

# UC Davis

## Dermatology Online Journal

### Title

Understanding eligibility creep in psoriasis assessments: a survey study

### Permalink

<https://escholarship.org/uc/item/8jv7r1q5>

### Journal

Dermatology Online Journal, 28(3)

### Authors

Rakita, Uros  
Guraya, Armaan  
Porter, Caroline L  
et al.

### Publication Date

2022

### DOI

10.5070/D328357780

### Copyright Information

Copyright 2022 by the author(s). This work is made available under the terms of a Creative Commons Attribution-NonCommercial-NoDerivatives License, available at <https://creativecommons.org/licenses/by-nc-nd/4.0/>

Peer reviewed

# Understanding eligibility creep in psoriasis assessments: a survey study

Uros Rakita<sup>1</sup> MSc, Armaan Guraya<sup>2</sup> BS, Caroline L Porter<sup>3</sup> MD, Jeremy K Bray<sup>3</sup> MD, Steven R Feldman<sup>3-5</sup> MD PhD

Affiliations: <sup>1</sup>Chicago Medical School, Rosalind Franklin University, North Chicago, Illinois, USA, <sup>2</sup>Chicago College of Osteopathic Medicine, Midwestern University, Chicago, Illinois, USA, <sup>3</sup>Center for Dermatology Research, Department of Dermatology, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA, <sup>4</sup>Department of Pathology, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA, <sup>5</sup>Department of Social Sciences & Health Policy, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA

Corresponding Author: Steven R Feldman MD PhD, Department of Dermatology, Wake Forest School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157-1071, Tel: 336-716-7740, Fax: 336-716-7732, Email: [sfeldman@wakehealth.edu](mailto:sfeldman@wakehealth.edu)

## Abstract

Psoriasis severity assessments for clinical trial entry may be unintentionally overestimated, especially if trial eligibility is chiefly dependent on rating of disease severity. When this results in patients with less severe phenotypes joining clinical trials it is referred to as eligibility creep. We investigated the potential impact of psychosocial incentives on psoriasis lesion severity grading. A survey was constructed and disseminated through Amazon Mechanical Turk. Participants completed two vignette-style questions prompted with a randomly allocated psychosocial incentive. Questions required participants to grade and select psoriasis lesion pictures for a fictional trial. Participants also decided whether or not to schedule re-evaluation of patients deemed ineligible at initial visit. There were 646 participants. There was no significant difference in number of total lesions selected for study inclusion between incentive groups (Kruskal-Wallis,  $P=0.30$ ). In general, participants completing empathy and professional uncertainty incentives selected the most and least number of lesion pictures for trial inclusion, respectively. Participants prompted with empathy incentives had significantly greater rates of choosing to schedule a follow-up visit for ineligible patients compared to participants prompted with other incentives (69.7% versus 59.1%, Chi square  $P=0.046$ ). Situations evoking empathy may contribute to eligibility creep.

*Keywords: clinical trial, eligibility creep, PASI, psoriasis, survey*

## Introduction

Observed disease severity improvements in placebo groups of psoriasis drug trials can range from 15% to 20% [1]. A proposed explanation is “eligibility creep” (EC): estimating baseline psoriasis severity on the high side of the subjective range such that subjects meet trial entry criteria [1]. Various psychosocial incentives may contribute toward its occurrence. Using a survey-based design, we investigated potential psychosocial incentives that may contribute to EC.

The study was approved by the Wake Forest School of Medicine Institutional Review Board (IRB00071987). A Qualtrics generated survey was disseminated through Amazon Mechanical Turk. Participants of  $\geq 18$  years old were included in the study. Participants were provided with a PASI scoring guide and asked to select psoriasis lesion images (derived with permission from the online dermatology educational resource DermNet) they determined were of PASI severity score three or more and therefore were eligible for a fictional research trial ([Supplemental material](#)). Survey images were selected from a pool of DermNet images, which were already categorized by PASI score. A board-certified dermatologist (S.R.F.) further

evaluated the selected images for PASI score accuracy and applicability to survey questions. Participants evaluated PASI redness, scale, and thickness severities independently in three separate rating questions. More specifically, each rating question contained three images (only one of which met the aforementioned study inclusion criteria); in total, 9 images were rated by each participant. Each participant's rating question also randomly included one of 7 ad hoc designed psychosocial incentives (including a control incentive). Incentive design was guided by expert opinion and literature sources. Subjects were told hypothetically that the investigator would receive \$3,000 per enrolled patient (clinical trials may pay upwards of \$12,000 per enrolled patient), [2].

We assessed the total number (9 maximum) of psoriasis patient images deemed eligible for the hypothetical trial. Participants were also asked if they would schedule a follow-up visit prior to study enrollment termination to re-evaluate a patient already deemed ineligible on multiple occasions including during the most recent evaluation, for the fictional trial. Socio-demographics were compared between groups using Monte-Carlo simulation method of significance testing for categorical variables. Mean number of total included lesion images were compared across incentive groups using nonparametric Kruskal-Wallis test.

There was no significant difference in sociodemographic traits between incentive groups (Monte-Carlo,  $P \geq 0.38$  for all), (Table 1). In total, 646 participants completed a severity rating question. There was no significant difference in total number of images selected for study inclusion between incentive groups (Kruskal-Wallis,  $P=0.30$ ). There was also no significant difference in subgroup analysis of participants with psoriasis ( $N=146$  [22.45%]; Kruskal-Wallis,  $P=0.36$ ) and those with no psoriasis history ( $N=501$  [77.56%]; Kruskal-Wallis,  $P=0.54$ ) also revealed no significant difference in total number of images selected for study inclusion between incentive groups. In general, participants completing empathy and professional uncertainty incentives selected the most and least amount of lesion images for trial inclusion, respectively (Table 2). Of the 644

**Table 1.** Study participant demographics.

Study participant traits	Frequency	Percent
<b>Age</b>		
18-30	200	30.96
31-40	265	41.02
41-50	104	16.10
51-60	51	7.89
61-70	25	3.87
71-80	1	0.15
<b>Gender</b>		
Female	364	56.35
Male	278	43.03
Other	4	0.62
<b>Race</b>		
American Indian or Alaskan Native	8	1.24
Asian	149	23.07
Black or African American	55	8.51
Caucasian	398	61.61
Native Hawaiian or other Pacific	4	0.62
Multiracial	16	2.48
Unknown/Not reported	16	2.48
<b>Highest Education</b>		
Did not graduate high school	9	1.39
High school or GED	77	11.92
Associates or college degree	156	24.15
Bachelor's degree	287	44.43
Graduate degree	117	18.11
<b>Personal history of psoriasis</b>		
Yes	146	22.45
No	477	73.84
Unsure	24	3.72
<b>Family history of psoriasis</b>		
Yes	208	32.20
No	388	60.06
Unsure	50	7.74
<b>Familiarity with medical terminology</b>		
Very familiar	69	10.68
Familiar	173	26.78
Somewhat familiar	347	53.72
Not familiar	57	8.82
<b>Last seen a dermatologist</b>		
Never	177	27.40
More than 2 years ago	180	27.86
Within last 1-2 years	128	19.81
Within last 6 months	125	19.35
Within last month	36	5.57

Of 646 participants, 24 were missing demographic values. Monte-Carlo simulation testing with sample number of 20,000 did not reveal any significant differences between incentive groups ( $P \geq 0.38$  for all).

participants completing the follow-up question, 391 (60.7%) elected to schedule a follow up visit. Those who were previously prompted with empathy (69.7% versus 59.1%, Chi square  $P=0.046$ ) and

**Table 2.** Mean number of psoriasis lesion images identified as eligible for inclusion by incentive group.

Incentive group	N	Mean (SD)	Lower 95% CI for mean	Upper 95% CI for mean
Empathy	99	4.23 (1.51)	3.93	4.53
Control	83	4.01 (1.44)	3.70	4.33
Professional/financial gain	93	4.00 (1.55)	3.68	4.32
Personal relationship	92	3.90 (1.25)	3.64	4.16
Logistic constraints	94	3.86 (1.36)	3.58	4.14
Research criteria	86	3.86 (1.26)	3.59	4.13
Professional uncertainty	98	3.77 (1.24)	3.52	4.01
Total	645	3.95 (1.38)	3.84	4.06

N, number; SD, standard deviation; CI, confidence interval.

personal relationship (51.1% versus 62.3%, Chi square  $P=0.041$ ) incentives had greater and lower rates of choosing to schedule a follow up visit, respectively, compared to participants not prompted with the aforementioned incentives.

## Discussion

We did not identify a specific psychosocial incentive that significantly impacted the number of included lesion images. This remained the case for participants with and without a known psoriasis history. Situations eliciting empathy trended toward higher inclusion. Participants in the empathy group also elected to re-evaluate ineligible patients at greater rates than those prompted with other incentives. Re-evaluation can directly cause apparent placebo effects [1].

Although our study had a large sample with randomized comparator groups, limitations exist. Namely, a non-validated survey was used and participants were selected from the general public. This experiment was not designed to evaluate the prevalence of EC or real-world factors contributing to EC in psoriasis drug trials. However, the phenomenon investigated in the current study is

based in general principles of psychology and might be expected to generalize across populations; patterns identified in the current study may be more prominent in physician populations in which the studied incentives are more salient. However, this requires further investigation.

## Conclusion

In conclusion, EC may contribute towards observed clinical improvements in placebo arms of clinical trials. Empathy may be a particularly relevant psychosocial incentive associated with artificially elevated severity rankings at baseline.

## Potential conflicts of interest

Dr. Feldman has received research grants from Lilly, Abbvie, Janssen, Pfizer, Almirall, and Galderma; speaking honoraria from Lilly, Abbvie, Janssen, Alvotech, Amgen and Sun; consulting fees Abbvie, Janssen, Alvotech, vTv, BMS, Samsung, Pfizer, Boehringer, Dermavant, Arcutis, Novartis, UCB, Helsinn, Sun, Almirall, Leo, Mylan, Forte, TwoXar, and Arena. He holds Stock/ownership of [www.DrScore.com](http://www.DrScore.com) <<http://www.DrScore.com>> and Causa Research.

## References

- Hick J, Feldman SR. Eligibility creep: a cause for placebo group improvement in controlled trials of psoriasis treatments. *J Am Acad Dermatol.* 2007;57:972-976. [PMID: 17884244].
- Department of Health and Human Services. Office of Inspector

General. Recruiting human subjects. Pressures in industry-sponsored clinical research. Washington, DC: Department of Health and Human Services; 2000.

**Supplemental material:**

Survey script (not including sociodemographic questions) with annotated headings:

*Introductory statements:*

Psoriasis is a skin disease which shows up as thick, red, scaly plaques on the skin. This survey is about psoriasis **redness, scaliness, and thickness** severity ratings.

For the following 4 questions, **pretend you are the doctor** seeing psoriasis patients.

For the first 3 questions you will see psoriasis pictures and evaluate them on 3 separate categories (redness, scaliness, and thickness) for 3 different patients. You will sequentially rate each patient's psoriasis pictures on the 3 categories (**redness, scaliness, and thickness**). Since the categories are rated independently of one another, **the rating of one category should not influence your rating of the others**.

The last question will be a simple multiple choice question where you will not need to evaluate psoriasis pictures.

**A severity guide is provided below** [not shown]. We recommend you review this picture before starting to evaluate psoriasis categories.

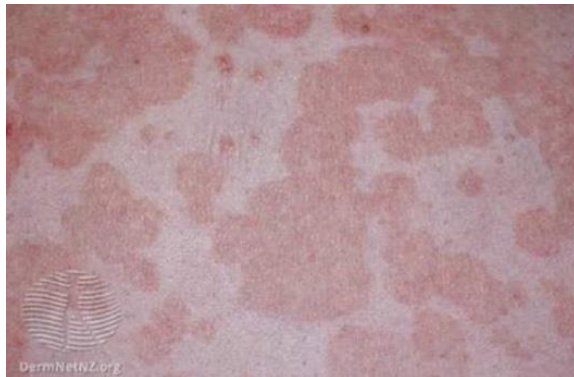
*Below is the control prompt and the nine psoriasis lesion pictures included in the survey. The lesion pictures were the same for every incentive and were presented in random order to every participant.*

**Control:** Three psoriasis patients come to your office. They tell you that their primary doctor recently diagnosed them with high blood pressure and recommended daily exercise. A new promising treatment for psoriasis is currently being researched which may benefit patients.

To enter this psoriasis treatment research study, a patient needs to have a **redness score of 3 or more**. Below are three images from three separate patients. Select any of the below patient images you think has/have a **redness of 3 or more** and therefore qualifies for the study.

**Redness**

A) Patient 1



B) Patient 2





C) Patient 3 [only patient that should meet study inclusion criteria]



D) None of the above patient images have a redness score of 3 or more, and therefore none of the above patients qualify to enter the study

Three psoriasis patients come to your office. They tell you that their primary doctor recently diagnosed them with high blood pressure and recommended daily exercise. A new promising treatment for psoriasis is currently being researched which may benefit patients.

To enter this psoriasis treatment research study, a patient needs to have a **scaliness score of 3 or more**. Below are three images from three separate patients. Select any of the below patient images you think has/have a **scaliness of 3 or more** and therefore qualifies for the study.

A) Patient 1



B) Patient 2



C) Patient 3 [only patient that should meet study inclusion criteria]



- D) None of the above patient images have a scaliness score of 3 or more, and therefore none of the above patients qualify to enter the study

Three psoriasis patients come to your office. They tell you that their primary doctor recently diagnosed them with high blood pressure and recommended daily exercise. A new promising treatment for psoriasis is currently being researched which may benefit patients.

To enter this psoriasis treatment research study, a patient needs to have a **thickness score of 3 or more**. Below are three images from three separate patients. Select any of the below patient images you think has/have a **thickness of 3 or more** and therefore qualifies for the study.

- A) Patient 1



- B) Patient 2



- C) Patient 3 [only patient that should meet study inclusion criteria]



- D) None of the above patient images have a thickness score of 3 or more, and therefore none of the above patients qualify to enter the study

*Below are the remaining incentive prompts without lesion pictures included. Including the control prompt above, all prompts were randomly allocated to survey participants*

**Empathy:** Three psoriasis patients come to your office. These patients have failed multiple treatment options. They are pleading for a treatment that works since their day-to-day lives have been completely ruined by their psoriasis. A new and promising treatment for psoriasis is currently being researched which may benefit patients.

**Personal relationship:** Three psoriasis patients come to your office. They are your close friends you have known since childhood. A new and promising treatment for psoriasis is currently being researched which may benefit patients.

**Personal/Financial gain:** Three psoriasis patients come into your office. A new and promising treatment for psoriasis is currently being researched which may benefit patients. You are a doctor working in a dermatology clinic that has agreed to enroll eligible patients into the study. The researchers want a total of 200 patients enrolled in their study. They are also extracting study patients from your competitor clinic, which has already enrolled 100 patients. For each patient you enroll, the pharmaceutical company will pay you \$3,000.

**Research criteria:** To qualify for enrollment into a new psoriasis research study offering a new and promising treatment, a patient needs to fulfill multiple disease related criteria. Initial criteria include: having stable psoriasis disease for 6 or more months, having already failed approved treatments, and having a low quality-of-life score. In addition to these initial criteria, a doctor needs to evaluate a patient's psoriatic plaque for redness, scaliness, and thickness. Three psoriasis patients come to your clinic. These patients already meet all of the initial criteria, but they have not received a doctor's evaluation of the severity of their psoriatic plaque lesions based on the characteristics of redness, scaliness, and thickness.

**Logistic constraints:** You are a doctor working in a rural dermatology clinic that sees 100 psoriasis patients per year. You have agreed to take part in a new psoriasis study that is researching a promising treatment which may benefit psoriasis patients. The study expects you to enroll 15 patients this year. The deadline is only one month away and you have enrolled only 11 patients so far. Three psoriasis patients come into your office.

**Professional uncertainty:** Another healthcare provider assessed three of your patients with psoriasis and referred them to you for your assessment. This provider initially assessed the patients' psoriatic plaques and gave them a redness score of 3, a scaling score of 3, and thickness score of 3. A new and promising treatment for psoriasis is currently being researched which may benefit psoriasis patients.

*Below is the second question of the survey. Every participant received this question:*

You are a doctor who has agreed to enroll eligible psoriasis patients into a new drug trial. To qualify for enrollment into this trial a patient needs to have a redness severity score of 3 or more (score ranges from 0-4). In general, you regularly see patients and if they happen to meet study criteria you offer enrollment to them.

Over the last 7 months, you've been treating a psoriasis patient (Patient A) once a month. At every visit you evaluate the redness of Patient A's psoriatic plaque. Your monthly evaluations of Patient A's redness severity score were: 0, 2, 1, 2, 2, 1, 2. You just finished today's visit with Patient A and like last month, you judge their redness score to be 2. You determine that clinically you do not need to see Patient A for another 6 months **by which time drug trial enrollment will be finished.**

Select the answer you want to choose with regards to Patient A:

- A. You would like to schedule a follow-up visit next month before the trial enrollment period ends in order to reassess Patient A's redness severity, just in case their next month's score happens to change and meet the study enrollment criteria.
- B. You do not want to schedule a follow-up visit next month since all of Patient A's prior redness severity scores did not meet study entry criteria, so chances are that the redness score will not change within one month.