Guidelines of care for the management of acne vulgaris

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Background: Acne vulgaris commonly affects adults, adolescents, and preadolescents aged 9 years or older.

Objective: The objective of this study was to provide evidence-based recommendations for the management of acne.

Methods: A work group conducted a systematic review and applied the Grading of Recommendations, Assessment, Development, and Evaluation approach for assessing the certainty of evidence and formulating and grading recommendations.

Results: This guideline presents 18 evidence-based recommendations and 5 good practice statements. Strong recommendations are made for benzoyl peroxide, topical retinoids, topical antibiotics, and oral doxycycline. Oral isotretinoin is strongly recommended for acne that is severe, causing psychosocial burden or scarring, or failing standard oral or topical therapy. Conditional recommendations are made for topical clascoterone, salicylic acid, and azelaic acid, as well as for oral minocycline, sarecycline, combined oral contraceptive pills, and spironolactone. Combining topical therapies with multiple mechanisms of action, limiting systemic antibiotic use, combining systemic antibiotics with topical therapies, and adding intralesional corticosteroid injections for larger acne lesions are recommended as good practice statements.

Limitations: Analysis is based on the best available evidence at the time of the systematic review.

Conclusions: These guidelines provide evidence-based recommendations for the management of acne vulgaris. (J Am Acad Dermatol 2024;90:1006.e1-30)

Key words: Acne; acne vulgaris; adapalene; antiandrogens; antibiotics; azelaic acid; azithromycin; benzoyl peroxide; clascoterone; clindamycin; contraceptives; corticosteroids; *Cutibacterium acnes*; diet and acne; doxycycline; erythromycin; grading and classification of acne; guidelines; hormonal therapy; isotretinoin; light therapies; microbiological and endocrine testing; minocycline; retinoids; salicylic acid; sarecycline; spironolactone; tazarotene; treatment; tretinoin; trifarotene.

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SCOPE AND OBJECTIVES

Acne vulgaris is one of the most common skin conditions diagnosed and treated by dermatologists in the United States (US) and worldwide.[1,2] These guidelines aim to provide evidence-based recommendations to guide the clinical management of acne vulgaris for adults, adolescents, and preadolescents aged 9 years or older from the perspectives of US and Canadian dermatologists, clinicians who treat acne, and patients. These guidelines update the 2016 American Academy of Dermatology guidelines of care for the management of acne.[3] We examine evidence based on a systematic review of the literature on acne grading and classification, laboratory testing, and treatment using topical therapies, systemic antibiotics, hormonal agents, oral isotretinoin, physical modalities, complementary and alternative medicine, and dietary and environmental interventions. These guidelines focus on acne treatments that are available, approved by the US Food and Drug Administration (FDA), and commonly used in the US. Acneiform eruptions and medication-induced acne are not addressed. Diagnosis and treatment of infantile acne, mid-childhood acne in children under the age of 9 years, and acne-induced hyperpigmentation and scarring are beyond of the scope of these guidelines.[4]

CAPSULE SUMMARY

- The American Academy of Dermatology's 2016 guidelines for the management of acne vulgaris are updated with a systematic review, which resulted in 18 evidence-based recommendations and 5 good practice statements.
- Strong recommendations are made for topical benzoyl peroxide, retinoids, and/or antibiotics and their fixed-dose combinations, and for oral doxycycline. Oral isotretinoin is strongly recommended for severe acne, acne causing psychosocial burden or scarring, or acne failing standard treatment with oral or topical therapy.
- Conditional recommendations are made for the use of topical clascoterone, salicylic acid, azelaic acid, oral minocycline, sarecycline, combined oral contraceptives, and spironolactone.
- Using topical therapies combining multiple mechanisms of action, limiting systemic antibiotic use, combining systemic antibiotics with benzoyl peroxide and other topical therapies, and adjuvant intralesional corticosteroid injections are recommended as good clinical practices.

METHODS

The American Academy of Dermatology (AAD) and Evidinno, Inc., conducted a series of focused and systematic reviews from May 2021 to November 2022 (see Detailed Methods in Supplementary Materials, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2) to determine the effectiveness and safety of treatments currently available and approved in the US for the management of acne vulgaris in adults, adolescents, and preadolescents aged 9 years or older based on the 9 clinical questions with prespecified patient, intervention, comparator, and outcome and study eligibility criteria (Table I and Supplementary Tables I-VII, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2). The Work Group consisted of 9 board-certified dermatologists (including 1 methodologist and 1 measure representative and medical writer), 3 board-certified pediatric dermatologists, 1 staff liaison, and 1 patient representative. The work group employed the Grading of Recommendations, Assessment, Development, and Evaluation approach for assessing the certainty of the evidence and formulating and grading clinical recommendations. This approach incorporates benefits and harms, patient values and preferences, resource use, and certainty of evidence as key factors in the evidence to decision framework (Supplementary Table X, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2). Strength of recommendation and strength of the supporting evidence were expressed as shown in Table II.[5-7] A strong recommendation means that the work group believes that the benefits clearly outweigh risks and burden (or that the risks and burden clearly outweigh the benefits), and a conditional recommendation means that the work group believes that the benefits are closely balanced with risks and burden. A conditional recommendation implies that we believe most people would want the recommended course of action.

DEFINITION

Acne vulgaris is a chronic, inflammatory skin disease of the pilosebaceous unit.[8] Acne primarily presents with open or closed comedones, papules, pustules, or nodules on the face or trunk and may result in pain, erythema, hyperpigmentation, or scars.[8]

Abbreviations used:

AAD: American Academy of Dermatology
BP: benzoyl peroxide
COC: combined oral contraceptive
EE: ethinyl estradiol
FDA: Food and Drug Administration
IBD: inflammatory bowel disease
IGA: Investigator Global Assessment
MD: mean difference
RCT: randomized controlled trial
RR: risk ratio
US: United States
VTE: venous thromboembolism

INTRODUCTION/BACKGROUND

Acne vulgaris is a common skin condition affecting 9.4% of the global population in 2010, representing the eighth most prevalent disease globally.[9] Acne affects approximately 85% of teenagers but can occur in most age groups and can persist into adulthood.[10] The burden of acne, as measured by disability-adjusted life years, ranked second among all skin diseases in 2013.[11] Over 50 million people in the US have acne.[12] In the US, more than 5.1 million Americans sought medical treatment for acne, leading to $846 million in medical costs and $398 million in lost productivity for patients and caregivers in 2013.[1] Acne has important impact on emotional functioning, social functioning, relationships, leisure activities, daily activities, sleep, school, and work.[13,14] The health-related quality of life impact of acne is comparable to that of chronic conditions such as asthma, psoriasis, and arthritis.[15,16] Acne is associated with increased risks of stigmatization, bullying, depression, anxiety, poor self-esteem, and suicidal ideation.[17-20]

Multifactorial pathogenesis of acne involves follicular hyperkeratinization, microbial colonization with *Cutibacterium acnes*, sebum production, complex inflammatory mechanisms involving both innate and acquired immunity, neuroendocrine mechanisms, and genetic and nongenetic factors. Risk factors for acne development include increasing age during adolescence, family history of acne, and oily skin type.[21]

ACNE GRADING AND CLASSIFICATION

Numerous acne clinical grading and classification systems have been used in research and clinical settings to assess overall acne disease severity, lesion number and morphologies, affected anatomic sites, and associated secondary changes such as dyspigmentation and scarring. Consistent use of an acne grading and classification system may help facilitate therapeutic decision-making and assess treatment response in clinical practice.[22] Available grading systems include the Investigator Global Assessment (IGA), Leeds revised acne grading system, Global Acne Grading System, Global Acne Severity Scale, and Comprehensive Acne Severity Scale, among others.[23-29]

While there is no universally accepted acne grading system in clinical settings, the IGA is most commonly used in the US[30] and demonstrates good agreement between clinician and patient ratings. The definition of IGA scales varied over time and will require harmonization efforts to facilitate use and future meta-analyses.[31] The IGA scale has been used in many randomized controlled trials (RCTs) for acne treatments and proposed as a cohesive framework upon which to establish an ideal acne grading system.[32] An ideal acne grading system should measure the types of primary acne lesions, number of lesions, and extent and region of skin involvement and should feature strong psychometric properties, ability to categorize severity via descriptive text or photographs, ease of use, and stakeholder acceptance.[33] Stakeholders from the International Dermatology Outcomes Measures and the American Academy of Dermatology reached consensus on a 5-point ordinal scale (ranging from 0-4: clear, almost clear, mild, moderate, and severe) to quantify severity of acne and other inflammatory dermatoses in routine clinical practice.[34] Descriptors of this scale remain to be standardized and validated for use in facial and truncal acne. Acne severity may also be measured via digital photography, as is increasingly used in clinical practice and trials, as well as fluorescent photography, polarized light photography, video microscopy, and multispectral imaging modalities.[35]

Beyond signs and symptoms, core acne outcomes measures should also include domains such as satisfaction with appearance, extent of scars/dark marks, satisfaction with treatment received, long-term acne control, adverse events, and health-related quality of life. Acne quality-of-life measures provide a more comprehensive and holistic perspective on the burden of acne on patients' lives and may not correlate well with clinical acne severity.[36] While multiple dermatology-specific and acne-specific health-related quality-of-life measures are available as research tools, shorter measures also exist for use in routine clinical practice.[37,38]

MICROBIOLOGICAL AND ENDOCRINE TESTING

C. acnes (formerly *Propionibacterium acnes)* is a Gram-positive anaerobic rod primarily implicated in acne pathogenesis, with some strains likely pathogenic while others commensal in the skin

Table I. Clinical questions and scope

Clinical questions
CQ 1. What systems are most commonly used for the grading and classification of acne vulgaris in adults, adolescents, and preadolescents (≥9 y)?
CQ 2. What is the role of microbiological and endocrine testing in evaluating acne vulgaris in adults, adolescents, and preadolescents (≥9 y)?
CQ 3. What are the effectiveness and safety of topical agents in the treatment of acne vulgaris in adults, adolescents, and preadolescents (≥9 y), including:
• Retinoids (adapalene, tazarotene, tretinoin, and trifarotene)
• Benzoyl peroxide
• Topical antibiotics (erythromycin, clindamycin, dapsone, and minocycline)
• Alpha hydroxy acid (glycolic acid)
• Beta hydroxy acid (salicylic acid)
• Azelaic acid
• Topical antiandrogen (clascoterone)
• Others (sulfur/sulfacetamide sodium and resorcinol)
• Combinations of topical agents
CQ 4. What are the effectiveness and safety of systemic antibiotics in the treatment of acne vulgaris in adults, adolescents, and preadolescents (≥9 y), including:
• Tetracyclines (doxycycline, minocycline, sarecycline)
• Macrolides (azithromycin, clarithromycin, and erythromycin)
• Penicillins (amoxicillin and ampicillin)
• Cephalosporin (cephalexin)
• Trimethoprim/sulfamethoxazole
• Other (dapsone)
CQ 5.a. What are the effectiveness and safety of hormonal agents in the treatment of acne vulgaris in adults, adolescents, and preadolescents (≥9 y), including:
• Combined contraceptive agents (estrogen and progestin)
• Aldosterone receptor antagonist (spironolactone)
• Oral corticosteroids (prednisolone and prednisone)
• Intralesional corticosteroid (triamcinolone)
CQ 5.b. For patients on spironolactone, how often and for how long should potassium level be monitored?
CQ 6.a. What are the effectiveness and safety of isotretinoin in the treatment of acne vulgaris in adults, adolescents, and preadolescents (≥9 y)?
CQ 6.b. For patients on isotretinoin, how often and for how long should lipids, liver enzymes, creatine kinase, and blood count levels be monitored?
CQ 7. What are the effectiveness and safety of physical modalities for the treatment of acne vulgaris in adults, adolescents, and preadolescents (≥9 y), including:
• Chemical peels (alpha hydroxy acid: glycolic acid, lactic acid, madelic acid; beta hydroxy acid: salicylic acid)
• Comedo extraction
• Lasers
• Photodynamic/light therapy (blue light therapy, red light therapy, ALA, and IPL)
CQ 8. What are the effectiveness and safety of complementary/alternative therapies in the treatment of acne vulgaris in adults, adolescents, and preadolescents (≥9 y), including:
• Botanicals/plant-derived agents (tea tree oil, green tea, and witch hazel)
• Vitamin oral formulation (zinc, niacinamide, pantothenic acid)
• Vitamin topical formulation (zinc and niacinamide)
CQ 9. What are the effectiveness and safety of diet in the treatment of acne vulgaris in adults, adolescents, and preadolescents (≥9 y), including:
• Low-glycemic diet
• Low-dairy diet
• Low-whey diet
• Omega-3 and chocolate

ALA, Aminolevulinic acid; *IPL*, intense pulsed light; *US*, United States.

microbiome.[39,40] *C. acnes* has specific culture requirements that prevent growth in routine bacterial culture. *Staphylococcus epidermidis, Staphylococcus aureus,* and *Malassezia* species have also been identified in acne lesions, although causal relationships remain to be demonstrated.[41-45]

Table II. Strength of recommendation and certainty of evidence

Strength of recommendation	Wording	Implication[5-7]
Strong recommendation *for* the use of an intervention	"We recommend…"	Benefits clearly outweigh risk and burdens; recommendation applies to most patients in most circumstances.
Strong recommendation *against* the use of an intervention	"We recommend against…"	Risk and burden clearly outweigh benefits; recommendation applies to most patients in most circumstances.
Good practice statement	"We recommend…"	Guidance was viewed by the Work Group as imperative to clinical practice and developed when the supporting evidence was considerable but indirect, and the certainty surrounding an intervention's impact was high with the benefits clearly outweighing the harms (or vice versa). Good Practice Statements are strong recommendations as the certainty surrounding the impact of the recommended intervention is high. Implementation of these strong recommendations is considered to clearly result in beneficial outcomes.[7]
Conditional recommendation *for* the use of an intervention	"We conditionally recommend…"	Benefits are closely balanced with risks and burden; recommendation applies to most patients, but the most appropriate action may differ depending on the patient or other stakeholder values.
Conditional recommendation *against* the use of an intervention	"We conditionally recommend against…"	Risks and burden closely balanced with benefits; recommendation applies to most patients, but the most appropriate action may differ depending on the patient or other stakeholder values
Certainty of evidence	**Wording**	**Implication[5,6]**
High	"high certainty evidence"	Very confident that the true effect lies close to that of the estimate of the effect.
Moderate	"moderate certainty evidence"	Moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	"low certainty evidence"	Confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect
Very low	"very low certainty evidence"	The estimate of effect is very uncertain; the true effect may be substantially different from the estimate of effect

While some *C. acnes* species have developed resistance to antibiotics[46,47] and certain strains are more strongly associated with acne, routine microbiologic and/or antibiotic susceptibility testing is not indicated for patients with acne since it does not affect management. Patients presenting with eruptive uniform pustules to nodules in periorificial areas, particularly in settings of prolonged tetracycline treatment, may benefit from lesion culture to diagnose Gram-negative folliculitis. Treatment with isotretinoin or another antibiotic may be required. Microbiologic testing may also be considered for patients presenting with monomorphic truncal papules and pustules to diagnose pityrosporum folliculitis.

Androgens, such as testosterone and dehydroepiandrosterone sulfate, have central roles in the pathogenesis of acne. The association between acne severity and androgen levels remains unclear, with some studies showing positive associations while others showed no associations.[48,49]

Routine endocrinologic testing is not indicated for most patients with acne. Patients who present with acne and clinical signs or symptoms of hyperandrogenism, such as hirsutism, oligomenorrhea or amenorrhea, androgenic alopecia, infertility, polycystic ovaries, clitoromegaly, and truncal obesity may warrant further endocrine testing for hyperandrogenism. Polycystic ovarian syndrome is a common cause of hyperandrogenism, characterized by ovulatory dysfunction or polycystic ovaries on ultrasonography. Tests for serum total and/or free testosterone, dehydroepiandrosterone sulfate, androstenedione, luteinizing hormone, follicle-stimulating hormone may be considered.[50-54] For women with hyperandrogenism, screening for

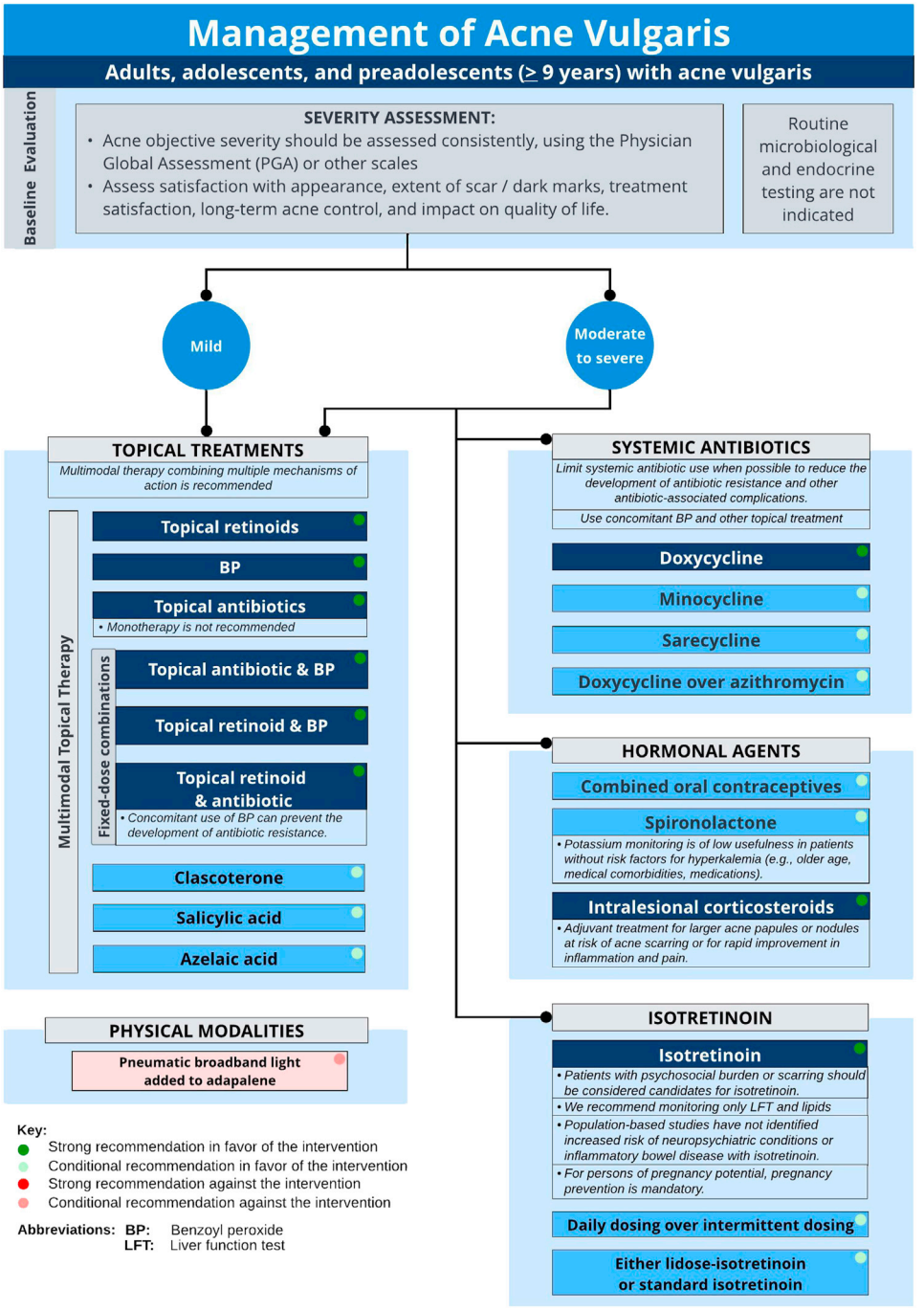

Fig 1. Management of acne vulgaris.

nonclassic congenital adrenal hyperplasia due to 21-hydroxylase deficiency by 17-hydroxyprogesterone levels may be indicated.[50] Serum growth hormone, insulin-like growth factor, sex hormone-binding globulin, free androgen index, lipid panel, insulin, prolactin, estrogen, and progesterone may also be abnormal in some patients with severe acne.[51,54-57] Patients with abnormal endocrine testing or in whom there is a persistent concern for underlying endocrine disorder should be evaluated by an endocrinologist.

ACNE MANAGEMENT

Treatment options available for acne include topical therapies (available over the counter or as prescriptions), systemic antibiotics, hormonal agents, oral isotretinoin, physical modalities,

Table III. Recommendation for the management of acne vulgaris in adults, adolescents, and preadolescents (≥9 years)

No.	Recommendation	Strength	Certainty of evidence	Evidence
Topical agents				
1.1	When managing acne with topical medications, we recommend multimodal therapy combining multiple mechanisms of action.		Good practice statement	
1.2	For patients with acne, we recommend benzoyl peroxide.	Strong	Moderate	63-70
1.3	For patients with acne, we recommend topical retinoids.	Strong	Moderate	59,60,62-64,71-83
1.4	For patients with acne, we recommend topical antibiotics Remark: Topical antibiotic monotherapy is not recommended.	Strong	Moderate	66,68,69,71,79,84-92
1.5	For patients with acne, we conditionally recommend clascoterone.	Conditional*	High	93,94
1.6	For patients with acne, we conditionally recommend salicylic acid.	Conditional	Low	95
1.7	For patients with acne, we conditionally recommend azelaic acid.	Conditional	Moderate	96-98
1.8	For patients with acne, we recommend fixed dose combination topical antibiotic with benzoyl peroxide	Strong	Moderate	66,68,69,99-106
1.9	For patients with acne, we recommend fixed dose combination topical retinoid with topical antibiotic. Remark: Concomitant use of benzoyl peroxide is recommended to prevent the development of antibiotic resistance.	Strong	Moderate	71,79,99,107,108
1.10	For patients with acne, we recommend fixed dose combination topical retinoid with benzoyl peroxide.	Strong	Moderate	63,64,99,109-113
Systemic antibiotics				
2.1	For patients with acne, we recommend doxycycline.	Strong	Moderate	114-118
2.2	For patients with acne, we conditionally recommend minocycline.	Conditional	Moderate	114,119-122
2.3	For patients with acne, we conditionally recommend sarecycline.	Conditional*	High	123-125
2.4	For patients with acne, we conditionally recommend doxycycline over azithromycin.	Conditional	Low	126-129
2.5	For patients with acne, we recommend limiting use of systemic antibiotics when possible to reduce the development of antibiotic resistance and other antibiotic associated complications.		Good practice statement	
2.6	It is recommended that systemic antibiotics are used concomitantly with benzoyl peroxide and other topical therapy.		Good practice statement	
Hormonal agents				
3.1	For patients with acne, we conditionally recommend combined oral contraceptive pills.	Conditional†	Moderate	130-139
3.2	For patients with acne, we conditionally recommend spironolactone. Remark: Potassium monitoring is not needed in healthy patients. However, consider potassium testing for those with risk factors for hyperkalemia (e.g., older age, medical comorbidities, medications).	Conditional	Moderate	140-147
3.3	For patients with larger acne papules or nodules, we recommend intralesional corticosteroid injections as an adjuvant therapy. Remark: Intralesional corticosteroid injections should be used judiciously for patients who are at risk of acne scarring and/or for rapid improvement in inflammation and pain. Using a lower concentration and volume of corticosteroid can minimize the risks of local corticosteroid adverse events.		Good practice statement	

Continued

Table III. Cont'd

No.	Recommendation	Strength	Certainty of evidence	Evidence
Isotretinoin				
4.1	For patients with severe acne or for patients who have failed standard treatment with oral or topical therapy, we recommend isotretinoin. Remark: Acne patients with psychosocial burden or scarring should be considered as having severe acne and to be candidates for isotretinoin. For patients undergoing treatment with isotretinoin, monitoring of LFTs and lipids should be considered, but CBC monitoring is not needed in healthy patients. Population-based studies have not identified increased risk of neuropsychiatric conditions or inflammatory bowel disease in acne patients undergoing treatment with isotretinoin. For persons of childbearing potential, pregnancy prevention is mandatory.		Good practice statement	
4.2	For patients with severe acne, we conditionally recommend traditional daily dosing of isotretinoin over intermittent dosing of isotretinoin.	Conditional	Low	[148-150]
4.3	For patients prescribed isotretinoin, we conditionally recommend either standard isotretinoin or lidose-isotretinoin.	Conditional	High	[151]
Physical modalities				
5.1	For patients with acne, we conditionally recommend against adding pneumatic broadband light to adapalene 0.3% gel.	Conditional	Low	[152]

*Conditional recommendations were made for clascoterone and sarecycline due to high current cost of treatment that may impact equitable acne treatment access.
†Conditional recommendation was made for combined oral contraceptive pills due to the variability in patient values and preferences related to contraception and hormonal medications.

complementary and alternative medicine, and dietary and environmental interventions. Given the diversity of treatment options for acne, shared decision-making is important to individualize acne care based on the potential treatment benefits and risks, the severity, extent, and region of acne involvement, treatment costs, patient preferences, and other factors (Fig 1).

TOPICAL THERAPIES

Topical therapies are the mainstay of acne treatment: they may be used for acne initial treatment and maintenance as monotherapy (except topical antibiotics) or used in combination with other topical or oral agents. Commonly used topical therapies include topical retinoids, benzoyl peroxide (BP), antibiotics, clascoterone, salicylic acid, and azelaic acid. When managing acne with topical therapies, multimodal therapy combining multiple mechanisms of actions is recommended as a good practice statement to optimize efficacy and to reduce the risk of antibiotic resistance.

Topical retinoids

Topical retinoids are vitamin A derivatives and serve as the cornerstone of acne treatment since they are comedolytic and anti-inflammatory, improve dyspigmentation, and enable maintenance of acne clearance. Four types of topical retinoids, including topical tretinoin,[58] adapalene,[59] tazarotene,[60,61] and trifarotene,[62] are FDA-approved for acne treatment in the US. Each retinoid binds to a different set of retinoic acid receptors and confers modest differences in activity, tolerability and efficacy.

We recommend topical retinoids for acne treatment based on moderate certainty evidence from 20 studies (Table III and Supplementary Table XII, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[59,62-64,71-81,153-155] Compared to vehicle at 12 weeks, a greater proportion of patients treated with topical retinoids achieved IGA success in 4 RCTs (risk ratio [RR], 1.57 [1.21, 2.04]).[59,63,64,71] Topical retinoid use may be limited by side effects, including increased risk of burning sensation, dryness, erythema, exfoliation, peeling, and pain. Treatment-emergent adverse events leading to discontinuation at 12 weeks were low (1.4%) in 3 RCTs.[63,80,155] Existing comparative effectiveness data do not suggest superiority of one topical retinoid against another, with efficacy and tolerability differing by specific concentrations and formulations.[153,156-159] Irritation may be particularly common at higher concentrations, which

may be mitigated by reduced frequency of use and concurrent emollients use.[160-163] Some tretinoin formulations should be applied in the evening due to its photolabile nature and should not be applied with BP to avoid oxidation and inactivation; topical tretinoin microsphere formulations, adapalene, and tazarotene lack similar restrictions. Topical retinoids may cause photosensitivity; concurrent daily sunscreen use can reduce sunburn risks. Adapalene 0.1% gel is available over the counter while other topical retinoids are available by prescription only.

Benzoyl peroxide

BP is an over-the-counter topical antimicrobial agent that releases free oxygen radicals and is mildly comedolytic.[164,165] We recommend BP for acne treatment based on moderate certainty evidence from 8 studies (Table III and Supplementary Table XIII, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[63-70] Compared to vehicle at 12 weeks, a greater proportion of patients treated with BP achieved IGA success in 3 RCTs (RR, 2.70 [1.10, 6.65]).[63-65] Greater reductions in both inflammatory (mean difference [MD] in the percentage change from baseline, −22.13% [−42.53%, −1.72%]) and noninflammatory (MD, −17.05% [−22.96%, −11.14%]) lesion counts were seen in BP versus vehicle at 12 weeks in 3 RCTs.[63,66,69] BP use is limited by concentration and formulation-dependent burning sensation, stinging, dryness, erythema, pain, peeling, irritation, fabric staining and bleaching, and uncommon contact allergy. Lower BP concentrations and water-based and wash-off formulations may be better tolerated.[166,167] No *C. acnes* resistance to BP has been reported.

Topical antibiotics

Topical antibiotics (including erythromycin, clindamycin, minocycline, and dapsone) treat acne through both antibacterial and anti-inflammatory effects.[168] We recommend topical antibiotics for acne treatment based on moderate certainty evidence from 14 studies (Table III and Supplementary Table XIV, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[66,68,69,71,79,84-91] Compared to vehicle at 12 weeks, a greater proportion of patients treated with topical antibiotics achieved IGA success in 3 RCTs (RR, 1.49 [1.28, 1.73]).[71,86,87]

A greater reduction in inflammatory lesions was seen with topical antibiotics versus vehicle at 12 weeks in 8 RCTs (MD in the percentage change from baseline, −10.86% [−18.81%, −2.91%]),[66,69,79,84-87,91] but the difference in reduction in noninflammatory lesion counts between the groups was not statistically significant at 12 weeks in 7 RCT (−3.33% [−7.90%, 1.24%]).[66,69,79,84-87] Notably, topical antibiotic monotherapy is not recommended due to concern for antibiotic resistance. Combining topical antibiotics with BP enhances efficacy and may prevent antibiotic resistance development. Concurrent topical application of BP with either dapsone or sulfacetamide causes an orange-brown skin discoloration, which can be washed off; thus BP should be used at a different time of day than topical dapsone.[169] Glucose-6-phosphate dehydrogenase screening is not required prior to starting topical dapsone. Topical antibiotics are generally well tolerated; there have been rare case reports describing diarrhea or *Clostridium difficile*-related colitis associated with topical clindamycin use.[92,170] There is a lack of active comparator studies to suggest if any one topical antibiotic is superior to another.

Fixed-dose topical combinations

Fixed-dose topical combinations of BP, retinoids, or antibiotics facilitate treatment regimen adherence.[171] We recommend fixed-dose topical combinations of BP and topical retinoid, BP and topical antibiotic, and topical retinoid and topical antibiotic for acne treatment based on moderate certainty evidence from 7[63,64,99,109-112] 9[66,68,69,99-104], and 3[71,79,99] studies, respectively (Table III and Supplementary Tables XV-XXIII, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2). Compared to vehicle at 12 weeks, a greater proportion of patients treated with combined BP and topical retinoid achieved IGA success in 3 RCTs (RR, 2.19 [1.77, 2.72]).[63,64,109] Greater reductions in both inflammatory (MD in the percentage change from baseline, −37.34% [−72.49%, −2.18%]) and noninflammatory (MD, −20.47% [−26.31, −14.62]) lesion counts were seen in combined BP and topical antibiotic versus vehicle at 12 weeks in 4 RCTs.[66,69,99,101] Concomitant BP use is recommended with combined topical retinoid and topical antibiotic to prevent the development of antibiotic resistance. Potential adverse effect profiles of the fixed-dose combinations generally reflect those of the individual agents in summation. Some fixed-dose combination products may be less expensive than prescribing their individual components separately.

Clascoterone

Clascoterone is a topical antiandrogen that directly binds the androgen receptor and inhibits androgen-mediated lipid and inflammatory cytokine synthesis from sebocytes.[172] We conditionally recommend clascoterone for acne treatment based on high certainty evidence from 2 studies (Table III

and Supplementary Table XXIV, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2) and based on work group discussions related to treatment access and cost.

Compared to vehicle at 12 weeks, a greater proportion of patients treated with clascoterone achieved IGA success in 2 RCTs (RR, 2.08 [1.39, 3.11]).[93] Despite high certainty of benefits over risks based on clinical trial evidence, the work group voted on a conditional recommendation due to concerns about the high current cost of clascoterone treatment that may impact equitable acne treatment access. This conditional recommendation may be revised in the future pending changes in treatment cost and access.

Salicylic acid

Salicylic acid is a topical comedolytic agent that is available over the counter, with concentration ranging in 0.5% to 2%. We conditionally recommend salicylic acid for acne treatment based on moderate certainty evidence from 1 RCT, showing a 25% greater reduction in inflammatory lesions, 11% greater reduction in open comedones, and no difference in closed comedones with 0.5% salicylic acid use compared to vehicle at 12 weeks (Table III and Supplementary Table XXV, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[95] Chemical peels using salicylic acid 10% to 30% are separately discussed in the physical modalities section.

Azelaic acid

Azelaic acid is a topical comedolytic, antibacterial, and anti-inflammatory agent, which may be particularly helpful for patients with sensitive skin or darker skin types due to its lightening effect on dyspigmentation.[96,97,173] We conditionally recommend topical azelaic acid for acne treatment based on moderate certainty evidence from 3 RCTs (Table III and Supplementary Table XXVI, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[96-98] In 1 RCT of 92 patients, 28% more patients receiving azelaic acid 20% cream twice daily achieved 50% to 100% reduction in total lesion count compared to vehicle at 3 months.[97]

Considerations in topical therapies

In patients who are pregnant, the risk of fetal harm from topical azelaic acid, BP, erythromycin, and clindamycin are not expected based on limited expected systemic absorption.[174,175] Salicylic acid can be used in pregnancy if the area of exposure and duration of therapy is limited; use for large areas or under occlusion are not recommended due to the potential for systemic absorption.[174] There are no data on the safety of topical dapsone and clascoterone during pregnancy or lactation. Tazarotene is contraindicated in pregnancy based on animal reproduction studies, retinoid pharmacology, and the potential for systemic absorption. No human studies have established causal relationships between the use of topical retinoids with birth defects; nevertheless, topical therapies other than topical retinoids are preferred during pregnancy. Topical minocycline is not recommended during pregnancy or lactation.

Salicylic acid is available over the counter. Fixed-dose combination BP 2.5%/adapalene 1% gel, tretinoin 0.1%/BP 3% cream, tretinoin 0.05% lotion, trifarotene 0.005% cream, dapsone 5% gel, and minocycline 4% foam are FDA-approved for ages 9 years and above, and most other topical retinoids, antibiotics, clascoterone, and azelaic acid are approved for age 12 years and above.

Available evidence is insufficient to develop a recommendation on the use of topical glycolic acid, sulfur, sodium sulfacetamide, and resorcinol for acne treatment or to make recommendations that compare topical BP, retinoids, antibiotics, and their combinations directly against each other (Supplementary Tables XXVII-XXXV, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).

SYSTEMIC ANTIBIOTICS

Systemic antibiotics have been used extensively to treat acne, typically moderate to severe acne. Oral tetracycline-class antibiotics, including doxycycline, minocycline, and sarecycline, are commonly used. Tetracycline-class antibiotics exhibit antibiotic properties by binding the 16S ribosomal RNA of the bacterial ribosome 30S subunit to inhibit protein synthesis, as well as anti-inflammatory properties by inhibiting neutrophil chemotaxis and matrix metalloproteinases and down-regulating inflammatory cytokines.[176] Notably, tetracycline-class antibiotics are contraindicated in pregnancy, lactation, and childhood below age 9 years during tooth development, since repeated exposure may cause permanent teeth enamel hypoplasia or discoloration.

Limiting the use of systemic antibiotics when possible is recommended as a good practice statement to reduce the development of antibiotic resistance and other antibiotic-associated complications. In 2021, dermatologists prescribed more oral antibiotics per clinician than all other specialties, with the majority of antibiotics used for acne treatment.[177,178]

In addition to concerns about antibiotic resistance, oral tetracycline-class antibiotic use has been associated with inflammatory bowel disease (IBD),[114] pharyngitis,[179] *Clostridium difficile* infection,[180,181] and *Candida* vulvovaginitis. Outpatient antibiotic stewardship promotes appropriate antibiotic use in which patients receive the *right* dose of the *right* antibiotic at the *right* time for the *right* duration. The Centers for Disease Control and Prevention recommend outpatient antibiotic stewardship programs to include (1) commitment to optimizing antibiotic prescribing and patient safety, (2) implementation action for stewardship policy or practice, (3) tracking prescribing practices through clinician feedback or self-assessment, and (4) access to educational resources and expertise.[182] When treating acne with systemic antibiotics, we recommend concomitant use of BP and other topical therapies as a good practice statement to decrease risk of antibiotic resistance and to limit the duration of systemic antibiotic exposure. Oral antibiotics should not be used as monotherapy for acne treatment. Systemic antibiotic use should also be limited to the shortest duration possible, typically no more than 3-4 months, as recommended by international guidelines.[3,183,184] For patients who have inadequate response or contraindications to nonantibiotic therapies and may require longer courses of systemic antibiotics, consistent follow up and re-evaluation should limit systemic antibiotic use to the shortest duration and should maintain treatment endpoints with concurrent topical therapies during and after systemic antibiotic treatment.[185-189]

Doxycycline

We recommend doxycycline for acne treatment based on moderate certainty evidence from 5 studies (Table III and Supplementary Table XXXVI, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[114-118] Compared to vehicle at 4 months, a greater proportion of patients treated with doxycycline achieved IGA success in 2 RCTs (RR, 1.80 [1.17, 2.77]).[116,117] Treatment withdrawal due to adverse effects was more common with doxycycline compared to placebo in 3 trials (1.3% vs 0.3%; RR, 2.25 [0.38, 13.21]).[115-117] Doxycycline may cause gastrointestinal disturbances (15.7% vs 5.9%; RR, 2.56 [1.05, 6.25]),[115-117] including nausea, vomiting, and diarrhea; esophagitis, phototoxicity; and rarely intracranial hypertension. Taking doxycycline with food and adequate fluids in the upright position may reduce gastrointestinal side effects. Low-dose doxycycline (20 mg twice daily or 40 mg extended release daily) has demonstrated efficacy in patients with moderate inflammatory acne,[115] but there remains insufficient evidence comparing oral doxycycline at different dosages directly.[190]

We conditionally recommend doxycycline over azithromycin for acne treatment based on low certainty evidence from 4 studies (Table III and Supplementary Table XXXVII, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[126-129] A greater reduction in total lesion counts was seen in doxycycline versus azithromycin at 12 weeks (MD in the change from baseline, −6.0 [-11.63, −0.37] in 1 RCT.[126] Azithromycin is a broad-spectrum macrolide antibiotic that covers respiratory and other infections; increasing azithromycin use could increase antibiotic resistance.

Minocycline

We conditionally recommend minocycline for acne treatment based on moderate certainty evidence from 5 studies and based on work group discussions related to uncommon potential treatment adverse effects (Table III and Supplementary Table XXXVIII, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[114,119-122] Compared to vehicle at 12 weeks, a greater proportion of patients treated with minocycline achieved IGA success in 2 RCTs (RR, 1.82 [1.28, 2.57]).[119-121] Adverse effects requiring treatment cessation were higher with minocycline compared to placebo in 2 RCTs (9.1% vs 1.0%; RR, 6.23 [1.20, 32.99]).[120,122] Oral minocycline confers similar common adverse effects as doxycycline. Despite moderate certainty of benefits over risks based on clinical trial evidence, the work group voted on a conditional recommendation due to concerns about rare potential adverse effects of minocycline, which include vertigo, autoimmune hepatitis, skin hyperpigmentation, drug-induced lupus, and hypersensitivity syndrome. As there is insufficient evidence comparing doxycycline and minocycline directly, the potential risks and benefits of each treatment option should be considered (Supplementary Table XXXIX, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2). Moreover, oral minocycline monotherapy is not superior to topical BP 5% or erythromycin 2%/BP 5% in mild to moderate acne in 1 RCT (Supplementary Tables XL-XLII, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[191] Available evidence is insufficient to develop a recommendation on the use of long-term minocycline monotherapy or in combination with tazarotene as maintenance therapy beyond 3-4 months over tazarotene gel alone (Supplementary Table XLIII, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[186]

Sarecycline

We conditionally recommend sarecycline for acne treatment based on high certainty evidence from 3 studies and based on Work Group discussions related to treatment access and cost (Table III and Supplementary Table XLIV, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[123-125] Sarecycline is a narrow-spectrum tetracycline-class antibiotic, and compared to vehicle at 12 weeks, a greater proportion of patients treated with sarecycline achieved IGA success in 2 RCTs (22.3% vs 13.0%; RR, 1.73 [1.23, 2.44]).[123-125] Sarecycline is dosed by weight at 1.5 mg/kg and is generally well tolerated with low incidence of gastrointestinal, photosensitivity, and Candida infection side effects. Despite high certainty of benefits over risks based on clinical trial evidence, the work group voted on a conditional recommendation due to concerns about the high current cost of sarecycline treatment that may impact equitable acne treatment access. This conditional recommendation may be revised in the future pending changes in treatment cost and access.

Considerations in systemic antibiotics

Oral doxycycline, minocycline, and sarecycline are FDA-approved for the management of acne. In patients who are pregnant or lactating, tetracycline-class antibiotics should be avoided due to potential for permanent teeth discoloration and bone growth inhibition in the fetus or nursing infant. The 2016 AAD acne guidelines discussed the limited use of oral erythromycin and azithromycin for pregnant persons and on the restricted use of trimethoprim-sulfamethoxazole or trimethoprim for patients unable to tolerate tetracyclines.[3] Available evidence is insufficient to develop a recommendation on the use of oral azithromycin or trimethoprim/sulfamethoxazole for acne treatment (Supplementary Tables XLV-XLVIII, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2). In addition, TMP-SMX may be associated with severe adverse reactions such as Stevens-Johnson syndrome/toxic epidermal necrolysis and acute respiratory failure. These antibiotics are also indicated for community-acquired infections, such as pneumonia and urinary tract infections, and broad use for acne should be discouraged to avoid selection of antibiotic-resistant bacteria. Available evidence is also insufficient to make recommendations that compare systemic antibiotics directly against each other or against topical therapies (Supplementary Tables XLIX-LIII, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).

HORMONAL AGENTS

Combined oral contraceptives

Combined oral contraceptives (COCs) contain combinations of estrogen and progestin. COC prevent ovulation and pregnancy by inhibiting gonadotropin-releasing hormone, follicle stimulating hormone, and luteinizing hormone. COC treat acne through their overall anti-androgenic properties, which decrease ovarian androgen production, increase sex hormone-binding globulin, and reduce free testosterone that would otherwise activate the androgen receptor. COC reduce 5α-reductase activity and block the androgen receptor.[192-195]

Ethinyl estradiol (EE) is the most common estrogen component in COC, with daily doses typically ranging from 10-50 μg. Progestins are synthesized progesterone analogues and are historically categorized by generations. First, second, and third generation progestins are derived from testosterone and have androgenic potential if used alone. Examples of first-generation oral progestins include norethindrone and ethynodiol diacetate; second-generation include levonorgestrel and norgestrel; and third-generation include norgestimate and desogestrel, which are considered less androgenic than prior generations. Progestin-only oral contraceptive pills, intramuscular injections, intrauterine devices, or subcutaneous implants may worsen acne.[196,197] Fourth-generation progestins include oral drospirenone and dienogest. Drospirenone is a spironolactone analogue not derived from testosterone and has antiandrogenic properties. Combined with estrogen, all COCs yield net antiandrogenic properties.[193,198] Four COCs are FDA-approved for treatment of acne in women who desire oral contraception, including norgestimate/EE, norethindrone acetate/EE/ferrous fumarate, drospirenone/EE, and drospirenone/EE/levomefolate. All COCs are currently available in generic forms in the US.

We conditionally recommend COCs for acne treatment based on moderate certainty evidence from 10 studies[130-139] and variability in patient values and preferences related to contraception (Table III and Supplementary Table LIV, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2). Data on all COC formulations with acne outcomes, regardless of specific approved indication for acne treatment, were pooled and compared against placebo. Compared to vehicle at the end of cycle 6, a greater proportion of patients treated with COCs achieved IGA success in 3 RCTs (RR, 1.45 [1.06, 1.97]).[130-132] Greater reductions in both inflammatory (MD in the percentage change from baseline,

−15.81% [−20.44%, −11.17%]) and noninflammatory (MD, −19.45% [−9.9, −9.0]) lesion counts were seen in COC versus vehicle at the end of cycle 6 in 9 RCTs[130-138] and 6 RCTs,[131-134,136,137] respectively. High dropout rates of 25% to 35% across multiple RCTs may in part reflect variability in patient preferences regarding COC continuation. Current data show no consistent difference in acne responses based on COC formulations or dosages and do not support the superiority of one COC over another for acne treatment (Supplementary Tables LVI-LXI, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[199-205] Reports of any adverse effects (54.0% vs 50.1%; RR, 1.15 [1.07, 1.24]) and treatment withdrawal due to adverse effects (5.1% vs 2.9%; 1.86 [1.32, 2.62]) are more common with COCs than with placebo. COC for acne treatment is not limited to patients with acne affecting the jawline or with premenstrual flares, hirsutism, or hyperandrogenism. Clinicians should counsel patients about expected time to acne improvement with COCs, usually notable within 3-6 months, and may consider combining COCs with other acne therapies early in treatment course to accelerate treatment response.

Obtaining a comprehensive medical history and measuring blood pressure are important before prescribing COCs.[206] Clinicians may be reasonably certain that a patient who has no symptoms or signs of pregnancy and who meets specific criteria (eg, who presents within 7 days after the start of normal menses or who have not had sexual intercourse since the start of last normal menses) is not pregnant.[207] Urine pregnancy tests may also be considered.[207] COC access may be expanded using patient eligibility self-screening tools.[208] Pelvic and breast examination, cervical cancer screening, and sexually transmitted infection screening are not required prior to COC initiation.[208] Recommendations for contraceptive selection for patients with specific characteristics or medical conditions are found in the US Medical Eligibility Criteria for Contraceptive Use, 2016, which is available as a mobile application to facilitate use in clinical settings.[209] Absolute and relative contraindications to COCs are summarized in Table IV.[209] Discussions weighing potential benefits and risks of COCs may differ depending on its indication: if a COC is indicated to prevent pregnancy, its risks and benefits should be contextualized against those of an unintended pregnancy; if a COC is indicated exclusively for acne treatment, its risks and benefits should be compared against those of acne.

Potential adverse effects of COCs include venous thromboembolism (VTE), myocardial infarction, stroke, breast cancer, cervical cancer, among others. Typical use of EE with daily dose below 50 μg is associated with lower VTE risks compared to historical use of EE with daily doses above 50 μg, which are no longer available in the US; existing data have not shown significant effect of further EE dose reductions below 50 μg on VTE risks.[208,210] The absolute risk of VTE associated with COC use is small compared to the risk of VTE in pregnancy.[208,210] Estimated VTE incidence per 10,000 person-years are estimated at approximately 1-5 in nonpregnant women who do not use COCs, 3-9 in COC users, 10 in drospirenone-containing COC users, 5-20 in pregnancy, and 40-65 in the 12-week postpartum period.[208,210] COC use is associated with small increases in myocardial infarction and stroke risks, particularly in patients above age 35 years who smoke tobacco or patients who have hypertension, diabetes mellitus, or migraines. While cardiovascular events are important safety concerns, they are uncommon in reproductive-aged patients, in which a small relative risk increase still represents an overall low absolute risk.[193,194,211] COCs have been associated with small increases in breast cancer and cervical cancer risks and decreases in endometrial, ovarian, and colorectal cancer risks in systematic reviews.[212-216] A long-term cohort study of 46,022 women in the United Kingdom showed an overall neutral balance between short- and long-term cancer risks and benefits in past COC users after 30 years of follow-up.[214]

COC confers benefits beyond contraception and acne treatment, including regulating menstrual cycles, induction of amenorrhea, prevention of menstrual migraines, and treatment of conditions such as dysmenorrhea, hirsutism, menorrhagia, endometriosis-associated pelvic pain, premenstrual syndrome, among others.[217] Due to numerous potential benefits, risks, and variability in patient values and preferences, patient-centered contraceptive counseling that prioritize patients' values, preferences, and lived experiences in the shared decision-making of initiation or discontinuation of contraceptive methods is critical.[218] To help all patients achieve reproductive goals, the American College of Obstetricians and Gynecologists recommends intentional application of a reproductive justice framework that acknowledges historical devaluation of reproductive desires of people of color and other marginalized individuals and conscious and unconscious clinician bias in contraceptive counseling.[218]

COC may be combined with other oral or topical acne medications, including tetracycline antibiotics and spironolactone. Tetracycline-class antibiotics have not been shown to reduce COC

Table IV. Summary of contraindications to combined oral contraceptive use based on the US Medical Eligibility Criteria for Contraceptive Use*

Absolute contraindications (Category 4: A condition that represents an unacceptable health risk if COC is used)	Relative contraindications (Category 3: A condition for which the theoretical or proven risks usually outweigh the benefits of COC)
Personal characteristics and reproductive history	
• Age ≥35 y and smoking ≥15 cigarettes daily	• Age ≥35 y and smoking <15 cigarettes daily
• <21 d postpartum, regardless of breastfeeding status	• Breastfeeding patient 21-29 d postpartum
	• Breastfeeding patient 30-42 d postpartum, with other VTE risk factors†
	• Nonbreastfeeding patient 21-42 d postpartum, with other VTE risk factors†
Cardiovascular disease	
• SBP ≥160 mmHg or DBP ≥100 mmHg	• SBP 140-159 mmHg or DBP 90-99 mmHg
• Vascular disease	• Adequately controlled hypertension
• Acute VTE or history of VTE with ≥1 risk factor for recurrence‡	• VTE with no risk factors for recurrence
	• Superficial venous thrombosis
• Major surgery with prolonged immobilization	• Peripartum cardiomyopathy with normal or mildly impaired cardiac function for ≥6 mo
• Known thrombogenic mutation§	
• Multiple risk factors for atherosclerosis‖	
• Current or history of ischemic heart disease	
• Current or history of stroke	
• Valvular heart disease with complications¶	
• Peripartum cardiomyopathy with normal or impaired cardiac function for <6 mo or moderate or severely impaired cardiac function	
Gastrointestinal conditions	
• Acute or flare of viral hepatitis	• History of malabsorptive procedures (Roux-en-Y gastric bypass or biliopancreatic diversion)
• Severe or decompensated cirrhosis	• Ulcerative colitis or Crohn disease with increased VTE risk#
• Hepatocellular adenoma	• Untreated or medically treated symptomatic gallbladder disease
• Malignant liver tumor (hepatoma)	• History of COC-related cholestasis
• Diabetes with nephropathy, retinopathy, neuropathy, other vascular disease, or with duration > 20 y**	
• Current breast cancer	• Past breast cancer with no evidence of disease for 5 y
• Migraine with aura	• Multiple sclerosis with prolonged immobility
• Systemic lupus erythematosus with positive or unknown antiphospholipid antibodies	
• Solid organ transplantation complicated by acute or chronic graft failure, rejection, or cardiac allograft vasculopathy	

BP, Blood pressure; *COC*, combined oral contraceptives; *VTE*, venous thromboembolism.

*Adapted from Curtis KM et al. Please refer to the US Medical Eligibility Criteria for Contraceptive Use 2016 for additional clarification, evidence, and comments related to important classification details on combined hormonal contraceptives.[209]

†Risk factors include age ≥35 years, previous VTE, thrombophilia, immobility, transfusion at delivery, peripartum cardiomyopathy, body mass index ≥30 kg/m^2, postpartum hemorrhage, post-Cesarean delivery, preeclampsia, or smoking.

‡Risk factors include history of estrogen-related VTE, pregnancy-related VTE, idiopathic VTE, known thrombophilia (including antiphospholipid syndrome), active cancer (metastatic, receiving therapy, or within 6 months after clinical remission) excluding nonmelanoma skin cancer, or history of recurrent VTE.

§Known thrombogenic mutations include factor V Leiden, prothrombin mutation, protein S deficiency, protein C deficiency, or anti-thrombin deficiency.

‖Risk factors include older age, smoking, diabetes mellitus, hypertension, low high-density lipoprotein, high low-density lipoprotein, or high triglycerides.

¶Complicated valvular heart disease includes pulmonary hypertension, risk for atrial fibrillation, or history of subacute bacterial endocarditis.

#Risk factors include active or extensive disease, surgery, immobilization, corticosteroid use, vitamin deficiencies, or fluid depletion.

**Classification as absolute (class 4) or relative (class 3) contraindication is assessed based on severity of diabetes-related complications.

effectiveness.[194,211,219,220] Among anti-infectives, rifampin and griseofulvin have demonstrably reduced COC effectiveness.[221] Concomitant use of spironolactone and drospirenone did not increase serum potassium or adverse effects requiring treatment discontinuation.[222,223] COC is FDA-approved for female patients above age 14 years (drospirenone/EE, drosperinone/EE/levomefolate) or 15 years (norgestimate/EE, norethindrone/EE/ferrous fumarate). A new type of COC with drospirenone/estetrol was approved by the FDA for contraception in 2021[224]; its use for acne was not evaluated in the current guidelines.

Spironolactone

Spironolactone is an aldosterone receptor antagonist that decreases testosterone production and competitively inhibits testosterone and dihydrotestosterone binding to androgen receptors in the skin.[225-228] Spironolactone may also inhibit 5α-reductase and increase steroid-hormone binding globulin.[229,230] Spironolactone is not FDA-approved for the treatment of acne.

We conditionally recommend spironolactone for acne treatment based on moderate certainty evidence from 8 studies (Table III and Supplementary Table LV, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[140-147] Compared to placebo combined with BP 2.5% alone at 12 weeks, a greater proportion of patients treated with spironolactone 50 mg daily combined with BP 2.5% achieved IGA success in a small RCT of 40 patients (75.0% vs 30.0%; RR, 2.50 [1.22, 5.11]).[140] Compared to vehicle at 12 weeks, a greater proportion of patients treated with spironolactone at daily doses ranging from 50-200 mg had improvement in patient global assessment in 2 small RCTs of 58 patients (77.4% vs 22.25; RR, 3.60 [1.75, 7.42]).[141,142] A cohort study comparing acne patients starting treatment with spironolactone to those starting treatment with oral tetracycline-class antibiotics found similar rates of treatment effectiveness, as assessed by treatment switching, between the 2 groups.[231] Menstrual irregularities were commonly reported (40.6% vs 0%; RR, 10.89 [1.54, 77.08]),[140,141] may be dose-dependent,[232] and are less common among those using COC.[233] Common side effects also include diuresis, breast tenderness, breast enlargement, gynecomastia, fatigue, headache, and dizziness.[234] Although spironolactone 50-100 mg/day showed a greater improvement in IGA at 12 weeks as well as acne-specific quality of life and patient global assessment at 24 weeks compared with placebo in a recent RCT of 410 patients,[235] it was published after the literature search was finalized for the current guidelines."

The work group remarked that potassium monitoring is of low usefulness without risk factors for hyperkalemia (eg, older age, medical co-morbidities, medications) based on very low certainty observational studies.[140-147] No significant changes in serum electrolytes were seen in 2 small RCT of spironolactone for acne treatment.[140,141] In a large cohort study of 108,547 patients with acne who received spironolactone for ≥30 days, 0.22% received a hyperkalemia diagnosis and 0.03% discontinued spironolactone within 30 days after hyperkalemia diagnosis. A 4-year retrospective cohort study reported 6 cases of hyperkalemia during 291 patient-years of follow-up. A retrospective review of 974 women aged 18-45 years receiving spironolactone 50-200 mg daily for acne showed that 15 (0.8%) of the 1802 associated potassium measurements exceeded 5.0 mmol/L; all patients with hyperkalemia were asymptomatic and continued spironolactone treatment.[145] In a cohort study of 139 male and female Japanese patients who received spironolactone for acne, with daily dose taper from 200 mg to 50 mg over 20 weeks, all 25 patients in the subset who received potassium monitoring had normal potassium levels in 32 weeks of follow-up.[146] In a cohort study of 124 healthy women with baseline normal serum potassium level, 3 (2.4%) patients aged 42-47 years had incident hyperkalemia upon follow-up.[147] Potassium monitoring should be considered in older patients; patients with medical co-morbidities such as hypertension, diabetes mellitus, chronic kidney disease, among others; and patients taking medications affecting renal, adrenal, and hepatic function, including angiotensin converting enzyme inhibitors, angiotensin receptor blockers, nonsteroidal anti-inflammatory drugs, digoxin, among others. Avoiding a diet high in potassium should be considered.[236]

Spironolactone should not be used in pregnancy. Spironolactone crosses the placenta and exposure in utero in animal studies may cause feminization of a male fetus. Human data are based on limited case reports, with 5 cases resulting in normal male genital development and 1 case of ambiguous genitalia in a newborn of a mother treated with spironolactone until week 5 of gestation.[237] Concurrent COC use is often indicated in treating acne with spironolactone.

Spironolactone carries a warning on tumorigenicity based on chronic toxicity studies in rats that were exposed to up to 150 times human doses of spironolactone or its metabolites. A systematic review of 7 studies of 4.5 million individuals showed no statistically significant association between

spironolactone use in men and women above age 18 years and risks of breast cancer (RR 1.04; 95% confidence interval 0.86-1.22), ovarian cancer (1.52; 0.84-2.20), bladder cancer (0.89; 0.71-1.07); kidney cancer (0.96; 0.85-1.07), gastric cancer (1.02; 0.80-1.24), or esophageal cancer (1.09; 0.91-1.27) based on low to very low certainty of evidence.[238] Spironolactone use is associated with decreased prostate cancer risk (0.79; 0.68-0.90) compared to non-users based on very low certainty of evidence.[238]

Intralesional corticosteroid

Intralesional corticosteroid therapy has been used as an adjuvant therapy for acne. Although there is limited clinical trial data evaluating intralesional corticosteroid injection for acne, in a small RCT of 9 patients, most acne cysts injected with triamcinolone resolved within 3-7 days of the treatment, and those injected with triamcinolone resolved faster than those with saline control.[239] In addition, intralesional corticosteroid injections are effective for a variety of other inflammatory skin conditions such as granuloma annulare, hidradenitis suppurativa, inflamed epidermal cysts, and keloids.[240-246] Together, these characteristics indirectly imply that intralesional corticosteroid injection can be a useful treatment option; therefore, the work group issued a good practice statement for intralesional corticosteroid injection use as an adjuvant therapy in patients with larger acne papules or nodules (Table III). Intralesional corticosteroid injections should be used judiciously for patients who are at risk of acne scarring and/or for rapid improvement in inflammation and pain. Localized skin atrophy, systemic absorption of steroids, and possible adrenal suppression may occur.[247] Using a lower concentration and volume of corticosteroid (eg, triamcinolone 2.5-5 mg/ml) can minimize the risks of local corticosteroid adverse events.[248]

Considerations in hormonal agents

Available evidence is insufficient to develop a recommendation on the use of oral corticosteroids, flutamide, or metformin for acne treatment (Supplementary Tables LXII-LXVIII, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2). The 2016 AAD acne guidelines discussed the temporary use of oral corticosteroids for patients with severe inflammatory acne while starting standard acne treatment and low-dose oral corticosteroids for patients with adrenal hyperandrogenism.[3] Prednisone 0.5-1 mg/kg/day has been used to treat acne fulminans, isotretinoin-induced acne fulminans and to prevent isotretinoin-induced acne flares in at-risk patients.[249,250] However, long-term adverse effects of oral corticosteroids prohibit their use as a primary acne treatment.

ISOTRETINOIN

Oral isotretinoin, or 13-*cis*-retinoic acid, is the only FDA-approved treatment for severe recalcitrant nodular acne vulgaris since 1982. While the exact mechanism of action is unknown, isotretinoin reduces the size and secretion of sebaceous glands, decreases surface and ductal level of sebum-dependent *C. acnes* indirectly, inhibits comedogenesis by normalizing keratinocyte keratinization, and possesses anti-inflammatory properties.[251]

Despite the remarkable effectiveness of isotretinoin observed in routine dermatology practice, clinical trial data regarding its efficacy are limited and of low quality. In a RCT of 33 patients with treatment-resistant cystic and conglobate acne, mean number of cystic lesions decreased by 17% and 33% at 1 and 2 months of isotretinoin treatment, but increased by 33% and 58% at 1 and 2 months of placebo (Supplementary Table LXIX, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[252] Moreover, 13 of 17 patients receiving placebo switched to isotretinoin due to acne worsening.[252] Earlier dose-response studies showed a significant improvement across all dosages (0.1, 0.5, and 1 mg/kg/day).[253-255] In a RCT of 925 patients comparing standard isotretinoin with lidose-isotretinoin, 81.0% of patients treated with standard isotretinoin experienced a 90% reduction in lesion count and 88.9% of patients treated with standard isotretinoin achieved treatment success after 20 weeks of treatment.[151] In another RCT of 60 patients, the low-dose isotretinoin (5 mg daily) group had fewer total lesions compared to those in the vehicle group after 16 weeks of treatment (MD in total lesion counts, −5.4 [-8.91, −1.89]).[256] Many global acne experts have agreed that isotretinoin is the most appropriate treatment option for those with severe or scarring acne.[183,184,257-262] Together, these characteristics indirectly imply the excellent efficacy of isotretinoin; therefore, WG issued a good practice statement for isotretinoin use in patients with severe acne or in patients who have failed standard treatment with oral or topical therapy (Table III). The work group remarked that patients with acne who present with acne-related psychosocial burden and/or scarring should be considered candidates for isotretinoin treatment. Isotretinoin has been extensively used to treat mild to moderate acne that is refractory to other topical and oral therapies or that relapses quickly after discontinuation of oral antibiotics.[148-150,263-265] Common adverse effects associated with isotretinoin involve the

mucocutaneous, musculoskeletal, and ophthalmic systems and generally resolve following isotretinoin discontinuation with standard treatment courses.[3]

Laboratory monitoring during isotretinoin treatment should include liver function tests, fasting lipid panel, and pregnancy test for patients with pregnancy potential and should not include complete blood count monitoring. While significant heterogeneity exist among study definitions, data from 5 isotretinoin cohort studies estimated that risks of abnormal liver function tests above reference limits ranged from 0.8% to 10.4%, with 0.9% to 4.7% requiring treatment discontinuation (Supplementary Table LXX, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[266-270] Data from 6 isotretinoin cohort studies estimated that the risks of abnormal triglycerides ranged from 7.1% to 39.0% and abnormal cholesterol levels ranged from 6.8% to 27.2% (Supplementary Table LXXI, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[266-271] Data from 2 isotretinoin cohort studies estimated the risk of mild normocytic anemia as 0.4%, abnormal platelet level at 1.2% to 2.9%, and abnormal white blood cell count at 7.0% to 10.8% (Supplementary Table LXXII, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[269,270] No grade 3 or greater abnormalities in the complete blood count was observed.[270] Prior meta-analyses of 26 studies showed that the proportion of patients with laboratory abnormalities was low.[272] A recent Delphi consensus study of 22 acne experts reached agreement on checking alanine aminotransferase and triglycerides prior to initiation and at peak isotretinoin dose and on not checking complete blood count, low-density lipoprotein or high-density lipoprotein.[273] Data on laboratory monitoring in patients treated with isotretinoin have been critically appraised, with little evidence to support the benefit of laboratory monitoring to detect adverse events.[274]

For persons with pregnancy potential, pregnancy prevention is mandatory with isotretinoin treatment. After introduction of isotretinoin in the US in 1982, there were hundreds of reports of isotretinoin-exposed pregnancies that resulted in fetal congenital malformations.[275] iPLEDGE is the current FDA-mandated Risk Evaluation and Mitigation Strategy aimed to prevent isotretinoin exposure in pregnancy. All patients receiving isotretinoin are required to enroll in and adhere to iPLEDGE. Recent iPLEDGE modification in 2021 categorized patients into 2 gender-neutral categories: patients who cannot become pregnant, per iPLEDGE definition, include a patient who has had a hysterectomy and/or bilateral oophorectomy, a patient who is postmenopausal, or a patient who was born with male reproductive organs. Patients who can become pregnant must adhere to complete abstinence or use 2 specified contraceptive methods at least 1 month before, during, and 1 month after isotretinoin treatment. Since the iPLEDGE implementation, approximately 150 isotretinoin-exposed pregnancies continue to occur in the US annually due to non-adherence with contraceptive requirements.[276,277] Among sexually active patients who reported non-adherence, 29% did not comply with consistent condom use and 39% missed 1 or more contraceptive pills in the previous month.[277] Patients with pregnancy potential receiving isotretinoin should be carefully counseled regarding various contraceptive methods that are available and the specific requirements of the iPLEDGE system at each clinic visit. Long-acting reversible contraceptives, including intrauterine devices and contraceptive implants, should be considered as the primary contraceptive method whenever clinically appropriate since they have higher effectiveness than COCs and condoms in reducing the risk of unintended pregnancy and do not depend on ongoing patient efforts.[278]

Population-based studies have not identified increased risk of neuropsychiatric conditions or IBD in patients with acne undergoing isotretinoin treatment (Supplementary Table LXIX, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2). Available low certainty evidence from 7 observational studies with substantial heterogeneity do not support a significant association between isotretinoin use and IBD incidence, including ulcerative colitis and Crohn's disease.[279-285] The overall RR of IBD between isotretinoin-exposed and unexposed groups is estimated at 1.13 (95% confidence interval, 0.89, 1.43).[279-285] Neuropsychiatric adverse effects, including changes in mood, depression, anxiety, suicidal ideation and completed suicide have been sporadically reported in patients receiving isotretinoin, including with positive challenge/dechallenge, suggesting a potential causal association.[286,287] However, available low certainty evidence from 4 observational studies with substantial heterogeneity do not support a significant association between isotretinoin use and neuropsychiatric adverse effect incidence.[288-291] The overall RR of adverse neuropsychiatric adverse effects between isotretinoin-exposed and unexposed group is estimated at 0.88 (95% confidence interval 0.77-1.00).[288-291] Multiple studies indicate that isotretinoin may improve quality of life and decrease symptoms of anxiety and

depression in patients with moderate to severe acne, which could reduce overall risks of neuropsychiatric adverse events at a population level.[292-294] However, given high prevalence of depression, anxiety and suicidal ideation/suicide in the general population, and especially the adolescent population who may be candidates for isotretinoin therapy, clinicians should monitor for depression, anxiety, suicidal ideation/suicidality, and other neuropsychiatric adverse effects and individualize therapeutic decisions based on individual differences in response to isotretinoin. Notably, the US Preventive Service Task Force recommends screening for depression in adults[291] and in adolescents aged 12-18 years[295] and recommends screening for anxiety in adolescents aged 8-18 years,[296] regardless of exposure to isotretinoin, each with grade B recommendations that concludes with moderate certainty that such screening yields moderate net benefits. The Patient Health Questionnaire-2 and Patient Health Questionnaire-9 have been proposed as efficient and validated instruments for depression screening with isotretinoin treatment.[297]

We conditionally recommend daily dosing over intermittent dosing of isotretinoin based on low certainty evidence from 3 RCTs (Supplementary Table LXXIII, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[148-150] Greater reductions in global acne grading system score (MD, −1.75 [−3.38, −0.12]), inflammatory lesion counts (MD, −3.87 [−5.57, −2.17]), and non-inflammatory lesion counts (MD, −4.53 [−6.89, −2.17]) were seen in daily dosing (0.5-0.7 mg/kg daily) versus intermittent dosing of isotretinoin (0.5-0.7 mg/kg daily for 1 week out of every 4 weeks) at 24 weeks in an RCT of 33 patients.[150] Withdrawal due to adverse effects were more common with daily dosing than intermittent dosing (6.7% vs 0%).[150]

We conditionally recommend either standard isotretinoin or lidose-isotretinoin based on high certainty evidence from 1 study (Supplementary Table LXXIV, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[151] Standard isotretinoin has better bioavailability when taken with a high fat meal, whereas the bioavailability of lidose-isotretinoin is less affected by whether it is taken with food. In an RCT of 782 patients, lidose-isotretinoin showed non-inferiority in reducing facial and truncal nodular lesions and in the proportion of patients achieving ≥90% reduction of total lesions at 20 weeks (76.9% vs 81.0%; RR, 0.95 [0.88, 1.02]).[151] No significant differences in adverse effects or treatment withdrawal was noted.[151] Both formulations are available as branded generic prescriptions in the US.

Additional potential adverse effects, such as cardiovascular risk, bone mineralization, scarring, and *S. aureus* colonization, were addressed in the 2016 acne guidelines. Expert consensus from the American Society of Dermatologic Surgery concluded that there is insufficient evidence to justify delaying treatment with superficial chemical peels and nonablative lasers, including hair removal lasers and lights, vascular lasers, and nonablative fractional devices for patients currently receiving or recently received isotretinoin.[298] Full-face dermabrasion, mechanical dermabrasion with rotary devices, and ablative laser treatment of the entire face or non-facial regions are not recommended within 6 months of isotretinoin use due to increased risks of adverse events.[298]

Available evidence is insufficient to directly compare between traditional dosage (0.5mg-1.0 mg/kg/day) and low-dosage (<0.5 mg/kg/day) isotretinoin regimens, between isotretinoin with systemic antibiotics with or without topical therapies, and between isotretinoin alone and isotretinoin with topical agents (Supplementary Tables LXXV-LXXX, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2). Although available evidence was insufficient to make a formal recommendation, a few small studies have suggested that low-dose regimens may be associated with similar efficacy and rates of relapse compared to higher-dose regimens.[150,254,255]

PHYSICAL MODALITIES

Physical modalities examined included acne lesion extraction, chemical peels, laser and light-based devices, microneedle radiofrequency devices, and photodynamic therapy. Available evidence is insufficient to develop a recommendation on the use of acne lesion/comedo extraction, chemical peels (including glycolic acid, trichloroacetic acid, salicylic acid, Jessner's solution, or mandelic acid), laser and light-based devices (including 585-595 nm pulsed dye laser, neodymium-doped yttrium aluminum garnet laser, 1450 diode laser, potassium titanyl phosphate laser, infrared light-emitting diode, 635-670 nm red light, combined 420 nm blue light and 660 nm red light, 589 nm/1319 nm laser, or intense pulsed light), microneedle radiofrequency device, or photodynamic therapy with aminolevulinic acid for the treatment of acne (Supplementary Tables LXXXI-CLIX, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2). We conditionally recommend against adding pneumatic broadband light to adapalene 0.3% gel based on low certainty evidence from 1 study (Table III

and Supplementary Table CLX, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).[152] Adding pneumatic broadband light to adapalene did not reduce acne lesion counts and was associated with risks of hyperpigmentation and purpura.[152] The 1726 nm laser was cleared by the FDA for acne treatment in 2022[299,300]; its evidence was not evaluated in the current guidelines due to lack of a RCT.

COMPLEMENTARY/ALTERNATIVE THERAPIES

Complementary and alternative therapies examined include botanical or plant-derived agents and vitamins. Available evidence is insufficient to develop a recommendation on the use of topical tea tree oil, topical green tea, topical witch hazel, oral pantothenic acid, oral or topical zinc, oral or topical niacinamide for acne treatment (Supplementary Tables CLXI-CLXXIII, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2).

DIET

Available evidence is conflicting on low-glycemic-load diet for acne treatment (Supplementary Tables CLXXIV-CLXXVI, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2). A greater reduction in facial acne score was seen in a low-glycemic-load diet versus a high-glycemic-load diet at 8 weeks in an RCT of 45 patients (MD in change from baseline, −0.3 [−0.39, −0.21]).[301] One RCT of 32 Korean patients showed improvement in the Leeds Revised Acne score at 12 weeks in a low-glycemic-load diet group, but not in control group.[247] A greater reduction in total lesion count was seen in a low-glycemic-load diet versus a high-glycemic-load diet at 12 weeks in an RCT of 43 Australian patients (MD in change from baseline, −8.1 [−14.89, −1.31])[302] However, in an RCT of 84 patients, the addition of a low-glycemic diet in patients starting BP 2.5% gel did not result in significant differences in acne lesion counts.[303] Available evidence is insufficient to develop a recommendation on the use of low dairy diet, low whey diet, omega-3 fatty acids, and chocolate on acne treatment.

GAPS IN RESEARCH AND STUDY LIMITATIONS

These guidelines identified important evidence gaps on the use of microbiology and endocrinology testing in acne, the use of systemic antibiotics beyond tetracycline-class antibiotics, physical modalities, complementary and alternative therapies, dietary interventions for the treatment of acne, and cost-effectiveness of acne treatments. RCT with long-term follow-up and comparative effectiveness research are necessary to examine and compare patient-centered acne treatment outcomes. Increased use of active comparator trials are needed when multiple interventions exist within a treatment class, such as among topical retinoids and topical antibiotics.[304,305] Additional research is needed on optimizing value of laboratory monitoring for patients receiving spironolactone and isotretinoin. A list of interventions and comparisons of interventions identified, evaluated, and not considered to be viable candidates for recommendation development due to insufficient evidence is available in Supplementary Table CLXXVII, available via Mendeley at https://data.mendeley.com/datasets/z2bmdwwdf9/2.

Tailoring acne management in diverse populations will require incorporation of diversity, equity, and inclusion efforts in the acne research pipeline. Women, patients of color, and sexual and gender minority patients may be disproportionately affected by acne.[21,306-308] Many acne RCT specify contraceptive requirements and exclusion criteria related to hormone therapy.[309] To optimize acne care in patients with pregnancy potential and LGBTQ + patients, future acne research should incorporate ongoing national efforts to collect high-quality information about sex, gender identity, and sexual orientation and to examine real-life acne treatment effects by including patients with variations in contraceptive use and hormone therapy status.[309-311] Additional research on the safety and efficacy of acne treatments in the context of pregnancy and lactation are required.[174,312]

Patients with skin of color may disproportionately suffer from acne sequelae, including acne-induced hyperpigmentation and keloidal scarring, which may be under-appreciated or undertreated by clinicians.[307] A systematic review of the treatments of acne-associated hyperpigmentation and scarring fall beyond the scope of these guidelines but is an area of important work. In addition to early treatment of acne, common treatments for acne-induced hyperpigmentation include topical retinoids, azelaic acid, hydroquinone, and physical modalities such as lasers and chemical peels. Common treatments for keloidal scars include topical silicone, intralesional corticosteroids, or lasers. A recent systematic review of 55 studies on acne in skin of color was unable to draw firm conclusions to guide distinct decisions in acne practice in patients with skin of color.[307] Only 4 of 55 studies evaluated acne outcomes in Fitzpatrick skin types IV to VI. The lack of research representation was most notable among Black, African

American, and Afro-Caribbean patients. Expanding diversity and inclusion of acne RCT will be critical to examine acne treatment in patients with skin of color.

This guideline is developed based on analysis of the best available data at the time it was conducted. The results of future studies may necessitate revision of current recommendations. Study limitations included the pragmatic decision to limit the literature review to English language, which may have excluded relevant data published in other languages. Due to the large scope of the review using Grading of Recommendations, Assessment, Development, and Evaluation methodology, the analysis included only RCTs, which may have limited identification of relevant long-term follow-up data.

SUMMARY

Analysis of the evidence from this systematic review based on 9 clinical questions resulted in 18 evidence-based recommendations and 5 good practice statements for the treatment of acne. Strong recommendations are made for benzoyl peroxide, topical retinoids, and topical antibiotics, as well as for oral doxycycline. Oral isotretinoin is strongly recommended for acne that is severe, causing psychosocial burden or scarring, or failing standard oral or topical therapy. Conditional recommendations are made for topical clascoterone, salicylic acid, azelaic acid, as well as for oral minocycline, sarecycline, COC pills, and spironolactone. Combining topical therapies with multiple mechanisms of action, limiting systemic antibiotic use, combining systemic antibiotics with topical therapies, and adding intralesional corticosteroid injections for larger acne lesions are recommended as good practice statements (Table III).

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Conflicts of interest

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