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## Trends in utilization of topical medications for treatment of rosacea in the United States (2005-2014): A cohort analysis

*To the Editor*: Rosacea is a common inflammatory skin disorder ( prevalence, 1.3%-2.1%).[1] In addition to gentle skin care and sun protection, metronidazole or azelaic acid are considered first-line topical therapy for papulopustular rosacea and topical $\alpha$-agonists are first-line topical therapy for erythrotelangiectatic rosacea.[2] The aim of this study was to evaluate real-world topical rosacea therapy utilization and costs.

We carried a retrospective cohort analysis of the MarketScan Commercial Claims and Encounters database (henceforth referred to as the database). The study was exempted by the Institutional Review Board at the Milton S. Hershey Medical Center. The validated database consists of reimbursed claims of approximately 50 million employees per year who are covered under private insurance plans across the United States. Uniquely, the database can track an individual across payers and geographic locations and it contains demographic data, dates, and costs for services, procedures, and pharmacy claims. Costs were adjusted for inflation and are reported in 2015 US dollars.

During the period from January 1, 2005, to December 31, 2014, a total of 72,173 adults were continuously enrolled with a diagnosis of rosacea, defined as 2 or more claims for treatment for *International Classification of Diseases, Ninth Revision*, code 695.3 by a dermatologist, primary care provider, and/or ophthalmologist over the course of 18 months (Table I).

Most patients (86% [n = 62,074]) were treated with topical agents; only 6% (n = 4463) were treated with oral therapy exclusively (a discussion of oral therapy in this cohort is presented elsewhere).[3] Single-agent topical therapy was used for 75.8% of patients (n = 47,035), whereas 24.2% (n = 15,039) received combination topical therapy. Metronidazole and azelaic acid comprised the most common combination regimen (Table II). More patients utilized branded topical medications than used

**Table I.** Topical treatments for rosacea 2005-2015: cohort characteristics

| Characteristic | Value |
|---|---|
| Overall cohort size, N | 72,173 |
| Median age, y (interquartile range) | 50, 13 |
| Female-to-male ratio, n (%) | 52,541:19,632 (72.80:27.20) |
| Ratio of those residing in a metropolitan area to those residing in a nonmetropolitan area, n (%) | 63,553:8620 (88.06:11.94) |
| Rosacea treatment, n (%) | |
| Enrollees with no treatment claims | 5636 (7.81) |
| Enrollees with only topical treatment claims | 27,684 (38.36) |
| Enrollees with only oral treatment claims | 4463 (6.18) |
| Enrollees with both oral and topical treatment claims | 34,390 (47.65) |
| Median time between visits, d (interquartile range) | 241; 476 |
| Enrollees by geographic region, n (%) | NE, 12,267 (17.00); NC, 18,043 (25.00); S, 31,239 (43.28); W, 9997 (13.85) |
| Type of provider, n, (%)* | |
| Dermatologist | 66,460 (92.08) |
| Ophthalmologist | 4927 (6.83) |
| Other provider | 786 (1.09) |

*NC*, North Central (Illinois, Indiana, Iowa, Kansas Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin); *NE*, Northeast [Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania Rhode Island, and Vermont), *S*, South (Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and West Virginia); *SD*, standard deviation, *W*, West (Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming).
*Provider associated with claim for initial visit for rosacea.

**Table II.** Comparison of generic and brand topical medications in the treatment of rosacea

| Generic | | | | | Branded | | | | | Difference between average annual cost of the branded drug and generic drug, $* |
|---|---|---|---|---|---|---|---|---|---|---|
| | Patients with claims | | Annual total cost per patient, $ | | | Patients with claims | | Annual total cost per patient, $ | | |
| Prescription topical | n | % | Mean | SD | Prescription topical | n | % | Mean | SD | |
| Any generic | 39,383 | 54.57 | 160.37 | 209.53 | Any branded | 50,334 | 69.51 | 308.02 | 314.71 | 147.65 |
| Metronidazole | 26,245 | 36.24 | 168.63 | 208.93 | MetroCream, MetroGel | 33,941 | 46.87 | 257.79 | 229.35 | 89.16 |
| Azelaic acid | 40 | 0.06 | 185.63 | 132.33 | Finacea, Azelex | 23,043 | 31.82 | 273.31 | 236.14 | 87.68 |
| Sodium sulfacetamide | 1065 | 1.47 | 167.56 | 191.39 | Sulfacet, Plexion, Rosula, Avar, Clenia, Ovace, Rosac, Klaron, Rosanil | 10,128 | 13.99 | 317.31 | 275.79 | 149.75 |
| Clindamycin | 7029 | 9.71 | 88.36 | 140.51 | Cleocin | 662 | 0.91 | 391.29 | 357.36 | 302.93 |
| Pimecrolimus | 25 | 0.03 | 272.06 | 194.16 | Elidel | 4021 | 5.55 | 303.44 | 377.10 | 31.38 |
| Brimonidine† | NA | 0.00 | NA | NA | Mirvaso | 2762 | 3.81 | 404.16 | 350.90 | NA |
| Tretinoin | 2019 | 2.79 | 114.43 | 121.09 | Retin A, Avita, Tretin-X, Ziana, Veltin | 136 | 0.19 | 242.74 | 166.63 | 128.31 |
| Tacrolimus | 15 | 0.02 | 365.40 | 306.72 | Protopic | 1875 | 2.59 | 336.26 | 527.05 | **−29.14** |
| Permethrin | 811 | 1.12 | 49.27 | 42.57 | Elimite, Acticin | 0 | 0.00 | NA | NA | |
| Adapalene | 148 | 0.20 | 301.87 | 218.98 | Differin, Epiduo | 413 | 0.57 | 264.25 | 228.83 | **−37.62** |
| Tazarotene† | NA | 0.00 | NA | NA | Tazarac | 449 | 0.62 | 405.76 | 457.44 | NA |
| Ivermectin† | NA | 0.00 | NA | NA | Soolantra | 10 | 0.01 | 264.52 | 15.89 | NA |

Manufacturers: Differin, Epiduo, MetroCream, MetroGel, Mirvaso, Rosanil, and Soolantra, Galderma, Fort Worth, TX; Finacea, Bayer, Whippany, NJ; Azelex, Elimite, Tazorac, Allergan, Inc, Irvine, CA; Sulfacet, Dermik Laboratories USA (discontinued); Rosula, PharmaDerm USA (discontinued); Avar, Ovace, and Plexion, Mission Pharmacal Company, San Antonio, TX; Clenia, Upsher-Smith Laboratories Inc USA (discontinued); Rosac, GlaxoSmithKline (discontinued); Elidel, Klaron, Retin A, and Ziana, Bausch Health Companies Inc, Laval, Canada; Cleocin, Pfizer, New York, NY; Avita and Acticin, Mylan Bertek Pharmaceuticals, Inc, Sugar Land, TX; Triax, Triax Pharmaceuticals, LLC, Cranford, NJ; Veltin, Almirall, LLC, Exton, PA; Protopic, LEO Laboratories Ltd, Dublin, Ireland; Tretin-X, Precision Dermatology, Inc, Cumberland, RI.

*NA*, Not applicable; *SD*, standard deviation.

*Positive numbers indicate that the generic has a lower cost, whereas negative numbers (highlighted with boldface) indicate that the generic medications have a higher cost.

†No generic was available during the study period.

generic versions (n = 50,334 versus n = 39,621, respectively). The mean annual costs of topical therapy per patient were $308.02 (standard deviation [SD], $314.71) and $160.37 (SD, $209.53) for branded and generic medications, respectively ($P < .0001$). The potential annual per-patient cost saving by switching from a branded medication to a generic was $147.65.

Our study is limited by its retrospective nature, lack of Medicare and Medicaid claims, and dependency on *International Classification of Diseases, Ninth Revision*, code for rosacea that has not been validated. However, validity is supported by the high proportion of patients with dermatologist care.

In summary, an important proportion of patients (24.2%) received combination topical therapy. These medications are thought to work by similar mechanisms (anti-inflammatory, antioxidant, and modulation of kallikrein related peptidase 5), and to our knowledge, they have not been studied together. Also, combination therapy is not discussed in most guidelines.

We defined the cost of a topical medication as the sum of insurance payments, patient copay, and deductible per medication over the period of a year. We found that the mean annual cost of topical therapy for branded medications per person was nearly twice the cost of generics, despite the rise in generic drug costs.[4] Thus, there is an opportunity to save health care costs, which amount to nearly $7.5 million annually for this cohort. Importantly, we analyzed the data from a health care system point of view, which provides more realistic overall cost analysis and is different from a patient point of view, in which, for example, coupons and other discounts reduce immediate out-of-pocket expense but increase societal cost.[5] Our analysis suggests that there is an opportunity to increase utilization of generic medications and that combination topical therapy is commonly used.

In addition, more research is needed to determine the most efficacious rosacea therapies. Topical therapy is common (used at a rate of 86% in this study) and may have lower adverse effects, yet topical agents can be more expensive than systemic medications.[6] This is pertinent, given that about 24% of patients received combination topical therapy. More cost-effectiveness studies for rosacea therapy could inform providers, patients, and future guidelines.

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## The associations of depression and coping methods on health-related quality of life for those with hidradenitis suppurativa

*To the Editor:* Hidradenitis suppurativa (HS) is a chronic inflammatory disease that can have negative effects on health-related quality of life (HRQOL).[1] A previous study showed that resilience moderates the association between depression and HRQOL.[2] Resilience is usually triggered by an adverse event