Clinical Severity of Psoriasis in Last 20 Years of PUVA Study

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Objective: To assess the severity of psoriasis over time.

Design: We analyzed the results of structured dermatologic examinations administered over a 20-year period beginning 10 years after study enrollment.

Setting: The PUVA [psoralen–UV-A] Follow-up Study, which is a prospective cohort study.

Patients: The analyses were restricted to 815 patients (83.2% of those eligible) who underwent at least 2 of 4 possible examinations between 1985 and 2005.

Main Outcome Measure: A 4-point physician global assessment (PGA).

Results: The distribution of the PGA levels in the study group did not change significantly over time, except that in 2005 more patients had no psoriasis compared with patients who underwent examinations in the previous study years (9.6% vs < 5.1%, P < .03). The PGA level changed more than 1 level between examinations in only 14% of patients. Multistate Markov models estimated that patients had a likelihood of about 80% to remain at the same PGA level 1 year later. After 10 years, this likelihood varied between 19% and 53%, depending on the PGA level. Except for patients who were clear of disease at baseline, on average patients had about 1 year without psoriasis over 20 years. On average, individuals with moderate to severe disease remained at these levels for 11 or more years.

Conclusion: Three decades after a large and diverse group of patients sought a cure for their psoriasis, consistent control of their psoriasis often had not been achieved.

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Psoriasis is a common chronic skin condition that affects about 2% of the people in the United States.1 Although it is widely accepted that psoriasis waxes and wanes and varies substantially in severity among patients, the severity of psoriasis over a long period in a single person or group has not been well documented. In the 1960s and 1970s, several cross-sectional studies based on self-reports and without clearly defined outcomes estimated that 40% of patients with psoriasis had experienced a “complete remission” at least once in their lifetime.2,4 In clinical trials with a maximum of 16 weeks of follow-up, the mean relative change of the psoriasis area and severity index ranged from −20% to 50% among almost 500 placebo-treated patients.5 A recent study using the General Practice Research Database found that the prevalence of psoriasis, as reported as an independent diagnosis, declined in patients older than 70 years, suggesting that psoriasis may go into remission in elderly patients.6

The severity of psoriasis in a given individual at any point reflects both endogenous (underlying disease activity) and exogenous factors, including treatment. The short- to intermediate-term effects of therapies on disease severity have been examined in hundreds of clinical trials, but they are unlikely to be representative of the psoriasis severity over a long period among individuals who have this disease for an average of 40 or more years. Also, persons entering clinical trials are likely to have worse psoriasis than their usual state. Patients who are receiving active treatment are likely to have less disease, and there is a discrepancy between the efficacy of treatments observed in clinical trials and their effectiveness in daily life.

For editorial comment see page 1191

The PUVA [psoralen–UV-A] Follow-up Study is a long-term prospective cohort safety study, which has included

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study-sponsored structured dermatologic examinations, including an assessment of psoriasis severity using a physician global assessment (PGA) scale administered over nearly 30 years.\(^7\) In contrast to earlier examinations in the first study decade, by 1985 the timing of these examinations was not coordinated with therapeutic decisions and/or disease status. Therefore, the results of the last 4 examinations were used in this study. The primary objective of the present study was to analyze change of psoriasis severity among participants in a prospective cohort study over the last 2 decades.

## METHODS

### THE PUVA FOLLOW-UP STUDY

The PUVA Follow-up Study is a long-term safety and efficacy study that has prospectively studied 1380 patients with moderate to severe psoriasis who were first treated with PUVA in 1975 and 1976 at 16 university centers in the United States. In 1977, a total of 1380 of 1450 patients who participated in the original trial enrolled in the PUVA Follow-up Study. By 2005, 22 cycles of follow-up interviews and 9 cycles of physical examinations had been completed. The Declaration of Helsinki protocols were followed, and at time of enrollment all patients provided written informed consent. A more detailed description of this cohort study has been published previously.\(^8,9\)

### GLOBAL PSORIASIS SEVERITY

During 5 periods of the cohort study, from entry (1975-1976) to 1983, members were invited to come to a participating center for an in-person follow-up interview (which assessed treatment exposures and health-related outcomes since last interview) and a structured dermatologic examination, both of which were performed annually by a local investigator (Figure 1). These examinations were very likely to coincide with medical care. By 1985, a coordinating center conducted telephone interviews, with the exception of 1 center, which interviewed its own patients. At the time of the telephone interview in designated years, the interviewer helped to arrange the patient's clinical examination, which, when possible, was performed at a participating center or, alternatively, at the patient's current dermatology department and was performed relatively independently of clinical status or care. Also, by 1985, PUVA use had decreased substantially (Figure 1). In this report, the dermatologic examinations analyzed were performed during 4 periods (1985-1986, 1990-1991, 2000-2001, and 2003-2005). The study provided instructions and standardized forms to all examining physicians for scoring several clinical cutaneous signs. Each clinical examination included a 4-point assessment of PGA (clear, mild, moderate, and severe).

### STUDY POPULATION

Cohort members were included in this analysis if they had undergone 2 or more PGA assessments between 1985 and 2005. To be eligible, patients must have undergone a second examination after 1985; therefore, they had to have received follow-up at least until 1991. In 1991, a total of 979 patients were still participating in the study, 351 had died, 37 were unavailable for follow-up, and 23 had withdrawn from the study (Figure 1). A comparison of the 979 cohort members who were followed up in 1991 and the 815 patients who were eligible to enter this study demonstrated that the study patients were significantly more likely to be male (66.6% vs 61.7%, \(P=0.03\)), but men and women were of comparable age (mean [SD], 56.7 [12.9] years vs 55.9 [15.9] years, \(P=0.16\)). Up to 1986, the cumulative exposures to PUVA, UV-B, and methotrexate were comparable between the study patients and those not included (mean [SD], 188.5 [137.6] PUVA treatments vs 203.3 [163.1] PUVA treatments, \(P=0.12\); 248.6 [351.1] UV-B treatments vs 288.5 [458.3] UV-B treatments, \(P=0.31\); and 15.6 [31.2] months of methotrexate therapy vs 17.4 [32.9] months of methotrexate therapy, \(P=0.27\), respectively).

At time of the enrollment in the PUVA study, the 815 study patients were significantly younger and more likely to be female than the other 565 cohort members (mean age, 41.5 years vs 47.1 years [\(P<0.001\)] and 64.2% women vs 36.4% women [\(P=0.005\)], respectively). At time of the first PGA assessment (1977, \(N=1192\)), study participants were significantly more likely to have more moderate to severe disease compared with the remaining patients (18.9% vs 32.9% [\(P<0.001\)], respectively).

### STATISTICAL ANALYSIS

We used the \(\chi^2\) test to determine the statistical significance of difference in the distribution of categorical variables and the \(t\) test for continuous variables. For paired comparisons, the Wilcoxon signed rank test and the McNemar test were used as appropriate. To test for statistical differences between multiple
groups, 2-way analysis of variance or the Kruskal-Wallis test was used as appropriate. To assess the intraindividual variability of the PGA scorings, we calculated turnover tables for all intervals and pooled them. We applied multistate Markov modeling, which describes the process in which an individual moves through a series of states in continuous time. Multivariate statistical modeling package for the statistical program R was used to estimate a transition intensity matrix (hazard matrix: hazard ratios with 95% confidence intervals \([CIs]\) \([data\ not\ shown\])\), which were subsequently transformed to proportions \(\) without 95% CIs because of software limitations. First, multistate Markov modeling was used to estimate the transit rates between levels of PGA after 1, 5, and 10 years. We chose a model that allowed changes only to subsequent PGA stages but used a likelihood ratio test to compare it with a model that allowed all possible changes. Second, Markov models estimated the length of stay of the total study period (20 years) in each of the PGA levels stratified by the patients\' PGA level at baseline in 1986.

To study the effect of aging and disease duration on the 4-point PGA, we compared the distribution of these variables across the PGA levels at each clinical examination. Also, a multivariate ordered logistic regression model, which is a type of logistic regression model with an ordinal-depending variable that has more than 2 categories, was used to calculate adjusted odds ratios (ORs) and 95% CIs. For the 4 analyses, collinearity was absent and the proportional odds assumption was tested using a likelihood ratio test and a Brant test, the results of which were nonsignificant \(P > .05\).

**RESULTS**

**THE COHORT OVER TIME**

Figure 2 demonstrates that of the patients who were actively followed up in each year of the PUVA study, the overwhelming majority were interviewed, and that the number of participants who were unavailable for follow-up or withdrew from the study was very small. Death of the cohort members was the primary reason for the decreasing number of participants between 1975 and 2005.

**CHARACTERISTICS OF STUDY POPULATION**

About three-quarters of the cohort members who were followed up participated in the clinical examinations (Table 1). Of the 979 patients, 815 (82.3%) underwent 2 or more clinical examinations between 1985 and 2005. The majority of 815 study participants were middle-aged male patients who had psoriasis for more than 25 years (Table 1). The age at onset of psoriasis ranged from 0 to 68 years (mean [SD] age, 19.0 [17.8] years). Graphically, no bimodal distribution was detected. A little fewer than 50% of the patients had PGA scores of moderate to severe psoriasis at 1 or more of the examinations. The distribution of PGA levels remained stable over a period of 20 years, except that a larger percentage of patients were reported clear of psoriasis at the 2005 examination \(P < .03\) compared with prior examinations \(P > .13\).

**DISTRIBUTION**

In 1986, 1991, 2001, and 2005, the total number of clinically examined patients was 889, 979, 580, and 424, respectively. Of the patients who were followed up after 1991, 92.2% of the 884 patients who underwent 1 examination between 1985 and 2005 underwent a second examination. Of the study patients who were followed up in 2005, 8.8% underwent 2, 30.5% underwent 3, and 60.8% underwent 4 examinations. The likelihood that a
second examination was reported increased significantly for each year a patient was followed up after the first examinations between 1985 and 2005 (OR, 1.31; 95% CI, 1.27-1.36). A total of 2378 examinations were included in this study (mean, 3 examinations per patient). The mode of PGA level was mild (48.0%). Of the 815 patients, 290 (35.6%) had the exact same PGA score, and 50.3% had a maximum difference of 1 level; 13.3%, of 2 levels; and 0.9%, of 3 levels (ie, had an examination reporting clear psoriasis and an examination reporting severe psoriasis) at examinations in which they participated. The difference between the 2 broad severity categories (none or mild vs moderate or severe psoriasis) changed in more than half of the participants (52.3%). Although the variance increased significantly (P < .001) with the maximum number of observations (Figure 3), the majority of patients remained within 1 level of their baseline assessment in 1986 (Figure 4). Of the 94 patients who had severe disease in 1986, almost half still had severe disease in 1991, about 25% remained at this level in 2001 and 2005, and between 65% to 85% had at least moderate disease at subsequent examinations. About 90% of 602 patients with mild and moderate psoriasis in 1986 remained within 1 PGA level at the subsequent examinations. About 70% of patients with no or mild disease in 1986 had these same levels of psoriasis severity at subsequent examinations.

### PAIRED COMPARISONS

The median change in PGA score between the 4 examination periods was 0 (25th percentiles of 0.0 and −1.0 and 75th percentiles of 0.0 and 1.0). Paired analyses between the 4 assessments showed no significant difference in PGA levels of patients (P > .06). After categorizing the PGA levels of patients with none to mild and moderate to severe psoriasis, paired analyses showed no statistical significant differences between periods (P > .33).

### INTRAINDIVIDUAL VARIABILITY

Patients’ probability of having the same global psoriasis severity 1 year later is about 80% but decreases at 5- and 10-year intervals (Table 2). Of patients with mild to moderate disease, about 85% were likely to still have the same level of disease after 10 years. It was estimated that almost half the patients with moderate disease will have mild disease after 10 years. About a third of patients with severe psoriasis are likely to have mild or moderate disease 10 years later, and almost a quarter of those with no psoriasis will have moderate disease.

### Table 1. Characteristics of Patients With Psoriasis Who Underwent 2 or More Clinical Examinations

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Participants, No. (%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>865 (73.7)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>743 (74.1)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>571 (78.3)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>400 (76.0)&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Women, No. (%)</td>
<td>333 (38.1)</td>
<td>280 (37.4)</td>
<td>221 (38.1)</td>
<td>151 (37.8)</td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>54.0 (13.9)</td>
<td>56.1 (13.0)</td>
<td>59.9 (12.6)</td>
<td>63.7 (13.5)</td>
<td></td>
</tr>
<tr>
<td>Duration of disease, mean (SD), y</td>
<td>32.6 (13.6)</td>
<td>34.9 (12.8)</td>
<td>41.6 (12.2)</td>
<td>45.0 (13.0)</td>
<td></td>
</tr>
<tr>
<td>Physician global assessment of psoriasis, No. (%)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Clear</td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
<td></td>
</tr>
<tr>
<td>40 (4.5)</td>
<td>404 (45.4)</td>
<td>308 (34.6)</td>
<td>121 (13.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29 (3.8)</td>
<td>340 (44.7)</td>
<td>270 (35.5)</td>
<td>109 (14.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29 (4.8)</td>
<td>289 (47.8)</td>
<td>193 (31.9)</td>
<td>63 (10.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>38 (9.5)</td>
<td>188 (47.0)</td>
<td>127 (31.8)</td>
<td>47 (11.8)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>Of the patients who underwent at least 2 examinations (n = 815).

<sup>b</sup>Percentage of patients who were followed up during that period.

<sup>c</sup>Statistically significant (P < .02) on x² test.
tients with moderate psoriasis in 1986 were expected to have moderate or severe disease in 11 of 20 subsequent years. Those with severe disease at the initial examination would average 6 years of mild, moderate, and severe psoriasis and should be clear of psoriasis for only half a year over 2 decades.

EFFECT OF AGING

A comparison of patients’ age and disease duration at the time of examination between the 4 PGA levels showed no statistical significant differences in any of the examination periods ($P > .18$). After adjustment for sex in a multivariate proportional logistic regression model, age and disease duration were not significantly associated with level of PGA in 1986, 1991, 2001, or 2005 (eg, age in 2005, adjusted OR, 0.98 [95% CI, 0.96-1.02]; and duration of disease in 2005, adjusted OR, 1.00 [95% CI, 0.98-1.03]).

SENSITIVITY ANALYSES

To study whether patients with active or persistent disease were more likely to accept an invitation for a study-sponsored clinical examination, several sensitivity analyses were performed. The demographic and disease characteristics of the patients who underwent all examinations during follow-up (72.2% of the study population) were comparable to those of the patients who missed intermediate examinations (data not shown). Restricting the analysis to the 241 participants who underwent all 4 examinations did not change the results substantially (data not shown). We compared the PGA levels of patients who were examined only in 1986 with those of...
patients who were assessed in both 1986 and 1991. The same comparison was performed for examinations in 1991 and 2001. There were no significant differences in the distribution of the PGA levels of the patients with 1 vs 2 observations, except that patients who underwent only 1 examination were significantly more likely to have severe psoriasis than those who underwent 2 examinations (11.9% vs 3.1%, P < .001). When we fitted a Markov model with all transitions possible (ie, also from PGA levels 1 to 4), the likelihood ratio test comparing this model with the presented model showed no significant difference (df = 6, P = .41).

Nearly all data concerning the variability in clinical psoriasis severity over time come from a few cross-sectional studies using self-reported psoriasis severity in time or from clinical trials with follow-up measured in weeks rather than years or decades. The PUVA Follow-up Study cohort is unique. Patients have been followed up for nearly 30 years from enrollment in a clinical trial irrespective of their use of PUVA or any other therapy. In the first 5 years of the study, many patients still relied on PUVA and the study protocol linked interviews and study-sponsored dermatologic examinations. By the mid-1980s, use of PUVA had decreased significantly. Also beginning in 1985, the timing of interviews and study-sponsored dermatologic examinations were no longer closely linked to each other or to patients seeking care for their psoriasis. As a result, the structured dermatologic examinations performed from 1985 to 2005 provide a unique assessment of the distribution of psoriasis severity over time in a group of patients who joined this cohort nearly a decade earlier and of the variability in individuals’ physician-assessed psoriasis severity over a 20-year period. To quantify the variation of the patients’ disease severity over these 20 years, we used new statistical techniques to estimate transition rates and the expected number of years that patients would be at the different PGA levels depending on their baseline assessment.

Table 2. The Transit Rate Between Levels of Physician Global Assessment of Psoriasis at Consecutive Examinations After 1, 5, and 10 Years<br>

<table>
<thead>
<tr>
<th>PGA of Psoriasis in 1986</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>5.79</td>
<td>9.28</td>
<td>3.90</td>
<td>1.03</td>
</tr>
<tr>
<td>Mild</td>
<td>1.23</td>
<td>11.80</td>
<td>5.42</td>
<td>1.55</td>
</tr>
<tr>
<td>Moderate</td>
<td>0.78</td>
<td>8.15</td>
<td>8.44</td>
<td>2.63</td>
</tr>
<tr>
<td>Severe</td>
<td>0.45</td>
<td>6.22</td>
<td>7.04</td>
<td>6.18</td>
</tr>
</tbody>
</table>

*Multistate Markov modeling (see “Methods” section).

Table 3. Of the Total of 20 Years, the Expected Number of Years That Patients Will Spend in Each of the Levels of the Physician Global Assessment (PGA) Stratified by PGA of Psoriasis in 1986

<table>
<thead>
<tr>
<th>PGA of Psoriasis in 1986</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
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<tr>
<td>None</td>
<td>5.79</td>
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COMMENT

Nearly all data concerning the variability in clinical psoriasis severity over time come from a few cross-sectional studies using self-reported psoriasis severity in time or from clinical trials with follow-up measured in weeks rather than years or decades. The PUVA Follow-up Study cohort is unique. Patients have been followed up for nearly 30 years from enrollment in a clinical trial irrespective of their use of PUVA or any other therapy. In the first 5 years of the study, many patients still relied on PUVA and the study protocol linked interviews and study-sponsored dermatologic examinations. By the mid-1980s, use of PUVA had decreased significantly. Also beginning in 1985, the timing of interviews and study-sponsored dermatologic examinations were no longer closely linked to each other or to patients seeking care for their psoriasis. As a result, the structured dermatologic examinations performed from 1985 to 2005 provide a unique assessment of the distribution of psoriasis severity over time in a group of patients who joined this cohort nearly a decade earlier and of the variability in individuals’ physician-assessed psoriasis severity over a 20-year period. To quantify the variation of the patients’ disease severity over these 20 years, we used new statistical techniques to estimate transition rates and the expected number of years that patients would be at the different PGA levels depending on their baseline assessment.

PSoriasis Severity in Time

Based on nearly 2400 structured dermatologic examinations, the distribution of psoriasis severity within this group assessed by dermatologists changed little for the PUVA cohort as a whole over a 20-year period. Only about 25% of individual study participants had more than 1 PGA level change (with up to 3 levels possible) in multiple examinations. Paired comparisons demonstrated no significant differences between patients’ PGA levels over time. Moreover, transition rate analysis estimated that patients had about an 80% chance to have the same level of psoriasis severity after 1 year, but these rates decreased after 5 and 10 years, especially for the 2 extreme PGA levels. At least 50% of patients with moderate to severe disease are likely to still be at this level 10 years later, but patients with severe psoriasis will have mild to moderate disease in at least two-thirds of the follow-up years. Therefore, at least in this heterogeneous population cared for by many dermatologists, including many with a special interest in psoriasis, the likelihood that the extent of disease will change more than 1 PGA level over 1 year and over 10 years is relatively small, and fewer than 5% will have no psoriasis. As expected, patients who had no psoriasis at baseline, which may reflect the natural course of their disease or may be attributable to therapy, have the best chance of having no or mild disease in the future. Although treatment exposure and PGA examination results were not linked in this study, overall treatment use has been substantial in this cohort. For example, from study entry to 1984, cohort members had used twice as many PUVA as UV-B treatments, but after 1984, UV-B was used 3 times as often (between 1985 and 2005, the cohort used more than 200,000 UV-B treatments). Despite substantial therapy use over time, only 9.0% and 2.3% of the 813 study participants were clear of disease at 1 or 2 examinations and only 5 (1.0%) of the 507 patients who underwent 3 or more clinical examinations were clear at 3 examinations, which may be a spontaneous outcome or attributable to therapy. These low proportions of clearance contrast with those observed in an older prospective study of an isolated population followed up for a median interval of 1 year as well as those of a study that noted that 75% of patients reported a com-
complete remission of their disease and that 2% of men and 8% of women had no signs of the disease for at least 5 years. Both of these studies relied on patient reports rather than on examination and included a much higher percentage of persons with mild psoriasis than did the PUVA Follow-up Study.

EFFICACY VS EFFECTIVENESS

The study findings confirm the discrepancy between the efficacy of treatments observed in clinical trials and our success in controlling psoriasis over the long term. In the original PUVA trial, 88% of the patients achieved clearance at completion of the study, but 1 year or more thereafter, including at time points close to the introduction of cyclosporine and the biologics, 55% or fewer of those patients were described as having no or mild psoriasis. This difference of 30% may suggest that clearing psoriasis over the short term is quite feasible but that it is much more difficult to substantially reduce psoriasis over the long term, which may be attributable to other issues such as care setting (clinical trials vs real life), access and availability, safety, convenience, satisfaction, and costs. Although our study was unable to differentiate which of these issues or what other factors may be the root cause, our findings indicate that those patients who sought a cure for their psoriasis 30 years ago and temporarily achieved good control of their disease have suffered from substantial disease over the long term.

Psoriasis severity reported at the first 5 examinations after the introduction of PUVA (1976-1982), which were excluded from the analyses, was significantly less than that at later examinations. In the years in which the first 5 examinations were performed, the use of PUVA was significantly greater than in the years before the examinations that were performed between 1985 and 2005 (Figure 1). However, this level of control diminished in association with the decline of PUVA use after it became widely accepted to be carcinogenic in the 1980s. At least in our cohort, the introduction of new treatments from 1985 to 1998 (ie, vitamin D derivatives, retinoids, and cyclosporine) did not seem to have substantially affected the severity of the patients’ psoriasis. However, the distribution of PGA levels of 400 patients with psoriasis who were examined in 2005 showed that a significantly larger percentage (9.6% vs <5.1%) of patients were rated clear compared with the patients at prior examinations. Fewer than one-fourth of those who were clear in 2005 had ever used biologics, but the availability of biologics and the publicity about psoriasis treatments may have stimulated more patients to seek care again. Therefore, these recent data, as well as our cohort’s experience from 1977 to 1982, are compatible with the hypothesis that more intensive therapy, both new and old, is able to reduce psoriasis, at least for short periods.

EFFECT OF AGING

A medical claims–based study that used prevalence estimates that were based on general physicians’ record-
time of patients’ enrollment in the PUVA study, nearly a decade before the first examinations included in these analyses were performed, the patients had sufficiently severe and/or treatment-resistant psoriasis that both patients and their treating dermatologists at 16 centers, which were selected for their expertise in the treatment of psoriasis, deemed them appropriate candidates for a then-experimental therapy, which included the systemic administration of drug. We believe that our results are likely to be representative of the course of psoriasis severity among patients with moderate to severe psoriasis who at least initially had access to care at a leading dermatologic center. Although mortality may be associated with clinical psoriasis severity (owing to increased incidence of comorbidities), it is not likely to be associated with the degree of disease fluctuations, which is the objective of this study. The Markov model was used to create the transition tables. As a statistical model, it is based on several assumptions. The results of these kinds of analyses should be interpreted with some caution and applied cautiously in advising individual patients. However, a sensitivity analysis with altered assumptions confirmed the findings of the presented model. Because of software limitations, we were unable to calculate 95% CIs for the transition rates. However, the 95% CIs were estimated for the transition intensities (hazard matrix), which is in an intermediate step in the process of the transition rate calculation, and were reasonably narrow (data not shown). We believe that a 4-point PGA scale, which was assessed by dermatologists who were trained at investigators’ meetings and through instructions, as part of a structured dermatologic examination, is likely to be a reliable and valid measurement in the assessment of psoriasis. However, the PGA was not strictly defined and did not include parameters such as percentage of body surface area affected and/or plaque characteristics but is widely used and has “face” validity.21–23 Although a global assessment may be relatively insensitive for measuring small changes over time, we believe it should be sensitive to clinically meaningful changes, which are the focus of this study. In addition to the intraobserver variability of the PGA, interobserver variability may also have affected our results, because different investigators may have assessed some patients over time. The extent to which observer bias affects the PGA in psoriasis is not well documented.22

In conclusion, even with substantial use of psoriasis therapies after 1984, including more than an average of 170 UV-B treatments, 50 PUVA treatments, and a year of methotrexate therapy, our cohort was assessed by dermatologists as having moderate or severe psoriasis at nearly half of almost 2400 examinations performed over a 20-year period. Although at some times the disease may improve or worsen, most individuals in our cohort had similar extents of psoriasis at subsequent examinations. Three decades after this large diverse group of patients sought a cure for their psoriasis, they have not achieved consistent control of their disease. Additional prospective longitudinal studies that assess the (natural) course of psoriasis and its determinants are warranted.

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Author Contributions: Dr Stern is the principal investigator of the PUVA Follow-up Study. Study concept and design: Nijsten and Stern. Acquisition of data: Stern. Analysis and interpretation of data: Nijsten, Looman, and Stern. Drafting of the manuscript: Nijsten. Critical revision of the manuscript for important intellectual content: Nijsten, Loo- man, and Stern. Statistical analysis: Nijsten and Loo- man. Obtained funding: Stern. Administrative, technical, and material support: Nijsten and Stern. Study supervision: Stern.

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