PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Impact of psoriasis severity on patient-reported clinical symptoms, health-related quality of life, and work productivity among US patients: real-world data from the Corrona Psoriasis Registry
AUTHORS	Strober, Bruce; Greenberg, Jeffrey; Karki, Chitra; Mason, Marc; Guo, Ning; Hur, Peter; Zhao, Yang; Herrera, Vivian; Lin, Feng; Lebwohl, Mark

VERSION 1 - REVIEW

REVIEWER	Marcus Schmitt-Egenolf Dermatology, Dep. of Public Health & Clinical Medicine, Umeå University, SE-901 85 Umeå, Sweden www.derma.org
REVIEW RETURNED	27-Nov-2018

GENERAL COMMENTS	This is an relevant manuscript providing psoriasis RWE in the US setting. It would be informative to charaterize the "Treatment history" in Table 1 more detailed by mentioning the distribution of the currently received drugs: 1) In the category biologics in % for each mentioned drug: adalimumab, alefacept, certolizumab, efalizumab, etanercept, golimumab, infliximab, ixekizumab, secukinumab, ustekinumab. 2) Likewise for nonbiologics: acitretin, apremilast, cyclosporine, hydroxyurea, methotrexate, mycophenolate, mofetil, sulfasalazine, tofacitinib, 6-thioguanine.

REVIEWER	Howard Thom University of Bristol, United Kingdom. Received consultancy fees from Novartis for work on psoriatic arthritis. However, no connection to manuscript authors or their work.
REVIEW RETURNED	18-Dec-2018

GENERAL COMMENTS	Thank you for the opportunity to review this mostly well written paper. I have a few comments below which I hope the authors can address. The results section in the abstract might benefit from quantifying the strength/magnitude of the association between baseline characteristics, BSA, IGA, and PROs, at least for some key outcomes. I would imagine it's expected that (SLQI, EQ-VAS, WPAI) scores would get worse in tandem with severity (BSA, IGA) but it's not known by how much.

	P9, L31. Why were none of the (non-gender) categorical variables included in the multivariable regression? Variables like history of comorbidities or employment status are as likely confounders as age or disease duration. P9, L42. Please clarify whether the "required" specification for variables of interest ensured that there was no missing data at all. Is the design such that patients would be omitted altogether if that variable was missing? Could this lead to an unrepresentative sample of you target population? Were there any non-responders? At the beginning of the results section, the authors say that 1525/1529 had complete BSA data and 1527/1529 had complete IGA, so there was some missingness. I think this just needs clarification. Supplementary table 1 giving results of the ordinal regression was a little difficult for me to understand. Could you please add a note below the table (or in the main text) clarifying why (for example) the odds of no fatigue vs mild/moderate/severe/very severe fatigue is 1.01 for BSA; this suggests, to me, that odds of no fatigue increases with BSA severity. A little more explanation is needed to ensure the model is understandable. Minor typo. Table 2 label should say by BSA and IGA severity.

VERSION 1 – AUTHOR RESPONSE

Responses to Reviewers

Reviewer #1:

Comment 1: This is an relevant manuscript providing psoriasis RWE in the US setting. It would be informative to charaterize the "Treatment history" in Table 1 more detailed by mentioning the distribution of the currently received drugs:

1) In the category biologics in % for each mentioned drug: adalimumab, alefacept, certolizumab, efalizumab, etanercept, golimumab, infliximab, ixekizumab, secukinumab, ustekinumab.

2) Likewise for nonbiologics: acitretin, apremilast, cyclosporine, hydroxyurea, methotrexate, mycophenolate, mofetil, sulfasalazine, tofacitinib, 6-thioguanine.

Response 1: Thank you for your comment. Unfortunately, it was not the objective of this manuscript to characterize treatment history and the approvals necessary to obtain this data from the Corrona registry would cause a substantial delay in resubmission of this manuscript. We do see value in reporting this information and we will consider publishing this data in a subsequent manuscript.

Reviewer #2:

Comment #1: The results section in the abstract might benefit from quantifying the strength/magnitude of the association between baseline characteristics, BSA, IGA, and PROs, at least for some key outcomes. I would imagine it's expected that (SLQI, EQ-VAS, WPAI) scores would get worse in tandem with severity (BSA, IGA) but it's not known by how much.

Response #1: Thank you for your comments. A full reporting of these associations does not lend itself to being included in the abstract. We have included P values for some key outcomes.

Comment #2: P9, L31. Why were none of the (non-gender) categorical variables included in the multivariable regression? Variables like history of comorbidities or employment status are as likely confounders as age or disease duration.

Response #2: Other factors were assessed in the original modeling and resulted in extreme variation of a feature set across all models. Given the cross-sectional observational exploratory nature of the objective that also included multiple outcome variables, we selected those known a priori common to all models to keep the model simplistic, yet applicable. Further analysis on each individual model would be beyond the approach and scope of this manuscript.

We included the following footnote for Table 2 in the originally submitted manuscript to address this concern: “All models adjusted a priori for age, gender, psoriasis duration, and body mass index at registry enrollment.”

Age and disease duration are not in the regression models. WPAI data was collected following the questionnaire use instruction. The question “daily activities affected” was answered by all patients, while “work time miss” and other work-related questions were answered by employed patients only.

Comment #3: P9, L42. Please clarify whether the "required" specification for variables of interest ensured that there was no missing data at all. Is the design such that patients would be omitted altogether if that variable was missing? Could this lead to an unrepresentative sample of you target population? Were there any non-responders? At the beginning of the results section, the authors say that 1525/1529 had complete BSA data and 1527/1529 had complete IGA, so there was some missingness. I think this just needs clarification.

Response #3: The “required” here indicates questionnaire fields which are required to be completed before submission. This procedure ensures the key variables’ data completeness. Even so, there are some data errors that existed, that is the reason why missingness is seen as 1525/1529 in BSA and 1527/1529 in IGA. The following text has been added to the 1st paragraph of the results to clarify this point, “No patients were omitted from the analysis, but some did not have complete data sets.”

Comment #4: Supplementary table 1 giving results of the ordinal regression was a little difficult for me to understand. Could you please add a note below the table (or in the main text) clarifying why (for example) the odds of no fatigue vs mild/moderate/severe/very severe fatigue is 1.01 for BSA; this suggests, to me, that odds of no fatigue increases with BSA severity. A little more explanation is needed to ensure the model is understandable.

Response #4: The following text has been added to the footnote of supplementary table 1 to clarify this point, “Each “vs” comparison implies the "0 vs 1” structure of a traditional logistic regression. The 0 group is the reference.”

Comment #5: Minor typo. Table 2 label should say by BSA and IGA severity.

Response #5: The title of table 2 has been revised accordingly.