Frequency of Primary Nonadherence to Acne Treatment

Kathryn L. Anderson, BS; Emily H. Dothard, BA; Karen E. Huang, MS; Steven R. Feldman, MD, PhD

IMPORTANCE Treatment outcomes depend on adherence to the prescribed regimen. Primary nonadherence refers to not obtaining and starting to take a prescribed medication. The frequency of primary nonadherence to acne treatment has not been well characterized. The complexity of multidrug acne regimens may add to this problem but, to our knowledge, has not been explored.

OBJECTIVES To estimate acne treatment primary nonadherence rates and to determine the relationship between primary nonadherence and the number of acne treatments prescribed.

DESIGN, SETTING, AND PARTICIPANTS A review of medical records from an outpatient university dermatology clinic identified patients with an acne diagnosis at a dermatology visit in the past 3 months who were prescribed 1, 2, or 3 or more treatments. Patients were excluded if they were not English speakers, were not prescribed treatment for their acne, or did not have an active telephone number. Using randomized lists, these patients were queried via telephone regarding which acne treatments they obtained. The results were analyzed using Fisher exact tests and multivariable logistic regression. For patients who were prescribed 1, 2, or 3 or more treatments, 47, 48, and 48 eligible patients were contacted, respectively.

MAIN OUTCOMES AND MEASURES The primary study outcomes were the overall rate of primary nonadherence and the rate for each treatment-number subgroup. Secondary outcomes included the association of sex, age, medication type, and electronic prescription status with primary nonadherence.

RESULTS Overall, 27% of patients did not fill all their prescriptions. Of patients who were given 1, 2, or 3 or more treatments, 9%, 40%, and 31%, respectively, did not fill all their prescriptions. There was no statistically significant difference by sex or age for primary nonadherence in any of the 3 treatment-number groups. Based on multivariable analyses, being prescribed a topical retinoid (odds ratio, 2.9; 95% CI, 1.0-8.0) or an over-the-counter product (odds ratio, 3.6; 95% CI, 1.1-12.3) was associated with primary nonadherence. Based on univariate analysis, there was less primary nonadherence with electronic prescriptions compared with paper prescriptions ($P < .001$).

CONCLUSIONS AND RELEVANCE Primary adherence to an acne treatment regimen is better when only 1 treatment is prescribed. Some patients may not complete acne treatment because 1 or more of their medications were never obtained.
Primary Nonadherence to Acne Treatment

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dherence is the extent to which a patient follows agreed-on treatment recommendations. Poor adherence can be characterized as primary nonadherence, or not obtaining and starting the treatment, and secondary nonadherence, or not using the treatment well or discontinuing the treatment early. Nonadherence is a pervasive problem in all fields of medicine, particularly when treating chronic conditions. Chronic conditions, including acne, have low secondary adherence rates because patients miss doses and discontinue treatments. There is less information on how often patients do not begin treatment.

In one study of patients with partial public health insurance coverage for yearly medication cost of more than $90, a total of 10% of prescriptions for acne were not redeemed. Many other studies have focused on the adherence frequency and increased secondary adherence in patients with acne, but the extent of primary nonadherence is not well characterized. Typically, multiple agents are used to address the multifactorial nature of acne; the resulting complexity of acne treatment reduces secondary adherence. As the number of treatments increases, primary adherence may also be affected, but the relationship between the number of treatments prescribed and the rate of primary nonadherence has not been defined.

The purpose of this study was to determine the frequency of primary nonadherence to acne treatments and to assess the effect of the number of recommended treatments, including prescriptions and over-the-counter products, on primary nonadherence. Secondary aims included determining the effect of the class of medication, patient sex, patient age, and electronic vs paper prescriptions on primary nonadherence.

Methods

The study was approved by the Wake Forest University School of Medicine Institutional Review Board. Oral patient consent was obtained. Inclusion criteria included patients diagnosed with acne (International Classification of Diseases, Ninth Revision, code 706.1) by a dermatologist in the Department of Dermatology at Wake Forest Baptist Medical Center in the past 3 months. Patients were excluded if they had not been prescribed a treatment at their acne-related visit, were not English speakers, or did not have an active telephone number. Patients may have been seen by 1 of 8 attending dermatologists, 9 resident dermatologists, or 2 physician assistants. Medication samples are neither stocked nor provided to patients in this clinic, and there was no compassionate provision of acne products by pharmaceutical companies.

Each patient’s age, sex, number of acne treatments, specific treatments for acne, and electronic prescribing status of each of those treatments were extracted from the electronic medical records. We characterized prescriptions into those that were electronically prescribed, those that were printed, and those that were recommended for over-the-counter purchase without a prescription. Patients were stratified into 3 treatment-number subgroups based on the number of treatments prescribed: 1, 2, or 3 or more treatments. We included over-the-counter products when counting the number of treatments “prescribed”; these were captured from the after visit summary each patient receives at the end of their clinic visit. A randomized list for calling patients (or a guardian if the patient was younger than 18 years) was generated for each of the 3 treatment-number subgroups. If the patient (or guardian) was unable to be contacted after 3 telephone call attempts, another patient from the same group was called from the randomized list until a sample size of approximately 50 patients from each group was reached. During the call, the patient (or guardian) was asked a series of questions (Box) to assess primary nonadherence.

Primary nonadherence was defined as not filling all of the prescriptions. Primary nonadherence rates for subgroups—treatment-number subgroup and treatment characteristic subgroups (including age, sex, over-the-counter medication, electronic prescription status, and medication class)—were compared using a Fisher exact test. Multivariable logistic regression was used to examine the primary effects of each prescription feature on primary nonadherence. Variables included in the model were the number of treatments prescribed (1, 2, or 3 or more); prescriptions for isotretinoin, topical retinoids, topical antibiotics, oral antibiotics, combination topical products, and over-the-counter products; and whether the patient was given a paper prescription (rather than only electronic prescriptions). We used SAS, version 9.3 (SAS Institute Inc), for data management and analysis.

Results

Of the patients who were prescribed 1 treatment, 97 eligible patients were called and 47 gave consent to participate; for 2 treatments, 113 eligible patients were called and 48 gave consent to participate; and for 3 or more treatments, 95 eligible patients were called and 48 gave consent to participate. Not all patients who were called gave consent because some patients did not answer the call after 3 attempts or declined to participate. A total of 40 males and 103 females gave consent to participate (mean [SD] age, 28 [14] years).

Thirty-eight (27%) patients did not fill all their prescriptions. Four patients (9%) who were given 1 treatment, 19 (40%) who were given 2 treatments, and 15 (31%) who were given 3 or more treatments did not fill all their prescriptions (global Fisher exact test, \( P = .001; 1 \text{ vs} 2 \text{ treatments, } P < .001; 1 \text{ vs } 3 \text{ or more treatments, } P = .009; \text{ and } 2 \text{ vs } 3 \text{ or more treatments, } P = .52\) (Table 1). There was no significant difference in primary adherence by sex (1 treatment, \( P = .62; 2 \text{ treatments, } P = .49; \text{ and } 3 \text{ or more treatments, } P = .70\) or age.

<table>
<thead>
<tr>
<th>Box. Questions Asked During Telephone Call to Assess Primary Adherence to the Acne Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. You were prescribed 1 or more treatments at your visit. Did you decide to fill any of those? If yes, which treatment(s) did you fill? If it would help, please grab the prescription and read the label.</td>
</tr>
<tr>
<td>2. Do you have any other treatment(s) for your acne, such as products that do not require a prescription? If yes, could you get that product and tell me what is written on the label?</td>
</tr>
<tr>
<td>3. Do you use any gentle cleansers? Antibacterial soaps? Benzoyl peroxide? Salicylic acid?</td>
</tr>
</tbody>
</table>
Primary nonadherence was greatest for topical retinoids (Table 2). The difference in primary adherence by treatment was not statistically significant between oral medications (including isotretinoin) and topical medications ($P = .06$), isotretinoin and other oral medications ($P = .16$), or topical retinoids and topical antibiotics ($P = .08$). Patients were more likely to fill electronic prescriptions compared with paper prescriptions ($P < .001$). They were also more likely to obtain a medication prescribed electronically compared with an over-the-counter treatment ($P = .003$) (Table 3).

In the multivariable logistic regression model, only prescriptions for topical retinoids (odds ratio, 2.9; $P = .04$) and over-the-counter products (odds ratio, 3.6; $P = .04$) significantly predicted patients not filling all their prescriptions (Table 4).

### Table 1. Primary Nonadherence Rates Based on Age and Number of Prescriptions

<table>
<thead>
<tr>
<th>No. of Treatments</th>
<th>No./Total No. (%)</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0/16</td>
<td>.30</td>
</tr>
<tr>
<td>2</td>
<td>5/13 (38)</td>
<td>.21</td>
</tr>
<tr>
<td>≥3</td>
<td>6/15 (40)</td>
<td>.10</td>
</tr>
<tr>
<td>Overall</td>
<td>11/44 (25)</td>
<td>.97</td>
</tr>
</tbody>
</table>

### Table 2. Primary Nonadherence Rates Specific to the Type of Medication

<table>
<thead>
<tr>
<th>Treatment Type</th>
<th>Total Prescribed, No.</th>
<th>Not Purchased, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topical medication, any type</td>
<td>109</td>
<td>14 (13)</td>
</tr>
<tr>
<td>Topical antibiotic</td>
<td>51</td>
<td>7 (14)</td>
</tr>
<tr>
<td>Topical retinoid</td>
<td>46</td>
<td>14 (30)</td>
</tr>
<tr>
<td>Oral medication, any type</td>
<td>85</td>
<td>4 (5)</td>
</tr>
<tr>
<td>Oral antibiotic</td>
<td>58</td>
<td>4 (7)</td>
</tr>
<tr>
<td>Isotretinoin</td>
<td>27</td>
<td>0</td>
</tr>
</tbody>
</table>

### Table 3. Primary Adherence Rates Based on Prescription Method

<table>
<thead>
<tr>
<th>Prescription Method</th>
<th>Total Prescribed, No.</th>
<th>Not Purchased, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electronic</td>
<td>130</td>
<td>8 (6)</td>
</tr>
<tr>
<td>Paper</td>
<td>15</td>
<td>5 (33)</td>
</tr>
<tr>
<td>Over-the-counter</td>
<td>53</td>
<td>11 (21)</td>
</tr>
</tbody>
</table>

### Table 4. Multivariable Logistic Regression Model Predicting Patient Nonadherence

<table>
<thead>
<tr>
<th>Treatments prescribed, No.</th>
<th>Odds Ratio (95% CI)</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1 [Reference]</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.9 (0.4-8.5)</td>
<td>.40</td>
</tr>
<tr>
<td>≥3</td>
<td>0.7 (0.1-5.4)</td>
<td>.74</td>
</tr>
</tbody>
</table>

### Medication type

- **Isotretinoin**: 0.2 (0.0-2.1); $P = .18$
- **Topical antibiotic**: 2.0 (0.7-5.7); $P = .20$
- **Topical retinoid**: 2.9 (1.0-8.0); $P = .04$
- **Combination product**: 0.8 (0.2-3.3); $P = .71$
- **Over-the-counter product**: 3.6 (1.1-12.3); $P = .04$
- **Oral antibiotic**: 1.0 (0.3-3.2); $P = .95$
- **Paper prescription**: 3.0 (0.8-11.1); $P = .10$

### Discussion

We found an overall primary nonadherence rate to acne treatments of 27%, greater than the 10% primary nonadherence rate previously reported.8 Our study was based on patient report rather than pharmacy data, we included over-the-counter treatments, and we defined primary nonadherence as a patient not obtaining their complete regimen rather than filling individual prescriptions. Treatment costs could also account for some of the difference between our findings and those of the previous study. Our study included patients with any type of insurance and medication coverage; the previous study was done in a public health insurance setting that provided at least 50% coverage for yearly medication expenses greater than $90.

Studies not related to acne have suggested that primary adherence rates vary little by sex, with a statistically nonsignificant trend for males to be more likely to fill their prescriptions.17,18 Our study found a similar pattern. Other studies have suggested that primary adherence rates differ by age, with young patients being less likely to obtain their medications; our study did not find significant differences by age.

Primary adherence was highest (100%) for isotretinoin. The lowest adherence was for topical retinoids. Although not statistically significant, topical medication prescriptions were filled less frequently than those for oral medications, even after excluding isotretinoin.

The use of electronic prescriptions increases primary adherence.9 However, when electronic prescriptions were compared directly with paper prescriptions for patients seen at an emergency department, there was no difference in the adherence.20 We found a trend for patients who received a paper prescription toward less likelihood of filling the prescription (odds ratio, 3.0; 95% CI, 0.8-11.1; $P = .10$). Over-the-counter products were associated with greater primary nonadherence (odds ratio, 3.6; 95% CI, 1.1-12.3; $P = .04$), consistent with previous studies.19

While our study was not designed to determine the reasons for primary nonadherence, many patients offered unprompted reasons for not filling their prescriptions. Common justifications included cost, forgetfulness, similar treatments already on hand, not agreeing with the prescribed regimen, and improvement of skin condition before obtaining the prescriptions. It may help to address these key issues when prescribing any medication.

This study is limited by self-reported response bias; patients may have overreported what prescriptions they actually filled, so our study likely provides a lower-bound estimate of primary nonadherence. In addition, some of the medications may have been prescribed with specific instructions not to fill unless experiencing a flare or if unable to purchase another medication owing to cost. The telephone calls for each group followed a random order; however, the sample size of females compared with males differed (103 and 40, respectively; 28% males); this reflects the ratio in the sample of patients who were called (220 females and 85 males; 28% males). This may be owing to women being...
more likely to seek treatment for acne. To better understand the cause of primary nonadherence, future studies may examine factors such as cost of treatment, patient dissatisfaction with the prescribed regimen, and forgetfulness on behalf of the patient.

Conclusions
A substantial proportion of patients with acne do not even fill their prescriptions; increasing the complexity of treatment by prescribing multiple treatments—particularly over-the-counter products and separate topical retinoid products—increases the likelihood that all the prescriptions will not be filled. Efforts to reduce the risk of primary nonadherence in patients with acne have not been tested but could include reminder systems and simplifying treatment regimens with the use of combination products that contain 2 or more active ingredients. Primary nonadherence can be considered when evaluating patients who have poor response to treatment.

REFERENCES
11. Del Rosso JJ. Study results of benzoyl peroxide 5%/clindamycin 1% topical gel, adapalene 0.1% gel, and use in combination for acne vulgaris. J Drugs Dermatol. 2007;6(6):616-622.