

**Fig 1.** Patients who received rituximab treatment showed a dramatic improvement in their nailfold capillaries over the first 6 months, and the changes in their nailfold capillary patterns completely resolved after 12 months of follow-up. Patients who received other immunosuppressive medications (prednisone, methotrexate, mycophenolate mofetil, IVIG) showed no changes in nailfold capillary patterns. IVIG, Intravenous immunoglobulin; 2 per. Mov. Avg (rituximab), curve of rituximab over time.

We identified 45 dermatomyositis patients. A review of history, capillaroscopy exam, medications, and timing was performed. We found that before initiation of therapy 10 patients (22%) had normal-appearing nailfold capillaries, and 35 patients (78%) had at least 1 remarkable change in their nailfold capillary pattern. Of those patients with nailfold capillary changes, all had them in multiple digits, and multiple types of capillary changes were seen. Of patients with capillary changes, 10 patients (29%) went on to receive rituximab treatment (2 infusions, 1 month apart), and 71% received  $\geq 1$  other immunosuppressive (prednisone, methotrexate, mycophenolate mofetil, intravenous immunoglobulin). Patients who did not receive rituximab treatment, but received other immunosuppressive treatment, showed no alterations in their nailfold capillary patterns on 6 months' follow-up or on 2-year follow-up, regardless of macroscopic clinical response (Fig 1). In contrast, 80% of patients who received rituximab treatment had normal-appearing nailfold capillaries on 6 months' follow-up and 100% at 2 years. Our data suggest that although inflammation might be suppressed by other immunosuppressants rituximab is unique in reversing remarkable nailfold capillaries.

Our data strongly suggest that rituximab targets microvasculature and restores the function of nailfold capillary in dermatomyositis; if rituximab is truly disease modifying, there might be a case for rituximab becoming the primary first-line agent for this disease. To help determine if rituximab is disease modifying and this skin marker also mirrors

recovery of microvascular damage in other organs, longitudinal studies examining if differences in long-term outcomes reflect these differences in outcome at the microvascular level should be performed.

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#### REFERENCES

1. Dalakas MC. Inflammatory muscle diseases. *N Engl J Med*. 2015; 373(4):393-394.
2. Schmeling H, Stephens S, Goia C, et al. Nailfold capillary density is importantly associated over time with muscle and skin disease activity in juvenile dermatomyositis. *Rheumatology (Oxford)*. 2011;50(5):885-893.
3. Barth Z, Schwartz T, Flatø B, et al. The association between nailfold capillary density and pulmonary and cardiac involvement in medium- to long-standing juvenile dermatomyositis. *Arthritis Care Res (Hoboken)*. 2018 [Epub ahead of print].

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#### Pharmacy costs of medications for the treatment of onychomycosis in the United States



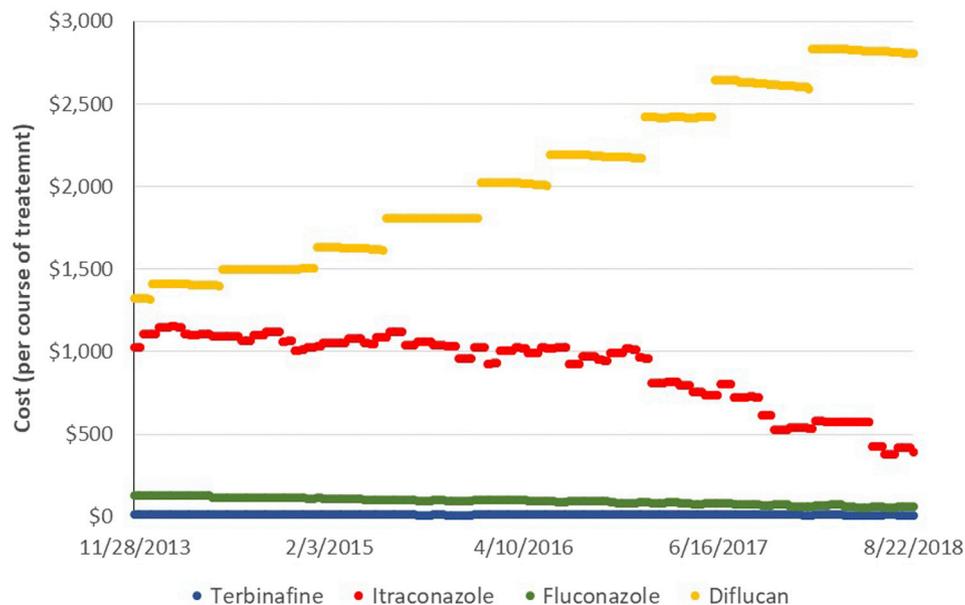
*To the Editor:* Onychomycosis affects approximately 5.5% of the world's population, causing significant physical and social impairment.<sup>1</sup> Studies on the economic burden of onychomycosis medications are dated,<sup>2,3</sup> and estimated costs based on manufacturer-reported retail prices may be inaccurate. The National Average Drug Acquisition Cost (NADAC) was developed to increase medication cost transparency and to more accurately represent the prices paid by pharmacies for medications, inclusive of manufacturer-to-pharmacy discounts. The NADAC is used by state Medicaid agencies to set reimbursement for ingredient costs of medications to more accurately reflect the spending burden of outpatient prescription medications.

**Table I.** Changes in the cost of topical and systemic medications for onychomycosis from November 28, 2013, to August 22, 2018

Medication type	November 28, 2013	June 22, 2016	August 22, 2018	Average annual change	Annual rate of change
<b>Topical</b>					
Ciclopirox 8% solution	\$4.15	\$3.97	\$2.35	−\$0.38	−11.3%
Kerydin 5% solution*		\$135.47	\$145.53	\$4.96	3.7%
Jublia 10% solution*		\$136.24	\$137.30	\$5.56	4.5%
<b>Systemic</b>					
Itraconazole	\$1027.68	\$1027.43	\$396.20	−\$133.39	−18.2%
Fluconazole	\$127.44	\$89.24	\$60.25	−\$14.19	−14.6%
Terbinafine	\$14.13	\$13.27	\$11.97	−\$0.46	−3.4%
Diflucan	\$1326.39	\$2195.46	\$2807.39	\$312.83	17.2%

A single course of systemic treatment of onychomycosis of the toenails consisted of (1) terbinafine (one 250-mg tablet daily for 12 weeks), (2) itraconazole (one 200-mg tablet daily for 12 weeks), and (3) fluconazole/Diflucan (one 150-mg tablet once per week for 12 months). Fluconazole (Diflucan) is prescribed until the toenail grows out, which takes 12 months on average.

\*Jublia (efinaconazole) (Valeant Pharmaceuticals, Bridgewater, NJ) and Kerydin were both approved for the treatment of onychomycosis in 2014.



**Fig 1.** Trends in the cost of systemic medications for a single course of treatment for onychomycosis of the toenails from November 28, 2013, to August 22, 2018. A single course of systemic treatment of onychomycosis of the toenails consisted of (1) terbinafine (one 250-mg tablet daily for 12 weeks), (2) itraconazole (one 200-mg tablet daily for 12 weeks), and (3) fluconazole/Diflucan (one 150-mg tablet once per week for 12 months).

NADAC data from the Medicaid Pharmacy Pricing database were analyzed to identify trends in the pharmacy costs of generic and brand name onychomycosis medications from November 28, 2013, to August 22, 2018. Costs of topical medications were calculated per milliliter of medication, whereas costs of systemic medications were calculated on the basis of a single treatment course per patient for toenail onychomycosis. Costs were adjusted for inflation, as measured by Consumer Price Index for All Urban Consumers to allow for comparison.

The per-milliliter cost of topical onychomycosis treatment in 2018 ranged from \$2.35 for ciclopirox 8% solution to \$145.53 for the brand name version of tavaborole 5% solution (Kerydin [Anacor Pharmaceuticals, Palo Alto, CA]) (Table I). The per patient cost of a single course of systemic treatment in 2018 ranged from \$12 for terbinafine to \$2807 for the brand name version of fluconazole (Diflucan [Pfizer, New York, NY]). The annual rate of change in inflation-adjusted cost for generic medications ranged from −18.2% for itraconazole to −3.4% for

terbinafine, and for brand name medications it ranged from 3.7% for Kerydin to 17.2% for Diflucan (Fig 1).

Overall, pharmacy costs of brand name topical and systemic medications are greater than pharmacy costs of generic alternatives for onychomycosis treatment and have increased substantially over the past 5 years. Conversely, the cost of generic treatments, all of which were being produced by 8 or more manufacturers, have dropped slightly over the past 5 years despite overall increases in drug spending over the same time period. These observed trends mirror the findings of previous analyses demonstrating that decreased manufacturer competition is associated with increased medication prices, and they will likely persist until expiration of the patents for these brand name medications.<sup>4</sup>

One limitation of our study is that NADAC is calculated only for medications covered by Medicaid and with sufficient cost data submitted by retail pharmacies. Thus, approved onychomycosis drugs, including brand name versions of oral terbinafine (Lamisil [Novartis Pharmaceuticals, East Hanover, NJ]), oral itraconazole (Sporonox [Janssen Pharmaceuticals, Titusville, NJ]), and Onmel [Merz Pharmaceuticals, Greensboro, NC]), and topical ciclopirox (Penlac [Aventis Pharmaceuticals, Berwyn, PA]) were not available for analysis. Additionally, our analysis does not account for rebates paid by manufacturers as part of the Medicaid Drug Rebate Program to offset drug expenditures.

Oral therapies are generally more effective than topicals in treating onychomycosis. Topical or oral therapies are indicated for mild-to-moderate disease. Only oral therapies are appropriate for patients with severe onychomycosis, as topical therapies are often ineffective.<sup>5</sup> Indiscriminant use of topicals for treating onychomycosis can be costly and can contribute significantly to the growing national prescription drug spending burden. Increased investigation into the efficacy and cost of these treatments is needed to deliver cost-effective care for patients with this common nail condition.

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#### REFERENCES

1. Lipner SR, Scher RK. Part I: onychomycosis: clinical overview and diagnosis. *J Am Acad Dermatol*. 2018. <https://doi.org/10.1016/j.jaad.2018.03.062> [Epub ahead of print]. Accessed August 23, 2018.
2. Stier DM, Henke C, Schein J, Doyle J, Schonfeld WH, Broering J. Cost of treatment for onychomycosis. Data from a 9-month observational study. *Pharmacoeconomics*. 2001;19(3):267-279.
3. Jansen R, Redekop WK, Rutten FF. Cost effectiveness of continuous terbinafine compared with intermittent itraconazole in the treatment of dermatophyte toenail onychomycosis: an analysis of based on results from the L.I.ON. study. Lamisil versus itraconazole in onychomycosis. *Pharmacoeconomics*. 2001;19(4):401-410.
4. Alpern JD, Zhang L, Stauffer WM, Kesselheim AS. Trends in pricing and generic competition within the oral antibiotic drug market in the United States. *Clin Infect Dis*. 2017;65(11):1848-1852.
5. Lipner SR, Scher RK. Part II: Onychomycosis: treatment and prevention of recurrence. *J Am Acad Dermatol*. 2018. <https://doi.org/10.1016/j.jaad.2018.05.1260> [Epub ahead of print]. Accessed August 23, 2018.

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#### Clinical differences in pediatric and adult *Malassezia* folliculitis: Retrospective analysis of 321 cases over 9 years



*To the Editor:* *Malassezia* folliculitis, a common disease in adolescents, is easily misdiagnosed as acne, rosacea, or bacterial folliculitis.<sup>1-3</sup> In this study, we aimed to investigate the clinical differences between pediatric (childhood plus adolescent) and adult *Malassezia* folliculitis and their treatment responses.

We retrospectively reviewed relevant cases using International Classification of Diseases (ICD) 9th Revision codes 704.8 (follicular disorder) and 117.9 (mycoses) or 111.0 (pityriasis versicolor) and ICD 10th Revision codes L73.9 (follicular disorder) and B48.8 (mycoses) or B36.0 (pityriasis versicolor) seen at our hospital during January 2008-December 2016. Only the patients given diagnoses after direct microscopic examination of specimens or biopsy were included. This study was approved by the institutional review board of MacKay Memorial Hospital (approval no. 16MMHIS156e).

A total of 321 patients with pediatric (<18 years; n = 79) and adult (n = 242) *Malassezia* folliculitis were included. Clinical information, including age, sex, season of diagnosis, symptoms, lesion locations,