National Institute for Health and Care Excellence

Draft for consultation

Acne vulgaris: management

[E2] Management options for mild to moderate 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 (excluding 1.5.8 and bullet points 2 and 3 of recommendation 1.5.10) and two research recommendations in the NICE guideline(see evidence review E1 for the committee's discussion of the evidence)

December 2020

Draft for consultation

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

Disclaimer

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ISBN:

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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 mild to moderate acne vulgaris. NMA has been the main method of analysis to inform these questions (see evidence review E1). 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 moderate to severe acne vulgaris are contained in the evidence reports F1 and F2, 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 mild to moderate acne – pairwise comparisons

Review question

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

Introduction

Mild to moderate acne is very common with a wide range of treatment modalities available including over the counter products. Management options should be effective and acceptable to the individual, taking into consideration potential side effects and contraindications. This evidence review therefore aims to find the most effective treatment option for people with mild to moderate 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, of all ages who have mild to moderate acne
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	**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.

2 Methods and process

3 This evidence review was developed using the methods and process described in
4 Developing NICE guidelines: the manual. Methods specific to this review question are

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 62 studies were included in this pairwise review. These are divided into the following categories of interventions: topical non-retinoids and retinoids, own class topicals, topical antibiotics, topical antiseptics, topical acids, oral antibiotics and combinations with other topicals, oral hormonal contraceptives and hormone-modifying agents, oral isotretinoin and physical treatments.

Topical non-retinoids and retinoids

Eighteen parallel group design RCTs (Adhikary 2014, Babaeinejad 2013, Berger 2007a, Chalker 1987, Dubey 2016, Gollnick 2009, Guerra-Tapia 2012, Hughes 1992, Iftikhar 2009, Langner 2000, Marazzi 2002a, Shwetha 2014, Stinco 2007, Thiboutout 2006, Tirado-Sanchez 2013, Trifu 2011, Tu 2001, Webster 2001) reported side effects of topical retinoid treatments or topical treatment combinations including a retinoid treatment in people with mild to moderate acne. Skin irritation was reported by the vast majority of studies.

Four parallel group design RCTs (Babayeva 2011, Berger 2007a, Berger 2007b, Marazzi 2002a) mentioned participants reported improvement of acne.

Four studies were conducted in the USA (Berger 2007a, Berger 2007b, Chalker 1987, Webster 2001), 3 studies in India (Adhikary 2014, Dubey 2016, Shwetha 2014), 2 studies in the UK (Hughes 1992, Marazzi 2002a), 1 study in China (Tu 2001), Italy (Stinco 2007), Iran (Babaeinejad 2013), Pakistan (Iftikhar 2009), Poland (Langner 2000), Mexico (Tirado-Sanchez 2013), Romania (Trifu 2011), Spain (Guerra-Tapia 2012), Turkey (Babayeva 2011); 2 studies were collaborations studies from North America/Europe (Gollnick 2009) and North America (Thiboutout 2006).

Own class topicals

Four parallel group design RCTs (Charakida 2007, Hanstead 1985, Katsambas 1989, Pazoki-Toroudi 2010) reported skin irritation as a side effect of treatment with Acnicare, topical azelaic acid and topical fucidic acid.

One study was conducted in Denmark (Hanstead 1985), Greece (Katsambas 1989), Iran (Pazoki-Toroudi 2010) and the UK (Charakida 2007).

Topical antibiotics

Fourteen parallel group design RCTs (Alirezai 2005, Carey 1996, Cunliffe 2002b, Eichenfield 2016, Hajheydari 2011, Jain 1998, Khanna 1990, Leyden 1987, Pazoki-Toroudi 2010, Pazoki-Toroudi 2011, Schaller 2016, Shalita 2005, Stein Gold 2016, Xu 2016) reported skin irritation as a side effect of treatment with topical antibiotics. Carey 1996 and Pazoki-Toroudi 2010 also mentioned participant reported improvement of acne.

Three studies were conducted in Iran (Hajheydari 2011, Pazoki-Toroudi 2010, Pazoki-Toroudi 2011) and the USA (Leyden 1987, Shalita 2005, Stein Gold 2016), 2 studies in India (Jain 1998, Khanna 1990), 1 study in Canada (Carey 1996), China (Xu 2016), Germany (Schaller 2016) and the UK (Cunliffe 2002b); 2 studies were collaboration studies from Europe (Alirezai 2005) and North America (Eichenfield 2016).

Topical antiseptics

Five parallel group design RCTs (Gollnick 2009, Hughes 1992, Milani 2003, Smith 1980b, Stoughton 1987) reported skin irritation as a side effects of treatment with topical antiseptics in people with mild to moderate acne.

Two studies were conducted in the USA (Smith 1980b-USA, Stoughton 1987), 1 in Italy (Milani 2003) and in the UK (Hughes 1992); 1 study was a collaboration study from Europe/North America (Gollnick 2009).

Topical acids

One parallel group design RCT (Boutli 2003) reported skin irritation and light sensitivity as side effects of treatment with topical acids. Three parallel group RCTs (Akarsu 2012, Poli 2005, Shalita 1981) mentioned participant reported improvement of acne.

One study was conducted in Greece (Boutli 2003), France (Poli 2005), Turkey (Akarsu 2012) and the USA (Shalita 1981).

Oral antibiotics and combinations with other topicals

Four parallel group design RCTs (Bleeker 1983, Maleszka 2011, Ozolins 2004, Rassai 2013) reported side effects of treatment with oral antibiotics or oral antibiotics in combination with topical antibiotics in people with mild to moderate acne. Ozolins 2004 and Rassai 2013 also mentioned participant reported improvement of acne.

One study was conducted in Iran (Rassai 2013), Poland (Maleszka 2011), Sweden (Bleeker 1983) and the UK (Ozolins 2004).

Oral hormonal contraceptives and hormone-modifying agents

Seven parallel group design RCTs (Alora Palli 2013, Jaisamrarn 2014, Jaisamrarn 2018, Leyden 2002, Palombo-Kinne 2009, Plewig 2009, Thorneycroft 2004) reported side effects of treatment with oral hormonal contraceptives and hormone-modifying agents in women with mild to moderate acne. Most often reported side effects were breast tenderness, breakthrough bleeding and neurological side effects. Plewig 2009 also mentioned participant reported improvement of acne.

Two studies were conducted in the USA (Alora Palli 2013, Leyden 2002), 2 studies in Thailand (Jaisamrarn 2014, Jaisamrarn 2018) and 1 study in Germany (Thorneycroft 2004); 2 studies were collaboration studies from Europe (Palombo-Kinne 2009-Europe, Plewig 2009).

Oral isotretinoin

One parallel group design RCT (Rademaker 2014, New Zealand) reported mucosal/cutaneous changes as a side effect of treatment with oral isotretinoin in people with mild to moderate acne.

Physical treatments

Chemical peels

Three parallel group design RCT (Dayal 2017, Dayal 2020, Sarkar 2019) reported side effects of treatments with chemical peels in people with mild to moderate acne. The most often reported side effects were erythema and changes in pigmentation. All 3 studies were conducted in India.

Energy based treatments (light/laser)

Three parallel group design RCTs (Papageorgiou 2000a, Ragab 2014, Seaton 2003) reported side effects of energy based treatments in people with mild to moderate acne. Most

often reported side effects were skin irritation and erythema. Ragab 2014 also mentioned participant reported improvement of acne.

Two studies were conducted in the UK (Papageorgiou 2000a, Seaton 2003) and 1 study in Egypt (Ragab 2014).

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

Excluded studies

Studies not included in this review with 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
Adhikary 2014 **Country**: India **Study type**: RCT	N=200 **Sex**: mixed **Number randomised: arm 1**: n=100 **Number randomised: arm 2**: n=100 **Inclusion details**: Age at least 10 years, grade I to grade II acne vulgaris of face, on the Indian grading scale.	**Intervention: arm 1**: topical Isotretinoin gel 0.05 % once daily at night and topical Clindamycin phosphate 1% lotion in the morning **Intervention: arm 2**: Adapalene 0.1 % gel once daily at night and topical Clindamycin phosphate 1% lotion in the morning.	• Skin irritation
Akarsu 2012 **Country**: Turkey **Study type**: RCT	N=50 **Sex**: mixed **Number randomised: arm 1**: n=25 **Number randomised: arm 2**: n=25 **Inclusion details**: Mild to moderate AV, between the ages of 18 and 35 years, and with between 10–50 IL and 10–100 NIL above the mandibular line at baseline.	**Intervention: arm 1**: SAL 3% + CLIND-topical 1% + BPO-topical 5% **Intervention: arm 2**: CLIND-topical 1% + BPO-topical 5%	• Participant reported improvement
Alirezai 2005 **Country**: Europe **Study type**: RCT	N=592 **Sex**: mixed **Number randomised: arm 1**: n=265 **Number randomised: arm 2**: n=261 **Number randomised: arm 3**: n=66	**Intervention: arm 1**: CLIND-topical 1% gel **Intervention: arm 2**: CLIND-topical 1% topical solution **Intervention: arm 3**: Vehicle gel	• Skin irritation

Study	Population	Interventions	Outcomes
	Inclusion details: At least age 12, acne vulgaris on face (severity grade of 2 to 5 on the Leeds revised scale), and 15-50 inflammatory facial lesions.		
Alora Palli 2013 **Country**: United States **Study type**: RCT	N=30 **Sex**: female **Number randomised: arm 1**: n=16 **Number randomised: arm 2**: n=14 **Inclusion details**: Female, age 18 to 45 years, who achieved spontaneous menarche, desired contraception and had a diagnosis of truncal acne of 10 to 50 inflammatory lesions on the back and chest combined with not more than 5 nodules.	**Intervention: arm 1**: EE-oral 0.02 mg + DROS-oral 3mg od **Intervention: arm 2**: PLC-oral	• Neurological side effects • Change in mood • Breakthrough bleeding
Babaeinejad 2013 **Country**: Iran **Study type**: RCT	N=60 **Sex**: mixed **Number randomised: arm 1**: n=30 **Number randomised: arm 2**: n=30 **Inclusion details**: Mild acne vulgaris (Evaluator Global Severity Score, EGSS, of 2).	**Intervention: arm 1**: BPO 2.5% gel **Intervention: arm 2**: ADAP 0.1% gel	• Skin irritation
Babayeva 2011 **Country**: Turkey **Study type**: RCT	N=46 **Sex**: mixed **Number randomised: arm 1**: n=23 **Number randomised: arm 2**: n=23 **Inclusion details**: 18 and 35 years of age, with 10–50 inflammatory lesions and 10–100 non-Inflammatory lesions above the mandibular line at baseline.	**Intervention: arm 1**: SAL 3% + CLIND-topical 1% **Intervention: arm 2**: TRET-topical 0.05% + CLIND-topical 1%	• Participant reported improvement
Berger 2007a **Country**: United States **Study type**: RCT	N=156 **Sex**: mixed **Number randomised: arm 1**: n=78 **Number randomised: arm 2**: n=78	**Intervention: arm 1**: TRET-topical 0.04% **Intervention: arm 2**: TRET-topical 0.1%	• Skin irritation • Light sensitivity • Participant reported improvement

Study	Population	Interventions	Outcomes
	Inclusion details: Ages 12 to 40 years, in good health, with mild to moderate acne vulgaris defined as 20 to 150 total facial lesions. Of these lesions, 10 to 100 were to be comedones (open and closed), and 10 to 50 were to be inflammatory lesions (papules and pustules). No more than 2 were to be nodules (defined as deep inflammatory lesions of 1 cm or greater).		
Berger 2007b **Country**: United States **Study type**: RCT	N=178 **Sex**: mixed **Number randomised: arm 1**: n=88 **Number randomised: arm 2**: n=90 **Inclusion details**: 19 and 45 years of age with mild to moderate acne vulgaris - between 15 and 80 total facial lesions that consisted of 10 to 40 inflammatory lesions and no more than 2 nodules.	**Intervention: arm 1**: TRET-topical 0.04% **Intervention: arm 2**: Vehicle gel	• Participant reported improvement
Bleeker 1983 **Country**: Sweden **Study type**: RCT	N=40 **Sex**: mixed **Number randomised: arm 1**: n=20 **Number randomised: arm 2**: n=20 **Inclusion details**: Mild to moderate papulopustular acne.	**Intervention: arm 1**: Erythromycin stearate capsules 500mg b.d. **Intervention: arm 2**: Erythromycin base capsules 500mg b.d.	• GI side effects
Boutli 2003 **Country**: Greece **Study type**: RCT	N=37 **Sex**: mixed **Number randomised: arm 1**: n=19 **Number randomised: arm 2**: n=18 **Inclusion details**: Age 13-25, moderate acne (grade 11, Pilsbury and Kligman), 20-50 comedones and 20-40 papulopustules.	**Intervention: arm 1**: Topical benzoil peroxide 5% gel **Intervention: arm 2**: Topical Nisal cream (chloroxylenol 0.5% + salicylic acid 2%)	• Skin irritation • Light sensitivity
Carey 1996 **Country**: Canada **Study type**: RCT	N=499 **Sex**: mixed **Number randomised:**	**Intervention: arm 1**: Topical fucidic acid 2% **Intervention: arm 2**:	• Skin irritation • Participant reported

Study	Population	Interventions	Outcomes
	arm 1: n=249 **Number randomised: arm 2**: n=250 **Inclusion details**: Under 25 years, 15 - 75 inflamed lesions on the face.	Topical erythromycin 2%	improvement
Chalker 1987 **Country**: United States **Study type**: RCT	N=313 **Sex**: mixed **Number randomised: arm 1**: n=156 **Number randomised: arm 2**: n=157 **Inclusion details**: Acne vulgaris with a minimum of 12 inflammatory lesions and 12 noninflammatory lesions and a maximum of 3 facial nodulocystic lesions, aged 13-30.	**Intervention: arm 1**: Topical ISO 0.05% gel b.d. **Intervention: arm 2**: Vehicle b.d.	• Skin irritation
Charakida 2007 **Country**: United Kingdom **Study type**: RCT	N=40 **Sex**: mixed **Number randomised: arm 1**: n=20 **Number randomised: arm 2**: n=20 **Inclusion details**: Participants aged between 16 and 45 years with mild to moderate facial inflammatory acne defined as the presence of at least 10 acne papules or pustules between the brow and jaw line and an acne severity score of between 2 and 7 on the Leeds revised acne grading system.	**Intervention: arm 1**: ACNICARE (triethyl citrate + ethyl linoleate) topical b.d. **Intervention: arm 2**: Vehicle topical b.d.	• Skin irritation
Cunliffe 2002b **Country**: United Kingdom **Study type**: RCT	N=79 **Sex**: mixed **Number randomised: arm 1**: n=40 **Number randomised: arm 2**: n=39 **Inclusion details**: Acne vulgaris, aged 13 to 30. Baseline or screening P acnes counts on facial skin (cheek or forehead) had to be at least 104 colony-forming units	**Intervention: arm 1**: topical clindamycin 1% / BPO 5% gel b.d. **Intervention: arm 2**: topical clindamycin 1%	• Skin irritation

Study	Population	Interventions	Outcomes
	(CFUs) per square centimetre, of which no more than 104 CFU/cm 2 could be erythromycin or clindamycin resistant. Eligible patients also had to have 15 to 100 inflammatory lesions, 15 to 100 comedones, and <2 nodules/cysts on the face. Sexually active female patients were required to use contraception for 28 days before the start and for the duration of the study.		
Dayal 2017 **Country**: India **Study type**: RCT	N=40 **Sex**: mixed **Number randomised: arm 1**: n=20 **Number randomised: arm 2**: n=20 **Inclusion details**: Mild-to-moderate (grade I and grade II) facial acne vulgaris, graded using a system taking into account the predominant lesions present: Grade 1 (mild): comedones, occasional papules. Grade 2 (moderate): papules, comedones, few pustules. Grade 3 (severe): predominant pustules, nodules, abscesses. Grade 4 (cystic): mainly cysts, abscesses, widespread scarring.	**Intervention: arm 1**: salicylic acid 30% **Intervention: arm 2**: Jessner's peel	• Skin redness • Pigment changes
Dayal 2020 **Country**: India **Study type**: RCT	N=50 **Sex**: mixed **Number randomised: arm 1**: n=25 **Number randomised: arm 2**: n=25 **Inclusion details**: Mild-to-moderate (grade I and grade II) facial acne vulgaris on the Vaishampayan grading system.	**Intervention: arm 1**: 30% salicylic acid peel **Intervention: arm 2**: 45% mandelic acid peel	• Skin redness • Pigment changes
Dubey 2016 **Country**: India **Study type**: RCT	N=100 **Sex**: mixed **Number randomised:**	**Intervention: arm 1**: adapalene (0.1%) o.d. **Intervention: arm 2**:	• Skin irritation

Study	Population	Interventions	Outcomes
	arm 1: n=50 **Number randomised: arm 2**: n=50 **Inclusion details**: Male and non-pregnant participants aged between 12 and 30 years. Participants with mild to moderate acne vulgaris; based on simple acne grading scale (grade 1 to grade 4). Participants with only comedones as noninflammatory lesions, and papules and pustules as inflammatory lesions were included in the study (mild to moderate acne vulgaris- grades 1 and 2).	benzoyl peroxide (2.5%) clindamycin (1%) combination o.d.	
Eichenfield 2016 **Country**: North America **Study type**: RCT	N=2238 **Sex**: mixed **Number randomised: arm 1**: n=1118 **Number randomised: arm 2**: n=1120 **Inclusion details**: At least 12 years of age, with a diagnosis of acne, with 20–50 facial inflammatory lesions (papules and pustules) and 30–100 facial noninflammatory lesions (open and closed comedones), and with an acne grade of 3 (indicating moderate severity) on the Global Acne Assessment Score (GAAS) at screening and at baseline.	**Intervention: arm 1**: Topical dapsone 7.5% gel o.d. **Intervention: arm 2**: Topical vehicle o.d.	• Skin irritation
Gollnick 2009 **Country**: North America/Europe **Study type**: RCT	N=1670 **Sex**: mixed **Number randomised: arm 1**: n=419 **Number randomised: arm 2**: n=418 **Number randomised: arm 3**: n=415 **Number randomised: arm 4**: n=418 **Inclusion details**: 12 years of age or older	**Intervention: arm 1**: Adapalene 0.1%–BPO 2.5% fixed combination topical gel o.d. **Intervention: arm 2**: Adapalene 0.1% topical gel o.d. **Intervention: arm 3**: BPO 2.5% topical gel o.d. **Intervention: arm 4**: Vehicle topical o.d.	• Skin irritation

Study	Population	Interventions	Outcomes
	with acne vulgaris, having on the face 20–50 inflammatory lesions, 30–100 noninflammatory lesions and an Investigator's Global Assessment (IGA) score of 3, corresponding to moderate acne.		
Guerra-Tapia 2012 **Country**: Spain **Study type**: RCT	N=168 **Sex**: mixed **Number randomised: arm 1**: n=83 **Number randomised: arm 2**: n=85 **Inclusion details**: Aged 12 to 39 years, with = 15 inflammatory lesions and/ or non-inflammatory lesions but = 3 nodulocystic lesions and an acne grade of = 2.0 and < 7.0 on the Leeds Revised Acne Grading System.	**Intervention: arm 1**: topical BPO % + CLIND 1% o.d. **Intervention: arm 2**: Adapalene 0.1% topical gel o.d.	• Skin irritation
Hajheydari 2011 **Country**: Iran **Study type**: RCT	N=96 **Sex**: mixed **Number randomised: arm 1**: n=32 **Number randomised: arm 2**: n=32 **Number randomised: arm 3**: n=32 **Inclusion details**: Aged 12-28 years with mild to moderate acne vulgaris.	**Intervention: arm 1**: Topical azithromycin 2% b.d. **Intervention: arm 2**: Topical erythromycin 2% b.d. **Intervention: arm 3**: Topical clindamycin 2% b.d.	• Skin irritation
Hanstead 1985 **Country**: Denmark **Study type**: RCT	N=79 **Sex**: mixed **Number randomised: arm 1**: n=40 **Number randomised: arm 2**: n=39 **Inclusion details**: Mild to moderate acne vulgaris.	**Intervention: arm 1**: Topical fucidin cream 2% **Intervention: arm 2**: Topical placebo cream	• Skin irritation
Hughes 1992 **Country**: United Kingdom **Study type**: RCT	N=77 **Sex**: mixed **Number randomised: arm 1**: n=25 **Number randomised: arm 2**: n=26 **Number randomised: arm 3**: n=26	**Intervention: arm 1**: Topical isotretinoin 0.05% b.d. **Intervention: arm 2**: Topical BPO 5% b.d. **Intervention: arm 3**: Vehicle b.d.	• Skin irritation

Study	Population	Interventions	Outcomes
	Inclusion details: 15-100 inflamed and/or 15-100 non-inflamed lesions but no more than three nodulocystic lesions on the face.		
Iftikhar 2009 **Country**: Pakistan **Study type**: RCT	N=200 **Sex**: mixed **Number randomised: arm 1**: na, n=100 completed **Number randomised: arm 2**: na, n=100 completed **Inclusion details**: More than 13 years of age, with mild to moderate acne (comedones, papulopustules and few nodules with no scarring) and free of intercurrent illness.	**Intervention: arm 1**: 0.1% ADAP topical o.d. **Intervention: arm 2**: 4% BPO topical o.d.	• Skin irritation
Jain 1998 **Country**: India **Study type**: RCT	N=40 **Sex**: Mixed **Number randomised: arm 1**: n=20 **Number randomised: arm 2**: n=20 **Inclusion details**: Moderately severe acne, with lesions on the face.	**Intervention: arm 1**: 5% benzoyl peroxide topical and 1% metronidazole gel o.d. **Intervention: arm 2**: 5% benzoyl peroxide topical and 1% clindamycin gel o.d.	• Skin irritation
Jaisamrarn 2014 **Country**: Thailand **Study type**: RCT	N=201 **Sex**: female **Number randomised: arm 1**: n=100 **Number randomised: arm 2**: n=101 **Inclusion details**: Healthy females aged between 18 and 45 years with mild to moderate acne vulgaris - defined as having no more than 5 comedones or papules and no pustule while moderate acne vulgaris was defined as 6–15 comedones or papules and/or a maximum of three pustules.	**Intervention: arm 1**: triphasic EE/NGM treatment at the dosage of 0.035/0.18, 0.035/0.215 and 0.035/0.25mg on days 1–7, 8–14 and 15–21, respectively, and took inactive tablets for 7 days before starting the next treatment cycle **Intervention: arm 2**: biphasic EE/DSG treatment at the dosage of 0.04/0.025 and 0.03/0.125mg on days 1–7 and 8–22 of each cycle, respectively, and discontinued treatment for 6 days before starting the next treatment cycle.	• Breast tenderness • Neurological side effects • Breakthrough bleeding
Jaisamrarn 2018 **Country**: Thailand	N=180 **Sex**: female	**Intervention: arm 1**: EE/CMA at the dosage of	• Breast tenderness

Study	Population	Interventions	Outcomes
Study type: RCT	**Number randomised: arm 1**: n=90 **Number randomised: arm 2**: n=90 **Inclusion details**: Healthy women between the ages of 18 to 45 years with mild to moderate acne vulgaris and who had dysmenorrhea of any degree of severity. Mild acne vulgaris was defined as having comedones as the main type of acne lesion with < 10 papules and pustules. Moderate acne was defined as having 10–40 papules and pustules, 10–40 comedones, and/or mild truncal disease.	30 mcg/2 mg once daily; treatment was for 21 consecutive days, starting on the first day of the menstruation, followed by 7 days of medication free before starting the next cycle of treatment. **Intervention: arm 2**: received EE/DRSP at the dosage of 30 mcg/3 mg once daily; treatment was for 21 consecutive days, starting on the first day of the menstruation, followed by 7 days of medication free before starting the next cycle of treatment.	• Neurological side effects • Breakthrough bleeding
Katsambas 1989; Trial 1 **Country**: Greece **Study type**: RCT	N=92 **Sex**: mixed **Number randomised: arm 1**: n=43 **Number randomised: arm 2**: n=49 **Inclusion details**: Papulo-pustular acne (degree II/III of Plewig-Kligmann).	**Intervention: arm 1**: 20% azelaic acid cream **Intervention: arm 2**: vehicle	• Skin irritation
Khanna 1990 **Country**: India **Study type**: RCT	N=26 **Sex**: Mixed **Number randomised: arm 1**: na, n=12 completed **Number randomised: arm 2**: na, n=14 completed **Inclusion details**: Moderately severe acne - defined as the presence, on the face (above the jawline) of the subject, of 5-15 inflammatory lesions (IN) but no more than 5 nodulocystic lesions and / or more than 50 non-inflammatory (NI) acne lesions.	**Intervention: arm 1**: topical clindamycin hydrochloride 1% twice a day **Intervention: arm 2**: hydro-alcoholic vehicle twice a day	• Skin irritation
Langner 2000 **Country**: Poland **Study type**: RCT	N=127 **Sex**: Mixed **Number randomised: arm 1**: n=43	**Intervention: arm 1**: isotretinoin 0.05%w/w cream formulated with standard sunscreen	• Skin irritation

Study	Population	Interventions	Outcomes
	Number randomised: arm 2: n=42 **Number randomised: arm 3**: n=42 **Inclusion details**: Acne vulgaris of the face (15–100 inflammatory lesions and/or 15–100 non-inflammatory lesions, but not more than three nodulocystic lesions).	**Intervention: arm 2**: isotretinoin (0.10%w/w) cream formulated with standard sunscreen **Intervention: arm 3**: placebo vehicle sunscreen cream	
Leyden 1987 **Country**: United States **Study type**: RCT	N=109 **Sex**: Mixed **Number randomised: arm 1**: n=55 **Number randomised: arm 2**: n=54 **Inclusion details**: At least 14 years of age and had to have a minimum of ten but no more than sixty facial papules and pustules, and no more than six facial nodular cystic lesions.	**Intervention: arm 1**: 2% erythromycin gel **Intervention: arm 2**: clindamycin phosphate 1% solution	• Skin irritation
Leyden 2002 **Country**: United States **Study type**: RCT	N=371 **Sex**: Female **Number randomised: arm 1**: n=185 **Number randomised: arm 2**: n=186 **Inclusion details**: Healthy women, at least 14 years of age, with regular menstrual cycles and moderate facial acne. Moderate facial acne was defined as a total facial count of 6 to 200 noninflammatory comedones, 10 to 75 inflammatory lesions (papules and pustules), and 5 or fewer nodules. Also required a normal Papanicolaou test result within the past 6 months or a low-grade abnormal Papanicolaou test result under medical evaluation, a negative pregnancy test result, and agreement to use a nonhormonal	**Intervention: arm 1**: tablets containing 20g of EE and 100g of LNG in a 28-day blister pack with 21 days of active medication followed by 7 days of placebo **Intervention: arm 2**: Placebo oral	• Breakthrough bleeding

Study	Population	Interventions	Outcomes
	method of contraception if at risk for pregnancy.		
Maleszka 2011 **Country**: Poland **Study type**: RCT	N=240 **Sex**: mixed **Number randomised: arm 1**: n=120 **Number randomised: arm 2**: n=120 **Inclusion details**: 14 years or older with a clinical diagnosis of moderate acne vulgaris.	**Intervention: arm 1**: Azithromycin 500mg o.d. for 3 days in the first week, followed by 500-mg tablets weekly to complete 10 weeks of treatment. **Intervention: arm 2**: Doxycycline (Hiramicin) 100-mg capsules twice a day on the first day of the treatment, followed by doxycycline 100-mg capsules once a day during 12 weeks of treatment.	• GI side effects
Marazzi 2002a **Country**: United Kingdom **Study type**: RCT	N=188 **Sex**: Mixed **Number randomised: arm 1**: n=95 **Number randomised: arm 2**: n=93 **Inclusion details**: Facial acne vulgaris having 15–100 inflammatory lesions and/or 15–100 non-inflammatory lesions, but not more than three nodulocystic lesions.	**Intervention: arm 1**: gel containing isotretinoin 0.1%w/w and erythromycin 4.0%w/w in a vehicle of butylated hydroxytoluene, hydroxypropylcellulose and ethanol **Intervention: arm 2**: comparator gel contained benzoyl peroxide 5.0%w/w and erythromycin 3.0%w/w	• Skin irritation • Participant reported improvement
Milani 2003 **Country**: Italy **Study type**: RCT	N=60 **Sex**: Mixed **Number randomised: arm 1**: n=30 **Number randomised: arm 2**: n=30 **Inclusion details**: 15-35 years with mild to moderate acne vulgaris, defined as at least 10 inflammatory lesions and 10 non-inflamatory lesions, and no more than two nodulo-cystic lesions.	**Intervention: arm 1**: Hydrogen peroxide gel (Crystacide 1%) **Intervention: arm 2**: Benzoyl peroxide gel (PanOxyl 4%)	• Skin irritation
Ozolins 2004 **Country**: United Kingdom **Study type**: RCT	N=649 **Sex**: mixed **Number randomised: arm 1**: n=131 **Number randomised: arm 2**: n=130 **Number randomised: arm 3**: n=130 **Number randomised:**	**Intervention: arm 1**: OXYTETRA-oral 500mg b.d. + PLC-topical **Intervention: arm 2**: MINO-oral 100mg + PLC-topical **Intervention: arm 3**: BPO- topical 5% + PLC-oral **Intervention: arm 4**:	• Skin irritation • GI side effects • Participant reported improvement

Study	Population	Interventions	Outcomes
	arm 4: n=127 **Number randomised: arm 5**: n=131 **Inclusion details**: Mild to moderate acne vulgaris (acne grade 3·0 or less) and at least 15 inflamed and 15 non-inflamed lesions on the face.	Combined formulation of BPO- topical 5%/ERYTH-topical 3%+ PLC-oral **Intervention: arm 5**: BPO-topical 5% + ERYTH-topical 2% + PLC-oral	
Palombo-Kinne 2009 **Country**: Europe **Study type**: RCT	N=1338 **Sex**: female **Number randomised: arm 1**: n=530 **Number randomised: arm 2**: n=541 **Number randomised: arm 3**: n=267 **Inclusion details**: Female patients between 16 and 45 years old with mild to moderate papulopustular acne and without contraindications to COC use. Mild to moderate facial papulopustular acne was defined as 10–50 comedones (non-inflammatory lesions), 10–50 papules and pustules together (inflammatory lesions) and not more than three small nodules (inflammatory lesions); a normal Papanicolaou test result within the past 6 months; use of a non-hormonal method of contraception for sexually active patients.	**Intervention: arm 1**: EE-oral 0.030mg + DNG-oral 2mg **Intervention: arm 2**: CPA-oral (2mg) + EE-oral (0.035mg) **Intervention: arm 3**: PLC-oral	• Breast tenderness • Neurological side effects • Breakthrough bleeding
Papageorgiou 2000a **Country**: United Kingdom **Study type**: RCT	N=107 **Sex**: mixed **Number randomised: arm 1**: n=27 **Number randomised: arm 2**: n=30 **Number randomised: arm 3**: n=25 **Number randomised: arm 4**: n=25 **Inclusion details**: Mild to moderate acne, age ranging from 14 to	**Intervention: arm 1**: BLU-PT 415nm **Intervention: arm 2**: BR-LED 415 and 660nm **Intervention: arm 3**: White light control **Intervention: arm 4**: BPO-topical 5%	• Skin irritation

Study	Population	Interventions	Outcomes
	50 years, otherwise healthy.		
Pazoki-Toroudi 2010 **Country**: Iran **Study type**: RCT	N=126 **Sex**: mixed **Number randomised: arm 1**: na, n=35 completed **Number randomised: arm 2**: na, n=31 completed **Number randomised: arm 3**: na, n=40 completed **Number randomised: arm 4**: n=20 **Inclusion details**: Age between 14 and 40 years, mild-to-moderate forms of acne vulgaris with at least 10 inflammatory lesions on the face (with a maximum of three nodules).	**Intervention: arm 1**: Azelaic acid 5% gel **Intervention: arm 2**: Erythromycin 2% gel **Intervention: arm 3**: Azelaic acid 5% + Erythromycin 2% gel **Intervention: arm 4**: Placebo	• Skin irritation • Participant reported improvement
Pazoki-Toroudi 2011 **Country**: Iran **Study type**: RCT	N=150 **Sex**: mixed **Number randomised: arm 1**: n=50 **Number randomised: arm 2**: n=50 **Number randomised: arm 3**: n=50 **Inclusion details**: Age between 14 and 40 years, mild-to-moderate forms of acne vulgaris with at least 10 inflammatory lesions on the face .	**Intervention: arm 1**: Azelaic acid 5% gel **Intervention: arm 2**: Clindamycin 2% gel **Intervention: arm 3**: Azelaic acid + Clindamycin gel	• Skin irritation
Plewig 2009 **Country**: Europe **Study type**: RCT	N=377 **Sex**: women **Number randomised: arm 1**: n=251 **Number randomised: arm 2**: n=126 **Inclusion details**: Women with moderate papulopustular acne of the face (8– 75 papules and/or pustules) aged between 18 and 40 years (smokers up to 30 years).	**Intervention: arm 1**: Ethinyl estradiol 0.03mg + chlormadinone acetate 2mg **Intervention: arm 2**: Placebo	• Breast tenderness • Neurological side effects • Change in mood • Breakthrough bleeding • Participant reported improvement
Poli 2005 **Country**: France	N=81 **Sex**: mixed **Number randomised:**	**Intervention: arm 1**: Diacneal (0.1% retinaldehyde and 6%	• Participant reported improvement

Study	Population	Interventions	Outcomes
Study type: RCT	**arm 1**: n=42 **Number randomised: arm 2**: n=39 **Inclusion details**: Greasy or normal or combination skin type, with phototypes II–IV, presenting with inflammatory (7–15 lesions) and retentional (15–30 lesions) mild to moderate acne vulgaris.	glycolic acid) **Intervention: arm 2**: Vehicle	
Rademaker 2014 **Country**: New Zealand **Study type**: RCT	N=58 **Sex**: mixed **Number randomised: arm 1**: n=29 **Number randomised: arm 2**: n=29 **Inclusion details**: 25–55 years of age, with low-grade adult acne - defined as three or more acne lesions/ month on the face, for at least the last 3 months.	**Intervention: arm 1**: 5mg isotretinoin once daily **Intervention: arm 2**: No treatment for 16 weeks	• Mucosal or cutaneous changes
Ragab 2014 **Country**: Egypt **Study type**: RCT	N=25 **Sex**: mixed **Number randomised: arm 1**: n=15 **Number randomised: arm 2**: n=10 **Inclusion details**: Participants aged 14 years or over. Participants with mild to moderate acne vulgaris; determined by Evaluator Global Severity score.Score of 2 or 3 on scale before treatment.	**Intervention: arm 1**: PDT using 5-aminolevulinic acid (ALA) with intense pulsed light (IPL) **Intervention: arm 2**: IPL alone	• Skin redness • Pigment changes • Participant reported improvement
Rassai 2013 **Country**: Iran **Study type**: RCT	N=144 **Sex**: mixed **Number randomised: arm 1**: na, n=74 completed **Number randomised: arm 2**: na, n=74 completed **Inclusion details**: Inflammatory acne vulgaris, at least 20 comedones, or with nodules or cysts disregarding the	**Intervention: arm 1**: 500mg azithromycin/day, 3 days a week + oral levamisole 150mg/day, 2 days a week **Intervention: arm 2**: 500mg azithromycin/day, 3 days a week	• Skin irritation • GI side effects • Participant reported improvement

Study	Population	Interventions	Outcomes
	number of comedones.		
Sarkar 2019 **Country**: India **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**: Patients with acne (grade 1 and 2) with postacne hyperpigmentation. Patients aged >12 years.	**Intervention: arm 1**: 35% glycolic acid peel **Intervention: arm 2**: 20% salicylic acid-10% mandelic acid **Intervention: arm 3**: Phytic acid	• Skin redness
Schaller 2016 **Country**: Germany **Study type**: RCT	N=217 **Sex**: mixed **Number randomised: arm 1**: n=108 **Number randomised: arm 2**: n=109 **Inclusion details**: 12–45 years old, having facial acne vulgaris (defined as having 17–60 inflammatory lesions [papules and pustules], =1 facial nodular cystic lesion, 20–125 non-inflammatory facial lesions and an Investigator's Static Global Assessment [ISGA] score of 'mild' or 'moderate').	**Intervention: arm 1**: Benzoyl peroxide 3% + clindamycin 1% QD **Intervention: arm 2**: Azelaic acid 20% BID	• Skin irritation
Seaton 2003 **Country**: United Kingdom **Study type**: RCT	N=41 **Sex**: mixed **Number randomised: arm 1**: n=31 **Number randomised: arm 2**: n=10 **Inclusion details**: Aged between 18 and 45 years with mild-to-moderate facial inflammatory acne defined as the presence of at least ten acne papules or pustules between the brow and jawline and an acne severity score of between 2 and 7 on the Leeds revised acne grading system.	**Intervention: arm 1**: Pulsed dye laser **Intervention: arm 2**: Sham laser	• Skin redness • Skin irritation

Study	Population	Interventions	Outcomes
Shalita 1981 **Country**: United States **Study type**: RCT	N=49 **Sex**: mixed **Number randomised: arm 1**: n=25 **Number randomised: arm 2**: n=24 **Inclusion details**: Teenagers (12 to 20) with mild to moderate acne vulgaris, classed by Pillsbury, Shelly and Kligman grades I or II, with at least fifteen comedones and no more than ten inflammatory lesions.	**Intervention: arm 1**: 0.5% salicylic acid (Stri-Dex medicated pads) **Intervention: arm 2**: Placebo	• Participant reported improvement
Shalita 2005 **Country**: United States **Study type**: RCT	N=1026 **Sex**: mixed **Number randomised: arm 1**: n=386 **Number randomised: arm 2**: n=127 **Number randomised: arm 3**: n=385 **Number randomised: arm 4**: n=128 **Inclusion details**: 12 years of age or older with mild to moderate facial acne vulgaris and an Investigator's Static Global Assessment (ISGA) score of 2 or greater at baseline. Also a minimum of 17 but no more than 40 facial inflammatory lesions, including nasal lesions, and a minimum of 20, but no more than 150 facial non-inflammatory lesions, excluding nasal lesions.	**Intervention: arm 1**: Clindamycin foam o.d. **Intervention: arm 2**: Vehicle foam o.d. **Intervention: arm 3**: Clindamycin gel 1% o.d. **Intervention: arm 4**: Vehicle gel o.d.	• Skin irritation
Shwetha 2014 **Country**: India **Study type**: RCT	N=120 **Sex**: mixed **Number randomised: arm 1**: n=60 **Number randomised: arm 2**: n=60 **Inclusion details**: Mild to moderate acne on face as per Indian Acne Alliance Grading for Severity of acne, aged between 12 to 25 years.	**Intervention: arm 1**: topical 1% clindamycin + 0.1% adapalene **Intervention: arm 2**: topical 1% clindamycin + 2.5% benzoyl peroxide	• Skin irritation

Study	Population	Interventions	Outcomes
Smith 1980b **Country**: United States **Study type**: RCT	N=59 **Sex**: mixed **Number randomised: arm 1**: n=29 **Number randomised: arm 2**: n=30 **Inclusion details**: At least ten inflammatory papules and/or pustules and no more than three nodulocystic lesions on the face, otherwise in good health.	**Intervention: arm 1**: 20% Benzoyl-peroxide b.d. **Intervention: arm 2**: Vehicle b.d.	• Skin irritation
Stein Gold 2016 **Country**: United States **Study type**: RCT	N=2102 **Sex**: mixed. **Number randomised: arm 1**: 1044 **Number randomised: arm 2**: 1058 **Inclusion details**: Moderate acne, with 20 to 50 inflammatory lesions (papules and pustules) and 30 to 100 noninflammatory lesions (open and closed comedones) on the face. Patients were also required to have an acne grade of 3 (indicating moderate acne) on the Global Acne Assessment Score. 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. **Number randomised: arm 3**: 69	**Intervention: arm 1**: Dapsone gel 7.5%. ADAP 0.3%/BPO 2.5% gel **Intervention: arm 2**: Vehicle. ADAP 0.1%/BPO 2.5% gel **Intervention: arm 3**: Vehicle	• Skin irritation
Stinco 2007 **Country**: Italy **Study type**: RCT	N=65 **Sex**: mixed **Number randomised: arm 1**: n=25	**Intervention: arm 1**: Azelaic acid o.d. **Intervention: arm 2**: Benzoyl peroxide o.d.	• Skin irritation

Study	Population	Interventions	Outcomes
	Number randomised: arm 2: n=20 **Number randomised: arm 3**: n=20 **Inclusion details**: Mild or moderate comedonic or papulopustular acne, localized on the face. each patient had a minimum of 20 facial non-inflammatory lesions (open and closed comedones) and 10 inflamed lesions. Also required to be in good health and have not received any oral or topical anti-acne therapy in the 8 weeks prior the study.	**Intervention: arm 3**: Adapalene o.d.	
Stoughton 1987 **Country**: United States **Study type**: RCT	N=110 **Sex**: mixed **Number randomised: arm 1**: n=55 **Number randomised: arm 2**: n=55 **Inclusion details**: Helathy participants aged between 12 and 35 years and with a minimum of 10 erythematous facial papules and pustules.	**Intervention: arm 1**: Chlorhexidine gluconate skin solution **Intervention: arm 2**: vehicle	• Skin irritation
Thiboutot 2006 **Country**: North America **Study type**: RCT	N=653 **Sex**: mixed **Number randomised: arm 1**: n=261 **Number randomised: arm 2**: n=258 **Number randomised: arm 3**: n=134 **Inclusion details**: Participants 12 years or older, with 20 to 100 noninflammatory facial lesions, 20 to 50 inflammatory facial lesions, and no nodules or cysts; specified washout periods were required for participants taking certain topical and systemic treatments.	**Intervention: arm 1**: Adapalene 0.1% gel **Intervention: arm 2**: Adapalene 0.3% gel **Intervention: arm 2**: Vehicle	• Skin irritation
Thorneycroft 2004	N=1154	**Intervention: arm 1**:	• Breast

Study	Population	Interventions	Outcomes
Country: Germany **Study type**: RCT	**Sex**: female **Number randomised: arm 1**: n=568 **Number randomised: arm 2**: n=586 **Inclusion details**: Otherwise healthy female subjects ranging in age from 15 to 40 years without contraindications for combined oral contraceptive use with mild to moderate acne vulgaris, having 6 to 100 comedones (noninflammatory lesions), 10 to 50 papules or pustules together, and not more than 5 nodules on the face (inflammatory lesions). Normal gynecologic examination and cervical smear within the last 6 months; negative pregnancy test; 3 spontaneous withdrawal bleedings following delivery, abortion, or lactation; and avoidance of comedogenic cosmetics or sunscreens, sex hormone preparations, and antiacne therapy.	30micrograms ethinyl estradiol + 3milligrams drospirenone **Intervention: arm 2**: 35micrograms ethinyl estradiol + 0.18, 0.215, 0.25mg norgestimate	tenderness • Neurological side effects
Tirado-Sanchez 2013 **Country**: Mexico **Study type**: RCT	N=171 **Sex**: mixed **Number randomised: arm 1**: n=43 **Number randomised: arm 2**: n=43 **Number randomised: arm 3**: n=45 **Number randomised: arm 4**: n=40 **Inclusion details**: 18 years or older with at least ten noninflammatory acne lesions and <30 inflammatory lesions on the entire face. Patients with childbearing potential were required to use birth control and to have a negative	**Intervention: arm 1**: Adapalene 0.1% gel **Intervention: arm 2**: Adapalene 0,3% gel **Intervention: arm 3**: Tretinoin 0.05% gel **Intervention: arm 4**: Placebo gel	• Skin irritation

Study	Population	Interventions	Outcomes
	pregnancy test result at the beginning of the study.		
Trifu 2011 **Country**: Romania **Study type**: RCT	N=47 **Sex**: men **Number randomised: arm 1**: n=32 **Number randomised: arm 2**: n=15 **Inclusion details**: White-skinned men with acne vulgaris of the face of mild-to-moderate severity, with a score of 2 or 3 on IGA, and with TLC between 20 and 100, and ILC between 10 and 50.	**Intervention: arm 1**: Tretinoin 0.05% cream **Intervention: arm 2**: Vehicle	• Skin irritation
Tu 2001 **Country**: China **Study type**: RCT	N=150 **Sex**: mixed **Number randomised: arm 1**: n=75 **Number randomised: arm 2**: n=75 **Inclusion details**: Grade II–III acne vulgaris	**Intervention: arm 1**: Adapalene gel 0.1% **Intervention: arm 2**: Tretinoin gel 0.025%	• Skin irritation
Webster 2001 **Country**: United States **Study type**: RCT	N=143 **Sex**: Mixed **Number randomised: arm 1**: n=72 **Number randomised: arm 2**: n=71 **Inclusion details**: At least 12 years old with mild to moderate facial acne vulgaris, defined as 10 to 60 facial inflammatory lesions, 10 to 200 facial noninflammatory lesions, and no more than 2 facial nodular cystic lesions (none more than 5mm in diameter).	**Intervention: arm 1**: once-daily application of tazarotene 0.1% gel **Intervention: arm 2**: tretinoin 0.025% gel	• Skin irritation
Xu 2016 **Country**: China **Study type**: RCT	N=1016 **Sex**: Mixed **Number randomised: arm 1**: n=500 **Number randomised: arm 2**: n=516 **Inclusion details**: Aged 12–45 years (inclusive) diagnosed	**Intervention: arm 1**: topical clindamycin 1%/benzoyl peroxide 5% once-daily gel **Intervention: arm 2**: clindamycin 1% twice-daily gel	• Skin irritation

Study	Population	Interventions	Outcomes
	with mild to moderate acne, with at least 17, but not more than 60 facial inflammatory lesions (papules plus pustules), at least 20 but not more than 125 facial non-inflammatory lesions (open and closed comedones), no more than 1 facial nodular lesion with no cystic lesions, and who had a baseline Investigator's Static Global Assessment (ISGA) score of 2 or 3.		

Abbreviations: AZE + SAL peel: azelaic acid and salicylic acid peel; 1319-LSR: 1319 nm laser photochemical therapy; 589-LSR: 589 nm laser photochemical therapy; 5ALA: 5-aminolevulinic acid withunspecified light source; 5ALA-IPL-PDT: 5 aminolevulinic acid using intense pulsed light; 5ALA-KTP-PDT: 5-aminolevulinic acid using KTP (potassium titanyl phosphate) laser; 5ALA-PDL-PDT: 5-aminolevulinic acid using pulsed dye laser; 5ALA-RED-PDT: 5-aminolevulinic acid using red light; 5ARI: 5-alpha-reductase inhibitors; ACTINAC: Actinac (4% chloramphenicol, 4% hydrocortisone acetate, 2.4% butoxyethyl nicotinate, 2.4% allantoin, 32% precipitated sulphur); ADAP + BPO: adapalene + benzoyl peroxide; ADAP: adapalene; AFA peel: amino fruit acid (available in creams, pads, lotions); AZE: azelaic acid; AZITH:azithromycin; BIFON: bifonazole; BiRF: bipolar radiofrequency; BLU-PT: blue light emitting diode therapy (LED) photochemical therapy; BPO + CLIND: benzoyl peroxide 5%/clindamycin 1%; BPO: benzoyl peroxide; BR-LED: blue + red light; BUTEN: butenifine; CD271: CD 271 alcoholic gel; CHLOR: chlorhexidine gluconate/digluconate; CIPRO: ciprofloxacine; CLIND: clindamycin; CLIND + TRET: clindamycin 1% + tretioin 0.025%; CLIND+ ZINC: clindamycin with zinc acetatedihydrate; CMA: chlormadinone acetate; CO2: fractional CO2 laser; CPA + EE: co-cyprindiol (ethinylestradiol with cyproterone acetate); CPA: cyproterone acetate; DAPS: dapsone; DEM: demeclocycline; DOXY: doxycycline; DRSP: drospirenone; EE + DNG: estradiol (valerate) + dienogest; EE + DROS: ethinylestradiol + drospirenone; EE + LNG: ethinylestradiol+levonorgestrel; EE: ethinylestradiol; EE+DSGethinylestradiol+ desogestrel; EE+NGM: ethinylestradiol+norgestimate; ERYTH + ZINC: erythromycin with zinc acetate dihydrate; ERYTH:erythromycin; FCA: fucidic acid (sodium fusidate); FMR: fractional microneedling radiofrequency; GLY peel: glycolic acid; GOLDMP: gold microparticles; HPS: hydrogen peroxide; IPL: intense pulsed light; IPL+VAC: intense pulsed light + vacuum; IRL: near infrared light; 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≥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: ISOisotretinoin ≥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 peel: Jessner's peel; KTP: potassium titanyl phosphate laser; LEVA: levamisole; LNG: levonorgestrel; LYME: lymecycline; MAL with occlusion: methyl aminolevulinate ; MAL without occlusion: methylaminolevulinate ; MAL-DL-PDT: methyl aminolevulinate using daylight; MAL-IPL-PDT: methyl aminolevulinate using intense pulsed light; MAL-KTP-PDT: methyl aminolevulinate using potassium titanyl phosphate (KTP) laser; 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; NAD:nadifloxacin; NAFL: fractional erbiumglass laser; NBUVB: nearband ultraviolet light; Nd:YAG: long-pulse neodymium-doped yttrium aluminum garnet laser; NELS: Nels Cream (chloroxylenol + zinc oxide); NICO: nicotinamide (NIACINAMID); no!no!: no!no! skin device (broad spectrum light of 450-2000nm, 6 J/cm-2); NOR + EE:norethisterone + ethinylestradiol; OXYTETRA: oxytetracycline; PBBL: pneumatic broadband light therapy; PDL: pulsed dye laser; PLC: placebo; PLC-physical: sham physical treatment; PRED:prednisolone; PYA peel: pyruvic acid; RED: red light; RETINOL: retinol (vitamin A); ROXI: roxithromycin; SAL peel: salicylic acid; SARE:sarecyclin; SOS: superoxidised solution (an electrochemically processed aqueous solution manufactured from pure water and sodium chloride); SPIRO: spironolactone; TAZ:tazarotene; TCA peel: trichloroaecetic acid; TETRA: tetracycline;TRET: tretinoin (retin A, all-trans reinoic acid); TRIC: triclozan; 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 E1).

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 E1.

Recommendations supported by this evidence review

Evidence review underpinning recommendations 1.5.1, 1.5.2 and 1.5.4 to 1.5.12 (excluding 1.5.8 and bullet points 2 and 3 of recommendation 1.5.10) and 2 research recommendation on the effectiveness of chemical peels and the effectiveness of physical modalities. Other evidence supporting these recommendations as well as the committee's discussion of the evidence can be found in the evidence review on mild to moderate acne network meta-analysis (evidence report E1).

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Appendices

Appendix A - Review protocol

Review protocol for review question: For people with mild to moderate 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?

Field	Content
	6.1 What is the effectiveness of oral hormonal contraceptives in the treatment of acne vulgaris? 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.

Field	Content
Condition or domain being studied	Acne vulgaris
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]

Field	Content
	Anthelmintics • 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]

Field	Content
	• 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)

Field	Content
	○ 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) • 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)

Field	Content

	• 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

Field	Content
	○ 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**

Field	Content

	• 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)
	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

Field	Content
	considered, as there is indication that these are efficacious while the rate of isotretinoin-related side effects is lower. 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

Field	Content
	Excluded study designs: • 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

Field	Content
	reported, the mean counts and standard error at baseline and treatment endpoint will be prioritised, accounting for correlations 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.

Field	Content

	For scales where these relative effects are found to be sufficiently linearly related, we will include the respective extracted scale 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***

Field	Content
	• Treatment discontinuation due to side effects by treatment endpoint ***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

Field	Content
	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 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** <u>Network meta-analysis</u> 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

Field	Content
	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 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

Field	Content
	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). 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.

Field	Content
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Field	Content
Analysis of sub-groups	**Severity** For all outcomes, we will conduct separate analyses for people with • 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

Field	Content	
	suitable for both sexes. **<u>Age</u>** If possible, a random effects meta-regression according to age will be conducted for NMA of efficacy (% change in acne lesion 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	

Field	Content		
Anticipated or actual start date	After protocol registered on PROSPERO		
Anticipated completion date	13 January 2021		
Stage of review at time of this submission	**Review stage**	**Started**	**Completed**
	Preliminary searches	☑	☑
	Piloting of the study selection process	☐	☐
	Formal screening of search results against eligibility criteria	☑	☑
	Data extraction	☑	☑
	Risk of bias (quality) assessment	☑	☑
	Data analysis	☑	☑
Named contact	**5a. Named contact** National Guideline Alliance **5b. Named contact e-mail** AcneManagement@nice.org.uk **5e. Organisational affiliation of the review** National Institute for Health and Care Excellence (NICE) and National Guideline Alliance		
Review team members	National Guideline Alliance		
Funding sources/sponsor	This systematic review is being completed by the National Guideline Alliance, which is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists. NICE funds the National Guideline Alliance to develop guidelines for those working in the NHS, public health, and social care in England.		

Field	Content
Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/gid-ng10109/documents/committee-member-list 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	Not applicable

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

1 *Crl: 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 mild to moderate 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/
16	exp economic evaluation/
17	exp health care cost/

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

Date of initial search: 12/12/2018

Date of updated search: 06/05/2020

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

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

Search for health utility values

Date of initial search: 29/01/2019

Date of updated search: 06/05/2020

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

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

#	Searches
1	exp Acne Vulgaris/ use ppez
2	exp acne/ use emez
3	acne.tw.
4	or/1-3
5	Quality-Adjusted Life Years/ use ppez
6	Sickness Impact Profile/
7	quality adjusted life year/ use emez
8	"quality of life index"/ use emez
9	(quality adjusted or quality adjusted life year*).tw.
10	(qaly* or qal or qald* or qale* or qtime* or qwb* or daly).tw.
11	(illness state* or health state*).tw.
12	(hui or hui2 or hui3).tw.
13	(multiattibute* or multi attribute*).tw.
14	(utilit* adj3 (score*1 or valu* or health* or cost* or measur* or disease* or mean or gain or gains or index*)).tw.
15	utilities.tw.
16	(eq-5d* or eq5d* or eq-5* or eq5* or euroqual* or euro qual* or euroqual 5d* or euro qual 5d* or euro qol* or euroqol*or euro quol* or euroquol* or euro quol5d* or euroquol5d* or eur qol* or eurqol* or eur qol5d* or eurqol5d* or eur?qul* or eur?qul5d* or euro* quality of life or european qol).tw.
17	(euro* adj3 (5 d* or 5d* or 5 dimension* or 5dimension* or 5 domain* or 5domain*)).tw.
18	(sf36 or sf 36 or sf thirty six or sf thirtysix).tw.
19	(time trade off*1 or time tradeoff*1 or tto or timetradeoff*1).tw.
20	Quality of Life/ and ((quality of life or qol) adj (score*1 or measure*1)).tw.
21	Quality of Life/ and ec.fs.
22	Quality of Life/ and (health adj3 status).tw.
23	(quality of life or qol).tw. and Cost-Benefit Analysis/ use ppez
24	(quality of life or qol).tw. and cost benefit analysis/ use emez
25	((qol or hrqol or quality of life).tw. or *quality of life/) and ((qol or hrqol* or quality of life) adj2 (increas* or decreas* or

#	Searches
	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 mild to moderate 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 mild to moderate acne (side effects and participant reported improvement)?

Table 4: Evidence table

Study details	Participants	Interventions	Outcomes and results	Comments
Study details **Reference** Adhikary, J. S., V.,Bhandare, B.,Vivekananda,A comparative study to evaluate the efficacy and safety of topical isotretinoin and clindamycin versus adapalene and clindamycin in the treatment of grade I - II acne vulgaris of face. 2014. International Journal of Pharmaceutical Sciences Review and Research **Trial ID** Adhikary 2014 **Country** India **Study type** RCT **Source of funding** Not industry funded ***Analysis method*** **Intention to treat or completers analysis** Completers	N=200 ***Characteristics*** **Sex** mixed **age (mean±SD)** 22.78±3.08 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Indian Grading Scale **Inclusion details** Age at least 10 years, grade I to grade II acne vulgaris of face on the Indian grading scale. **Exclusion details** Allergy to any of the studied medication and photosensitivity; History of drug use for the treatment of acne within one month; Patients with endocrinal problems. ***Number included*** **Number randomised: arm 1** 100 **Number randomised: arm 2** 100 **Number completed: arm 1** 94 **Number completed: arm 2**	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <26 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** topical Isotretinoin gel 0.05 % once daily at night and topical Clindamycin phosphate 1% lotion in the morning **Intervention: arm 2** Adapalene 0.1 % gel once daily at night and topical Clindamycin phosphate 1% lotion in the morning **Coded intervention: arm 1** ISO-topical + CLIND-topical **Coded intervention:**	***Results*** **Skin irritation (n/N): arm 1** 56/94 **Skin irritation (n/N): arm 2** 32/97	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns; randomised trial, but methods not reported **2. Deviation from intervention** High;open-labeled; not reported if ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;between 6 and 3% withdrawals **4. Outcome measurement (efficacy)** High;open labeled; outcomes - lesion counting and adverse effects **5. Selective reporting** Some concerns;there was a study protocol that was reviewed and approved by the

Study details	Participants	Interventions	Outcomes and results	Comments
	97	**arm 2** ADAP-topical + CLIND-topical **Treatment category** Topical retinoids ± other treatment		Institutional Ethics Committee at the Institute, but unclear whether it was a pre-registered protocol **6. Overall bias** High
Study details **Reference** Akarsu, S. F., E.,Yücel, F.,Gül, E.,Günes, A. T.Efficacy of the addition of salicylic acid to clindamycin and benzoyl peroxide combination for acne vulgaris. 2012. Journal of dermatology **Trial ID** Akarsu 2012 **Country** Turkey **Study type** RCT **Source of funding** Unstated ***Analysis method*** **Intention to treat or completers analysis** completers	N=50 ***Characteristics*** **Sex** mixed **age (median)** 19 **age (min/max)** 18/29 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** Mild to moderate AV, between the ages of 18 and 35 years, and with between 10–50 IL and 10–100 NIL above the mandibular line at baseline. **Exclusion details** Cystic or nodular acne lesions, those who had used topical anti-acne preparations within the prior 2 weeks, used systemic antibiotics for acne within the prior 1 month, used systemic retinoids within the prior 6 months, or received a facial cosmetic procedure within the prior 6 months. Also pregnant or lactating women, patients who had known allergy or hypersensitivity to any of the study medication ingredients, or a	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** SAL 3% + CLIND-topical 1% + BPO-topical 5% **Intervention: arm 2** CLIND-topical 1% + BPO-topical 5% **Coded intervention: arm 1** SAL topical + CLIND-topical + BPO-topical **Coded intervention: arm 2** CLIND-topical + BPO-topical	***Results*** **Participant reported improvement (n/N): arm 1** 24/24 **Participant reported improvement (n/N): arm 2** 25/25	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;methods not reported **2. Deviation from intervention** Some concerns;not clear if participants and personnel were blinded; not reported if ITT analysis was done **3. Missing outcome data (efficacy)** Low;less than 5% loss to follow-up or withdrawals **4. Outcome measurement (efficacy)** Low;investigator-blinded; outcomes - lesion counting, adverse effects, biophysical measurements, quality of life **5. Selective reporting** Some concerns;not

Study details	Participants	Interventions	Outcomes and results	Comments
	history of regional enteritis, ulcerative colitis or antibacterial-associated colitis. ***Number included*** **Number randomised: arm 1** 25 **Number randomised: arm 2** 25 **Number completed: arm 1** 24 **Number completed: arm 2** 25			reported whether there was a pre-registered protocol **6. Overall bias** Some concerns
Study details **Reference** Alirezai, M. G., B.,Horvath, A.,Forsea, D.,Briantais, P.,Guyomar, M.Results of a randomised, multicentre study comparing a new water-based gel of clindamycin 1% versus clindamycin 1% topical solution in the treatment of acne vulgaris. 2005. European Journal of Dermatology **Trial ID** Alirezai 2005 **Country** Europe **Study type** RCT **Source of funding** Industry funded ***Analysis method*** **Intention to treat or completers analysis** ITT	N=592 ***Characteristics*** **Sex** mixed **age (mean±SD)** 20.5±5.1 **age (min/max)** 12/35 ***Inclusion/exclusion criteria*** **Used validated acne scale** yes **Acne scale** Leeds Revised Grading Scale **Inclusion details** At least age 12, acne vulgaris on face (severity grade of 2 to 5 on the Leeds revised scale), and 15-50 inflammatory facial lesions. **Exclusion details** Acne conglobata, acne fulminans, chloracne, drug enduced acne, pregnant or nursing or planning for a baby, and men with beards that may interfere with assessment. ***Number included*** **Number randomised: arm 1** 265	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 3 **Split face design** No **Intervention: arm 1** CLIND-topical 1% gel **Intervention: arm 2** CLIND-topical 1% topical solution **Intervention: arm 3** Vehicle gel **Coded intervention: arm 1** CLIND-topical **Coded intervention: arm 2** CLIND-topical **Coded intervention:**	***Results*** **Skin irritation (n/N): arm 1** 5/265 **Skin irritation (n/N): arm 2** 5/261 **Skin irritation (n/N): arm 3** 0/66	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;participants were randomised in a 4:4:1 ratio, but methods not reported for allocation concealment **2. Deviation from intervention** Some concerns;participants aware of treatment regimen and product packaging and asked not to inform the Investigator in order to maintain blinding; ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;more than 5% loss to follow-up or

Study details	Participants	Interventions	Outcomes and results	Comments
Method of ITT imputation LOCF	**Number randomised: arm 2** 261 **Number randomised: arm 3** 66 **Number completed: arm 1** 233 **Number completed: arm 2** 240 **Number completed: arm 3** 57	**arm 3** Vehicle **Treatment category** Topical non-retinoids ± other treatment		withdrawals (10.5%) - similar between arms **4. Outcome measurement (efficacy)** Low;investigator-blinded; outcomes - lesion counting, Global Assessment of Improvement, adverse effects **5. Selective reporting** Some concerns;not reported whether there was a pre-registered protocol **6. Overall bias** Some concerns
Study details **Reference** Alora Palli, M. R.-H., C. M.,Lima, X. T.,Kimball, A. B.A single-center, randomized double-blind, parallel-group study to examine the safety and efficacy of 3mg drospirenone/0.02mg ethinyl estradiol compared with placebo in the treatment of moderate truncal acne vulgaris. 2013. Journal of drugs in dermatology **Trial ID** Alora Palli 2013 **Country** United States	N=30 ***Characteristics*** **Sex** female **age (mean±SD)** 24±4.5 **age (min/max)** 19/40 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** Female, age 18 to 45 years, who achieved spontaneous menarche, desired contraception and had a diagnosis of truncal acne of 10 to 50 inflammatory lesions on the	***Interventions*** **Treatment duration (weeks)** 24 **Treatment duration category** 24+ weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** EE-oral 0.02 mg + DROS-oral 3mg od **Intervention: arm 2** PLC-oral **Coded intervention: arm 1**	***Results*** **Neurological side effects (n/N): arm 1** 2/15 **Neurological side effects (n/N): arm 2** 0/10 **Change in mood (n/N): arm 1** 1/15 **Change in mood (n/N): arm 2** 0/10 **Breakthrough bleeding (n/N): arm 1** 1/15 **Breakthrough bleeding (n/N): arm 2**	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;participants randomly assigned in 1:1 ratio by Research Randomiser; methods not reported for allocation concealment **2. Deviation from intervention** Low;double-blinded (participants and study staff not aware of treatment assignment); ITT analysis appears to

Study details	Participants	Interventions	Outcomes and results	Comments
Study type RCT **Source of funding** Industry funded ***Analysis method*** **Intention to treat or completers analysis** completers	back and chest combined with not more than 5 nodules **Exclusion details** Smokers, medical conditions that increased their risk of developing adverse events from study medication, patients who had used topical acne medications (tretinoin, benzoyl peroxide, or topical antibiotics) within 2 weeks, systemic antibiotics or oral steroids within 4 weeks, oral contraceptive within 12 weeks, isotretinoin in the past six months, and phototherapy devices (ClearLight, Zenozapper, tanning booths or lamps) within 1 week. ***Number included*** **Number randomised: arm 1** 16 **Number randomised: arm 2** 14 **Number completed: arm 1** 11 **Number completed: arm 2** 10	EE-oral + DROS-oral **Coded intervention: arm 2** PLC-oral **Treatment category** Hormonal contraceptives / Hormone-modifying agents	0/10	have been performed **3. Missing outcome data (efficacy)** High;40% loss to follow-up or withdrawals - more in the active arm; last observation carried forward **4. Outcome measurement (efficacy)** Low;assessor was blinded; outcomes - lesion counting, Investigator and Subject Global Assessment, quality of life, adverse effects **5. Selective reporting** Low;registered with ClinicalTrials.gov **6. Overall bias** High
Study details **Reference** Babaeinejad, S. H. F., R. F.The efficacy, safety, and tolerability of adapalene versus benzoyl peroxide in the treatment of mild acne vulgaris; a randomized trial. 2013. Journal of Drugs in Dermatology **Trial ID** Babaeinejad 2013	N=60 ***Characteristics*** **Sex** mixed **age (mean±SD)** 21.1±3.64 **age (min/max)** 18/31 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale**	***Interventions*** **Treatment duration (weeks)** 8 **Treatment duration category** 6 to <12 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1**	***Results*** **Skin irritation (n/N): arm 1** 6/30 **Skin irritation (n/N): arm 2** 8/30	***Cochrane RoB Tool v2.0*** **1. Randomisation** Low;randomisation conducted using standard computer randomisation software; medications were in identical tubes and coding not disclosed until after data were analysed **2. Deviation from**

Study details	Participants	Interventions	Outcomes and results	Comments
Country Iran, Islamic Republic of **Study type** RCT **Source of funding** Not industry funded ***Analysis method*** **Intention to treat or completers analysis** completers	Evaluator's Global Severity Scale (EGSS) **Inclusion details** Mild acne vulgaris (Evaluator Global Severity Score, EGSS, of 2) **Exclusion details** Severe acne or other dermatologic conditions requiring systemic therapy, nursing/pregnant women, and those who were planning for pregnancy. No use within the past 2 weeks of topical antibiotics and corticosteroid, 1 month of oral antibiotics and corticosteroid, and 6 months of oral retinoid agent. ***Number included*** **Number randomised: arm 1** 30 **Number randomised: arm 2** 30 **Number completed: arm 1** 30 **Number completed: arm 2** 30	BPO 2.5% gel **Intervention: arm 2** ADAP 0.1% gel **Coded intervention: arm 1** BPO-topical **Coded intervention: arm 2** ADAP-topical **Treatment category** Topical retinoids ± other treatment		**intervention** Some concerns;double blind; not reported if ITT analysis performed **3. Missing outcome data (efficacy)** Low;all participants completed the study **4. Outcome measurement (efficacy)** Low;outcomes - lesion count, adverse effects, overall satisfaction **5. Selective reporting** Some concerns;not reported whether there was a pre-registered protocol **6. Overall bias** Some concerns
Study details **Reference** Babayeva, L. A., S.,Fetil, E.,Gunes, A. T.Comparison of tretinoin 0.05% cream and 3% alcohol-based salicylic acid preparation in the treatment of acne vulgaris. 2011. Journal of the European Academy of Dermatology and Venereology **Trial ID**	N=46 ***Characteristics*** **Sex** mixed **age (mean±SD)** 20.78±2.69 **age (min/max)** 18/31 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale**	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1**	***Results*** **Participant reported improvement (n/N): arm 1** 23/23 **Participant reported improvement (n/N): arm 2** 23/23	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;randomisation using 1:1 ratio (no other information provided); unclear whether allocation sequence concealed **2. Deviation from intervention** Some

Study details	Participants	Interventions	Outcomes and results	Comments
Babayeva 2011 **Country** Turkey **Study type** RCT **Source of funding** Not industry funded ***Analysis method*** **Intention to treat or completers analysis** completers	None **Inclusion details** 18 and 35 years of age, with 10–50 inflammatory lesions and 10–100 non-Inflammatory lesions above the mandibular line at baseline **Exclusion details** Pregnant or lactating women, patients who had known sensitivity to any of the study medication ingredients, those who used topical anti-acne preparations, medicated shampoos or cleansers within 2 weeks; systemic antibiotic treatments for acne within 1 month; or systemic retinoid treatments within 6 months, prior to start of the study. ***Number included*** **Number randomised: arm 1** 23 **Number randomised: arm 2** 23 **Number completed: arm 1** 23 **Number completed: arm 2** 23	SAL 3% + CLIND-topical 1% **Intervention: arm 2** TRET-topical 0.05% + CLIND-topical 1% **Coded intervention: arm 1** SAL topical + CLIND-topical **Coded intervention: arm 2** TRET-topical + CLIND-topical		concerns;single-blinded but not clear who was blinded; not reported if ITT analysis was performed **3. Missing outcome data (efficacy)** Low;all participants completed the study **4. Outcome measurement (efficacy)** High;"Evaluations were performed by an investigator aware of the treatment allocation" **5. Selective reporting** Some concerns;not reported whether there was a pre-registered protocol, but all outcomes mentioned appear to have findings reported **6. Overall bias** High
Study details **Reference** Berger, R. B., A.,Fleischer, A.,Leyden, J. J.,Lucky, A.,Pariser, D.,Rafal, E.,Thiboutot, D.,Wilson, D.,Grossman, R.,et al.,A double-blinded, randomized, vehicle-controlled,	N=156 ***Characteristics*** **Sex** mixed **age (mean±SD)** 18.399999999999999 **age (min/max)** 12/41	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms**	***Results*** **Skin irritation (n/N): arm 1** 2/78 **Skin irritation (n/N): arm 2** 6/78 **Light sensitivity (n/N):**	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;randomisation on a 1:1 ratio using computer-generated randomisation schedule provided by

Study details	Participants	Interventions	Outcomes and results	Comments
multicenter, parallel-group study to assess the safety and efficacy of tretinoin gel microsphere 0.04% in the treatment of acne vulgaris in adults. 2007a. Cutis; cutaneous medicine for the practitioner **Trial ID** Berger 2007a **Country** United States **Study type** RCT **Source of funding** Industry funded ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** Ages 12 to 40 years, in good health, with mild to moderate acne vulgaris defined as 20 to 150 total facial lesions. Of these lesions, 10 to 100 were to be comedones (open and closed), and 10 to 50 were to be inflammatory lesions (papules and pustules). No more than 2 were to be nodules (defined as deep inflammatory lesions of 1 cm or greater). **Exclusion details** Pregnant, lactating, or had been using systemic birth control for <6 months, erythema not attributed to the acne lesions, peeling, dryness, burning/stinging, and itching on the face, excessive facial hair (ie, beard, sideburns, or mustache) that would obstruct evaluation; use of photosensitizing, phototherapy, or selftanning agents; and the presence of skin cancer or actinic keratosis on the face. No use of systemic retinoid treatment for at least 1 year before the study, and topical retinoids, systemic antibiotics, nicotinamide, or systemic steroids for at least 1 month. Other topical medications applied to the face (including corticosteroids, antimicrobials, salicylic acid, and benzoyl peroxide) were to be discontinued at least 2 weeks before study initiation. ***Number included***	2 **Split face design** No **Intervention: arm 1** TRET-topical 0.04% **Intervention: arm 2** TRET-topical 0.1% **Coded intervention: arm 1** TRET-topical **Coded intervention: arm 2** TRET-topical **Treatment category** Topical retinoids ± other treatment	**arm 1** 3/78 **Light sensitivity (n/N): arm 2** 1/78 **Participant reported improvement (n/N): arm 1** 67/78 **Participant reported improvement (n/N): arm 2** 67/78	thte manufacturer, prepared using a pre-specified block size; methods not reported for allocation concealment **2. Deviation from intervention** Low;double-blinded; ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;more than 5% loss to follow-up or withdrawals - balanced between arms **4. Outcome measurement (efficacy)** Low;investigator was blinded **5. Selective reporting** Some concerns;"study protocol approved by an independent review board and conducted in accordance with the Declearation of Helsinki and the good clinical practice guidelines", but no further details provided **6. Overall bias**

Study details	Participants	Interventions	Outcomes and results	Comments
	Number randomised: arm 1 78 **Number randomised: arm 2** 78 **Number completed: arm 1** 73 **Number completed: arm 2** 72			Some concerns
Study details **Reference** Berger, R. R., R.,Barba, A.,Wilson, D.,Stewart, D.,Grossman, R.,Nighland, M.,Weiss, J.Tretinoin gel microspheres 0.04% versus 0.1% in adolescents and adults with mild to moderate acne vulgaris: a 12-week, multicenter, randomized, double-blind, parallel-group, phase IV trial. 2007b. Clinical therapeutics **Trial ID** Berger 2007b **Country** United States **Study type** RCT **Source of funding** Industry funded ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	N=178 ***Characteristics*** **Sex** mixed **age (min/max)** 19/45 **age (other information)** mean age in TRET group 26.7 yrs; Vehicle group 29.0 yrs ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** 19 and 45 years of age with mild to moderate acne vulgaris - between 15 and 80 total facial lesions that consisted of 10 to 40 inflammatory lesions and no more than 2 nodules. **Exclusion details** - ***Number included*** **Number randomised: arm 1** 88 **Number randomised: arm 2** 90 **Number completed: arm 1**	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** TRET-topical 0.04% **Intervention: arm 2** Vehicle gel **Coded intervention: arm 1** TRET-topical **Coded intervention: arm 2** Vehicle **Treatment category** Topical retinoids ± other treatment	***Results*** **Participant reported improvement (n/N): arm 1** 23/88 **Participant reported improvement (n/N): arm 2** 13/90	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;methods not reported **2. Deviation from intervention** Low;double-blinded; ITT analysis was done **3. Missing outcome data (efficacy)** High;more than 20% discontinued; "most" were lost to follow up and 4 participants in the tretinoin treatment group discontinued for adverse events **4. Outcome measurement (efficacy)** Some concerns;blinding not reported **5. Selective reporting** Some concerns;study protocol was reviewed

Study details	Participants	Interventions	Outcomes and results	Comments
	68 **Number completed: arm 2** 68			by appropriate institutional review boards at each study site, but no further details provided **6. Overall bias** High
Study details **Reference** Bleeker, J.Tolerance and efficacy of erythromycin stearate tablets versus enteric-coated erythromycin base capsules in the treatment of patients with acne vulgaris. 1983. Journal of International Medical Research **Trial ID** Bleeker 1983 **Country** Sweden **Study type** RCT **Source of funding** Unstated ***Analysis method*** **Intention to treat or completers analysis** completers	N=40 ***Characteristics*** **Sex** mixed **age (other information)** Mean age 20.6 in erythromycin stearate group, 19.7 in the other ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** Mild to moderate papulopustular acne **Exclusion details** Acne conglobata, comedonal ace, hypersensitivity to erythromycin, antibiotic treatment in the past month ***Number included*** **Number randomised: arm 1** 20 **Number randomised: arm 2** 20 **Number completed: arm 1** 18 **Number completed: arm 2** 16	***Interventions*** **Treatment duration (weeks)** 2 **Treatment duration category** 0 to <6 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** Erythromycin stearate capsules 500mg b.d. **Intervention: arm 2** Erythromycin base capsules 500mg b.d. **Coded intervention: arm 1** ERYTH-oral **Coded intervention: arm 2** ERYTH-oral **Treatment category** Oral antibiotics	***Results*** **GI side effects (n/N): arm 1** 3/18 **GI side effects (n/N): arm 2** 4/16	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;methods not reported **2. Deviation from intervention** Some concerns;not reported if participants were blinded; no ITT analysis was done **3. Missing outcome data (efficacy)** High;more than 5% discontinued due to side effects (20% enteric-coated erythromycin base capsules vs 10% erythromycin stearate tablets) **4. Outcome measurement (efficacy)** Low;investigator-blinded **5. Selective reporting** Some concerns;not reported whether

Study details	Participants	Interventions	Outcomes and results	Comments
				there was a pre-registered protocol **6. Overall bias** High
Study details **Reference** Boutli, F. Z., M.,Koussidou, T.,Ioannides, D.,Mourellou, O.Comparison of chloroxylenol 0.5% plus salicylic acid 2% cream and benzoyl peroxide 5% gel in the treatment of acne vulgaris: a randomized double-blind study. 2003. Drugs under experimental and clinical research **Trial ID** Boutli 2003 **Country** Greece **Study type** RCT **Source of funding** Unstated ***Analysis method*** **Intention to treat or completers analysis** completers	N=37 ***Characteristics*** **Sex** mixed **age (min/max)** 13/25 **age (other information)** mean age 21.4 in BP group & 20.8 in other group (SDs not reported) ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Pillsbury **Inclusion details** Age 13-25, moderate acne (grade 11, Pilsbury and Kligman), 20-50 comedones and 20-40 papulopustules **Exclusion details** Pregnant or nursing women, other systemic diseases, nodulocystic acne, taking oral contraceptives, taking systemic antibiotics, or any topical treatment for other reasons during the study ***Number included*** **Number randomised: arm 1** 19 **Number randomised: arm 2** 18 **Number completed: arm 1** 18 **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** Topical benzoil peroxide 5% gel **Intervention: arm 2** Topical Nisal cream (chloroxylenol 0.5% + salicylic acid 2%) **Coded intervention: arm 1** BPO-topical **Coded intervention: arm 2** NISAL topical **Treatment category** Topical non-retinoids ± other treatment	***Results*** **Skin irritation (n/N): arm 1** 14/18 **Skin irritation (n/N): arm 2** 2/16 **Light sensitivity (n/N): arm 1** NA **Light sensitivity (n/N): arm 2** 0/16	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;randomised trial, but methods not reported **2. Deviation from intervention** Some concerns;double-blinded but not clear who was blinded; No ITT analysis was done **3. Missing outcome data (efficacy)** High;more than 5% discontinued or lost to follow-up (8.1%); 5.3% in group 1 and 11.1% in group 2 **4. Outcome measurement (efficacy)** Some concerns;blinding not reported **5. Selective reporting** Some concerns;not reported whether there was a pre-registered protocol

Study details	Participants	Interventions	Outcomes and results	Comments
	16			**6. Overall bias** High
Study details **Reference** Carey, W. B., J. C.A Canadian multicentre study to compare fusidic acid lotion and erythromycin solution in the treatment of acne vulgaris of the face. 1996. European journal of clinical research **Trial ID** Carey 1996 **Country** Canada **Study type** RCT **Source of funding** Not industry funded ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** na	N=499 ***Characteristics*** **Sex** mixed **age (mean±SD)** 18.2±3.5 **age (min/max)** 11/25 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** Under 25 years, 15 - 75 inflammed lesions on the face **Exclusion details** Any established or suspected dermatalogical disease or who had used topical treatments within the past week. Women of childbearing age not considered to be using adequate contraception. Received ultraviolet radiation treatment within the past 4 weeks, systemic anti-infectives or corticosteroids o and hormones (except contraception) within the previous 4 weeks, or acne treament with retinoid within the past 12 months. ***Number included*** **Number randomised: arm 1** 249 **Number randomised: arm 2** 250 **Number completed: arm 1** 195	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** Topical fucidic acid 2% **Intervention: arm 2** Topical erythromycin 2% **Coded intervention: arm 1** FCA-topical **Coded intervention: arm 2** ERYTH-topical **Treatment category** Topical non-retinoids ± other treatment	***Results*** **Skin irritation (n/N): arm 1** 9/245 **Skin irritation (n/N): arm 2** 7/246 **Participant reported improvement (n/N): arm 1** 210/242 **Participant reported improvement (n/N): arm 2** 211/243	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;computer-generated randomisation schedule used; methods not reported for allocation concealment **2. Deviation from intervention** High;open-labeled; ITT analysis was done **3. Missing outcome data (efficacy)** High;more than 15% loss to follow-up or withdrawals (21.7% receiving fusidic acid lotion and 15.6% receiving erythromycin) **4. Outcome measurement (efficacy)** Low;evaluator-blinded **5. Selective reporting** Some concerns;not reported whether there was a pre-registered protocol **6. Overall bias**

Study details	Participants	Interventions	Outcomes and results	Comments
	Number completed: arm 2 211			High
Study details **Reference** Chalker, D. K. L., J. L.,Smith, J. G.,Klauda, H. C.,Pochi, P. E.,Jacoby, W. S.,Yonkosky, D. M.,Voorhees, J. J.,Ellis, C. N.,Matsuda-John, S.Efficacy of topical isotretinoin 0.05% gel in acne vulgaris: results of a multicenter, double-blind investigation. 1987. Journal of the American Academy of Dermatology **Trial ID** Chalker 1987 **Country** United States **Study type** RCT **Source of funding** Unstated ***Analysis method*** **Intention to treat or completers analysis** completers	N=313 ***Characteristics*** **Sex** mixed **age (min/max)** 13/33 **age (other information)** Mean age in completers: ISO 19.3 yrs; Vechilce 19.8 yrs. In withdrawals: ISO 21.0 Vehicle 21.6 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** Acne vulgaris with a minimum of 12 inflammatory lesions and 12 noninflammatory lesions and a maximum of 3 facial nodulocystic lesions, aged 13-30. **Exclusion details** Pregnancy or lactation, female patients not using effective form of contraceptive for a period of 3 months before the study, throughout the study period, and for 1 month after stopping use of the study medication ***Number included*** **Number randomised: arm 1** 156 **Number randomised: arm 2** 157 **Number completed: arm 1** 130	***Interventions*** **Treatment duration (weeks)** 14 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** Topical ISO 0.05% gel b.d. **Intervention: arm 2** Vehicle b.d. **Coded intervention: arm 1** ISO-topical **Coded intervention: arm 2** Vehicle **Treatment category** Topical retinoids ± other treatment	***Results*** **Skin irritation (n/N): arm 1** 99/130 **Skin irritation (n/N): arm 2** 86/138	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;randomised trial, but methods not reported **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;more than 10% withdrew (16.7% in intervention group and 12.1% in vehicle group) - most not related to the study medication **4. Outcome measurement (efficacy)** Some concerns;not clear if blinded **5. Selective reporting** Some concerns;not reported whether there was a pre-

Study details	Participants	Interventions	Outcomes and results	Comments
	Number completed: arm 2 138			registered protocol **6. Overall bias** High
Study details **Reference** Charakida, A. C., M.,Chu, A. C.Double-blind, randomized, placebo-controlled study of a lotion containing triethyl citrate and ethyl linoleate in the treatment of acne vulgaris. 2007. British Journal of Dermatology **Trial ID** Charakida 2007 **Country** United Kingdom **Study type** RCT **Source of funding** Not industry funded ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** na	N=40 ***Characteristics*** **Sex** mixed **age (other information)** median (IQR) age: 24 (20-30.75) in active group, 27.5 (18.25 - 33) in vehicle group ***Inclusion/exclusion criteria*** **Used validated acne scale** yes **Acne scale** Leeds Revised Grading Scale **Inclusion details** Patients aged between 16 and 45 years with mild to moderate facial inflammatory acne defined as the presence of at least 10 acne papules or pustules between the brow and jaw line and an acne severity score of between 2 and 7 on the Leeds revised acne grading system. **Exclusion details** Severe acne, rosacea, pregnancy, breastfeeding, known allergy to constituents of the lotions, use of medication for acne or use of antibiotics for other medical conditions ***Number included*** **Number randomised: arm 1** 20 **Number randomised: arm 2** 20 **Number completed: arm 1** 17 **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** ACNICARE (triethyl citrate + ethyl linoleate) topical b.d. **Intervention: arm 2** Vehicle topical b.d. **Coded intervention: arm 1** ACNICARE **Coded intervention: arm 2** Vehicle **Treatment category** Topical non-retinoids ± other treatment	***Results*** **Skin irritation (n/N): arm 1** 1/17 **Skin irritation (n/N): arm 2** 0/16	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;randomisation using computer-generated sequence; no other methods reported **2. Deviation from intervention** Low;double-blinded (2 lotions provided in identical bottles to ensure anonymity for both investigator and participant); ITT analysis was done **3. Missing outcome data (efficacy)** High;more than 15% withdrew (15% intervention; 20% vehicle); participants withdrew from vehicle because of dissatisfaction with clinical response **4. Outcome measurement (efficacy)** Low;investigator-blinded; outcomes measured at 4, 8 and 12 weeks but only

Study details	Participants	Interventions	Outcomes and results	Comments
	16			results at 4 and 12 weeks appear to have been reported. However, study endpoints appear to be change from baseline to after 12 weeks **5. Selective reporting** Some concerns;study protocol mention, but not clear whether this was a pre-registered protocol **6. Overall bias** High
Study details **Reference** Cunliffe, W. J. H., K. T.,Bojar, R.,Levy, S. F.A randomized, double-blind comparison of a clindamycin phosphate/benzoyl peroxide gel formulation and a matching clindamycin gel with respect to microbiologic activity and clinical efficacy in the topical treatment of acne vulgaris. 2002. Clinical Therapeutics **Trial ID** Cunliffe 2002b **Country** United Kingdom **Study type** RCT	N=79 ***Characteristics*** **Sex** mixed **age (mean±SD)** 18.2±1.7 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** Acne vulgaris, aged 13 to 30. Baseline or screening P acnes counts on facial skin (cheek or forehead) had to be at least 104 colony-forming units (CFUs) per square centimeter, of which no more than 104 CFU/cm 2 could be erythromycin or clindamycin resistant. Eligible patients also had to have 15 to 100 inflammatory lesions,	***Interventions*** **Treatment duration (weeks)** 16 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** topical clindamycin 1% / BPO 5% gel b.d. **Intervention: arm 2** topical clindamycin 1% **Coded intervention: arm 1** BPO-topical + CLIND-topical	***Results*** **Skin irritation (n/N): arm 1** 11/40 **Skin irritation (n/N): arm 2** 2/39	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;participants ranked in descending order in accordance with their total lesion counts at baseline and assigned to treatments alternatively; treatment assignments performed by statistician not involved in the data collection, management or analysis and medication dispensed

Study details	Participants	Interventions	Outcomes and results	Comments
Source of funding Industry funded ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	15 to 100 comedones, and <2 nodules/cysts on the face. Sexually active female patients were required to use contraception for 28 days before the start and for the duration of the study. **Exclusion details** Excluded if they had used oral antibiotics, topical antibiotics, or systemic hormones, including tablets containing cyproterone acetate 2 mg plus ethinylestradiol 35 pg, within 12 weeks before the start of the study. They were not to have used topical steroids on the face for 2 weeks, topical retinoids for 4 weeks, or oral retinoids for 6 months before entry. Patients with beards and sideburns, or with systemic or dermatologic diseases that may have afaffected their acne conditions or treatment assessments, and patients whose activities involved prolonged exposure to sunlight were excluded from the study. Pregnant or breast-feeding women and patients with known sensitivity to any ingredients in the study medications also were excluded. ***Number included*** **Number randomised: arm 1** 40 **Number randomised: arm 2** 39 **Number completed: arm 1** 30 **Number completed: arm 2** 32	**Coded intervention: arm 2** CLIND-topical **Treatment category** Topical non-retinoids ± other treatment		by a pharmacist not an evaluator **2. Deviation from intervention** Low;double-blinded; ITT analysis was done **3. Missing outcome data (efficacy)** High;more than 5% withdrawals (15% combination gel; 7.7% clindamycin monotherapy) resulting from loss to follow-up **4. Outcome measurement (efficacy)** Low;evaluator blinded **5. Selective reporting** Some concerns;not reported whether there was a pre-registered protocol **6. Overall bias** High
Study details **Reference**	N=40	***Interventions*** **Treatment duration**	***Results*** **Skin redness (n/N): arm 1**	***Cochrane RoB Tool v2.0***

Study details	Participants	Interventions	Outcomes and results	Comments
Dayal, S. A., A.,Sahu, P.,Jain, V. K.Jessner's solution vs. 30% salicylic acid peels: a comparative study of the efficacy and safety in mild-to-moderate acne vulgaris. 2017. Journal of cosmetic dermatology **Trial ID** Dayal 2017 **Country** India **Study type** RCT **Source of funding** Unstated ***Analysis method*** **Intention to treat or completers analysis** completers	***Characteristics*** **Sex** mixed **age (mean±SD)** 17.3±2.03 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Indian Grading Scale **Inclusion details** Mild-to-moderate (grade I and grade II) facial acne vulgaris, graded using a system taking into account the predominant lesions present: Grade 1 (mild): comedones, occasional papules. Grade 2 (moderate): papules, comedones, few pustules. Grade 3 (severe): predominant pustules, nodules, abscesses. Grade 4 (cystic): mainly cysts, abscesses, widespread scarring. **Exclusion details** Patients with severe acne vulgaris (patients with abscesses and nodulo-cystic lesions), who were on any anti-acne therapy since last 4 weeks, pregnancy and lactation, history of hypersensitivity to formulations used, history of keloid formation, photosensitivity, active dermatoses such as facial warts or herpes simplex infection, and patients with unrealistic expectations. ***Number included*** **Number randomised: arm 1** 20 **Number randomised: arm 2** 20 **Number completed: arm 1** 20	**(weeks)** 12 **Treatment duration category** 12 to <24 weeks **Treatment intensity** 6 sessions (once every 2 weeks for 12 weeks) **Number of arms** 2 **Split face design** No **Intervention: arm 1** salicylic acid 30% **Intervention: arm 2** Jessner's peel **Coded intervention: arm 1** SAL peel **Coded intervention: arm 2** JES peel **Treatment category** Chemical peels	4/20 **Skin redness (n/N): arm 2** 6/20 **Pigment changes (n/N): arm 1** 1/20 **Pigment changes (n/N): arm 2** 3/20	**1. Randomisation** Some concerns;randomisation using computerised randomisation, no other methods reported **2. Deviation from intervention** Some concerns;not reported if participants or personnel were blinded; not reported if ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;not reported if/how many particiants discontinued **4. Outcome measurement (efficacy)** Low;evaluator blinded **5. Selective reporting** Some concerns;not reported whether there was a pre-registered protocol **6. Overall bias** Some concerns

Study details	Participants	Interventions	Outcomes and results	Comments
	Number completed: arm 2 20			
Study details **Reference** 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. 2020. Journal of Cosmetic DermatologyJ **Trial ID** Dayal 2020 **Country** India **Study type** RCT **Source of funding** Not reported ***Analysis method*** **Intention to treat or completers analysis** Completers	N=50 ***Characteristics*** **Sex** mixed **age (mean±SD)** 19.5±2.30 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Vaishampayan scale **Inclusion details** Mild-to-moderate (grade I and grade II) facial acne vulgaris on the Vaishampayan grading system. **Exclusion details** Patients with infiltrates, abscesses, and nodulocystic lesions, taking any oral or topical treatment for acne for the past 4 weeks, pregnant and nursing women, history of hypersensitivity to study medication used,patients having keloidal tendency, history of photosensitivity, active or recurrent herpes simplex infection, facial warts or molluscum contagiosum, active dermatosis, and those having impractical expectations. ***Number included*** **Number randomised: arm 1** 25 **Number randomised: arm 2** 25 **Number completed: arm 1** 25 **Number completed: arm 2** 25	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <26 weeks **Treatment intensity** Total 6 sessions **Number of arms** 2 **Split face design** No **Intervention: arm 1** 30% salicylic acid peel **Intervention: arm 2** 45% mandelic acid peel **Coded intervention: arm 1** SAL peel **Coded intervention: arm 2** MAND peel **Treatment category** Chemical peels	***Results*** **Skin redness (n/N): arm 1** 9/25 **Skin redness (n/N): arm 2** 2/25 **Pigment changes (n/N): arm 1** 3/25 **Pigment changes (n/N): arm 2** 0/25	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;insufficient information on methods **2. Deviation from intervention** Some concerns;not reported if participants were blinded **3. Missing outcome data (efficacy)** Low;it appears that all participants completed the study **4. Outcome measurement (efficacy)** Low;dermatologist was blinded **5. Selective reporting** Some concerns;Not reported whether there was a pre-registered protocol **6. Overall bias** Some concerns

Study details	Participants	Interventions	Outcomes and results	Comments
Study details **Reference** Dubey, A., Amane, H.Comparison of efficacy and safety of adapalene and benzoyl peroxide-clindamycin combination in the topical treatment of acne vulgaris. 2016. International journal of basic & clinical pharmacology **Trial ID** Dubey 2016 **Country** India **Study type** RCT **Source of funding** No funding sources ***Analysis method*** **Intention to treat or completers analysis** Completers	N=100 ***Characteristics*** **Sex** mixed **age (min/max)** 12/30 **age (other information)** Age (In years) = Number of patients (n = 93) 12-15 = 6 16-19 = 30 20-23 = 30 24-27 = 15 28-31 = 12 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Indian Grading Scale **Inclusion details** Male and non-pregnant participants aged between 12 and 30 years.Participants with mild to moderate acne vulgaris; based on simple acne grading scale (grade 1 to grade 4).Participants with only comedones as noninflammatory lesions, and papules and pustules as inflammatory lesions were included in the study (mild to moderate acne vulgaris- grades 1 and 2). **Exclusion details** Presence of severe inflammatory lesions of acne like nodulo-cystic lesions (grades 3 and 4).Use of any other drug for the treatment of acne vulgaris within 1 month ***Number included*** **Number randomised: arm 1** 50 **Number randomised: arm 2**	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <26 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** adapalene (0.1%) o.d. **Intervention: arm 2** benzoyl peroxide (2.5%) clindamycin (1%) combination o.d. **Coded intervention: arm 1** ADAP-topical **Coded intervention: arm 2** BPO-topical + CLIND-topical **Treatment category** Topical retinoids ± other treatment	***Results*** **Skin irritation (n/N): arm 1** 1/47 **Skin irritation (n/N): arm 2** 1/46	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;methods not reported **2. Deviation from intervention** High;open-label; not reported if ITT analysis was done **3. Missing outcome data (efficacy)** High;more than 5% discontinued in both arms **4. Outcome measurement (efficacy)** High;open-label **5. Selective reporting** Some concerns;Not reported whether there was a pre-registered protocol **6. Overall bias** High

Study details	Participants	Interventions	Outcomes and results	Comments
	50 **Number completed: arm 1** 47 **Number completed: arm 2** 46			
Study details **Reference** Eichenfield, L. F. L., T.,Frankel, E. H.,Jones, T. M.,Chang-Lin, J. E.,Berk, D. R.,Ruan, S.,Kaoukhov, A.Efficacy and safety of once-daily dapsone gel, 7.5% for treatment of adolescents and adults with acne vulgaris: Second of two identically designed, large, multicenter, randomized, vehicle-controlled trials. 2016. Journal of Drugs in Dermatology **Trial ID** Eichenfield 2016 **Country** North America **Study type** RCT **Source of funding** Industry funded ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** na	N=2238 ***Characteristics*** **Sex** mixed **age (mean±SD)** 20.45±7.77 **age (median)** 18 **age (min/max)** 12/61 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Global Acne Assessment Score (GAAS) **Inclusion details** At least 12 years of age, with a diagnosis of acne, with 20–50 facial inflammatory lesions (papules and pustules) and 30–100 facial noninflammatory lesions (open and closed comedones), and with an acne grade of 3 (indicating moderate severity) on the Global Acne Assessment Score (GAAS) at screening and at baseline. **Exclusion details** A diagnosis of severe cystic acne, acne conglobata, acne fulminans, or secondary acne; any nodule or cyst above the mandibular line; use of systemic therapy, including anti-inflammatory drugs within 2 weeks of screening, antibiotics within 4 weeks of screening, and isotretinoin or anti-	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** Topical dapsone 7.5% gel o.d. **Intervention: arm 2** Topical vehicle o.d. **Coded intervention: arm 1** DAPS-topical **Coded intervention: arm 2** Vehicle **Treatment category** Topical non-retinoids ± other treatment	***Results*** **Skin irritation (n/N): arm 1** 19/1117 **Skin irritation (n/N): arm 2** 11/1118	***Cochrane RoB Tool v2.0*** **1. Randomisation** Low;randomisation in a 1:1 ratio and stratified by sex; an interactive voice or web response system was used by study staff to obtain participant numbers and corresponding medication kit numbers **2. Deviation from intervention** Some concerns;double-blinded but not clear who was blinded; ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;more than 5% discontinued in both arms (8.2% dapsone gel; 8.3% vehicle) - similar between arms (most lost to follow-up) **4. Outcome measurement (efficacy)**

Study details	Participants	Interventions	Outcomes and results	Comments
	androgens within the previous 6 months; existence of skin abnormalities other than acne, excessive hair, or other physical characteristics in or around the test sites that could confound study results; other clinically significant findings or conditions that could, in the investigator's opinion, confound the study or interfere with study participation; topical procedures, such as use of phototherapy or energy-based devices, or cosmetic procedures within 1 week of screening, or use of topical acne treatments, including anti-inflammatory drugs, salicylic acid, corticosteroids, and retinoids, within 2 weeks of screening; and use of oral contraceptives solely for the control of acne or plans to use any systemic therapy that could potentially affect acne during the study. ***Number included*** **Number randomised: arm 1** 1118 **Number randomised: arm 2** 1120 **Number completed: arm 1** 1026 **Number completed: arm 2** 1027			Some concerns;not clear who was blinded **5. Selective reporting** Low;registration trial registered with US and Canada clinicaltrials.gov and protocol approved by an institutional review board or independent ethics committee prior to study initiation **6. Overall bias** Some concerns
Study details **Reference** Gollnick, H. P. D., Z.,Glenn, M. J.,Rosoph, L. A.,Kaszuba, A.,Cornelison, R.,Gore, B.,Liu, Y.,Graeber, M.Adapalene-benzoyl peroxide, a unique fixed-dose combination topical gel for the treatment of acne vulgaris: a transatlantic,	N=1670 ***Characteristics*** **Sex** mixed **age (mean±SD)** 19 **age (min/max)** 12/55 ***Inclusion/exclusion criteria*** **Used validated acne scale**	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 4 **Split face design**	***Results*** **Skin irritation (n/N): arm 1** 70/332 **Skin irritation (n/N): arm 2** 47/331 **Skin irritation (n/N): arm 3** 29/350	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;participants randomised in a 1:1:1:1 ratio, but no other information provided on methods **2. Deviation from intervention**

Study details	Participants	Interventions	Outcomes and results	Comments
randomized, double-blind, controlled study in 1670 patients. 2009. British journal of dermatology **Trial ID** Gollnick 2009 **Country** North America/Europe **Study type** RCT **Source of funding** Industry funded ***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** 12 years of age or older with acne vulgaris, having on the face 20–50 inflammatory lesions, 30–100 noninflammatory lesions and an Investigator's Global Assessment (IGA) score of 3, corresponding to moderate acne. **Exclusion details** No more than one active nodule at baseline. Severe acne requiring isotretinoin therapy or other dermatological conditions requiring interfering treatment. Women were excluded if they were pregnant, nursing or planning a pregnancy, as were men with facial hair that would interfere with the assessments. ***Number included*** **Number randomised: arm 1** 419 **Number randomised: arm 2** 418 **Number randomised: arm 3** 415 **Number randomised: arm 4** 418 **Number completed: arm 1** 366 **Number completed: arm 2** 369 **Number completed: arm 3** 363 **Number completed: arm 4** 361	No **Intervention: arm 1** Adapalene 0.1%–BPO 2.5% fixed combination topical gel o.d. **Intervention: arm 2** Adapalene 0.1% topical gel o.d. **Intervention: arm 3** BPO 2.5% topical gel o.d. **Intervention: arm 4** Vehicle topical o.d. **Coded intervention: arm 1** ADAP-topical + BPO-topical **Coded intervention: arm 2** ADAP-topical **Coded intervention: arm 3** BPO-topical **Coded intervention: arm 4** Vehicle **Treatment category** Topical retinoids ± other treatment	**Skin irritation (n/N): arm 4** 18/341	Low;double-blinded (blinding ensured through providing medication in identical packaging; a third party dispensed the treatment); ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;more than 10% discontinued in all arms (12.6%; 11.7%; 12.5%, 13.6%), reasons provided with most discontinuing through participant request or loss to follow-up; last observation carried forward used; sensitivity analysis conducted **4. Outcome measurement (efficacy)** Low;double-blinded (blinding ensured through providing medication in identical packaging; a third party dispensed the treatment) **5. Selective reporting** Low;registered with ClinicalTrials.gov

Study details	Participants	Interventions	Outcomes and results	Comments
				6. Overall bias Some concerns
Study details **Reference** Guerra-Tapia, A.Effects of benzoyl peroxide 5% clindamycin combination gel versus adapalene 0.1% on quality of life in patients with mild to moderate acne vulgaris: A randomized single-blind study. 2012. Journal of Drugs in Dermatology **Trial ID** Guerra-Tapia 2012 **Country** Spain **Study type** RCT **Source of funding** Industry funded ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	N=168 ***Characteristics*** **Sex** mixed **age (mean±SD)** 19.10±5.3 **age (min/max)** 12/39 ***Inclusion/exclusion criteria*** **Used validated acne scale** yes **Acne scale** Leeds Revised Grading Scale **Inclusion details** Aged 12 to 39 years, with = 15 inflammatory lesions and/ or non-inflammatory lesions but = 3 nodulocystic lesions and an acne grade of = 2.0 and < 7.0 on the Leeds Revised Acne Grading System. **Exclusion details** The use of any significant concomitant medicinal product within the past month that may have affected a patient's acne; a history of photosensitivity; severe systemic disease, including colitis; hypersensitivity to any of the investigational agents or their components; participation in an investigational drug study within 30 days of the baseline visit; pregnancy or breastfeeding; and sexually active patients who were not using medically safe contraception (oral or injectable contraceptives or implants, intrauterine devices, or correctly used barrier methods). Patients using contraceptives containing anti-androgens were excluded, as were those	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** topical BPO % + CLIND 1% o.d. **Intervention: arm 2** Adapalene 0.1% topical gel o.d. **Coded intervention: arm 1** BPO-topical + CLIND-topical **Coded intervention: arm 2** ADAP-topical **Treatment category** Topical retinoids ± other treatment	***Results*** **Skin irritation (n/N): arm 1** 2/83 **Skin irritation (n/N): arm 2** 5/85	***Cochrane RoB Tool v2.0*** **1. Randomisation** Low;participants randomised on a 1:1 ratio using a computer-generated table of random numbers; study treatments correlated with a participant number; participant numbers were allocated in strict ascending numerical order with no numbers omitted **2. Deviation from intervention** Some concerns;participants were not blinded because of treatment differences in appearance and size of tubes - participants were instructed to keep study treatment confidential; "unblinded pharmacists dispensed study products." ITT analysis was done **3. Missing outcome data (efficacy)**

Study details	Participants	Interventions	Outcomes and results	Comments
	using oral or topical steroids or any type of oral treatment that may have interfered with acne. Patients who had used any form of topical treatment for acne (including natural or UV light) in the 2 weeks before enrollment were also excluded, and those using oral isotretinoin needed to have discontinued this agent 6 month before enrollment. ***Number included*** **Number randomised: arm 1** 83 **Number randomised: arm 2** 85 **Number completed: arm 1** 56 **Number completed: arm 2** 58			Some concerns;more than 30% discontinued in both arms, mainly because participants considered themselves cured or were lost to follow-up **4. Outcome measurement (efficacy)** Low;investigator-blinded **5. Selective reporting** Low;registered with ClinicalTrials.gov **6. Overall bias** Some concerns
Study details **Reference** Hajheydari, Z. M., M.,Vahidshahi, K.,Nozari, A.Comparison of efficacy of Azithromycin vs. Clindamycin and erythromycin in the treatment of mild to moderate acne vulgaris. 2011. Pakistan Journal of Medical Sciences **Trial ID** Hajheydari 2011 **Country** Iran, Islamic Republic of **Study type** RCT **Source of funding** Not industry funded	N=96 ***Characteristics*** **Sex** mixed **age (mean±SD)** 19.53±3.45 **age (min/max)** 12/28 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** Aged 12-28 years with mild to moderate acne vulgaris **Exclusion details** Patients using any kind of acne treatment in	***Interventions*** **Treatment duration (weeks)** 16 **Treatment duration category** 12 to <24 weeks **Number of arms** 3 **Split face design** No **Intervention: arm 1** Topical azithromycin 2% b.d. **Intervention: arm 2** Topical erythromycin 2% b.d. **Intervention: arm 3**	***Results*** **Skin irritation (n/N): arm 1** 10/32 **Skin irritation (n/N): arm 2** 1/32 **Skin irritation (n/N): arm 3** 4/32	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;participants randomised and divided into 3 groups , matched together based on Acne Severity Index; no other details reported **2. Deviation from intervention** Some concerns;double-blinded but it is not clear if participants were blinded (a pharmacist dispensed

Study details	Participants	Interventions	Outcomes and results	Comments
	the previous month, using drugs, and females with polycystic ovarian syndrome were excluded. ***Number included*** **Number randomised: arm 1** 32 **Number randomised: arm 2** 32 **Number randomised: arm 3** 32 **Number completed: arm 1** na **Number completed: arm 2** na **Number completed: arm 3** na	Topical clindamycin 2% b.d. **Coded intervention: arm 1** AZITH-topical **Coded intervention: arm 2** ERYTH-topical **Coded intervention: arm 3** CLIND-topical **Treatment category** Topical non-retinoids ± other treatment		study treatment to maintain blinding); not reported if ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;not clear if all participants completed the study **4. Outcome measurement (efficacy)** Low;assessor were blinded **5. Selective reporting** Some concerns;not reported whether there was a pre-registered protocol **6. Overall bias** Some concerns
Study details **Reference** Hansted, B. J., J.,Reymann, F.,Christiansen, J.Fucidin cream for topical treatment of acne vulgaris. 1985. Current Therapeutic Research - Clinical and Experimental **Trial ID** Hanstead 1985 **Country** Denmark **Study type** RCT **Source of funding**	N=79 ***Characteristics*** **Sex** mixed **age (mean±SD)** 19 **age (min/max)** 14/30 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** Mild to moderate acne vulgaris	***Interventions*** **Treatment duration (weeks)** 8 **Treatment duration category** 6 to <12 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** Topical fucidin cream 2% **Intervention: arm 2**	***Results*** **Skin irritation (n/N): arm 1** 1/36 **Skin irritation (n/N): arm 2** 0/34	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;methods not reported **2. Deviation from intervention** Some concerns;double-blinded but not clear who was blinded; not reported if ITT analysis was done **3. Missing outcome**

Study details	Participants	Interventions	Outcomes and results	Comments
Industry funded ***Analysis method*** **Intention to treat or completers analysis** completers	**Exclusion details** - ***Number included*** **Number randomised: arm 1** 40 **Number randomised: arm 2** 39 **Number completed: arm 1** 36 **Number completed: arm 2** 34	Topical placebo cream **Coded intervention: arm 1** FCA-topical **Coded intervention: arm 2** PLC-topical **Treatment category** Topical non-retinoids ± other treatment		**data (efficacy)** Some concerns;10% participants receiving fusidin discontinued and 12.8% receiving placebo) , most due to not attending for control examinations, although 2 (5.1%) participants in the placebo group discontinued because of aggravation of their acne **4. Outcome measurement (efficacy)** Some concerns;not clear if blinded **5. Selective reporting** Some concerns;not reported whether there was a pre-registered protocol **6. Overall bias** High
Study details **Reference** Hughes, B. R. N., J. F.,Cunliffe, W. J.A double-blind evaluation of topical isotretinoin 0.05%, benzoyl peroxide gel 5% and placebo in patients with acne. 1992. Clinical & Experimental Dermatology **Trial ID**	N=77 ***Characteristics*** **Sex** mixed **age (mean±SD)** 18.7 **age (min/max)** 14/29 ***Inclusion/exclusion criteria*** **Used validated acne scale**	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 3 **Split face design**	***Results*** **Skin irritation (n/N): arm 1** 10/25 **Skin irritation (n/N): arm 2** 10/26 **Skin irritation (n/N): arm 3** 1/26	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;random allocation stratified for sex, age, duration and severity of acne; no other methods reported **2. Deviation from**

Study details	Participants	Interventions	Outcomes and results	Comments
Hughes 1992 **Country** United Kingdom **Study type** RCT **Source of funding** Not industry funded ***Analysis method*** **Intention to treat or completers analysis** completers	no **Acne scale** None **Inclusion details** 15-100 inflamed and/or 15-100 non-inflamed lesions but no more than three nodulocystic lesions on the face **Exclusion details** Pregnant females and those using antiandrogen contraceptives were exclude ***Number included*** **Number randomised: arm 1** 25 **Number randomised: arm 2** 26 **Number randomised: arm 3** 26 **Number completed: arm 1** 24 **Number completed: arm 2** 24 **Number completed: arm 3** 25	No **Intervention: arm 1** Topical isotretinoin 0.05% b.d. **Intervention: arm 2** Topical BPO 5% b.d. **Intervention: arm 3** Vehicle b.d. **Coded intervention: arm 1** ISO-topical **Coded intervention: arm 2** BPO-topical **Coded intervention: arm 3** Vehicle **Treatment category** Topical retinoids ± other treatment		**intervention** Some concerns;double-blinded but not clear who was blinded; not reported if ITT analysis was done **3. Missing outcome data (efficacy)** High;8% participants receiving isotretinoin withdrew because of side effects; 3.8% in the placebo group because of lack of efficacy; 7.7% in the benzoyl peroxide group because of side effects or lack of efficacy **4. Outcome measurement (efficacy)** Some concerns;not clear who was blinded **5. Selective reporting** Some concerns;not reported whether there was a pre-registered protocol **6. Overall bias** High
Study details **Reference** Iftikhar, U. A., S.,Nadeem, M.,Kazmi, A. H.A comparison of efficacy and safety of	N=200 ***Characteristics*** **Sex** mixed	***Interventions*** **Treatment duration (weeks)** 24 **Treatment duration**	***Results*** **Skin irritation (n/N): arm 1** 66/100 **Skin irritation (n/N): arm**	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;randomisati

Study details	Participants	Interventions	Outcomes and results	Comments
topical 0.1% adapalene and 4% benzoyl peroxide in the treatment of mild to moderate acne vulgaris. 2009. J pak assoc derma **Trial ID** Iftikhar 2009 **Country** Pakistan **Study type** RCT **Source of funding** Unstated ***Analysis method*** **Intention to treat or completers analysis** completers	**age (mean±SD)** 20.895±4.3 **age (min/max)** 13/32 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** More than 13 years of age, with mild to moderate acne (comedones, papulopustules and few nodules with no scarring) and free of intercurrent illness **Exclusion details** No other topical medication for acne during the last 2 weeks or oral medications during the last 4 weeks. Pregnant and lactating female patients. ***Number included*** **Number randomised: arm 1** na **Number randomised: arm 2** na **Number completed: arm 1** 100 **Number completed: arm 2** 100	**category** 24+ weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** 0.1% ADAP topical o.d. **Intervention: arm 2** 4% BPO topical o.d. **Coded intervention: arm 1** ADAP-topical **Coded intervention: arm 2** BPO-topical **Treatment category** Topical retinoids ± other treatment	**2** 68/100	on using random number tables, no other methods reported **2. Deviation from intervention** High;open trial; ITT analysis was not done **3. Missing outcome data (efficacy)** High;10% discontinued, not reported how many in which arm **4. Outcome measurement (efficacy)** High;open-labeled **5. Selective reporting** Some concerns;not reported whether there was a pre-registered protocol **6. Overall bias** High
Study details **Reference** Jain, V. K. C., K. L.,Dayal, S.Comparative evaluation of topical benzoyl peroxide, metronidazole and benzoyl peroxide - clindamycin combination in treatment of acne vulgaris. 1998. Indian	N=40 ***Characteristics*** **Sex** Mixed **age (min/max)** 16/22 ***Inclusion/exclusion criteria*** **Used validated acne scale**	***Interventions*** **Treatment duration (weeks)** 8 **Treatment duration category** 6 to <12 weeks **Number of arms**	***Results*** **Skin irritation (n/N): arm 1** 3/20 **Skin irritation (n/N): arm 2** 3/20	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;methods not reported **2. Deviation from intervention** Some

Study details	Participants	Interventions	Outcomes and results	Comments
journal of dermatology, venerology and leprology **Trial ID** Jain 1998 **Country** India **Study type** RCT **Source of funding** Not industry funded ***Analysis method*** **Intention to treat or completers analysis** Completers	No **Acne scale** None **Inclusion details** Moderately severe acne, with lesions on the face **Exclusion details** Patients on antiacne treatment within one month or having serious concomitant illness or endocrinal problems like hirsutism, menstrual dysfunction, diabetes or females on oral contraceptives ***Number included*** **Number randomised: arm 1** 20 **Number randomised: arm 2** 20 **Number completed: arm 1** 20 **Number completed: arm 2** 20	2 **Split face design** No **Intervention: arm 1** 5% benzoyl peroxide topical and 1% metronidazole gel o.d. **Intervention: arm 2** 5% benzoyl peroxide topical and 1% clindamycin gel o.d. **Coded intervention: arm 1** BPO-topical + MET-topical **Coded intervention: arm 2** BPO-topical + CLIND-topical **Treatment category** Topical non-retinoids ± other treatment		concerns;blinding not reported **3. Missing outcome data (efficacy)** Low;it appears that all participants completed the study **4. Outcome measurement (efficacy)** Some concerns;blinding not reported **5. Selective reporting** Some concerns;not reported whether there was a pre-registered protocol **6. Overall bias** Some concerns
Study details **Reference** Jaisamrarn, U. C., S.,Angsuwathana, S.,Nerapusee, O.A comparison of multiphasic oral contraceptives containing norgestimate or desogestrel in acne treatment: A randomized trial. 2014. Contraception **Trial ID** Jaisamrarn 2014 **Country** Thailand	N=201 ***Characteristics*** **Sex** female **age (mean±SD)** 30.2±6.15 ***Inclusion/exclusion criteria*** **Used validated acne scale** No **Acne scale** None **Inclusion details** Healthy females aged between 18 and 45 years with mild to moderate acne vulgaris -	***Interventions*** **Treatment duration (weeks)** 26 **Treatment duration category** 24+ weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** triphasic EE/NGM treatment at the	***Results*** **Breast tenderness (n/N): arm 1** 5/100 **Breast tenderness (n/N): arm 2** 9/101 **Neurological side effects (n/N): arm 1** 5/101 **Neurological side effects (n/N): arm 2** 10/101 **Breakthrough bleeding**	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;participants randomly assigned to treatment on a 1:1 ratio using pre-generated permuted block randomisation sheme; methods not reported for allocation concealment **2. Deviation from intervention**

Study details	Participants	Interventions	Outcomes and results	Comments
Study type RCT **Source of funding** Not industry funded ***Analysis method*** **Intention to treat or completers analysis** completers	defined as having no more than 5 comedones or papules and no pustule while moderate acne vulgaris was defined as 6–15 comedones or papules and/or a maximum of three pustules. **Exclusion details** Subjects who were pregnant or breastfeeding; who had experienced hypersensitivity to EE, NGM, DSG or any of the study medication ingredients; the use of a concomitant medication that was likely to interfere with the safety of EE/NGM and or EE/DSG, the use of topical acne treatments, systemic antimicrobials or a systemic retinoid within 2 weeks, 1 month and 6 months prior to enrollment, respectively; having a contraindication to OCs ***Number included*** **Number randomised: arm 1** 100 **Number randomised: arm 2** 101 **Number completed: arm 1** 93 **Number completed: arm 2** 95	dosage of 0.035/0.18, 0.035/0.215 and 0.035/0.25mg on days 1–7, 8–14 and 15–21, respectively, and took inactive tablets for 7 days before starting the next treatment cycle **Intervention: arm 2** biphasic EE/DSG treatment at the dosage of 0.04/0.025 and 0.03/0.125mg on days 1–7 and 8–22 of each cycle, respectively, and discontinued treatment for 6 days before starting the next treatment cycle **Coded intervention: arm 1** EE-oral+NGM-oral **Coded intervention: arm 2** EE-oral+DSG-oral **Treatment category** Hormonal contraceptives / Hormone-modifying agents	**(n/N): arm 1** 10/100 **Breakthrough bleeding (n/N): arm 2** 7/101	High;"lack of double-blind methodology was this study's important limitation because single-blinded (here, investigator-blinded) studies may be affected by bias"; per-protocol analysis was used for efficacy assessment (ITT analysis used for safety and tolerability) **3. Missing outcome data (efficacy)** High;more than 5% discontinued in both arms because of poor compliance, discomfort from adverse events and loss to follow-up with reason unknown **4. Outcome measurement (efficacy)** Low;investigator-blinded **5. Selective reporting** Low;registered with ClinicalTrials.gov **6. Overall bias** High
Study details **Reference** Jaisamrarn, U. S., S.A	N=180 ***Characteristics*** **Sex**	***Interventions*** **Treatment duration (weeks)**	***Results*** **Breast tenderness (n/N): arm 1**	***Cochrane RoB Tool v2.0*** **1. Randomisation**

Study details	Participants	Interventions	Outcomes and results	Comments
comparison of combined oral contraceptives containing chlormadinone acetate versus drospirenone for the treatment of acne and dysmenorrhea: a randomized trial. 2018. Contraception & Reproductive Medicine **Trial ID** Jaisamrarn 2018 **Country** Thailand **Study type** RCT **Source of funding** Not industry funded ***Analysis method*** **Intention to treat or completers analysis** ITT	female **age (mean±SD)** 27.85±6.55 ***Inclusion/exclusion criteria*** **Used validated acne scale** No **Acne scale** None **Inclusion details** Healthy women between the ages of 18 to 45 years with mild to moderate acne vulgaris and who had dysmenorrhea of any degree of severity. Mild acne vulgaris was defined as having comedones as the main type of acne lesion with < 10 papules and pustules. Moderate acne was defined as having 10–40 papules and pustules, 10–40 comedones, and/or mild truncal disease. **Exclusion details** Women who were pregnant, lactating and/or had any hypersensitivity to the study medication were excluded from the study. Subjects with any coexisting medical condition or were taking any concomitant medication that is likely to interfere with the safe administration of EE/CMA or EE/DRSP as per the opinion of the investigator were also excluded from the study. Other exclusion criteria included the use of systemic retinoids within 6 months, systemic antimicrobials within 1 month, topical acne treatment within 2 weeks prior to study enrollment and having a contraindication to OCs. ***Number included*** **Number randomised: arm 1** 90 **Number randomised: arm 2** 90	26 **Treatment duration category** 24+ weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** EE/CMA at the dosage of 30 mcg/2 mg once daily; treatment was for 21 consecutive days, starting on the first day of the menstruation, followed by 7 days of medication free before starting the next cycle of treatment. **Intervention: arm 2** received EE/DRSP at the dosage of 30 mcg/3 mg once daily; treatment was for 21 consecutive days, starting on the first day of the menstruation, followed by 7 days of medication free before starting the next cycle of treatment **Coded intervention: arm 1** EE-oral + CMA-oral **Coded intervention: arm 2** EE-oral + DROS-oral	12/90 **Breast tenderness (n/N): arm 2** 12/90 **Neurological side effects (n/N): arm 1** 6/90 **Neurological side effects (n/N): arm 2** 9/90 **Breakthrough bleeding (n/N): arm 1** 0/90 **Breakthrough bleeding (n/N): arm 2** 2/90	Some concerns;participants randomly assigned to treatment on a 1:1 ratio using computer-generated randomisation sheme; methods not reported for allocation concealment **2. Deviation from intervention** Some concerns;single-blinded (investigator); ITT analysis was done **3. Missing outcome data (efficacy)** Low;less than 5% discontinued **4. Outcome measurement (efficacy)** Low;investigator-blinded **5. Selective reporting** Some concerns;registered on the Thai Clinical Trial Registry, but registered retrospectively **6. Overall bias** Some concerns

Study details	Participants	Interventions	Outcomes and results	Comments
	Number completed: arm 1 89 **Number completed: arm 2** 89	**Treatment category** Hormonal contraceptives / Hormone-modifying agents		
Study details **Reference** Katsambas, A. G., K.,Stratigos, J.Clinical studies of 20% azelaic acid cream in the treatment of acne vulgaris. Comparison with vehicle and topical tretinoin. 1989. Acta Dermato-Venereologica, Supplement **Trial ID** Katsambas 1989;Trial 1 **Country** Greece **Study type** RCT **Source of funding** Unstated ***Analysis method*** **Intention to treat or completers analysis** Completers	N=92 ***Characteristics*** **Sex** mixed **age (median)** 19 **age (min/max)** 13/34 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Plewig & Kligman **Inclusion details** Papulo-pustular acne (degree II/III of Plewig-Kligmann) **Exclusion details** Multiple large nodules, cysts and draining sinuses ***Number included*** **Number randomised: arm 1** 43 **Number randomised: arm 2** 49 **Number completed: arm 1** 36 **Number completed: arm 2** 44	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** 20% azelaic acid cream **Intervention: arm 2** vehicle **Coded intervention: arm 1** AZE-topical **Coded intervention: arm 2** Vehicle **Treatment category** Topical non-retinoids ± other treatment	***Results*** **Skin irritation (n/N): arm 1** 4/43 **Skin irritation (n/N): arm 2** 1/49	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;methods not reported **2. Deviation from intervention** Some concerns;double-blinding but not clear who was blinded; not reported if ITT analysis was done **3. Missing outcome data (efficacy)** High;11.6% participants discontinued in the azlaic acid group and 6.1% in the vehicle group because of irritant effects or insufficient efficacy **4. Outcome measurement (efficacy)** Some concerns;not clear if blinded **5. Selective reporting** Some concerns;not

Study details	Participants	Interventions	Outcomes and results	Comments
				reported whether there was a pre-registered protocol **6. Overall bias** High
Study details **Reference** Khanna, N.Topical clindamycin hydrochloride 1% in acne vulgaris. 1990. Indian journal of dermatology, venerology and leprology **Trial ID** Khanna 1990 **Country** India **Study type** RCT **Source of funding** Not industry funded ***Analysis method*** **Intention to treat or completers analysis** Comleters	N=26 ***Characteristics*** **Sex** Mixed **age (min/max)** 14/23 ***Inclusion/exclusion criteria*** **Used validated acne scale** No **Acne scale** None **Inclusion details** Moderately severe acne - defined as the presence, on the face (above the jawline) of the subject, of 5-15 inflammatory lesions (IN) but no more than 5 nodulocystic lesions and / or more than 50 non-inflammatory (NI) acne lesions. **Exclusion details** Any anti-acne therapy within the previous 30 days. Female patients currently taking any oral contraceptives or pregnant. ***Number included*** **Number randomised: arm 1** na **Number randomised: arm 2** na **Number completed: arm 1** 12 **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** topical clindamycin hydrochloride 1% twice a day **Intervention: arm 2** hydro-alcoholic vehicle twice a day **Coded intervention: arm 1** CLIND-topical **Coded intervention: arm 2** Vehicle **Treatment category** Topical non-retinoids ± other treatment	***Results*** **Skin irritation (n/N): arm 1** 2/12 **Skin irritation (n/N): arm 2** 3/14	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;methods not reported **2. Deviation from intervention** Low;double-blinded but not clear who was blinded; not reported if ITT analysis was done **3. Missing outcome data (efficacy)** High;10% dropouts - not reported how many participants were randomised in each arm, no reasons **4. Outcome measurement (efficacy)** Some concerns;not clear **5. Selective reporting** Some concerns;not reported whether there was a pre-registered protocol **6. Overall bias** High

Study details	Participants	Interventions	Outcomes and results	Comments
Study details **Reference** Langner, A. S., W.,Donald, A. E.,Boorman, G. C.Double-blind, placebo-controlled study of the efficacy and safety of isotretinoin cream (0.05% w/w and 0.10% w/w) with sunscreens in the treatment of mild to moderate acne vulgaris. 2000. Journal of Dermatological Treatment **Trial ID** Langner 2000 **Country** Poland **Study type** RCT **Source of funding** Unstated ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** na	N=127 ***Characteristics*** **Sex** Mixed **age (mean±SD)** 18.6 **age (min/max)** 12/42 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** None **Inclusion details** Acne vulgaris of the face (15–100 inflammatory lesions and/or 15–100 non-inflammatory lesions, but not more than three nodulocystic lesions) **Exclusion details** Pregnant, breast-feeding or sexually active females not using adequate contraception for at least 1 month before the study, not prepared to use adequate precautions during the study and then for at least 1 month after the study were excluded. Also excluded were patients using anti-androgen contraceptives; those who had received oral retinoids during the previous year or steroids or antibiotics (oral or topical) or any other treatment for acne during the previous month; patients receiving any significant concomitant medication; and those with a history of hypersensitivity or idiosyncratic reaction to tretinoin, isotretinoin, sunscreen or any component of the study medication. Patients were also excluded if they had a history of	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 3 **Split face design** No **Intervention: arm 1** isotretinoin 0.05%w/w cream formulated with standard sunscreen **Intervention: arm 2** isotretinoin (0.10%w/w) cream formulated with standard sunscreen **Intervention: arm 3** placebo vehicle sunscreen cream **Coded intervention: arm 1** ISO-topical **Coded intervention: arm 2** ISO-topical **Coded intervention: arm 3** PLC-topical **Treatment category** Topical retinoids ± other treatment	***Results*** **Skin irritation (n/N): arm 1** 4/40 **Skin irritation (n/N): arm 2** 8/40 **Skin irritation (n/N): arm 3** 1/39	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;participants randomised using a pre-determined randomisation schedule; methods not reported for allocation concealment **2. Deviation from intervention** High;double-blinded but not clear who was blinded; ITT analysis was done; major protocol violations (<50% compliance, attendance of <27 +/- 7 days, no-show for more than 35 days after planned visit, not receiving study treatment for 42 days, or using a concomitant medication believed to affect the study results) occurred in 23.8% placebo group, 23.2% in the 0.05% isotretinoin group and 9.5% in the 0.10% isotretinoin group because of

Study details	Participants	Interventions	Outcomes and results	Comments
	photosensitivity, suffered from any systemic disease (for example severe renal or hepatic impairment, cardiovascular or neurological disease) or any skin disease other than acne vulgaris (for example psoriasis, rosacea, allergic rash, or bacterial, viral or fungal infection) which might interfere with the evaluation of the study medication. ***Number included*** **Number randomised: arm 1** 43 **Number randomised: arm 2** 42 **Number randomised: arm 3** 42 **Number completed: arm 1** 33 **Number completed: arm 2** 38 **Number completed: arm 3** 32			**3. Missing outcome data (efficacy)** Some concerns;7% discontinued in 2 arms and 5% in one arm because of lack of efficacy or refusal to co-operate **4. Outcome measurement (efficacy)** Some concerns;not clear **5. Selective reporting** Some concerns;not reported whether there was a pre-registered protocol **6. Overall bias** High
Study details **Reference** Leyden, J. J. S., A. R.,Saatjian, G. D.,Sefton, J.Erythromycin 2% gel in comparison with clindamycin phosphate 1% solution in acne vulgaris. 1987. Journal of the American Academy of Dermatology **Trial ID** Leyden 1987 **Country** United States **Study type**	N=109 ***Characteristics*** **Sex** Mixed **age (mean±SD)** 17.8 **age (min/max)** 14/34 ***Inclusion/exclusion criteria*** **Used validated acne scale** No **Acne scale** None **Inclusion details**	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** 2% erythromycin gel **Intervention: arm 2**	***Results*** **Skin irritation (n/N): arm 1** 6/48 **Skin irritation (n/N): arm 2** 2/47	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;methods not reported **2. Deviation from intervention** Some concerns;single-blinded; not reported if ITT analysis was done **3. Missing outcome data (efficacy)** High;more than 5% of

Study details	Participants	Interventions	Outcomes and results	Comments
RCT **Source of funding** Unstated ***Analysis method*** **Intention to treat or completers analysis** Completers	At least 14 years of age and had to have a minimum of ten but no more than sixty facial papules and pustules, and no more than six facial nodular cystic lesions **Exclusion details** Regular use of oral or topical antibiotics or other effective antiacne medication (for example, benzoyl peroxide or tretinoin) within 30 days of study entry; Use of any topical antiacne agent within 14 days of study entry; treatment with estrogens for 12 weeks or less immediately preceding study entry; or previous treatment with isotretinoin ***Number included*** **Number randomised: arm 1** 55 **Number randomised: arm 2** 54 **Number completed: arm 1** 52 **Number completed: arm 2** 50	clindamycin phosphate 1% solution **Coded intervention: arm 1** ERYTH-topical **Coded intervention: arm 2** CLIND-topical **Treatment category** Topical non-retinoids ± other treatment		participants were excluded (5.45% erythromycin group and 7.4% clindomycin group) because of treatment-unrelated protocol violations, no further details provided; facial lesions (including nodules) were counted at baseline, but analysis of nodule data was not performed because no participant had more than 2 nodules at any time during the study **4. Outcome measurement (efficacy)** Low;investigator-blinded **5. Selective reporting** Some concerns;not reported whether there was a pre-registered protocol **6. Overall bias** High
Study details **Reference** Leyden, J. J. T., E. A.,Miller, B.,Ung, M.,Berson, D.,Lee, J.Once-daily tazarotene 0.1 % gel versus once-daily	N=371 ***Characteristics*** **Sex** Female **age (mean±SD)** 24.9±7.09	***Interventions*** **Treatment duration (weeks)** 26 **Treatment duration category**	***Results*** **Breakthrough bleeding (n/N): arm 1** 45/177 **Breakthrough bleeding (n/N): arm 2**	***Cochrane RoB Tool v2.0*** **1. Randomisation** Low;randomisation using blocks of 4 participants within

Study details	Participants	Interventions	Outcomes and results	Comments
tretinoin 0.1 % microsponge gel for the treatment of facial acne vulgaris: a double-blind randomized trial. 2002. Cutis; cutaneous medicine for the practitioner **Trial ID** Leyden 2002 **Country** United States **Study type** RCT **Source of funding** Industry funded ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	**age (min/max)** 14/48 ***Inclusion/exclusion criteria*** **Used validated acne scale** No **Acne scale** None **Inclusion details** Healthy women, at least 14 years of age, with regular menstrual cycles and moderate facial acne. Moderate facial acne was defined as a total facial count of 6 to 200 noninflammatory comedones, 10 to 75 inflammatory lesions (papules and pustules), and 5 or fewer nodules. Also required a normal Papanicolaou test result within the past 6 months or a low-grade abnormal Papanicolaou test result under medical evaluation, a negative pregnancy test result, and agreement to use a nonhormonal method of contraception if at risk for pregnancy. **Exclusion details** Known contraindications to OCs; cigarette smoking in a woman aged 35 or older; use of injectable estrogens, progestogens, or androgens within the 6 months before enrollment; and use of oral or implantable hormonal contraceptives for 3 months before the study. ***Number included*** **Number randomised: arm 1** 185 **Number randomised: arm 2** 186 **Number completed: arm 1** na	24+ weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** tablets containing 20 g of EE and 100 g of LNG in a 28-day blister pack with 21 days of active medication followed by 7 days of placebo **Intervention: arm 2** Placebo oral **Coded intervention: arm 1** EE-oral + LNG-oral **Coded intervention: arm 2** PLC-oral **Treatment category** Hormonal contraceptives / Hormone-modifying agents	6/177	each study site, according to a computerised randomisation schedule; medication code provided in sealed envelopes labeled according to the randomisation schedule and kept by the investigator **2. Deviation from intervention** Some concerns;double-blinded (participants blinded but not clear who else blinded); ITT analysis was done **3. Missing outcome data (efficacy)** High;more than 30% discontinued (overall) - numbers not reported for each arm; according to the paper significantly more participants in the placebo group than in the active treatment group were lost to follow-up; last observation carried forward used **4. Outcome measurement (efficacy)** Some concerns;not

Study details	Participants	Interventions	Outcomes and results	Comments
	Number completed: arm 2 na			clear (medication code provided in sealed envelopes and kept by the investigator, but not clear whether kept blind until after assessment/analysis) **5. Selective reporting** Some concerns;not reported whether there was a pre-registered protocol **6. Overall bias** High
Study details **Reference** Maleszka R, Turek-Urasinska K, Oremus M, Vukovic J, Barsic B.Pulsed azithromycin treatment is as effective and safe as 2-week longer daily doxycycline treatment of acne vulgaris: a randomized, double-blind, noninferiority study.. 2011. Skinmed **Trial ID** Maleszka 2011 **Country** Poland **Study type** RCT **Source of funding** PLIVA Croatia Ltd. ***Analysis method***	N=240 ***Characteristics*** **Sex** mixed **age (mean±SD)** 20.4 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Unknown, 4-point scale **Inclusion details** 14 years or older with a clinical diagnosis of moderate acne vulgaris. **Exclusion details** Patients with severe acne vulgaris, other facial dermatoses, and other diseases with acne as a part of clinical presentation, and patients with beards and moustaches, and signs of hirsutism. Women of childbearing potential were asked to use reliable methods	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** Azithromycin 500mg o.d. for 3 days in the first week, followed by 500-mg tablets weekly to complete 10 weeks of treatment. **Intervention: arm 2** Doxycycline (Hiramicin) 100-mg	***Results*** **GI side effects (n/N): arm 1** 2/115 **GI side effects (n/N): arm 2** 9/116	***Cochrane RoB Tool v2.0*** **1. Randomisation** Low;participants randomised on a 1:1 ratio and using a computer random number generator to select random blocks; numbers sealed in separate envelopes and centrally packed for distribution **2. Deviation from intervention** Low;double blinded (all study personnel in contact with participants and participants blinded); ITT analysis performed

Study details	Participants	Interventions	Outcomes and results	Comments
Intention to treat or completers analysis Completers	of mechanical contraception, following negative pregnancy test before treatment. ***Number included*** **Number randomised: arm 1** 120 **Number randomised: arm 2** 120 **Number completed: arm 1** 109 **Number completed: arm 2** 115	capsules twice a day on the first day of the treatment, followed by doxycycline 100-mg capsules once a day during 12 weeks of treatment **Coded intervention: arm 1** AZITH-oral **Coded intervention: arm 2** DOXY-oral **Treatment category** Oral antibiotics		**3. Missing outcome data (efficacy)** Low;< 5% withdrawn from each arm in ITT analysis, >5% from each arm withdrawn from per-protocol analysis for similar reasons across groups; last observation carried forward used **4. Outcome measurement (efficacy)** Low; all study personnel in contact with participants were blinded **5. Selective reporting** Some concerns;not reported whether there was a pre-registered protocol **6. Overall bias** Some concerns
Study details **Reference** Marazzi,Clinical evaluation of Double Strength Isotrexin versus Benzamycin in the topical treatment of mild to moderate acne vulgaris. 2002a. Journal of Dermatological Treatment **Trial ID** Marazzi 2002a	N=188 ***Characteristics*** **Sex** Mixed **age (mean±SD)** 17±4.3 **age (min/max)** 12/33 ***Inclusion/exclusion criteria*** **Used validated acne scale**	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design**	***Results*** **Skin irritation (n/N): arm 1** 5/91 **Skin irritation (n/N): arm 2** 3/92 **Participant reported improvement (n/N): arm 1** 90/95	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;randomisation using pre-determined randomisation schedule; methods not reported for allocation

Study details	Participants	Interventions	Outcomes and results	Comments
Country United Kingdom **Study type** RCT **Source of funding** Industry funded ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** na	No **Acne scale** Leeds Grading Scale, Cunliffe **Inclusion details** Facial acne vulgaris having 15–100 in• ammatory lesions and/or 15–100 non-in• ammatory lesions, but not more than three nodulocystic lesions. **Exclusion details** - ***Number included*** **Number randomised: arm 1** 95 **Number randomised: arm 2** 93 **Number completed: arm 1** 74 **Number completed: arm 2** 63	No **Intervention: arm 1** gel containing isotretinoin 0.1%w/w and erythromycin 4.0%w/w in a vehicle of butylated hydroxytoluene, hydroxypropylcellulose and ethanol **Intervention: arm 2** comparator gel contained benzoyl peroxide 5.0%w/w and erythromycin 3.0%w/w **Coded intervention: arm 1** ISO-topical + ERYTH-topical **Coded intervention: arm 2** BPO-topical + ERYTH-topical **Treatment category** Topical retinoids ± other treatment	**Participant reported improvement (n/N): arm 2** 91/93	concealment **2. Deviation from intervention** Some concerns;single-blinded; ITT analysis was done **3. Missing outcome data (efficacy)** High;22% participants from one and 32% from the other arm discontinued because of lack of treatment efficacy, adverse events, refusal to co-operate, development of exclusion criteria and other reasons **4. Outcome measurement (efficacy)** Low;investigator-blinded **5. Selective reporting** Some concerns;not reported whether there was a pre-registered protocol **6. Overall bias** High
Study details **Reference** Milani, M. B., A.,Zavattarelli, M.Efficacy and safety of stabilised hydrogen peroxide cream (Crystacide) in mild-	N=60 ***Characteristics*** **Sex** Mixed **age (mean±SD)**	***Interventions*** **Treatment duration (weeks)** 8 **Treatment duration**	***Results*** **Skin irritation (n/N): arm 1** 2/30 **Skin irritation (n/N): arm**	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;methods not reported

Study details	Participants	Interventions	Outcomes and results	Comments
to-moderate acne vulgaris: A randomised, controlled trial versus benzoyl peroxide gel. 2003. Current Medical Research and Opinion **Trial ID** Milani 2003 **Country** Italy **Study type** RCT **Source of funding** Not industry funded ***Analysis method*** **Intention to treat or completers analysis** Completers	25±6 ***Inclusion/exclusion criteria*** **Used validated acne scale** No **Acne scale** None **Inclusion details** 15-35 years with mild to moderate acne vulgaris, defined as at least 10 inflammatory lesions and 10 non-inflamatory lesions, and no more than two nodulo-cystic lesions. **Exclusion details** Acne conglobata, severe acne, or otherwise requiring more than topical treatment ***Number included*** **Number randomised: arm 1** 30 **Number randomised: arm 2** 30 **Number completed: arm 1** 30 **Number completed: arm 2** 30	**category** 6 to <12 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** Hydrogen peroxide gel (Crystacide 1%) **Intervention: arm 2** Benzoyl peroxide gel (PanOxyl 4%) **Coded intervention: arm 1** HPS-topical **Coded intervention: arm 2** BPO-topical **Treatment category** Topical non-retinoids ± other treatment	**2** 7/30	**2. Deviation from intervention** Some concerns;single-blinded; ITT analysis was done **3. Missing outcome data (efficacy)** Low;all participants completed the trial **4. Outcome measurement (efficacy)** Low;investigator-blinded **5. Selective reporting** Some concerns;not reported whether there was a pre-registered protocol **6. Overall bias** Some concerns
Study details **Reference** Ozolins, M. A. E., E.,Avery, P. A. J.,Cunliffe, P. W. J.,Wan Po, P. A. L.,O'Neill, P. C.,Simpson, N. B.,Walters, C. E.,Carnegie, E.,Lewis, J. B.,Dada, J.,Haynes, M.,Williams, K.,Williams, P. H. C.Comparison of five antimicrobial regimens for treatment of mild to moderate	N=649 ***Characteristics*** **Sex** mixed **age (mean±SD)** 19.7±6.1 **age (min/max)** 11/42 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale**	***Interventions*** **Treatment duration (weeks)** 18 **Treatment duration category** 12 to <24 weeks **Number of arms** 5 **Split face design** No **Intervention: arm 1**	***Results*** **Skin irritation (n/N): arm 1** 1/131 **Skin irritation (n/N): arm 2** 2/130 **Skin irritation (n/N): arm 3** 3/130 **Skin irritation (n/N): arm 4**	***Cochrane RoB Tool v2.0*** **1. Randomisation** Low;randomisation using a computer-generated randomisation code known only to trial co-ordinator and pharmacy staff; randomisation in blocks of 11, without stratification;

Study details	Participants	Interventions	Outcomes and results	Comments
inflammatory facial acne vulgaris in the community: Randomised controlled trial. 2004. Lancet **Trial ID** Ozolins 2004 **Country** United Kingdom **Study type** RCT **Source of funding** Not industry funded ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF/LOCB	Leeds Grading Scale, Cunliffe **Inclusion details** Mild to moderate acne vulgaris (acne grade 3·0 or less) and at least 15 inflamed and 15 non-inflamed lesions on the face **Exclusion details** Acne that was primarily truncal, nodular, comedonal, or due to secondary causes; pregnancy, breastfeeding, or intention to become pregnant; onset of acne after age 26 years; fear of developing a physical deformity; another dermatological disease of the face; significant systemic disease; previous treatment with oral isotretinoin; current acne treatment from a consultant dermatologist; interacting medication; participation in any other clinical trial within the previous 3 months; and known hypersensitivity to study medications ***Number included*** **Number randomised: arm 1** 131 **Number randomised: arm 2** 130 **Number randomised: arm 3** 130 **Number randomised: arm 4** 127 **Number randomised: arm 5** 131 **Number completed: arm 1** 94 **Number completed: arm 2** 90 **Number completed: arm 3** 92 **Number completed: arm 4**	OXYTETRA-oral 500mg b.d. + PLC-topical **Intervention: arm 2** MINO-oral 100mg + PLC-topical **Intervention: arm 3** BPO- topical 5% + PLC-oral **Intervention: arm 4** Combined formulation of BPO- topical 5%/ERYTH-topical 3%+ PLC-oral **Intervention: arm 5** BPO-topical 5% + ERYTH-topical 2% + PLC-oral **Coded intervention: arm 1** OXYTETRA-oral + PLC-topical **Coded intervention: arm 2** MINO-oral + PLC-topical **Coded intervention: arm 3** BPO-topical + PLC-oral **Coded intervention: arm 4** BPO-topical + ERYTH-topical + PLC-oral **Coded intervention: arm 5** BPO-topical + ERYTH-	2/127 **Skin irritation (n/N): arm 5** 1/131 **GI side effects (n/N): arm 1** 1/131 **GI side effects (n/N): arm 2** 2/130 **GI side effects (n/N): arm 3** 0/130 **GI side effects (n/N): arm 4** 4/127 **GI side effects (n/N): arm 5** 1/131 **Participant reported improvement (mean±SD): arm 1** 72±131 **Participant reported improvement (mean±SD): arm 2** 70±130 **Participant reported improvement (mean±SD): arm 3** 78±130 **Participant reported improvement (mean±SD): arm 4** 84±127 **Participant reported improvement (mean±SD):**	treatments provided in sealed opaque boxes labelled with participant's unique identification number (see 2005 HTA report for full details) **2. Deviation from intervention** Some concerns;ITT used; the authors stated that "participants were not blinded because of the prohibitive costs of manufacturing identical placebos and reformulating the active treatments to make all five interventions look the same however, it was estimated that around half of the participants were unsure of which of their treatments was active" (see 2005 HTA report for full details) **3. Missing outcome data (efficacy)** High;27% withdrew (range 19.7% to 30.8% across treatment groups) because of loss to follow-up, unwilling/unable to

Study details	Participants	Interventions	Outcomes and results	Comments
	102 **Number completed: arm 5** 93	topical + PLC-oral **Treatment category** Oral antibiotics	**arm 5** 82±131	attend visit, exacerbation of acne, adverse events **4. Outcome measurement (efficacy)** Low;Assessors blinded **5. Selective reporting** Low;trial included on the Cochrane skin group trials register **6. Overall bias** High
Study details **Reference** Palombo-Kinne, E. S., I.,Schumacher, U.,Graser, T.Efficacy of a combined oral contraceptive containing 0.030 mg ethinylestradiol/2 mg dienogest for the treatment of papulopustular acne in comparison with placebo and 0.035 mg ethinylestradiol/2 mg cyproterone acetate. 2009. Contraception **Trial ID** Palombo-Kinne 2009 **Country** Europe **Study type** RCT **Source of funding**	N=1338 ***Characteristics*** **Sex** female **age (mean±SD)** 24.4±5.9 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Investigator's Global Assessment scale (IGA) **Inclusion details** Female patients between 16 and 45 years old with mild to moderate papulopustular acne and without contraindications to COC use. Mild to moderate facial papulopustular acne was defined as 10–50 comedones (non-inflammatory lesions), 10–50 papules and pustules together (inflammatory lesions) and not more than three small nodules (inflammatory lesions); a normal	***Interventions*** **Treatment duration (weeks)** 24 **Treatment duration category** 24+ weeks **Number of arms** 3 **Split face design** no **Intervention: arm 1** EE-oral 0.030mg + DNG-oral 2mg **Intervention: arm 2** CPA-oral (2mg) + EE-oral (0.035mg) **Intervention: arm 3** PLC-oral **Coded intervention: arm 1**	***Results*** **Breast tenderness (n/N): arm 1** 8/525 **Breast tenderness (n/N): arm 2** 15/537 **Breast tenderness (n/N): arm 3** na/264 **Neurological side effects (n/N): arm 1** 28/525 **Neurological side effects (n/N): arm 2** 28/537 **Neurological side effects (n/N): arm 3** 14/264 **Breakthrough bleeding (n/N): arm 1**	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;participants randomised on a 2:2:1 ratio, but no other methods reported **2. Deviation from intervention** Low;ITT used; double blinded (double-dummy approach used to maintain participant blinding; not clear who else blinded) **3. Missing outcome data (efficacy)** Low;loss to follow-up or withdrawals

Study details	Participants	Interventions	Outcomes and results	Comments
Industry funded ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	Papanicolaou test result within the past 6 months; use of a non-hormonal method of contraception for sexually active patients **Exclusion details** Presence of known contraindications to OCs; smoking, if age at inclusion is N30 years; pregnancy and lactation (at least three regular cycles were to elapse before start of treatment); and a body mass index N30 kg/m2. Dermatological exclusion criteria were as follows: other forms of acne and atopy and intake of preparations with known or suspected acne-inducing effects (for example, vitamins B, anabolics, corticoids). ***Number included*** **Number randomised: arm 1** 530 **Number randomised: arm 2** 541 **Number randomised: arm 3** 267 **Number completed: arm 1** 497 **Number completed: arm 2** 512 **Number completed: arm 3** 243	EE-oral + DNG-oral **Coded intervention: arm 2** CPA-oral + EE-oral **Coded intervention: arm 3** PLC-oral **Treatment category** Hormonal contraceptives / Hormone-modifying agents	11/525 **Breakthrough bleeding (n/N): arm 2** na/537 **Breakthrough bleeding (n/N): arm 3** na/264	(reasons provided): 5.3% vs 4.7% vs 8% **4. Outcome measurement (efficacy)** Some concerns;Trial was double blind, but not clear who else was blinded in addition to participants **5. Selective reporting** Some concerns;Not reported whether there was a pre-registered protocol **6. Overall bias** Some concerns
Study details **Reference** Papageorgiou, P. K., A.,Chu, A.Phototherapy with blue (415 nm) and red (660 nm) light in the treatment of acne vulgaris. 2000a. British Journal of Dermatology **Trial ID** Papageorgiou 2000a	N=107 ***Characteristics*** **Sex** mixed **age (mean±SD)** 25.01±na ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale**	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Treatment intensity** 84 sessions as irradiation carried out	***Results*** **Skin irritation (n/N): arm 1** 3/27 **Skin irritation (n/N): arm 2** 1/30 **Skin irritation (n/N): arm 3** 2/25	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;randomisation using a computerised randomisation list; methods not reported for allocation

Study details	Participants	Interventions	Outcomes and results	Comments
Country United Kingdom **Study type** RCT **Source of funding** Unstated ***Analysis method*** **Intention to treat or completers analysis** Completers	Unclear **Inclusion details** Mild to moderate acne, age ranging from 14 to 50 years, otherwise healthy **Exclusion details** Patients who were pregnant, on oral contraceptives, had taken oral antibiotics during the previous 2 weeks, and patients whose acne was assessed as very mild (with fewer than five inflammatory lesions) or severe (cystic) ***Number included*** **Number randomised: arm 1** 27 **Number randomised: arm 2** 30 **Number randomised: arm 3** 25 **Number randomised: arm 4** 25 **Number completed: arm 1** 23 **Number completed: arm 2** 25 **Number completed: arm 3** 21 **Number completed: arm 4** 22	daily for 15 minutes **Number of arms** 4 **Split face design** no **Intervention: arm 1** BLU-PT 415nm **Intervention: arm 2** BR-LED 415 and 660nm **Intervention: arm 3** White light control **Intervention: arm 4** BPO-topical 5% **Coded intervention: arm 1** BLU-PT **Coded intervention: arm 2** BR-LED **Coded intervention: arm 3** PLC-physical **Coded intervention: arm 4** BPO-topical **Treatment category** Energy based (light / laser)	**Skin irritation (n/N): arm 4** 8/25	concealment **2. Deviation from intervention** Some concerns;Not blinded; not reported if ITT analysis was done **3. Missing outcome data (efficacy)** High;23% withdrawals or loss to follow-up - main reason in the phototherapy groups was non-compliance on using the light boxes, but no other reasons reported; 9/107 stopped treatment for efficacy reasons (unclear from which treatment arms) **4. Outcome measurement (efficacy)** Low;Assessors blinded **5. Selective reporting** Some concerns;Not reported whether there was a pre-registered protocol **6. Overall bias** High
Study details **Reference** Pazoki-Toroudi, H. N.-K., M.,Tabatabaie, H.,Ajami, M.,Habibey, R.,Shizarpour,	N=126 ***Characteristics*** **Sex** mixed	***Interventions*** **Treatment duration (weeks)** 12	***Results*** **Skin irritation (n/N): arm 1** 3/35	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;Methods not

Study details	Participants	Interventions	Outcomes and results	Comments
M.,Babakoohi, S.,Rahshenas, M.,Firooz, A.Combination of azelaic acid 5% and erythromycin 2% in the treatment of acne vulgaris. 2010. Journal of Dermatological Treatment **Trial ID** Pazoki-Toroudi 2010 **Country** Iran, Islamic Republic of **Study type** RCT **Source of funding** Industry funded ***Analysis method*** **Intention to treat or completers analysis** Completers	**age (mean±SD)** 20.53±2.44 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Unclear, type of lesion x counts scale **Inclusion details** Age between 14 and 40 years, mild-to-moderate forms of acne vulgaris with at least 10 inflammatory lesions on the face (with a maximum of three nodules) **Exclusion details** Patients with other types of acne such as acne conglobata, acne fulminans and acne secondary to pregnancy or lactation; those suffering from other skin diseases such as psoriasis, dermatitis, and papulopustular rosacea, which affect the treatment course; patients with a history of hepatic or kidney disease, allergic drug reaction, malnutrition, or those receiving topical or systemic anti-acne antibiotic therapy within 45 days or isotretinoin within 6 months before the beginning of the study; in addition, anyone taking drugs such as theophyllin, phenytoin, barbiturates, carbamazepine, cyclosporine, warfarin, ergotamine and triazolam within 1 week before the beginning of the study. ***Number included*** **Number randomised: arm 1** na **Number randomised: arm 2** na **Number randomised: arm 3** na **Number randomised: arm 4**	**Treatment duration category** 12 to <24 weeks **Number of arms** 4 **Split face design** no **Intervention: arm 1** Azelaic acid 5% gel **Intervention: arm 2** Erythromycin 2% gel **Intervention: arm 3** Azelaic acid 5% + Erythromycin 2% gel **Intervention: arm 4** Placebo **Coded intervention: arm 1** AZE-topical **Coded intervention: arm 2** ERYTH-topical **Coded intervention: arm 3** AZE-topical+ERYTH-topical **Coded intervention: arm 4** PLC-topical **Treatment category** Topical non-retinoids ± other treatment	**Skin irritation (n/N): arm 2** 5/31 **Skin irritation (n/N): arm 3** 2/40 **Skin irritation (n/N): arm 4** 1/20 **Participant reported improvement (n/N): arm 1** 8/35 **Participant reported improvement (n/N): arm 2** 7/31 **Participant reported improvement (n/N): arm 3** 11/40 **Participant reported improvement (n/N): arm 4** na/20	reported **2. Deviation from intervention** High;double blind (participants and dermatologists); no ITT (placebo group changed to routine treatment after 4 weeks) **3. Missing outcome data (efficacy)** High;16.5% non-placebo participants discontinued because of loss to follow-up - unclear which treatment arm and unclear for placebo group **4. Outcome measurement (efficacy)** High;placebo group outcomes not measured after 4 weeks; dermatologist blinded **5. Selective reporting** High;Not reported whether there was a pre-registered protocol; unclear why placebo group changed to routine treatment, whether this was pre-specified

Study details	Participants	Interventions	Outcomes and results	Comments
	20 **Number completed: arm 1** 35 **Number completed: arm 2** 31 **Number completed: arm 3** 40 **Number completed: arm 4** 20			or because of worsening of participant symptoms **6. Overall bias** High
Study details **Reference** Pazoki-Toroudi, H. N., M. A.,Ajami, M.,Jaffary, F.,Aboutaleb, N.,Nassiri-Kashani, M.,Firooz, A.Combination of azelaic acid 5% and clindamycin 2% for the treatment of acne vulgaris. 2011. Cutaneous and Ocular Toxicology **Trial ID** Pazoki-Toroudi 2011 **Country** Iran, Islamic Republic of **Study type** RCT **Source of funding** Not industry funded ***Analysis method*** **Intention to treat or completers analysis** Completers	N=150 ***Characteristics*** **Sex** mixed **age (mean±SD)** 22.66±2.4 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Unclear, type of lesion x counts scale **Inclusion details** Age between 14 and 40 years, mild-to-moderate forms of acne vulgaris with at least 10 inflammatory lesions on the face . **Exclusion details** Nodulocystic lesions (>3), Other types of acne such as acne conglubata or fulminans and acne secondary to pregnancy or lactation, Other skin diseases such as psoriasis, dermatitis, or papulopustular rosacea that affect the therapeutic course, History of hepatic or kidney disease, Malnutrition, Topical antiacne therapy or systemic therapy with antibiotics 45 days before the beginning of the study, History of allergic reaction to prescribed drugs, Taking	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 3 **Split face design** no **Intervention: arm 1** Azelaic acid 5% gel **Intervention: arm 2** Clindamycin 2% gel **Intervention: arm 3** Azelaic acid + Clindamycin gel **Coded intervention: arm 1** AZE-topical **Coded intervention: arm 2** CLIND-topical **Coded intervention: arm 3**	***Results*** **Skin irritation (n/N): arm 1** 4/45 **Skin irritation (n/N): arm 2** 6/43 **Skin irritation (n/N): arm 3** 3/44	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;Methods not reported **2. Deviation from intervention** Some concerns;double blind (participants and dermatologists); no ITT **3. Missing outcome data (efficacy)** High;16% discontinued (similar across treatment arms); 2 patients for lack of efficacy in AA group, other reasons not reported **4. Outcome measurement (efficacy)** Low;dermatologist blinded

Study details	Participants	Interventions	Outcomes and results	Comments
	drugs such as theophyllin, phenytoin, barbiturates, carbamazepine, cyclosporine, warfarin, ergotamine, and triazolam within 1 week before beginning the study, and Pregnant or lactating patients. ***Number included*** **Number randomised: arm 1** 50 **Number randomised: arm 2** 50 **Number randomised: arm 3** 50 **Number completed: arm 1** 45 **Number completed: arm 2** 43 **Number completed: arm 3** 44	AZE-topical+CLIND-topical **Treatment category** Topical non-retinoids ± other treatment		**5. Selective reporting** Some concerns;Not reported whether there was a pre-registered protocol **6. Overall bias** High
Study details **Reference** Plewig, G. C., W. J.,Binder, N.,Hoschen, K.Efficacy of an oral contraceptive containing EE 0.03 mg and CMA 2 mg (Belara) in moderate acne resolution: a randomized, double-blind, placebo-controlled Phase III trial. 2009. Contraception **Trial ID** Plewig 2009 **Country** Europe **Study type** RCT **Source of funding** Industry funded	N=377 ***Characteristics*** **Sex** women **age (min/max)** 18/40 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Cook **Inclusion details** Women with moderate papulopustular acne of the face (8– 75 papules and/or pustules) aged between 18 and 40 years (smokers up to 30 years) **Exclusion details** Subjects were not allowed to take hormonal	***Interventions*** **Treatment duration (weeks)** 24 **Treatment duration category** 24+ weeks **Number of arms** 2 **Split face design** no **Intervention: arm 1** Ethinyl estradiol 0.03mg + chlormadinone acetate 2mg **Intervention: arm 2** Placebo	***Results*** **Breast tenderness (n/N): arm 1** 61/251 **Breast tenderness (n/N): arm 2** 10/126 **Neurological side effects (n/N): arm 1** 98/251 **Neurological side effects (n/N): arm 2** 41/126 **Change in mood (n/N): arm 1** 17/251 **Change in mood (n/N): arm 2** 5/126	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;participants randomised on a 2:1 ratio, but no other methods reported **2. Deviation from intervention** Some concerns;double blind but not clear who was blinded; ITT analysis appears to have been conducted; 10 participants excluded for non-adherence **3. Missing outcome**

Study details	Participants	Interventions	Outcomes and results	Comments
Analysis method **Intention to treat or completers analysis** ITT **Method of ITT imputation** na	contraception or topical or systemic moderate acne therapy during the trial. Exclusion criteria included systemic moderate acne therapy (for example, with antiandrogens and/or retinoids) during the previous 6 months; hormonal combinations containing antiandrogens, norgestimate or desogestrel during the previous 3 months; oral antibiotic or topical moderate acne treatment during the previous 4 weeks. ***Number included*** **Number randomised: arm 1** 251 **Number randomised: arm 2** 126 **Number completed: arm 1** 214 **Number completed: arm 2** 103	**Coded intervention: arm 1** EE-oral + CMA-oral **Coded intervention: arm 2** PLC-oral **Treatment category** Hormonal contraceptives / Hormone-modifying agents	**Breakthrough bleeding (n/N): arm 1** 22/251 **Breakthrough bleeding (n/N): arm 2** 4/126 **Participant reported improvement (n/N): arm 1** 77/251 **Participant reported improvement (n/N): arm 2** 52/126	**data (efficacy)** Some concerns;discontiuation - 14% in active & 18% in placebo arm. Unclear how many due to efficacy and differences between treatments in those withdrawing because of adverse events (5.6% vs 0.8%) **4. Outcome measurement (efficacy)** Some concerns;not clear **5. Selective reporting** Some concerns;the authors state that the trial protocol was approved by the local ethics committee, but no further details reported **6. Overall bias** High
Study details **Reference** Poli, F. R., V.,Lauze, C.,Adhoute, H.,Morinet, P.Efficacy and safety of 0.1% retinaldehyde/ 6% glycolic acid (diacneal) for mild to moderate acne vulgaris. A multicentre, double-blind, randomized, vehicle-	N=81 ***Characteristics*** **Sex** mixed **age (mean±SD)** 18.65±4.24 ***Inclusion/exclusion criteria*** **Used validated acne scale** no	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2	***Results*** **Participant reported improvement (n/N): arm 1** 37/42 **Participant reported improvement (n/N): arm 2** 25/39	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;Methods not reported **2. Deviation from intervention** Some concerns;double blind

Study details	Participants	Interventions	Outcomes and results	Comments
controlled trial. 2005. Dermatology (basel, switzerland) **Trial ID** Poli 2005 **Country** France **Study type** RCT **Source of funding** Unstated ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	**Acne scale** Unclear, type of lesion x counts scale **Inclusion details** Greasy or normal or combination skin type, with phototypes II–IV, presenting with inflammatory (7–15 lesions) and retentional (15–30 lesions) mild to moderate acne vulgaris **Exclusion details** Patients presenting with a beard, suffering from nodulocystic lesions or secondary acne (occupational, cosmetic or drug induced) or severe acne that required an additional therapy were not included. In addition, subjects could not be included if they suffered from systemic disease, had potential allergy or required topical or systemic therapy that might interfere with the study as well as pregnant or nursing females or subjects under oral contraception lasting for less than 3 months or including cyproterone acetate. ***Number included*** **Number randomised: arm 1** 42 **Number randomised: arm 2** 39 **Number completed: arm 1** 32 **Number completed: arm 2** 29	**Split face design** no **Intervention: arm 1** Diacneal (0.1% retinaldehyde and 6% glycolic acid) **Intervention: arm 2** Vehicle **Coded intervention: arm 1** DIACNEAL topical **Coded intervention: arm 2** Vehicle **Treatment category** Chemical peels		but not clear who blinded; around 10% temporary discontinuation of treatment in active arm **3. Missing outcome data (efficacy)** High;discontinuation 30% - Unclear how many due to efficacy. Not all randomised patients included in ITT. **4. Outcome measurement (efficacy)** Some concerns;not clear **5. Selective reporting** Some concerns;Not reported whether there was a pre-registered protocol **6. Overall bias** High
Study details **Reference** Rademaker, M. W., J. M.,Birchall, N. M.Isotretinoin 5 mg daily for low-grade adult acne vulgaris - A placebo-controlled,	N=58 ***Characteristics*** **Sex** mixed **age (mean±SD)** 38.049999999999997±7.49 **age (min/max)**	***Interventions*** **Treatment duration (weeks)** 16 **Treatment duration category** 12 to <24 weeks	***Results*** **Mucosal or cutaneous changes (n/N): arm 1** 14/23 **Mucosal or cutaneous changes (n/N): arm 2** 2/23	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;study centres randomised independently using a computer-generated

Study details	Participants	Interventions	Outcomes and results	Comments
randomized double-blind study. 2014. Journal of the European Academy of Dermatology and Venereology **Trial ID** Rademaker 2014 **Country** New Zealand **Study type** RCT **Source of funding** Industry funded ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	25/55 ***Inclusion/exclusion criteria*** **Used validated acne scale** yes **Acne scale** Leeds Revised Grading Scale **Inclusion details** 25–55 years of age, with low-grade adult acne - defined as three or more acne lesions/ month on the face, for at least the last 3 months **Exclusion details** Any patients with acne greater than grade 2, by the Modified Leeds Acne Assessment scale. Pregnancy (or unwilling to adopt contraception), breast-feeding, any significant systemic illness, BMI over 35, or any systemic agent likely to influence the patient's acne (including systemic glucocorticoids or antibiotics). Patients were not allowed any topical or systemic anti-acne products in the preceding 4 weeks, or during the study period. Oestrogen and/or progesterone therapy (including levonorgestrel-releasing intrauterine device) was acceptable, but only if on a stable dose for at least 6 months preceding the start of the study. Patients were excluded if they had been on a systemic retinoid in the preceding 6 months. ***Number included*** **Number randomised: arm 1** 29 **Number randomised: arm 2** 29 **Number completed: arm 1** 29 **Number completed: arm 2**	**Number of arms** 2 **Split face design** no **Intervention: arm 1** 5mg isotretinoin once daily **Intervention: arm 2** No treatment for 16 weeks **Coded intervention: arm 1** ISO<120.Daily<0.5 **Coded intervention: arm 2** PLC-oral **Treatment category** Oral isotretinoin		randomisation schedule, no other methods reported **2. Deviation from intervention** High;double-blinded for group 1 (isotretinoin), double-blinded then open label for group 2 (placebo then active treatment); placebo and isotretinoin capsules similar in smell, taste and appearance; protocol deviations reported (n=12, unclear whether similar across treatment groups); ITT analysis was done **3. Missing outcome data (efficacy)** High;around 25% discontinued but not clear how many from which group; not clear how many were randomised to each group; last observation carried forward used to impute data **4. Outcome measurement (efficacy)** Low;all data processed and

Study details	Participants	Interventions	Outcomes and results	Comments
	29			analysed by an independent organisation; to ensure assessor blinding to adverse events, assessments were performed by a study nurse separately **5. Selective reporting** Some concerns;registered with the Australia/New Zealand Clinical Trials Registry (retrospectively due to an administrative error) **6. Overall bias** High
Study details **Reference** Ragab, Magdy A., Hussein, Tarek M., Salem, Mona A.Photodynamic therapy using 5-aminolevulinic acid and intense pulsed light against intense pulsed light alone in the treatment of acne vulgaris. 2014. Journal of the Egyptian Womenâ<U+0080><U+0099>s Dermatologic Society **Trial ID** Ragab 2014 **Country** Egypt	N=25 ***Characteristics*** **Sex** mixed **age (mean±SD)** 19.4 **age (min/max)** 14/39 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Evaluator's Global Severity Scale (EGSS) **Inclusion details** Participants aged 14 years or over.Participants with mild to moderate acne	***Interventions*** **Treatment duration (weeks)** 2 **Treatment duration category** 0 to <6 weeks **Treatment intensity** 2 sessions **Number of arms** 2 **Split face design** No **Intervention: arm 1** PDT using 5-aminolevulinic acid	***Results*** **Skin redness (n/N): arm 1** 14/15 **Skin redness (n/N): arm 2** 8/10 **Pigment changes (n/N): arm 1** 4/15 **Pigment changes (n/N): arm 2** 1/10 **Participant reported improvement (n/N): arm 1** 15/15 **Participant reported improvement (n/N): arm 2**	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;methods not reported for allocation **2. Deviation from intervention** Some concerns;not reported if participants were blinded **3. Missing outcome data (efficacy)** Low;all participants completed the study **4. Outcome measurement**

Study details	Participants	Interventions	Outcomes and results	Comments
Study type RCT **Source of funding** No funding sources ***Analysis method*** **Intention to treat or completers analysis** completers	vulgaris; determined by Evaluator Global Severity score.Score of 2 or 3 on scale before treatment **Exclusion details** Therapy with oral isotretinoin in the past 6 months, the use of topical or systemic antibiotics 2 weeks before the study, photosensitive dermatoses, pregnancy, or lactation ***Number included*** **Number randomised: arm 1** 15 **Number randomised: arm 2** 10 **Number completed: arm 1** 15 **Number completed: arm 2** 10	(ALA) with intense pulsed light (IPL) **Intervention: arm 2** IPL alone **Coded intervention: arm 1** 5ALA-IPL-PDT **Coded intervention: arm 2** IPL **Treatment category** Energy based (light / laser)	8/10	**(efficacy)** Some concerns;not reportedif/who was blinded; it mentioned only that the evaluation of efficacy was based on photographs taken before the first treatment and at follow-up visits. **5. Selective reporting** Some concerns;Not reported whether there was a pre-registered protocol **6. Overall bias** Some concerns
Study details **Reference** Rassai, S. M., M.,Yaghoobi, R.,Sina, N.,Mohebbipour, A.,Feily, A.Superior efficacy of azithromycin and levamisole vs. azithromycin in the treatment of inflammatory acne vulgaris: An investigator-blind randomized clinical trial in 169 patients. 2013. International Journal of Clinical Pharmacology and Therapeutics **Trial ID** Rassai 2013 **Country** Iran, Islamic Republic of	N=144 ***Characteristics*** **Sex** mixed **age (min/max)** 12/34 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Unclear, type of lesion x counts scale **Inclusion details** Inflammatory acne vulgaris, at least 20 comodones, or with nodules or cysts disregarding the number of comodomes. **Exclusion details** Using any type of systemic treatment for acne, any hematological, renal or hepatic	***Interventions*** **Treatment duration (weeks)** 8 **Treatment duration category** 6 to <12 weeks **Number of arms** 2 **Split face design** no **Intervention: arm 1** 500mg azithromycin/day, 3 days a week + oral levamisole 150mg/day, 2 days a week **Intervention: arm 2**	***Results*** **Skin irritation (n/N): arm 1** 1/76 **Skin irritation (n/N): arm 2** 0/77 **GI side effects (n/N): arm 1** 2/76 **GI side effects (n/N): arm 2** 11/77 **Participant reported improvement (n/N): arm 1** 16/76 **Participant reported improvement (n/N): arm 2**	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;randomisation using simple random table, no other methods reported **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;not reported how

Study details	Participants	Interventions	Outcomes and results	Comments
Study type RCT **Source of funding** Not industry funded ***Analysis method*** **Intention to treat or completers analysis** Completers	disease, were pregnant or lactating, had drug-induced acne, or were using alcohol, anti-convulsants or anti-coagulants ***Number included*** **Number randomised: arm 1** na **Number randomised: arm 2** na **Number completed: arm 1** 74 **Number completed: arm 2** 74	500mg azithromycin/day, 3 days a week **Coded intervention: arm 1** AZITH-oral+LEVA-oral **Coded intervention: arm 2** AZITH-oral **Treatment category** Oral antibiotics	2/77	many were randomised to each arm; overall 12% discontinued because of refusal to continue treatment or because of side effects. **4. Outcome measurement (efficacy)** Low;investigator-blinded **5. Selective reporting** Low;registered in clinicaltrial.gov **6. Overall bias** High
Study details **Reference** Sarkar, R., Ghunawat, S., Garg, V. K.Comparative Study of 35% Glycolic Acid, 20% Salicylic-10% Mandelic Acid, and Phytic Acid Combination Peels in the Treatment of Active Acne and Postacne Pigmentation. 2019. **Trial ID** Sarkar 2019 **Country** India **Study type** RCT **Source of funding** No funding received	N=45 ***Characteristics*** **Sex** mixed **age (mean±SD)** 23.17±na **age (min/max)** 16/38 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Michaelson **Inclusion details** Patients with acne (grade 1 and 2) with postacne hyperpigmentation.Patients with age >12 years **Exclusion details** Patients with active/recurrent herpes	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <26 weeks **Treatment intensity** 6 sessions **Number of arms** 3 **Split face design** no **Intervention: arm 1** 35% glycolic acid peel **Intervention: arm 2** 20% salicylic acid-10% mandelic acid **Intervention: arm 3**	***Results*** **Skin redness (n/N): arm 1** 0/15 **Skin redness (n/N): arm 2** 1/15 **Skin redness (n/N): arm 3** 0/15	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;randomised by random numbers table, methods not reported for allocation **2. Deviation from intervention** Some concerns;not reported if participants were blinded **3. Missing outcome data (efficacy)** Low;it appears that all participants completed the study **4. Outcome**

Study details	Participants	Interventions	Outcomes and results	Comments
Analysis method **Intention to treat or completers analysis** completers	infection.Patients with a history of hypertrophic scarring/keloid.Patients with hypersensitivity to aspirin.Patients with oral isotretinoin intake in the past 6 months.Pregnant and lactating women.Patients refusing consent ***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	Phytic acid **Coded intervention: arm 1** GLY peel **Coded intervention: arm 2** SAL peel + MAND peel **Coded intervention: arm 3** PHY peel **Treatment category** Chemical peels		**measurement (efficacy)** Some concerns;blinding not reported **5. Selective reporting** Some concerns;Not reported whether there was a pre-registered protocol **6. Overall bias** Some concerns
Study details **Reference** Schaller, M., Sebastian, M., Rees, C., Seidel, D., Hennig, M.A multicentre, randomized, single-blind, parallel-group study comparing the efficacy and tolerability of benzoyl peroxide 3%/clindamycin 1% with azelaic acid 20% in the topical treatment of mild-to-moderate acne vulgaris. 2016. Journal of the european academy of dermatology and venereology. 30 (6) (pp 966-973), 2016. Date of publication: 2016.	N=217 ***Characteristics*** **Sex** mixed **age (mean±SD)** 20.10±7 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Investigator's Static Global Assessment (ISGA)/Investigator's global severity Assessment **Inclusion details** 12–45 years old, having facial acne vulgaris (defined as having 17–60 inflammatory lesions [papules and pustules], =1 facial nodular cystic lesion, 20–125 non-	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** no **Intervention: arm 1** Benzoyl peroxide 3% + clindamycin 1% QD **Intervention: arm 2** Azelaic acid 20% BID **Coded intervention:**	***Results*** **Skin irritation (n/N): arm 1** 8/108 **Skin irritation (n/N): arm 2** 25/109	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;randomisation on a 1:1 ratio using computer-generated schedule, no other methods reported **2. Deviation from intervention** Some concerns;single-blinded (participants, site staff responsible for dispensing treatment and individuals involved in

Study details	Participants	Interventions	Outcomes and results	Comments
Trial ID Schaller 2016 **Country** Germany **Study type** RCT **Source of funding** Industry funded ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	inflammatory facial lesions and an Investigator's Static Global Assessment [ISGA] score of 'mild' or 'moderate'). **Exclusion details** Being pregnant (or at risk of becoming pregnant), breastfeeding, a history of non-acne facial disease or severe systemic disease, having received medications that could interfere with the evaluation of the study treatments within the 6 months pre-study (antibiotics, corticosteroids, retinoids), facial procedures within the last month, or known hypersensitivity or allergy to active constituents of the study drugs. ***Number included*** **Number randomised: arm 1** 108 **Number randomised: arm 2** 109 **Number completed: arm 1** 104 **Number completed: arm 2** 102	**arm 1** BPO-topical+CLIND-topical **Coded intervention: arm 2** AZE-topical **Treatment category** Topical non-retinoids ± other treatment		study conduct were not blinded to treatment); ITT and modified ITT analyses were done **3. Missing outcome data (efficacy)** Some concerns;3.7% vs 6.4% discontinued (reasons provided) **4. Outcome measurement (efficacy)** Low;assessor-blinded **5. Selective reporting** Low;registered on clincial trials **6. Overall bias** Some concerns
Study details **Reference** Seaton, E. D. C., A.,Mouser, P. E.,Grace, I.,Clement, R. M.,Chu, A. C.Pulsed-dye laser treatment for inflammatory acne vulgaris: Randomised controlled trial. 2003. Lancet **Trial ID** Seaton 2003 **Country** United Kingdom **Study type**	N=41 ***Characteristics*** **Sex** mixed **age (min/max)** 18/45 **age (other information)** median (IQR) in PDL group: 26 (23-32); in PLC 31 (20-36) ***Inclusion/exclusion criteria*** **Used validated acne scale** yes **Acne scale** Leeds Revised Grading Scale	***Interventions*** **Treatment intensity** 1 session **Number of arms** 2 **Split face design** no **Intervention: arm 1** Pulsed dye laser **Intervention: arm 2** Sham laser **Coded intervention: arm 1** PDL	***Results*** **Skin redness (n/N): arm 1** 1/31 **Skin redness (n/N): arm 2** 0/10 **Skin irritation (n/N): arm 1** 1/31 **Skin irritation (n/N): arm 2** 2/10	***Cochrane RoB Tool v2.0*** **1. Randomisation** Low;randomisation using computer-generated sequence; allocations contained in opaque, sequentially-numbered, sealed envelopes and concealed from participants and assessorrs - only known to investigator

Study details	Participants	Interventions	Outcomes and results	Comments
RCT **Source of funding** Not industry funded ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	**Inclusion details** Aged between 18 and 45 years with mild-to-moderate facial inflammatory acne defined as the presence of at least ten acne papules or pustules between the brow and jawline and an acne severity score of between 2 and 7 on the Leeds revised acne grading system. **Exclusion details** Washout periods for previous treatments were 4 weeks for oral antibiotics, 12 weeks for cyproterone acetatecontaining contraceptives, 52 weeks for oral isotretinoin, and 2 weeks for topical treatments. Acne treatments were not allowed during the study. ***Number included*** **Number randomised: arm 1** 31 **Number randomised: arm 2** 10 **Number completed: arm 1** 27 **Number completed: arm 2** 9	**Coded intervention: arm 2** PLC-physical **Treatment category** Energy based (light / laser)		providing treatment; some differences in baseline characteristics, but not considered excessive **2. Deviation from intervention** Some concerns;double-blinded (participants and assessors blinded); ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;12.9% discontinued from laser treatment (change of residence or need for antibiotic treatment for acne), 10% discontinuation in sham treatment due to dissatisfaction with clinical response **4. Outcome measurement (efficacy)** Low;assessor blinded **5. Selective reporting** High;local ethics committee approved protocol, but no further details provided; some

Study details	Participants	Interventions	Outcomes and results	Comments
				results reported only at 12 weeks after treatment (not at other visits, that is 2, 4, 8 weeks) **6. Overall bias** High
Study details **Reference** Shalita, A. R.Treatment of mild and moderate acne vulgaris with salicylic acid in an alcohol detergent vehicle. 1981. Cutis **Trial ID** Shalita 1981 **Country** United States **Study type** RCT **Source of funding** Industry funded ***Analysis method*** **Intention to treat or completers analysis** Completers	N=49 ***Characteristics*** **Sex** mixed **age (min/max)** 12/20 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Pillsbury **Inclusion details** Teenagers (12 to 20) with mild to moderate acne vulgaris, classed by Pillsbury, Shelly and Kligman grades I or II, with at least fifteen comedones and no more than ten inflammatory lesions. **Exclusion details** Patients with systemic disease; Patients taking antibiotics or oral contraceptives during the study or who had taken them less than one month prior to the start of the study; Patients using scrub cleansers or other topical acne therapy during the study or who had used them less than two weeks prior to entering the study; Patients known to be allergic to any of the ingredients in the test medication; Patients with beards ***Number included*** **Number randomised: arm 1**	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** no **Intervention: arm 1** 0.5% salicylic acid (Stri-Dex medicated pads) **Intervention: arm 2** Placebo **Coded intervention: arm 1** SAL topical **Coded intervention: arm 2** PLC-physical	***Results*** **Patient reported improvement (n/N): arm 1** 18/25 **Participant reported improvement (n/N): arm 2** 8/24	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;treatments were rndomised and coded by the study sponsor, but no other methods reported **2. Deviation from intervention** Some concerns;double-blinded, but not clear whether participants were blinded; unclear if ITT analysis was done **3. Missing outcome data (efficacy)** Low;it looks like all participants were included in the analysis **4. Outcome measurement (efficacy)** Some concerns;blinding not reported **5. Selective**

Study details	Participants	Interventions	Outcomes and results	Comments
	25 **Number randomised: arm 2** 24 **Number completed: arm 1** 25 **Number completed: arm 2** 24			**reporting** Some concerns;Not reported whether there was a pre-registered protocol **6. Overall bias** Some concerns
Study details **Reference** 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 **Trial ID** Shalita 2005 **Country** United States **Study type** RCT **Source of funding** Industry funded ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** na	N=1026 ***Characteristics*** **Sex** mixed **age (mean±SD)** 18.89±6.39 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Investigator's Static Global Assessment (ISGA)/Investigator's global severity Assessment **Inclusion details** 12 years of age or older with mild to moderate facial acne vulgaris and an Investigator's Static Global Assessment (ISGA) score of 2 or greater at baseline. Also a minimum of 17 but no more than 40 facial inflammatory lesions, including nasal lesions, and a minimum of 20, but no more than 150 facial non-inflammatory lesions, excluding nasal lesions. **Exclusion details** Any active nodulo-cystic lesions and those who had used topical or systemic treatment within 4 weeks prior to study entrance. ***Number included*** **Number randomised: arm 1** 386	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 4 **Split face design** no **Intervention: arm 1** Clindamycin foam o.d. **Intervention: arm 2** Vehicle foam o.d. **Intervention: arm 3** Clindamycin gel 1% o.d. **Intervention: arm 4** Vehicle gel o.d. **Coded intervention: arm 1** CLIND-topical **Coded intervention: arm 2** Vehicle **Coded intervention: arm 3** CLIND-topical	***Results*** **Skin irritation (n/N): arm 1** 24/386 **Skin irritation (n/N): arm 2** 9/127 **Skin irritation (n/N): arm 3** 3/385 **Skin irritation (n/N): arm 4** 2/128	***Cochrane RoB Tool v2.0*** **1. Randomisation** Low;randomisation in a 3:1:3:1 ratio and stratified by study site; randomisation codes were sealed and only revealed in emergency **2. Deviation from intervention** Some concerns;authors reported that the study was double-blinded, but not clear who else blinded other than investigators (participants and co-ordinators not blinded); ITT analysis was done **3. Missing outcome data (efficacy)** Some concerns;around 10% participants lost to follow up overall (10.9% vs 10.1% vs

Study details	Participants	Interventions	Outcomes and results	Comments
	Number randomised: arm 2 127 **Number randomised: arm 3** 385 **Number randomised: arm 4** 128 **Number completed: arm 1** 344 **Number completed: arm 2** 112 **Number completed: arm 3** 346 **Number completed: arm 4** 113	**Coded intervention: arm 4** Vehicle **Treatment category** Topical non-retinoids ± other treatment		11.8% vs 11.7%) **4. Outcome measurement (efficacy)** Low;evaluator blinded **5. Selective reporting** Some concerns;Not reported whether there was a pre-registered protocol **6. Overall bias** Some concerns
Study details **Reference** Shwetha, H. G., A.,Revathi, T. N.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 at a tertiary care hospital. 2014. Journal of Chemical and Pharmaceutical Research **Trial ID** Shwetha 2014 **Country** India **Study type** RCT **Source of funding**	N=120 ***Characteristics*** **Sex** mixed **age (mean±SD)** 18.03±1.85 **age (min/max)** 12/25 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Indian Grading Scale **Inclusion details** Mild to moderate acne on face as per Indian Acne Alliance Grading for Severity of acne, aged between 12 to 25 years **Exclusion details** Other variants of acne, drug induced acne, pregnant and lactating mothers and those with history of hypersensitivity to any	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** no **Intervention: arm 1** topical 1% clindamycin + 0.1% adapalene **Intervention: arm 2** topical 1% clindamycin + 2.5% benzoyl peroxide **Coded intervention: arm 1** CLIND-topical+ADAP-	***Results*** **Skin irritation (n/N): arm 1** 59/59 **Skin irritation (n/N): arm 2** 58/58	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;randomisation list using table of random numbers; methods not reported for allocation concealment **2. Deviation from intervention** Some concerns;not reported if participants were blinded; not clear whether ITT analysis was done **3. Missing outcome data (efficacy)** Low;<5% lost to follow up **4. Outcome**

Study details	Participants	Interventions	Outcomes and results	Comments
Not industry funded ***Analysis method*** **Intention to treat or completers analysis** Completers	component of the drug ***Number included*** **Number randomised: arm 1** 60 **Number randomised: arm 2** 60 **Number completed: arm 1** 59 **Number completed: arm 2** 58	topical **Coded intervention: arm 2** CLIND-topical+BPO-topical **Treatment category** Topical retinoids ± other treatment		**measurement (efficacy)** Some concerns;blinding not reported **5. Selective reporting** Some concerns;Not reported whether there was a pre-registered protocol **6. Overall bias** Some concerns
Study details **Reference** Smith, E. B. P., R. S.,McCabe, J. M.,Becker, L. E.Benzoyl peroxide lotion (20 percent) in acne. 1980b. Cutis **Trial ID** Smith 1980b **Country** United States **Study type** RCT **Source of funding** Industry funded ***Analysis method*** **Intention to treat or completers analysis** Completers	N=59 ***Characteristics*** **Sex** mixed **age (mean±SD)** 22.55 **age (min/max)** 18/30 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Unclear, type of lesion x counts scale **Inclusion details** At least ten inflammatory papules and/or pustules and no more than three nodulocystic lesions on the face, otherwise in good health **Exclusion details** Not topical medication for acne during the week before the study, and no oral antibioti cs, oral contraceptives, or systemic corticosteroids for one month before the study began. Also no pregnant women or	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** no **Intervention: arm 1** 20% Benzoyl-peroxide b.d. **Intervention: arm 2** Vehicle b.d. **Coded intervention: arm 1** BPO-topical **Coded intervention: arm 2** Vehicle **Treatment category** Topical non-retinoids	***Results*** **Skin irritation (n/N): arm 1** 21/26 **Skin irritation (n/N): arm 2** 17/25	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;methods not reported **2. Deviation from intervention** Some concerns;double-blinded (participants blinded); not clear if ITT done **3. Missing outcome data (efficacy)** Some concerns;13.8% vs 13.3% discontinued (reasons not reported) **4. Outcome measurement (efficacy)** Low;evaluator blinded **5. Selective**

Study details	Participants	Interventions	Outcomes and results	Comments
	subjects with a history of hypersensitivity to benzoyl peroxide ***Number included*** **Number randomised: arm 1** 29 **Number randomised: arm 2** 30 **Number completed: arm 1** 25 **Number completed: arm 2** 26	± other treatment		**reporting** Some concerns;Not reported whether there was a pre-registered protocol **6. Overall bias** Some concerns
Study details **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 **Source of funding** Industry funded.Galderma Research & Development	N=2102 ***Characteristics*** **Sex** mixed.mixed **age (mean±SD)** 20±7.47±19.58 **age (median)** 17 **age (min/max)** 12/63/12/57 **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.no **Acne scale** Global Acne Assessment Score (GAAS).Investigator's Global Assessment scale (IGA) **Inclusion details** Moderate acne, with 20 to 50 inflammatory lesions (papules and pustules) and 30 to 100 noninflammatory lesions (open and closed comedones) on the face. Patients were also	***Interventions*** **Treatment duration (weeks)** 12.12 **Treatment duration category** 12 to <24 weeks.12 to <24 weeks **Number of arms** 2.3 **Split face design** no.No **Intervention: arm 1** Dapsone gel 7.5%.ADAP 0.3%/BPO 2.5% gel **Intervention: arm 2** Vehicle.ADAP 0.1%/BPO 2.5% gel **Coded intervention: arm 1** DAPS-topical.ADAP-topical + BPO-topical **Coded intervention: arm 2** Vehicle.ADAP-topical	***Results*** **Skin irritation (n/N): arm 1** 11/1044 **Skin irritation (n/N): arm 2** 8/1058	***Cochrane RoB 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)**

Study details	Participants	Interventions	Outcomes and results	Comments
(conflicts of interest reported). ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	required to have an acne grade of 3 (indicating moderate acne) on the Global Acne Assessment Score.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. **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 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** 1044	+ BPO-topical **Treatment category** Topical non-retinoids ± other treatment.Topical or combination **Intervention: arm 3** Vehicle **Coded intervention: arm 3** Vehicle		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 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 participants, but

Study details	Participants	Interventions	Outcomes and results	Comments
	Number randomised: arm 2 1058 **Number completed: arm 1** 948 **Number completed: arm 2** 976 **Number randomised: arm 3** 69 **Number completed: arm 3** 61			no results appear to have been reported;Low **6. Overall bias** Some concerns
Study details **Reference** Stinco, G. B., G.,Trotter, D.,Pillon, B.,Patrone, P.Relationship between sebostatic activity, tolerability and efficacy of three topical drugs to treat mild to moderate acne. 2007. Journal of the European Academy of Dermatology and Venereology **Trial ID** Stinco 2007 **Country** Italy **Study type** RCT **Source of funding** Unstated ***Analysis method*** **Intention to treat or completers analysis** Completers	N=65 ***Characteristics*** **Sex** mixed **age (mean±SD)** 18.25 **age (min/max)** 12/24 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Unclear, type of lesion x counts scale **Inclusion details** Mild or moderate comedonic or papulopustular acne, localized on the face. each patient had a minimum of 20 facial non-inflammatory lesions (open and closed comedones) and 10 inflamed lesions. Also required to be in good health and have not received any oral or topical anti-acne therapy in the 8 weeks prior the study. **Exclusion details** Subjects over the age of 24, patients who were taking systemic drugs of any type of treatment	***Interventions*** **Treatment duration (weeks)** 8 **Treatment duration category** 6 to <12 weeks **Number of arms** 3 **Split face design** no **Intervention: arm 1** Azelaic acid o.d. **Intervention: arm 2** Benzoyl peroxide o.d. **Intervention: arm 3** Adapalene o.d. **Coded intervention: arm 1** AZE-topical **Coded intervention: arm 2** BPO-topical **Coded intervention: arm 3** ADAP-topical	***Results*** **Skin irritation (n/N): arm 1** 1/24 **Skin irritation (n/N): arm 2** 5/18 **Skin irritation (n/N): arm 3** 3/19	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;methods not reported; 20 volunteers also recruited for control group (no details provided) **2. Deviation from intervention** Some concerns;not clear if participants were blinded; not reported if ITT was done **3. Missing outcome data (efficacy)** Some concerns;4% (azelaic acid) vs 10% (BPO) vs 5% (adapalne) vs 20% (control) participants lost to follow up overall **4. Outcome**

Study details	Participants	Interventions	Outcomes and results	Comments
	Number included **Number randomised: arm 1** 25 **Number randomised: arm 2** 20 **Number randomised: arm 3** 20 **Number completed: arm 1** 24 **Number completed: arm 2** 18 **Number completed: arm 3** 19	**Treatment category** Topical retinoids ± other treatment		**measurement (efficacy)** Some concerns;blinding not reported **5. Selective reporting** Some concerns;Not reported whether there was a pre-registered protocol; no outcome data reported on control group **6. Overall bias** High
Study details **Reference** Stoughton, R.R., Leyden, J.J. Efficacy of 4 percent chlorhexidine gluconate skin cleanser in the treatment of acne vulgaris. 1987. Cutis **Trial ID** Stoughton 1987 **Country** United States **Study type** RCT **Source of funding** Unstated ***Analysis method*** **Intention to treat or completers analysis** Completers	N=110 ***Characteristics*** **Sex** mixed **age (mean±SD)** not reported **age (min/max)** not reported ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Unclear, type of lesion x counts scale **Inclusion details** Helathy participants aged between 12 and 35 years and with a minimum of 10 erythematous facial papules and pustules. **Exclusion details** Patients were excluded if they had chronic illness or skin disease other than acne vulgaris (eg, acne conglobata), severe acne	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** no **Intervention: arm 1** Chlorhexidine gluconate skin solution **Intervention: arm 2** Vehicle **Coded intervention: arm 1** CHLOR-topical **Coded intervention:**	***Results*** **Skin irritation (n/N): arm 1** 2/55 **Skin irritation (n/N): arm 2** 1/55	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns; methods not reported for allocation concealment **2. Deviation from intervention** Some concerns; not clear if participants were blinded; not reported if ITT was done **3. Missing outcome data (efficacy)** low concerns; <5% loss to follow-up or withdrawals **4. Outcome measurement (efficacy)**

Study details	Participants	Interventions	Outcomes and results	Comments
	that would require more than topical therapy, systemic treatment with antibiotics or other therapy for acne within one month before entering the study, and pregnancy. ***Number included*** **Number randomised: arm 1** 55 **Number randomised: arm 2** 55 **Number completed: arm 1** 48 **Number completed: arm 2** 45	**arm 2** vehicle **Treatment category** Topical non-retinoids ± other treatment		Low concerns; evaluator blinded **5. Selective reporting** Some concerns; not reported whether there was a pre-registered protocol **6. Overall bias** Some concerns
Study details **Reference** Thiboutot, D., Pariser, D.M., Egan, N., Flores, J., Herndon, J.H. Jr, Kanof, N.B., Kempers, S.E., Maddin, S., Poulin, Y.P., Wilson, D.C., Hwa, J., Liu, Y., Graeber, M. Adapalene Study Group. Adapalene gel 0.3% for the treatment of acne vulgaris: A multicenter, randomized, double-blind, controlled, phase III trial. 2006. J Am Acad Dermatol **Trial ID** Thiboutot 2006 **Country** North America **Study type** RCT **Source of funding** The investigating authors	N=653 ***Characteristics*** **Sex** mixed **age (mean±SD)** 18.2±6.14 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** no scale used **Inclusion details** Participants 12 years or older, with 20 to 100 noninflammatory facial lesions, 20 to 50 inflammatory facial lesions, and no nodules or cysts; specified washout periods were required for participants taking certain topical and systemic treatments. **Exclusion details** Participants with severe acne requiring isotretinoin therapy or other dermatologic conditions requiring interfering treatment; women were excluded if they were pregnant,	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 3 **Split face design** no **Intervention: arm 1** Adapalene 0.1% gel **Intervention: arm 2** Adapalene 0.3% gel **Intervention: arm 2** Vehicle **Coded intervention: arm 1** ADAP-topical **Coded intervention: arm 2** ADAP-topical	***Results*** **Skin irritation (n/N): arm 1** 18/261 **Skin irritation (n/N): arm 2** 36/258 **Skin irritation (n/N): arm 3** 0/134	***Cochrane RoB Tool v2.0*** **1. Randomisation** Low concerns **2. Deviation from intervention** Low concerns; participants blinded; ITT analysis performed **3. Missing outcome data (efficacy)** Some concerns; 10% participants lost to follow up overall **4. Outcome measurement (efficacy)** Low concerns; investigator-blinded **5. Selective reporting** Some concerns; not reported whether

Study details	Participants	Interventions	Outcomes and results	Comments
received payments for this research study; 3 of the authors are employees of Galderma Research and Development ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** not reported	nursing, or planning a pregnancy as well as men with facial hair that would interfere with the assessments. ***Number included*** **Number randomised: arm 1** 261 **Number randomised: arm 2** 258 **Number randomised: arm 3** 134 **Number completed: arm 1** 240 **Number completed: arm 2** 227 **Number completed: arm 2** 120	**Coded intervention: arm 3** Vehicle **Treatment category** Topical retinoids ± other treatment		there was a pre-registered protocol **6. Overall bias** Some concerns
Study details **Reference** Thorneycroft, I. H. G., H.,Schellschmidt, I.Superiority of a combined contraceptive containing drospirenone to a triphasic preparation containing norgestimate in acne treatment. 2004. Cutis **Trial ID** Thorneycroft 2004 **Country** Germany **Study type** RCT **Source of funding** Industry funded ***Analysis method*** **Intention to treat or**	N=1154 ***Characteristics*** **Sex** female **age (mean±SD)** 24.05±5.8 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Unclear, type of lesion x counts scale **Inclusion details** Otherwise healthy female subjects ranging in age from 15 to 40 years without contraindications for combined oral contraceptive use with mild to moderate acne vulgaris, having 6 to 100 comedones (noninflammatory lesions), 10 to 50 papules or pustules together, and not more than 5 nodules on the face (inflammatory lesions).	***Interventions*** **Treatment duration (weeks)** 24 **Treatment duration category** 24+ weeks **Number of arms** 2 **Split face design** no **Intervention: arm 1** 30micrograms ethinyl estradiol + 3milligrams drospirenone **Intervention: arm 2** 35micrograms ethinyl estradiol + 0.18, 0.215, 0.25mg norgestimate **Coded intervention:**	***Results*** **Breast tenderness (n/N): arm 1** 16/566 **Breast tenderness (n/N): arm 2** 17/582 **Neurological side effects (n/N): arm 1** 22/566 **Neurological side effects (n/N): arm 2** 21/582	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;randomisation in 1:1 ratio using computer-generated randomisation list; methods not reported for allocation concealment **2. Deviation from intervention** Some concerns;double-blind but not clear if participants were blinded; full analysis set included, but unclear whether this was ITT analysis

Study details	Participants	Interventions	Outcomes and results	Comments
completers analysis Completers	Normal gynecologic examination and cervical smear within the last 6 months; negative pregnancy test; 3 spontaneous withdrawal bleedings following delivery, abortion, or lactation; and avoidance of comedogenic cosmetics or sunscreens, sex hormone preparations, and antiacne therapy **Exclusion details** Subjects older than 30 years who smoked and those who were pregnant or lactating, acne comedonica or nodulocystic/conglobate acne; acne with multiple large nodes, cysts, fistular comedones, or abscessing fistular ducts; previous acne treatment failure with (antiandrogenic) sex hormone preparations given for at least 3 months; and the need for other medication with known acne-inducing effects, such as lithium, vitamin B1, or corticoids. ***Number included*** **Number randomised: arm 1** 568 **Number randomised: arm 2** 586 **Number completed: arm 1** 533 **Number completed: arm 2** 545	**arm 1** EE-oral + DROS-oral **Coded intervention: arm 2** EE-oral+NGM-oral **Treatment category** Hormonal contraceptives / Hormone-modifying agents		**3. Missing outcome data (efficacy)** Some concerns;discontinuations 6.2% vs 7% due to adverse events, other reasons, withdrawal of consent, protocol deviation, or lack of efficacy (similar across trials) **4. Outcome measurement (efficacy)** Some concerns;blinding not reported **5. Selective reporting** Some concerns;Not reported whether there was a pre-registered protocol **6. Overall bias** High
Study details **Reference** Tirado-Sanchez, A. E., Y. S.,Ponce-Olivera, R. M.,Bonifaz, A.Efficacy and safety of adapalene gel 0.1% and 0.3% and tretinoin gel 0.05% for acne vulgaris: Results of a single-center, randomized, double-blinded,	N=171 ***Characteristics*** **Sex** mixed **age (mean±SD)** 20±6.15 ***Inclusion/exclusion criteria*** **Used validated acne scale** no	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 4	***Results*** **Skin irritation (n/N): arm 1** 5/42 **Skin irritation (n/N): arm 2** 12/42 **Skin irritation (n/N): arm 3**	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;methods not reported **2. Deviation from intervention** Some

Study details	Participants	Interventions	Outcomes and results	Comments
placebo-controlled clinical trial on Mexican patients (skin type III-IV). 2013. Journal of Cosmetic Dermatology **Trial ID** Tirado-Sanchez 2013 **Country** Mexico **Study type** RCT **Source of funding** Unstated ***Analysis method*** **Intention to treat or completers analysis** Completers	**Acne scale** Unclear, type of lesion x counts scale **Inclusion details** 18 years or older with at least ten noninflammatory acne lesions and <30 inflammatory lesions on the entire face. Patients with childbearing potential were required to use birth control and to have a negative pregnancy test result at the beginning of the study **Exclusion details** Patients who had received topical treatment within 1 week prior to inclusion or systemic anti-acne drugs within 2 weeks beforehand were excluded from the study, as were those treated with systemic retinoids within 3 months prior to inclusion or those patients having any concomitant skin conditions on the study area, which could interfere with the study results ***Number included*** **Number randomised: arm 1** 43 **Number randomised: arm 2** 43 **Number randomised: arm 3** 45 **Number randomised: arm 4** 40 **Number completed: arm 1** 42 **Number completed: arm 2**	**Split face design** no **Intervention: arm 1** Adapalene 0.1% gel **Intervention: arm 2** Adapalene 0,3% gel **Intervention: arm 3** Tretinoin 0.05% gel **Intervention: arm 4** Placebo gel **Coded intervention: arm 1** ADAP-topical **Coded intervention: arm 2** ADAP-topical **Coded intervention: arm 3** TRET-topical **Coded intervention: arm 4** PLC-topical **Treatment category** Topical retinoids ± other treatment	15/43 **Skin irritation (n/N): arm 4** na/na	concerns;double-blinded but not clear if participants were blinded; not reported if ITT was done **3. Missing outcome data (efficacy)** Low;<5% loss to follow-up or withdrawals **4. Outcome measurement (efficacy)** Some concerns;blinding not reported **5. Selective reporting** Some concerns;Not reported whether there was a pre-registered protocol **6. Overall bias** Some concerns

Study details	Participants	Interventions	Outcomes and results	Comments
	42 **Number completed: arm 3** 43 **Number completed: arm 4** 37			
Study details **Reference** Trifu, V. T., G. S.,Naumescu, E.,Zalupca, L.,Moro, L.,Celasco, G.Cortexolone 17alpha-propionate 1% cream, a new potent antiandrogen for topical treatment of acne vulgaris. A pilot randomized, double-blind comparative study vs. placebo and tretinoin 0.05% cream. 2011. British Journal of Dermatology **Trial ID** Trifu 2011 **Country** Romania **Study type** RCT **Source of funding** Industry funded ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	N=47 ***Characteristics*** **Sex** men **age (mean±SD)** 20.82±3.1 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Investigator's Global Assessment scale (IGA) **Inclusion details** White-skinned men with acne vulgaris of the face of mild-to-moderate severity, with a score of 2 or 3 on IGA, and with TLC between 20 and 100, and ILC between 10 and 50. **Exclusion details** Women, presence of facial lesions other than acne vulgaris, use of systemic antiacne medications or any kind of light treatment in the month before starting the study, or topical application of acne medications in the last 2 weeks, history of hypersensitivity to any ingredient of the trial drugs, severe liver or renal impairment, presence of diabetes, glaucoma, psychoses, or severe diseases in other organs including viral or bacterial infections. ***Number included*** **Number randomised: arm 1** 32	***Interventions*** **Treatment duration (weeks)** 8 **Treatment duration category** 6 to <12 weeks **Number of arms** 2 **Split face design** no **Intervention: arm 1** Tretinoin 0.05% cream **Intervention: arm 2** Vehicle **Coded intervention: arm 1** TRET-topical **Coded intervention: arm 2** Vehicle **Treatment category** Topical retinoids ± other treatment	***Results*** **Skin irritation (n/N): arm 1** 3/30 **Skin irritation (n/N): arm 2** 3/14	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;treatments assigned to participants in identical tubes according to blinded randomisation list, stratified every 6 participants, generated by the sponsor; no other methods reported **2. Deviation from intervention** Low;double-blind (participants blinded); ITT analysis performed **3. Missing outcome data (efficacy)** High;6.7% vs 18.75% vs 11.1% discontinued because of withdrawal of consent or lack of compliance **4. Outcome measurement (efficacy)** Low;investigator-

Study details	Participants	Interventions	Outcomes and results	Comments
	Number randomised: arm 2 15 **Number completed: arm 1** 26 **Number completed: arm 2** 14			blinded **5. Selective reporting** Low;study protocol and other relevant documentation approved by the Romanian National Authorities **6. Overall bias** High
Study details **Reference** Tu, P. L., G. Q.,Zhu, X. J.,Zheng, J.,Wong, W. Z.A comparison of adapalene gel 0.1% vs. tretinoin gel 0.025% in the treatment of acne vulgaris in China. 2001. Journal of the European Academy of Dermatology and Venereology **Trial ID** Tu 2001 **Country** China **Study type** RCT **Source of funding** Unstated ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** na	N=150 ***Characteristics*** **Sex** mixed **age (mean±SD)** 19 **age (min/max)** 14/30 ***Inclusion/exclusion criteria*** **Used validated acne scale** no **Acne scale** Global Acne Grading System (GAGS) **Inclusion details** Grade II–III acne vulgaris **Exclusion details** - ***Number included*** **Number randomised: arm 1** 75 **Number randomised: arm 2** 75 **Number completed: arm 1** 71 **Number completed: arm 2**	***Interventions*** **Treatment duration (weeks)** 8 **Treatment duration category** 6 to <12 weeks **Number of arms** 2 **Split face design** no **Intervention: arm 1** Adapalene gel 0.1% **Intervention: arm 2** Tretinoin gel 0.025% **Coded intervention: arm 1** ADAP-topical **Coded intervention: arm 2** TRET-topical **Treatment category** Topical retinoids ± other treatment	***Results*** **Skin irritation (n/N): arm 1** 23/72 **Skin irritation (n/N): arm 2** 31/67	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;methods not reported **2. Deviation from intervention** Some concerns;double-blind, but not clear if participants were blinded; not reported if ITT was done **3. Missing outcome data (efficacy)** Some concerns;4% vs 10.7% discontinued; reasons not provided **4. Outcome measurement (efficacy)** Some concerns;blinding not reported **5. Selective**

Study details	Participants	Interventions	Outcomes and results	Comments
	66			**reporting** Some concerns;Not reported whether there was a pre-registered protocol **6. Overall bias** High
Study details **Reference** Webster, G. F. B., D.,Stein, L. F.,Fivenson, D. P.,Tanghetti, E. A.,Ling, M.Efficacy and tolerability of once-daily tazarotene 0.1% gel versus once-daily tretinoin 0.025% gel in the treatment of facial acne vulgaris: a randomized trial. 2001. Cutis; cutaneous medicine for the practitioner **Trial ID** Webster 2001 **Country** United States **Study type** RCT **Source of funding** Not industry funded ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** na	N=143 ***Characteristics*** **Sex** Mixed **age (mean±SD)** 22.5±9.5 **age (min/max)** 7/56 ***Inclusion/exclusion criteria*** **Used validated acne scale** No **Acne scale** None **Inclusion details** At least 12 years old with mild to moderate facial acne vulgaris, defined as 10 to 60 facial inflammatory lesions, 10 to 200 facial noninflammatory lesions, and no more than 2 facial nodular cystic lesions (none more than 5mm in diameter) **Exclusion details** Any uncontrolled systemic disease, known hypersensitivity to any components in the study medication, use of any topical treatments during the study period, acne known to be resistant to antibiotics, use of birth control for less than 12 weeks prior to the study, other skin diseases, participation in any other studies within 30 days, pregancy, lactation, intention to become pregnant	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** once-daily application of tazarotene 0.1% gel **Intervention: arm 2** tretinoin 0.025% gel **Coded intervention: arm 1** TAZ-topical **Coded intervention: arm 2** TRET-topical **Treatment category** Topical retinoids ± other treatment	***Results*** **Skin irritation (n/N): arm 1** 4/61 **Skin irritation (n/N): arm 2** 2/70	***Cochrane RoB Tool v2.0*** **1. Randomisation** Low;randomisation using computer-generated treatment allocation list (performed by independent organisation); randomisation code kept in tamper-evidence sealed envelopes **2. Deviation from intervention** Low;none of the clinical personnel had access to randomisation codes at any time during the study; blinding maintained by labeling the study medications with opaque, permanent adhesive labels and dispensed to participants in preseaeled cardboard boxes; ITT analysis was done

Study details	Participants	Interventions	Outcomes and results	Comments
	Number included **Number randomised: arm 1** 72 **Number randomised: arm 2** 71 **Number completed: arm 1** 61 **Number completed: arm 2** 70			**3. Missing outcome data (efficacy)** Some concerns;15.3% vs 1.4% loss to follow-up or withdrawals; reasons provided **4. Outcome measurement (efficacy)** Low;investigator-blinded **5. Selective reporting** Some concerns;not reported whether there was a pre-registered protocol **6. Overall bias** Some concerns
Study details **Reference** Xu, J. H. L., Q. J.,Huang, J. H.,Hao, F.,Sun, Q. N.,Fang, H.,Gu, J.,Dong, X. Q.,Zheng, J.,Luo, D.,et al.,A multicentre, randomized, single-blind comparison of topical clindamycin 1%/benzoyl peroxide 5% once-daily gel versus clindamycin 1% twice-daily gel in the treatment of mild to moderate acne vulgaris in Chinese patients. 2016. Journal of the european academy of dermatology and venereology: JEADV	N=1016 ***Characteristics*** **Sex** Mixed **age (mean±SD)** 23.3±4.5 ***Inclusion/exclusion criteria*** **Used validated acne scale** No **Acne scale** Investigator's Static Global Assessment (ISGA)/Investigator's global severity Assessment **Inclusion details** Aged 12–45 years (inclusive) diagnosed with mild to moderate acne, with at least 17, but not more than 60 facial inflammatory lesions	***Interventions*** **Treatment duration (weeks)** 12 **Treatment duration category** 12 to <24 weeks **Number of arms** 2 **Split face design** No **Intervention: arm 1** topical clindamycin 1%/benzoyl peroxide 5% once-daily gel **Intervention: arm 2** clindamycin 1% twice-	***Results*** **Skin irritation (n/N): arm 1** 22/500 **Skin irritation (n/N): arm 2** 2/516	***Cochrane RoB Tool v2.0*** **1. Randomisation** Some concerns;randomisation on a 1:1 ratio using comput-ergenerated randomisation schedule; Methods not reported for allocation concealment **2. Deviation from intervention** Some concerns;participants and perosnnel do not appear to have been

Study details	Participants	Interventions	Outcomes and results	Comments
Trial ID Xu 2016 **Country** China **Study type** RCT **Source of funding** Industry funded ***Analysis method*** **Intention to treat or completers analysis** ITT **Method of ITT imputation** LOCF	(papules plus pustules), at least 20 but not more than 125 facial non-inflammatory lesions (open and closed comedones), no more than 1 facial nodular lesion with no cystic lesions, and who had a baseline Investigator's Static Global Assessment (ISGA) score of 2 or 3 **Exclusion details** Cystic acne lesions, acne conglobata, acne fulminans or secondary acne (for example chloracne or druginduced acne) were excluded from the study. Women of childbearing potential had to use medically acceptable method of contraception during the study; pregnant and lactating women ***Number included*** **Number randomised: arm 1** 500 **Number randomised: arm 2** 516 **Number completed: arm 1** 430 **Number completed: arm 2** 445	daily gel **Coded intervention: arm 1** CLIND-topical + BPO-topical **Coded intervention: arm 2** CLIND-topical **Treatment category** Topical non-retinoids ± other treatment		blinded; ITT analysis was done **3. Missing outcome data (efficacy)** High;around 14% participants discontinued; higher rate for adverse events in clindamycin combination (2.4%) vs clincamycin alone (0.8%); last observation carried forward used **4. Outcome measurement (efficacy)** Low;assessor-blinded **5. Selective reporting** Low;registered on clinical trials.gov **6. Overall bias** High

5ALA-IPL-PDT: 5-aminolevulinic acid using intense pulsed light; ADAP: adapalene; AZE: azelaic acid; AZITH: azithromycin; BLU-PT: blue light; BPO: benzoyl peroxide; BR-LED: blue + red light; CHLOR: chlorhexidine gluconate; CLIND: clindamycin; CMA: chlormadinone acetate; CPA: co-cyprindiol; DAPS: dapsone; DNG: dienogest; DOXY: doxycycline; DROS: drospirenone; EE: ethinylestradiol; ERYTH: erythromycin; FCA: fucidic acid; GLY: glycolic acid; HPS: hydrogen peroxide; IPL: intense pulsed light; ISO: isotretinoin; IQR: interquartile range; ITT: intension to treat; LEVA: levamisole; LNG: levonorgestrel; LOCB: last observation carried backward; LOCF: last observation carried forward; MAND: mandelic; MET: metronidazole; MINO: minocycline; NGM: norgestimate; OXYTETRA: oxytetracycline; PDL: pulsed dye laser; PDT: photochemical therapy; PHY: phytic acid; PLC: placebo; RCT: randomised controlled trial; RoB: risk of bias; SAL: salicylic acid; SD: standard deviation; TAZ: tazarotene; TRET: tretinoin.

Appendix E

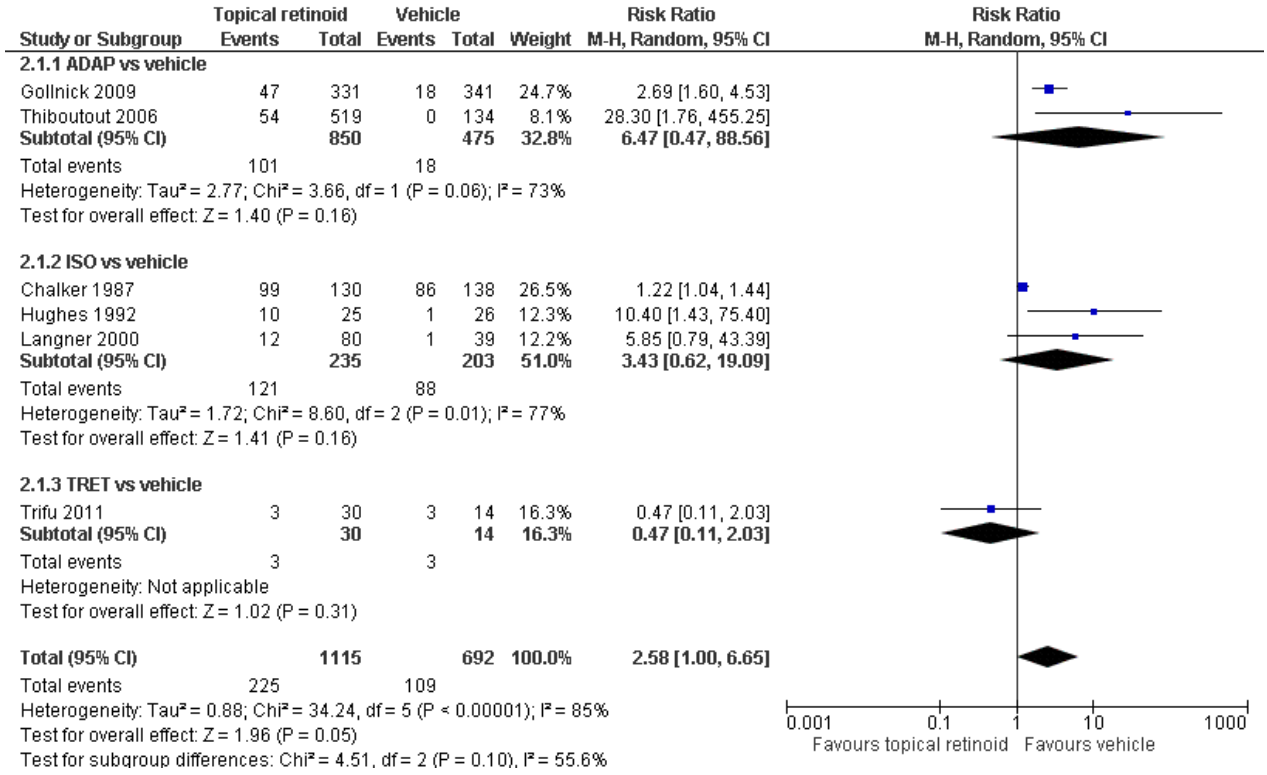
Appendix E - Forest plots

Forest plots for review question: What is the effectiveness and acceptability of interventions for the treatment of mild to moderate 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.

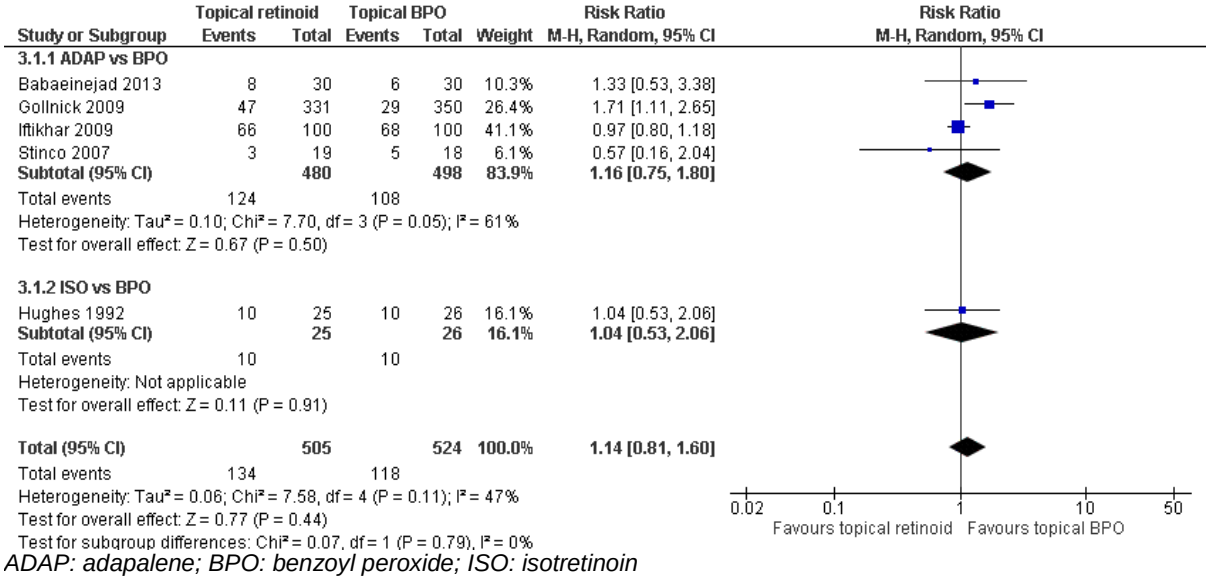
Topical non-retinoids and retinoids

Figure 2: Comparison of topical retinoid treatments with vehicle for the outcome of skin irritation



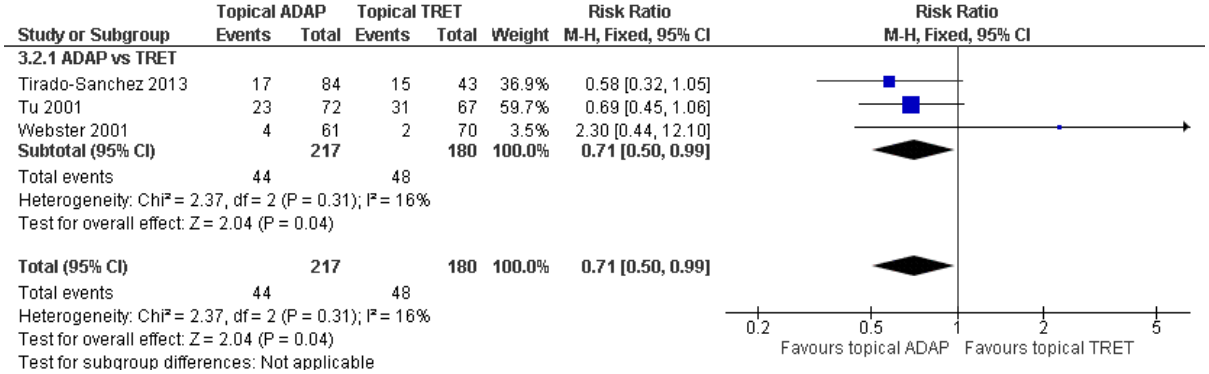
ADAP: adapalene; ISO: isotretinoin; TRET: tretinoin

Figure 3: Comparison of topical retinoid treatments with topical benzoyl peroxide treatment for the outcome of skin irritation



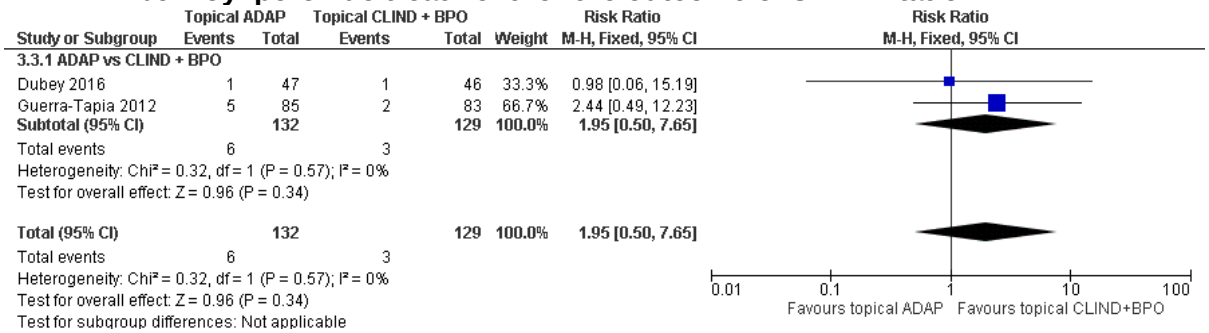
ADAP: adapalene; BPO: benzoyl peroxide; ISO: isotretinoin

Figure 4: Comparison of topical adapalene treatment with topical tretinoin treatment for the outcome of skin irritation



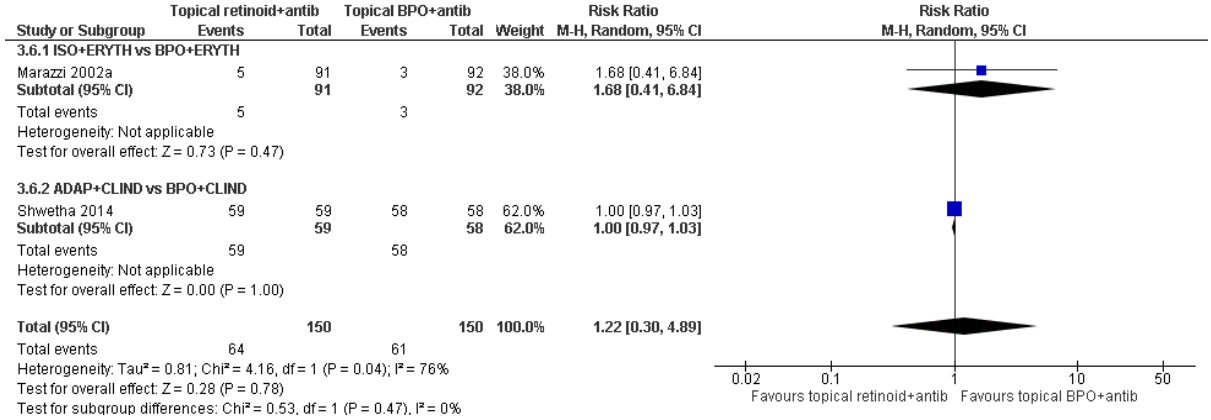
ADAP: adapalene; TRET: tretinoin

Figure 5: Comparison of topical adapalene treatment with topical clindamycin and benzoyl peroxide treatment for the outcome of skin irritation



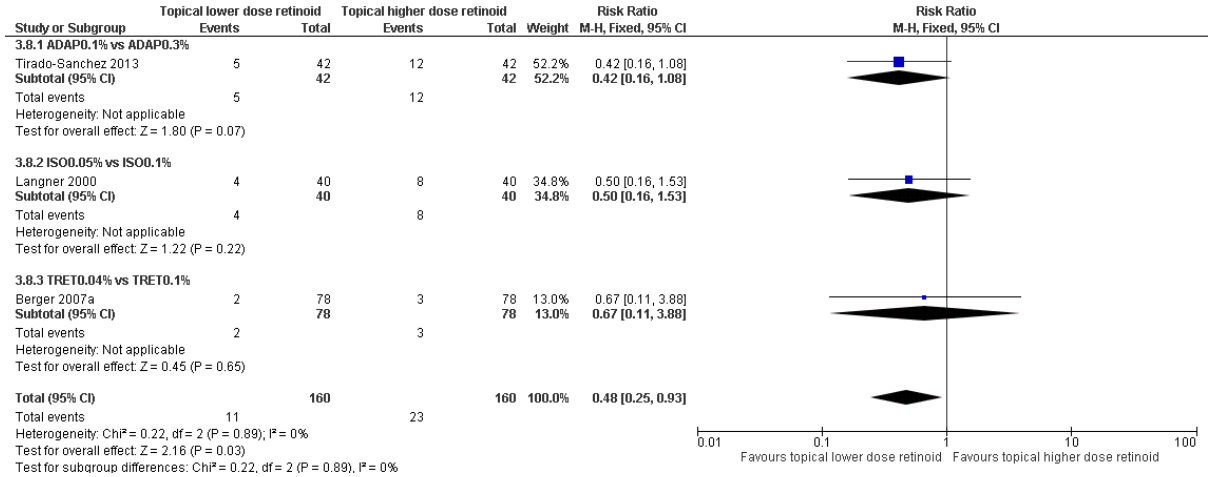
ADAP: adapalene; BPO: benzoyl peroxide; CLIN: clindamycin

Figure 6: Comparison of topical retinoid treatment in combination with topical antibiotics with topical benzoyl peroxide treatment in combination with topical antibiotics for the outcome of skin irritation



ADAP: adapalene; BPO: benzoyl peroxide; CLIN: clindamycin; ERYTH: erythromycin; ISO: isotretinoin

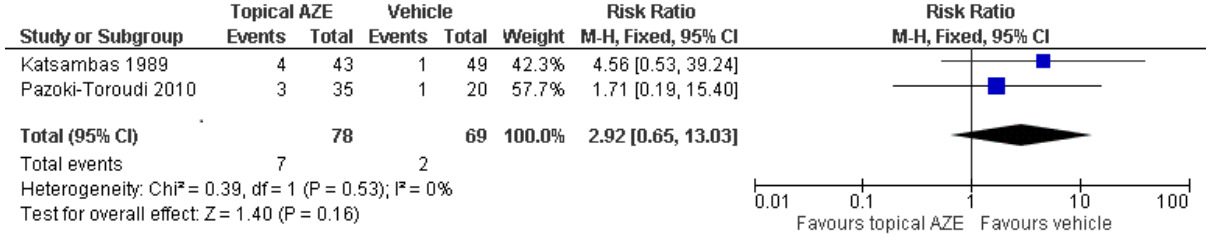
Figure 7: Comparison of topical lower dose retinoid treatment with topical higher dose retinoid treatment for the outcome of skin irritation



ADAP: adapalene; ISO: isotretinoin; TRET: tretinoin

Own class topicals

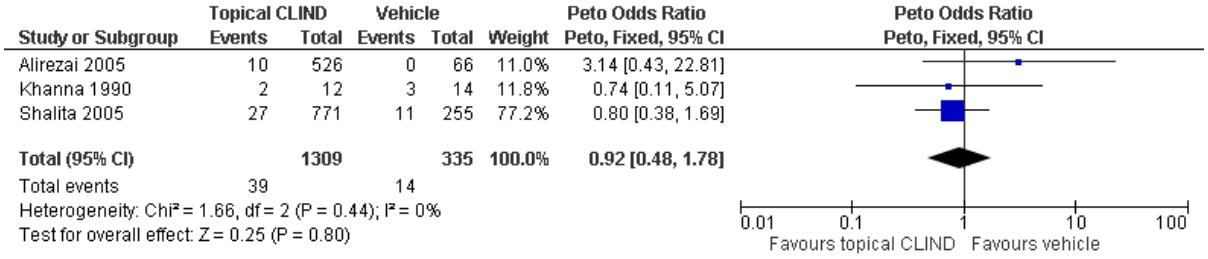
Figure 8: Comparison of topical azelaic acid with vehicle for the outcome of skin irritation



AZE: azelaic acid

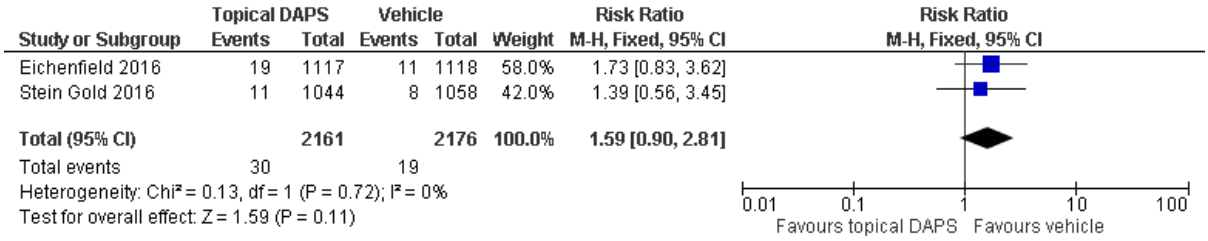
Topical antibiotics

Figure 9: Comparison of topical clindamycin with vehicle for the outcome of skin irritation



CLIND: clindamycin

Figure 10: Comparison of topical dapsone with vehicle for the outcome of skin irritation



DAPS: dapsone

Figure 11: Comparison of topical antibiotic with topical antibiotic for the outcome of skin irritation

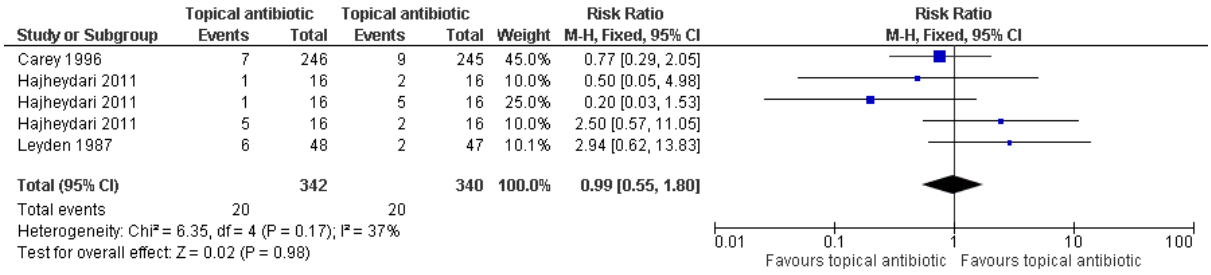
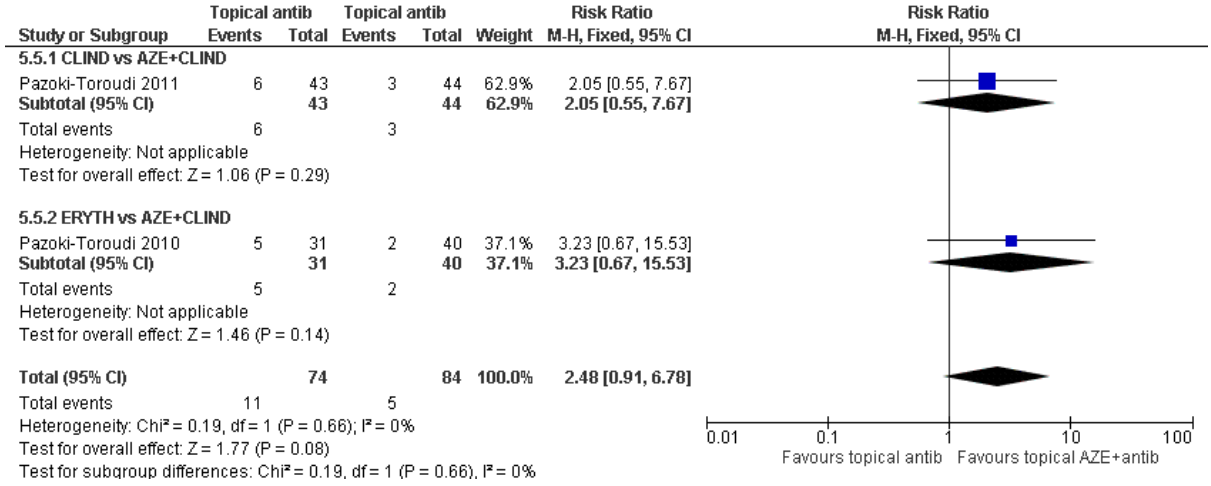


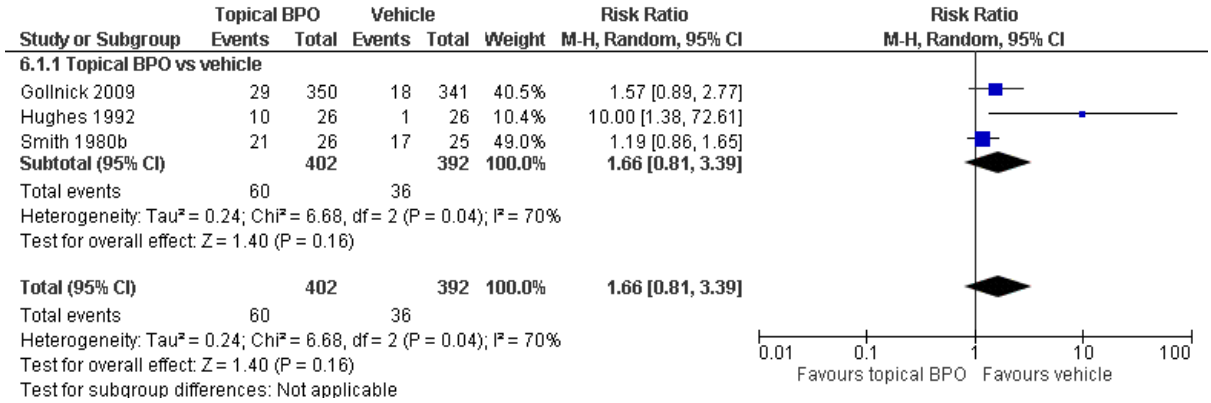
Figure 12: Comparison of topical antibiotic with topical antibiotic for the outcome of skin irritation



AZE: azelaic acid; CLIND: clindamycin; ERYTH: erythromycin

Topical antiseptics

Figure 13: Comparison of topical benzoyl peroxide treatment with vehicle for the outcome of skin irritation



BPO: benzoyl peroxide

Topical acids

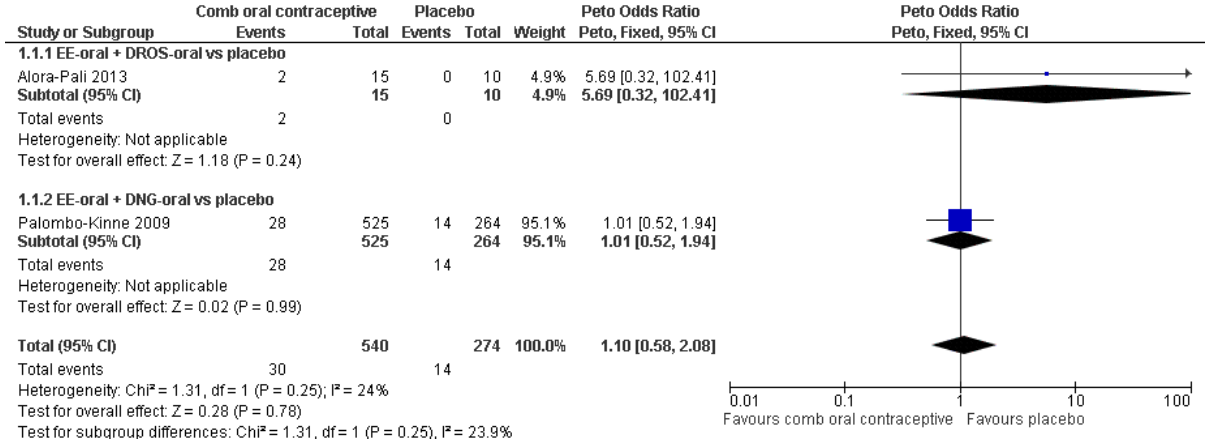
No meta-analysis was conducted for topical acid treatments and so there are no forest plots.

Oral antibiotics and combinations with other topicals

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

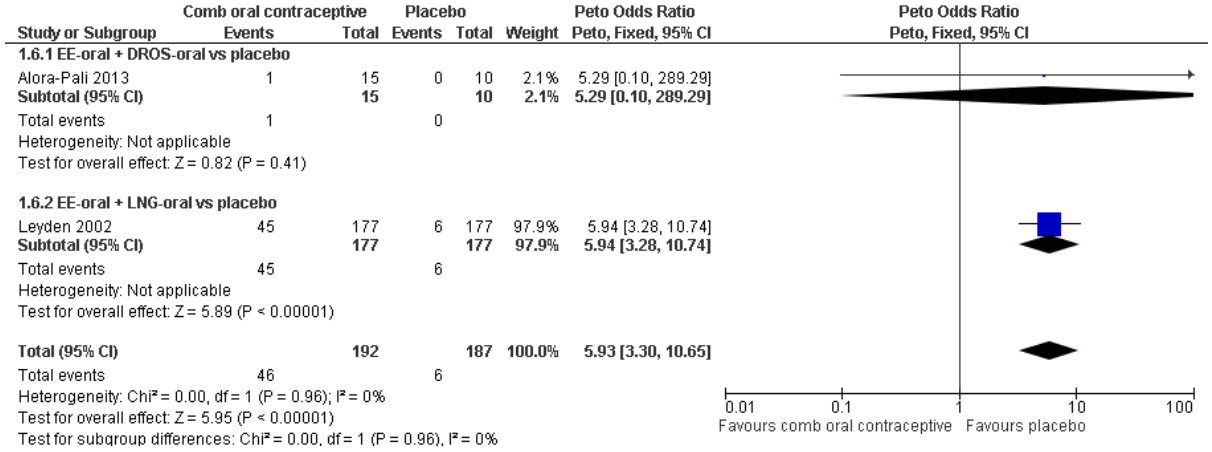
Oral hormonal contraceptives or hormone-modifying agents

Figure 14: Comparison of combined oral contraceptive treatment with placebo for the outcome of neurological side effect



EE-oral + DROS-oral: ethhinylestradiol + drospirenone; EE-oral + DNG-oral: estradiol (valerate) + dienogest

Figure 15: Comparison of combined oral contraceptive treatment with placebo for the outcome of breakthrough bleeding



EE-oral + DROS-oral: ethhinylestradiol + drospirenone; EE-oral + LNG-oral: ethhinylestradiol + levonorgestrel

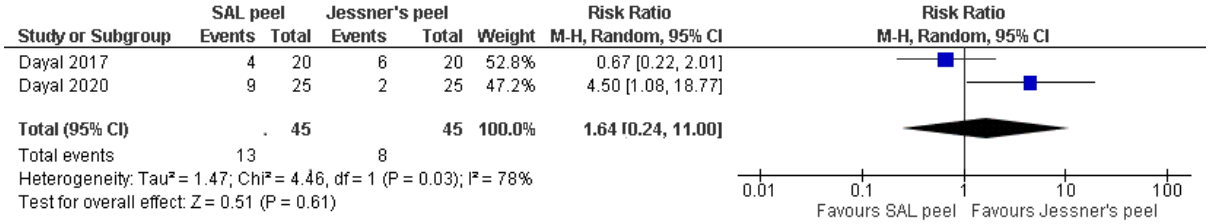
Oral isotretinoin

No meta-analysis was conducted for treatment with oral isotretinoin and so there are no forest plots.

Physical treatments

Chemical peels

Figure 16: Comparison of salicylic acid peel treatment with Jessner's peel treatment for the outcome of skin redness



SAL: salicylic acid

Energy based treatments (light/laser)

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

Appendix F - GRADE tables

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

Topical non-retinoids and retinoids

Table 5: Clinical evidence profile for comparison of topical retinoid treatments 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		
Skin irritation (retinoids) vs vehicle												
6[1]	randomised trials	very serious[2]	very serious[3]	no serious indirectness	serious[4]	none	225/1115 (20.2%)	109/692 (15.8%)	RR 2.58 (1.00 to 6.65)	249 more per 1000 (from 0 more to 890 more)	⊕OOO VERY LOW	IMPORTANT
Skin irritation (topical retinoid + non-retinoid) - ADAP+BPO vs vehicle												
1[5]	randomised trials	serious[6]	no serious inconsistency	no serious indirectness	no serious imprecision	none	70/332 (21.1%)	18/341 (5.3%)	RR 3.99 (2.43 to 6.56)	158 more per 1000 (from 75 more to 293 more)	⊕⊕⊕O MODERATE	IMPORTANT
Participant reported improvement (retinoids) - TRET vs vehicle												
1[7]	randomised trials	very serious[8]	no serious inconsistency	no serious indirectness	serious[4]	none	23/88 (26.1%)	13/90 (14.4%)	RR 1.81 (0.98 to 3.34)	117 more per 1000 (from 3 fewer to 338 more)	⊕OOO VERY LOW	IMPORTANT

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

[1] Gollnick 2009, Thiboutout 2006, Chalker 1987, Hughes 1992, Langner 2000, Trifu 2011

[2] Overall risk of bias judgement: serious/very serious risk of bias in the evidence contributing to the outcomes

[3] Evidence downgraded by 2 levels due to very serious inconsistency

[4] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes

[5] Gollnick 2009

[6] Overall risk of bias judgement: serious risk of bias in the evidence contributing to the outcomes

[7] Berger 2007b

[8] Overall risk of bias judgement: very serious risk of bias in the evidence contributing to the outcomes

Table 6: Clinical evidence profile for comparison of topical retinoid treatments or topical treatment combinations including a retinoid treatment versus topical treatments or their combinations

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical treatment	Topical treatment	Relative (95% CI)	Absolute		
Skin irritation (topical retinoids (adapalene, isotretinoin) vs topical benzoyl peroxide)												
5[1-5]	randomised trials	very serious[17]	no serious inconsistency	no serious indirectness	serious[18]	none	134/505 (26.5%)	118/524 (22.5%)	RR 1.14 (0.81 to 1.6)	32 more per 1000 (from 43 fewer to 135 more)	⊕OOO VERY LOW	IMPORTANT
Skin irritation (topical adapalene vs topical tretinoin)												
3[6-8]	randomised trials	very serious[17]	no serious inconsistency	no serious indirectness	serious[18]	none	44/217 (20.3%)	48/180 (26.7%)	RR 0.71 (0.5 to 0.99)	77 fewer per 1000 (from 3 fewer to 133 fewer)	⊕OOO VERY LOW	IMPORTANT
Skin irritation (topical adapalene vs topical clindamycin + benzoyl peroxide)												
2[9-10]	randomised trials	very serious[17]	no serious inconsistency	no serious indirectness	very serious[19]	none	6/132 (4.5%)	3/129 (2.3%)	RR 1.95 (0.5 to 7.65)	22 more per 1000 (from 12 fewer to 155 more)	⊕OOO VERY LOW	IMPORTANT
Skin irritation (topical adapalene vs topical adapalene + benzoyl peroxide)												
1[1]	randomised trials	serious[20]	no serious inconsistency	no serious indirectness	serious[18]	none	47/331 (14.2%)	70/332 (21.1%)	RR 0.67 (0.48 to 0.94)	70 fewer per 1000 (from 13 fewer to 110 fewer)	⊕⊕OO LOW	IMPORTANT
Skin irritation (topical adapalene + benzoyl peroxide vs topical benzoyl peroxide)												
1[1]	randomised trials	serious[20]	no serious inconsistency	no serious indirectness	no serious imprecision	none	70/332 (21.1%)	29/350 (8.3%)	RR 2.54 (1.7 to 3.82)	128 more per 1000 (from 58 more to 234 more)	⊕⊕⊕O MODERATE	IMPORTANT
Skin irritation (topical retinoids (adapalene, isotretinoin) + topical antibiotics vs + topical retinoids (adapalene, isotretinoin) + antibiotics)												
2[11-12]	randomised trials	very serious[17]	serious[21]	no serious indirectness	very serious[19]	none	64/150 (42.7%)	61/150 (40.7%)	RR 1.22 (0.3 to 4.89)	89 more per 1000 (from 285 fewer to 1000 more)	⊕OOO VERY LOW	IMPORTANT
Skin irritation (topical isotretinoin + clindamycin vs topical adapalene + clindamycin												
1[13]	randomised	very	no serious	no serious	no serious	none	56/94	32/97	RR 1.81 (1.3	267 more per 1000	⊕⊕OO	IMPORTANT

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical treatment	Topical treatment	Relative (95% CI)	Absolute		
	trials	serious[22]	inconsistency	indirectness	imprecision		(59.6%)	(33%)	to 2.51)	(from 99 more to 498 more)	LOW	
Skin irritation (topical lower dose retinoid (adapalene, isotretinoin, tretinoin) vs higher dose retinoid (adapalene, isotretinoin, tretinoin))												
3[6,14,15]	randomised trials	very serious[17]	no serious inconsistency	no serious indirectness	serious[18]	none	11/160 (6.9%)	23/160 (14.4%)	RR 0.48 (0.25 to 0.93)	75 fewer per 1000 (from 10 fewer to 108 fewer)	⊕OOO VERY LOW	IMPORTANT
Light sensitivity (topical lower dose tretinoin vs higher dose tretinoin)												
1[15]	randomised trials	serious[20]	no serious inconsistency	no serious indirectness	very serious[19]	none	6/78 (7.7%)	1/78 (1.3%)	RR 6 (0.74 to 48.68)	64 more per 1000 (from 3 fewer to 611 more)	⊕OOO VERY LOW	IMPORTANT
Participant reported improvement (topical isotretinoin + erythromycin vs topical benzoyl peroxide + erythromycin)												
1[11]	randomised trials	very serious[22]	no serious inconsistency	no serious indirectness	no serious imprecision	none	90/95 (94.7%)	91/95 (95.8%)	RR 0.99 (0.93 to 1.05)	10 fewer per 1000 (from 67 fewer to 48 more)	⊕⊕OO LOW	IMPORTANT
Participant reported improvement (topical tretinoin + clindamycin vs topical salicylic acid + clindamycin)												
1[16]	randomised trials	very serious[22]	no serious inconsistency	no serious indirectness	no serious imprecision	none	23/23 (100%)	23/23 (100%)	RR 1 (0.92 to 1.09)	0 fewer per 1000 (from 80 fewer to 90 more)	⊕⊕OO LOW	IMPORTANT
Participant reported improvement (topical lower dose tretinoin vs higher dose tretinoin)												
1[15]	randomised trials	serious[20]	no serious inconsistency	no serious indirectness	no serious imprecision	none	67/78 (85.9%)	67/78 (85.9%)	RR 1 (0.88 to 1.14)	0 fewer per 1000 (from 103 fewer to 120 more)	⊕⊕⊕O MODERATE	IMPORTANT

CI: confidence interval; MID: minimally important difference; RR: relative risk
[1] Gollnick 2009
[2] Hughes 1992
[3] Babaeinejad 2013
[4] Iftikhar 2009
[5] Stinco 2007
[6] Tirado-Sanchez 2013
[7] Tu 2001
[8] Webster 2001
[9] Dubey 2016
[10] Guerra-Tapia 2012

[11] *Marazzi 2002a*
[12] *Swetha 2014*
[13] *Adhikary 2014*
[14] *Langner 2000*
[15] *Berger 2007a*
[16] *Babayeva 2001*
[17] *Overall risk of bias judgement: very serious risk of bias in the evidence contributing to the outcomes*
[18] *Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes*
[19] *Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes*
[20] *Overall risk of bias judgement: serious risk of bias in the evidence contributing to the outcomes*
[21] *Evidence downgraded by 1 level due to serious inconsistency*
[22] *Overall risk of bias judgement: very serious risk of bias in the evidence contributing to the outcomes*

Own class topicals

Table 7: Clinical evidence profile for comparison of topical own class treatments versus vehicle

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical treatments	Vehicle	Relative (95% CI)	Absolute		
Skin irritation (topical acnicare)												
1[1]	randomised trials	very serious[5]	no serious inconsistency	no serious indirectness	very serious[6]	none	1/17 (5.9%)	0/16 (0%)	POR 6.97 (0.14 to 351.74)	-	⊕OOO VERY LOW	IMPORTANT
Skin irritation (topical azelaic acid)												
2[2-3]	randomised trials	very serious[5]	no serious inconsistency	no serious indirectness	very serious[6]	none	7/78 (9%)	2/69 (2.9%)	RR 2.92 (0.65 to 13.03)	56 more per 1000 (from 10 fewer to 349 more)	⊕OOO VERY LOW	IMPORTANT
Skin irritation (topical azelaic acid + erythromycin)												
1[3]	randomised trials	very serious[5]	no serious inconsistency	no serious indirectness	very serious[6]	none	2/40 (5%)	1/20 (5%)	RR 1 (0.1 to 10.38)	0 fewer per 1000 (from 45 fewer to 469 more)	⊕OOO VERY LOW	IMPORTANT
Skin irritation (topical fucidic acid)												

1[4]	randomised trials	very serious[5]	no serious inconsistency	no serious indirectness	very serious[6]	none	1/36 (2.8%)	0/34 (0%)	POR 6.99 (0.14 to 352.83)	-	⊕OOO VERY LOW	IMPORTANT

CI: confidence interval; MID: minimally important difference; POR: peto odds ratio; RR: relative risk
[1] Charakida 2007
[2] Katsambas 1989
[3] Pazoki-Toroudi 2010
[4] Hanstead 1985
[5] Overall risk of bias judgement: very serious risk of bias in the evidence contributing to the outcomes
[6] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes

Topical antibiotics

Table 8: Clinical evidence profile for comparison of topical antibiotic treatments versus vehicle

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Topical antibiotics**	**Vehicle**	**Relative (95% CI)**	**Absolute**		
Skin irritation (topical clindamycin)												
3[1-3]	randomised trials	very serious[7]	no serious inconsistency	no serious indirectness	very serious[8]	none	39/1309 (3%)	14/335 (4.2%)	POR 0.92 (0.48 to 1.78)	3 fewer per 1000 (from 21 fewer to 30 more)	⊕OOO VERY LOW	IMPORTANT
Skin irritation (topical dapsone)												
2[4-5]	randomised trials	very serious[7]	no serious inconsistency	no serious indirectness	serious[9]	none	30/2161 (1.4%)	19/2176 (0.87%)	RR 1.59 (0.9 to 2.81)	5 more per 1000 (from 1 fewer to 16 more)	⊕OOO VERY LOW	IMPORTANT
Skin irritation (topical erythromycin)												
1[6]	randomised trials	very serious[10]	no serious inconsistency	no serious indirectness	very serious[8]	none	5/31 (16.1%)	1/20 (5%)	RR 3.23 (0.41 to 25.62)	112 more per 1000 (from 30 fewer to 1000 more)	⊕OOO VERY LOW	IMPORTANT

CI: confidence interval; MID: minimally important difference; POR: peto odds ratio; RR: relative risk
[1] Alirezai 2005

[2] Khanna 1990
[3] Shalita 2005
[4] Eichenfield 2016
[5] Stein Gold 2016,
[6] Pazoki-Toroudi 2010
[7] Overall risk of bias judgement: very serious risk of bias in the evidence contributing to the outcomes
[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] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes
[10] Overall risk of bias judgement: very serious risk of bias in the evidence contributing to the outcomes

Table 9: Clinical evidence profile for comparison of topical antibiotic treatments or topical combinations versus topical antibiotic treatments or topical combinations

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical antibiotics	Control	Relative (95% CI)	Absolute		
Skin irritation (topical antibiotic vs topical antibiotic)												
3[1-3]	randomised trials	very serious[10]	no serious inconsistency	no serious indirectness	very serious[11]	none	20/342 (5.8%)	20/340 (5.9%)	RR 0.99 (0.55 to 1.8)	1 fewer per 1000 (from 26 fewer to 47 more)	⊕OOO VERY LOW	IMPORTANT
Skin irritation (topical antibiotic vs topical antibiotic + azelaic acid)												
2[4-5]	randomised trials	very serious[13]	no serious inconsistency	no serious indirectness	serious[12]	none	11/74 (14.9%)	5/84 (6%)	RR 2.48 (0.91 to 6.78)	88 more per 1000 (from 5 fewer to 344 more)	⊕OOO VERY LOW	IMPORTANT
Skin irritation (topical clindamycin vs topical clindamycin + benzoyl peroxide)												
1[6]	randomised trials	very serious[13]	no serious inconsistency	no serious indirectness	no serious imprecision	none	2/516 (0.39%)	22/500 (4.4%)	RR 0.09 (0.02 to 0.37)	40 fewer per 1000 (from 28 fewer to 43 fewer)	⊕⊕OO LOW	IMPORTANT
Skin irritation (topical clindamycin + benzoyl peroxide vs topical clindamycin + zink acetate dihydrate)												
1[7]	randomised trials	very serious[13]	no serious inconsistency	no serious indirectness	no serious imprecision	none	11/40 (27.5%)	2/39 (5.1%)	RR 5.36 (1.27 to 22.65)	224 more per 1000 (from 14 more to 1000 more)	⊕⊕OO LOW	IMPORTANT
Skin irritation (topical clindamycin + benzoyl peroxide vs topical azelaic acid)												
1[8]	randomised trials	serious[14]	no serious inconsistency	no serious indirectness	no serious imprecision	none	8/108 (7.4%)	25/109 (22.9%)	RR 0.32 (0.15 to 0.68)	156 fewer per 1000 (from 73 fewer to 195 fewer)	⊕⊕⊕O MODERATE	IMPORTANT

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical antibiotics	Control	Relative (95% CI)	Absolute		
Skin irritation (topical clindamycin + benzoyl peroxide vs topical metronidazole + benzoyl peroxide)												
1[9]	randomised trials	serious[14]	no serious inconsistency	no serious indirectness	very serious[11]	none	3/20 (15%)	3/20 (15%)	RR 1 (0.23 to 4.37)	0 fewer per 1000 (from 116 fewer to 506 more)	⊕OOO VERY LOW	IMPORTANT
Participant reported improvement (topical erythromycin vs topical fucidic acid)												
1[1]	randomised trials	very serious[13]	no serious inconsistency	no serious indirectness	no serious imprecision	none	211/243 (86.8%)	210/242 (86.8%)	RR 1 (0.93 to 1.07)	0 fewer per 1000 (from 61 fewer to 61 more)	⊕⊕OO LOW	IMPORTANT
Participant reported improvement (topical erythromycin vs topical clindamycin + azelaic acid)												
1[5]	randomised trials	very serious[13]	no serious inconsistency	no serious indirectness	very serious[11]	none	7/31 (22.6%)	11/40 (27.5%)	RR 0.82 (0.36 to 1.87)	50 fewer per 1000 (from 176 fewer to 239 more)	⊕OOO VERY LOW	IMPORTANT

CI: confidence interval; MID: minimally important difference; RR: relative risk
[1] Carey 1996
[2] Hajheydari 2011
[3] Leyden 1987
[4] Pazoki-Toroudi 2011
[5] Pazoki-Toroudi 2010
[6] Xu 2016
[7] Cunliffe 2002b
[8] Schaller 2016
[9] Jain 1998
[10] Overall risk of bias judgement: very serious risk of bias in the evidence contributing to the outcomes
[11] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes
[12] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes
[13] Overall risk of bias judgement: very serious risk of bias in the evidence contributing to the outcomes
[14] Overall risk of bias judgement: serious risk of bias in the evidence contributing to the outcomes

Topical antiseptics

Table 10: Clinical evidence profile for comparison of topical antiseptic treatments versus vehicle

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical antiseptics	Vehicle	Relative (95% CI)	Absolute		
Skin irritation (topical benzoyl peroxide)												
3[1-3]	randomised trials	very serious[5]	serious[6]	no serious indirectness	serious[7]	none	60/402 (14.9%)	36/392 (9.2%)	RR 1.66 (0.81 to 3.39)	61 more per 1000 (from 17 fewer to 219 more)	⊕OOO VERY LOW	IMPORTANT
Skin irritation (topical chlorhexidine gluconate / digluconate)												
1[4]	randomised trials	very serious[8]	no serious inconsistency	no serious indirectness	very serious[9]	none	2/55 (3.6%)	1/55 (1.8%)	RR 2 (0.19 to 21.42)	18 more per 1000 (from 15 fewer to 371 more)	⊕OOO VERY LOW	IMPORTANT

CI: confidence interval; MID: minimally important difference; RR: relative risk
[1] Gollnick 2009
[2] Hughes 1992
[3] Smith 1980b
[4] Stoughton 1987
[5] Overall risk of bias judgement: very serious risk of bias in the evidence contributing to the outcomes
[6] Evidence downgraded by 1 level due to serious inconsistency
[7] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes
[8] Overall risk of bias judgement: very serious risk of bias in the evidence contributing to the outcomes
[9] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes

Table 11: Clinical evidence profile for comparison of topical hydrogen peroxide treatment versus topical benzoyl peroxide treatment

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical hydrogen peroxide	Topical benzoyl peroxide	Relative (95% CI)	Absolute		

Skin irritation												
1[1]	randomised trials	serious[6]	no serious inconsistency	no serious indirectness	very serious[3]	none	2/30 (6.7%)	7/30 (23.3%)	RR 0.29 (0.06 to 1.26)	166 fewer per 1000 (from 219 fewer to 61 more)	⊕OOO VERY LOW	IMPORTANT

CI: confidence interval; MID: minimally important difference; RR: relative risk
[1] Milani 2003
[2] Overall risk of bias judgement: serious risk of bias in the evidence contributing to the outcomes
[3] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes

Topical acids

Table 12: Clinical evidence profile for comparison of topical acid treatments with vehicle

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Topical acids**	**Vehicle**	**Relative (95% CI)**	**Absolute**		
Participant reported improvement (topical salicylic acid)												
1[1]	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	18/25 (72%)	8/24 (33.3%)	RR 2.16 (1.17 to 4)	387 more per 1000 (from 57 more to 1000 more)	⊕⊕OO LOW	IMPORTANT
Participant reported improvement (topical diacneal)												
1[2]	randomised trials	very serious[5]	no serious inconsistency	no serious indirectness	serious[4]	none	37/42 (88.1%)	25/39 (64.1%)	RR 1.37 (1.06 to 1.78)	237 more per 1000 (from 38 more to 500 more)	⊕OOO VERY LOW	IMPORTANT

CI: confidence interval; MID: minimally important difference; RR: relative risk
[1] Shalita 1981,
[2] Poli 2005
[3] Overall risk of bias judgement: serious risk of bias in the evidence contributing to the outcomes
[4] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes
[5] Overall risk of bias judgement: very serious risk of bias in the evidence contributing to the outcomes

Table 13: Clinical evidence profile for comparison of topical acid treatments with topical benzoyl peroxide treatment or in combination with other topical treatments

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical acids	Topical treatments	Relative (95% CI)	Absolute		
Skin irritation (topical nisal vs topical benzoyl peroxide)												
1[1]	randomised trials	very serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	2/16 (12.5%)	14/18 (77.8%)	RR 0.16 (0.04 to 0.6)	653 fewer per 1000 (from 311 fewer to 747 fewer)	⊕⊕OO LOW	IMPORTANT
Light sensitivity (topical nisal vs topical benzoyl peroxide)												
1[1]	randomised trials	very serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/16 (0%)	5/18 (27.8%)	POR 0.12 (0.02 to 0.76)	234 fewer per 1000 (from 52 fewer to 270 fewer)	⊕⊕OO LOW	IMPORTANT
Participant reported improvement (topical salicylic acid + clindamycin + benzoyl peroxide vs topical clindamycin + benzoyl peroxide)												
1[2]	randomised trials	serious[4]	no serious inconsistency	no serious indirectness	no serious imprecision	none	24/24 (100%)	25/25 (100%)	RR 1 (0.93 to 1.08)	0 fewer per 1000 (from 70 fewer to 80 more)	⊕⊕⊕O MODERATE	IMPORTANT

CI: confidence interval; MID: minimally important difference; POR: peto odds ratio; RR: relative risk
[1] Boutli 2003
[2] Akarsu 2012
[3] Overall risk of bias judgement: very serious risk of bias in the evidence contributing to the outcomes
[4] Overall risk of bias judgement: serious risk of bias in the evidence contributing to the outcomes

Oral antibiotics and combinations with other topicals

Table 14: Clinical evidence profile for comparison of oral antibiotics and their combination with oral antibiotics and their combination

Quality assessment	No of participants	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Oral antibiotic	Oral antibiotic	Relative (95% CI)	Absolute		
Skin irritation (oral azithromycin vs oral azithromycin + levamisole)												
1[1]	randomised trials	very serious[5]	no serious inconsistency	no serious indirectness	very serious[6]	none	1/76 (1.3%)	0/77 (0%)	POR 7.49 (0.15 to 377.35)	-	⊕OOO VERY LOW	CRITICAL
Skin irritation (oral oxytetracycline + placebo vs oral minocycline + placebo)												
1[2]	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	very serious[6]	none	1/131 (0.76%)	2/130 (1.5%)	RR 0.5 (0.05 to 5.41)	8 fewer per 1000 (from 15 fewer to 68 more)	⊕OOO VERY LOW	CRITICAL
Gastrointestinal side effects (oral erythromycin vs oral erythromycin)												
1[3]	randomised trials	very serious[5]	no serious inconsistency	no serious indirectness	very serious[6]	none	3/18 (16.7%)	4/18 (22.2%)	RR 0.75 (0.2 to 2.88)	56 fewer per 1000 (from 178 fewer to 418 more)	⊕OOO VERY LOW	CRITICAL
Gastrointestinal side effects (oral oxytetracycline + placebo vs oral minocycline + placebo)												
1[2]	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	very serious[6]	none	1/131 (0.76%)	2/130 (1.5%)	RR 0.50 (0.05 to 5.41)	8 fewer per 1000 (from 15 fewer to 68 more)	⊕OOO VERY LOW	CRITICAL
Gastrointestinal side effects (oral azithromycin vs oral azithromycin + levamisole)												
1[1]	randomised trials	very serious[5]	no serious inconsistency	no serious indirectness	serious[8]	none	2/76 (2.6%)	11/77 (14.3%)	RR 0.18 (0.04 to 0.8)	117 fewer per 1000 (from 29 fewer to 137 fewer)	⊕OOO VERY LOW	CRITICAL
Gastrointestinal side effects (oral azithromycin + topical tretinoin vs oral doxycycline + topical tretinoin)												
1[4]	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	serious[8]	none	2/115 (1.7%)	9/116 (7.8%)	RR 0.22 (0.06 to 0.80)	61 fewer per 1000 (from 74 fewer to 2 more)	⊕⊕OO LOW	CRITICAL
Participant reported improvement (oral azithromycin vs oral azithromycin + levamisole)												
1[1]	randomised trials	very serious[5]	no serious inconsistency	no serious indirectness	no serious imprecision	none	16/76 (21.1%)	2/77 (2.6%)	RR 8.11 (1.93 to 34.05)	185 more per 1000 (from 24 more to 858 more)	⊕⊕OO LOW	CRITICAL
Participant reported improvement (oral oxytetracycline + placebo vs oral minocycline + placebo)												

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Oral antibiotic	Oral antibiotic	Relative (95% CI)	Absolute		
1[2]	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	serious[8]	none	72/131 (55%)	70/130 (53.8%)	RR 1.02 (0.82 to 1.27)	11 more per 1000 (from 97 fewer to 145 more)	⊕⊕OO LOW	CRITICAL

CI: confidence interval; MID: minimally important difference; POR: peto odds ratio; RR: relative risk
[1] Rassai 2013
[2] Ozolins 2004
[3] Bleeker 1983
[4] Maleszka 2011
[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

Table 15: Clinical evidence profile for comparison of topical antibiotic in combination with oral antibiotic with topical antibiotic in combination with oral antibiotic

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Oral + topical	Oral + topical	Relative (95% CI)	Absolute		
Skin irritation (oral oxytetracycline + placebo vs topical benzoyl peroxide + placebo)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	1/131 (0.76%)	3/130 (2.3%)	RR 0.33 (0.03 to 3.14)	15 fewer per 1000 (from 22 fewer to 49 more)	⊕OOO VERY LOW	CRITICAL
Skin irritation (oral oxytetracycline + placebo vs topical benzoyl peroxide + topical erythromycin + placebo)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	1/131 (0.76%)	2/127 (1.6%)	RR 0.48 (0.04 to 5.28)	8 fewer per 1000 (from 15 fewer to 67 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Oral + topical	Oral + topical	Relative (95% CI)	Absolute		
Skin irritation (oral oxytetracycline + placebo vs topical benzoyl peroxide + topical erythromycin + placebo)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	1/131 (0.76%)	1/131 (0.76%)	RR 1 (0.06 to 15.82)	0 fewer per 1000 (from 7 fewer to 113 more)	⊕OOO VERY LOW	CRITICAL
Skin irritation (oral minocycline + placebo vs topical benzoyl peroxide + placebo)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	2/130 (1.5%)	3/130 (2.3%)	RR 0.67 (0.11 to 3.92)	8 fewer per 1000 (from 21 fewer to 67 more)	⊕OOO VERY LOW	CRITICAL
Skin irritation (oral minocycline + placebo vs topical benzoyl peroxide/erythromycin + placebo)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	2/130 (1.5%)	2/127 (1.6%)	RR 0.98 (0.14 to 6.83)	0 fewer per 1000 (from 14 fewer to 92 more)	⊕OOO VERY LOW	CRITICAL
Skin irritation (oral minocycline + placebo vs topical benzoyl peroxide + topical erythromycin + placebo)												
1[1]	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	2/130 (1.5%)	1/131 (0.76%)	RR 2.02 (0.19 to 21.95)	8 more per 1000 (from 6 fewer to 160 more)	⊕OOO VERY LOW	CRITICAL
Skin irritation (topical benzoyl peroxide + placebo topical benzoyl peroxide/erythromycin + placebo)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	3/130 (2.3%)	2/127 (1.6%)	RR 1.47 (0.25 to 8.62)	7 more per 1000 (from 12 fewer to 120 more)	⊕OOO VERY LOW	CRITICAL
Skin irritation (topical benzoyl peroxide + placebo vs topical benzoyl peroxide + topical erythromycin + placebo)												
1[1]	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	3/130 (2.3%)	1/131 (0.76%)	RR 3.02 (0.32 to 28.69)	15 more per 1000 (from 5 fewer to 211 more)	⊕OOO VERY LOW	CRITICAL
Skin irritation (topical benzoyl peroxide/erythromycin + placebo vs BPO + ERYTH + placebo)												

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Oral + topical	Oral + topical	Relative (95% CI)	Absolute		
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	2/127 (1.6%)	1/131 (0.76%)	RR 2.06 (0.19 to 22.47)	8 more per 1000 (from 6 fewer to 164 more)	⊕OOO VERY LOW	CRITICAL
Gastrointestinal side effects (oral oxytetracycline + placebo vs topical benzoyl peroxide + placebo)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	1/131 (0.76%)	0/130 (0%)	POR 7.33 (0.15 to 369.56)	-	⊕OOO VERY LOW	CRITICAL
Gastrointestinal side effects (oral oxytetracycline + placebo vs topical benzoyl peroxide/erythromycin + placebo												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	1/131 (0.76%)	4/127 (3.1%)	RR 0.24 (0.03 to 2.14)	24 fewer per 1000 (from 31 fewer to 36 more)	⊕OOO VERY LOW	CRITICAL
Gastrointestinal side effects (oral oxytetracycline + placebo vs topical benzoyl peroxide + topical erythromycin + placebo)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	1/131 (0.76%)	1/131 (0.76%)	RR 1 (0.06 to 15.82)	0 fewer per 1000 (from 7 fewer to 113 more)	⊕OOO VERY LOW	CRITICAL
Gastrointestinal side effects (oral minocycline + placebo vs topical benzoyl peroxide + placebo)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	2/130 (1.5%)	0/130 (0%)	POR 7.45 (0.46 to 119.69)	-	⊕OOO VERY LOW	CRITICAL
Gastrointestinal side effects (oral minocycline + placebo vs topical benzoyl peroxide/erythromycin + placebo)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	2/130 (1.5%)	4/127 (3.1%)	RR 0.49 (0.09 to 2.62)	16 fewer per 1000 (from 29 fewer to 51 more)	⊕OOO VERY LOW	CRITICAL
Gastrointestinal side effects (oral minocycline + placebo vs topical benzoyl peroxide + topical erythromycin + placebo)												
1[1]	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	2/130 (1.5%)	1/131 (0.76%)	RR 2.02 (0.19 to 21.95)	8 more per 1000 (from 6 fewer to 160 more)	⊕OOO VERY	CRITICAL

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Oral + topical	Oral + topical	Relative (95% CI)	Absolute		
											LOW	
Gastrointestinal side effects (topical benzoyl peroxide + placebo vs topical benzoyl peroxide/erythromycin + placebo)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/130 (0%)	4/127 (3.1%)	POR 0.13 (0.02 to 0.93)	27 fewer per 1000 (from 2 fewer to 31 fewer)	⊕OOO VERY LOW	CRITICAL
Gastrointestinal side effects (topical benzoyl peroxide + placebo vs topical benzoyl peroxide + erythromycin + placebo)												
1[1]	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/130 (0%)	1/131 (0.76%)	POR 0.14 (0 to 6.87)	7 fewer per 1000 (from 8 fewer to 45 more)	⊕OOO VERY LOW	CRITICAL
Gastrointestinal side effects (topical benzoyl peroxide/erythromycin + placebo vs topical benzoyl peroxide + topical erythromycin + placebo)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	4/127 (3.1%)	1/131 (0.76%)	RR 4.13 (0.47 to 36.41)	24 more per 1000 (from 4 fewer to 270 more)	⊕OOO VERY LOW	CRITICAL
Participant reported improvement (oral oxytetracycline + placebo vs topical benzoyl peroxide + placebo)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	72/131 (55%)	78/130 (60%)	RR 0.92 (0.74 to 1.13)	48 fewer per 1000 (from 156 fewer to 78 more)	⊕⊕OO LOW	CRITICAL
Participant reported improvement (oral oxytetracycline + placebo vs topical benzoyl peroxide/erythromycin + placebo)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	72/131 (55%)	84/127 (66.1%)	RR 0.83 (0.68 to 1.01)	112 fewer per 1000 (from 212 fewer to 7 more)	⊕⊕OO LOW	CRITICAL
Participant reported improvement (oral oxytetracycline + placebo vs topical benzoyl peroxide + topical erythromycin + placebo)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	72/131 (55%)	82/131 (62.6%)	RR 0.88 (0.72 to 1.08)	75 fewer per 1000 (from 175 fewer to 50 more)	⊕⊕OO LOW	CRITICAL
Participant reported improvement (oral minocycline + placebo vs topical benzoyl peroxide + placebo)												
1[1]	randomised	serious[1]	no serious	no serious	serious[4]	none	70/130	78/130	RR 0.9 (0.73 to	60 fewer per 1000 (from 162	⊕⊕OO	CRITICAL

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Oral + topical	Oral + topical	Relative (95% CI)	Absolute		
	trials		inconsistency	indirectness			(53.8%)	(60%)	1.11)	fewer to 66 more)	LOW	
Participant reported improvement (oral minocycline + placebo vs topical benzoyl peroxide/erythromycin + placebo)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	70/130 (53.8%)	84/127 (66.1%)	RR 0.81 (0.69 to 0.96)	126 fewer per 1000 (from 218 fewer to 0 more)	⊕⊕OO LOW	CRITICAL
Participant reported improvement (oral minocycline + placebo vs topical benzoyl peroxide + topical erythromycin + placebo)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	70/130 (53.8%)	82/131 (62.6%)	RR 0.86 (0.7 to 1.06)	88 fewer per 1000 (from 188 fewer to 38 more)	⊕⊕OO LOW	CRITICAL
Participant reported improvement (topical benzoyl peroxide + placebo vs topical benzoyl peroxide/erythromycin + placebo)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	78/130 (60%)	84/127 (66.1%)	RR 0.91 (0.75 to 1.09)	60 fewer per 1000 (from 165 fewer to 60 more)	⊕⊕OO LOW	CRITICAL
Participant reported improvement (topical benzoyl peroxide + placebo vs topical benzoyl peroxide + topical erythromycin + placebo)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	78/130 (60%)	82/131 (62.6%)	RR 0.96 (0.79 to 1.16)	25 fewer per 1000 (from 131 fewer to 100 more)	⊕⊕OO LOW	CRITICAL
Participant reported improvement (topical benzoyl peroxide/erythromycin + placebo vs topical benzoyl peroxide + topical erythromycin + placebo)												
1[1]	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[4]	none	84/127 (66.1%)	82/131 (62.6%)	RR 1.06 (0.88 to 1.27)	38 more per 1000 (from 75 fewer to 169 more)	⊕OOO VERY LOW	CRITICAL

CI: confidence interval; MID: minimally important difference; POR: peto odds ratio; RR: relative risk
[1] Ozolins 2004
[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
[4] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes

Oral hormonal contraceptives and hormone-modifying agents

Table 16: Clinical evidence profile for comparison of treatment with oral hormonal contraceptives or hormone modifying agents versus placebo

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hormonal treatment	Placebo	Relative (95% CI)	Absolute		
Neurological side effect (combined oral contraceptive)												
2[1-2]	randomised trials	Serious[5]	no serious inconsistency	no serious indirectness	very serious[6]	none	30/540 (5.6%)	14/274 (5.1%)	POR 1.1 (0.58 to 2.08)	5 more per 1000 (from 21 fewer to 50 more)	⊕OOO VERY LOW	IMPORTANT
Neurological side effect (oral co-cyprindiol												
1[2]	randomised trials	serious[5]	no serious inconsistency	no serious indirectness	very serious[6]	none	28/537 (5.2%)	7/132 (5.3%)	RR 0.98 (0.44 to 2.2)	1 fewer per 1000 (from 30 fewer to 64 more)	⊕OOO VERY LOW	IMPORTANT
Neurological side effect (oral ethinylestradiol+ oral chlormadinone acetate)												
1[3]	randomised trials	serious[5]	no serious inconsistency	no serious indirectness	serious[7]	none	98/251 (39%)	41/126 (32.5%)	RR 1.2 (0.89 to 1.61)	65 more per 1000 (from 36 fewer to 198 more)	⊕⊕OO LOW	IMPORTANT
Mood disturbance (oral ethinylestradiol + oral drospirenone)												
1[1]	randomised trials	serious[5]	no serious inconsistency	no serious indirectness	very serious[6]	none	1/15 (6.7%)	0/10 (0%)	POR 5.29 (0.1 to 289.29)	-	⊕OOO VERY LOW	IMPORTANT
Mood disturbance (oral ethinylestradiol+ oral chlormadinone acetate)												
1[3]	randomised trials	serious[5]	no serious inconsistency	no serious indirectness	very serious[6]	none	17/251 (6.8%)	5/126 (4%)	RR 1.71 (0.64 to 4.52)	28 more per 1000 (from 14 fewer to 140 more)	⊕OOO VERY LOW	IMPORTANT
Breakthrough bleeding (combined oral contraceptive)												
2[1,4]	randomised trials	very serious[8]	no serious inconsistency	no serious indirectness	no serious imprecision	none	46/192 (24%)	6/187 (3.2%)	POR 5.93 (3.3 to 10.65)	132 more per 1000 (from 67 more to 229 more)	⊕⊕OO LOW	IMPORTANT
Breakthrough bleeding (oral ethinylestradiol+ oral chlormadinone acetate)												

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hormonal treatment	Placebo	Relative (95% CI)	Absolute		
1[3]	randomised trials	serious[5]	no serious inconsistency	no serious indirectness	serious[7]	none	22/251 (8.8%)	4/126 (3.2%)	RR 2.76 (1.15 to 6.63)	56 more per 1000 (from 5 more to 179 more)	⊕⊕OO LOW	IMPORTANT
Participant improvement (oral ethinylestradiol+ oral chlormadinone acetate)												
1[3]	randomised trials	serious[5]	no serious inconsistency	no serious indirectness	no serious imprecision	none	177/251 (70.5%)	52/126 (41.3%)	RR 1.71 (1.37 to 2.14)	293 more per 1000 (from 153 more to 470 more)	⊕⊕⊕O MODERATE	IMPORTANT

CI: confidence interval; MID: minimally important difference; POR: peto odds ratio; RR: relative risk
[1] Alora-Pali 2013,
[2] Palombo-Kinne 2009,
[3] Plewig 2009,
[4] Leyden 2002
[5] Overall risk of bias judgement: serious risk of bias in the evidence contributing to the outcomes
[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] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes
[8] Overall risk of bias judgement: very serious risk of bias in the evidence contributing to the outcomes

Table 17: Clinical evidence profile for comparison of treatment with oral hormonal contraceptives and hormone modifying agents versus treatment with oral hormonal contraceptives and hormone modifying agents

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hormonal treatment	Hormonal treatment	Relative (95% CI)	Absolute		
Neurological side effect (oral ethinylestradiol + norgestimate vs oral ethinylestradiol + desogestrel)												
1[1]	randomised trials	very serious[5]	no serious inconsistency	no serious indirectness	very serious[6]	none	5/101 (5%)	10/101 (9.9%)	RR 0.5 (0.18 to 1.41)	50 fewer per 1000 (from 81 fewer to 41 more)	⊕OOO VERY LOW	IMPORTANT
Neurological side effect (oral ethinylestradiol + chlormadinone acetate vs oral ethinylestradiol + drospirenone)												
1[2]	randomised	Serious[7]	no serious	no serious	very serious[6]	none	6/90	9/90	RR 0.67 (0.25	33 fewer per 1000	⊕OOO	IMPORTANT

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hormonal treatment	Hormonal treatment	Relative (95% CI)	Absolute		
	trials		inconsistency	indirectness			(6.7%)	(10%)	to 1.8)	(from 75 fewer to 80 more)	VERY LOW	
Neurological side effect (oral estradiol (valerate) + dienogest vs oral ethinylestradiol + cyproterone acetate)												
1[3]	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	very serious[6]	none	28/525 (5.3%)	28/537 (5.2%)	RR 1.02 (0.61 to 1.7)	1 more per 1000 (from 20 fewer to 36 more)	⊕OOO VERY LOW	IMPORTANT
Neurological side effect (oral ethinylestradiol + norgestimate vs oral ethinylestradiol + drospirenone)												
1[4]	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	very serious[6]	none	21/582 (3.6%)	22/566 (3.9%)	RR 0.93 (0.52 to 1.67)	3 fewer per 1000 (from 19 fewer to 26 more)	⊕OOO VERY LOW	IMPORTANT
Breakthrough bleeding (oral ethinylestradiol + norgestimate vs oral ethinylestradiol + desogestrel)												
1[1]	randomised trials	very serious[5]	no serious inconsistency	no serious indirectness	very serious[6]	none	10/100 (10%)	7/101 (6.9%)	RR 1.44 (0.57 to 3.64)	30 more per 1000 (from 30 fewer to 183 more)	⊕OOO VERY LOW	IMPORTANT
Breakthrough bleeding (oral ethinylestradiol + chlormadinone acetate vs oral ethinylestradiol + drospirenone)												
1[2]	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	very serious[6]	none	0/90 (0%)	2/90 (2.2%)	POR 0.13 (0.01 to 2.16)	19 fewer per 1000 (from 22 fewer to 25 more)	⊕OOO VERY LOW	IMPORTANT
Breast tenderness (oral ethinylestradiol + norgestimate vs oral ethinylestradiol + desogestrel)												
1[1]	randomised trials	very serious[5]	no serious inconsistency	no serious indirectness	very serious[6]	none	5/100 (5%)	9/101 (8.9%)	RR 0.56 (0.19 to 1.62)	39 fewer per 1000 (from 72 fewer to 55 more)	⊕OOO VERY LOW	IMPORTANT
Breast tenderness (oral ethinylestradiol + chlormadinone acetate vs oral ethinylestradiol + drospirenone)												
1[2]	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	very serious[6]	none	12/90 (13.3%)	12/90 (13.3%)	RR 1 (0.47 to 2.11)	0 fewer per 1000 (from 71 fewer to 148 more)	⊕OOO VERY LOW	IMPORTANT
Breast tenderness (oral estradiol (valerate) + dienogest vs oral ethinylestradiol + cyproterone acetate)												

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hormonal treatment	Hormonal treatment	Relative (95% CI)	Absolute		
1[3]	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	no serious imprecision	none	58/525 (11%)	15/537 (2.8%)	RR 3.96 (2.27 to 6.89)	83 more per 1000 (from 35 more to 165 more)	⊕⊕⊕O MODERATE	IMPORTANT
Breast tenderness (oral ethinylestradiol + norgestimate vs oral ethinylestradiol + drospirenone)												
1[4]	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	very serious[6]	none	17/582 (2.9%)	16/566 (2.8%)	RR 1.03 (0.53 to 2.02)	1 more per 1000 (from 13 fewer to 29 more)	⊕OOO VERY LOW	IMPORTANT

CI: confidence interval; MID: minimally important difference; POR: peto odds ratio; RR: relative risk
[1] Jaisamran 2014
[2] Jaisamran 2018
[3] Palombo-Kinne 2009
[4] Thorneycroft 2004
[5] Overall risk of bias judgement: very serious risk of bias in the evidence contributing to the outcomes
[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 in the evidence contributing to the outcomes

Oral isotretinoin

Table 18: Clinical evidence profile for comparison of treatment with oral isotretinoin versus inactive control

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Oral isotretinoin	Control	Relative (95% CI)	Absolute		
Mucosal/cutaneous changes (oral ISO<120.Daily<0.5)												
1[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	14/23 (60.9%)	2/23 (8.7%)	RR 7.00 (1.79 to 27.39)	522 more per 1000 (from 69 more to 1000 more)	⊕⊕OO LOW	CRITICAL

CI: confidence interval; RR: relative risk

[1] *Rademaker 2014*
[2] *Overall risk of bias judgement: very serious risk of bias*

Physical treatments

Chemical peels

Table 19: Clinical evidence profile for comparison of treatment with chemical peel versus treatment with chemical peel

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Peel	Peel	Relative (95% CI)	Absolute		
Skin irritation (salicylic acid peel vs Jessner's peel)												
1[1]	randomised trials	serious[4]	no serious inconsistency	no serious indirectness	very serious[5]	none	1/20 (5%)	3/20 (15%)	RR 0.33 (0.04 to 2.94)	101 fewer per 1000 (from 144 fewer to 291 more)	⊕OOO VERY LOW	IMPORTANT
Skin redness (salicylic acid peel vs Jessner's peel)												
2[1,2]	randomised trials	serious[4]	serious[6]	no serious indirectness	very serious[5]	none	13/45 (28.9%)	8/45 (17.8%)	RR 1.64 (0.24 to 11)	114 more per 1000 (from 135 fewer to 1000 more)	⊕OOO VERY LOW	IMPORTANT
Skin redness (glycolic acid peel vs salicylic + mandelic acid peel)												
1[3]	randomised trials	serious[4]	no serious inconsistency	no serious indirectness	very serious[5]	none	0/15 (0%)	1/15 (6.7%)	POR 0.14 (0 to 6.82)	57 fewer per 1000 (from 67 fewer to 261 more)	⊕OOO VERY LOW	IMPORTANT
Skin redness (glycolic acid peel vs phytic acid peel)												
1[3]	randomised trials	serious[4]	no serious inconsistency	no serious indirectness	very serious[7]	none	0/15 (0%)	0/15 (0%)	RD 0 (-0.12 to 0.12)	-	⊕OOO VERY LOW	IMPORTANT
Skin redness (salicylic acid peel + mandelic acid peel vs phytic acid peel)												

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Peel	Peel	Relative (95% CI)	Absolute		
1[3]	randomised trials	serious[4]	no serious inconsistency	no serious indirectness	very serious[5]	none	1/15 (6.7%)	0/15 (0%)	POR 7.39 (0.15 to 372.38)	-	⊕OOO VERY LOW	IMPORTANT
Change in pigmentation (salicylic acid peel vs mandelic acid peel)												
1[2]	randomised trials	serious[4]	no serious inconsistency	no serious indirectness	serious[8]	none	3/25 (12%)	0/25 (0%)	POR 8.05 (0.8 to 81.12)	-	⊕⊕OO LOW	IMPORTANT

CI: confidence interval; MID: minimally important difference; POR: peto odds ratio; RD: risk difference; RR: relative risk
[1] Dayal 2017,
[2] Dayal 2020,
[3] Sarkar 2019
[4] Overall risk of bias judgement: serious risk of bias in the evidence contributing to the outcomes
[5] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes
[6] Evidence downgraded by 1 level due to serious inconsistency
[7] Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events
[8] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes

Energy based treatments (light/laser)

Table 20: Clinical evidence profile for comparison of treatment with pulsed dye laser vs placebo

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Energy device (laser)	Placebo	Relative (95% CI)	Absolute		
Skin irritation (pulsed dye laser)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	1/31 (3.2%)	2/10 (20%)	RR 0.16 (0.02 to 1.6)	168 fewer per 1000 (from 196 fewer to 120 more)	⊕OOO VERY LOW	IMPORTANT
Skin redness (pulsed dye laser)												

1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	1/31 (3.2%)	0/10 (0%)	POR 3.75 (0.04 to 360.19)	-	⊕OOO VERY LOW	IMPORTANT

CI: confidence interval; MID: minimally important difference; POR: peto odds ratio; RR: relative risk
[1] Seaton 2003
[2] Overall risk of bias judgement: serious risk of bias in the evidence contributing to the outcomes

[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 21: Clinical evidence profile for comparison of treatment with energy device versus placebo

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Energy device (light)**	**Placebo**	**Relative (95% CI)**	**Absolute**		
Skin irritation (blue light led photochemical therapy)												
1[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	3/27 (11.1%)	2/25 (8%)	RR 1.39 (0.25 to 7.64)	31 more per 1000 (from 60 fewer to 531 more)	⊕OOO VERY LOW	IMPORTANT
Skin irritation (blue + red light photochemical therapy)												
1[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	1/30 (3.3%)	2/25 (8%)	RR 0.42 (0.04 to 4.33)	46 fewer per 1000 (from 77 fewer to 266 more)	⊕OOO VERY LOW	IMPORTANT

CI: confidence interval; MID: minimally important difference; RR: relative risk
[1] Papageoriou 2000
[2] Overall risk of bias judgement: very serious risk of bias in the evidence contributing to the outcomes
[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 22: Clinical evidence profile for comparison of treatment with energy device versus treatment with energy device

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Energy device (light)**	**Energy device (light)**	**Relative (95% CI)**	**Absolute**		

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Energy device (light)	Energy device (light)	Relative (95% CI)	Absolute		
Skin irritation (blue light led photochemical therapy vs blue + red light photochemical therapy)												
1[1]	randomised trials	very serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	3/27 (11.1%)	1/30 (3.3%)	RR 3.33 (0.37 to 30.16)	78 more per 1000 (from 21 fewer to 972 more)	⊕OOO VERY LOW	IMPORTANT
Skin redness (5-AMINOLEVULINIC ACID photodynamic therapy using intense pulsed light vs intense pulsed light therapy)												
1[2]	randomised trials	serious[5]	no serious inconsistency	no serious indirectness	serious[6]	none	14/15 (93.3%)	8/10 (80%)	1.17 (0.83 to 1.64)	136 more per 1000 (from 136 fewer to 512 more)	⊕⊕OO LOW	IMPORTANT
Change in pigmentation (5-AMINOLEVULINIC ACID photodynamic therapy using intense pulsed light therapy vs intense pulsed light therapy)												
1[2]	randomised trials	serious[5]	no serious inconsistency	no serious indirectness	very serious[4]	none	4/15 (26.7%)	1/20 (5%)	RR 5.33 (0.66 to 42.97)	216 more per 1000 (from 17 fewer to 1000 more)	⊕OOO VERY LOW	IMPORTANT
Participant reported improvement (5-AMINOLEVULINIC ACID photodynamic therapy using intense pulsed light vs intense pulsed light therapy)												
1[2]	randomised trials	serious[5]	no serious inconsistency	no serious indirectness	no serious imprecision	none	15/15 (100%)	8/20 (40%)	RR 2.39 (1.41 to 4.05)	556 more per 1000 (from 164 more to 1000 more)	⊕⊕⊕O MODERATE	IMPORTANT

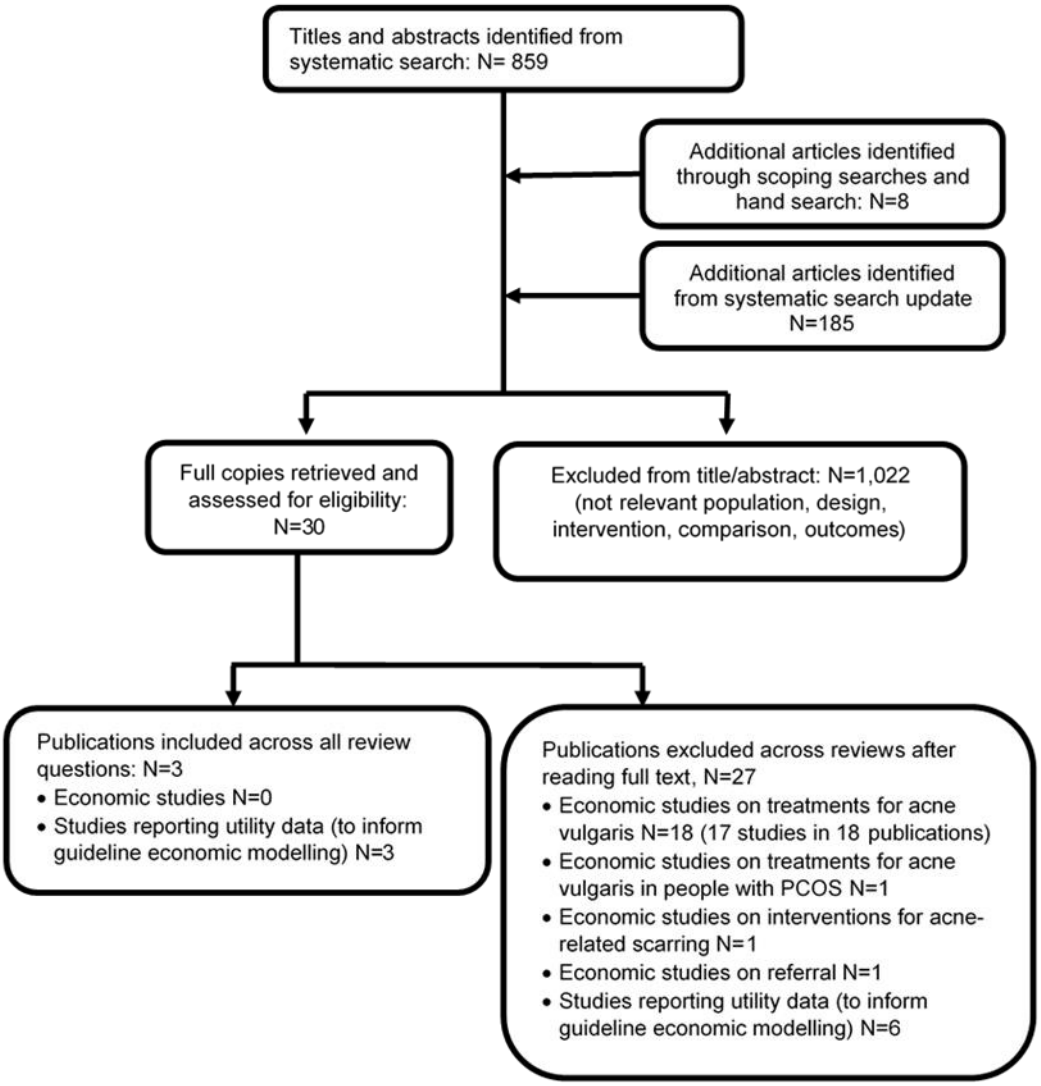
CI: confidence interval; MID: minimally important difference; RR: relative risk
[1] Papageorgiou 2000
[2] Ragab 2014
[3] Overall risk of bias judgement: very serious risk of bias in the evidence contributing to the outcomes
[4] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes
[5] Overall risk of bias judgement: serious risk of bias in the evidence contributing to the outcomes
[6] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID 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 mild to moderate 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 17. 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 mild to moderate 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 model for review question: What is the effectiveness and acceptability of interventions for the treatment of mild to moderate 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 E1.

Appendix J - Economic analysis

Economic analysis for review question: What is the effectiveness and acceptability of interventions for the treatment of mild to moderate 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 E1.

Appendix K - Excluded studies

Excluded clinical and economic studies for review question: What is the effectiveness and acceptability of interventions for the treatment of mild to moderate 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 23: Excluded studies and reasons for their exclusion

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

Reference	Reason for exclusion
cyproterone acetate-ethinyl estradiol combination in moderate acne: a pilot randomized clinical trial. 2011. Clinical, Cosmetic and Investigational Dermatology CCID	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 trial. 2009. Journal of Pakistan Association of Dermatologists	No relevant outcomes reported

Reference	Reason for exclusion
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 3.75% gel. 2017. Journal of clinical and aesthetic dermatology	No relevant data reported - post hoc subgroup analysis for Hispanic population of Pariser 2014

Reference	Reason for exclusion
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, Evaluation of Efficacy, Safety and Optimal Concentration of CLDM-T Gel in the Treatment of Acne Vulgaris. 1999a. Rinsho iyaku (journal of	Not in English language

Reference	Reason for exclusion
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 vulgaris: What is the role of age?. 2011. Journal of Dermatological Treatment	No relevant study population - sample includes people with moderate acne but

Reference	Reason for exclusion
	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
Behrangi, E., Sadeghi, S., Sadeghzadeh-Bazargan, A., Goodarzi, A., Ghassemi, M., Sepasgozar, S., Rohaninasab, M. The effect of	No relevant data reported - reports combined results

Reference	Reason for exclusion
metformin in the treatment of intractable and late onset acne: A comparison with oral isotretinoin. 2019. Iranian Journal of Dermatology	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
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	No relevant study population - sample includes people with mild

Reference	Reason for exclusion
Vulgaris: Results of a Randomized, Active Controlled, Multicentre, Phase IV Clinical Trial. 2014. Journal of Clinical and Diagnostic Research JCDR	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
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	No relevant study population - sample includes people with mild

Reference	Reason for exclusion
vulgaris. 1991. Acta Dermato-Venereologica	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 Tretinoin Formulations. 2003b. Cutis	No relevant study population - participants did not have acne
Brand, E. L. R., A. Study of the therapeutic effectiveness of clindamycin phosphate (1% solution) versus tetracycline (solution)	Not in English language

Reference	Reason for exclusion
administered topically in the treatment of acne vulgaris. 1986. Medicina cutÃ¡nea ibero-latino-americana	
Brandt, H. A., P.,Ahokas, T.,Forstrom, L.,Jarvinen, T.,Keskitalo, R.,Lehtonen, L.,Plosila, M.,Rita, H.,Suramo, M. L.Erythromycin acistrate - An alternative oral treatment for acne. 1994. Journal of Dermatological Treatment	No relevant comparison - suboptimal dose
Breneman, D. L. A., M. C. Successful treatment of acne vulgaris in women with a new topical sodium sulfacetamide/sulfur lotion. 1993. International Journal of Dermatology	No relevant study design - not RCT
Breno, B. K., A.,Richard, A.,Rougier, A.Interest of a new salicylic acid derivative in the prevention of acne relapses. 2002. European journal of dermatology : EJD	No relevant article type - conference abstract
Brickman, S. S. L., W. D.,Gareau, J. Y.A double-blind evaluation of a topical antibiotic preparation in acne. 1980. Current Therapeutic Research - Clinical and Experimental	No relevant intervention - intervention & class not available in the UK
Brodell, R. T. S., B. J.,Rafal, E.,Toth, D.,Tyring, S.,Wertheimer, A.,Kerrouche, N.,Bucher, D.A fixed-dose combination of adapalene 0.1%BPO 2.5% allows an early and sustained improvement in quality of life and patient treatment satisfaction in severe acne. 2012. Journal of Dermatological Treatment	No relevant outcomes reported
Brogden, R. N. S., T. M.,Avery, G. S.Benzoyl peroxide acne lotions : an independent report. 1974. Drugs	No relevant article type - expert review
Brookes, D. B. M., R. M.,Sheil, L. P.,Flowers, I. M.,Poulter, G. A. Comparison of Tretinoin and a composite formulation in the treatment of acne. 1978. British Journal of Clinical Practice	No relevant study population - insufficient details reported to determine acne severity and study is not relevant for PCOS, maintenance or refractory treatments
Bubna, A. K.Metformin - For the dermatologist. 2016. Indian Journal of Pharmacology	Duplicate record
Bucknall, J. H. M., P. N. Comparison of tretinoin solution and benzoyl peroxide lotion in the treatment of acne vulgaris. 1977. Current Medical Research & Opinion	Not obtainable
Budden, M. G. Topical and oral tetracycline in the treatment of acne vulgaris. 1988. Practitioner	No relevant intervention - intervention & class not available in the UK
Burke, B. E., E. A.,Cunliffe, W. J.Benzoylperoxide versus topical erythromycin in the treatment of acne vulgaris. 1983. British Journal of Dermatology	No relevant study design - not RCT
Burkhart, C. G. B., C. N.Treatment of acne vulgaris without antibiotics: tertiary amine-benzoyl peroxide combination vs. benzoyl peroxide alone (Proactiv Solution). 2007. International Journal of Dermatology	Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments
Burton, J. E., G.A placebo-controlled study to evaluate the efficacy of topical tetracycline and oral tetracycline in the treatment of mild to moderate acne. 1990. Journal of International Medical Research	No relevant intervention - intervention & class not available in the UK
Burton, J. L. P., R. J.,Harris, J. I.Effect of 1% cyproterone acetate in Cetomacrogol cream BPC (formula A) on sebum excretion rate in patients with acne. 1976. British Journal of Dermatology	No relevant data reported - pharmokinetic study

Reference	Reason for exclusion
Callender, V. D.Fitzpatrick skin types and clindamycin phosphate 1.2%/benzoyl peroxide gel: Efficacy and tolerability of treatment in moderate to severe acne. 2012a. Journal of Drugs in Dermatology	No relevant data reported - post hoc analysis reporting results for people receiving clindamycin 2.1%/BPO 2.5% gel
Cambazard, F.Clinical efficacy of Velac, a new tretinoin and clindamycin phosphate gel in acne vulgaris. 1998. Journal of the European Academy of Dermatology & Venereology	No relevant study design - non-systematic review of tretinoin treatment
Cannizzaro, M. V. D., A.,Garofalo, V.,Del Duca, E.,Bianchi, L.Reducing the oral Isotretinoin skin side effects: Efficacy of 8% omega-ceramides, hydrophilic sugars, 5% niacinamide cream Compound in acne patients. 2018. Giornale Italiano di Dermatologia e Venereologia	Not in English language
Cao, J., Yang, G., Wang, Y., Liu, J. Acupoint Stimulation for Acne: A Systematic Review of Randomized Controlled Trials. 2013. Med Acupunct. 2013	No relevant intervention - systematic review about acupoint stimulation techniques used to treat acne
Cao, J., Yang, G., Wang, Y., Ping Liu, J., Smith, C.A., Luo, H., Liu. Y. Complementary therapies for acne vulgaris. 2015. Cochrane Database Syst Rev	Not relevant intervention - systematic review about complementary and alternative medicine for acne
Cao, T. T., E. S.,Chan, Y. H.,Yosipovitch, G.,Tey, H. L.Anti-pruritic efficacies of doxycycline and erythromycin in the treatment of acne vulgaris: a randomized single-blinded pilot study. 2018. Indian journal of dermatology, venereology and leprology	No relevant study design - not RCT
Carlborg, L. Cyproterone acetate versus Levonorgestrel combined with ethinyl estradiol in the treatment of acne. Results of a multicenter study. 1986. Acta Obstetricia et Gynecologica Scandinavica	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Carlborg, L. Cyproterone acetate versus levonorgestrel combined with ethinylestradiol in the treatment of acne. Results of a multicenter study. 1987. Contraception fertilite sexualite	Duplicate record
Carmina, E. L., R. A.A comparison of the relative efficacy of antiandrogens for the treatment of acne in hyperandrogenic women. 2002. Clinical Endocrinology	Duplicate record
Caron, D. S., V.,Clucas, A.,Verschoore, M.Skin tolerance of adapalene 0.1% gel in combination with other topical antiacne treatments. 1997a. Journal of the American Academy of Dermatology	No relevant study population - participants did not have acne
Caron, D. S., V.,Kerrouche, N.,Clucas, A.Split-face comparison of adapalene 0. 1% gel and tretinoin 0.025% gel in acne patients. 1997b. Journal of the American Academy of Dermatology	No relevant outcomes reported
Cavicchini, S. C., R.Long-term treatment of acne with 20% azelaic acid cream. 1989. Acta Dermato-Venereologica, Supplement	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Cestone, E. M., A.,Zanoletti, V.,Zanardi, A.,Mantegazza, R.,Dossena, M.Acne RA-1,2, a novel UV-selective face cream for patients with acne: Efficacy and tolerability results of a randomized, placebo-	Efficacy outcomes reported in figures only

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

Reference	Reason for exclusion
topical nadifloxacin and benzoyl peroxide versus clindamycin and benzoyl peroxide in acne vulgaris: A randomized controlled trial. 2011. Indian Journal of Pharmacology	intervention & class not available in the UK
Christian, G. L. K., G. G. Clindamycin vs placebo as adjunctive therapy in moderately severe acne. 1975. Archives of Dermatology	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Christiansen, J. H., P.,Reymann, F.The retinoic acid derivative Ro 11 1430 in Acne vulgaris. A controlled multicenter trial against retinoic acid. 1977. Dermatologica	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Christiansen, J. H., P.,Reymann, F.Treatment of acne vulgaris with the retinoic acid derivative Ro 11-1430. A controlled clinical trial against retinoic acid. 1976. Dermatologica	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Christiansen, J. V. G., E.,Ludvigsen, K.,Konstman Meier, C. H.,Norholm, A.,Osmundsen, P. E.,Pedersen, D.,Rasmussen, K. A.,Reiter, H.,Reymann, F.,et al.,Topical vitamin A acid (Airol) and systemic oxytetracycline in the treatment of acne vulgaris. A controlled clinical trial. 1974a. Dermatologica	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Christiansen, J. V. G., E.,Ludvigsen, K.,Meier, C. H.,Norholm, A.,Pedersen, D.,Rasmussen, K. A.,Reiter, H.,Reymann, F.,Sylvest, B.,et al.,Topical tretinoin, vitamin A acid (Airol) in acne vulgaris. A controlled clinical trial. 1974b. Dermatologica	No relevant study population - sample includes people with mild to severe acne and study is not relevant for PCOS, maintenance or refractory treatments
Chu, A. H., F. J.,Plott, R. T.The comparative efficacy of benzoyl peroxide 5%/erythromycin 3% gel and erythromycin 4%/zinc 1.2% solution in the treatment of acne vulgaris. 1997. British Journal of Dermatology	No relevant study population - sample includes people with too narrow range of acne severity criteria and study is not relevant for PCOS, maintenance or refractory treatments
Chularojanamontri, L. T., P.,Kulthanan, K.,Varothai, S.,Winayanuwattikun, W.A double-blinded, randomized, vehicle-controlled study to access skin tolerability and efficacy of an anti-inflammatory moisturizer in treatment of acne with 0.1% adapalene gel. 2016. Journal of Dermatological Treatment	No relevant intervention - Adaplene with or without Eucerin mositurizer
Clucas, A. V., M.,Sorba, V.,Poncet, M.,Baker, M.,Czernielewski, J.Adapalene 0.1% gel is better tolerated than tretinoin 0.025% gel in acne patients. 1997. Journal of the American Academy of Dermatology	Duplicate publication from Cunliffe 1997 trial
Cochran, R. J. T., S. B.,Flannigan, S. A.Topical zinc therapy for acne vulgaris. 1985. International Journal of Dermatology	No relevant study design - not RCT

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Reference	Reason for exclusion
	maintenance and refractory treatments
Shie Morteza, M., Hayati, Z., Namazi, N., Abdollahimajd, F.Efficacy and safety of oral silymarin in comparison with oral doxycycline and their combination therapy in the treatment of acne vulgaris. 2019. Dermatologic Therapy	No relevant intervention - silymarin
Shin JU, Lee SH, Jung JY, Lee JH.A split-face comparison of a fractional microneedle radiofrequency device and fractional carbon dioxide laser therapy in acne patients.. 2012. J Cosmet Laser Ther	Reported outcomes relevant for the network meta-analysis but not in enough detail to include in the analysis. Outcomes were not relevant for pairwise comparisons - including PCOS, maintenance and refractory treatments
Shwetha, H. G., A.A comparative study of efficacy and safety of combination of topical 1% clindamycin and 0.1% adapalene with 1% clindamycin and 2.5% benzoyl peroxide in mild to moderate acne in a tertiary care hospital. 2013. Indian Journal of Pharmacology	No relevant article type - conference abstract
Sidgiddi, 2019Efficacy of oral isotretinoin in combination with desloratadine in the treatment of common vulgaris acne in Vietnamese Patients. 2019. Open Access Macedonian Journal of Medical Sciences	Duplication of Van 2019
Sidgiddi, S., Allenby, K., Okumu, F., Gautam, A.Bioavailability, Pharmacokinetics, and Transepidermal Water Loss of Short Contact Tazarotene Lotion 0.1% Versus Tazarotene (Tazorac^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

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

Economic studies	Reason for exclusion
Straight CE, Lee YH, Liu G, Kirby JS (2015). Duration of oral 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.	Retrospective analysis of 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

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

For research recommendations associated with this review question see appendix L in evidence report E1.