JAMA Dermatology | Consensus Statement

# Pediatric Psoriasis Comorbidity Screening Guidelines

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**IMPORTANCE** Psoriasis is a complex inflammatory skin condition associated with serious medical comorbidities in adults, including obesity, hypertension, dyslipidemia, type 2 diabetes mellitus, psoriatic arthritis, nonalcoholic fatty liver disease, depression, anxiety, and decreased quality of life. Because psoriasis begins in childhood in almost one-third of patients, early identification of risk may be critical to minimizing effects on future health.

**OBJECTIVE** To develop the first set of guidelines for comorbidity screening for patients with pediatric psoriasis based on current evidence.

**EVIDENCE REVIEW** A literature review was performed using PubMed from January 1999 through December 2015. Limiting the search to human studies published in English and removing reviews and editorials produced 153 relevant manuscripts. An expert panel in psoriasis, pediatric dermatology, pediatric rheumatology, pediatric gastroenterology, pediatric endocrinology, and adult and pediatric cardiology used the patient-centered Strength of Recommendation Taxonomy (SORT) method to evaluate and grade the quality of evidence.

**FINDINGS** Because of the limited number of pediatric studies published on these topics, the strength of the panel's recommendations is classified as SORT level C expert consensus recommendations. The majority of recommendations coincide with those endorsed by the American Academy of Pediatrics for the general pediatric patient but with added attention to signs and symptoms of arthritis, depression, and anxiety. The panel also identified key areas for further investigation.

**CONCLUSIONS AND RELEVANCE** Patients with pediatric psoriasis should receive routine screening and identification of risk factors for associated comorbidities. These guidelines are relevant for all health care providers caring for patients with pediatric psoriasis, including primary care clinicians, dermatologists, and pediatric specialists. Because these are the first pediatric guidelines, re-review and refinement will be necessary as studies further detail, and possibly stratify, risk in affected children.

Supplemental content

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*JAMA Dermatol*. doi:10.1001/jamadermatol.2017.0499
Published online May 17, 2017.



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Psoriasis is a common chronic, inflammatory disorder, beginning in childhood in almost one-third of cases and affecting 0.05% to 2.20% of children (Egypt and Italy, respectively, at the 2 limits).[1,2] It is often not an isolated condition, with affected adults having increased incidence of myocardial infarction, diabetes mellitus, hypertension, hyperlipidemia, obesity, metabolic syndrome, arthritis, and liver disease.[1-3] Patients with psoriasis frequently have depression,[1,3] suicidality, anxiety, and impaired quality of life.[4] Studies of children with psoriasis have begun to identify similar associations with systemic and behavioral comorbidities.[1,5-7] Early identification of risk factors for these comorbidities may allow interventions to minimize health effects over a lifetime and lessen the impact of psoriatic disease.

In 2008, the National Psoriasis Foundation (NPF) published a consensus document with recommendations for comorbidity screening of adults with psoriasis,[8] followed by similar work by several other organizations.[9,10] No equivalent guidance document, however, exists for affected children. Members of the Pediatric Dermatology Research Alliance (PeDRA) and NPF established the NPF-PeDRA–Pediatric Psoriasis Comorbidity Screening Initiative to assess the current literature and establish screening recommendations for children. This article outlines the findings and resulting recommendations, along with identified gaps in research. By increasing awareness and providing a tool to help address these important health issues, we hope to optimize the comprehensive care of patients with pediatric psoriasis.

## Methods

A panel with expertise in clinical and research work in psoriasis (including dermatoepidemiology and comorbidity research), pediatric dermatology, pediatric rheumatology, pediatric gastroenterology, pediatric endocrinology, adult and pediatric cardiology and with publication on relevant topics, and/or experience with consensus recommendation processes, was identified. A literature review was performed using PubMed, searching articles published from January 1999 through December 2015, to identify relevant publications using the search term "psoriasis" in combination with "comorbidities," "screening," "arthritis," "diabetes mellitus," "non-alcoholic fatty liver disease," "cardiovascular disease," "lipids," "hypertension," "obesity," "inflammatory bowel disease," "polycystic ovary syndrome," "metabolic syndrome," "depression," "anxiety," and "quality of life." The initial search identified a total of 919 manuscripts. We limited the pool to studies involving humans and those published in English. After removing redundant studies, reviews, and editorials, 153 manuscripts remained, with 26 involving pediatric patients. We used the patient-centered Strength of Recommendation Taxonomy (SORT) method to grade the quality of the evidence.[11] We also reviewed the American Academy of Pediatrics (AAP) Preventive Pediatric Health Care recommendations, other recognized pediatric specialty screening recommendations (eg, the American Diabetes Association), as well as the NPF, and other adult psoriasis comorbidity screening recommendations (**Table**).

### Consensus Process

The expert panel was organized into 4 teams assessing the following comorbidity topic areas: cardiovascular, lipids, obesity, endocrinology, rheumatology, gastroenterology, mood disorders, quality of life, and other less common comorbidities. The panel reviewed the results of the literature search to ensure that all relevant articles were included. Each team evaluated the relevant literature and composed preliminary recommendations based on the evidence and identified areas where further investigation is needed. Preliminary recommendations were reviewed and edited by the entire panel in an iterative process to finalize the expert consensus document.

**Table. Strength of Recommendation Taxonomy[a]**

| Recommendation Strength | Evidence Quality |
|---|---|
| **A** = Based on consistent and good quality patient-oriented evidence | **Level 1** = Good quality, patient-oriented |
| **B** = Based on inconsistent or limited quality patient-oriented evidence | **Level 2** = Limited quality, patient-oriented |
| **C** = Based on consensus, usual practice, opinion, disease-oriented evidence or case series | **Level 3** = Other evidence (ie, usual practice, opinion, disease-oriented evidence) |

[a] Adapted from Maymone et al.[11]

### Strength and Scope of Recommendations

Because of the paucity of pediatric studies published on these topics, the strength of recommendation for all recommendations in this document is SORT level C (based on consensus, usual practice, opinion, disease-oriented evidence or case series). The majority of the evidence is drawn from publications with study quality level 2 (limited quality, patient-oriented evidence) in adults and level 3 (usual practice, opinion, disease-oriented evidence) in children.

These recommendations are directed toward all pediatric patients with psoriasis, without risk stratification based on type (eg, plaque, guttate, palmoplantar. or inverse), severity, or duration of disease. The majority of the studies identified in our literature search involved patients with chronic plaque-type psoriasis (when specified) and insufficient data were available to parse out any significant differences among psoriasis types. Data from adult studies suggests that those with moderate-to-severe skin disease have increased comorbidities,[12,13] but there has not been adequate study to further stratify children at this time.

The screening recommendations derived are largely consistent with those endorsed by the AAP for the general pediatric patient. With a few highlighted exceptions, there is currently insufficient evidence to justify more intensive screening protocols for children with psoriasis. While some children may have had screening performed as part of their yearly health maintenance visits with their primary care physician, as they enter the preteen and teenage years, only 70% will have had an annual visit with their primary care physician, and only 10% will have received all recommended preventive services (including physical parameters measurement [height, weight, blood pressure], anticipatory guidance [including healthy eating, exercise, secondhand smoke], and for adolescents, time alone with physician to discuss sensitive topics).[14] Thus, all health care providers caring for patients with pediatric psoriasis should help assess and ensure that appropriate screening has been performed.

### Comorbidity Background and Screening Recommendations

#### Overweight or Obesity

Overweight (body mass index [BMI], calculated as weight in kilograms divided by height in meters squared, ≥85th percentile to



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<95th percentile for age and sex) and obesity (BMI ≥ 95th percentile) are epidemics in children and adolescents in the United States. Obesity prevalence in 2-year-olds to 19-year-olds rapidly increased from approximately 5% from 1963 to 1970 to 17% from 2011 to 2014.[15] Several studies have shown that patients with pediatric psoriasis in the United States and around the world have a higher prevalence of overweight and obesity compared with unaffected controls.[6,16] It is unclear whether being overweight or obese predisposes to psoriasis or affects the severity of disease in children, but a preliminary study noted overweight or obesity predated psoriasis by at least 2 years in 25 of 27 children.[17] It is hypothesized that having excess adipose tissue and an associated proinflammatory state with increased cytokine (eg, tumor necrosis factor [TNF]) expression, may predispose susceptible individuals to development of psoriasis.

### Screening Recommendation

- Screen for overweight and obesity yearly using BMI percentile, starting at 2 years of age.

For those identified as being overweight or obese, Barlow et al[18] details treatment and intervention approaches. Since psoriasis alone has been found to be an independent risk factor for cardiovascular disease in adulthood, health care providers should discuss with patients and families the importance of making lifestyle changes to minimize any additional risk from overweight or obesity. Motivational interviewing,[19] a patient-centered communication style with strategies such as reflective listening, shared decision making, and agenda setting, may be helpful in facilitating this conversation. Nutritional counseling should be considered if available. Referral to a pediatric tertiary weight management center is particularly important for those children with a BMI greater than 120% of the 95th percentile.

## Type 2 Diabetes Mellitus

The prevalence of type 2 diabetes mellitus (DM) has also increased significantly in US youths 20 years or younger (30.5% increase from 2001 to 2009).[20] Individuals of American Indian, African, Hispanic, and Asian descent appear to be disproportionately affected.[21] The adult literature shows that psoriasis is an independent risk factor for diabetes (pooled odds ratio [OR], 1.59 [95% CI, 1.38-1.83] even after adjusting for confounding comorbidities).[22] Earlier age of psoriasis onset (<40 years old)[23] and presence of psoriatic arthritis[1,5,6] may impart an even greater risk of DM, although the actual risk for children with psoriasis remains to be delineated.

### Screening Recommendations

- Screen every 3 years starting at age 10 years or the onset of puberty if the patient is overweight and has 2 risk factors from **Box 1**.
- Screen patients with obesity every 3 years starting at age 10 years or the onset of puberty regardless of the presence of risk factors.
- Screening should be performed by measuring fasting serum glucose.

These recommendations reflect the most recent 2016 guidelines from the American Diabetes Association for all children,[24] which have not yet been officially endorsed by the AAP. Although the guidelines note the option of screening with glycated hemoglobin, fasting glucose is the preferred measurement for children because glycated hemoglobin often leads to variably correct classification of DM status in this age group. Given the remarkably small risk of DM in prepubertal children, screening for type 2 DM is not routinely recommended in this population. When diagnosed, management approaches for pediatric DM are outlined in detail by Copeland et al.[25]

**Box 1. Risk Factors for Type 2 Diabetes Mellitus[a]**

- Body mass index ≥ 85th percentile
- Family history of type 2 diabetes in a first-degree or second-degree relative
- Native American, African American, Latino, Asian American, Pacific Islander race/ethnicity
- Conditions associated with insulin resistance: polycystic ovary syndrome, acanthosis nigricans, hypertension, dyslipidemia, small-for-gestational-age birth weight
- Maternal history of diabetes or gestational diabetes during the child's gestation

[a]Adapted from Barlow et al[18] and the American Diabetes Association 2016 Guidelines.[24]

## Dyslipidemia

Adult studies consistently support the association between psoriasis, dyslipidemia, and abnormal lipid function and composition,[26] and there is evidence for early metabolic and lipid abnormalities in children associated with psoriatic inflammation.[7,27,28] But as the literature is still limited, at present, having psoriasis does not warrant additional lipid screening beyond the general age-related recommendations for all children.[29]

Psoriasis is associated with increased risk for cardiovascular disease (CVD) in adults, specifically acute myocardial infarction (MI), peripheral vascular disease, and stroke.[30] Most concerning is the risk of early MI, as a 30-year-old with severe psoriasis has a relative risk of 3.1 compared with nonpsoriatic controls.[31] This increased CVD risk remains after controlling for other known risk factors such as obesity and diabetes and is higher in those with more severe skin disease.[30,31] Acute MI, peripheral vascular disease, and stroke are rare in children, and no studies to our knowledge have evaluated the risk in children with psoriasis. However, imaging studies performed in adults with psoriasis demonstrated that early features of atherosclerosis, including vascular inflammation[32] and noncalcified coronary plaque burden,[33] can start early in life. We urge health care providers to be aware of the risk of early MI as patients with pediatric psoriasis transition to adulthood and to consider this risk when evaluating each of the individual cardiovascular risk factors.

### Screening Recommendations

- Universal lipid screening should be performed during the following 2 age ranges: 9 to 11 years old and 17 to 21 years old.
- Outside of the specified age ranges, screening is also recommended in the presence of any additional cardiovascular risk factors (**Box 2**).
- Recommended lipid screening is with a fasting lipid panel (total, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol, and triglycerides).

The National Heart, Lung and Blood Institute and the AAP support universal screening for all children, regardless of risk factors, between the ages of 9 and 11 years old and again at 17 and 21 years old.[29] This screen was designed to identify children with



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**Box 2. Risk Factors for Dyslipidemia[a]**

- Family history of cardiovascular disease: myocardial infarction, angina, coronary artery bypass graft/stent/angioplasty, sudden cardiac death; relevant if occurs in a parent, grandparent, aunt, or uncle at early ages (<55 years for men; <65 years for women)
- Hypertension
- Tobacco use
- Body mass index ≥ 95th percentile
- High-density lipoprotein cholesterol <40 mg/dL
- Type 1 or type 2 diabetes mellitus
- Renal disease: chronic kidney disease, end-stage renal disease, postrenal transplant
- Nephrotic syndrome
- Postorthotopic heart transplant
- Kawasaki disease with current or regressed aneurysms
- Human immunodeficiency virus infection
- Chronic inflammatory disease (ie, systemic lupus erythematosus, juvenile rheumatoid arthritis)

[a]Adapted from Daniels et al.[34]

hereditary dyslipidemias but has the additional benefit of identifying dyslipidemias related to other risk factors. A nonfasting test can be performed to measure non–high-density lipoprotein cholesterol, but a fasting lipid panel is preferred to more accurately assess for elevated triglycerides.

Additional or repeat screening should be considered for patients younger than 9 years or 12 to 16 years of age in the presence of other risk factors (Box 2). To assess family history, appropriate screening questions include asking about sudden or early death, stroke, MI, hyperlipidemia, and whether family members have been treated or are taking medications to control these problems. The time frame and frequency of additional screening are at the discretion of the health care provider because there are no specific limits from the AAP.[29] Health care providers should be aware that lipids, particularly low density lipoprotein cholesterol, have a physiologic nadir during adolescence (at approximately 12-17 years of age), and results should be interpreted with this in mind.

For patients with elevated lipids, health care providers should refer to the AAP and National Heart, Lung and Blood Institute guidelines for lipid testing, treatments, and lifestyle changes.[29,34]

## Hypertension

Adult studies support that psoriasis is associated with hypertension, but only a single retrospective study supports the association between pediatric psoriasis and hypertension.[1]

### Screening Recommendation

- Screen for hypertension yearly starting at 3 years of age, using age, sex, and height reference charts.[29]

The committee recommends following the AAP guidelines for annual blood pressure screening. Screening should be performed using properly fitted equipment with the correct cuff size because this varies based on the size of the patient (the inflatable bladder should cover 80%-100% of the midpoint arm circumference).

## Nonalcoholic Fatty Liver Disease

Nonalcoholic fatty liver disease (NAFLD) is a term that encompasses simple steatosis, as well as nonalcoholic steatohepatitis (NASH). Because of the association of NAFLD with overweight, obesity, and insulin resistance, screening for NAFLD is recommended for pediatric patients with these health conditions.[18] Several studies have found an increased risk for NAFLD independent of obesity in adults with psoriasis.[35,36] Pediatric studies are needed to test for this risk in childhood psoriasis.

### Screening Recommendations

- All children with obesity or who are overweight with additional risk factors (central adiposity, insulin resistance [see Box 1 for associated conditions], prediabetes or diabetes, dyslipidemia, obstructive sleep apnea or family history of NAFLD/NASH) should be screened with alanine aminotransferase (ALT) measurement starting at 9 to 11 years of age.
- Earlier screening can be considered in younger patients with risk factors such as severe obesity, family history of NAFLD or NASH or hypopituitarism.

When the initial screening test is normal, consider repeating ALT every 2 to 3 years if risk factors remain unchanged. Consider repeating screening sooner if risk factors increase in number or severity (ie, excessive weight gain or development of other medical problems that increase NAFLD risk, such as type 2 diabetes or obstructive sleep apnea). Some guidelines recommend screening with both ALT and aspartate transaminase. ALT is the better screening test to detect NAFLD; because the cost of laboratory tests often varies across institutions, this may influence ordering a single test (ALT) vs a panel of tests. For detection of pediatric chronic liver disease, the upper limit of normal for ALT is suggested to be 22 U/L in girls and 25 U/L in boys.[37] To our knowledge, there is currently no evidence supporting screening of patients with psoriasis with normal BMI.

## Polycystic Ovary Syndrome

Polycystic ovary syndrome is an insulin resistance syndrome that overlaps and is associated with some of the other comorbidities discussed. While the adult literature suggests that psoriasis may be associated with polycystic ovary syndrome,[38] similar studies have not yet been performed in the pediatric population. Health care providers should be aware of the possible coexistence of polycystic ovary syndrome and consider directed testing if suggestive symptoms or signs are present (eg, oligomenorrhea, hirsutism).[38]

## Gastrointestinal Diseases

Patients with psoriasis have increased rates of inflammatory bowel disease, both Crohn disease and ulcerative colitis.[39] For patients who have decreased growth rate, unexplained weight loss, or symptoms consistent with inflammatory bowel disease (nausea, vomiting, abdominal pain, chronic diarrhea), formal gastrointestinal evaluation should be considered.

Although there are some reports of celiac disease in adults with psoriasis, there are no studies to our knowledge supporting screening for celiac disease in patients with pediatric psoriasis.



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## Arthritis

Psoriatic arthritis can be destructive and debilitating, making early identification and intervention a priority. Pediatric psoriatic arthritis has a bimodal peak. Clinical characteristics during the first peak at 2 to 3 years of age mirror those of juvenile idiopathic arthritis, with female predisposition, antinuclear antibody positivity, and oligoarthritis or polyarthritis with a tendency for small joint and wrist involvement. Characteristics during the second peak at 10 to 12 years of age have more in common with spondyloarthritis: male predisposition, enthesitis, axial disease, and HLA-B27 positivity.[40] Dactylitis, or inflammation of an entire digit, is a common finding in pediatric psoriatic arthritis. Notably, 80% of children with psoriatic arthritis develop arthritis 2 to 3 years prior to skin findings,[40,41] whereas adult patients tend to develop cutaneous manifestations of psoriasis first, on average 8.5 years before arthritis symptoms.

### Screening Recommendations

- Pediatric patients with psoriasis should be screened for the development of arthritis by a directed review of systems and physical examination (**Box 3**).

Questioning for arthritis symptoms should be part of the standard ongoing management of patients with psoriasis. Several arthritis screening tools have been created for use in adult patients with psoriasis, but none have been validated in children to our knowledge. Pediatric arthritis can be more insidious, and screening questions need to evaluate for limp and stiffness, particularly in the morning.[41] Screening for complaints of pain alone may not adequately identify arthritis in young children.

The aim of arthritis screening is to identify symptomatic patients who may not know they have a disease because the adverse effects on the joints are irreversible. There is currently no laboratory test available (such as a biomarker) to identify patients prior to the development of arthritis. Thus, patients should be screened for arthritis at the time of psoriasis diagnosis and periodically thereafter. Further studies are needed to determine the optimum interval for repeat screening and to assess the impact of such screening on health outcomes.

**Box 3. Features of Pediatric Psoriatic Arthritis**

- Pain and/or swelling in 1 or more joints
- Inflammation of a digit (dactylitis)
- Joint stiffness after rest or sleep that improves with activity
- Limp
- Heel pain or back pain (enthesitis)
- Eye pain or redness (uveitis)

## Uveitis

Uveitis (also known as iridocyclitis) is characterized by acute-onset eye pain, redness, miosis, photophobia, and blurred vision. This inflammatory eye condition has been reported to occur in 1.5% to 25% of patients with psoriatic arthritis,[42] but it does not appear to be associated with skin-limited psoriasis. Thus, screening for uveitis, via routine ophthalmology examinations, is only warranted for patients with psoriatic arthritis.[42]

## Mood Disorders and Substance Abuse

Psoriasis is associated with psychiatric comorbidities in all age groups.[43] In fact, pediatric patients with psoriasis were found to have an approximately 25% to 30% higher risk of developing depression and/or anxiety compared to children without psoriasis.[43] Excess alcohol intake has been shown to exacerbate psoriasis as well as mood disorders. Young and middle-aged men with psoriasis, in particular, appear to have higher rates of excessive alcohol use. Adult studies have also shown that alcohol-related mortality is higher in patients with psoriasis than in healthy controls,[44] but more data are needed to determine the risk of developing alcohol abuse in patients with pediatric psoriasis.

### Screening Recommendations

- Screen yearly for depression and anxiety regardless of age.
- Screen yearly for substance abuse beginning at 11 years of age.

This recommendation is an adjustment to the AAP recommendation to screen children for depression and substance abuse annually starting at 11 years of age.[45] Because affected individuals are more likely to have negative social experiences, such as bullying, with resultant adverse effects on their self-esteem and sense of well-being, early recognition of psychiatric disorders and active intervention are essential.

Screening can be performed with a number of tools or engaging in discussion with the patient. For example, the Patient Health Questionnaire (PHQ)-4 tool (eTable 1 in the Supplement) is a simple screen for both depression and anxiety.[46] Positive screens may require a more formal evaluative tool or referral to a mental health provider.

## Quality of Life

Health care providers should recognize the profound psychosocial ramifications of psoriasis and the potential significant impact on quality of life (QOL) of patients and their caregivers. Physical symptoms of pain, pruritus, and fatigue contribute to poor QOL, even in individuals with clinically mild skin disease.[47] In fact, one study[48] found the degree of QOL impairment in patients with pediatric psoriasis to be greater than that of children with diabetes, comparable to that of children with arthritis and asthma, and only less than the impairment of children with psychiatric disorders. Children with psoriasis exhibit notable impairment of emotional, social, and school functioning and often experience stigmatization as well as teasing or bullying in school.[47,48] Younger children with psoriasis and those with joint symptoms appear to have more significantly impaired QOL. There is also a significant burden on the parents as well as the affected child, which further impacts QOL.[49]

Questions that promote conversation about the effects of psoriasis on the patient's home, school, and social lives are an important part of overall management. Health care providers may consider using a formal QOL instrument as part of the overall evaluation and rationale for using systemic therapies, especially in the setting of worsening disease. The most commonly used QOL screen for pediatric psoriasis is the Children's Dermatology Life Quality Index.



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### Systemic Therapy

Prior to initiating systemic therapies for psoriasis, health care providers should consider the existence of comorbidities because they may impact choice of medication, tolerability, and adverse effects. Certain systemic agents could increase the risk of hepatotoxicity (eg, methotrexate), especially in an overweight or obese patient with possible NAFLD. Monitoring of serum lipids and blood pressure while on therapy may also be necessary, depending on the medication (eg, cyclosporine). Directed baseline screening and monitoring tests should be performed as indicated by each individual's therapeutic plan. Discussion of specific laboratory testing for available systemic agents is beyond the scope of this article but is addressed in other publications.[50]

## Discussion

Over the last 2 decades, a rapidly growing body of literature in adults and more recently in children has provided strong evidence for the multidimensional impact of having psoriasis. Not only do the risks span multiple organ systems, but they also involve significant impairment of QOL and a propensity for concomitant psychiatric disorders, especially depression and anxiety. Educating patients and their families about associated conditions, improving their lifestyle choices early, and providing a supportive environment are key components to their overall health management. Communication and collaboration between dermatologists, primary care providers, and other pediatric specialists will be critical to accomplish the recommended screenings and to limit the sequelae of this disorder.

## Conclusions

These mainly consensus-based recommendations provide a starting point for screening that will be refined as more is learned. As studies further detail the comorbidity risks in children, there may be a need to further stratify screening (eg, by age group, disease subtype, severity). It will also be important to assess the effectiveness of early detection and proactive intervention in preventing future complications. Many unanswered questions remain. We have listed some key questions in eTable 2 in the Supplement with the hopes of inspiring future research on these important topics.

ARTICLE INFORMATION

**Accepted for Publication:** February 14, 2017.

**Published Online:** May 17, 2017. doi:10.1001/jamadermatol.2017.0499

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**Conflict of Interest Disclosures:** None reported.

**Funding/Support:** Project support was provided by the National Psoriasis Foundation (NPF) and the Rady Children's Hospital/University of California, San Diego-Eczema and Inflammatory Skin Disease Center. Dr Osier was partially funded by an NPF Medical Dermatology Research Fellowship grant that supported her participation throughout the 2014 to 2016 academic years. Dr Tom was supported by a Career Development Award (award No. K23AR060274) from the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), part of the National Institutes of Health. Dr Gelfand was supported by the NIAMS (grant No. K24-AR064310).

**Role of the Funder/Sponsor:** The funders/sponsors had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

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