Irritable Bowel Syndrome Risk in Acne Patients: Implications for Dermatologic Care

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PRACTICE **POINTS**

- Clinicians should consider monitoring for early signs of irritable bowel syndrome (IBS) in adult patients with acne to facilitate prompt diagnosis and intervention.
- Clinicians should remain judicious when prescribing antibiotics for acne management to minimize potential disruptions to the gut microbiota and the risk for IBS.
- Isotretinoin may serve as a safer alternative to antibiotics in patients with acne, particularly those with gastrointestinal concerns.

To the Editor:

Acne vulgaris and irritable bowel syndrome (IBS) are both associated with microbial dysbiosis and chronic inflammation.[1-3] While the prevalence of IBS among patients with acne has been examined previously,[4,5] there has been limited focus on the risk for new-onset IBS following acne diagnosis. Current evidence suggests isotretinoin may be associated with a lower risk for IBS compared to oral antibiotics[6]; however, evidence supporting this association is limited outside these cohorts, highlighting the need for further investigation. In this large-scale study, we sought to investigate the incidence of new-onset IBS among patients with acne compared with healthy controls as well as to evaluate whether oral acne treatments (ie, oral antibiotics or isotretinoin) are associated with new-onset IBS in this population.

A retrospective cohort study was conducted using data from the US Collaborative Network in TriNetX from October 2014 to October 2024. Patients were identified using *International Classification of Diseases, Tenth Revision, Clinical Modification* codes, *Current Procedural Terminology* codes, Anatomical Therapeutic Chemical Classification System codes, and RxNorm codes (Table 1). These codes were selected based on prior literature review, clinical relevance, and their ability to capture diagnoses of acne and IBS as well as relevant exclusion criteria. Patients were considered eligible if they were between the ages of 18 and 90 years. Individuals with a history of IBS, inflammatory bowel disease, infectious gastroenteritis, or celiac disease were excluded from our analysis.

To examine potential associations between acne and IBS, 2 primary cohorts were established: patients with acne who were managed without systemic medications and healthy controls (ie, patients with no history of acne) who had no exposure to systemic acne treatments (Figure). Further, to assess the relationship between oral acne treatments (macrolides, tetracyclines, isotretinoin) and IBS, additional cohorts were created for each therapy and were compared to a cohort of patients with acne who were managed without systemic medications. To control for potential concomitant treatments, patients who had received any systemic treatment other than the specific therapy for their treatment cohort were excluded from our analysis.

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The eTable is available in the Appendix online at www.mdedge.com/cutis.

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TABLE 1. Codes Used to Source Data From the US Collaborative Network in TriNetX

Code	Description
ICD-10-CM	
L70.0	Acne vulgaris
K58	Irritable bowel syndrome
K50-K52	Noninfective enteritis and colitis
K90.0	Celiac disease
E66	Overweight and obesity
F41.1	Generalized anxiety disorder
F17	Nicotine dependence
F33	Major depressive disorder, recurrent
E11	Type 2 diabetes mellitus
F10	Alcohol-related disorders
A09	Infectious gastroenteritis and colitis, unspecified
Z00.00	Encounter for general adult medical examination without abnormal findings
CPT	
99213	Office or other outpatient visit for the evaluation and management of an established patient, which requires a medically appropriate history and/or examination and low level of medical decision-making; when using time for code selection, 20-29 min of total time is spent on the date of the encounter
99212	Office or other outpatient visit for the evaluation and management of an established patient, which requires a medically appropriate history and/or examination and straightforward medical decision-making; when using time for code selection, 10-19 min of total time is spent on the date of the encounter
RxNorm	
6064	Isotretinoin
ATC	
J01FA	Macrolides
J01A	Tetracyclines

Abbreviations: ATC, Anatomical Therapeutic Chemical Classification System; *CPT*, *Current Procedural Terminology*; *ICD-10-CM*, *International Classification of Diseases, Tenth Revision, Clinical Modification*.

To account for potential confounders, all cohorts were 1:1 propensity score matched by demographics, tobacco and alcohol use, type 2 diabetes, obesity, anxiety, and depression (eTable). Each cohort was followed for 2 years after their index of event: the date of acne diagnosis for the acne cohort, the date of systemic treatment initiation for the treatment cohorts, and the date of the general adult encounter without abnormal findings for the control cohort. The primary outcome was the incidence of IBS, assessed by odds ratio (OR) and 95% CIs.

We identified 375,944 patients with acne managed without systemic treatment and 3,148,443 healthy controls who met study criteria. After the 1:1 propensity score match, each cohort included 49,690 patients (eTable). In the 2-year period after acne diagnosis, patients were more likely to develop IBS compared with controls (1421 vs 1285 [OR, 1.10; 95% CI, 1.02-1.19]) (Table 2). Patients with acne who were treated with tetracyclines (n=208,971) were 30% more likely to develop IBS than those managed without systemic medications

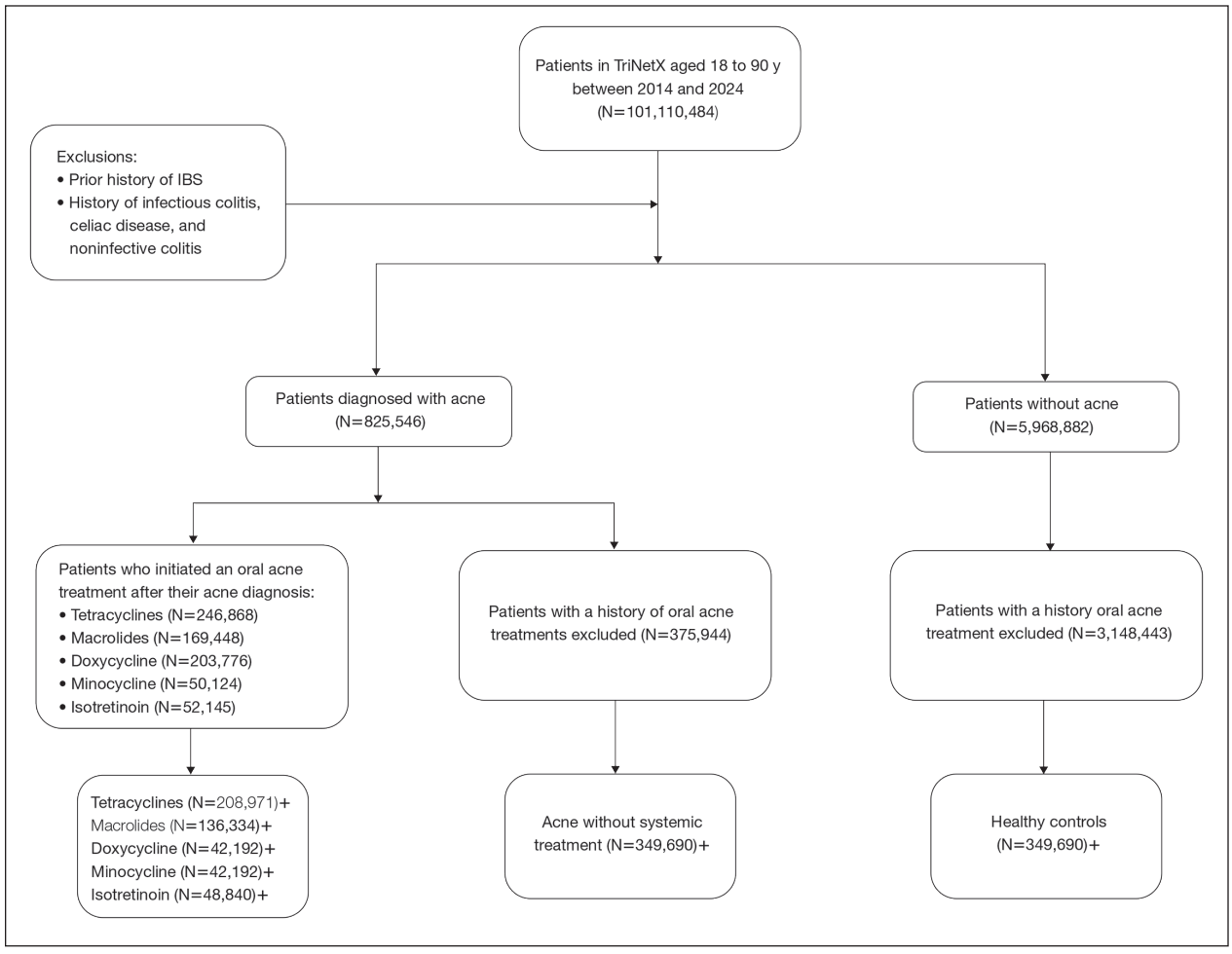

FIGURE. Flowchart of cohort construction in TriNetX followed by propensity-score matching (+). Cohorts were matched for demographics, overweight and obesity status, tobacco and alcohol use, generalized anxiety disorder, major depressive disorder and type 2 diabetes mellitus.

(1114 vs 856 [OR, 1.30; 95% CI, 1.19-1.42]). Within the tetracycline cohort, doxycycline-treated patients were 25% more likely to develop IBS compared with those treated with minocycline (213 vs 170 [OR, 1.25; 95% CI, 1.02-1.53]). Similarly, the use of macrolides (n=136,334) for acne treatment was significantly associated with an increased risk for IBS (1023 vs 595 [OR, 1.73; 95% CI, 1.57-1.92; $P<.0001$]) compared with controls. No statistically significant association was observed between isotretinoin and the incidence of IBS (Table 2).

In this large-scale cohort study, acne was associated with an increased likelihood of developing IBS within 2 years of an acne diagnosis compared with healthy controls. While a prior study also identified this association, it had a broader follow-up window ranging from 8 to 10 years.[2] In contrast, our analysis specifically quantified the risk within the first 2 years of diagnosis. This distinction suggested potential for earlier IBS onset in patients with acne than has previously been recognized and may serve as an early clinical indicator for IBS risk in this population.

Our findings further suggested an association between oral tetracyclines and macrolides and an increased risk for IBS. This aligns with existing literature suggesting that oral antibiotic use can disrupt the gut microbiota and lead to potential gastrointestinal complications[7] and reinforces the importance of careful antibiotic stewardship in dermatologic practice.

Although isotretinoin initially was surrounded by substantial controversy regarding its potential impact on gut health—particularly in inflammatory bowel disease[8]—our results do not support an increased risk for IBS among patients with acne who use isotretinoin. These findings challenge previous concerns and align with research suggesting that isotretinoin could be a safer alternative to antibiotic use for eligible patients who have a history of gastrointestinal disorders.[6]

This study highlights an important but underrecognized link between acne and IBS risk, emphasizing the need for early monitoring of gastrointestinal symptoms and careful antibiotic stewardship in dermatologic practice. Gastroenterology consultation may be advisable for patients with acne who

TABLE 2. Incidence and Likelihood of Irritable Bowel Syndrome After 2 Years

Analysis	No. of patients in cohort	No. of patients with IBS (%)	Odds ratio (95% CI)
Overall			
Acne without systemic treatment	349,690	1421 (0.4)	1.10 (1.02-1.19)
Healthy controls	349,690	1285 (0.4)	
Tetracyclines			
Tetracyclines	208,971	1114 (0.5)	1.30 (1.19-1.42)
Acne without systemic treatment	208,971	856 (0.4)	
Macrolides			
Macrolides	136,334	1023 (0.8)	1.73 (1.57-1.92)
Acne without systemic treatment	136,334	595 (0.4)	
Doxycycline vs minocycline			
Doxycycline	42,192	213 (0.5)	1.25 (1.02-1.53)
Minocycline	42,192	170 (0.4)	
Isotretinoin			
Isotretinoin	46,840	157 (0.3)	0.98 (0.79-1.23)
Acne without systemic treatment	46,840	159 (0.3)	

Abbreviation: IBS, Irritable bowel syndrome.

have persistent gastrointestinal symptoms to facilitate a more integrated, patient-centered approach to care.

Limitations of this study include potential misclassification of *International Classification of Diseases, Tenth Revision, Clinical Modification* codes, selection bias, and residual confounding from unmeasured factors such as diet, lifestyle, disease severity, and treatment adherence due to the reliance on electronic health record data.

Our findings build upon prior evidence linking acne and IBS and offer important insights into the timing of this association following acne diagnosis. Future research should explore biological mechanisms underlying the gut-skin axis and evaluate targeted interventions to mitigate IBS risk in patients with acne.

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eTABLE. Baseline Characteristics of Patients With Acne Managed Without Systemic Treatments Compared With Healthy Controls

	Before propensity score matching				After propensity score matching			
Characteristic	Acne (n=375,944)	Control (n=3,148,443)	*P* value	SD	Acne (n=349,690)	Control (n=349,690)	*P* value	SD
Mean (SD) age at index of event, y	27.9 (15)	48.8 (18.6)	<.001	1.238	28.8 (15.1)	29.8 (14.4)	<.001	0.065
Sex, n (%)								
Female	249,777 (66.4)	1,633,920 (51.9)	<.001	0.299	225,802 (64.6)	249,917 (71.4)	<.001	0.148
Male	105,145 (28)	1,297,560 (41.2)	<.001	0.281	103,231 (29.5)	78,313 (22.4)	<.001	0.163
Unknown	21,022 (5.6)	216,963 (6.9)	<.001	0.053	20,657 (5.9)	21,460 (6.1)	<.001	0.009
Race, n (%)								
White	212,664 (56.6)	2,074,624 (65.9)	<.001	0.192	203,109 (58.1)	189,050 (54.1)	<.001	0.081
Black	47,183 (12.6)	362,875 (11.5)	<.001	0.031	43,291 (12.4)	44,650 (12.8)	<.001	0.011
Asian	22,852 (6.1)	145,933 (4.6)	<.001	0.064	21,296 (6.1)	23,157 (6.6)	<.001	0.021
American Indian	1788 (0.5)	7568 (0.2)	<.001	0.039	1426 (0.4)	2011 (0.6)	<.001	0.023
Native Hawaiian	1710 (0.5)	6976 (0.2)	<.001	0.040	1398 (0.4)	1958 (0.6)	<.001	0.023
Other	24,086 (6.4)	112,086 (3.6)	<.001	0.131	20,794 (.6)	23,212 (6.6)	<.001	0.028
Unknown	65,661 (17.5)	438,381 (13.9)	<.001	0.097	58,376 (16.7)	65,652 (18.8)	<.001	0.054
Ethnicity, n (%)								
Hispanic	40,151 (10.7)	286,666 (9.1)	<.001	0.052	38,315 (11)	37,478 (10.7)	<.001	0.007
Non-Hispanic	251,119 (66.8)	2,331,534 (74.1)	<.001	0.159	237,476 (67.9)	224,060 (64.1)	<.001	0.081
Unknown	84,674 (22.5)	530,243 (16.8)	<.001	0.143	73,899 (21.1)	88,152 (25.2)	<.001	0.096
Comorbidity, n (%)								
Overweight/obesity	29,220 (7.8)	570,645 (18.1)	<.001	0.312	29,123 (8.3)	26,922 (7.7)	<.001	0.023
Generalized anxiety disorder	14,179 (3.8)	164,355 (5.2)	<.001	0.070	14,083 (4.0)	15,015 (4.3)	<.001	0.013
Major depressive disorder	9105 (2.4)	107,255 (3.4)	<.001	0.058	9007 (2.6)	11,143 (3.2)	<.001	0.036
Nicotine dependence	8900 (2.4)	261,949 (8.3)	<.001	0.267	8900 (2.5)	9510 (2.7)	<.001	0.010
Type 2 diabetes mellitus	7252 (1.9)	358,619 (11.4)	<.001	0.386	7237 (2.1)	7681 (2.2)	<.001	0.008
Alcohol-related disorders[a]	3475 (0.9)	84,265 (2.7)	<.001	0.132	3468 (1.0)	3761 (1.0)	<.001	0.008

[a]Encompasses alcohol abuse, alcohol dependence, and alcohol use (unspecified).