

# **Evidence informing best treatment for acne vulgaris in clinical practice**

Eugene Healy

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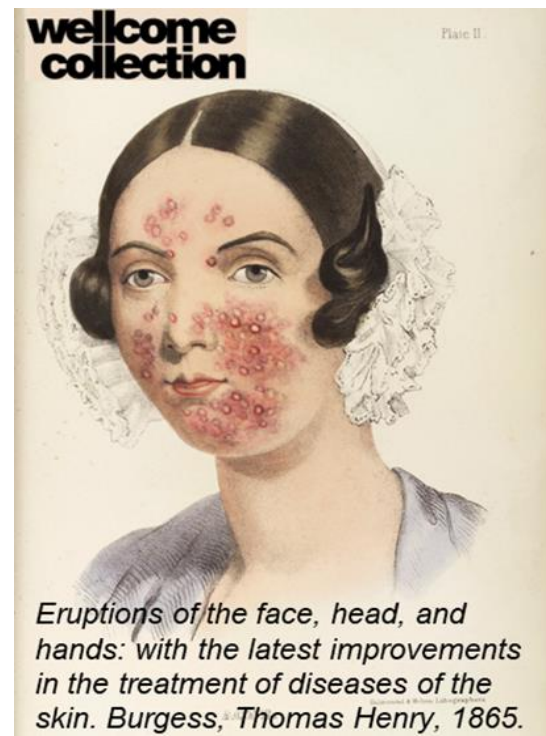
# Acne vulgaris

- Face / Chest / Back / Shoulders
- Comedones
- Papules / Pustules
- Nodules / Cysts
- Scars (ice pick, rolling, boxcar, hypertrophic, keloid)
- Seborrhoea
- Pigmentary changes

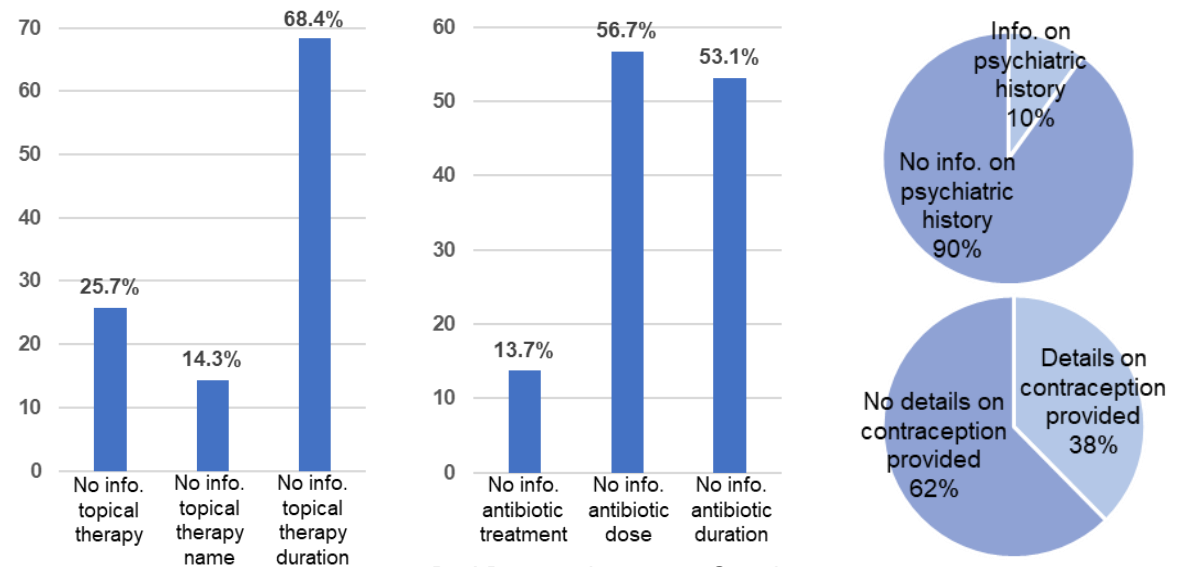


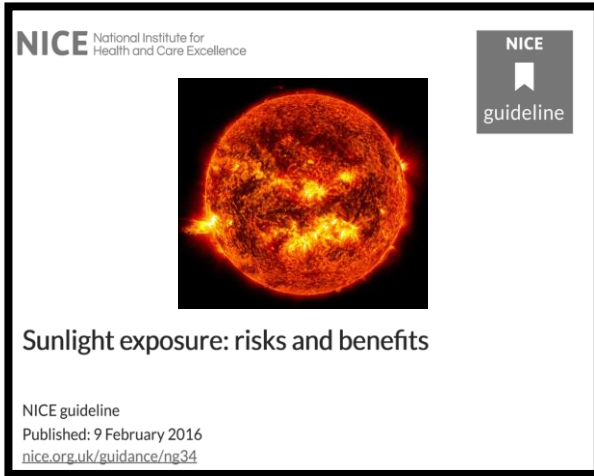
# Acne vulgaris / Need for guidance

- 8<sup>th</sup> most common disease in the world (*Lancet* 2012;380:2163-96)
- Skin disease + psychosocial effects  
59.6% reported reduced self-confidence (*Br J Dermatol* 2022;186:191-3)
- Range of treatments available
- Variation in clinical practice (treatments, duration, etc.)
- Variation in provision of relevant information during referral to secondary care



307 sequential referral letters for patients (127 male, 180 female) with acne





Expert Advisor to NICE



The guideline referred to in this presentation was produced by the National Guideline Alliance for the National Institute for Health and Care Excellence (NICE). The views expressed in this presentation are those of the author and not necessarily those of NICE.

National Institute for Health and Care Excellence (2021) Acne vulgaris: management. Available from <https://www.nice.org.uk/guidance/ng198>

NICE worked with the British Association of Dermatologists (BAD) to develop this guideline.

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# Many potential treatments for acne; which ones are best?

SYSTEMATIC REVIEW

BJD  
British Journal of Dermatology

## A systematic review and network meta-analysis of topical pharmacological, oral pharmacological, physical and combined treatments for acne vulgaris\*

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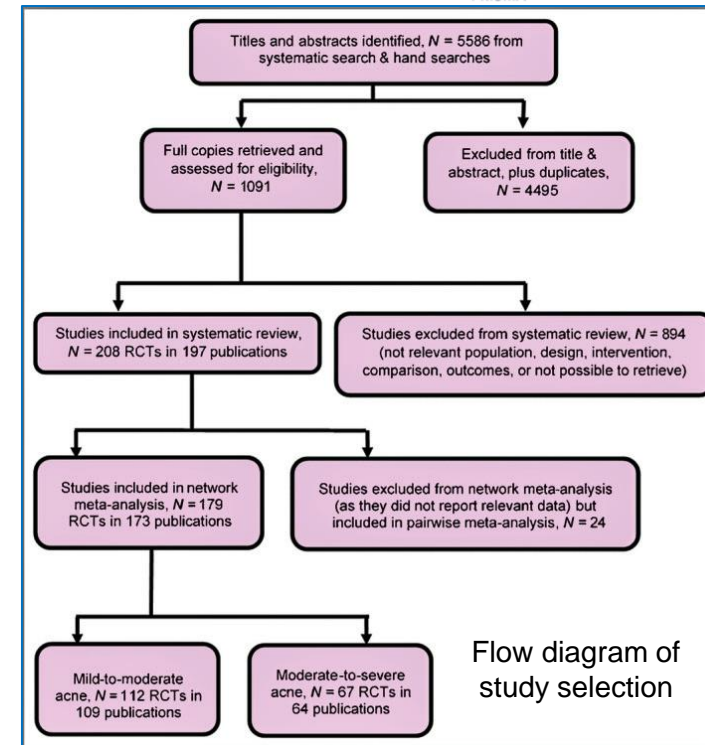
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BJD 2022;187:639–649

PROSPERO  
International prospective register of systematic reviews

PRISMA  
guidelines



### Supplementary data

[bjd21739-sup-0001-AppendixS1](#)

**Appendix S1** Search strategy.

- docx file

[bjd21739-sup-0002-AppendixS2](#)

**Appendix S2** Study protocol.

- docx file

[bjd21739-sup-0003-AppendixS3](#)

**Appendix S3** Methods of the statistical analysis and codes for data synthesis.

- docx file

[bjd21739-sup-0004-AppendixS4](#)

**Appendix S4** Methods of inconsistency checks and statistical codes.

- docx file

[bjd21739-sup-0005-AppendixS5](#)

**Appendix S5** Methods of bias adjustment models and statistical codes.

- docx file

[bjd21739-sup-0006-AppendixS6](#)

**Appendix S6** Methods of threshold analysis.

- docx file

[bjd21739-sup-0007-AppendixS7](#)

**Appendix S7** Characteristics of studies included in the network meta-analysis, and full references.

- docx file

[bjd21739-sup-0008-AppendixS8](#)

**Appendix S8** List of excluded studies with reasons for exclusion.

- docx file

[bjd21739-sup-0009-AppendixS9](#)

**Appendix S9** Network meta-analysis data files.

- xlsx file

[bjd21739-sup-0010-AppendixS10](#)

**Appendix S10** Treatment classes, interventions and numbers of observations made on each, for each outcome considered in the network meta-analysis.

- docx file

[bjd21739-sup-0011-AppendixS11](#)

**Appendix S11** Model fit statistics.

- docx file

[bjd21739-sup-0012-AppendixS12](#)

**Appendix S12** Inconsistency checks – results.

- docx file

[bjd21739-sup-0013-AppendixS13](#)

**Appendix S13** Risk of bias of studies included in the network meta-analysis.

- docx file

[bjd21739-sup-0014-AppendixS14](#)

**Appendix S14** Bias adjustment models – results.

- docx file

[bjd21739-sup-0015-AppendixS15](#)

**Appendix S15** Network meta-analysis additional results.

- docx file

[bjd21739-sup-0016-AppendixS16](#)

**Appendix S16** Relative effects between all pairs of treatment classes: results of direct (head-to-head), indirect and network meta-analysis comparisons.

- xlsx file

[bjd21739-sup-0017-AppendixS17](#)

**Appendix S17** Threshold analysis on the efficacy outcome – results.

- docx file

[bjd21739-sup-0018-FigureS1-S2](#)

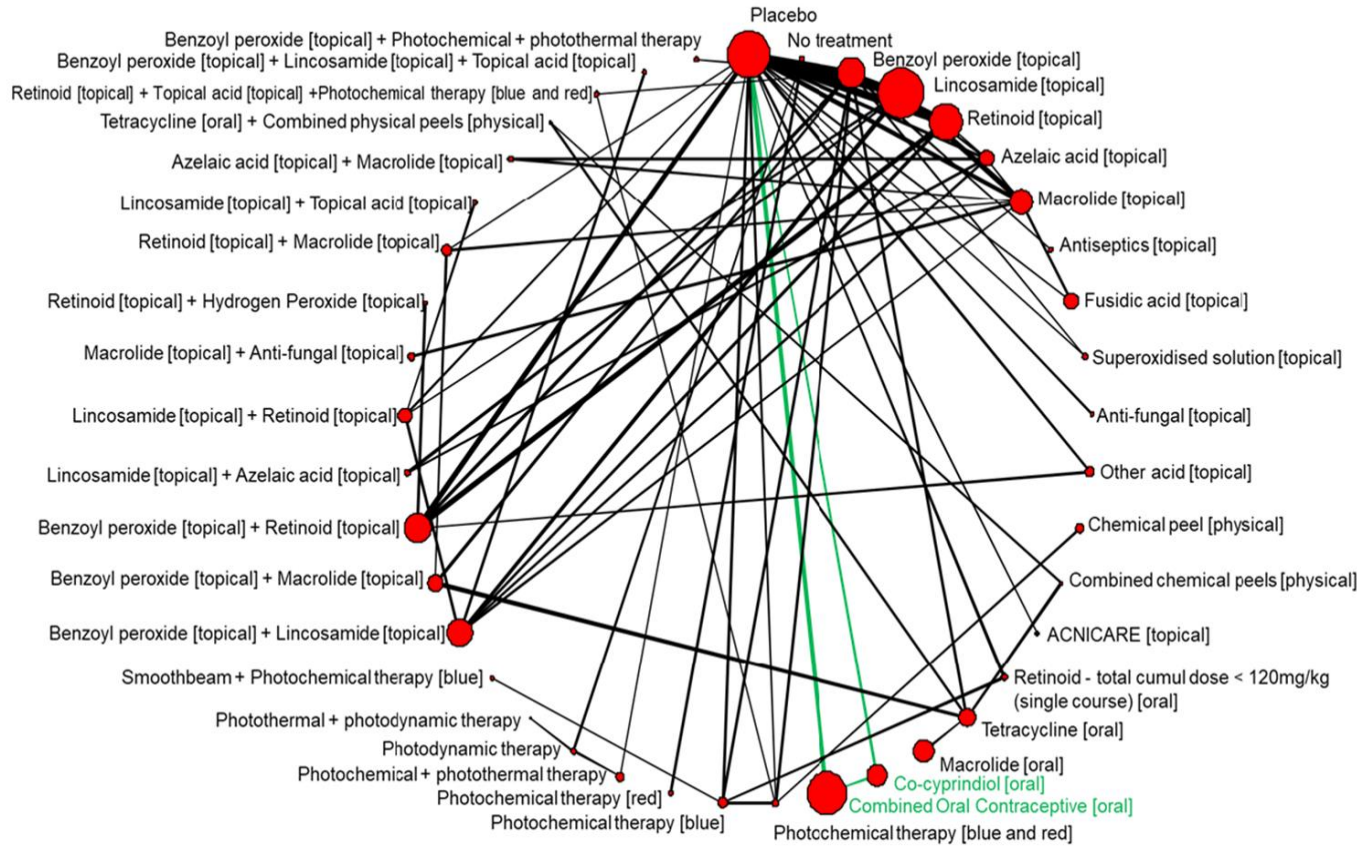
**Figure S1** Network of treatment classes for people with (a) mild-to-moderate acne and (b) moderate-to-severe acne on discontinuation for any reason.

**Figure S2** Network of treatment classes for people with (a) mild-to-moderate acne and (b) moderate-to-severe acne on discontinuation owing to side-effects.

- Systematic literature search identified 5,586 potentially eligible publications.
- 173 publications reporting on 179 RCTs (112 for mild-to-moderate acne and 67 for moderate-to-severe acne) met eligibility criteria for Network Meta Analysis (NMA).
- For mild-to-moderate acne, the NMA of efficacy included 90 RCTs, 41 treatment classes and 17,260 observations.
- For moderate-to-severe acne, the NMA of efficacy included 56 RCTs, 27 treatment classes and 16,493 observations.

# Network Meta Analysis (NMA); mild to moderate acne

Figure 1. Efficacy network of treatment classes for people with mild to moderate acne.



Treatment classes and lines in green indicate treatments and comparisons relevant to females only.

Width of each line proportional to number of trials in which each direct comparison is made.

Size of each circle proportional to number of observations made on each treatment class (number of participants in parallel trials and number of observations in split-face/body trials).

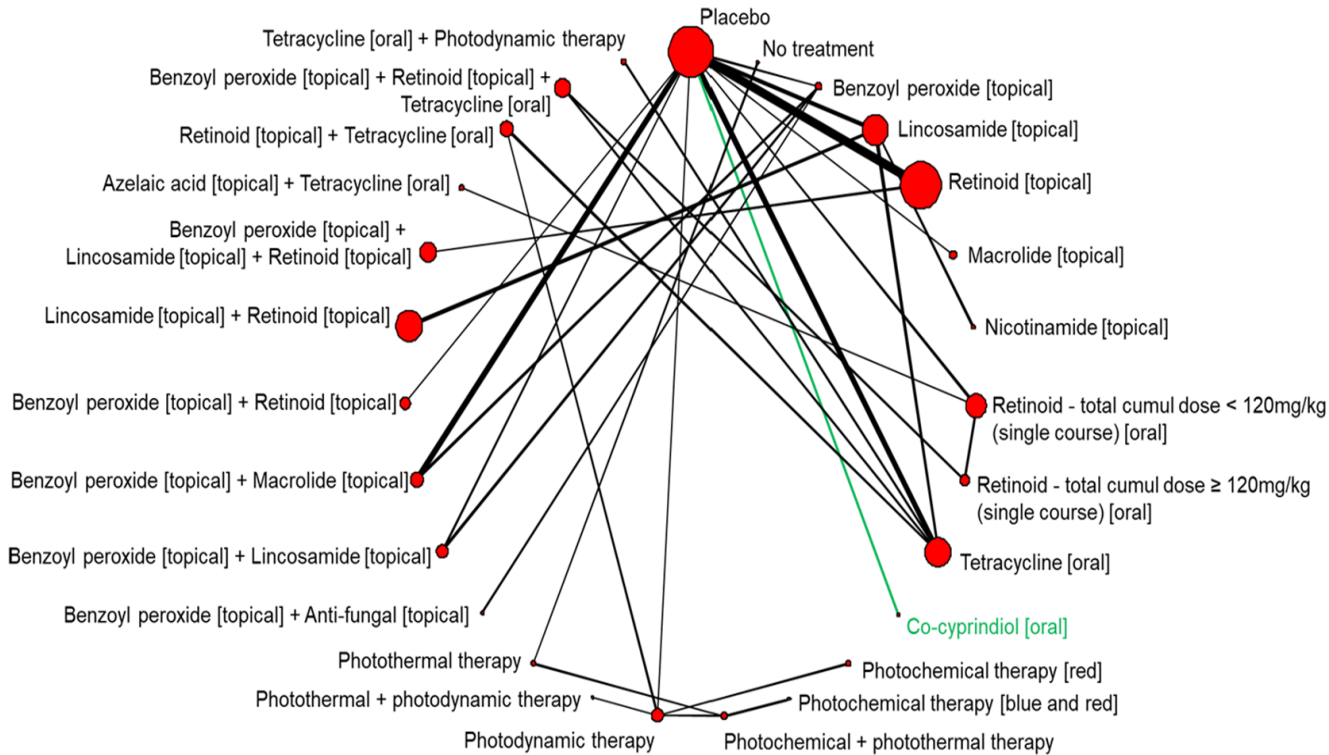
Table 1 Network meta-analysis: treatment efficacy (percentage change in total acne lesion count from baseline) in mild-to-moderate acne: bias-adjusted treatment class effects vs. placebo and rankings

Class	N	Effect vs. placebo (mean, 95% CrI)	Rank, females (mean, 95% CrI)	Rank, males (mean, 95% CrI)
ACNICARE (topical)	20	81.57 (32.49–135.70)	2.73 (1–10)	2.72 (1–10)
Photothermal + photodynamic therapy	9	67.87 (16.51–118.00)	4.30 (1–22)	4.27 (1–22)
Photochemical therapy (red)	28	84.57 (3.34–163.80)	4.34 (1–35)	4.26 (1–33)
Smoothbeam + photochemical therapy (blue)	24	54.34 (19.99–88.78)	5.51 (1–20)	5.49 (1–20)
<b>Chemical peels (physical)</b>	<b>101</b>	<b>39.70 (12.54–66.78)</b>	9.23 (2–28)	9.18 (2–27)
<b>Photochemical therapy (combined blue/red light)</b>	<b>69</b>	<b>35.36 (17.75–53.08)</b>	10.05 (4–21)	10.03 (4–21)
Benzoyl peroxide (topical) + lincosamide (Clindamycin) (topical) + other acid (topical)	24	32.37 (11.97–52.76)	12.13 (4–28)	12.06 (4–28)
Retinoid (topical) + Hydrogen Peroxide (topical)	26	32.16 (11.94–52.16)	12.27 (4 to 29)	12.20 (4–28)
Azelaic acid (topical) + lincosamide (Clindamycin) (topical)	44	30.24 (10.97–49.54)	13.38 (4–29)	13.29 (4–29)
Superoxidized solution (topical)	39	31.07 (3.94–58.38)	13.93 (3–35)	13.76 (3–34)
Photodynamic therapy (physical)	36	33.95 (–9.34–75.64)	14.03 (3–39)	13.74 (3–37)
<b>Photochemical therapy (blue) (physical)</b>	<b>138</b>	<b>28.58 (12.55–44.72)</b>	14.14 (6–27)	14.06 (6–26)
Benzoyl peroxide (topical) + photochemical + photothermal therapy (physical)	29	29.37 (6.81–52.22)	14.38 (4–33)	14.24 (4–32)
<b>Benzoyl peroxide (topical) + retinoid (topical)</b>	<b>1057</b>	<b>26.16 (16.75–35.36)</b>	15.44 (8–24)	15.39 (8–24)
Azelaic acid (topical) + macrolide (topical)	40	25.92 (7.96–43.87)	16.31 (6–32)	16.16 (6–31)
<b>Lincosamide (clindamycin) (topical) + retinoid (topical)</b>	<b>276</b>	<b>24.23 (10.84–37.51)</b>	17.22 (8–29)	17.08 (8–28)
No treatment	39	29.88 (–36.27–93.56)	17.83 (2–41)	17.28 (2–39)
<b>Macrolide (topical) + antifungal (topical)</b>	<b>74</b>	<b>22.77 (0.74–44.65)</b>	19.18 (5–37)	18.85 (5–35)
<b>Benzoyl peroxide (topical) + Macrolide (topical)</b>	<b>351</b>	<b>20.14 (1.44–38.73)</b>	21.00 (8–35)	20.62 (8–34)
Retinoid (topical) + other acid (topical) + photochemical therapy (combined blue/red light) (physical)	35	20.26 (–5.28–45.98)	21.49 (6–39)	21.00 (6–38)
Lincosamide (clindamycin) (topical) + other acid (topical)	23	18.67 (–4.10–41.07)	22.61 (7–39)	22.09 (7–37)
<b>Retinoid (topical)</b>	<b>1623</b>	<b>18.27 (10.28–26.14)</b>	22.71 (15–31)	22.43 (15–30)
<b>Photochemical + photothermal therapy [physical]</b>	<b>107</b>	<b>18.42 (–21.39–56.29)</b>	23.02 (5–41)	22.34 (5–39)
<b>Benzoyl peroxide (topical) + lincosamide (clindamycin) (topical)</b>	<b>992</b>	<b>17.91 (8.01–27.73)</b>	23.14 (15–32)	22.80 (15–31)
Tetracycline (oral) + combined chemical peels (physical)	13	16.44 (–10.96–43.82)	24.17 (6–40)	23.49 (6–38)
Combined chemical peels (physical)	14	16.06 (–11.37–43.40)	24.49 (6–40)	23.78 (6–38)
<b>Retinoid (topical) + macrolide (topical)</b>	<b>135</b>	<b>16.19 (–3.65–35.89)</b>	24.67 (9–39)	24.05 (9–37)
<b>Benzoyl peroxide (topical)</b>	<b>1109</b>	<b>15.60 (6.02–25.11)</b>	25.53 (18–33)	25.04 (18–32)
Antiseptics (topical)	30	13.41 (–9.20–36.05)	26.94 (9–40)	26.12 (9–38)
<b>Other acid (topical)</b>	<b>106</b>	<b>12.28 (–3.38–28.30)</b>	28.27 (14–39)	27.42 (13–37)
<b>Retinoid - total cumulative dose &lt; 120 mg kg<sup>-1</sup> (single course) (oral)</b>	<b>54</b>	<b>11.40 (–12.13–34.87)</b>	28.50 (10–41)	27.56 (10–39)
<b>Macrolide (topical)</b>	<b>765</b>	<b>11.71 (1.50–21.87)</b>	29.19 (20–36)	28.34 (20–35)
Cocypriindiol (oral)	584	10.49 (–5.10–26.01)	29.65 (14–40)	Not relevant
<b>Combined oral contraceptive (oral)</b>	<b>2313</b>	<b>10.18 (–0.47–20.85)</b>	30.36 (19–38)	Not relevant
<b>Tetracycline (oral)</b>	<b>388</b>	<b>9.41 (–10.54–29.32)</b>	30.54 (15–40)	29.48 (15–38)
Azelaic acid (topical)	301	9.54 (–1.83–20.59)	31.15 (22–38)	30.08 (21–37)
<b>Macrolide (oral)</b>	<b>143</b>	<b>3.54 (–24.34–31.38)</b>	33.35 (13–41)	32.00 (13–39)
<b>Lincosamide (clindamycin) (topical)</b>	<b>3073</b>	<b>6.28 (–1.67–14.18)</b>	34.02 (27–39)	32.59 (26–37)
Antifungal (topical)	20	–7.12 (–51.55–37.13)	35.37 (8–41)	33.81 (8–39)
Fusidic acid (topical)	310	0.34 (–15.84–16.89)	36.65 (25–41)	34.97 (25–39)
<b>Placebo</b>	<b>2698</b>	<b>Reference</b>	37.80 (33–41)	35.93 (31–39)

CrI, credible interval; N, number of observations across trials included in the analysis. Classes ordered by mean rank for females (rank = 1 indicates highest efficacy). Treatment classes and values in bold indicate treatment classes with N ≥ 50 each across randomized controlled trials included in the analysis. Treatment classes and values in italics indicate treatment classes with 95% CrI crossing the 'no effect' line.

# Network Meta Analysis (NMA); moderate to severe acne

Figure 1. Efficacy network of treatment classes for people with moderate to severe acne.



Treatment classes and lines in green indicate treatments and comparisons relevant to females only.

Width of each line proportional to number of trials in which each direct comparison is made.

Size of each circle proportional to number of observations made on each treatment class (number of participants in parallel trials and number of observations in split-face/body trials).

Table 2 Network meta-analysis: treatment efficacy (percentage change in total acne lesion count from baseline) in moderate-to-severe acne: treatment class effects vs. placebo and rankings

Class	N	Effect vs. placebo (mean, 95% CrI)	Rank, females (mean, 95% CrI)	Rank, males (mean, 95% CrI)
<b>Retinoid - total cumulative dose <math>\geq 120 \text{ mg kg}^{-1}</math> (single course) (oral)</b>	<b>182</b>	<b>58.09 (36.99–79.29)</b>	3.39 (1–11)	3.35 (1–10)
Photothermal therapy (physical)	46	57.60 (23.38–91.34)	4.29 (1–17)	4.21 (1–16)
Nicotinamide (topical)	29	49.75 (22.74–76.82)	6.43 (1–19)	6.31 (1 to 19)
<b>Retinoid - total cumulative dose <math>&lt; 120 \text{ mg kg}^{-1}</math> (single course) (oral)</b>	<b>938</b>	<b>47.72 (19.76–75.65)</b>	7.10 (1–20)	6.96 (1 to 20)
Photothermal + photodynamic therapy [physical]	14	47.82 (17.10–77.78)	7.33 (1–22)	7.18 (1–21)
<b>Lincosamide (clindamycin) (topical) + retinoid (topical)</b>	<b>1548</b>	<b>44.43 (29.20–60.02)</b>	7.66 (2–15)	7.53 (2–15)
Tetracycline (oral) + photodynamic therapy (physical)	48	44.84 (26.19–63.58)	7.75 (2–17)	7.61 (2–17)
<b>Benzoyl peroxide (topical) + retinoid (topical) + tetracycline (oral)</b>	<b>556</b>	<b>43.53 (29.49–57.70)</b>	8.15 (3–16)	8.01 (3–15)
Photodynamic therapy (physical)	298	40.45 (26.17–54.11)	9.47 (4–16)	9.29 (4–16)
No treatment	25	39.44 (2.64–75.70)	11.02 (2–25)	10.74 (2–24)
<b>Azelaic acid (topical) + tetracycline (oral)</b>	<b>50</b>	<b>38.55 (7.31–69.87)</b>	11.48 (2–25)	11.20 (2–24)
<b>Retinoid (topical) + tetracycline (oral)</b>	<b>379</b>	<b>35.22 (23.55–46.75)</b>	12.50 (7–19)	12.22 (6–18)
<b>Benzoyl peroxide (topical) + retinoid (topical)</b>	<b>217</b>	<b>33.97 (12.04–55.53)</b>	13.14 (3–24)	12.81 (3–23)
<b>Lincosamide (clindamycin) (topical)</b>	<b>1479</b>	<b>34.08 (21.26–47.02)</b>	13.22 (6–21)	12.92 (6–20)
<b>Photochemical therapy (red) (physical)</b>	<b>53</b>	<b>29.72 (6.81–52.10)</b>	15.46 (5–25)	15.06 (5–24)
<b>Benzoyl peroxide (topical)</b>	<b>80</b>	<b>28.75 (12.08–45.65)</b>	15.62 (6–23)	15.20 (6–22)
<b>Photochemical + photothermal therapy (physical)</b>	<b>71</b>	<b>28.21 (–2.54–58.82)</b>	16.09 (4–26)	15.65 (4–25)
Cocypirindiol (oral)	12	25.25 (–5.24–55.96)	17.12 (3–27)	Not relevant
<b>Tetracycline (oral)</b>	<b>1386</b>	<b>24.23 (16.24–32.28)</b>	18.63 (14–23)	18.10 (13–22)
<b>Benzoyl peroxide (topical) + lincosamide (clindamycin) (topical) + retinoid (topical)</b>	<b>600</b>	<b>23.09 (8.21–37.97)</b>	18.82 (10–25)	18.27 (10–24)
Benzoyl peroxide (topical) + antifungal (topical)	25	21.98 (–2.11–46.13)	18.99 (6–26)	18.43 (6–25)
<b>Benzoyl peroxide (topical) + lincosamide (clindamycin) (topical)</b>	<b>276</b>	<b>22.64 (6.24–39.14)</b>	19.11 (10–25)	18.55 (10–24)
<b>Benzoyl peroxide (topical) + macrolide (topical)</b>	<b>365</b>	<b>22.14 (12.76–31.79)</b>	19.53 (13–24)	18.96 (13–23)
Photochemical therapy (combined blue/red light) (physical)	15	8.76 (–43.29–53.96)	21.88 (5–27)	21.17 (5–26)
<b>Retinoid (topical)</b>	<b>3570</b>	<b>13.15 (8.30–18.05)</b>	23.60 (20–26)	22.82 (19–25)
<b>Macrolide (topical)</b>	<b>109</b>	<b>10.91 (–3.66–25.39)</b>	23.80 (17–27)	23.00 (17–26)
<b>Placebo</b>	<b>4122</b>	<b>Reference</b>	26.43 (25–27)	25.48 (24–26)

CrI, credible interval; N, number of observations across trials included in the analysis. Classes ordered by mean rank for females (rank = 1 indicates highest efficacy). Treatment classes and values in bold indicate treatment classes with  $N \geq 50$  each across randomized controlled trials included in the analysis. Treatment classes and values in italics indicate treatment classes with 95% CrI crossing the 'no effect' line.

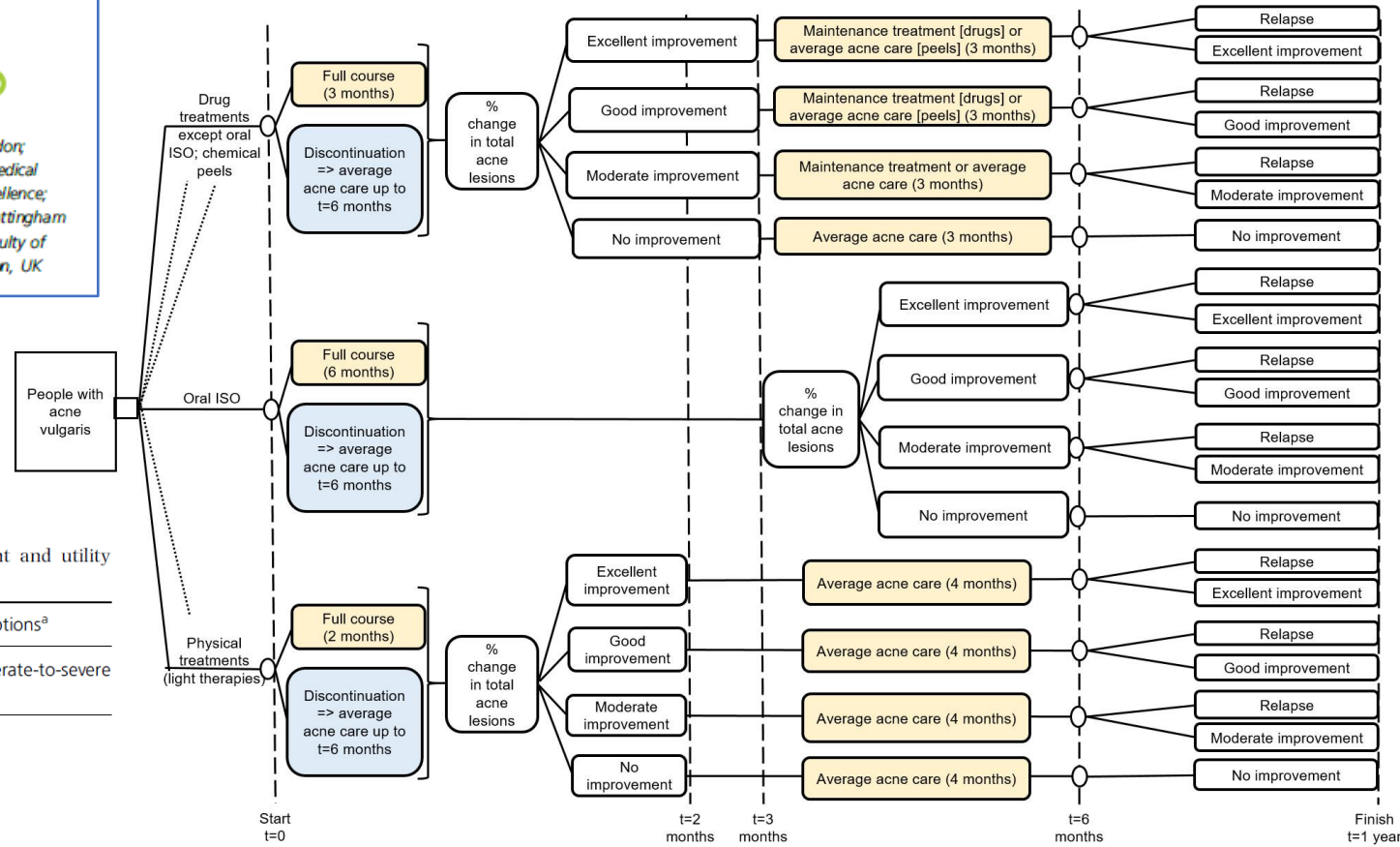
# Health Economic Analysis (economic model)

**Original article** CED  
Clinical and Experimental Dermatology

## Cost-effectiveness of topical pharmacological, oral pharmacological, physical and combined treatments for acne vulgaris

Ifigeneia Mavranetzouli,<sup>1,2</sup> Nicky J. Welton,<sup>3</sup> Caitlin H. Daly,<sup>3</sup> Jane Wilcock,<sup>4</sup> Nathan Bromham,<sup>2,5</sup> Laura Berg,<sup>2,5</sup> Jingyuan Xu,<sup>2,6</sup> Damian Wood,<sup>7</sup> Jane C. Ravenscroft,<sup>8</sup> Katharina Dworzynski,<sup>2,5</sup> and Eugene Healy<sup>9,10</sup>

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**Table 2** Relationship between percentage change in total acne lesion count from baseline, perceived acne improvement and utility value.

Acne health state	Perceived improvement <sup>8</sup>	Utility value <sup>9-12</sup> and further assumptions <sup>9</sup>	
		Mild-to-moderate acne	Moderate-to-severe acne
Health states relating to %CFB			
71.26–100% reduction in acne lesions	Excellent	0.94	0.94
53.14–71.26% reduction in acne lesions	Good	0.90	0.87
28.20–53.14% reduction in acne lesions	Moderate	0.86	0.79
< 28.20% reduction or any % increase in acne lesions	None	0.82	0.72
Other health states			
Baseline (start of model)	NA	0.82	0.72
Reduction in utility due to intolerable side effects	NA	-0.04	-0.07

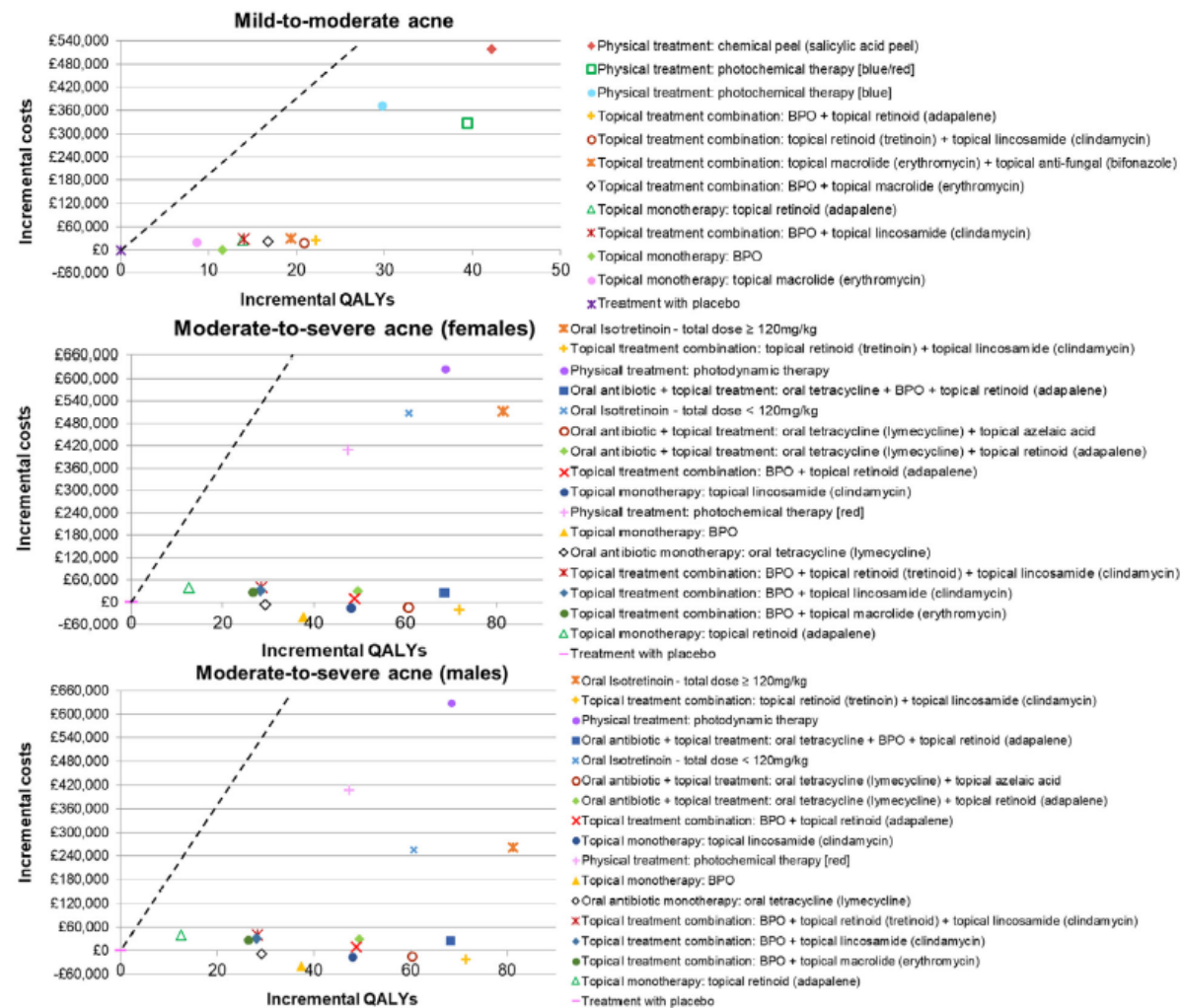
%CFB, percentage change in total lesion count from baseline; NA, not applicable. <sup>9</sup>Supplementary Data S5.



# Health Economic Analysis (economic model)

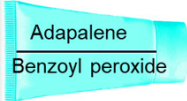

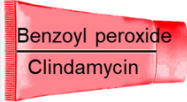
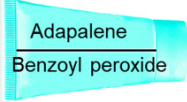
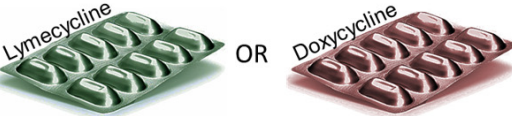
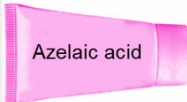
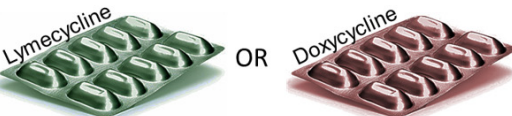
**Table 4** Cost-effectiveness results for treatments for mild-to-moderate and moderate-to-severe acne.<sup>a,b</sup>

Type of treatment	Class/int	n <sup>c</sup>	NMB/ person	Mean per person			Mean rank (95% CI)
				QALY	Int cost	Total cost	
<b>Mild-to-moderate acne (both sexes)</b>							
Physical treatment	Photochemical therapy (blue/red light)	69	£17 163	0.885	£370	£545	4.42 (1–11)
Topical treatment combination	BPO + topical retinoid (adapalene)	1057	£17 123	0.868	£121	£242	3.39 (1–7)
Topical treatment combination	Topical retinoid (tretinoin) + topical lincosamide (clindamycin)	276	£17 105	0.867	£120	£234	3.94 (1–9)
Topical treatment combination	Topical macrolide (erythromycin) + topical anti-fungal (bifonazole)	74	£17 061	0.865	£112	£247	5.37 (1–12)
Physical treatment	Chemical peel (salicylic acid peel)	101	£17 029	0.888	£621	£736	6.63 (1–12)
Topical treatment combination	BPO + topical macrolide (erythromycin)	351	£17 017	0.863	£112	£239	5.83 (1–11)
Topical monotherapy	Topical retinoid: adapalene	1623	£16 957	0.860	£107	£242	6.59 (3–10)
Topical treatment combination	BPO + topical lincosamide (clindamycin)	992	£16 956	0.860	£115	£245	6.75 (3–10)
Topical monotherapy	BPO	1109	£16 937	0.858	£79	£216	7.14 (3–11)
Physical treatment	Photochemical therapy (blue light)	138	£16 928	0.876	£410	£588	7.75 (1–12)
Topical antibiotic monotherapy	Topical macrolide: erythromycin	765	£16 859	0.855	£97	£236	8.96 (5–11)
Treatment with placebo	Treatment with placebo	2005	£16 704	0.846	£67	£217	11.23 (9–12)
<b>Moderate-to-severe acne (females)</b>							
Topical treatment combination	Topical retinoid (tretinoin) + topical lincosamide (clindamycin)	1548	£16 460	0.838	£160	£299	2.92 (1–8)
Oral antibiotic + topical treatment	Oral tetracycline (lymecycline) + BPO + topical retinoid (adapalene)	556	£16 351	0.835	£196	£344	3.43 (1–9)
Oral antibiotic + topical treatment	Oral tetracycline (lymecycline) + topical azelaic acid	50	£16 231	0.827	£132	£306	5.54 (1–15)
Oral isotretinoin	Oral isotretinoin; total cumulative dose ≥ 120 mg/kg	182	£16 122	0.848	£755	£832	5.91 (1–16)
Topical antibiotic monotherapy	Topical lincosamide (clindamycin)	1479	£15 986	0.814	£134	£303	6.44 (2–12)
Topical treatment combination	BPO + topical retinoid (adapalene)	217	£15 975	0.815	£146	£329	6.96 (1–15)
Oral antibiotic + topical treatment	Oral tetracycline (lymecycline) + topical retinoid (adapalene)	379	£15 969	0.816	£162	£349	6.33 (2–11)
Topical monotherapy	BPO	80	£15 798	0.804	£97	£280	8.22 (2–14)
Physical treatment	Photodynamic therapy	298	£15 755	0.835	£705	£945	9.26 (2–16)
Oral isotretinoin	Oral isotretinoin; total cumulative dose < 120 mg/kg	938	£15 715	0.827	£726	£827	9.84 (2–17)
Oral antibiotic monotherapy	Oral tetracycline (lymecycline)	1386	£15 600	0.796	£106	£313	10.69 (7–14)
Physical treatment	Photochemical therapy (red light)	53	£15 547	0.814	£473	£727	11.46 (2–17)
Topical treatment combination	BPO + topical lincosamide (clindamycin)	276	£15 539	0.795	£157	£352	11.43 (4–16)
Topical treatment combination	BPO + topical lincosamide (clindamycin) + topical retinoid (tretinoin)	600	£15 534	0.795	£155	£360	11.29 (4–16)
Topical treatment combination	BPO + topical macrolide (erythromycin)	365	£15 511	0.793	£148	£346	11.70 (6–15)
Topical monotherapy	Topical retinoid: adapalene	3570	£15 219	0.779	£120	£359	14.97 (12–16)
Treatment with placebo	Treatment with placebo	4122	£15 006	0.766	£68	£319	16.62 (15–17)



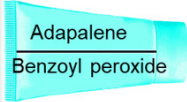

**Figure 2** Cost-effectiveness planes. Results for 1000 people with acne vulgaris. In each graph, the points for each treatment show its incremental quality-adjusted life years (QALYs) (horizontal axis) and costs (vertical axis) vs. treatment with placebo, which is placed at the origin. The slope of the dotted line indicates the National Institute for Health and Care Excellence lower cost-effectiveness threshold of £20 000/QALY. Moving towards the right of the horizontal axis, treatments result in more QALYs. For both acne severity levels, all treatments produce more QALYs compared with treatment with placebo. Moving towards the top of the vertical axis, treatments become more costly. For both acne severity levels, all treatments are more costly than treatment with placebo, with the exception of BPO in mild-to-moderate acne, and with the exception of BPO, topical clindamycin, combined topical tretinoin with clindamycin, oral lymecycline, and azelaic acid combined with oral lymecycline in moderate-to-severe acne. In all three graphs, treatments lie on the right side of the dotted line, suggesting that in all three analyses all assessed treatments are cost-effective compared with treatment with placebo.

BPO, benzoyl peroxide; CI, confidence interval; Int, intervention; NMB, net monetary benefit; QALY, quality-adjusted life year. <sup>a</sup>Classes are ordered by NMB (highest NMB indicates highest cost-effectiveness); <sup>b</sup>NMB and ranking estimated using a cost-effectiveness threshold (willingness to pay) of £20 000/QALY; <sup>c</sup>n, number of observations across randomized controlled trials included in the network meta-analysis of efficacy that informed the economic analysis.

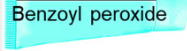
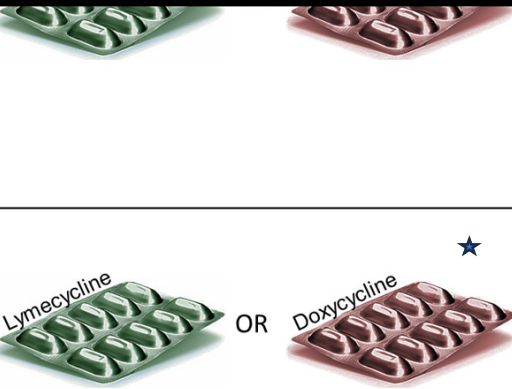
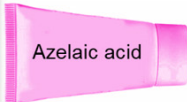

Topical	Oral	Severity	Advantages	Disadvantages
 <p>Adapalene Benzoyl peroxide</p>		All severity	<ul style="list-style-type: none"> <li>• Topical</li> <li>• Does not contain antibiotics</li> </ul>	<ul style="list-style-type: none"> <li>• Not for use during pregnancy</li> <li>• Use with caution during breastfeeding</li> <li>• Can cause skin irritation, photosensitivity, and bleaching of hair and fabrics</li> </ul>
 <p>Tretinoin Clindamycin</p>		All severity	<ul style="list-style-type: none"> <li>• Topical</li> </ul>	<ul style="list-style-type: none"> <li>• Not for use during pregnancy or breastfeeding (see recommendation 1.5.8)</li> <li>• Can cause skin irritation (see recommendation 1.5.7), and photosensitivity</li> </ul>
 <p>Benzoyl peroxide Clindamycin</p>		Mild to moderate	<ul style="list-style-type: none"> <li>• Topical</li> <li>• Can be used with caution during pregnancy and breastfeeding.</li> </ul>	<ul style="list-style-type: none"> <li>• Can cause skin irritation (see recommendation 1.5.7), photosensitivity, and bleaching of hair and fabrics</li> </ul>
 <p>Adapalene Benzoyl peroxide</p>	 <p>Lymecycline OR Doxycycline ★</p>	Moderate to severe	<ul style="list-style-type: none"> <li>• Oral component may be effective in treating affected areas that are difficult to reach with topical treatment (such as the back)</li> <li>• Treatment with adequate courses of standard therapy with systemic antibiotics and topical therapy is a Medicines and Healthcare products Regulatory Agency (MHRA) requirement for subsequent oral isotretinoin</li> </ul>	<ul style="list-style-type: none"> <li>• Not for use in pregnancy, during breastfeeding, or under the age of 12</li> <li>• Topical adapalene and topical benzoyl peroxide can cause skin irritation, photosensitivity, and bleaching of hair and fabrics</li> <li>• Oral antibiotics may cause systemic side effects and antimicrobial resistance</li> <li>• Oral tetracyclines can cause photosensitivity</li> </ul>
 <p>Azelaic acid</p>	 <p>Lymecycline OR Doxycycline ★</p>	Moderate to severe	<ul style="list-style-type: none"> <li>• Oral component may be effective in treating affected areas that are difficult to reach with topical treatment (such as the back)</li> <li>• Treatment with adequate courses of standard therapy with systemic antibiotics and topical therapy is a Medicines and Healthcare products Regulatory Agency (MHRA) requirement for subsequent oral isotretinoin</li> </ul>	<ul style="list-style-type: none"> <li>• Not for use in pregnancy, during breastfeeding, or under the age of 12</li> <li>• Oral antibiotics may cause systemic side effects and resistance</li> <li>• Oral tetracyclines can cause photosensitivity</li> </ul>

★ Or trimethoprim or oral macrolide (e.g. erythromycin).

Topical benzoyl peroxide; consider if above treatment options contraindicated, or the person wishes to avoid antibiotic or topical retinoid.

Topical	Oral	Severity	Advantages	Disadvantages
 <p>Adapalene Benzoyl peroxide</p>		All severity	<ul style="list-style-type: none"> <li>• Topical</li> <li>• Does not contain antibiotics</li> </ul>	<ul style="list-style-type: none"> <li>• Not for use during pregnancy</li> <li>• Use with caution during breastfeeding</li> <li>• Can cause skin irritation, photosensitivity, and bleaching of hair and fabrics</li> </ul>
 <p>Tretinoin Clindamycin</p>		All severity	<ul style="list-style-type: none"> <li>• Topical</li> </ul>	<ul style="list-style-type: none"> <li>• Not for use during pregnancy or breastfeeding (see recommendation 1.5.8)</li> <li>• Can cause skin irritation (see recommendation 1.5.7), and photosensitivity</li> </ul>
			<ul style="list-style-type: none"> <li>• Topical</li> </ul>	<ul style="list-style-type: none"> <li>• Can cause skin irritation (see</li> </ul>

Consider maintenance treatment in people with history of frequent relapse after treatment, e.g. fixed combination of topical adapalene and topical benzoyl peroxide; - if not tolerated, or if a component of combination is contraindicated, consider topical monotherapy with adapalene, azelaic acid, or benzoyl peroxide

 <p>Benzoyl peroxide</p>	 <p>Lymecycline OR Doxycycline</p>		<p>standard therapy with systemic antibiotics and topical therapy is a Medicines and Healthcare products Regulatory Agency (MHRA) requirement for subsequent oral isotretinoin</p>	<p>cause skin irritation, photosensitivity, and bleaching of hair and fabrics</p> <ul style="list-style-type: none"> <li>• Oral antibiotics may cause systemic side effects and antimicrobial resistance</li> <li>• Oral tetracyclines can cause photosensitivity</li> </ul>
 <p>Azelaic acid</p>	 <p>Lymecycline OR Doxycycline ★</p>	Moderate to severe	<ul style="list-style-type: none"> <li>• Oral component may be effective in treating affected areas that are difficult to reach with topical treatment (such as the back)</li> <li>• Treatment with adequate courses of standard therapy with systemic antibiotics and topical therapy is a Medicines and Healthcare products Regulatory Agency (MHRA) requirement for subsequent oral isotretinoin</li> </ul>	<ul style="list-style-type: none"> <li>• Not for use in pregnancy, during breastfeeding, or under the age of 12</li> <li>• Oral antibiotics may cause systemic side effects and resistance</li> <li>• Oral tetracyclines can cause photosensitivity</li> </ul>

★ Or trimethoprim or oral macrolide (e.g. erythromycin).

Topical benzoyl peroxide; consider if above treatment options contraindicated, or the person wishes to avoid antibiotic or topical retinoid.

## Oral isotretinoin treatment

Consider oral isotretinoin for people older than 12 years who have a severe form of acne that is resistant to adequate courses of standard therapy with systemic antibiotics and topical therapy.

Follow MHRA's safety advice on isotretinoin for severe acne.

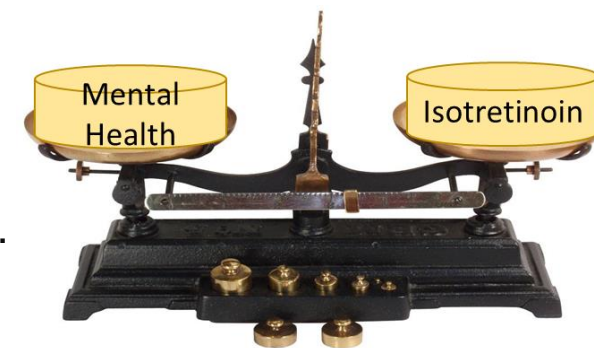
Consider referral to mental health services at referral to dermatology before starting treatment if significant psychological distress or mental health disorder, including current or past history of.

- Suicidal ideation or self harm
- a severe depressive or anxiety disorder
- body dysmorphic disorder.

Prescribe oral isotretinoin at standard daily dose of 0.5 to 1 mg/kg; - consider reduced daily dose (<0.5 mg/kg) for people at increased risk of, or experiencing, adverse effects.

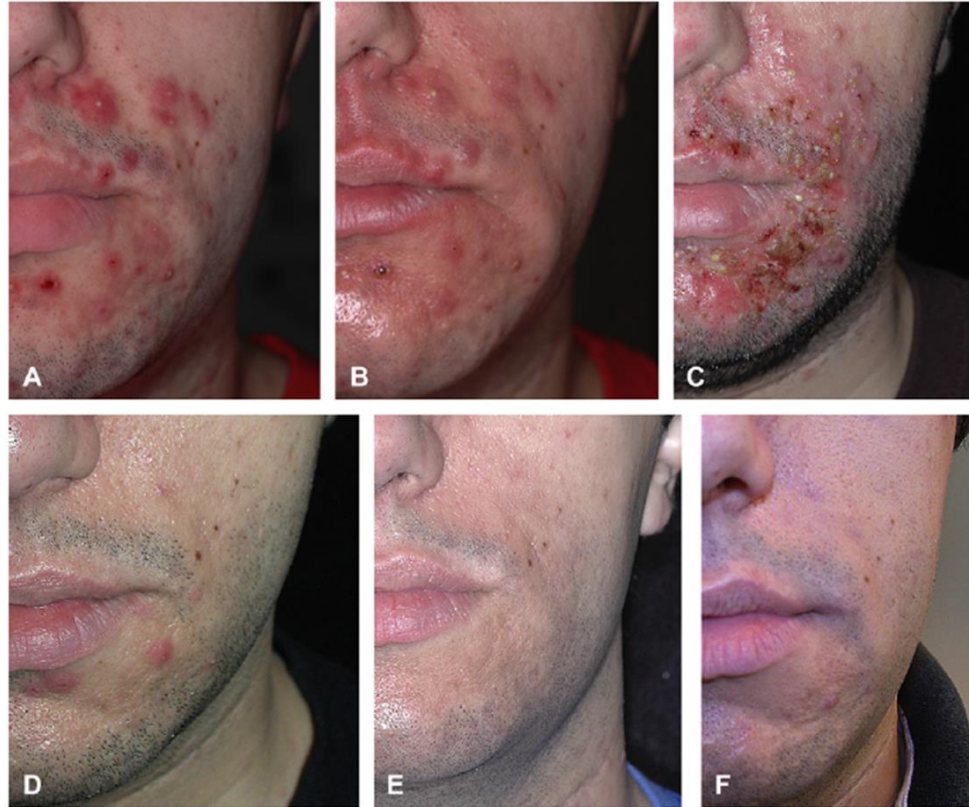
Continue oral isotretinoin until total cumulative dose of 120 to 150 mg/kg reached; - consider discontinuing treatment sooner if no new acne lesions for 4 to 8 weeks.

Review patient's psychological wellbeing during treatment, and monitor for symptoms or signs of depression, and advise them to seek help if they feel their mental health is affected or is worsening.



## Photodynamic therapy

Consider photodynamic therapy for people aged 18 and over with moderate to severe acne if other treatments ineffective, not tolerated or contraindicated.





**Fig 3.** Improvement of inflammatory acne and cicatricial lesions after topical application of 20% 5-aminolevulinic acid (ALA) for 3 hours of incubation under occlusion and 200 J/cm<sup>2</sup> of 633 nm red light (Omnilux; Photo Therapeutics, Cheshire, UK) at 100 mW/cm<sup>2</sup>. **A**, Before treatment. **B**, Immediately after the first session. **C**, Two days after the first session. **D**, Seven months after the first session and before the second session. **E**, Ten months after the first session, 3 months after the second session. **F**, One year and 2 months after the first session, after total of four sessions. Note the important inflammatory reaction after high dose red light ALA photodynamic therapy, with no long lasting side effects. (Courtesy R. Rox Anderson, MD.) *J Am Acad Dermatol* 2010;63:195-211

# Treatment options for people with polycystic ovary syndrome

For people with polycystic ovary syndrome and acne:

- treat their acne using first-line treatment options.
- if the chosen first-line treatment is not effective, consider adding ethinylestradiol with cyproterone acetate (co-cyprindiol) or an alternative combined oral contraceptive pill to their treatment.
- for those using co-cyprindiol, review at 6 months and discuss continuation or alternative treatment options.

Topical	Oral	Severity	Advantages	Disadvantages
Adapalene Benzoyl peroxide		All severity	• Topical • Does not contain antibiotics	• Not for use during pregnancy • Use with caution during breastfeeding • Can cause skin irritation, photosensitivity, and bleaching of hair and fabric
Topical Clindamycin		All severity	• Topical	• Not for use during pregnancy or breastfeeding (see recommendation 1.5.6) • Can cause skin irritation (see recommendation 1.5.7), and photosensitivity
Retinoid peroxide Clindamycin		Mild to moderate	• Topical • Can be used with caution during pregnancy and breastfeeding	• Can cause skin irritation (see recommendation 1.5.7), photosensitivity, and bleaching of hair and fabric
Adapalene Benzoyl peroxide		Moderate to severe	• Oral component may be effective in treating affected areas that are difficult to reach with topical treatment (such as the back) • Treatment with adequate courses of standard therapy with systemic antibiotics and topical therapy is a Medicine and Healthcare products Regulatory Agency (MHRA) requirement for subsequent oral subtherapy	• Not for use in pregnancy during breastfeeding, or under the age of 12 • Topical adapalene and topical benzoyl peroxide can cause skin irritation, photosensitivity, and bleaching of hair and fabric • Oral antibiotics may cause systemic side effects and antimicrobial resistance • Oral tetracyclines can cause photosensitivity
Aspirin acid		Moderate to severe	• Oral component may be effective in treating affected areas that are difficult to reach with topical treatment (such as the back) • Treatment with adequate courses of standard therapy with systemic antibiotics and topical therapy is a Medicine and Healthcare products Regulatory Agency (MHRA) requirement for subsequent oral subtherapy	• Not for use in pregnancy during breastfeeding, or under the age of 12 • Oral antibiotics may cause systemic side effects and antimicrobial resistance • Oral tetracyclines can cause photosensitivity



Consider referring people with acne and polycystic ovary syndrome with additional features of hyperandrogenism to an appropriate specialist (for example, a reproductive endocrinologist).

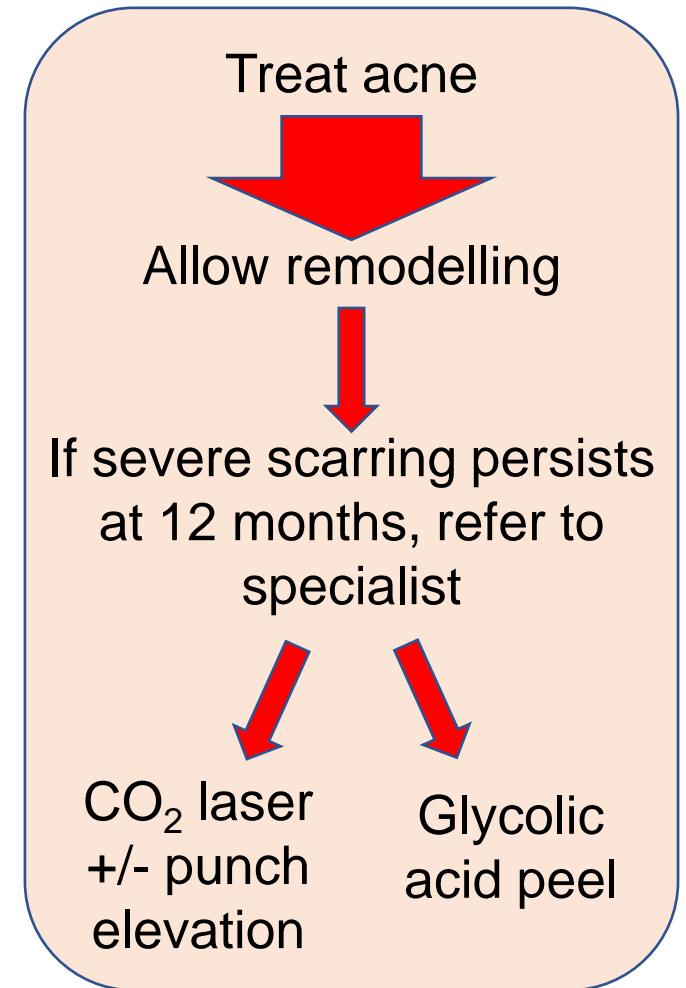
## Management of acne-related scarring

If a person has acne-related scarring, treat ongoing acne to prevent additional scarring.

Explain that skin remodels, and that acne scars may change / improve over time.

If acne-related scarring is severe & persists for a year after acne cleared:

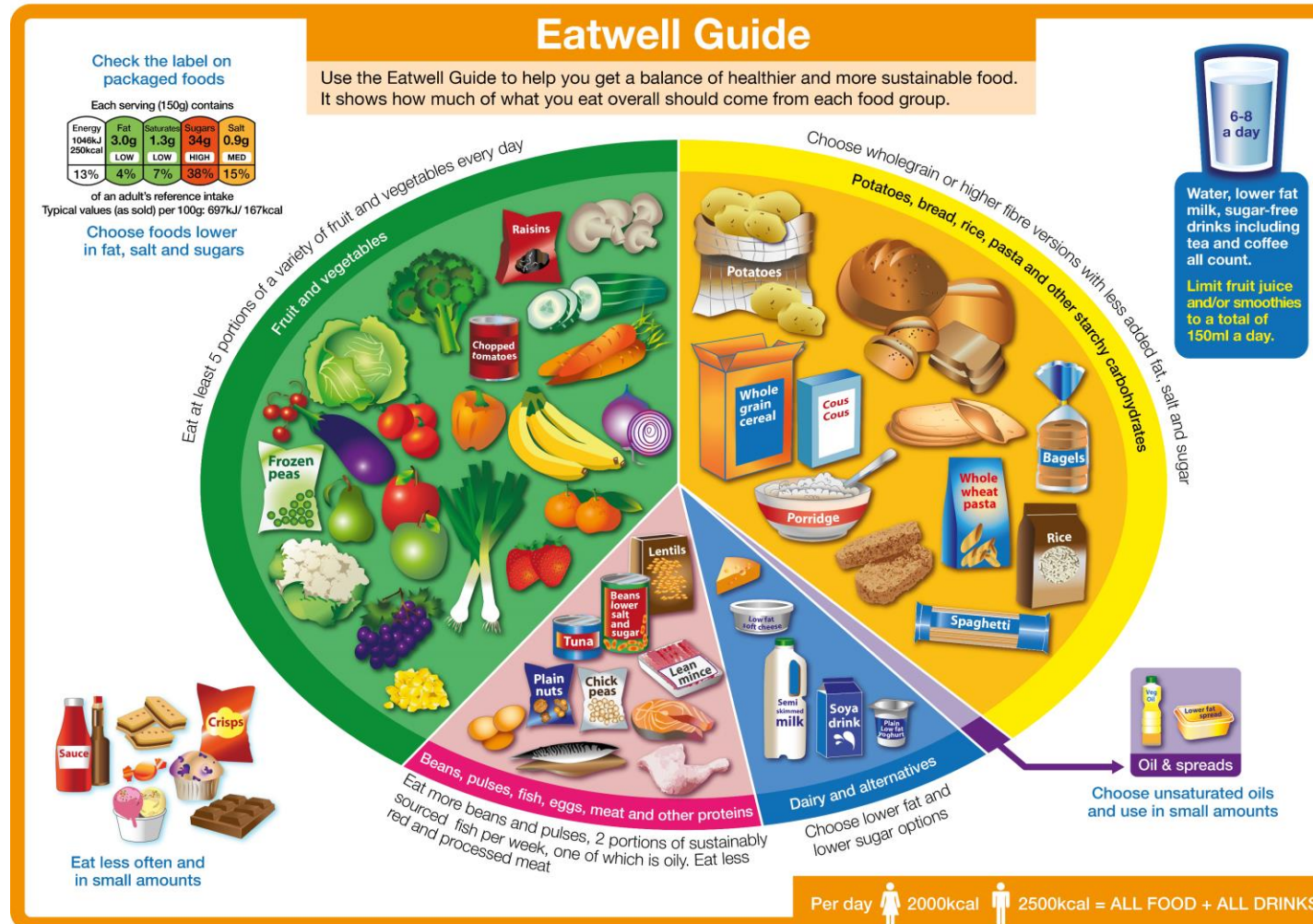
- refer to consultant dermatologist-led team with expertise in scarring management.
- in a consultant dermatologist-led team setting, consider CO<sub>2</sub> laser treatment (alone or after a session of punch elevation) or glycolic acid peel.



# Diet

Not enough evidence to support specific diets for treating acne.

Information on balanced diet; -see Public Health England's Eatwell Guide.





## Research recommendations

1. What is the efficacy of reduced dose oral isotretinoin in the management of acne vulgaris?
2. What is the most effective first-line treatment option for any severity of acne vulgaris for people with polycystic ovary syndrome?
3. What is the effect of dietary interventions or dietary changes on acne?
4. What skin care advice is appropriate for people with acne?
5. What is the effectiveness of physical treatments (such as light devices) in the treatment of acne vulgaris or persistent acne vulgaris-related scarring?
6. What are the risk factors for acne vulgaris-related scarring?
7. What is the effectiveness of chemical peels for the treatment of acne vulgaris or persistent acne vulgaris-related scarring?
8. What is the effectiveness of hormone-modifying agents in the treatment of acne vulgaris?
9. What information and support is valued by people with acne vulgaris?



**ACNE-ID**

**Comparison of low  
dose versus  
conventional dose  
oral isotretinoin**