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

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## Abstract

**Objective**—To compare the effectiveness of biologics, non-biologic systemic therapies, and phototherapy for psoriasis.

**Design**—Cross-sectional

**Setting**—Ten outpatient dermatology sites across the U.S.

**Participants**—713 plaque psoriasis patients receiving monotherapy: methotrexate, adalimumab, etanercept, ustekinumab, or narrowband ultraviolet B phototherapy.

**Main Outcome Measures**—Primary outcome: Clear or almost clear on the Physician Global Assessment. Secondary outcomes: Psoriasis Area and Severity Index, affected body surface area, and Dermatology Life Quality Index.

**Results**—The proportion of patients clear or almost clear on the Physician Global Assessment differed among treatments: methotrexate (23.8%), adalimumab (47.7%), etanercept (34.2%), ustekinumab (36.1%), NB-UVB (27.6%) ( $p < 0.001$ ). In adjusted analyses, patients on adalimumab (relative response rate 2.15, 95% CI 1.60–2.90), etanercept (1.45, 95% CI 1.06–1.97) and ustekinumab (1.57, 95% CI 1.06–2.32) were more likely to have clear or almost clear skin versus patients on methotrexate, while patients receiving phototherapy showed no significant difference (1.35, 95% CI 0.93–1.96) compared to methotrexate. No response difference was observed with respect to quality of life. 36.1% of etanercept and 11.8% of adalimumab patients received double the recommended doses, while 10.6% of phototherapy patients received the recommended treatment frequency.

**Conclusions**—The effectiveness of psoriasis therapies in clinical practice may be lower than previously reported in 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.

## Introduction

Psoriasis is a common, chronic Th1 and Th17 mediated inflammatory disease of the skin and joints<sup>1,2</sup>. It can occur at any age but onset most commonly occurs in young adulthood. The disease is felt 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 or phototherapy (i.e., those with moderate-to-severe disease) have an increased risk of major cardiovascular events and mortality independent of traditional risk factors<sup>3-9</sup>.

Moderate-to-severe psoriasis is typically defined as disease affecting 3–5% of body surface area (BSA) or requiring systemic treatment or phototherapy for successful management<sup>10,11</sup>. It is estimated that over 1.4 million Americans and 25 million individuals worldwide have moderate-to-severe psoriasis<sup>12</sup>. Traditional oral systemic therapies such as methotrexate, acitretin, and cyclosporine have been available for several decades but their use can be limited by patient intolerance or organ-specific toxicity with long-term use<sup>13</sup>. In the last decade, the treatment of moderate-to-severe psoriasis has undergone a revolution with the U.S. Food and Drug Administration (FDA) approval of six biologic drugs that target T-cells and cytokines critical to the pathogenesis of psoriasis<sup>14</sup>. Although these new therapies have been proven 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 side effects that are still being defined<sup>15</sup>. For example, efalizumab, which targets T-cells, was voluntarily removed from the market due to a rare risk of progressive multifocal leukoencephalopathy identified in post-marketing spontaneous reports<sup>16</sup>.

Despite the growing repertoire of psoriasis treatments, insufficient data exist to determine which therapies are first-, second-, and third-line<sup>17</sup>. Only a few short-term comparative trials 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 under real-world conditions, which is a critical and recognized data gap in comparative effectiveness research<sup>18-20</sup>. Therefore, the purpose of this multi-center 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 human subject protections

We conducted a cross-sectional study to determine the effectiveness of commonly used systemic or phototherapy treatments 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 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 two academic medical centers (University of Pennsylvania and University of Utah, each with a hospital-based site and a separate community-based site) and six private practices in Georgia, Pennsylvania, New York, and Colorado (see [www.dermcern.org](http://www.dermcern.org) for details). Data were collected from February 2010 through June 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. Study subjects were established patients who met at least one of the following criteria: currently receiving a biologic, oral systemic, or phototherapy prescribed by the dermatologist or PA for their psoriasis, were candidates for systemic therapy as defined by a history of  $\geq 5\%$  BSA involvement as documented in the medical record, or were previously treated with a biologic, oral systemic or phototherapy for their psoriasis. To further reduce bias, new patients 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 the above 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 here, we included patients if they were currently receiving a single commonly used (i.e.,  $>5\%$  of subjects) systemic therapy or phototherapy for a primary indication of plaque psoriasis. We excluded patients from this analysis who were not currently receiving systemic or phototherapy for their psoriasis, who were receiving more than one systemic or phototherapy at the time of their visit, and whose primary indication was another variant of psoriasis other than plaque (e.g., guttate, palmar/plantar, etc).

## 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, socio-demographic factors, psoriasis characteristics, height, weight, alcohol use, 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 Physician Global Assessment of psoriasis lesions (0=clear, 1=minimal, 2=mild, 3=moderate, 4=marked, 5=severe, individually scored for erythema, induration, and scaling and then averaged), dichotomized as clear or almost clear disease (0–1) versus mild to severe disease (2–5). which has been widely used in psoriasis clinical trials<sup>21–23</sup>. The Psoriasis Area and Severity Index (PASI) and 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 last 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 to PGA scores). A BSA of  $< 3\%$  was considered mild disease based on National Psoriasis Foundation definitions which have been extensively used in research, and previously published banding of DLQI scores were used to determine cut points upon which to dichotomize this endpoint<sup>12,24</sup>.

## Study size

The study is descriptive in nature and 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% confidence interval around rates for dichotomous variables being approximately 0.02.

## Statistical Analysis

We first conducted descriptive statistics of the patient population and evaluated univariate analyses using the Kruskal-Wallis test for grouped ordinal data, t-tests and Mann-Whitney

tests for pair-wise comparisons of continuous data, and chi-square or Fisher's exact test for dichotomous data. We then performed modified Poisson regression with robust error variance to determine which factors independently predicted optimal patient outcomes as defined above (see "Variables" section)<sup>25</sup>. Methotrexate was chosen as the base (reference) treatment as it is often considered the standard to 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 a p-value <0.10 in univariate analyses were included in the initial multivariable model<sup>26</sup>. Non-significant 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 (i.e., 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 (OR) to relative risks (RR) using previously published formulae<sup>27</sup>. We also performed a variety of sensitivity analyses, including varying the outcome definition by using PASI, BSA, DLQI, and more stringent cut points of PGA and examining different durations of treatment use.

## Results

We collected data on 1755 consecutively eligible psoriasis patients (5% of patients declined to participate), which was within 12% of our projected sample size; the 713 patients who were receiving commonly used mono- systemic or phototherapy for plaque psoriasis are included in this analysis (Figure 1). Missing data did not exceed 2.8% for any of the variables analyzed. Patients were 48.6 (standard deviation (SD) 16) years old on average, had a median (interquartile range (IQR) 1–4) of 2 co-morbidities in addition to psoriasis, and were overweight on average (Table 1). The study sample consisted of nearly equal numbers of males and females; patients of higher socioeconomic groups tended to be over-represented. The patients' median age at psoriasis onset was 25 years, with median disease duration of 19 years; forty percent of 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 or phototherapy treatment prior to the current therapy being evaluated at their visit.

The most commonly used monotherapies (and their corresponding median duration of use) were methotrexate 10.5 months (IQR 4–24), adalimumab 11.0 months (IQR 3–17), etanercept 12.0 months (IQR 6–36), ustekinumab 4.0 months (IQR 2.0–6.0), and narrowband ultraviolet B phototherapy (NB-UVB) 1.8 months (IQR 1.0–4.0) (Table 2). Further, there were differences in duration of current treatment use with patients on ustekinumab and NB-UVB having had shorter durations of use compared to methotrexate, adalimumab, and etanercept ( $p < 0.001$ ). Noteworthy findings regarding dosing of psoriasis therapies were observed: 36.1% of etanercept patients received 50mg twice a week and 11.8% of adalimumab patients received either 80mg every two weeks or 40mg weekly. After excluding patients with treatment duration of less than 3 months, 30.1% and 11.5% of patients on etanercept and adalimumab received these drug doses, respectively. Moreover, 10.6% of NB-UVB patients received twelve or more phototherapy treatments in the past 4 weeks.

In terms of objective response measurements, we observed statistically significant differences in median PGA ( $p < 0.001$ ), PASI ( $p = 0.02$ ), and BSA ( $p = 0.01$ ) across these therapies, however absolute differences were small and there was no statistically significant difference in DLQI ( $p = 0.15$ ). There were differences in the frequency of topical prescription

use within the last week with patients on NB-UVB reporting the most frequent usage ( $p < 0.001$ ). The crude response rate (“clear” or “almost clear” on PGA) was highest for adalimumab (47.7%, 95% confidence interval (CI) 39.5–56.0%), followed by ustekinumab (36.1%, 95% CI 25.1–48.3%), etanercept (34.2%, 95% CI 27.5–41.4%), NB-UVB (27.6%, 95% CI 20.0–36.4%), and methotrexate (23.8%, 95% CI 17.7–30.9%) (Figure 2a). Using DLQI to assess outcome provides a different profile; the response rate, defined as no or small effect (as indicated by scores of 5 or less), was higher and more closely aggregated among the treatments, ranging from 68.3% (95% CI 59.2–76.5%) with NB-UVB to 78.0% (95% CI 70.5–84.3%) with adalimumab (Figure 2b).

Patients who were responders based on PGA were more likely to be female, normal or underweight, treated in a private practice setting, and have had longer duration of current treatment use, and less likely to have used topical prescription therapy within the last week (data not shown). The unadjusted and adjusted relative rate of PGA responses are shown in Table 3; in comparison to patients on methotrexate, those receiving adalimumab, etanercept, and ustekinumab all had significantly higher response rates. Those on NB-UVB 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 4 to 10 (Table 3); for instance, 4 patients (rounded up from 3.6 as per convention) would need to be treated with adalimumab in order to achieve one additional treatment response over what would be expected if those same four patients were treated with methotrexate.

In sensitivity analyses, there was no evidence of any 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 (at least 3, 6, or 12 months), estimates for adalimumab remained stable and those for ustekinumab showed evidence of increasing efficacy with longer duration of treatment while results for etanercept and NB-UVB were attenuated and lost statistical significance. The crude response rates for patients treated for three or more months were 26.4% (95% CI 19.3–34.5) for methotrexate, 50.4% (95% CI 41.2–59.6) for adalimumab, 36.4% (95% CI 29.0–44.3) for etanercept, 46% (95% CI 31.8–60.7) for ustekinumab, and 41.5% (95% CI 26.3–57.9) for NB-UVB.

## Discussion

This study comprehensively details the effectiveness of commonly used systemic and phototherapy treatments for moderate-to-severe psoriasis in the real-world clinical practice setting. Based on a single assessment of PGA, only 24–48% of psoriasis patients currently receiving systemic or phototherapy treatment were clear or almost clear of their psoriasis. Of special importance, the effectiveness of systemic psoriasis therapies was lower in the real world practice setting compared to their reported efficacy in the randomized controlled trial (RCT) setting. For example, the rate of being clear or almost clear of psoriasis in our study in contrast to that in the CHAMPION trial (RCT of methotrexate vs. adalimumab vs. placebo) was 24% vs. 30%, respectively, for methotrexate and 48% vs. 73%, respectively, for adalimumab<sup>28</sup>. Similarly, the PGA response rate in our study compared to that in the ACCEPT trial (RCT of etanercept vs. ustekinumab) was 34% vs. 49%, respectively, for etanercept, and 36% vs. 65–71%, respectively, for ustekinumab<sup>29</sup>. Moreover, 36.1% of etanercept patients and 11.8% of adalimumab patients received twice the maintenance dose recommended based on clinical trial data,<sup>30,31</sup> while only 10.6% of patients on phototherapy were receiving the frequency of treatments (i.e. at least three times per week) necessary to optimize response.<sup>32</sup> Patients who participate in clinical trials may differ from “real world” patients in their health status, willingness to adhere to treatment regimens, and other factors

which may result in discrepancies between idealized clinical trial results and real world outcomes, thus further emphasizing the need for effectiveness studies in real-world clinical practice settings. In our multivariable model, the three biologics studied – adalimumab, etanercept, and ustekinumab – were all 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. Importantly, although PGA has been recommended for community-based psoriasis research, there is no widely accepted gold 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 endpoint evaluated<sup>33,34</sup>. 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 PGA's with different ranges or a dynamic approach (i.e. relying on the investigators memory of baseline severity in comparison to current severity) and thus caution may be indicated in comparing studies that used different types of PGA's.

In patient-reported outcomes on the DLQI, 68–78% of patients reported no or only 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<sup>24</sup>. Importantly, 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 (i.e. BSA), was nearly identical across the therapies we evaluated. Similarly, the differences 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 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 to consider. 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 fully exclude confounding and selection bias as potential sources of error. Additionally, phototherapy patients tend to be purposefully evaluated at intermediate time points (i.e., it is necessary to individually fine-tune dosing prior to achieving a clinical response) so assessment patterns for NB-UVB may have systematically differed from assessment patterns of systemic medications. Similarly, ustekinumab became available in the U.S. in September 2009 resulting in differing duration of use compared to 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. Importantly, since 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 remain on 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 differences in health-related quality of life, it is possible that the DLQI was not sensitive enough to detect differences which may exist among patients taking systemic or phototherapy treatments in the real world practice setting despite its ability to distinguish between methotrexate and adalimumab in the clinical trial setting<sup>35</sup>. Additionally, we have focused only 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 U.S. might further improve the generalizability of the findings.

In conclusion, we conducted a large cross-sectional study evaluating the effectiveness of commonly used systemic and phototherapy treatments 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 previously observed in controlled clinical trials. Future longitudinal comparative effectiveness studies in real world practice settings are necessary to confirm and extend our findings.

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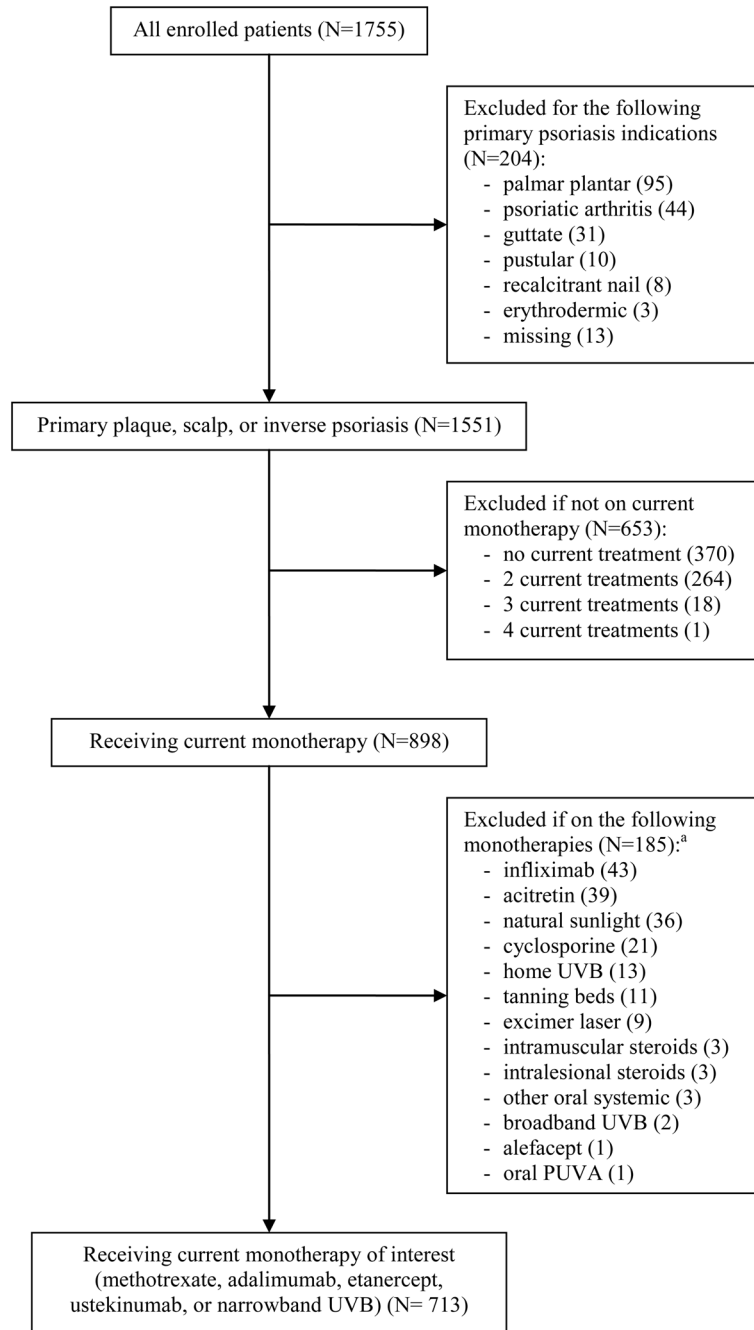
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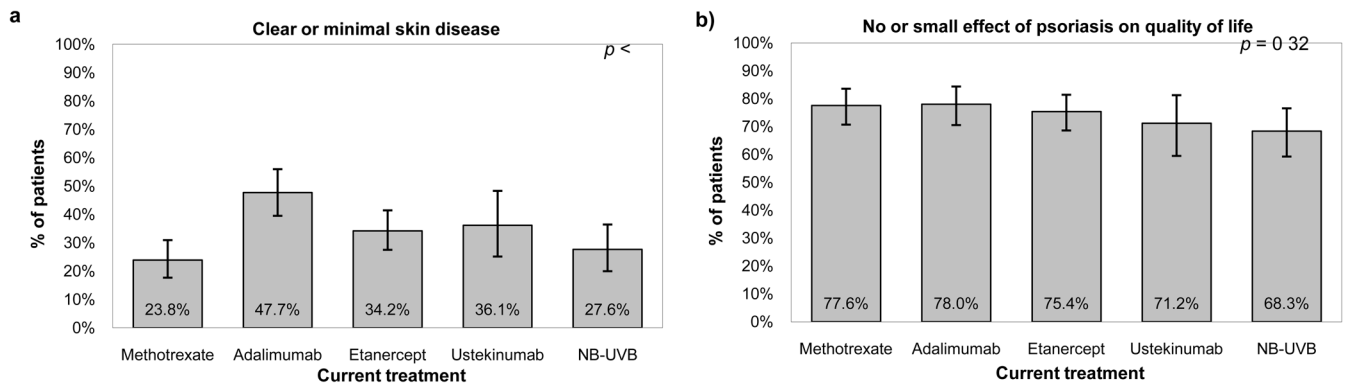


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**Figure 1.** Flow diagram of patient inclusion.  
<sup>a</sup>Current monotherapies of interest were selected if received by more than 5% of patients on current monotherapy.



**Figure 2.**

Figure 2a. PGA clearance (PGA = 1) by current psoriasis monotherapy. Figure 2b. No or small effect of psoriasis on quality of life (DLQI ≤ 5) by current psoriasis monotherapy. PGA, Physician Global Assessment; NB-UVB, Narrowband ultraviolet B; DLQI, Dermatology Life Quality Index

Note: Error bars indicate 95% confidence interval.

**Table 1**

## Baseline patient and psoriasis characteristics (N=713)

Characteristic	N (%)
Age, mean, median (SD, IQR), y	48.6, 49 (15.5, 38–60)
Female sex	352 (49.37)
Practice setting of dermatologist	
Academic	409 (57.36)
Private	304 (42.64)
White/Caucasian race	606 (84.99)
Body mass index (BMI) (kg/m <sup>2</sup> ), median (IQR)	28.8 (25.3, 33.0)
Total number of comorbidities, median (IQR) <sup>a</sup>	2 (1–4)
Duration of psoriasis, median (IQR), y	19 (8–29)
No. of days of topical medication use in last week, Median (IQR)	2 (0–6)
Psoriatic arthritis diagnosed by a physician	161 (22.58)
No. of previous biologic, oral systemic, or phototherapy treatments, median (IQR)	1 (0–2)
Previous type(s) of psoriasis treatment used <sup>b</sup>	
Biologic	266 (37.31)
Oral systemic	314 (44.04)
Phototherapy	295 (41.37)
None	184 (25.81)

IQR, interquartile range; SD, standard deviation

Note: Percentages may not total 100% due to missing data, which did not exceed 1.5% for any particular characteristic.

<sup>a</sup>Including cardiovascular, lung, infection, gastrointestinal, renal, endocrine, musculoskeletal, psychiatric, neurologic, malignant or autoimmune diseases

<sup>b</sup>Percentages do not total 100% because some patients may have used more than one previous treatment

**Table 2**  
Current monotherapy use with corresponding physician- and patient-reported outcomes (N=713)

	Current treatment					P value <sup>a</sup>
	Methotrexate N=174 (24.4%)	Adalimumab N=152 (21.3%)	Etanercept N=191 (26.8%)	Ustekinumab N=73 (10.2%)	Narrowband UVB N=123 (17.3%)	
PGA, median (IQR)	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)	<0.001
PASI, median (IQR)	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)	0.02
BSA, median (IQR)	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)	0.01
DLQI, median (IQR)	3 (1–5)	2 (0–5)	2 (1–5)	3 (1–6)	3 (1–7)	0.15
	Weekly dose:	Dose:	Dose:	Three-month dose:	No. of treatments in the past 4 weeks:	
	<7.5 mg	40mg q2w	50mg q2w	45mg/kg:	<3:	5.7%
	7.5–15mg	80mg q2w	25mg qw	90mg/kg:	3–5:	23.6%
	17.5–25mg	40mg qw	50mg qw		6–8:	31.7%
	30mg		25mg 2x/wk		9–11:	28.5%
	Other	Other	Other	Other	12:	10.6%
Prescription topical use in past week, median (IQR), days	2 (0–7)	2 (0–6)	1 (0–4)	0 (0–4)	4 (1–7)	<0.001
Duration of use without interruptions, median (IQR), months	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)	<0.001

BSA, body surface area (%); DLQI, Dermatology Life Quality Index; IQR, interquartile range; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment; UV, ultraviolet; qw, every two weeks; qw, weekly; 2x/wk, twice a week

Note: Percentages may not total 100% due to missing data, which did not exceed 2.8% for any particular outcome.

<sup>a</sup>Kruskal-Wallis test

**Table 3**

Relative rates of Physician Global Assessment clearance and risk differences by current monotherapy (N=704)

Current Treatment	Unadjusted RR (95% CI)	Adjusted RR <sup>a</sup> (95% CI)	Risk difference <sup>b</sup> (95% CI)	NNT <sup>c</sup>
Methotrexate (ref.)	1.00	1.00	-	-
Adalimumab	2.00 (1.46–2.74)	2.15 (1.60–2.90)	0.27 (0.14–0.45)	3.6
Etanercept	1.44 (1.03–2.00)	1.45 (1.06–1.97)	0.11 (0.01–0.23)	9.4
Ustekinumab	1.51 (1.01–2.28)	1.57 (1.06–2.32)	0.13 (0.01–0.31)	7.4
Narrowband UVB	1.16 (0.78–1.72)	1.35 (0.93–1.96)	0.08 (–0.02–0.23)	11.9

CI, confidence interval; NNT, number needed to treat; RR, relative rate; UVB, ultraviolet B

<sup>a</sup>Adjusted for sex, race, ethnicity, body mass index, skin type, frequency of topical use, practice setting of dermatologist, marital status, income, and insurance<sup>b</sup>Difference between adjusted and baseline risk<sup>c</sup>Number of patients needed to treat with the particular treatment to gain 1 additional patient with PGA clearance relative to the response achieved with methotrexate