Supplementary Methods Text

We performed an observational cohort study data from the Pediatric Eczema Elective Registry (PEER). PEER is an ongoing prospective observational registry that began enrollment in 2004 and aims to follow 7,000 subjects over 10 years. Inclusion criteria include: AD diagnosis by a physician based on the UK Working Party Criteria,(1) ages 2-17 at the time of enrollment, and use of 1% topical pimecrolimus cream for at least 42 out of the 180 days prior to enrollment. There was no objective disease severity requirement, but the study was advertised for patients with mild-to-moderate disease because pimecrolimus was originally FDA approved for this indication. Subjects were excluded from enrollment into the cohort if they had a history of lymphoproliferative disease, systemic malignancy, skin malignancy, or had used oral immunosuppressive medications such as cyclosporine, tacrolimus, or methotrexate. Subjects filled out an initial enrollment questionnaire and were followed longitudinally with repeat questionnaires every 6 months. Importantly, data collection was completely independent of physician visits and medication decisions after enrollment; subjects were not expected to continue to see the enrolling provider or to continue treatment with pimecrolimus if other medications were determined to be more appropriate for their condition. Written informed consent was obtained for each of the study participants, and the research protocol was approved by the institutional review board at the University of Pennsylvania.

The primary outcome measure, disease control, was based on treatment use and the following question: “during the last 6 months, would you say you or your child’s skin has shown complete disease control, good disease control, limited disease control, or uncontrolled disease?” This question was chosen because it is easily interpretable, patient-centered, and comprehensive.

It has been used in Randomized Controlled Trials and has been shown to correlate with a well-validated objective eczema severity measure, the Eczema Area and Severity Index (Spearman correlation coefficient at 6 months, 0.794).(2-6) Subjects were also asked about the use of any prescription creams or ointments for AD, and about the number of visits made to a health professional (nurse, family doctor, pediatrician, dermatologist, hospital emergency department, and other health care provider) for AD over the last 6 months. The medication data were used to sub-categorize those with self-described complete control into two groups: those with apparent remission (i.e. complete control without using any medications for AD over the last 6 months), and those with complete control who were using medications. Duration of follow-up was calculated from the date of enrollment and the last available survey date. Lost to follow-up was defined as no surveys returned in the preceding 18 months. Personal history of atopy was defined as a personal history of asthma or seasonal allergies if greater than or equal to age four, or a family history of asthma seasonal allergies or eczema in a parent or sibling if under age four.(7)

Baseline characteristics of the cohort were summarized descriptively. The proportion of all responses with each level of disease control are presented in table format. It is important to note that these analyses do not account for repeated measures within subject (i.e. a subject may have returned more than one survey within each age group). The proportion of responses with each level disease control by age is also presented graphically using kernel-weighted local polynomial smoothed graphs with 95% confidence bands.(8) In order to account for repeated disease control measurements, we created a separate generalized linear latent and mixed model (GLLAMM) with binomial logistic links for each level of disease control. We included random slopes and intercepts to account for individual heterogeneity in disease trajectories, and time was modeled as a linear term for age.(9) Adjusted odds ratios were calculated using multivariable

models controlling for potential confounders specified a priori including age at onset, enrollment age, sex, race, family income and history of atopic disease at enrollment. Finally, in an exploratory secondary analysis, GLAMM models were used to assess the subject-specific odds of dermatologist visits by age, and potential effect modification by level of disease control and age was addressed by including a multiplicative interaction term. We reported missing data where applicable, and checked the missing at random assumption in sensitivity analyses. Stata version 12.1 (StataCorp, College Station, TX) was used for all data analyses.

Supplemental References

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Supplementary Table 1. Characteristics of the study population

	N= 5,798
Mean age of onset, years (SD)	2.2 (3.0)
Mean age at enrollment, years (SD)	7.2 (4.1)
Median number of surveys (IQR)	8 (2-16)
Sex, male N (%)	2,709 (47%)
History of atopic disease*	4,365 (75%)
Race N (%)**	
White	2,523 (44%)
Hispanic or Latino	541 (9%)
African American	2,919 (50%)
American Indian or Alaskan Native	73 (1%)
Asian	231 (4%)
Hawaiian or other Pacific Islander	21 (0%)
Income, in thousands of US dollars N(%)	
<25	2,240 (39%)
25-50	900 (16%)
50-75	501 (9%)
75-100	294 (5%)
>100	361 (6%)
Prefer not to answer	1,498 (26%)
Mean duration of follow up, years (SD)	4.2 (2.6)
Lost to follow up***	1, 544 (27%)

Notes: *Personal history of atopy was defined as a personal history of asthma or seasonal allergies if greater than or equal to age four, or a family history of asthma seasonal allergies or eczema in a parent or sibling if under age four. **Numbers sum to >100% because respondents could select more than one racial category. ***Drop out, or loss to follow-up was defined as no surveys returned in the preceding 18 months.

Supplementary Table 2. Results of binomial logistic GLLAMM regression model for subject-specific the odds of a dermatologist visit over a 6-month period

	Dermatologist visit OR (95%CI) [#]
Age at visit	0.84 (0.81-0.87)
Complete control with treatment*	6.84 (4.45-10.5)
Good control*	12.33 (7.83-19.43)
Limited control*	23.55 (13.70-40.48)
Poor control*	42.15 (22.13-80.27)
Interaction term for age and level of disease control	1.00 (0.99-1.02)

Notes: *Odds relative to complete control without treatment; #Model adjusted for age of onset, enrollment age, sex, race, family income and history of atopic disease at enrollment.