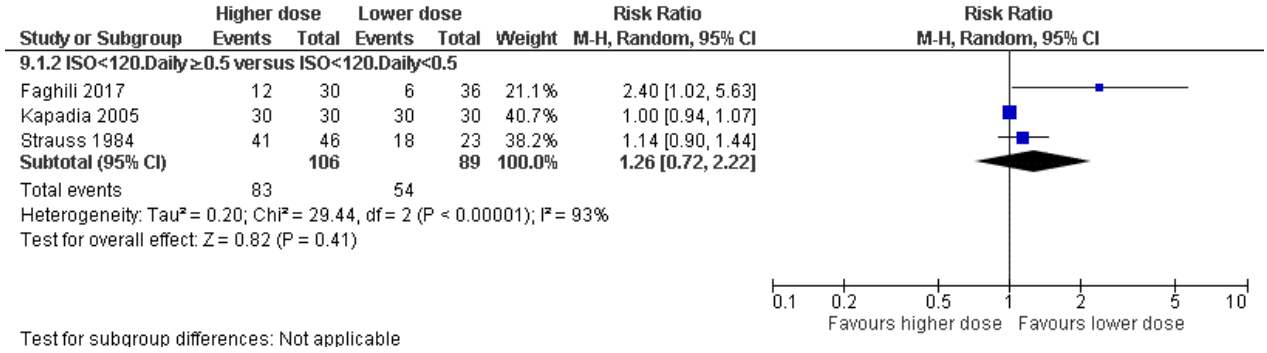


Oral hormonal contraceptives and hormone-modifying agents

No meta-analysis was conducted for oral hormonal contraceptives and hormone-modifying agents and so there are no forest plots.

Oral isotretinoin

Figure 4: Comparison of higher dose isotretinoin with lower dose isotretinoin for the outcome of mucosal/cutaneous changes



ISO: isotretinoin

Physical treatments

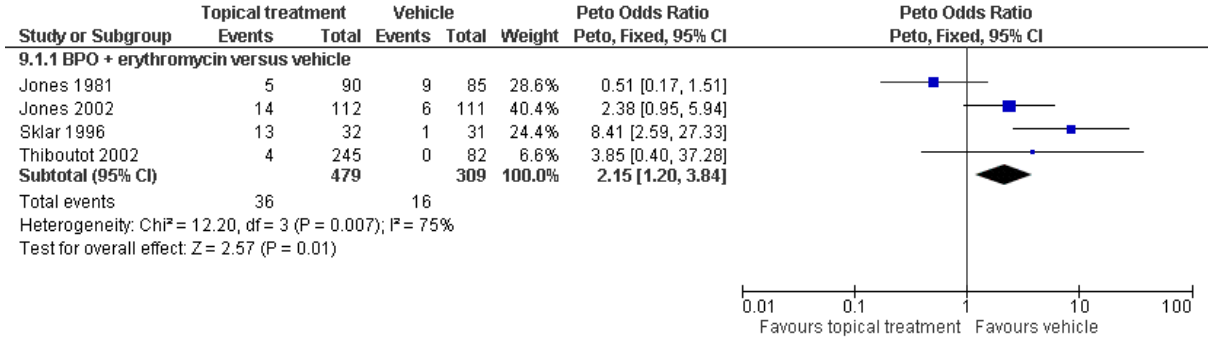
No meta-analysis was conducted for physical treatments and so there are no forest plots.

Topical and oral combination interventions

No meta-analysis was conducted for topical and oral combination interventions and so there are no forest plots.

Topical non-retinoids

Figure 5: Comparison of topical non-retinoid with vehicle for the outcome of skin irritation



BPO: benzoyl peroxide

Figure 6: Comparison of topical clindamycin with vehicle for the outcome of participant reported improvement

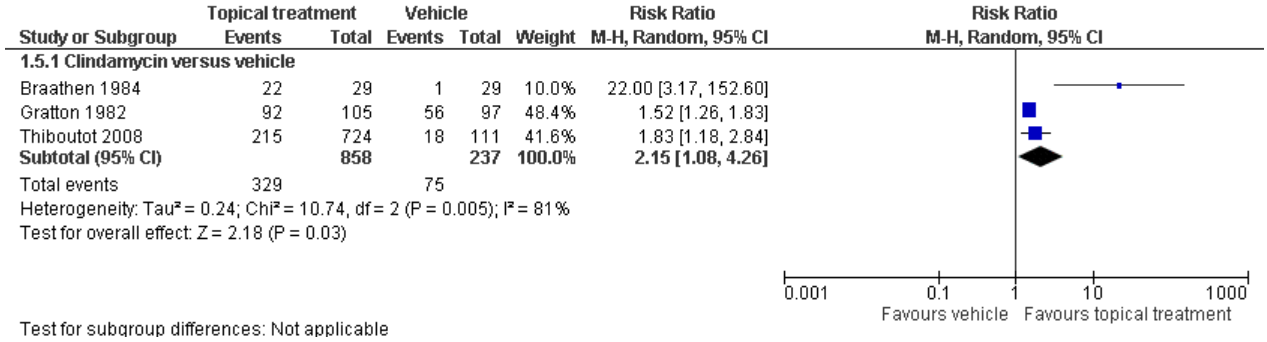
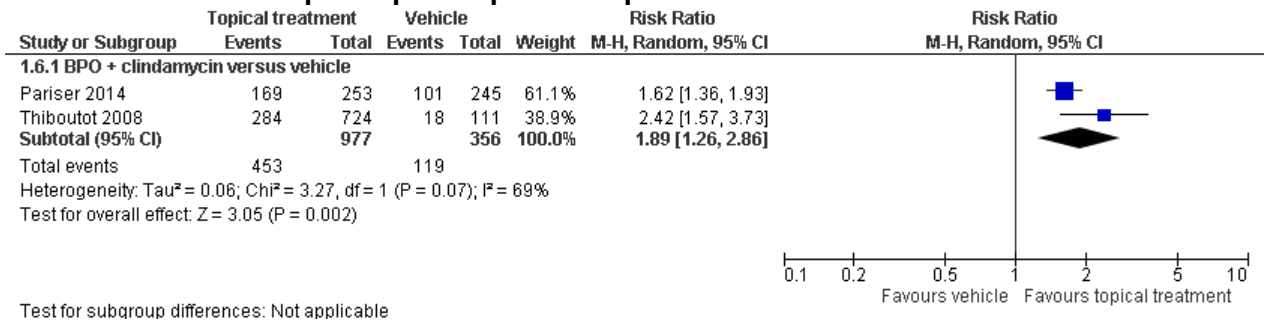


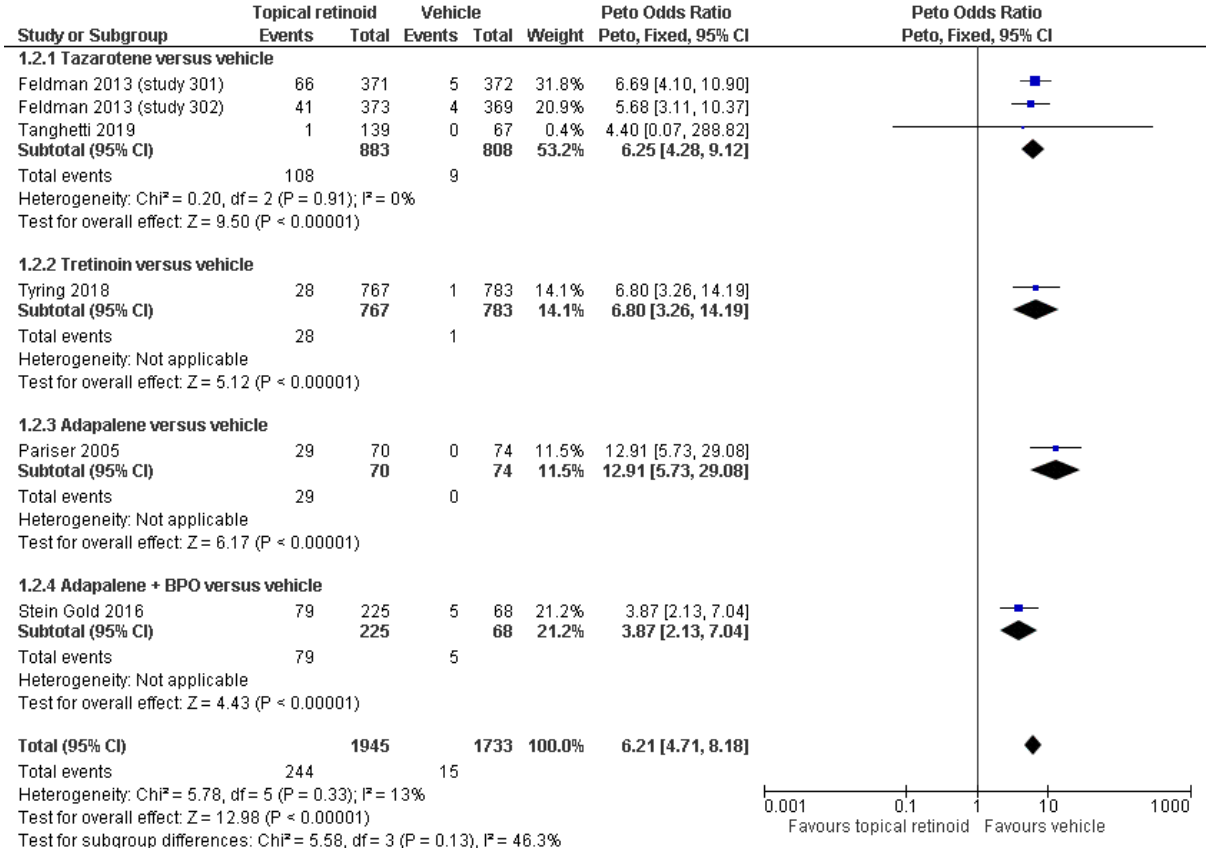
Figure 7: Comparison of topical benzoyl peroxide plus clindamycin with vehicles for the outcome of participant reported improvement



BPO: benzoyl peroxide

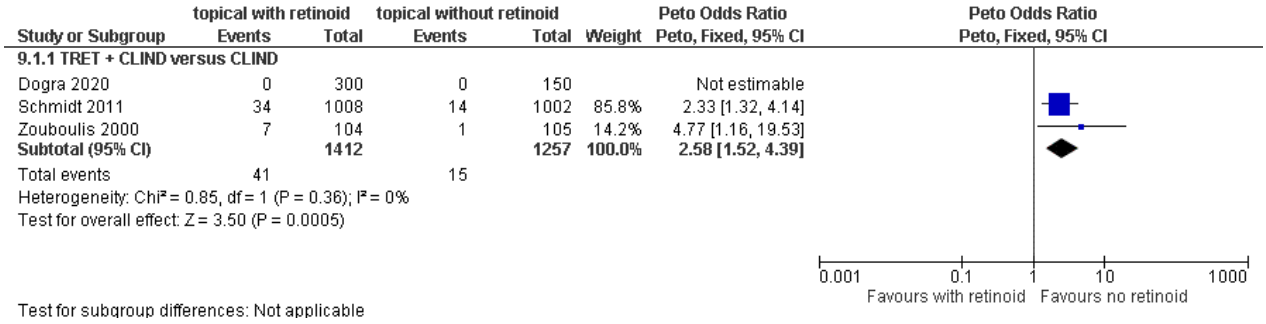
Topical retinoids

Figure 8: Comparison of topical retinoid with vehicle for the outcome of skin irritation



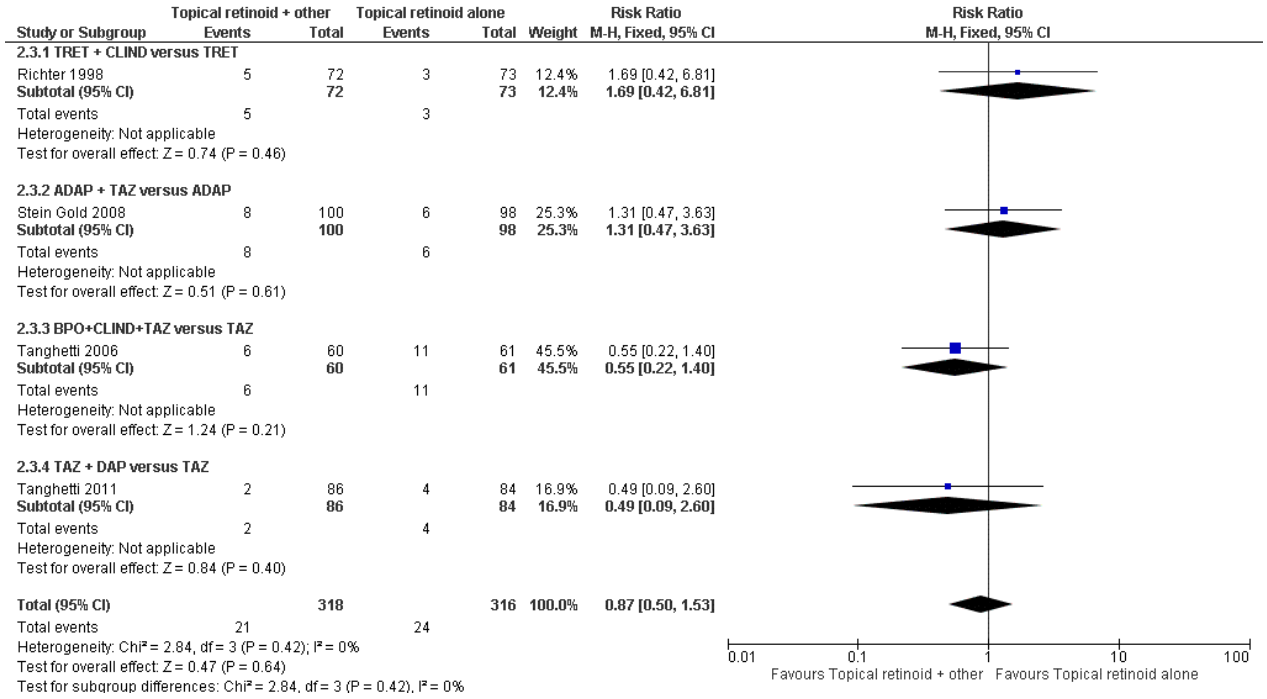
BPO: benzoyl peroxide

Figure 9: Comparison of topical plus retinoid with topical without retinoid for the outcome of skin irritation



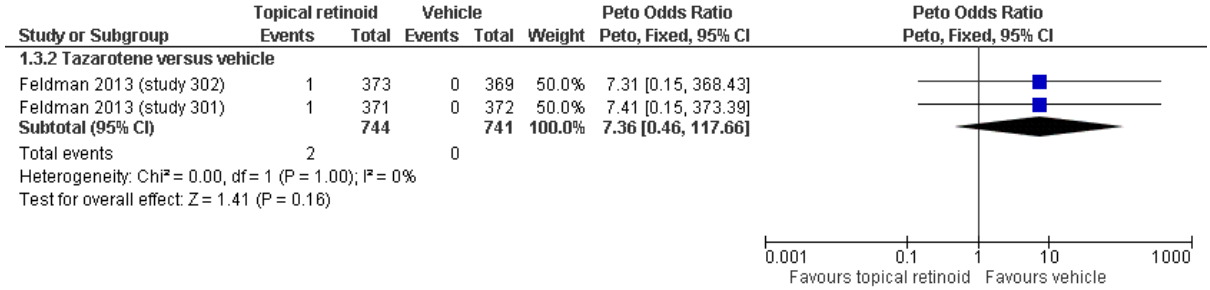
CLIND: clindamycin; TRET: tretinoin

Figure 10: Comparison of topical retinoid plus another topical agent with topical retinoid for the outcome of skin irritation



ADAP: adapalene; CLIND: clindamycin; TAZ: tazarotene; TRET: tretinoin

Figure 11: Comparison of topical retinoid with vehicle for the outcome of light sensitivity



Appendix F - GRADE tables

GRADE tables for review question: What is the effectiveness and acceptability of interventions for the treatment of moderate to severe acne (side effects and participant reported improvement)?

Oral antibiotics

Table 5: Clinical evidence profile for comparison of oral antibiotic versus placebo in participants with moderate to severe acne

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Oral antibiotic	Placebo	Relative (95% CI)	Absolute		
Skin irritation - Minocycline versus placebo												
1[1]	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	very serious[8]	none	5/119 (4.2%)	1/55 (1.8%)	RR 2.31 (0.28 to 19.31)	24 more per 1000 (from 13 fewer to 333 more)	⊕OOO VERY LOW	CRITICAL
GI side effects												
5[1,2,3,4,5]	randomised trials	very serious[9]	serious[10]	no serious indirectness	very serious[8]	none	82/1543 (5.3%)	41/1177 (3.5%)	RR 1.11 (0.62 to 2)	4 more per 1000 (from 13 fewer to 35 more)	⊕OOO VERY LOW	CRITICAL
Thrush / candiasis - Sarecyline versus placebo												
2[4,5]	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	serious[11]	none	4/994 (0.4%)	0/996 (0%)	Peto OR 7.44 (1.05 to 52.86)	-	⊕⊕OO LOW	CRITICAL
Patient reported improvement - Tetracycline versus placebo												
1[6]	randomised trials	very serious[9]	no serious inconsistency	no serious indirectness	no serious imprecision	none	21/29 (72.4%)	1/29 (3.4%)	RR 21 (3.02 to 145.98)	690 more per 1000 (from 70 more to 1000 more)	⊕⊕OO LOW	CRITICAL

CI: confidence interval; GI: gastrointestinal; POR: peto odds ratio; RR: risk ratio
[1] Stewart 2006

[2] *Dubertret 2003*
[3] *Leyden 2018*
[4] *Moore 2018 (SC1401)*
[5] *Moore 2018 (SC1402)*
[6] *Braathen 1984*
[7] *Overall risk of bias judgement: serious risk of bias.*
[8] *Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.*
[9] *Overall risk of bias judgement: very serious risk of bias*
[10] *Evidence downgraded by 1 level due to serious inconsistency.*
[11] *Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes.*

Table 6: Clinical evidence profile for comparison of oral antibiotic versus oral antibiotic in participants with moderate to severe acne

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Oral antibiotic	Oral antibiotic	Relative (95% CI)	Absolute		
GI side effects - LYME vs MINO												
1[1]	randomised trials	very serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	3/56 (5.4%)	2/53 (3.8%)	RR 1.42 (0.25 to 8.16)	16 more per 1000 (from 28 fewer to 270 more)	⊕OOO VERY LOW	CRITICAL
Thrush / candiasis - TETRA versus MINO												
1[2]	randomised trials	very serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	1/21 (4.8%)	1/23 (4.3%)	RR 1.1 (0.07 to 16.43)	4 more per 1000 (from 40 fewer to 671 more)	⊕OOO VERY LOW	CRITICAL
Patient reported improvement - LYME vs MINO												
1[1]	randomised trials	very serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	53/66 (80.3%)	53/68 (77.9%)	RR 1.03 (0.87 to 1.23)	23 more per 1000 (from 101 fewer to 179 more)	⊕⊕OO LOW	CRITICAL

CI: confidence interval; LYME: lymecycline; MINO: minocycline; RR: risk ratio; TETRA: tetracycline
[1] *Bossuyt 2003*
[2] *Khanna 2013*
[3] *Overall risk of bias judgement: very serious risk of bias.*
[4] *Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.*

Oral hormonal contraceptives and hormone-modifying agents

Table 7: Clinical evidence profile for comparison of hormonal treatments versus hormonal treatments in participants with moderate to severe acne

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hormonal treatments	Hormonal treatments	Relative (95% CI)	Absolute		
Breast tenderness - CPA/EE (Diane 50) versus NOR/EE (Minovlar)												
1[1]	randomised trials	very serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	5/26 (19.2%)	3/24 (12.5%)	RR 1.54 (0.41 to 5.76)	67 more per 1000 (from 74 fewer to 595 more)	⊕OOO VERY LOW	CRITICAL
Breast tenderness - CPA/EE (Diane 50) versus CPA/EE (high dose CPA)												
1[1]	randomised trials	very serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	5/26 (19.2%)	4/26 (15.4%)	RR 1.25 (0.38 to 4.14)	38 more per 1000 (from 95 fewer to 483 more)	⊕OOO VERY LOW	CRITICAL
Sexual dysfunction - CPA/EE (Diane 50) versus CPA/EE (high dose CPA)												
1[1]	randomised trials	very serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/26 (0%)	1/24 (4.2%)	Peto OR 0.12 (0 to 6.29)	37 fewer per 1000 (from 42 fewer to 220 more)	⊕OOO VERY LOW	CRITICAL
Sexual dysfunction - CPA/EE (Diane 50) versus NOR/EE (Minovlar)												
1[1]	randomised trials	very serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/26 (0%)	1/24 (4.2%)	Peto OR 0.12 (0 to 6.29)	37 fewer per 1000 (from 42 fewer to 220 more)	⊕OOO VERY LOW	CRITICAL
Mood disturbance - CPA/EE (Diane 50) versus CPA/EE (high dose CPA)												
1[1]	randomised trials	very serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	3/26 (11.5%)	3/26 (11.5%)	RR 1 (0.22 to 4.5)	0 fewer per 1000 (from 90 fewer to 404 more)	⊕OOO VERY LOW	CRITICAL
Mood disturbance - CPA/EE (Diane 50) versus NOR/EE (Minovlar)												
1[1]	randomised trials	very serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	3/26 (11.5%)	3/24 (12.5%)	RR 0.92 (0.21 to 4.14)	10 fewer per 1000 (from 99 fewer to 392 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hormonal treatments	Hormonal treatments	Relative (95% CI)	Absolute		
Breakthrough bleeding - CPA/EE (Diane 50) versus CPA/EE (Diane 35)												
1[2]	randomised trials	very serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	4/33 (12.1%)	2/40 (5%)	RR 2.42 (0.47 to 12.42)	71 more per 1000 (from 26 fewer to 571 more)	⊕OOO VERY LOW	CRITICAL
Breakthrough bleeding - CPA/EE (Diane 50) versus NOR/EE (Minovlar)												
1[1]	randomised trials	very serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	2/26 (7.7%)	3/24 (12.5%)	RR 0.62 (0.11 to 3.37)	47 fewer per 1000 (from 111 fewer to 296 more)	⊕OOO VERY LOW	CRITICAL
Breakthrough bleeding - CPA/EE (Diane 50) versus CPA/EE (high dose CPA)												
1[1]	randomised trials	very serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	2/26 (7.7%)	4/26 (15.4%)	RR 0.5 (0.1 to 2.5)	77 fewer per 1000 (from 138 fewer to 231 more)	⊕OOO VERY LOW	CRITICAL

CI: confidence interval; CPA: cyproterone acetate; EE: ethinyl estradiol; NOR: northisterone; OR: odds ratio; RR: risk ratio
[1] Miller 1986
[2] Fugere 1990
[3] Overall risk of bias judgement: very serious risk of bias.
[4] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.

Oral isotretinoin

Table 8: Clinical evidence profile for comparison of isotretinoin versus isotretinoin in participants with moderate to severe acne

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Isotretinoin	Isotretinoin	Relative (95% CI)	Absolute		
mucosal / cutaneous changes - ISO≥120.Daily≥0.5 versus ISO<120.Daily<0.5												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Isotretinoin	Isotretinoin	Relative (95% CI)	Absolute		
1[1]	randomised trials	very serious[6]	no serious inconsistency	no serious indirectness	serious[7]	none	46/49 (93.9%)	18/23 (78.3%)	RR 1.2 (0.96 to 1.51)	157 more per 1000 (from 31 fewer to 399 more)	⊕OOO VERY LOW	CRITICAL
mucosal / cutaneous changes - ISO<120.Daily≥0.5 versus ISO<120.Daily<0.5												
3[1,2,3]	randomised trials	very serious[6]	very serious[9]	no serious indirectness	very serious[10]	none	83/106 (78.3%)	54/89 (60.7%)	RR 1.26 (0.72 to 2.22)	158 more per 1000 (from 170 fewer to 740 more)	⊕OOO VERY LOW	CRITICAL
mucosal / cutaneous changes - ISO<120.Daily≥0.5 versus ISO<120.Other≥0.5												
1[4]	randomised trials	very serious[6]	no serious inconsistency	no serious indirectness	serious[7]	none	37/38 (97.4%)	16/22 (72.7%)	RR 1.34 (1.03 to 1.74)	247 more per 1000 (from 22 more to 538 more)	⊕OOO VERY LOW	CRITICAL
mucosal / cutaneous changes - ISO<120.Daily<0.5 versus ISO<120.Alt<0.5												
1[5]	randomised trials	serious[11]	no serious inconsistency	no serious indirectness	no serious imprecision	none	115/118 (97.5%)	111/116 (95.7%)	RR 1.02 (0.97 to 1.07)	19 more per 1000 (from 29 fewer to 67 more)	⊕⊕⊕O MODERATE	CRITICAL
New psychiatric diagnosis - ISO<120.Daily≥0.5 versus ISO<120.Daily<0.5												
1[2]	randomised trials	serious[11]	no serious inconsistency	no serious indirectness	very serious[10]	none	2/30 (6.7%)	2/36 (5.6%)	RR 1.2 (0.18 to 8.02)	11 more per 1000 (from 46 fewer to 390 more)	⊕OOO VERY LOW	CRITICAL
Change in mood - ISO<120.Daily≥0.5 versus ISO<120.Daily<0.5												
1[3]	randomised trials	serious[11]	no serious inconsistency	no serious indirectness	very serious[10]	none	3/30 (10%)	0/30 (0%)	Peto OR 7.93 (0.79 to 79.26)	-	⊕OOO VERY LOW	CRITICAL
Relapse - ISO≥120.Daily≥0.5 versus ISO<120.Daily<0.5												
1[1]	randomised trials	very serious[6]	no serious inconsistency	no serious indirectness	no serious imprecision	none	14/95 (14.7%)	38/92 (41.3%)	RR 0.25 (0.1 to 0.61)	310 fewer per 1000 (from 161 fewer to 372 fewer)	⊕⊕OO LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Isotretinoin	Isotretinoin	Relative (95% CI)	Absolute		
Relapse - ISO<120.Daily≥0.5 versus ISO<120.Daily<0.5												
1[1]	randomised trials	very serious[6]	no serious inconsistency	no serious indirectness	serious[7]	none	9/46 (19.6%)	19/46 (41.3%)	RR 0.47 (0.24 to 0.93)	219 fewer per 1000 (from 29 fewer to 314 fewer)	⊕OOO VERY LOW	CRITICAL
Relapse - ISO<120.Daily≥0.5 versus ISO<120.Other≥0.5												
1[4]	randomised trials	very serious[6]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/38 (0%)	3/22 (13.6%)	Peto OR 0.06 (0.01 to 0.65)	128 fewer per 1000 (from 48 fewer to 135 fewer)	⊕⊕OO LOW	CRITICAL
Relapse - ISO<120.Daily<0.5 versus ISO<120.Alt<0.5												
1[5]	randomised trials	serious[11]	no serious inconsistency	no serious indirectness	very serious[12]	none	0/118 (0%)	0/116 (0%)	RD 0 (-0.02 to 0.02)	-	⊕OOO VERY LOW	CRITICAL

Alt: alternative; ISO: isotretinoin; POR: peto odds ratio; RD: risk difference; RR: risk ratio
[1] Strauss 1984a
[2] Faghihi 2017
[3] Kapadia 2005
[4] Akman 2007
[5] Dhaked 2016
[6] Overall risk of bias judgement: very serious risk of bias.
[7] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes.
[8] Evidence downgraded by 2 levels due to very serious inconsistency.
[9] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.
[10] Overall risk of bias judgement: serious risk of bias.
[11] Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events.

Physical treatments

Table 9: Clinical evidence profile for comparison of physical treatments versus inactive control in participants with moderate to severe acne

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Physical treatments	Inactive control	Relative (95% CI)	Absolute		
Skin irritation - Photodynamic therapy												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	7/24 (29.2%)	2/23 (8.7%)	RR 3.35 (0.78 to 14.5)	204 more per 1000 (from 19 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL

CI: confidence interval; RR: risk ratio
[1] Chen 2015
[2] Overall risk of bias judgement: serious risk of bias.
[3] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.

Table 10: Clinical evidence profile for comparison of physical treatments versus physical treatments in participants with moderate to severe acne

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Physical treatments	Physical treatments	Relative (95% CI)	Absolute		
Skin irritation - 5ALA-IPL-PDT versus IPL												
1[1]	randomised trials	very serious[6]	no serious inconsistency	no serious indirectness	no serious imprecision	none	21/21 (100%)	20/20 (100%)	RR 1 (0.91 to 1.1)	0 fewer per 1000 (from 90 fewer to 100 more)	⊕⊕OO LOW	CRITICAL
Skin redness - Photodynamic + photothermal therapy versus photodynamic therapy												
1[2]	randomised trials	very serious[6]	no serious inconsistency	no serious indirectness	very serious[7]	none	0/14 (0%)	2/14 (14.3%)	Peto OR 0.13 (0.01 to 2.11)	124 fewer per 1000 (from 141 fewer to 159 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Physical treatments	Physical treatments	Relative (95% CI)	Absolute		
Skin redness - 5ALA-IPL-PDT versus IPL												
1[1]	randomised trials	very serious[6]	no serious inconsistency	no serious indirectness	very serious[7]	none	3/21 (14.3%)	0/20 (0%)	Peto OR 7.81 (0.77 to 79.66)	-	⊕OOO VERY LOW	CRITICAL
Skin redness - MAL-RED-PDT versus RED												
1[3]	randomised trials	serious[8]	no serious inconsistency	no serious indirectness	very serious[7]	none	4/100 (4%)	0/53 (0%)	Peto OR 4.76 (0.59 to 38.13)	-	⊕OOO VERY LOW	CRITICAL
Changes in pigmentation - Photodynamic + photothermal therapy versus photodynamic therapy												
1[2]	randomised trials	very serious[6]	no serious inconsistency	no serious indirectness	very serious[7]	none	1/14 (7.1%)	1/14 (7.1%)	RR 1 (0.07 to 14.45)	0 fewer per 1000 (from 66 fewer to 961 more)	⊕OOO VERY LOW	CRITICAL
Changes in pigmentation - PDL versus IPL												
1[4]	randomised trials	very serious[6]	no serious inconsistency	no serious indirectness	serious[9]	none	3/15 (20%)	0/15 (0%)	Peto OR 8.57 (0.82 to 89.45)	-	⊕OOO VERY LOW	CRITICAL
Changes in pigmentation - MAL-RED-PDT versus RED												
1[3]	randomised trials	serious[8]	no serious inconsistency	no serious indirectness	very serious[7]	none	2/100 (2%)	0/53 (0%)	Peto OR 4.67 (0.25 to 86.7)	-	⊕OOO VERY LOW	CRITICAL
Changes in pigmentation - PDL versus BR-LED												
1[4]	randomised trials	very serious[7]	no serious inconsistency	no serious indirectness	serious[9]	none	3/15 (20%)	0/15 (0%)	Peto OR 8.57 (0.82 to 89.45)	-	⊕OOO VERY LOW	CRITICAL
Patient reported improvement - Photodynamic + photothermal therapy versus photodynamic therapy												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Physical treatments	Physical treatments	Relative (95% CI)	Absolute		
1[2]	randomised trials	very serious[6]	no serious inconsistency	no serious indirectness	serious[9]	none	14/14 (100%)	12/14 (85.7%)	RR 1.16 (0.91 to 1.48)	137 more per 1000 (from 77 fewer to 411 more)	⊕OOO VERY LOW	CRITICAL
Patient reported improvement - PDL versus IPL												
1[4]	randomised trials	very serious[7]	no serious inconsistency	no serious indirectness	serious[9]	none	15/15 (100%)	12/15 (80%)	RR 1.24 (0.94 to 1.63)	192 more per 1000 (from 48 fewer to 504 more)	⊕OOO VERY LOW	CRITICAL
Patient reported improvement - PDL versus BR-LED												
1[4]	randomised trials	very serious[7]	no serious inconsistency	no serious indirectness	serious[9]	none	15/15 (100%)	6/15 (40%)	RR 2.38 (1.31 to 4.34)	552 more per 1000 (from 124 more to 1000 more)	⊕OOO VERY LOW	CRITICAL

5ALA: 5-aminolevulinic acid; BR: blue red; CI: confidence interval; IPL: intense pulsed light; LED: light emitting diode; MAL: methyl aminolevulinate; OR: odds ratio; PDL: pulsed dye laser; RR: risk ratio
[1] Mei 2013
[2] Kim 2017
[3] Pariser 2016
[4] Sami 2008
[5] Overall risk of bias judgement: very serious risk of bias.
[6] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.
[7] Overall risk of bias judgement: serious risk of bias.
[8] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes.

Topical and oral combination interventions

Table 11: Clinical evidence profile for comparison of topical+oral versus topical+oral in participants with moderate to severe acne

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical+oral	Topical+oral	Relative (95% CI)	Absolute		
Skin irritation - BPO + CLIND-topical + DOXY versus BPO + DOXY												
1[1]	randomised trials	very serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	3/32 (9.4%)	2/28 (7.1%)	RR 1.31 (0.24 to 7.3)	22 more per 1000 (from 54 fewer to 450 more)	⊕OOO VERY LOW	CRITICAL
Skin irritation - DOXY+ TRET versus AZITH + TRET												
1[2]	randomised trials	very serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	3/22 (13.6%)	4/28 (14.3%)	RR 0.95 (0.24 to 3.83)	7 fewer per 1000 (from 109 fewer to 404 more)	⊕OOO VERY LOW	CRITICAL
GI side effects - BPO + CLIND-topical + DOXY versus BPO + DOXY												
1[1]	randomised trials	very serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	1/33 (3%)	5/33 (15.2%)	RR 0.2 (0.02 to 1.62)	121 fewer per 1000 (from 148 fewer to 94 more)	⊕OOO VERY LOW	CRITICAL

AZITH: azithromycin; BPO: benzoyl peroxide; CI: confidence interval; CLIND: clindamycin; DOXY: doxycycline; RR: risk ratio; TRET: tretinoin
[1] Del Rosso 2007
[2] Parsad 2001
[3] Overall risk of bias judgement: very serious risk of bias.
[4] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.

Topical non-retinoids and retinoids

Table 12: Clinical evidence profile for comparison of topical interventions versus vehicle in participants with moderate to severe acne

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical	Vehicle	Relative (95% CI)	Absolute		
Skin irritation (non-retinoids) - Erythromycin versus vehicle												
1[1]	randomised trials	very serious[20]	no serious inconsistency	no serious indirectness	very serious[21]	none	26/109 (23.9%)	26/90 (28.9%)	RR 0.83 (0.52 to	49 fewer per 1000 (from 139 fewer to 92	⊕OOO VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical	Vehicle	Relative (95% CI)	Absolute		
									1.32)	more)		
Skin irritation (non-retinoids) - Clindamycin versus vehicle												
1[2]	randomised trials	very serious[20]	no serious inconsistency	no serious indirectness	very serious[21]	none	2/21 (9.5%)	0/14 (0%)	Peto OR 5.57 (0.32 to 98.36)	-	⊕OOO VERY LOW	CRITICAL
Skin irritation (non-retinoids) - BPO versus vehicle												
1[3]	randomised trials	serious[22]	no serious inconsistency	no serious indirectness	very serious[21]	none	4/30 (13.3%)	1/31 (3.2%)	Peto OR 3.75 (0.61 to 23.01)	89 more per 1000 (from 13 fewer to 710 more)	⊕OOO VERY LOW	CRITICAL
Skin irritation (non-retinoids) - BPO + erythromycin versus vehicle												
4[3,4,5,6]	randomised trials	very serious[20]	serious[23]	no serious indirectness	serious[24]	none	36/479 (7.5%)	16/309 (5.2%)	Peto OR 2.15 (1.2 to 3.84)	60 more per 1000 (from 10 more to 147 more)	⊕OOO VERY LOW	CRITICAL
Skin irritation (retinoids)												
6[7,8,9,10,11,12]	randomised trials	very serious[20]	no serious inconsistency	no serious indirectness	no serious imprecision	none	244/1945 (12.5%)	15/1733 (0.87%)	Peto OR 6.21 (4.71 to 8.18)	45 more per 1000 (from 32 more to 62 more)	⊕⊕OO LOW	CRITICAL
Light sensitivity (retinoids) - Tazarotene versus vehicle												
2[7,12]	randomised trials	serious[22]	no serious inconsistency	no serious indirectness	very serious[21]	none	2/744 (0.27%)	0/741 (0%)	Peto OR 7.36 (0.46 to 117.66)	-	⊕OOO VERY LOW	CRITICAL
Participant reported improvement - BPO versus vehicle												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical	Vehicle	Relative (95% CI)	Absolute		
1[15]	randomised trials	serious[22]	no serious inconsistency	no serious indirectness	serious[24]	none	211/711 (29.7%)	18/111 (16.2%)	RR 1.83 (1.18 to 2.84)	135 more per 1000 (from 29 more to 298 more)	⊕⊕OO LOW	CRITICAL
Participant reported improvement - Clindamycin versus vehicle												
3[13,15,16]	randomised trials	very serious[20]	very serious[25]	no serious indirectness	serious[24]	none	329/858 (38.3%)	75/237 (31.6%)	RR 2.15 (1.08 to 4.26)	364 more per 1000 (from 25 more to 1000 more)	⊕OOO VERY LOW	CRITICAL
Participant reported improvement - BPO + clindamycin versus vehicle												
2[15,17]	randomised trials	serious[22]	serious[24]	no serious indirectness	no serious imprecision	none	453/977 (46.4%)	119/356 (33.4%)	RR 1.89 (1.26 to 2.86)	298 more per 1000 (from 87 more to 622 more)	⊕⊕OO LOW	CRITICAL
Participant reported improvement - BPO + adapalene versus vehicle												
1[8]	randomised trials	serious[22]	no serious inconsistency	no serious indirectness	no serious imprecision	none	182/204 (89.2%)	26/65 (40%)	RR 2.23 (1.65 to 3.02)	492 more per 1000 (from 260 more to 808 more)	⊕⊕⊕O MODERATE	CRITICAL
Participant reported improvement - Tazarotene versus vehicle												
1[9]	randomised trials	serious[22]	no serious inconsistency	no serious indirectness	serious[24]	none	53/141 (37.6%)	20/69 (29%)	RR 1.3 (0.85 to 1.99)	87 more per 1000 (from 43 fewer to 287 more)	□□□□ LOW	CRITICAL
% change in scar count from baseline – Adapalene versus vehicle												
1[17]	randomised trials	serious[19]	no serious inconsistency	no serious indirectness	serious[25]	none	increase in scars from baseline by	increase in scars from baseline by 24.8% (p=0.036)	-	-	⊕⊕OO LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical	Vehicle	Relative (95% CI)	Absolute		
							4.5%					
% change in scar count from baseline – Adapalene versus vehicle												
1[18]	randomised trials	serious[19]	no serious inconsistency	no serious indirectness	serious[25]	none	decrease in scars from baseline by 15.5%	increase in scars from baseline by 14.4% (p value not reported, reported only that there was a statistical difference)	-	-	⊕⊕OO LOW	CRITICAL

BPO: benzoyl peroxide; CI: confidence interval; POR: peto odds ratio; RR: risk ratio; SD: standard deviation

[1] *Dobson 1980*
[2] *Kuhlman 1986*
[3] *Sklar 1996*
[4] *Jones 1981*
[5] *Jones 2002*
[6] *Thiboutot 2002*
[7] *Feldman 2013 (study 301)*
[8] *Feldman 2013 (study 302)*
[9] *Stein Gold 2016*
[10] *Tanghetti 2019*
[11] *Tyring 2018*
[12] *Pariser 2005*
[13] *Thiboutot 2008*
[14] *Braathen 1984*
[15] *Gratton 1982*
[16] *Pariser 2014*
[17] *Dreno 2017*
[18] *Dreno 2018*
[19] *Overall risk of bias judgement: very serious risk of bias.*
[20] *Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.*
[21] *Overall risk of bias judgement: serious risk of bias.*
[22] *Evidence downgraded by 1 level due to serious inconsistency. Random effects model was not possible.*
[23] *Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes.*
[24] *Evidence downgraded by 2 levels due to very serious inconsistency.*
[25] *Evidence downgraded by 1 level due to serious imprecision surrounding small sample size.*

Table 13: Clinical evidence profile for comparison of topical interventions versus topical interventions in participants with moderate to severe acne

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical	Topical	Relative (95% CI)	Absolute		
Skin irritation (non-retinoids) - BPO + ERYTH versus BPO												
1[1]	randomised trials	serious[12]	no serious inconsistency	no serious indirectness	serious[13]	none	13/32 (40.6%)	4/30 (13.3%)	RR 3.05 (1.12 to 8.31)	273 more per 1000 (from 16 more to 975 more)	⊕⊕OO LOW	CRITICAL
Skin irritation (topical ± retinoid) - Motretinide versus BPO												
1[2]	randomised trials	very serious[14]	no serious inconsistency	no serious indirectness	no serious imprecision	none	1/15 (6.7%)	11/15 (73.3%)	Peto OR 0.07 (0.02 to 0.29)	682 fewer per 1000 (from 521 fewer to 719 fewer)	⊕⊕OO LOW	CRITICAL
Skin irritation (topical ± retinoid) - BPO+CLIND+TAZ versus BPO+CLIND												
1[3]	randomised trials	serious[12]	no serious inconsistency	no serious indirectness	very serious[15]	none	1/20 (5%)	0/20 (0%)	Peto OR 7.39 (0.15 to 372.38)	-	⊕OOO VERY LOW	CRITICAL
Skin irritation (topical ± retinoid) - TRET + CLIND versus CLIND												
3[4,5,6]	randomised trials	serious[12]	no serious inconsistency	no serious indirectness	no serious imprecision	none	41/1412 (2.9%)	15/1257 (1.2%)	Peto OR 2.58 (1.52 to 4.39)	19 more per 1000 (from 6 more to 40 more)	⊕⊕⊕O MODERATE	CRITICAL
Skin irritation (topical ± retinoid) - TRET + CLIND versus TRET												
1[4]	randomised trials	serious[12]	no serious inconsistency	no serious indirectness	very serious[15]	none	0/300 (0%)	2/300 (0.67%)	Peto OR 0.13 (0.01 to 2.16)	6 fewer per 1000 (from 7 fewer to 8 more)	⊕OOO VERY LOW	CRITICAL
Skin irritation (topical ± retinoid) - TRET versus CLIND												
1[4]	randomised trials	serious[12]	no serious inconsistency	no serious indirectness	very serious[15]	none	2/300 (0.67%)	0/150 (0%)	Peto OR 4.50 (0.24 to 85.33)	-	⊕OOO VERY LOW	CRITICAL
Skin irritation (topical retinoid ± other)												
4[7,8,9,10]	randomised trials	very serious[14]	no serious inconsistency	no serious indirectness	very serious[15]	none	21/318 (6.6%)	24/316 (7.6%)	RR 0.87 (0.5 to 1.53)	10 fewer per 1000 (from 38 fewer to 40 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical	Topical	Relative (95% CI)	Absolute		
Patient reported improvement - BPO+MICO versus BPO												
1[11]	randomised trials	serious[12]	no serious inconsistency	no serious indirectness	no serious imprecision	none	45/51 (88.2%)	27/51 (52.9%)	RR 1.67 (1.26 to 2.2)	355 more per 1000 (from 138 more to 635 more)	⊕⊕⊕O MODERATE	CRITICAL

BPO: benzoyl peroxide; CLIND: clindamycin; CI: confidence interval; ERYTH: erythromycin; MICO: miconazole nitrate; POR: peto odds ratio; RR: risk ratio; TAZ: tazarotene TRET: tretinoin

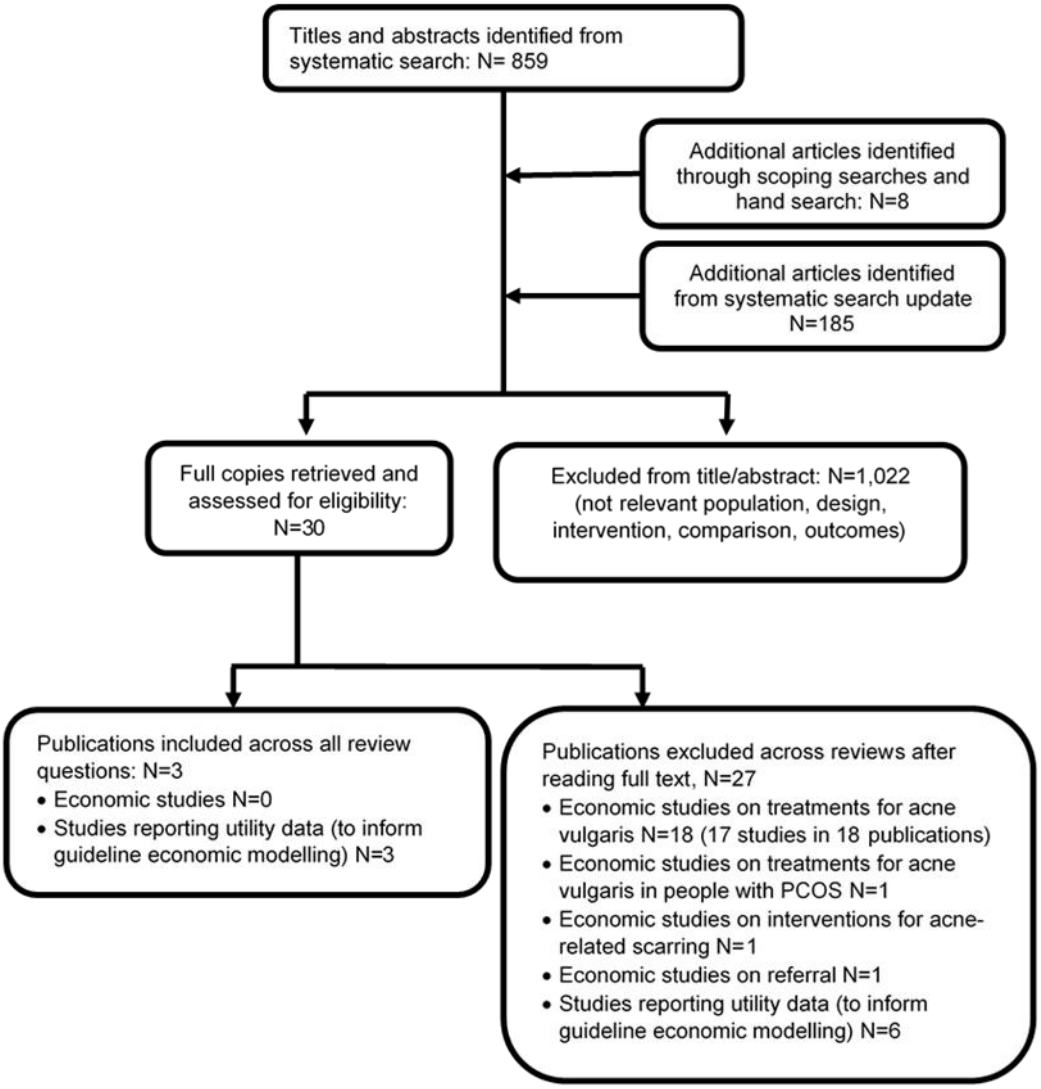
[1] *Sklar 1996*
[2] *Lassus 1984*
[3] *Dhawan 2013*
[4] *Dogra 2020*
[5] *Schmidt 2011*
[6] *Zouboulis 2000*
[7] *Richter 1998*
[8] *Stein Gold 2008*
[9] *Tanghetti 2006*
[10] *Tanghetti 2011*
[11] *Degreef 1982*
[12] *Overall risk of bias judgement: serious risk of bias.*
[13] *Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes.*
[14] *Overall risk of bias judgement: very serious risk of bias.*
[15] *Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.*

Appendix G - Economic evidence study selection

Economic evidence study selection for review question: What is the effectiveness and acceptability of interventions for the treatment of moderate to severe acne (side effects and participant reported improvement)?

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

Figure 12. Flow diagram of selection process for economic evaluations of interventions and strategies associated with the care of people with acne vulgaris and studies reporting acne vulgaris-related health state utility data



Appendix H - Economic evidence tables

Economic evidence tables for review question: What is the effectiveness and acceptability of interventions for the treatment of moderate to severe acne (side effects and participant reported improvement)?

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

Appendix I - Economic evidence profiles

Economic evidence profiles for review question: What is the effectiveness and acceptability of interventions for the treatment of moderate to severe acne (side effects and participant reported improvement)?

The economic model associated with this review question was based on the NMA results. So for the economic evidence profile see evidence report F1.

Appendix J – Economic analysis

Economic analysis for review question: What is the effectiveness and acceptability of interventions for the treatment of moderate to severe acne (side effects and participant reported improvement)?

The economic model associated with this review question was based on the NMA results. So for the economic analysis see evidence report F1.

Appendix K - Excluded studies

Excluded clinical and economic studies for review question: What is the effectiveness and acceptability of interventions for the treatment of moderate to severe acne (side effects and participant reported improvement)?

Clinical studies

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

Table 14: Excluded clinical 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

Reference	Reason for exclusion
Adalatkhah, 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 Investigational Dermatology CCID	Moderate acne - no information on lesion counts at baseline and study is not relevant for PCOS, maintenance or refractory treatments
Adams, J. T., P. Topical fusidic acid versus peroral doxycycline in the treatment of patients with acne vulgaris of the face. 1991. Current Therapeutic Research - Clinical and Experimental	No relevant intervention - suboptimal dose of doxycycline
Adams, R. M. B., K. H. An antiandrogen delta 1 chlormadinone acetate in acne: lack of effect topically. 1970a. Acta Dermato-Venereologica	Duplicate record
Adams, U. M. B., K. H. An antiandrogen delta 1 chlormadinone acetate in acne: lack of effect topically. 1970b. Acta Dermatologica	No relevant study population -insuficient 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	No relevant outcomes reported

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

Reference	Reason for exclusion
3.75% gel. 2017. Journal of clinical and aesthetic dermatology	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 p.100 adapalene gel and 0.025 p.100 tretinoin gel in the treatment of acne. 1996. Annales de dermatologie ET de venereologie	Not in English language
Alirezai, M. V., K.,Humbert, P.,Valensi, P.,Cambon, L.,Dupuy, P.A low-salt medical water reduces irritancy of retinoic acid in facial acne. 2000. European Journal of Dermatology	Intervention not targeted at acne but at treatment side effects
Allen, H.F., Mazzoni, C., Heptulla, R.A., Murray, M.A., Miller, N., Koenigs, L., Reiter, E.O. Randomized controlled trial evaluating response to metformin versus standard therapy in the treatment of adolescents with polycystic ovary syndrome. 2005. Journal of Pediatric Endocrinology and Metabolism	Not clear what proportion of participants had acne at baseline
Al-Mishari, M. A. Clinical and bacteriological evaluation of tetracycline and erythromycin in acne vulgaris. 1987. Clinical Therapeutics	Unclear if RCT
Amer, S. S., Nasr, M., Abdel-Aziz, R. T. A., Moftah, N. H., El Shaer, A., Polycarpou, E., Mamdouh, W., Sammour, O. Cosm-nutraceutical nanovesicles for acne treatment: Physicochemical characterization and exploratory clinical experimentation. 2020. International Journal of PharmaceuticsInt J Pharm	No relevant study design - not RCT
Amiri, M., Nahidi, F., Bidhendi-Yarandi, R., Khalili, D., Tohidi, M., Ramezani Tehrani, F.A comparison of the effects of oral contraceptives on the clinical and biochemical manifestations of polycystic ovary syndrome: A crossover randomized controlled trial. 2020. Human Reproduction	No relevant outcomes reported
An, W. X. Z., Z. H. Curative observation on herbal tea combined with ear acupoint in treating 120 middle school students with acne. 2016. Western journal of traditional chinese medicine[xi bu zhong yi yao]	Not in English language
Anadolu, R. Y. S., T.,Tarimci, N.,Birol, A.,Erdem, C.Improved efficacy and tolerability of retinoic acid in acne vulgaris: A new topical formulation with cyclodextrin complex PSI. 2004. Journal of the European Academy of Dermatology and Venereology	Insufficient information about severity of acne at baseline and study is not relevant for PCOS, maintenance or refractory treatments
Anonymous, Management of acne vulgaris. 1966. Drug & Therapeutics Bulletin	Duplicate record
Anonymous, Pharmacokinetic profile, safety, and tolerability of clascoterone topical cream 1% in subjects with moderate-to-severe acne vulgaris: an open-label phase IIa study. 2019. Journal of the American Academy of Dermatology	No relevant article type - conference abstract
Anonymous, Phase III Clinical Study of Clindamycin Phosphate Topical Gel (CLDM-T) in the Treatment of Acne Vulgaris: randomized Comparatie Study with Nadifloxacin Cream as a Control Drug. 1999b. Rinsho iyaku (journal of clinical therapeutics and medicines)	Not in English language
Anonymous, Retinoic acid in the treatment of acne. A report from the General Practitioner Research Group. 1974. Practitioner	No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Anonymous, The Clinical Phase II Study of CLDM-T Gel in the Treatment of Acne Vulgaris: double-Blind Comparative Study,	Not in English language

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

Reference	Reason for exclusion
vulgaris: What is the role of age?. 2011. Journal of Dermatological Treatment	includes people with moderate acne but baseline severity not reported according to lesion counts and study is not relevant for PCOS, maintenance or refractory treatments
Bae, B. G. P., C. O.,Shin, H.,Lee, S. H.,Lee, Y. S.,Lee, S. J.,Chung, K. Y.,Lee, K. H.,Lee, J. H.Salicylic acid peels versus Jessner's solution for acne vulgaris: a comparative study. 2013. Dermatologic surgery	Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments
Barak-Shinar, D. D., Z. D.A randomized controlled study of a novel botanical acne spot treatment. 2017. Journal of Drugs in Dermatology	No relevant intervention - study product was based on 10% herbal botanical ingredients with anti-inflammatory and anti-bacterial activity
Barranco, V. P.Effect of androgen-dominant and estrogen-dominant oral contraceptives on acne. 1974. Cutis; cutaneous medicine for the practitioner	No relevant study population - no information on the baseline severity of acne and study is not relevant for PCOS, maintenance or refractory treatments
Bassett, I. B. P., D. L.,Barnetson, R. S.A comparative study of tea-tree oil versus benzoylperoxide in the treatment of acne. 1990. Medical Journal of Australia	No relevant intervention - tea-tree oil
Baugh, W. P. K., W. D.Nonablative phototherapy for acne vulgaris using the KTP 532 nm laser. 2005. Dermatologic Surgery	Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments
Baumann, L. S. O., C.,Yatskayer, M.,Dahl, A.,Figueras, K.Comparison of clindamycin 1% and benzoyl peroxide 5% gel to a novel composition containing salicylic acid, capryloyl salicylic acid, HEPES, glycolic acid, citric acid, and dioic acid in the treatment of acne vulgaris. 2013. Journal of drugs in dermatology	Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments
Behrangi, E. A., E.,Tavakoli, T.,Mehran, G.,Atefi, N.,Esmaeeli, S.,Azizian, Z.Comparing efficacy of montelukast versus doxycycline in treatment of moderate acne. 2015. Journal of Research in Medical Sciences	No relevant intervention - montelukast

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

Reference	Reason for exclusion
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. Journal of Clinical and Diagnostic Research JCDR	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Bissonnette, R. B., C., Seite, S.,Nigen, S.,Provost, N.,Maari, C.,Rougier, A.Randomized study comparing the efficacy and tolerance of a lipophillic hydroxy acid derivative of salicylic acid and 5% benzoyl peroxide in the treatment of facial acne vulgaris. 2009. Journal of Cosmetic Dermatology	No relevant intervention - intervention & class not available in the UK
Bissonnette, R. M., C., Nigen, S.,Provost, N.,Bolduc, C.Photodynamic therapy with methylaminolevulinate 80 mg/g without occlusion improves acne vulgaris. 2010. Journal of Drugs in Dermatology	No relevant comparison - photodynamic therapy with methylaminolevulinate with occlusion vs without occlusion
Bissonnette, R. P., Y., Drew, J.,Hofland, H.,Tan, J.Olumacostat glasaretil, a novel topical sebum inhibitor, in the treatment of acne vulgaris: A phase IIa, multicenter, randomized, vehicle-controlled study. 2017. Journal of the American Academy of Dermatology	No relevant intervention - intervention not licensed in the UK
Biswas, S. M., K. K., Dutta, R. N.,Sarkar, D. K.Comparative evaluation of the efficacy of four topical medications individually or in combination to treat grade I acne vulgaris. 2009. Journal of the Indian Medical Association	No relevant outcomes reported
Biyun, C.The clinical observation of treating acne vulgaris with "xiao cuo fang". 2004. Zhong yao cai = Zhongyaocai [Journal of Chinese medicinal materials]	Not in English language
Bladon, P. T. B., B. M., Cunliffe, W. J.Topical azelaic acid and the treatment of acne: A clinical and laboratory comparison with oral tetracycline. 1986. British Journal of Dermatology	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Blaney, D. J. C., C. H. Topical use of tetracycline in the treatment of acne. A double blind study comparing topical and oral tetracycline therapy and placebo. 1976. Archives of Dermatology	No relevant intervention - intervention & class not available in the UK
Bleeker, J. H., L.,Vincent, J.Effect of systemic erythromycin stearate on the inflammatory lesions and skin surface fatty acids in acne vulgaris. 1981. Dermatologica	No relevant study population - sample includes people with mild to severe acne
Bodokh, I. J., Y., Lacour, J. Ph,Ortonne, J. P.Minocycline induces an increase in the number of excreting pilosebaceous follicles in acne vulgaris. A randomised study. 1997. Acta Dermato-Venereologica	No relevant data reported - pharmokinetic study
Bojar, R. A. E., E. A., Jones, C. E.,Cunliffe, W. J.,Holland, K. T.Inhibition of erythromycin-resistant propionibacteria on the skin of acne patients by topical erythromycin with and without zinc. 1994. British Journal of Dermatology	Efficacy outcomes reported in figures only
Borglund, E. H., O., Nord, C. E.Impact of topical clindamycin and systemic tetracycline on the skin and colon microflora in patients with acne vulgaris. 1984. Scandinavian Journal of Infectious Diseases	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments

Reference	Reason for exclusion
Borglund, E. K., B., Larsson-Stymne, B.,Strand, A.,Veien, N. K.,Jakobsen, H. B.Topical meclocycline sulfosalicylate, benzoyl peroxide, and a combination of the two in the treatment of acne vulgaris. 1991. Acta Dermato-Venereologica	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Borhan, W. H. H., H. A.,Aboelnour, N. H.Efficacy of pulsed dye laser on acne vulgaris. 2014. Journal of american science	Insufficient information about treatment (unspecified topical antibiotic)
Botsali, A. K., P.,Uran, P.The effects of isotretinoin on affective and cognitive functions are disparate in adolescent acne vulgaris patients. 2019. Journal of Dermatological Treatment.	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Bouloc, A. R., E.,Imko-Walczuk, B.,Moga, A.,Chadoutaud, B.,Dreno, B.A skincare combined with combination of adapalene and benzoyl peroxide provides a significant adjunctive efficacy and local tolerance benefit in adult women with mild acne. 2017. Journal of the European Academy of Dermatology and Venereology	No relevant intervention - compares emolients
Bourne, M. S.Comparison of two lotions for acne vulgaris. 1979. Practitioner	No relevant intervention - intervention & class not available in the UK
Bowman, S. G., M.,Nasir, A.,Vamvakias, G.Comparison of clindamycin/benzoyl peroxide, tretinoin plus clindamycin, and the combination of clindamycin/benzoyl peroxide and tretinoin plus clindamycin in the treatment of acne vulgaris: a randomized, blinded study. 2005. Journal of drugs in dermatology : JDD	No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Bradford, L. G. M., L. F.Topical application of vitamin A acid in acne vulgaris. 1974. Southern Medical Journal	Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments
Bran, E. L. R. A., A. Therapeutic effectiveness of clindamycin phosphate (1% solution) compared with tetracycline (solution) administered topically in the treatment of acne vulgaris. 1986. Medicina cutanea ibero-latino-americana	Not in English language
Brand, B. G., R.,Baker, M. D.,Poncet, M.,Greenspan, A.,Georgeian, K.,Soloff, A. M.Cumulative irritancy comparison of adapalene gel 0.1% versus other retinoid products when applied in combination with topical antimicrobial agents. 2003a. Journal of the American Academy of Dermatology	No relevant study population - participants did not have acne
Brand, B. G., R.,Baker, M. D.,Poncet, M.,Greenspan, A.,Georgeian, K.,Soto, P.,Arsonnaud, S.Cumulative Irritancy Potential of Adapalene Cream 0.1% Compared with Adapalene Gel 0.1% and Several	No relevant study population - participants did not have acne

Reference	Reason for exclusion
Tretinoin Formulations. 2003b. Cutis	
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 cutÃ¡nea ibero-latino-americana	Not in English language
Brandt, H. A., P.,Ahokas, T.,Forstrom, L.,Jarvinen, T.,Keskitalo, R.,Lehtonen, L.,Plosila, M.,Rita, H.,Suramo, M. L.Erythromycin acistrate - An alternative oral treatment for acne. 1994. Journal of Dermatological Treatment	No relevant comparison - suboptimal dose
Breneman, D. L. A., M. C. Successful treatment of acne vulgaris in women with a new topical sodium sulfacetamide/sulfur lotion. 1993. International Journal of Dermatology	No relevant study design - not RCT
Breno, B. K., A.,Richard, A.,Rougier, A.Interest of a new salicylic acid derivative in the prevention of acne relapses. 2002. European journal of dermatology : EJD	No relevant article type - conference abstract
Brickman, S. S. L., W. D.,Gareau, J. Y.A double-blind evaluation of a topical antibiotic preparation in acne. 1980. Current Therapeutic Research - Clinical and Experimental	No relevant intervention - intervention & class not available in the UK
Brodell, R. T. S., B. J.,Rafal, E.,Toth, D.,Tyring, S.,Wertheimer, A.,Kerrouche, N.,Bucher, D.A fixed-dose combination of adapalene 0.1%BPO 2.5% allows an early and sustained improvement in quality of life and patient treatment satisfaction in severe acne. 2012. Journal of Dermatological Treatment	No relevant outcomes reported
Brogden, R. N. S., T. M.,Avery, G. S.Benzoyl peroxide acne lotions : an independent report. 1974. Drugs	No relevant article type - expert review
Brookes, D. B. M., R. M.,Sheil, L. P.,Flowers, I. M.,Poulter, G. A. Comparison of Tretinoin and a composite formulation in the treatment of acne. 1978. British Journal of Clinical Practice	No relevant study population - insufficient details reported to determine acne severity and study is not relevant for PCOS, maintenance or refractory treatments
Bubna, A. K.Metformin - For the dermatologist. 2016. Indian Journal of Pharmacology	Duplicate record
Bucknall, J. H. M., P. N. Comparison of tretinoin solution and benzoyl peroxide lotion in the treatment of acne vulgaris. 1977. Current Medical Research & Opinion	Not obtainable
Budden, M. G. Topical and oral tetracycline in the treatment of acne vulgaris. 1988. Practitioner	No relevant intervention - intervention & class not available in the UK
Burke, B. E., E. A.,Cunliffe, W. J.Benzoylperoxide versus topical erythromycin in the treatment of acne vulgaris. 1983. British Journal of Dermatology	No relevant study design - not RCT
Burkhart, C. G. B., C. N.Treatment of acne vulgaris without antibiotics: tertiary amine-benzoyl peroxide combination vs. benzoyl peroxide alone (Proactiv Solution). 2007. International Journal of Dermatology	Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments
Burton, J. E., G.A placebo-controlled study to evaluate the efficacy of topical tetracycline and oral tetracycline in the treatment of mild to moderate acne. 1990. Journal of International Medical Research	No relevant intervention - intervention & class not available in the UK

Reference	Reason for exclusion
Burton, J. L. P., R. J.,Harris, J. I.Effect of 1% cyproterone acetate in Cetomacrogol cream BPC (formula A) on sebum excretion rate in patients with acne. 1976. British Journal of Dermatology	No relevant data reported - pharmokinetic study
Callender, V. D.Fitzpatrick skin types and clindamycin phosphate 1.2%/benzoyl peroxide gel: Efficacy and tolerability of treatment in moderate to severe acne. 2012a. Journal of Drugs in Dermatology	No relevant data reported - post hoc analysis reporting results for people receiving clindamycin 2.1%/BPO 2.5% gel
Cambazard, F.Clinical efficacy of Velac, a new tretinoin and clindamycin phosphate gel in acne vulgaris. 1998. Journal of the European Academy of Dermatology & Venereology	No relevant study design - non-systematic review of tretinoin treatment
Cannizzaro, M. V. D., A.,Garofalo, V.,Del Duca, E.,Bianchi, L.Reducing the oral Isotretinoin skin side effects: Efficacy of 8% omega-ceramides, hydrophilic sugars, 5% niacinamide cream Compound in acne patients. 2018. Giornale Italiano di Dermatologia e Venereologia	Not in English language
Cao, J., Yang, G., Wang, Y., Liu, J. Acupoint Stimulation for Acne: A Systematic Review of Randomized Controlled Trials. 2013. Med Acupunct. 2013	No relevant intervention - systematic review about acupoint stimulation techniques used to treat acne
Cao, J., Yang, G., Wang, Y., Ping Liu, J., Smith, C.A., Luo, H., Liu. Y. Complementary therapies for acne vulgaris. 2015. Cochrane Database Syst Rev	Not relevant intervention - systematic review about complementary and alternative medicine for acne
Cao, T. T., E. S.,Chan, Y. H.,Yosipovitch, G.,Tey, H. L.Anti-pruritic efficacies of doxycycline and erythromycin in the treatment of acne vulgaris: a randomized single-blinded pilot study. 2018. Indian journal of dermatology, venereology and leprology	No relevant study design - not RCT
Carlborg, L. Cyproterone acetate versus Levonorgestrel combined with ethinyl estradiol in the treatment of acne. Results of a multicenter study. 1986. Acta Obstetricia et Gynecologica Scandinavica	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Carlborg, L. Cyproterone acetate versus levonorgestrel combined with ethinylestradiol in the treatment of acne. Results of a multicenter study. 1987. Contraception fertilite sexualite	Duplicate record
Carmina, E. L., R. A.A comparison of the relative efficacy of antiandrogens for the treatment of acne in hyperandrogenic women. 2002. Clinical Endocrinology	Duplicate record
Caron, D. S., V.,Clucas, A.,Verschoore, M.Skin tolerance of adapalene 0.1% gel in combination with other topical antiacne treatments. 1997a. Journal of the American Academy of Dermatology	No relevant study population - participants did not have acne
Caron, D. S., V.,Kerrouche, N.,Clucas, A.Split-face comparison of adapalene 0. 1% gel and tretinoin 0.025% gel in acne patients. 1997b. Journal of the American Academy of Dermatology	No relevant outcomes reported
Cavicchini, S. C., R.Long-term treatment of acne with 20% azelaic acid cream. 1989. Acta Dermato-Venereologica, Supplement	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments

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

Reference	Reason for exclusion
fractional photothermolysis system with dynamic operating mode on acne scars and enlarged facial pores. 2009. Dermatologic Surgery	
Choudhury, S. C., S.,Sarkar, D. K.,Dutta, R. N.Efficacy and safety of topical nadifloxacin and benzoyl peroxide versus clindamycin and benzoyl peroxide in acne vulgaris: A randomized controlled trial. 2011. Indian Journal of Pharmacology	No relevant intervention - intervention & class not available in the UK
Christian, G. L. K., G. G. Clindamycin vs placebo as adjunctive therapy in moderately severe acne. 1975. Archives of Dermatology	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Christiansen, J. H., P.,Reymann, F.The retinoic acid derivative Ro 11 1430 in Acne vulgaris. A controlled multicenter trial against retinoic acid. 1977. Dermatologica	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Christiansen, J. H., P.,Reymann, F.Treatment of acne vulgaris with the retinoic acid derivative Ro 11-1430. A controlled clinical trial against retinoic acid. 1976. Dermatologica	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Christiansen, J. V. G., E.,Ludvigsen, K.,Konstman Meier, C. H.,Norholm, A.,Osmundsen, P. E.,Pedersen, D.,Rasmussen, K. A.,Reiter, H.,Reymann, F.,et al.,Topical vitamin A acid (Airol) and systemic oxytetracycline in the treatment of acne vulgaris. A controlled clinical trial. 1974a. Dermatologica	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Christiansen, J. V. G., E.,Ludvigsen, K.,Meier, C. H.,Norholm, A.,Pedersen, D.,Rasmussen, K. A.,Reiter, H.,Reymann, F.,Sylvest, B.,et al.,Topical tretinoin, vitamin A acid (Airol) in acne vulgaris. A controlled clinical trial. 1974b. Dermatologica	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Chu, A. H., F. J.,Plott, R. T.The comparative efficacy of benzoyl peroxide 5%/erythromycin 3% gel and erythromycin 4%/zinc 1.2% solution in the treatment of acne vulgaris. 1997. British Journal of Dermatology	No relevant study population - sample includes people with too narrow range of acne severity criteria and study is not relevant for PCOS, maintenance or refractory treatments
Chularojanamontri, L. T., P.,Kulthanan, K.,Varothai, S.,Winayanuwattikun, W.A double-blinded, randomized, vehicle-controlled study to access skin tolerability and efficacy of an anti-inflammatory moisturizer in treatment of acne with 0.1% adapalene gel. 2016. Journal of Dermatological Treatment	No relevant intervention - Adaplene with or without Eucerin mositurizer
Clucas, A. V., M.,Sorba, V.,Poncet, M.,Baker, M.,Czernielewski, J.Adapalene 0.1% gel is better tolerated than tretinoin 0.025% gel in acne patients. 1997. Journal of the American Academy of	Duplicate publication from Cunliffe 1997 trial

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

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

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

Reference	Reason for exclusion
0.5% liposomal spray and intense pulsed light in combination with topical keratolytic agents. 2010. Journal of the European Academy of Dermatology and Venereology	RCT but does not report comparative data
Degreef, H. V. B., G. Double-blind evaluation of a miconazole - benzoyl peroxide combination for the topical treatment of acne vulgaris. 1982a. Dermatologica	Duplicate record
Del Rosso JQ, Kircik L, Gallagher CJ.Comparative efficacy and tolerability of dapsone 5% gel in adult versus adolescent females with acne vulgaris. https://www.ncbi.nlm.nih.gov/pubmed/25610522	Posthoc analysis of Draelos 2007
Del Rosso, J. Q. Clindamycin phosphate 1.2%/tretinoin 0.025% gel for the treatment of acne vulgaris: Which patients are most likely to benefit the most?. 2015. Journal of Clinical and Aesthetic Dermatology	Duplicate record
Del Rosso, J. Q. K., L.,Gallagher, C. J.Comparative efficacy and tolerability of dapsone 5% gel in adult versus adolescent females with acne vulgaris. 2015. Journal of Clinical and Aesthetic Dermatology	No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Del Rosso, J. Q. Study results of benzoyl peroxide 5%/clindamycin 1% topical gel, adapalene 0.1% gel, and use in combination for acne vulgaris. 2007. Journal of drugs in dermatology : JDD	No relevant study population - no details of inclusion criteria reported and study is not relevant for PCOS, maintenance or refractory treatments
Del Rosso, J. Q. The use of topical azelaic acid for common skin disorders other than inflammatory rosacea. 2006. Cutis	Duplicate record
Deshmukh, S. N. B., V. A.,Mahajan, M. M.,Sujata Dudhgaonkar, D.,Mishra, D.Comparison of efficacy and safety of topical 1% nadifloxacin and tretinoin 0.025% combination therapy with 1% clindamycin and tretinoin 0.025% combination therapy in patients of mild-to-moderate acne. 2018. Perspectives in Clinical Research	No relevant intervention - intervention & class not available in the UK
DeVillez, R. L.Clinical comparison of the safety and efficacy of Brevoxyl gel and Benzamycin gel. 1992. Drug Investigation	No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Dhawan, S. S. Comparison of 2 clindamycin 1%-benzoyl peroxide 5% topical gels used once daily in the management of acne vulgaris. 2009. Cutis; cutaneous medicine for the practitioner	No relevant comparison - clindamycin/BPO topical gel with the hydrating excipients dimethicone and glycerin vs without hydrating excipients
Dieben Th, O. M. V., L.,Theeuwes, A.,Coelingh Bennink, H. J. T.The effects of CTR-24, a biphasic oral contraceptive combination, compared to Diane-35 in women with acne. 1994. Contraception	No relevant study population - insufficient details about types of lesions to determine severity of participants
Divers, L. S.A new preparation for the topical treatment of acne vulgaris. Report of a year's study. 1966. Journal of the College of	No relevant study design -

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

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

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

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

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

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

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

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

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

Reference	Reason for exclusion
oxytetracycline in the treatment of inflammatory acne vulgaris. 1982. British Journal of Dermatology	population - insufficient information reported about acne severity and study is not relevant for PCOS, maintenance or refractory treatments
Gibson, J. R.Azelaic acid 20% cream (AZELEX) and the medical management of acne vulgaris. 1997. Dermatology Nursing	No relevant article type - expert review
Gloor, M. H., A.,Friederich, H. C.Trial of benzoyl peroxide treatment of acne vulgaris. EXPERIMENTELLE UNTERSUCHUNGEN ZUR BENZOYLPEROXYDTHERAPIE DER ACNE VULGARIS. 1975. ZHAUTKR	Not in English language
Goforoushan, F. A., H.,Goldust, M.Efficacy of vitamin E to prevent dermal complications of isotretinoin. 2013. Pakistan Journal of Biological Sciences	No relevant comparison - compares efficacy of treatment to alleviate isotretinoin dermal complications
Goh, C. L. T., M. B.,Briantais, P.,Kaoukhov, A.,Soto, P.Adapalene gel 0.1% is better tolerated than tretinoin gel 0.025% among healthy volunteers of various ethnic origins. 2009. Journal of Dermatological Treatment	No relevant study population - participants did not have acne
Gold, L. S. B., H.,Rueda, M. J.,Kerrouche, N.,Dreno, B.Adapalene-benzoyl peroxide gel is efficacious and safe in adult female acne, with a profile comparable to that seen in teen-aged females. 2016. Journal of Clinical and Aesthetic Dermatology	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Gold, L. S., Dhawan, S., Weiss, J., Draelos, Z. D., Ellman, H., Stuart, I.Open-label extension study evaluating long-term safety and efficacy of FMX101 4% minocycline foam for moderate-to-severe acne vulgaris. 2019. Journal of Clinical and Aesthetic Dermatology	No relevant data reported - reported reports results on open-label part of trial only
Gold, M. H. B., V. L.,Boring, M. M.,Bridges, T. M.,Biron, J. A.,Carter, L. N.The use of a novel intense pulsed light and heat source and ALA-PDT in the treatment of moderate to severe inflammatory acne vulgaris. 2004. Journal of Drugs in Dermatology: JDD	No relevant study design - not RCT
Gold, M. H. R., J.,Goldman, M. P.,Bridges, T. M.,Bradshaw, V. L.,Boring, M. M.,Guider, A. N.A multicenter clinical evaluation of the treatment of mild to moderate inflammatory acne vulgaris of the face with visible blue light in comparison to topical 1% clindamycin antibiotic solution. 2005. Journal of drugs in dermatology : JDD	Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments
Gold, M. H. S., N. S.,Bradshaw, V. L.,Boring, M. M.A randomized, controlled, double-blind study of localized low-heat treatment of acne lesions. 2007. Cosmetic Dermatology	No relevant data reported - response study
Gold, M. H. S., W.,Biron, J. A.Clinical efficacy of home-use blue-light therapy for mild-to moderate acne. 2011. Journal of Cosmetic and Laser Therapy	No relevant intervention - only 2 individual lesions treated per patient
Gold, M. H., Korotkor., A.Sub-group analyses from a trial of a fixed combination of clindamycin phosphate 1.2% and benzoyl peroxide 3.75% gel for the treatment of moderate-to-severe acne vulgaris. 2015. Journal of Clinical and Aesthetic Dermatology	No relevant article type - non-systematic review

Reference	Reason for exclusion
Gold, M. R. M., A. P.A randomised, double-blind, multicentre, multinational comparison of 2% fusidic acid lotion and 1% clindamycin lotion in patients with acne vulgaris on the face. 1996. European journal of clinical research	Not obtainable
Goldman, M. P. B., S. M.A single-center study of aminolevulinic acid and 417 NM photodynamic therapy in the treatment of moderate to severe acne vulgaris. 2003. Journal of Drugs in Dermatology: JDD	No relevant study design - not RCT
Goldstein, J. A. S.-S., A.,Thomsen, R. J.,Pochi, P. E.,Shalita, A. R.,Strauss, J. S.Comparative effect of isotretinoin and etretinate on acne and sebaceous gland secretion. 1982. Journal of the American Academy of Dermatology	No relevant comparison - isotretinoin vs etretinate
Gollnick, H. G., K.Azelaic acid for the treatment of acne: Comparative trials. 1989. Journal of Dermatological Treatment	No relevant article type - expert review
Gollnick, H. P. G., K.,Zaumseil, R. P.Azelaic acid 15% gel in the treatment of acne vulgaris. Combined results of two double-blind clinical comparative studies. 2004. Journal der Deutschen Dermatologischen Gesellschaft [Journal of the German Society of Dermatology]	Not in English language
Gollnick, H. P. M. V., K.,Hermann, J.,Blume, U.,Hahn, H.,Haustein, U. F.,Orfanos, C. E.Topical quinolone OPC-7251: A clinical and microbiological study in acne. 1994. European Journal of Dermatology	No information on the baseline severity of acne and study is not relevant for PCOS, maintenance or refractory treatments
Goltz, R. W. C., G. M.,Schnieders, J. R.,Neidert, G. L.A comparison of Cleocin T 1 percent solution and Cleocin T 1 percent lotion in the treatment of acne vulgaris. 1985. Cutis	No relevant data - insufficient data reported
Goltz, R. W. K., S.Oral tetracycline treatment on bacterial flora in acne vulgaris. 1966. Archives of Dermatology	No relevant data reported - bacterial flora study
Gonzalez, P. V., R.,Cirigliano, M.The tolerability profile of clindamycin 1%/benzoyl peroxide 5% gel vs. adapalene 0.1%/benzoyl peroxide 2.5% gel for facial acne: Results of a randomized, single-blind, split-face study. 2012. Journal of Cosmetic Dermatology	No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Goodfellow, A. A.-Z., J.,Carter, G.Oral spironolactone improves acne vulgaris and reduces sebum excretion. 1984. British Journal of Dermatology	No relevant outcomes reported
Goreshi, R. S., A.,Ehst, B. D.A double-blind, randomized, bilateral comparison of skin irritancy following application of the combination acne products clindamycin/tretinoin and benzoyl peroxide/adapalene. 2012. Journal of Drugs in Dermatology	No relevant outcomes reported
Goswami, B. C. B., B.,Barua, A. B.,Olson, J. A. Topical retinoyl beta-glucuronide is an effective treatment of mild to moderate acne vulgaris in Asian-Indian patients. 1999. Skin Pharmacology & Applied Skin Physiology	No relevant intervention - retinoyl beta-glucuronide
Goujon, C. G., P.,Violin, L.,Larnier, C.Biometric and clinical comparative assay of Roaccutane gel (0.05% isotretinoin) versus Retacnyl cream (0.05% tretinoin) in the treatment of moderate retentional acne on the face. 1995. Nouvelles Dermatologiques	Not in English language
Gould, D. J. E., R.,Cunliffe, W. J.Oral tetracycline and retinoic acid gel in acne. 1978. Practitioner	No relevant study design - unclear if RCT
Graupe, K. C., W. J.,Gollnick, H. P.,Zaumseil, R. P.Efficacy and safety	No relevant study design -

Reference	Reason for exclusion
of topical azelaic acid (20 percent cream): an overview of results from European clinical trials and experimental reports. 1996. Cutis	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
Green, L. J. D. R., J. Q.Efficacy and Tolerability of a Three-Step Acne System Containing a Solubilized Benzoyl Peroxide Lotion versus a Benzoyl Peroxide/Clindamycin Combination Product: An Investigator-Blind, Randomized, Parallel-Group Study. 2008. The Journal of Clinical & Aesthetic Dermatology	Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments
Green, L. K., L. H.,Gwazdauskas, J.Randomized, controlled, evaluator-blinded studies conducted to compare the efficacy and tolerability of 3 over-the-counter acne regimens in subjects with mild or moderate acne. 2013. Journal of drugs in dermatology	No relevant comparison - compares over-the-counter 3-part skin care regimens inclunding BPO, SAL etc which have been discontinued (MaxClarity, Proactiv, Murad)
Greenwood, R. B., B.,Cunliffe, W. J.Evaluation of a therapeutic strategy for the treatment of acne vulgaris with conventional therapy. 1986. British Journal of Dermatology	No relevant study design - not RCT
Gregory, A. N. T., C. R.,Leibowitz, K. R.,Lane, M.A study on the use of a novel light and heat energy system to treat acne vulgaris. 2004. Cosmetic Dermatology	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Griffiths, C. E. E., J. T.,Bernard, B. A.,Rossio, P.,Cromie, M. A.,Finkel, L. J.,Shroot, B.,Voorhees, J. J.Comparison of CD271 (adapalene) and all-trans retinoic acid in human skin: dissociation of epidermal effects and CRABP-II mRNA expression. 1993. Journal of Investigative Dermatology	No relevant study population - participants did not have acne
Grimes, P. C., V.Tazarotene cream for postinflammatory hyperpigmentation and acne vulgaris in darker skin: A double-blind, randomized, vehicle-controlled study. 2006. Cutis	No relevant study population - sample includes people with post-inflammatory hyperpigmentation and acne and study is not relevant for PCOS, maintenance or refractory treatments
Grosshans, E. F., A.,Guibaud, B.Clinical evaluation of a topical ethyl lactate treatment of acne vulgaris (author's transl). 1978. Annales de dermatologie ET de venereologie	Not English language
Grosshans, E. M., R.,Mascaro, J. M.,Torras, H.,Meynadier, J.,Alirezai, M.,Finlay, A. Y.,Soto, P.,Poncet, M.,Verschoore, M.,Clucas, A.Evaluation of clinical efficacy and safety of adapalene 0.1% gel versus tretinoin 0.025% gel in the treatment of acne vulgaris, with particular reference to the onset of action and impact on quality of life. 1998. British Journal of Dermatology, Supplement	Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for

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

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

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

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

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

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

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

Reference	Reason for exclusion
suspension. 2010b. Journal of Dermatology. Conference: 1st Eastern Asia Dermatology Congress, EADC2010. Fukuoka Japan. Conference Publication:	
Jurairattanaporn, N. C., T.,Ophaswongse, S.,Udompataikul, M.Comparative trial of silver nanoparticle gel and 1% clindamycin gel when use in combination with 2.5% benzoyl peroxide in patients with moderate acne vulgaris. 2017. Journal of the Medical Association of Thailand	No relevant study population - sample does not meet the inclusion criteria for mild-to-moderate or moderate-to-severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Jurzyk, R. S. S., R. L.,Rose, L. I.Antiandrogens in the treatment of acne and hirsutism. 1992. American Family Physician	No relevant studyd design - not RCT
Kabir, M. S., S.,Raza, A.,Kanwal, S.,Tanvir, T.Comparison of efficacy of adapalene (0.1% gel) monotherapy ve adapalene (0.1%) plus benzyl peroxide (2.5%) combination therapy for treatment of mild to moderate acne vulgaris. 2018. Pakistan Journal of Medical and Health Sciences	No relevant data reported
Kainz, J. T. B., G.,Auer-Grumbach, P.,Lackner, V.,Perl-Convalexius, S.,Popa, R.,Wolfesberger, B.Azelaic acid 20 % cream: effects on quality of life and disease severity in adult female acne patients. 2016. Journal der Deutschen Dermatologischen Gesellschaft	Duplicate record
Kakita, L. Tazarotene versus tretinoin or adapalene in the treatment of acne vulgaris. 2000. Journal of the American Academy of Dermatology	No relevant article type - commentary article
Kaminaka, C. U., M.,Matsunaka, H.,Furukawa, F.,Yamomoto, Y.Clinical evaluation of glycolic acid chemical peeling in patients with acne vulgaris: a randomized, double-blind, placebo-controlled, split-face comparative study. 2014. Dermatologic surgery	Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments
Kang, A. L., A.,Herrmann, J.,Moy, R.Treatment of moderate-to-severe facial acne vulgaris with solid-state fractional 589/1,319-nm laser. 2019. Journal of Clinical and Aesthetic Dermatology	Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments
Kantikosum, K. C., Y.,Chottawornsak, N.,Asawanonda, P.The efficacy of glycolic acid, salicylic acid, gluconolactone, and licochalcone a combined with 0.1% adapalene vs adapalene monotherapy in mild-to-moderate acne vulgaris: A double-blinded within-person comparative study. 2019. Clinical, Cosmetic and Investigational Dermatology	No relevant study design - not RCT
Kantner, V. S., E. Topical effects of oxytetracycline in acne vulgaris. 1970. Ceskoslovenska dermatologie	Not in English language
Kar, B. R. T., S.,Panda, M.Comparative study of oral isotretinoin versus oral isotretinoin + 20% salicylic Acid peel in the treatment of active acne. 2013. Journal of Cutaneous & Aestheic Surgery	Reported outcomes relevant for the network meta-analysis but not in enough detail to include in

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

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

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

Reference	Reason for exclusion
randomized prospective clinical trial of split-face model therapy. 1999. Dermatologic surgery	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
Kim, W. J. P., J. M.,Ko, H. C.,Kim, B. S.,Kim, M. B.,Song, M.A split-faced, observer-blinded comparison study of topical adapalene/benzoyl peroxide and adapalene in the treatment of Asian acne patients. 2013. Journal of Drugs in Dermatology: JDD	No relevant article type - letter to editor
King, K. J., D. H.,Daltrey, D. C.,Cunliffe, W. J.A double-blind study of the effects of 13-cis-retinoic acid on acne, sebum excretion rate and microbial population. 1982. British Journal of Dermatology	No relevant data reported - sebum excretion study
Kircik, L. H. B., V.,Martin, G.,Pillai, R.Randomized, double-blind, split-face study to compare the irritation potential of two topical acne formulations over a 21-day treatment period. 2016. Journal of Drugs in Dermatology	No relevant study population - participants did not have acne
Kircik, L. H.Comparative efficacy and safety results of two topical combination acne regimens. 2009b. Journal of Drugs in Dermatology	No relevant data reported - study recruited participants for 4 (n=23) or 12 wk (n=42) trial of BPO/CLIND gel vs solubilized BPO gel but reports data for all participants
Kircik, L. H.Fixed Combination of Clindamycin Phosphate 1.2% and Benzoyl Peroxide 3.75% Aqueous Gel: Long-Term Use in Adult Females With Moderate Acne Vulgaris. 2017. Journal of Drugs in Dermatology: JDD	No relevant study design - not RCT
Kircik, L. H.Tretinoin microsphere gel pump 0.04% versus tazarotene cream 0.05% in the treatment of mild-to-moderate facial acne vulgaris. 2009. Journal of Drugs in Dermatology	Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments
Kligman, A. M. F., J. E., Jr.,Plewig, G.Topical vitamin A acid in acne vulgaris. 1969. Archives of Dermatology	No relevant study design - not RCT
Kligman, A. M. P., G.,Mills, O. H., Jr.Topically applied tretinoin for senile (solar) comedones. 1971. Archives of Dermatology	No relevant study design - not RCT
Kligman, A. M.Comparison of a topical benzoyl peroxide gel, oral minocycline, oral doxycycline and a combination for suppression of P. acnes in acne patients. 1998. Journal of dermatological treatment	No relevant outcmoes reported - bacterial counts
Knutson, D. D. S., L. J.,Smoot, W. H.Meclocycline sulfosalicylate. Topical antibiotic agent for the treatment of acne vulgaris. 1981. Cutis	No relevant article type - non-systematic review
Ko, H. C. S., M.,Seo, S. H.,Oh, C. K.,Kwon, K. S.,Kim, M. B.Prospective, open-label, comparative study of clindamycin 1%/benzoyl peroxide 5% gel with adapalene 0.1% gel in Asian acne patients: Efficacy and tolerability. 2009. Journal of the European Academy of Dermatology and Venereology	Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS,

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

Reference	Reason for exclusion
	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
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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Reference	Reason for exclusion
	with antibacterial soap wash alone
Sen, A. K., S.,Chatterjee, R. N.,Sarkar, M.,Bhattacharjee, S.,Ram, A. K.Acomparativestudyof efficacy and safetyoftopical clindamycingelversus combination of clindamycingeland benzoylperoxidecreamin patients ofmildtomoderateacnevulgaris. 2013. Indian Journal of Pharmacology	No relevant article type - conference abstract
Shafiq, Y. N., B. S.,Rizwani, G. H.,Usman, M.,Shah, B. A.,Aslam, M.,Hina, B.Anti-acne activity of Casuarina equisetifolia bark extract: a randomized clinical trial. 2014. Bangladesh journal of pharmacology	No relevant intervention - Casuarina equisetifolia bark extract (5% cream)
Shaheen, J. A. K., M.,Kareem, A.,Ahmad, M.,Ansari, N. U. H.,Ahmad, I.Clinical evaluation of roxithromyin in acne vulgaris: Comparison of daily versus alternate day regimen. 2005. Journal of Pakistan Association of Dermatologists	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Shahid, J. K., T.Tretinoin cream versus benzoyl peroxide(10%) gel in the tropical treatment of mild acne vulgaris. 1996. Biomedica	Not obtainable
Shahlita, A. R. S., E. B.,Bauer, E.Topical erythromycin v clindamycin therapy for acne. A multicenter, double-blind comparison. 1984. Archives of Dermatology	No relevant study population - insufficient information to determine severity of acne
Shahmoradi, Z. I., F.,Siadat, A. H.,Ghorbaini, A.,Nilforoushzadeh, M. A.Comparison of topical 5% nicotinamid and 2% clindamycin gels in the treatment of the mild to moderate acne vulgaris: a double-blinded randomized clinical trial. 2015. Journal of isfahan medical school	Not in English language
Shahmoradi, Z. I., F.,Siadat, A. H.,Ghorbaini, A.Comparison of topical 5% nicotinamid gel versus 2% clindamycin gel in the treatment of the mild-moderate acne vulgaris: A double-blinded randomized clinical trial. 2013. Journal of Research in Medical Sciences	Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments
Shalita, A. M., B.,Menter, A.,Abramovits, W.,Loven, K.,Kakita, L.Tazarotene cream versus adapalene cream in the treatment of facial acne vulgaris: a multicenter, double-blind, randomized, parallel-group study. 2005. Journal of drugs in dermatology : JDD	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Shalita, A. R. B., D. S.,Thiboutot, D. M.,Leyden, J. J.,Parizadeh, D.,Sefton, J.,Walker, P. S.,Gibson, J. R.Effects of tazarotene 0.1% cream in the treatment of facial acne vulgaris: Pooled results from two multicenter, double-blind, randomized, vehicle-controlled, parallel-group trials. 2004. Clinical Therapeutics	No relevant data reported - reports pooled result from 2 trials combined
Shalita, A. R. C., D. K.,Parish, L. C.,Bernstein, J. E.,Evans, C. S.The effects of topical nicotinamide on acne vulgaris. 1992. Journal of investigative dermatology	No relevant article type - conference abstract
Shalita, A. R. R., E. S.,Anderson, D. N.,Yavel, R.,Landow, S.,Lee, W. L.Compared efficacy and safety of tretinoin 0.1% microsphere gel alone and in combination with benzoyl peroxide 6% cleanser for the treatment of acne vulgaris. 2003. Cutis	No relevantinternvention - facial cleanser; No relevant study population - insufficient information to determine seveirty of acne

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

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

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

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

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

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

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

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

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

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

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

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

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

Reference	Reason for exclusion
	includes 11% people with 11% acne
Yoon, J. H. P., E. J.,Kwon, I. H.,Kim, C. W.,Lee, G. S.,Hann, S. K.,Kim, K. H.,Kim, K. J.Concomitant use of an infrared fractional laser with low-dose isotretinoin for the treatment of acne and acne scars. 2014. Journal of dermatological treatment	No relevant intervention - laser treatment for acne scarring
Yoon, J. Y. K., H. H.,Min, S. U.,Thiboutot, D. M.,Suh, D. H.Epigallocatechin-3-gallate improves acne in humans by modulating intracellular molecular targets and inhibiting P. acnes. 2013. Journal of Investigative Dermatology	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Yu, Z. S., J.,Lew-Kaya, D.,Walker, P.,Yu, D.,Tang-Liu, D. D.Pharmacokinetics of tazarotene cream 0.1% after a single dose and after repeat topical applications at clinical or exaggerated application rates in patients with acne vulgaris or photodamaged skin. 2003. Clinical Pharmacokinetics	No relevant study population - sample includes people with acne or photodamage - relevant outcomes not reported separately
Zachariae, H.Topical vitamin-A-acid in acne. 1980. Acta dermato-venereologica	No relevant study design - not RCT
Zander, E. W., S.Treatment of acne vulgaris with salicylic acid pads. 1992. Clinical Therapeutics	Duplicate record
Zarate, A. M., V. B.,Greenblatt, R. B.Effect of an antiandrogen, 17-alpha-methyl-B-nortestosterone, on acne and hirsutism. 1966. Journal of Clinical Endocrinology & Metabolism	No relevant study design - not RCT
Zeichner, J. A. H., M.,Linkner, R. V.,Wong, V.Efficacy and safety of tretinoin 0.025%/clindamycin phosphate 1.2% gel in combination with benzoyl peroxide 6% cleansing cloths for the treatment of facial acne vulgaris. 2013. Journal of Drugs in Dermatology	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Zeichner, J. A. P., R. V.,Haddican, M.,Wong, V.Efficacy and safety of a ceramide containing moisturizer followed by fixed-dose clindamycin phosphate 1.2%/benzoyl peroxide 2.5% gel in the morning in combination with a ceramide containing moisturizer followed by tretinoin 0.05% gel in the evening for the treatment of facial acne vulgaris. 2012. Journal of Drugs in Dermatology: JDD	No relevant study design - not RCT
Zeichner, J. A., Harper, J. C., Roberts, W. E., Guenin, E., Bhatt, V., Pillai, R.Novel tretinoin 0.05% lotion for the once-daily treatment of moderate-to-severe acne vulgaris: assessment of safety and tolerability in subgroups. 2019. Journal of Clinical and Aesthetic Dermatology	Not obtainable
Zeichner, J. A.The Efficacy and Tolerability of a Fixed Combination Clindamycin (1.2%) and Benzoyl Peroxide (3.75%) Aqueous Gel in Adult Female Patients with Facial Acne Vulgaris. 2015. The Journal of Clinical & Aesthetic Dermatology	Reports post hoc analysis of >=25 years old for Pariser 2014
Zeichner, J.Strategies to minimize irritation and potential iatrogenic post-inflammatory pigmentation when treating acne patients with skin of color. 2011. Journal of Drugs in Dermatology: JDD	Duplicate record
Zeng, R., Liu, Y., Zhao, W., Yang, Y., Wu, Q., Li, M., Lin, T.A split-face comparison of a fractional microneedle radiofrequency device and fractional radiofrequency therapy for moderate-to-severe acne vulgaris. 2020. Journal of Cosmetic Dermatology.	Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes

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

PCOS: polycystic ovary syndrome; RCT: randomised controlled trial

Economic studies and studies reporting utility data

Economic studies	Reason for exclusion
Borgonjen RJ, de Lange JA, van de Kerkhof PCM. Guideline-based clinical decision support in acne patients receiving isotretinoin: improving adherence and cost-effectiveness. J Eur Acad Dermatol Venereol. 2017; 31(10): ve440-e442	Intervention outside scope (clinical decision support)
Bossuyt L, Bosschaert J, Richert B, Cromphaut P, Mitchell T, Al Abadie M, Henry I, Bewley A, Poyner T, Mann N, Czernielewski J. Lymecycline in the treatment of acne: an efficacious, safe and cost-effective alternative to minocycline. Eur J Dermatol 2003; 13(2):130-5.	Only intervention costs (drug acquisition) considered
Czilli T, Tan J, Knezevic S, Peters C. Cost of Medications Recommended by Canadian Acne Clinical Practice Guidelines. J Cutan Med Surg. 2016; 20(6): 542-545.	Only intervention costs (drug acquisition) considered
Haddock ES, Eichenfield LF. High-dose isotretinoin: Bigger dents in wallets? J Am Acad Dermatol. 2016 Aug;75(2):e75-6. EXTRA	Letter
Hansen, L. A., Vermeulen, L. C., Bland, S., & Wetterneck, T. B. (2007). Guideline for Low-Cost Antimicrobial Use in the Outpatient Setting. American Journal of Medicine, 120(4), 295-302.	Not an economic evaluation - identification of drugs with low acquisition cost that are effective
Joish VN, Boklage S, Lynen R, Schmidt A, Lin J. Use of drospirenone/ ethinyl estradiol (DRSP/EE) among women with acne reduces acne treatment-related resources. J Med Econ. 2011; 14(6): 681-9.	Retrospective analysis of administrative data
Lee YH, Liu G, Thiboutot DM, Leslie DL, Kirby JS. A retrospective analysis of the duration of oral antibiotic therapy for the treatment of acne among adolescents: investigating practice gaps and potential cost-savings. J Am Acad Dermatol. 2014; 71(1): 70-6.	Retrospective analysis of administrative data
Leyden JJ, Tanghetti EA, Miller B, Ung M, Berson D, Lee J. Once-daily tazarotene 0.1% gel versus once-daily tretinoin 0.1% microsponge gel for the treatment of facial acne vulgaris: a double-blind randomized trial. Cutis 2002; 69(2 Suppl):12-9.	Only intervention costs (drug acquisition) considered
Ozolins M, Eady EA, Avery A, Cunliffe WJ, O'Neill C, Simpson NB, Williams HC. Randomised controlled multiple treatment comparison to provide a cost-effectiveness rationale for the selection of antimicrobial therapy in acne. Health Technol Assess 2005; 9(1)	Average CE ratios reported, no incremental analysis and not possible to estimate ICERs as costs per intervention not reported
Ozolins M, Eady EA, Avery AJ, Cunliffe WJ, Po AL, O'Neill C, Simpson NB, Walters CE, Carnegie E, Lewis JB, Dada J, Haynes M, Williams K, Williams HC. Comparison of five antimicrobial regimens for treatment of mild to moderate inflammatory facial acne vulgaris in the community: randomised controlled trial. Lancet 2004; 364(9452): 2188-95.	Average CE ratios reported, no incremental analysis and not possible to estimate ICERs as costs per intervention not reported
Penna P, Meckfessel MH, Preston N. Fixed-Dose Combination Gel of Adapalene and Benzoyl Peroxide plus Doxycycline 100 mg versus Oral Isotretinoin for the Treatment of Severe Acne: Efficacy and Cost Analysis. Am Health Drug Benefits. 2014; 7(1):37-45.	Only drug acquisition costs considered; efficacy based on naïve synthesis of RCT arm data
Rosamilia LL. Economic stewardship in acne management. Cutis. 2018; 102(1): 8-9.	Not an economic evaluation
Rubin CB, Lipoff JB. Primary Nonadherence in Acne Treatment: The Importance of Cost Consciousness. JAMA Dermatol. 2015; 151(10):1144-5.	Letter - not an economic evaluation
Straight CE, Lee YH, Liu G, Kirby JS (2015). Duration of oral	Retrospective analysis of

Economic studies	Reason for exclusion
antibiotic therapy for the treatment of adult acne: a retrospective analysis investigating adherence to guideline recommendations and opportunities for cost-savings. Journal of the American Academy of Dermatology, 72(5), 822-827.	administrative data
Tassavor M, Payette MJ. Estimated cost efficacy of U.S. Food and Drug Administration-approved treatments for acne. Dermatol Ther. 2019; 32(1): e12765	Letter - description of costs associated with different pharmacological interventions (drug + lab testing + clinician visit costs)
Webster GF, Guenther L, Poulin YP, Solomon BA, 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. Cutis. 2002 Feb;69(2 Suppl):4-11.	Only intervention costs (drug acquisition) considered
Yuwnate AH, Chandane RD, Sah RK, et al. Efficacy and cost-effective analysis of benzyl benzoate, permethrin, and ivermectin in the treatment of scabies and azithromycin versus doxycycline in the treatment of acne vulgaris. Natl J Physiol Pharm Pharmacol. 2019; 9(10): 977-982	Economic evaluation conducted in India
Zeitany AE, Bowers EV, Morrell DS. High-dose isotretinoin has lower impact on wallets: A cost analysis of dosing approaches. J Am Acad Dermatol. 2016; 74(1):174-6.	Letter; cost analysis using data based on a letter reporting a retrospective analysis

Studies reporting utility data	Reason for exclusion
Afsar FS, Seremet S, Demirlendi Duran H, Karaca S, Mumcu Sonmez N. Sexual quality of life in female patients with acne. Psychol Health Med. 2020; 25(2):171-178.	No utility data for acne health states
Altunay IK, Özkur E, Dalgard FJ, et al. Psychosocial Aspects of Adult Acne: Data from 13 European Countries. Acta Derm Venereol. 2020 Feb 5;100(4):adv00051.	No utility data reported
Balkrishnan R, Kulkarni AS, Cayce K, Feldman SR. Predictors of healthcare outcomes and costs related to medication use in patients with acne in the United States. Cutis. 2006 Apr;77(4): 251-5.	No utility data reported
Dreno B, Bordet C, Seite S, Taieb C, 'Registre Acné' Dermatologists. Acne relapses: impact on quality of life and productivity. J Eur Acad Dermatol Venereol. 2019; 33(5): 937-43.	No utility data reported
Seidler AM, Bayoumi AM, Goldstein MK, Cruz PD Jr, Chen SC. Willingness to pay in dermatology: assessment of the burden of skin diseases. J Invest Dermatol. 2012; 132(7):1785-90.	Utility data obtained from people valuing their own health state
VanBeek MJ. Integrating patient preferences with health utilities: a variation on health-related quality of life. Arch Dermatol. 2008; 144(8): 1037-41.	Editorial - no utility data reported

Appendix L - Research recommendations – full details

Research recommendations for review question: What is the effectiveness and acceptability of interventions for the treatment of moderate to severe acne (side effects and participant reported improvement)?

For research recommendations associated with this review question see appendix L in evidence report F.

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