STUDY

Comparative Effectiveness of Commonly Used Systemic Treatments or Phototherapy for Moderate to Severe Plaque Psoriasis in the Clinical Practice Setting

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Objective: To compare the effectiveness of biologic systemic therapy, nonbiologic systemic therapy, and phototherapy for treatment of psoriasis.

Design: A cross-sectional design was used.

Setting: Ten outpatient dermatology sites across the United States participating in the Dermatology Clinical Effectiveness Research Network contributed to the study.

Participants: A total of 713 patients with plaque psoriasis receiving systemic monotherapy (ie, methotrexate sodium, adalimumab, etanercept, or ustekinumab) or narrowband UV-B phototherapy.

Main Outcome Measures: The primary outcome of the study was clear or almost clear skin on the Physician Global Assessment scale. Secondary outcomes were score on the Psoriasis Area and Severity Index, affected body surface area, and score on the Dermatology Life Quality Index.

Results: The proportion of patients with clear or almost clear ratings on the Physician Global Assessment scale differed among treatments: methotrexate (23.8%), adalimumab (47.7%), etanercept (34.2%), ustekinumab (36.1%), and narrowband UV-B (27.6%) ($P<.001$). In adjusted analyses, patients receiving adalimumab (relative response rate, 2.15; 95% CI, 1.60-2.90), etanercept (1.45; 1.06-1.97), and ustekinumab (1.57; 1.06-2.32) were more likely to have clear or almost clear skin vs patients receiving methotrexate. Patients receiving phototherapy showed no significant difference (1.35; 95% CI, 0.93-1.96) compared with those receiving methotrexate. No response difference was observed with respect to quality of life. Treatment doses were double the recommended doses in 36.1% of patients taking etanercept and 11.8% of those taking adalimumab;10.6% of patients undergoing phototherapy received the recommended treatment frequency.

Conclusions: The effectiveness of psoriasis therapies in clinical practice may be lower than that reported in previous trials. Although relative differences in objective response rates among therapies may exist, absolute differences are small and may not be clinically significant. Dosing of common therapies varied from trial recommendations. These results provide novel benchmarks emphasizing the critical importance of studying effectiveness in real-world practice.

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Psoriasis is a common, chronic inflammatory disease of the skin and joints mediated by types 1 and 17 helper T cells.[1,2] It can develop at any age, but onset most commonly occurs in young adulthood. The disease is believed to be incurable and long-term spontaneous remissions are rare. Psoriasis is associated with impairment in physical and emotional health even in patients with mild disease, and patients with psoriasis requiring systemic therapy or phototherapy (ie, those with moderate to severe disease) have an increased risk of major cardiovascular events and mortality independent of traditional risk factors.[3-9]

Moderate to severe psoriasis is typically defined as disease affecting more than 3% to 5% of body surface area (BSA) or requiring systemic treatment or phototherapy for successful management.[10,11] It is estimated that more than 1.4 million Americans and 25 million individuals worldwide have moderate to severe psoriasis.[12] Traditional oral systemic therapies, such as methotrexate sodium, acitretin, and cyclosporine, have been available for several decades, but their use can be limited by patient intolerance or organ-specific toxic effects with long-term

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use.[13] In the past decade, the treatment of moderate to severe psoriasis has undergone a revolution with the US Food and Drug Administration approval of 6 biologic drugs that target T cells and cytokines critical to the pathogenesis of psoriasis.[14] Although these new therapies have proved efficacious for psoriasis in short-term studies, they are associated with high costs, diminished efficacy with long-term treatment, and risks of rare but serious adverse effects that are still being recognized.[15] For example, efalizumab, which targets T cells, was voluntarily removed from the market because of a rare risk of progressive multifocal leukoencephalopathy identified in postmarketing spontaneous reports.[16]

Despite the growing repertoire of psoriasis treatments, insufficient data exist to determine which therapies are first-, second-, and third-line.[17] Only a few short-term comparative trials[18-20] of oral systemic and biologic agents for psoriasis have been conducted and, to our knowledge, there are no data available to evaluate the effectiveness of these therapies in real-world conditions, which is a critical and recognized data gap in comparative effectiveness research. Therefore, the purpose of this multicenter study was to describe and compare the effectiveness of commonly used systemic and phototherapy treatments for moderate to severe psoriasis in patients being evaluated as part of routine medical care.

METHODS

STUDY DESIGN AND PARTICIPANT PROTECTION

We conducted a cross-sectional study to determine the effectiveness of commonly used systemic therapy or phototherapy for moderate to severe psoriasis. The study was approved by the University of Pennsylvania and University of Utah institutional review boards, and informed consent was obtained from all patients. The study was conducted in accordance with the Declaration of Helsinki.

SETTING

Data were collected by 12 clinicians (10 dermatologists [J.M.G., K.C., G.G.K., R.E.K., J.D.W., B.R.S., M.B.S., B.A.B., S.M.S., and A.S.V.] and 2 physician assistants) who are members of the Dermatology Clinical Effectiveness Research Network (DCERN). Developed through funding received from the American Recovery and Reinvestment Act, DCERN includes 2 academic medical centers (University of Pennsylvania and University of Utah, each with a hospital-based site and a separate community-based site) and 6 private practices in Georgia, Pennsylvania, New York, and Colorado (see http://www.dermcern.org for details). Data were collected from February 10, 2010, through June 30, 2011. Patient data were collected prospectively at a single, regularly scheduled clinic appointment, and no follow-up data were collected.

PARTICIPANTS

To minimize bias, broad inclusion criteria were used for the enrollment of consecutive patients being seen by their dermatology provider in DCERN practices for a routine follow-up appointment. Participants were established patients who met at least 1 of the following criteria: were currently receiving a biologic, oral systemic, or phototherapy prescribed by the dermatologist or physician assistant for psoriasis; were candidates for systemic therapy as defined by a history of 5% or more BSA involvement as documented in the medical record; or were previously treated with a biologic, oral systemic, or phototherapy for psoriasis. To further reduce bias, patients new to the practice became eligible for study inclusion only at their next regularly scheduled visit subsequent to the initial appointment. Patients were excluded if they did not meet these criteria or were unable or unwilling to provide consent. Enrolled patients were compensated $10 for completing the study surveys and interviews. In the analyses presented herein, we included patients if they were currently receiving a single commonly used systemic therapy or phototherapy for a primary indication of plaque psoriasis (ie, >5% of participants). We excluded patients from this analysis who were not currently receiving systemic or phototherapy for psoriasis, who were receiving more than 1 systemic or phototherapy at the time of their visit, and whose primary indication was a variant of psoriasis other than plaque (eg, guttate, palmar plantar).

VARIABLES

Trained study coordinators collected data using standardized case report forms. Data were gathered via patient self-report with confirmation by the patient's dermatology clinic record and assessments by the clinician investigators. Detailed data were collected on exposure factors, including medical history, current and past psoriasis treatments, sociodemographic factors, psoriasis characteristics, height, weight, alcohol use history, and tobacco use history. Current psoriasis monotherapy was the main exposure, with the other variables serving as potential confounders or effect modifiers. The primary outcome variable was a widely used Physician Global Assessment (PGA) scale of psoriasis lesions (0, clear; 1, minimal; 2, mild; 3, moderate; 4, marked; and 5, severe; scored for erythema, induration, and scaling and then averaged), dichotomized as clear or almost clear disease (0-1) vs mild to severe disease (2-5).[21-23] The Psoriasis Area and Severity Index (PASI) and affected BSA were also evaluated as objective outcomes, and the Dermatology Life Quality Index (DLQI) and patient report of current prescription topical treatment use within the past week were assessed as patient-reported outcomes. The PASI was dichotomized such that a score of 2 or less was considered to indicate no or minimal disease (based on a receiver operating characteristic analysis comparing PASI scores with PGA scores). Presence of psoriasis on less than 3% of the BSA was considered to be mild disease based on National Psoriasis Foundation definitions, which have been extensively used in research,[12] and previously published[24] banding of DLQI scores was used to determine cutoff points upon which to dichotomize this end point.

STUDY SIZE

The study was descriptive; therefore, a sample size for specific analyses was not determined a priori. We estimated that DCERN would collect data on approximately 2000 patients, which would yield precise estimates, with the half-width of the 95% CI around rates for dichotomous variables being approximately 0.02.

STATISTICAL ANALYSIS

We first conducted descriptive statistical analysis of the patient population and evaluated univariate analyses using the Kruskal-Wallis test for grouped ordinal data; unpaired, 2-tailed *t* tests and Mann-Whitney tests for pairwise comparisons of continuous data; and χ^2 or Fisher exact test for dichotomous data. We then performed modified Poisson regression with robust

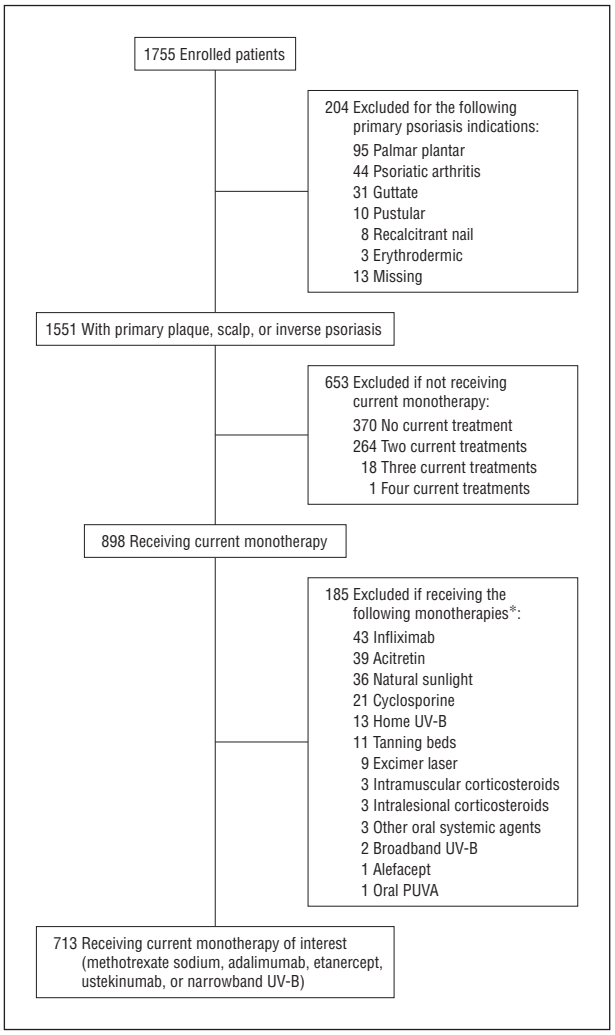

Figure 1. Flow diagram of patient inclusion. *Current monotherapies of interest were selected if received by more than 5% of patients receiving current monotherapy. PUVA indicates psoralen–UV-A.

error variance to determine which factors independently predicted optimal patient outcomes as defined in the "Variables" subsection of the "Methods" section.[25] Methotrexate was chosen as the base (reference) treatment, since it is often considered the standard with which novel therapies are compared. To build our model, we used a purposeful selection approach in which all covariates thought to be clinically important a priori as well as any covariates with significance at $P < .10$ in univariate analyses were included in the initial multivariable model.[26] Nonsignificant covariates were eliminated from the model if their removal did not change the risk ratio estimates of other covariates by more than 10%. Variables were considered for removal first if they were included in the model based on *P* value and then subsequently based on their perceived clinical importance. Model fit was assessed using goodness-of-fit tests based on deviance and Pearson statistics. The modified Poisson modeling approach was used to yield the clinically relevant statistic of relative response rates (ie, relative risk), which were then used to calculate the relative response difference and the number needed to treat. As a sensitivity analysis, we performed logistic regression and converted odds ratios to relative risks using published formulas.[27] We also performed a variety of sensitivity analyses, including varying the outcome definition by using PASI, BSA, DLQI, and more stringent cutoff points of PGA and examining different durations of treatment use.

Table 1. Baseline Patient and Psoriasis Characteristics in 713 Patients With Psoriasis

Characteristic	No. (%)[a]
Age, y	
Mean (SD)	48.6 (15.5)
Median (IQR)	49 (38-60)
Female sex	352 (49.4)
Practice setting of dermatologist	
Academic	409 (57.4)
Private	304 (42.6)
White race	606 (85.0)
BMI, median (IQR)	28.8 (25.3-33.0)
No. of comorbidities, median (IQR)[b]	2 (1-4)
Duration of psoriasis, median (IQR), y	19 (8-29)
No. of days of topical medication use in past week, median (IQR)	2 (0-6)
Psoriatic arthritis diagnosed by a physician	161 (22.6)
No. of previous biologic, oral systemic, or phototherapy treatments, median (IQR)	1 (0-2)
Previous psoriasis treatment[c]	
Biologic	266 (37.3)
Oral systemic	314 (44.0)
Phototherapy	295 (41.4)
None	184 (25.8)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); IQR, interquartile range.
[a] Percentages may not total 100 because of missing data, which did not exceed 1.5% for any particular characteristic.
[b] Including cardiovascular, lung, infection, gastrointestinal, renal, endocrine, musculoskeletal, psychiatric, neurologic, malignant, or autoimmune diseases.
[c] Percentages do not total 100 because some patients may have used more than one previous treatment.

RESULTS

We collected data on 1755 consecutively eligible patients with psoriasis (5% of patients declined to participate), which was within 12% of our projected sample size; the 713 patients who were receiving commonly used monotherapy with systemic agents or phototherapy for plaque psoriasis were included in this analysis (**Figure 1**). Missing data did not exceed 2.8% for any of the variables analyzed. Mean (SD) age of the patients was 48.6 (15.5) years; they had a median of 2 comorbidities (interquartile range [IQR], 1-4) in addition to psoriasis and were overweight, on average (**Table 1**). The study sample consisted of nearly equal numbers of men and women; patients of higher socioeconomic groups tended to be overrepresented. The patients' median age at psoriasis onset was 25 years, with median disease duration of 19 years; 40.0% of the patients had a family history of psoriasis and 22.6% had a physician diagnosis of psoriatic arthritis. Patients had used a median of 1 (IQR, 0-2) systemic therapy or phototherapy treatment before the current treatment being evaluated at their visit.

The most commonly used monotherapies and their corresponding median duration of use were methotrexate, 10.5 months (IQR, 4.0-24.0); adalimumab, 11.0 months (IQR, 3.0-16.8); etanercept, 12.0 months (IQR, 6.0-36.0); ustekinumab, 4.0 months (IQR, 2.0-6.0); and narrowband (NB) UV-B phototherapy, 1.8 months (IQR, 1.0-4.0) (**Table 2**). Furthermore, there were signifi-

Table 2. Dosage and Frequency of Treatment[a]

Characteristic	Methotrexate Sodium (n=174) [24.4%]	Adalimumab (n=152) [21.3%]	Etanercept (n=191) [26.8%]	Ustekinumab (n=73) [10.2%]	NB UV-B (n=123) [17.3%]	*P* Value[b]
Dosage (%)	<7.5 mg/wk (1.7)	40 mg every 2 wk (86.8)	50 mg every 2 wk (4.7)	45 mg/kg every 3 mo (56.2)	<3 Treatments in past 4 wk (5.7)	
	7.5-15 mg (62.6)	80 mg every 2 wk (0.7)	25 mg once/wk (3.1)	90 mg/kg every 3 mo (35.6)	3-5 Treatments in past 4 wk (23.6)	
	17.5-25 mg (27.6)	40 mg once/wk (11.2)	50 mg once/wk (49.7)	Other (5.5)	6-8 Treatments in past 4 wk (31.7)	
	≥30 mg (5.2)		25 mg twice/wk (3.1)		9-11 Treatments in past 4 wk (28.5)	
	Other (2.9)	Other (1.3)	50 mg twice/wk (36.1)		≥12 Treatments in past 4 wk (10.6)	
			Other (2.6)			
Use of topical prescription drug in past wk, median (IQR), d	2 (0-7)	2 (0-6)	1 (0-4)	0 (0-4)	4 (1-7)	<.001
Duration without interruption, median (IQR), mo	10.5 (4.0-24.0)	11.0 (3.0-16.8)	12.0 (6.0-36.0)	4.0 (2.0-6.0)	1.8 (1.0-4.0)	<.001

Abbreviations: IQR, interquartile range; NB, narrowband.
[a] Percentages may not total 100% because of missing data, which did not exceed 2.8% for any particular outcome.
[b] Kruskal-Wallis test.

Table 3. Current Monotherapy Use Among 713 Patients With Psoriasis With Physician- and Patient-Reported Outcomes

	Median (IQR)					
Outcome	Methotrexate Sodium (n=174) [24.4%]	Adalimumab (n=152) [21.3%]	Etanercept (n=191) [26.8%]	Ustekinumab (n=73) [10.2%]	NB UV-B (n=123) [17.3%]	*P* Value[a]
PGA	1.7 (1.3-2.0)	1.3 (1.0-1.7)	1.7 (1.0-2.0)	1.7 (1.0-2.1)	1.7 (1.0-2.0)	<.001
PASI	3.8 (1.8-6.6)	2.5 (1.2-4.8)	2.9 (1.8-4.9)	4.0 (1.0-7.9)	3.5 (2.0-5.5)	.02
BSA, %	3.0 (1.0-6.0)	2.0 (0.7-5.0)	2.0 (0.5-4.5)	3.0 (0.6-9.1)	3.3 (1.0-6.5)	.01
DLQI	3 (1-5)	2 (0-5)	2 (1-5)	3 (1-6)	3 (1-7)	.15

Abbreviations: BSA, body surface area; DLQI, Dermatology Life Quality Index; IQR, interquartile range; NB, narrowband; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment.
[a] Kruskal-Wallis test.

cant differences in duration of current treatment use, with patients receiving ustekinumab and NB UV-B having had shorter durations of use compared with patients receiving methotrexate, adalimumab, and etanercept ($P<.001$). Noteworthy findings regarding dosing of psoriasis therapies were observed: 36.1% of patients taking etanercept received 50 mg twice a week and 11.8% of those taking adalimumab received either 80 mg every 2 weeks or 40 mg weekly. After excluding patients with treatment duration of less than 3 months, 30.1% and 11.5% of patients taking etanercept or adalimumab received these doses, respectively. Moreover, 10.6% of patients undergoing NB UV-B therapy received 12 or more phototherapy treatments in the past 4 weeks.

In terms of objective response measurements, we observed statistically significant differences in median PGA ($P<.001$), PASI ($P=.02$), and BSA ($P=.01$) across these therapies; however, absolute differences were small and there was no statistically significant difference in DLQI ($P=.15$) (**Table 3**). There were significant differences in the frequency of topical prescription use within the past week, with patients receiving NB UV-B reporting the most frequent use ($P<.001$). The crude response rate (clear or almost clear on the PGA, as indicated by scores of ≤1) was highest for adalimumab (47.7%; 95% CI, 39.5%-56.0%), followed by ustekinumab (36.1%; 25.1%-48.3%), etanercept (34.2%; 27.5%-41.4%), NB UV-B (27.6%; 20.0%-36.4%), and methotrexate (23.8%; 17.7%-30.9%) (**Figure 2**A). Using the DLQI to assess outcome provides a different profile; the response rate, defined as no effect or a small effect (as indicated by scores of ≤5), was higher and more closely aggregated among the treatments, ranging from 68.3% (95% CI, 59.2%-76.5%) with NB UV-B to 78.0% (70.5%-84.3%) with adalimumab (Figure 2B).

Patients who were responders based on PGA were more likely to be female, to be of normal weight or underweight, to be treated in a private practice setting, and to have had longer duration of current treatment and were less likely to have used topical prescription therapy within the past week (data not shown). The unadjusted and adjusted relative rates of PGA responses are shown in **Table 4**; in comparison with patients taking methotrexate, those receiving adalimumab, etanercept, and ustekinumab had significantly higher response rates. Those using NB UV-B also had a higher, although not

statistically significant, response rate. Among therapies with statistically significant differences in response rates, the number needed to treat ranged from 3.6 to 9.4 (Table 4); for instance, 4 patients (rounded up from 3.6 as per convention) would need to be treated with adalimumab to achieve 1 additional treatment response over what would be expected if those same 4 patients were given methotrexate.

In sensitivity analyses, there was no evidence of response rate differences when using DLQI as the outcome (data not shown). When we evaluated outcomes of BSA or PASI, the differences in response rates were attenuated and occasionally lost statistical significance, particularly in the cases of etanercept and ustekinumab. When evaluating duration of current therapy use (≥3, 6, or 12 months), estimates for adalimumab remained stable and those for ustekinumab showed evidence of increasing efficacy with longer treatment; results for etanercept and NB UV-B were attenuated and lost statistical significance. The crude response rates for patients treated for 3 or more months were 26.4% (95% CI, 19.3-34.5) for methotrexate, 50.4% (41.2-59.6) for adalimumab, 36.4% (29.0-44.3) for etanercept, 46% (31.8-60.7) for ustekinumab, and 41.5% (26.3-57.9) for NB UV-B.

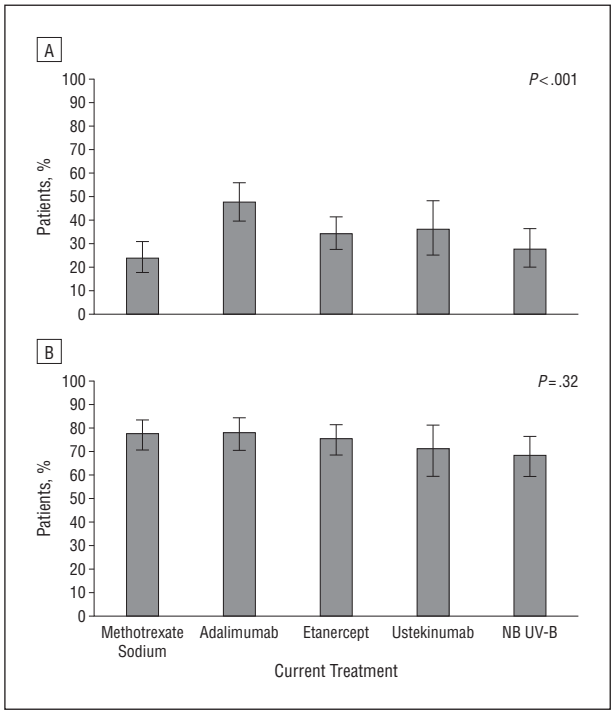

Figure 2. Response measures by current psoriasis monotherapy. A, Clear or minimal skin disease (Physician Global Assessment score, ≤1). B, No or small effect of psoriasis on quality of life (Dermatology Life Quality Index score, ≤5). NB indicates narrowband. Limit lines indicate 95% CI.

COMMENT

This study comprehensively detailed the effectiveness of commonly used systemic therapy and phototherapy treatments for moderate to severe psoriasis in the real-world clinical practice setting. Based on a single assessment of PGA, only 23.8% to 47.7% of patients with psoriasis currently receiving systemic therapy or phototherapy had achieved a clear or almost clear response to the treatment. Of special importance, the effectiveness of systemic psoriasis therapies was lower in the real-world practice setting compared with their reported efficacy in the randomized controlled trial setting. For example, the rate of being clear or almost clear of psoriasis in our study in contrast to that in the Comparative Study of Humira vs Methotrexate vs Placebo in Psoriasis Patients (CHAMPION) trial[28] (a randomized controlled trial of methotrexate vs adalimumab vs placebo) was 23.8% vs 30% for methotrexate and 47.7% vs 73% for adalimumab. Similarly, the PGA response rate in our study compared with that in the Active Comparator (CNTO 1275/Enbrel) Psoriasis Trial (ACCEPT)[29] (a randomized controlled trial of etanercept vs 2 different doses of ustekinumab) was 34.2% vs 49% for etanercept and 36.1% vs 65% (for the 45-mg arm) to 71% (for the 90-mg arm) for ustekinumab. Moreover, 36.1% of patients taking etanercept and 11.8% of those taking adalimumab received twice the maintenance dose recommended based on clinical trial data[30,31]; only 10.6% of patients receiving phototherapy were receiving the frequency of treatments (ie, ≥3 times per week) necessary to optimize response.[32] Patients who participate in trials may differ from those in the real-world setting in their health status, willingness to adhere to treatment regimens, and other factors that may result in discrepancies between idealized trial results and real-world outcomes, further emphasizing the need for effectiveness studies. In our multivariable model, all 3 biologics studied—adalimumab, etanercept, and ustekinumab—were more effective than the reference standard methotrexate based on PGA, even after comprehensively adjusting for numerous potential confounding factors. However, absolute differences in PGA were small, and the relative rate of response was attenuated, and in some cases no longer statistically significant, when evaluating other physician-reported outcomes, such as PASI and BSA. Although PGA has been recommended for community-based psoriasis research, there is no widely accepted criterion standard for defining a psoriasis treatment response at a static point in time, and our primary objective response analysis was sensitive to the type of end point evaluated.[33,34] Additionally, although to our knowledge we used the identical PGA as reported in ACCEPT and a nearly identical PGA as used in CHAMPION, other studies may use PGAs with different ranges or a dynamic approach; thus, caution is indicated in comparing studies that used different types of PGAs.

In patient-reported outcomes on the DLQI, 68.3% to 78.0% of patients reported no or only a mild effect of psoriasis on their health-related quality of life, indicating higher response to therapy on subjective, patient-reported measures than on objective, physician-reported outcomes.[24] The adjusted response rate for health-related quality of life, which has been suggested to be a better metric of psoriasis severity than objective measures (ie, BSA), was nearly identical across the therapies we evaluated. Similarly, the differences that we observed in PGA response rates were not mirrored by differences in patient self-report of topical prescription treatment use. In summary, these findings suggest that,

Table 4. Relative Rates of Physician Global Assessment Clearance and Risk Differences by Current Monotherapy in 704 Patients With Psoriasis

Current Treatment	Unadjusted RR (95% CI)	Adjusted RR (95% CI)[a]	Risk Difference (95% CI)[b]	NNT[c]
Methotrexate sodium	1 [Reference]	1 [Reference]		
Adalimumab	2.00 (1.46 to 2.74)	2.15 (1.60 to 2.90)	0.27 (0.14 to 0.45)	3.6
Etanercept	1.44 (1.03 to 2.00)	1.45 (1.06 to 1.97)	0.11 (0.01 to 0.23)	9.4
Ustekinumab	1.51 (1.01 to 2.28)	1.57 (1.06 to 2.32)	0.13 (0.01 to 0.31)	7.4
NB UV-B	1.16 (0.78 to 1.72)	1.35 (0.93 to 1.96)	0.08 (–0.02 to 0.23)	11.9

Abbreviations: NB, narrowband; NNT, number needed to treat; RR, relative rate.
[a] Adjusted for sex, race, ethnicity, body mass index, skin type, frequency of topical use, practice setting of dermatologist, marital status, income, and insurance.
[b] Difference between adjusted and baseline risk.
[c] Number of patients needed to treat with the particular treatment to gain 1 additional patient with Physician Global Assessment clearance relative to the response achieved with methotrexate.

although there are differences in treatment response rates based on objective measures, these differences are small and may not be of clinical significance.

Our study has important limitations. Despite our inclusion of a broad range of consecutively enrolled patients and a multivariable analysis that comprehensively adjusted for covariates, treatment assignment was not randomized and therefore we cannot exclude confounding and selection bias as potential sources of error. Additionally, patients receiving phototherapy tend to be purposefully evaluated at intermediate time points (ie, it is necessary to individually fine-tune dosing before achieving a clinical response), so assessment patterns for NB UV-B may have systematically differed from assessment patterns of systemic medications. Similarly, ustekinumab became available in the United States in September 2009, resulting in differing duration of use compared with more established therapies. Moreover, study assessments were not conducted by individuals blinded to treatment status, which could introduce information bias, although such error is unlikely to have systematically affected the results in any particular direction. Because this was not a longitudinal study, the phenomenon of clinical drift is likely present, and thus our results may overestimate the effectiveness of therapies in clinical practice; in other words, only patients with successful response to treatment continue the therapy. Similarly, given the cross-sectional nature of the study, we were not able to compare the relative safety of the therapies. Moreover, although we found no significant differences in health-related quality of life, it is possible that the DLQI was not sensitive enough to detect differences that may exist among patients receiving systemic therapy or phototherapy in the real-world practice setting despite its ability to distinguish between methotrexate and adalimumab effectiveness in the clinical trial setting.[35] Additionally, we focused on current monotherapy in this analysis and thus cannot speak to the comparative effectiveness of combination therapies. Finally, inclusion of more practices and patients from various regions of the United States might further improve the generalizability of the findings.

In conclusion, we conducted a large cross-sectional study evaluating the effectiveness of commonly used systemic therapy and phototherapy for moderate to severe psoriasis in real-world settings that provides important benchmarks to guide future research and policy. Our findings suggest that, although differences in objective responses may exist among these treatment options, absolute differences are small and may not be clinically significant. Furthermore, the absolute response rate to therapies for moderate to severe psoriasis may be lower in the real-world setting than what has been observed in randomized controlled trials. Longitudinal comparative effectiveness studies in real-world practice settings are necessary to confirm and extend our findings.

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Notable Notes

Dermatology for Poets and Bird-watchers

The following questions test your knowledge of dermatology as it relates to literature, the Bible, history, and culture. The final question is for bird-watchers. Answers are provided below.

Questions:

1. The word *pox* appears in a number of William Shakespeare's plays. To what illness does it refer?
2. Samson's hair was arranged into how many tresses (Judges 16:13)?
3. In Henry Wadsworth Longfellow's epic poem *The Song of Hiawatha*, what gesture of peace involves washing (Part I: "The Peace-Pipe")?
4. Karl Herxheimer (1861-1942), a German-Jewish dermatologist, helped to describe the Jarisch-Herxheimer reaction in syphilis therapy. In 1942, he was deported by the Nazis to a ghetto, where he perished. What was the ghetto's name?
5. General George Washington's face was scarred by smallpox. What method was used to prevent this disease in his troops?
6. Which king of Israel had a ruddy complexion (Samuel I 16:12)?
7. In Henrik Ibsen's play *Ghosts*, the character Oswald Alving suffers from congenital neurosyphilis. What French word does Ibsen use in the play for syphilis (Act 2)?
8. In Shakespeare's play *Henry IV* (Part I, Act 3, Scene 3), Falstaff tells Bardolph: "Thou art our admiral, thou bearest the lantern in the poop, but 'tis in the nose of thee." What is the diagnosis of Bardolph's nose malady?
9. In the original "Star Trek" television series episode "Let That Be Your Last Battlefield," the character Bele has a striking dermatologic feature. What is it?
10. What scar did Harry Potter have on his forehead?
11. Names of birds such as "pigeon chest" and "seagull murmur" have become part of medical terminology. What bird term describes a facial feature that many people get (2 words)?

Answers:

1. Syphilis.
2. Seven.
3. "Wash the war-paint from your faces, Wash the blood-stains from your fingers."
4. Terezin, located in the present-day Czech Republic.
5. Variolation.
6. David.
7. *Vermoulu*, which means worm-eaten.
8. Rosacea.
9. Bele's skin is half black and half white; the 2 halves are split exactly down the center of his body.
10. A scar in the shape of a lightning bolt from a failed murder attempt by Lord Voldemort.
11. Crow's feet.

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