Table I. Botanical ingredients found in >10% of topical cannabinoids

Ingredient	Frequency, n (%)
Coconut	52 (51)
Peppermint and/or menthol*	37 (36)
Lavender*	33 (32)
Beeswax	30 (29)
Shea	27 (26)
Sunflower	25 (24)
Aloe vera*	23 (22)
Arnica*	18 (18)
Eucalyptus*	17 (17)
Rosemary*	17 (17)
Ginger*	15 (15)
Almond	14 (14)
Jojoba	14 (14)
Tea tree*	14 (14)
Avocado	13 (13)
Chamomile*	13 (13)
Marigold*	11 (11)
Cocoa	11 (11)
Orange*	11 (11)
Argan	10 (10)
Frankincense*	10 (10)
Grapefruit*	10 (10)
Tamanu	10 (10)

Oils, extracts, infusions, butters, and esters were included in the ingredient list. Similar/related botanicals were combined to reduce redundancy (eg, orange with sweet orange oil and peppermint oil with its main component, menthol).
*Botanical allergen.[4,5]

might reflect cannabis consumer preference for nongreasy vehicles featuring natural/organic ingredients.

Cannabis has been reported to cause immunologic contact urticaria[7] and airborne allergic contact dermatitis.[8] Commercial preparations containing cannabinoid derivatives also contain a host of cannabinoid-unrelated allergens. However, inclusion of an allergen in the NACDG screening series does not necessarily imply high clinical relevance; the most recent prevalence of patch test positivity was <1% for tocopherol, parabens, and peppermint and lavender oils.[3] The generalizability of our findings is limited by geographic restriction of the sample.

Cannabinoids might have a future role to play in dermatology.[1] As evidence accumulates, consumers and dermatologists should be aware of the potential allergenicity of common ingredients, particularly botanicals, in topical cannabinoids.

The authors would like to thank Sean McKeown for providing the inspiration for this project.

Brandon L. Adler, MD, and Vincent A. DeLeo, MD

From the Department of Dermatology, Keck School of Medicine, University of Southern California, Los Angeles, California

Funding sources: None.

Conflicts of interest: None disclosed.

Reprints not available from the authors.

Correspondence to: Brandon L. Adler, MD, 1441 Eastlake Ave, Ezralow Tower, Ste 5301, Los Angeles, CA 90033

E-mail: brandon.adler@med.usc.edu

REFERENCES

1. Eagleston LRM, Kalani NK, Patel RR, Flaten HK, Dunnick CA, Dellavalle RP. Cannabinoids in dermatology: a scoping review. *Dermatol Online J*. 2018;24(6).
2. Lim M, Kirchhof MG. Dermatology-related uses of medical cannabis promoted by dispensaries in Canada, Europe, and the United States. *J Cutan Med Surg*. 2018:1203475418808761.
3. DeKoven JG, Warshaw EM, Zug KA, et al. North American Contact Dermatitis Group patch test results: 2015-2016. *Dermatitis*. 2018;29(6):297-309.
4. de Groot AC, Schmidt E. Essential oils, part iv: contact allergy. *Dermatitis*. 2016;27(4):170-175.
5. Mortimer S, Reeder M. Botanicals in dermatology: essential oils, botanical allergens, and current regulatory practices. *Dermatitis*. 2016;27(6):317-324.
6. Xu S, Kwa M, Lohman ME, Evers-Meltzer R, Silverberg JI. Consumer preferences, product characteristics, and potentially allergenic ingredients in best-selling moisturizers. *JAMA Dermatol*. 2017;153(11):1099-1105.
7. Williams C, Thompstone J, Wilkinson M. Work-related contact urticaria to Cannabis sativa. *Contact Dermatitis*. 2008;58(1):62-63.
8. Foster E, Nguyen C, Norris P. Contact buzz: allergic contact dermatitis to cannabis. *Dermatitis*. 2018;29(4):223-224.

https://doi.org/10.1016/j.jaad.2019.03.015

Real-world drug usage survival of spironolactone versus oral antibiotics for the management of female patients with acne

To the Editor: Acne often persists into adulthood, particularly for female patients.[1] For those with persistent moderate-to-severe disease requiring treatment with systemic agents, it is important to identify which options can provide a durable treatment effect over time. Spironolactone is emerging as a potential alternative to oral antibiotics.[2,3] However, little is known about long-term outcomes with spironolactone for those who have an initial positive response and how it compares with other alternatives.

To understand the drug usage survival of spironolactone compared with oral antibiotics for acne, we performed a retrospective analysis using OptumInsight Clinformatics DataMart (OptumInsight, Eden Prairie,

Table I. Patient characteristics and HRs for treatment discontinuation

Characteristic	Spironolactone, n = 4321	Tetracyclines, n = 7517	Other antibiotics,* n = 1606
Age at diagnosis, y, median (IQR)	27 (18-32)	16 (14-22)	16 (14-23)
Age at treatment, y, median (IQR)	29 (22-35)	18 (15-24)	19 (16-25)
Course duration, d, mean (SD)	697.8 (333.3)†	604.4 (261.0)	612.1 (261.7)
12-20 y at start of therapy	653.6 (296.1)†	594.4 (245.5)	599.1 (238.7)
21-30 y at start of therapy	679.1 (313.0)†	587.6 (239.6)	596.1 (251.1)
31-40 y at start of therapy	730.9 (359.3)†	664.1 (328.9)	688.6 (342.2)

		Age at start of therapy, HR (95% CI)		
	Overall, HR (95% CI)	12-20 y	21-30 y	31-40 y
Treatment				
Tetracyclines	Reference	Reference	Reference	Reference
Spironolactone	0.74 (0.71-0.77)	0.77 (0.71-0.83)	0.69 (0.64-0.75)	0.77 (0.71-0.83)
Other antibiotics	0.96 (0.91-1.02)	0.98 (0.91-1.05)	0.97 (0.86-1.10)	0.89 (0.77-1.03)
History of combined oral contraceptive use	1.04 (1.00-1.08)	1.07 (1.01-1.13)	1.01 (0.92-1.10)	1.03 (0.95-1.11)
History of topical retinoid use	1.05 (1.00-1.10)	1.03 (0.95-1.12)	1.09 (1.00-1.19)	1.05 (0.98-1.13)
History of polycystic ovarian syndrome	0.95 (0.88-1.02)	0.94 (0.84-1.06)	0.85 (0.75-0.97)	1.08 (0.96-1.21)
Age at start of therapy, y				
12-20	Reference			
21-30	1.02 (0.95-1.09)			
31-40	0.86 (0.78-0.96)			
Age at diagnosis, y				
<20	Reference			
21-30	0.93 (0.86-1.00)			
>31	0.91 (0.81-1.01)			

CI, Confidence interval; *HR*, hazard ratio; *IQR*, interquartile range; *SD*, standard deviation.
*Other antibiotics includes azithromycin, amoxicllin, trimethoprim-sulfamethoxazole, and cephalexin.
†$P < .001$ compared with tetracyclines, unpaired Student *t* test.

MN) to identify female patients 12-40 years of age with ≥2 diagnosis codes for acne during January 1, 2010-December 31, 2016. Prescriptions for spironolactone and oral antibiotics were identified by their National Drug Codes. The primary outcome was drug usage survival (duration of therapy) for patients who received treatment for ≥12 months. In addition, multivariate Cox proportional hazard models were used to evaluate for differences in drug usage survival for spironolactone compared with oral antibiotics. Statistical analyses were performed in Stata 15 (StataCorp, College Station, TX). The study was deemed exempt by the Institutional Review Board at the University of Pennsylvania.

The mean course duration was 697.8 days (standard deviation 333.3) among 4321 female patients treated with spironolactone and 604.4 days (standard deviation 261) among 7517 female patients treated with oral tetracycline-class antibiotics ($P < .001$, Table I). After controlling for age at diagnosis, age at treatment, history of polycystic ovarian syndrome, and history of combined oral contraceptive or topical retinoid use, the hazard ratio for treatment discontinuation was 0.74 (95% confidence interval 0.71-0.77) for spironolactone compared with oral tetracycline-class antibiotics (Table I, Fig 1). Similar findings were observed in sensitivity analyses including patients who received treatment ≥6 months.

These findings suggest that spironolactone might have superior drug usage survival compared with oral antibiotics for the treatment of female patients with acne. Prior studies have suggested that spironolactone might have similar effectiveness as oral antibiotics for acne and can decrease the duration of therapy with antibiotics in this patient population.[3,4] Considering that female patients often have persistent acne into adulthood and concerns regarding antibiotic overuse among acne patients, it is possible that using spironolactone as a first-line agent before oral antibiotics could improve outcomes for female patients with acne.[5]

This study has several limitations given its retrospective, observational design. It is important to recognize that spironolactone and oral antibiotics can be prescribed to different patient populations; however, similar findings are observed when stratified by age and after controlling for potential modifying factors, such as history of polycystic ovarian syndrome and concomitant medication use. Guidelines recommend limiting the duration of treatment with oral antibiotics to 3-6 months; thus, patients receiving oral antibiotics might have

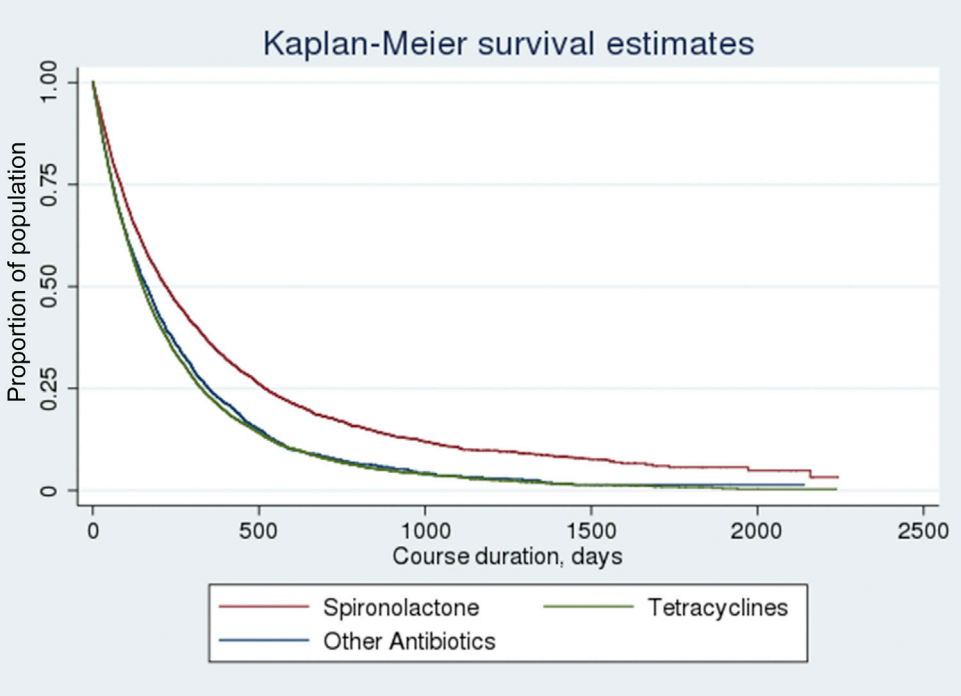

Fig 1. Kaplan-Meier survival curve for spironolactone versus oral antibiotics. Time zero was defined as the time point at which the patient had been stable on therapy for 1 year. Other antibiotics includes azithromycin, amoxicillin, trimethoprim-sulfamethoxazole, and cephalexin.

discontinued therapy because of these recommendations. However, by limiting the analysis to patients who had already been on therapy for ≥12 months (and hence not being treated in accordance with guidelines), this risk of bias is reduced. Although it is not possible to determine whether medication discontinuation occurred due to lack of efficacy, cost, side effects, resolution of acne, or other factors, the extended drug usage survival of spironolactone suggests that in routine clinical practice, spironolactone might have good long-term effectiveness and tolerability. Future prospective studies are needed to identify the optimal treatment approaches for female patients with moderate-to-severe acne.

John S. Barbieri, MD, MBA,[a] Juliana K. Choi, MD, PhD,[a,b] William D. James, MD,[a] and David J. Margolis, MD, PhD[a,c]

From the Department of Dermatology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania[a]; Department of Veteran Affairs, Philadelphia, Pennsylvania[b]; and Department of Biostatistics and Epidemiology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania[c]

Funding sources: Supported in part through the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS 1P30AR069589-01). Dr Barbieri is supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health under award number T32-AR-007465 and receives partial salary support through a Pfizer Fellowship in Dermatology Patient-Oriented Research grant to the Trustees of the University of Pennsylvania.

Conflicts of interest: None disclosed.

Disclaimer: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Reprints not available from the authors.

Correspondence to: John S. Barbieri, MD, MBA, 2 Maloney, 3600 Spruce St, Philadelphia, PA 19104

E-mail: john.barbieri@uphs.upenn.edu

REFERENCES

1. Collier CN, Harper JC, Cafardi JA, et al. The prevalence of acne in adults 20 years and older. *J Am Acad Dermatol*. 2008;58(1):56-59.

2. Barbieri JS, Bhate K, Hartnett KP, Fleming-Dutra KE, Margolis DJ. Trends in oral antibiotic prescription in dermatology, 2008 to 2016. *JAMA Dermatol*. 2019.
3. Barbieri JS, Choi JK, Mitra N, Margolis DJ. Frequency of treatment switching for spironolactone compared to oral tetracycline-class antibiotics for women with acne: a retrospective cohort study 2010-2016. *J Drugs Dermatol*. 2018;17(6):632-638.
4. Park JH, Bienenfeld A, Orlow SJ, Nagler AR. The use of hormonal antiandrogen therapy in female patients with acne: a 10-year retrospective study. *Am J Clin Dermatol*. 2018;19(3):449-455.
5. Barbieri JS, Spaccarelli N, Margolis DJ, James WD. Approaches to limit systemic antibiotic use in acne: systemic alternatives, emerging topical therapies, dietary modification, and laser and light-based treatments. *J Am Acad Dermatol*. 2019;80(2):538-549.

https://doi.org/10.1016/j.jaad.2019.03.036

Adult acne in women is not associated with a specific type of *Cutibacterium acnes*

To the Editor: Acne vulgaris in adult women is a well-known entity that may be distinguished from teenage acne. However, *Cutibacterium acnes* (*C acnes*), which is formerly named *Propionibacterium acnes*, has never been characterized in adult women with acne. The aim of this study was to compare the characteristics of *C acnes* (including phylotype, clonal complex, single-locus sequence typing (SLST) scheme, and resistance profile) between 2 groups with acne: adult women (defined as women aged 20 years or older) and adolescents/teenagers (individuals aged 11-18 years). Women older than 20 years were included to achieve adequate power.

In this prospective single-center study conducted over a 4-year period (2014-2017), the skin samples taken from patients with acne clinically confirmed by expert clinicians (M.S.J. or B.D.) and collected for *C acnes* bacteriologic analysis were selected. The study was approved by our local ethics committee, and all patients signed an informed consent to participate in the study. One sample per patient was taken from an inflammatory lesion with a cotton swab. All isolates were identified by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry as previously described.[1] In vitro susceptibility was tested by using the disk diffusion method as previously reported. Phylotype was determined according to the method recently developed by Barnard et al.[2] SLST was performed on all isolates as described by Scholz et al.[3] Macrolide and tetracycline resistance were investigated as previously described. Wilcoxon and Fisher exact tests were used to compare both groups. Statistical significance was set at a P value less than .05.

A total of 100 bacteriologic samples were collected. After diagnoses other than acne (n = 18 samples) had been ruled out, 51 samples from adult women were compared with 31 samples from teenagers. Demographics and clinical data are summarized in Table I. The comparison of *C acnes* phylotypes and clonal complexes is detailed in Table II. There was no significant difference in the distribution of *C acnes* phylotypes, clonal complexes, or SLST (details not shown) between the groups (P = .36, .43, and .12 respectively). The results were unchanged (ie, no difference between the 2 groups) when the comparison was restricted to female teenagers versus adult women. Likewise, there was no difference between adult women and teenagers when we included only the subpopulation of women older than age 25 years (n = 28), corresponding to the definition of adult acne in women in the literature. Most *C acnes* strains identified in this study were fully susceptible: 70% in the adult women group and 61% in the teenager group, with no statistically significant difference (P = .59). There was no significant difference in the proportion of macrolide-, tetracycline-, and macrolide- and tetracycline-resistant strains between the 2 groups.

Table I. Demographic and clinical data of the 2 groups (adult women vs adolescents/teenagers)

Characteristics	Adult women (n = 51)	Adolescents/teenagers (n = 31)	*P* value*
Sex repartition, female/male, n	51/0	18/13	
Median age, y (range)	29.7 (20-50)	16.1 (11-18)	
Median GEA score	2.1	2.9	.007
Acne subtype persistent/late-onset, n	43/7		
Cosmetic use, n (%)	30 (59)	15 (48)	.37
Smoking, n (%)	11 (22)	6 (19)	1
Previous systemic treatments			
Tetracyclines, n (%)	32 (63)	24 (77)	.22
Isotretinoin, n (%)	19 (37)	13 (42)	.82
Previous topical antibiotic use, n (%)	19 (37)	7 (23)	.22

GEA, Global Evaluation Assessment.
**P* value less than .05 is considered significant.