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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

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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

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Conflict of interest disclosure

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Dr. Strober has served as a consultant for AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol-Myers-Squibb, Celgene, Dermavant, Dermira, Janssen, Leo, Eli Lilly, Leo, Medac, Meiji Seika Pharma, Sebela Pharmaceuticals, Menlo Therapeutics, Novartis, Pfizer, GlaxoSmithKline, UCB Pharma, Sirtris, Sun Pharma, Ortho Dermatologics/Valeant, Regeneron, Sanofi-Genzyme; as an investigator for AbbVie, Celgene, Eli Lilly, Janssen, Merck, Boeheringer Ingelheim, GlaxoSmithKline, Pfizer, Galderma, and Sienna; as Co-scientific Director of the Corrona Psoriasis Registry; and has received grant support for the University of Connecticut fellowship program from AbbVie, Janssen, and the National Psoriasis Foundation. Dr. Lebwohl is an employee of Mount Sinai and receives research funds from: Abbvie, Boehringer Ingelheim, Celgene, Eli Lilly, Incyte, Janssen/Johnson & Johnson, Leo Pharmaceuticals, Medimmune/Astra Zeneca, Novartis, Pfizer, Sciderm, Valeant, and ViDac. Dr. Lebwohl is also a consultant for Allergan, Aqua, Boehringer Ingelheim, Corrona, LEO Pharma, Menlo, and Promius. Dr. Greenberg is an employee and shareholder of Corrona, LLC, and has been a consultant to Genentech, Janssen, Novartis, Pfizer, and Eli Lilly. Mr. Mason is an employee of Corrona, LLC, and at the time of the study, was a member of the University of Delaware, Dept. of Behavioral Health and Nutrition Affiliate Faculty (non-remunerative position). Ms. Guo is an employee of Corrona, LLC, and Ms. Karki was an employee of Corrona, LLC, at the time of the study. Drs. Herrera and Dr. Hur are employees of Novartis, and Dr. Zhao and Dr. Lin were employees of Novartis at the time of the study.

Running head: Psoriasis Severity and Quality of Life

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ABSTRACT

Objectives: This analysis examined the association between psoriasis severity, assessed by body surface area (BSA) and the Investigator's Global Assessment (IGA; previously used only in clinical trials) and patient-reported outcomes (PROs) in a real-world setting.

Design: Cross-sectional analysis within the Corrona Psoriasis Registry, an independent, prospective registry

Setting: 70 dermatology practices in the United States by May 31, 2016

Participants: 1529 adult patients with psoriasis being treated with biologic or nonbiologic systemic psoriasis treatment by May 31, 2016

Primary and secondary outcome measures: Psoriasis severity was assessed by percentage of affected BSA (mild [0–5%], moderate [>5–10%], severe [>10–15%], very severe [>15%]), and IGA scores (clear/almost clear [0–1], mild [2], moderate [3], severe [4]). PROs (pain, itch, fatigue; Dermatology Life Quality Index [DLQI]; EuroQoL Visual Analog Scale [EQ-VAS]; Work Productivity and Activity Impairment [WPAI]) were compared across BSA and IGA levels using ANOVA and chi-square tests. The association between psoriasis severity and PROs was examined using multivariable regression models.

Results: The mean age was 50.6 years and 47% of patients were female. Consistently, symptoms worsened, DLQI scores increased, EQ-VAS decreased, and WPAI scores increased with more severe disease when assessed by BSA and IGA. By BSA score, moderate to very severe psoriasis was associated with poorer outcomes for the "impairment while working" and "daily activities compared" WPAI domains. Very severe psoriasis was associated with increased "work hours missed" and "work hours affected." Findings were similar by IGA. Results were confirmed by multivariable regression analyses.

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Conclusions: In a real-world setting, more severe psoriasis, assessed by BSA and IGA, was consistently associated with worse PROs.

Strengths and limitations of this study

- This is the first study to explore the link between psoriasis severity measured by the Investigator's Global Assessment (IGA) and patient reported outcomes (PROs) in a real-world setting
- Due to the cross-sectional study design, causal inferences regarding the relationship between psoriasis severity and PROs cannot be made, and changes in psoriasis severity or PROs over time were not measured
- Patients were recruited from specific dermatology practices, which may have been more focused on psoriasis therapy and, therefore, may not be representative of the general US psoriasis population

Keywords: Psoriasis – Disease Severity – Health-related Quality of Life – Patient-reported Outcomes – Work Productivity

INTRODUCTION

Psoriasis is a chronic, immune-mediated, systemic, inflammatory, and often debilitating skin disease, affecting 2.6%–3.7% of the population in the United States (US).[1] With itching, pain, and scaling as its key symptoms, psoriasis can have a significant impact on patients' health-related quality of life (QoL) and work productivity, depending on disease severity.[2–4]

A growing body of real-world evidence has shown greater psoriasis severity is associated with worse QoL and higher impairments in work productivity.[4,5] Survey data from the National Psoriasis Foundation in the US revealed patients with severe psoriasis had a greater likelihood of

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being unemployed than those having mild disease.[5] In another US survey, Korman and colleagues found increased psoriasis severity was associated with more itching, pain, and scaling; poorer QoL; and greater productivity impairment.[4]

However, methods of measuring psoriasis severity are not used consistently across studies. Affected body surface area (BSA) is a widely known and used measure of psoriasis severity in clinical practice,[6,7] and dermatologists prefer this tool for evaluating patient outcomes.[7] Although BSA has been used in studies of psoriasis-associated QoL, BSA-defined disease severity varies across studies (eg, no/little <1%, mild 1%–2%, severe ≥3%, as used by the National Health and Nutrition Examination Survey[8] vs mild 0%–<3%, moderate 3%–<10%, severe ≥10%, as used by the National Psoriasis Foundation[5]). In addition, using BSA alone does not capture information regarding disease location or symptoms.[7]

Several other severity measures exist, with their respective strengths and limitations. The Psoriasis Area and Severity Index (PASI) score is the most widely used and most thoroughly validated severity measure as a primary endpoint in clinical trials. However, it has not been employed routinely in clinical practice and tends to be poorly understood by clinicians and patients.[6,9,10] In addition, it shows low sensitivity to changes in disease severity in cases with low BSA involvement (ie, <10%).[6] The physician's global assessment (PGA) has been described as being easier to understand compared with the PASI and more similar to assessments of disease used in clinical practice.[10] However, definitions and criteria for points within the PGA values lack standardization, and expert consensus has not yet been reached.[9] Further, a large discordance may exist between PGA and BSA, resulting in either an over- or underestimate of true disease severity.[11]

The 5-point investigator's global assessment (IGA) modified (mod) 2011 scale is typically used in clinical trials and gauges psoriasis severity according to the patient's degree of skin redness,

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thickening, and scaling. Its advantage over other tools (6-point IGA and PGA) is that it more narrowly defines the lowest level of disease severity.[9] However, the IGA mod 2011 scale has not been examined in real-world studies of psoriasis-associated QoL.

Although the IGA mod 2011 scale provides a useful framework for the assessment of disease features, use of this scale alone and without accounting for BSA may not accurately reflect disease severity. In clinical practice, physicians may use a combination of objective assessments of psoriasis severity, such as the IGA mod 2011 scale, BSA, and symptoms, and more subjective measures, such as the emotional impact of psoriasis on the patient.[6]

This analysis aims to define the relationship between psoriasis severity and symptom severity, QoL, and work productivity among US patients with psoriasis in a real-world setting. Separate analyses were conducted, with psoriasis severity defined using both BSA and IGA.

METHODS

Study Design

A cross-sectional study was conducted using the enrollment data from the Corrona Psoriasis Registry to identify associations between disease severity and patient-reported outcomes (PROs).

Patient and Public Involvement

Patients were not involved in determining the design, the recruitment to, or the conduct of this study. All patients enrolled in the Corrona Psoriasis Registry receive a patient newsletter that shares study results twice per year.

Data Source

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The Corrona Psoriasis Registry is an independent, prospective observational cohort launched in April 2015 in collaboration with the National Psoriasis Foundation, with a target enrollment of 10,000 patients with psoriasis from 200 sites throughout the US. The study inclusion criteria matched those for registry enrollment: Patients must be at least 18 years old, must have been given a psoriasis diagnosis by a dermatologist, and had to have begun treatment with a qualifying biologic or nonbiologic systemic psoriasis treatment either within the 12 months preceding or on the day of the enrollment visit. Data collected from the registry launch date (April 2015) through May 31, 2016 were analyzed for the study.

Study Measures

Data related to demographics, disease severity (BSA and IGA scores), disease duration, prior and current use of systemic treatments for psoriasis, physician-reported medical history (eg, cardiovascular disease, diabetes mellitus, cardiovascular disease and diabetes risk factors, lymphoma/malignancy, Crohn's disease, anxiety/depression), and PROs collected at registry enrollment were examined. Patients reported their levels of pain, itching, and fatigue on a visual analog scale (VAS) of 0 (none) to 100 (very severe) and completed 2 validated and commonly used health-related quality-of-life (HRQoL) assessment instruments: the Dermatology Life Quality Index (DLQI)[12] and the visual analog component of the EuroQoL Five Dimensions Questionnaire VAS (EQ-VAS).[13] In addition, the patients completed the Work Productivity and Activity Impairment (WPAI) questionnaire.[14] Dermatologists assessed disease severity in terms of the percentage of total BSA affected and/or the IGA mod 2011 scale score. BSA percentages were categorized as mild (0–5%), moderate (>5–10%), severe (>10–15%), and very severe (>15%). The 5-point IGA was used to categorize levels of skin induration, scaling, and redness as clear/almost clear (0–1), mild (2), moderate (3), and severe (4).

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Dermatology Life Quality Index

The DLQI, which is a dermatology-specific tool to measure HRQoL, requires respondents to answer 10 questions classified within 6 domains: symptoms and feelings, daily activities, leisure activities, work and school, personal relationships, and treatment. Respondents indicate the degree to which they experienced problems for a recall period of 1 week, and responses are assessed with a 4-point Likert scale: 0 (not at all/not relevant), 1 (a little), 2 (a lot), and 3 (very much). Responses are calculated for the total DLQI score, which is 0–30. Higher scores indicate worse HRQoL.

EuroQol Visual Analog Scale

The EuroQol Visual Analog Scale (EQ-VAS) is a non-disease–specific HRQoL assessment tool in which respondents indicate their state of health on the day of assessment on a scale of 0–100, with 100 being the best imaginable state of health and 0 being the worst imaginable state of health.

Work Productivity and Activity Impairment

The WPAI questionnaire measures impairment in work hours missed, work productivity and impairment, and daily activities. Based on a scale of 1 (no effect) to 10 (completely prevented patient from working/participating), respondents report the following domains for the previous week: work hours missed, work hours affected, impairment while working, and daily activities impaired. Daily activities include housework, shopping, exercise, and studying. Responses for all domains, except for daily activities, are valid only if the respondent is employed.

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Statistical Analysis

Data regarding patient characteristics, disease characteristics, comorbidities, treatment history, and PROs collected at registry enrollment were reported for the overall study population and by BSA and IGA disease severity groups. Frequency counts and percentages were reported for all categorical variables (sex, employment status, disability status, psoriatic arthritis diagnosis, treatment history, and history of comorbidities). Means and standard deviations (SDs) were reported for all continuous variables (age, body mass index [BMI], psoriasis duration, BSA, and IGA). Significance testing with analysis of variance (ANOVA) was used for continuous variables, and chi-square tests of association were employed for categorical variables to investigate if any differences in values were present across the levels of BSA and IGA disease severity.

Multivariable linear regression was used to model the association between disease severity levels and PROs. To address potential confounding, the model adjusted a priori for age, gender, disease duration, and BMI at enrollment. IGA and BSA were modeled separately. Ordinal regression modeling was performed as a confirmatory sensitivity analysis.

Statistical analyses included patients who had complete data on analysis variables at enrollment. To minimize the potential impact of missing data, variables of interest were specified as "required" during data collection; therefore, no statistical techniques were needed to account for missing data. All analyses were performed using STATA (StataCorp LP 2015, Stata Statistical Software: Release 14, Version 2, College Station, TX) with significance set at the $P < 0.05$ level.

Protection of Patients

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The study used blinded data to maintain patient confidentiality. The Corrona Psoriasis Registry was approved by both local and central review boards at the participating sites. All patients provided written informed consent prior to their enrollments in the registry.

RESULTS

Study Sample Characteristics

As of May 31, 2016, 1529 patients were enrolled in the registry; the mean age was 50 years and 47% were female. Among these patients, 1525 had complete BSA data and 1527 had complete IGA data, and the BSA and IGA patients were similar in age and gender types.

Similar proportions of patients were biologic experienced and had prior nonbiologic systemic therapy across disease severity groups (BSA and IGA). The proportion of patients who were biologic experienced ranged from 53%–59% across BSA categories and 53%–57% across IGA categories. Proportions of patients who had been treated with nonbiologic systemic therapies ranged from 45%–49% across BSA categories, and 42%–54% across IGA categories. The disease severity groups also had similar disease durations (**Table 1**).

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Table 1. Baseline patient characteristics by BSA severity categories

	BSA Severity Groups (n = 1525)				IGA Severity Groups (n = 1527)			
	Mild: 0–5% (n = 873)	**Moderate: >5–10% (n = 316)**	**Severe: >10–15% (n = 109)**	**Very Severe: >15% (n = 227)**	**Clear/ almost clear: 0/1 (n = 375)**	**Mild: 2 (n = 404)**	**Moderate: 3 (n = 586)**	**Severe: 4 (n = 162)**
Patient characteristics								
Female, n (%)	439 (50)	136 (43)	53 (49)	88 (39)	186 (50)	205 (51)	262 (45)	64 (40)
Age (years), mean (SD)	50.6 (14.4)	50.8 (13.9)	49.8 (14.8)	50.4 (14.9)	50 (14.3)	51.5 (14.8)	50.7 (14.1)	49.5 (14.9)
Body weight (kg), mean (SD)	87.5 (22.2)	88.7 (24.8)	92.3 (23.8)	95.4 (27.3)	85.6 (19.6)	89.6 (24.3)	90.0 (25.3)	94.1 (24.9)
Body mass index (kg/m^2), mean (SD)	30.1 (6.8)	30.2 (7.3)	32.0 (8.1)	32.2 (8.4)	29.2 (5.7)	31.0 (7.6)	30.8 (7.7)	32.0 (8.0)
Employed, n (%)	575 (66)	209 (67)	72 (66)	137 (61)	261 (70)	258 (64)	374 (64)	101 (63)

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Disabled, n (%)	59 (7)	28 (9)	8 (7)	31 (14)	20 (5)	22 (5)	60 (10)	24 (15)
Disease characteristics								
Psoriasis duration (years), mean (SD)	15.6 (13.8)	15.1 (12.9)	15.7 (13.7)	17.2 (13.4)	15.8 (13.2)	17.0 (14.8)	15.2 (13.2)	14.1 (12.4)
Psoriatic arthritis diagnosis, n (%)	369 (42)	120 (38)	37 (34)	90 (40)	152 (41)	165 (41)	223 (38)	78 (48)
Treatment history								
Biologic naïve, n (%)	410 (47)	148 (47)	48 (44)	93 (41)	165 (44)	188 (47)	277 (47)	70 (43)
Biologic experienced, n (%)	463 (53)	168 (53)	61 (56)	134 (59)	210 (56)	216 (53)	309 (53)	92 (57)
Nonbiologic systemic therapy, n (%)	389 (45)	141 (45)	52 (48)	111 (49)	169 (45)	170 (42)	268 (46)	88 (54)
Psoriasis severity								
BSA (%), mean (SD)	2.2 (1.7)	8.3 (1.6)	13.4 (1.5)	34.8 (18.8)	1.3 (3.3)	5.7 (8.5)	11.7 (12.1)	26.6 (21.9)
IGA, mean (SD)	1.7 (1.1)	2.8 (0.6)	3.1 (0.5)	3.3 (0.7)	0.6 (0.5)	2.0 (0.0)	3.0 (0.0)	4.0 (0.0)

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History of comorbidities								
Cardiovascular disease, n (%)	103 (12)	35 (11)	13 (12)	30 (13)	48 (13)	52 (13)	66 (11)	16 (10)
Coronary artery disease, n (%)	25 (3)	4 (1)	2 (2)	12 (5)	9 (2)	16 (4)	12 (2)	6 (4)
Congestive heart failure, n (%)	7 (1)	9 (3)	0 (0)	5 (2)	3 (1)	5 (1)	11 (2)	2 (1)
Stroke, n (%)	15 (2)	3 (1)	2 (2)	1 (0)	6 (2)	8 (2)	6 (1)	1 (1)
Cardiovascular disease/diabetes risk factors, n (%)	413 (47)	159 (50)	51 (47)	113 (50)	167 (45)	190 (47)	296 (51)	84 (52)
Hypertension, n (%)	327 (38)	126 (40)	45 (41)	95 (42)	139 (37)	152 (38)	239 (41)	64 (40)
Hyperlipidemia, n (%)	253 (29)	97 (31)	23 (21)	60 (26)	96 (26)	123 (31)	168 (29)	46 (28)
Metabolic syndrome, n (%)	13 (1)	3 (1)	3 (3)	7 (3)	5 (1)	8 (2)	7 (1)	6 (4)
Diabetes mellitus, n (%)	111 (13)	50 (16)	17 (16)	38 (17)	40 (11)	55 (14)	92 (16)	29 (18)

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Lymphoma/malignancy, n (%)	40 (5)	20 (6)	5 (5)	9 (4)	18 (5)	17 (4)	34 (6)	5 (3)
Crohn's disease, n (%)	4 (0)	3 (1)	0 (0)	1 (0)	2 (1)	3 (1)	2 (0)	1 (1)
Depression, n (%)	161 (18)	58 (18)	24 (22)	48 (21)	56 (15)	79 (20)	120 (20)	36 (22)
Anxiety, n (%)	154 (18)	52 (16)	25 (23)	44 (19)	69 (18)	75 (19)	98 (17)	33 (20)

BSA, body surface area; IGA, Investigator's Global Assessment; SD, standard deviation.

History of comorbidities/medical history: cardiovascular disease: combined histories of myocardial infarction, acute coronary syndrome, coronary artery disease, congestive heart failure, peripheral artery disease, cardiac revascularization procedure, ventricular arrhythmia, cardiac arrest, unstable angina, stroke, transient ischemic attack, pulmonary embolism, carotid artery disease, deep vein thrombosis or other cardiovascular event; cardiovascular/diabetes risk factors: hypertension, hyperlipidemia, or metabolic syndrome; lymphoma/malignancy: lymphoma, breast, lung, skin (excluding nonmelanoma skin cancer), or other.

Prior use of biologics: adalimumab, alefacept, certolizumab, efalizumab, etanercept, golimumab, infliximab, ixekizumab, secukinumab, ustekinumab, investigational drugs, and other patient-specified biologics.

Prior use of nonbiologics: acitretin, apremilast, cyclosporine, hydroxyurea, methotrexate, mycophenolate, mofetil, sulfasalazine, tofacitinib, 6-thioguanine, and other patient-specified nonbiologics.

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The most common comorbidities were hypertension (BSA range: 38%–42%; IGA range: 37%–41%), hyperlipidemia (BSA range: 21%–31%; IGA range: 26%–31%), depression (BSA range 18%–22%; IGA range 15%–22%), and anxiety (BSA range: 16%–23%; IGA range: 17%–20%; **Table 1**). Across BSA and IGA groups, at least 60% of patients worked full-time or part-time. Increasing proportions of patients were disabled as severity increased according to BSA (range: 7%–14%) and IGA (range: 5%–15%; **Table 1**).

Patient-Reported Outcomes Descriptive Analysis Results

Fatigue, itching, and pain VAS scores worsened with disease severity as assessed by both BSA and IGA (**Figures 1A and 1B**). Across BSA categories, mean fatigue scores ranged from 26.5–40.2, itching was 24.7–55.7, and pain was 15.2–41.7. Among IGA categories, mean fatigue scores ranged from 21.9–41.8, itching was 12.1–57.3, and pain was 7.4–44.3.

DLQI scores worsened and EQ-VAS health status decreased with increasing disease severity (**Figures 2A and 2B** and **Figures 3A and 3B**). Across BSA and IGA categories, mean DLQI scores ranged from 5.2–10.2 and 4.3–9.7, respectively. Mean EQ-VAS scores ranged from 62.9 (very severe) to 76.4 (mild) across BSA categories and 62.1 (severe) to 78.8 (clear/almost clear) across IGA categories, with higher scores indicating better health. Work productivity impairment also increased with greater disease severity (**Figures 4A and 4B).** By BSA category, the "work hours missed" domain was 2.3%–5.9%, "impairment while working" was 8.4%–19.0%, "work hours affected" was 9.5%–20.0%, and "daily activities impaired" was 13.1%–31.5%. By IGA category, the "work hours missed" domain was 1.2%–4.2%, "impairment while working" was 5.5%–19.9%, "work hours affected" was 6.0%–20.9%, and "daily activities impaired" was 8.2%–34.1%.

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Multivariable Linear Regression Model

The multivariable linear regression models confirmed the overall pattern in the descriptive results, demonstrating an association between greater disease severity when assessed by BSA and IGA, and worsening symptoms, worse QoL, and greater work productivity and activity impairment. Worsening itch, pain, and fatigue were significantly associated with increases in BSA and IGA levels: $P < 0.001$ for moderate, severe, and very severe BSA (reference: mild) and for mild, moderate, and severe IGA (reference: clear/almost clear). Overall DLQI and EQ-VAS scores also worsened with disease severity ($P < 0.05$ for each level of BSA and IGA) (**Table 2**).

In BSA models, the moderate, severe, and very severe psoriasis categories were significantly associated with poorer outcomes in the WPAI domains of "impairment while working" and "daily activities impaired" compared with mild severity (all $P < 0.05$) (**Table 2**). Very severe disease was significantly associated with increased "work hours missed" ($P < 0.05$), and moderate and very severe disease were associated with increased "work hours affected" (both $P < 0.05$) compared with mild disease.

Table 2. Linear regression results by BSA severity

	BSA Severity Groups (reference = mild: 0–5%)			**IGA Severity Groups (reference = clear/almost clear: 0/1)**		
Parameter, coefficient (95% CI)	**Moderate: >5–10%**	**Moderate: 3**	**Severe: 4**	**Mild: 2**	**Moderate: 3**	**Severe: 4**
Symptoms						

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Fatigue	9.50 (5.87, 13.14)*	13.13 (7.49, 18.76)*	12.67 (8.52, 16.82)*	7.52 (3.55, 11.49)*	12.45 (8.79, 16.11)*	19.69 (14.48, 24.91)*
Itch	23.17 (19.27, 27.06)*	25.42 (19.40, 31.44)*	32.10 (27.66, 36.54)*	18.27 (14.21, 22.33)*	37.15 (33.41, 40.90)*	45.70 (40.36, 51.04)*
Pain	15.09 (11.46, 18.71)*	19.37 (13.76, 24.97)*	27.68 (23.55, 31.82)*	10.36 (6.48, 14.24)*	25.15 (21.57, 28.72)*	37.37 (32.27, 42.47)*
DLQI	1.91 (1.17, 2.66)*	3.40 (2.25, 4.56)*	5.26 (4.41, 6.11)*	0.85 (0.04, 1.67)*	3.76 (3.01, 4.52)*	5.47 (4.40, 6.55)*
EQ-VAS	–5.14 (–7.91, –2.36)*	–7.34 (–11.64, –3.04)*	–12.98 (–16.14, –9.81)*	–3.47 (-6.51, –0.43)*	–7.35 (–10.16, –4.55)*	–15.15 (–19.15, –11.55)*
WPAI questionnaire						
Work time missed	0.58 (–1.38, 2.55)	–0.71 (-3.68, 2.26)*	3.50 (1.17, 5.82)*	1.13 (–1.01, 3.27)	2.96 (1.01, 4.92)*	2.87 (0.01, 5.73)*
Impairment while working	8.00 (4.58, 11.39)*	5.22 (0.06, 10.39)*	11.52 (7.49, 15.55)*	2.87 (–0.78, 6.53)	11.56 (8.22, 14.91)*	15.14 (10.29, 20.00)*

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Working hours affected	8.79 (5.20, 12.37)*	5.17 (–0.27, 10.61)	11.44 (7.19, 15.70)*	3.49 (–0.35, 7.33)*	13.05 (9.54, 16.55)*	15.65 (10.54, 20.77)*
Daily activities affected	10.28 (7.01, 13.54)*	11.54 (6.50, 16.59)*	19.69 (15.97, 23.40)*	7.88 (4.34, 11.42)*	15.04 (11.78, 18.31)*	26.36 (21.70, 31.01)*

*Significant at $P < 0.05$.

BSA, body surface area; CI, confidence interval; DLQI, Dermatology Life Quality Index; EQ-VAS, EuroQoL visual analog scale; IGA, Investigator's Global Assessment, WPAI, Work Productivity and Activity Impairment.

Fatigue, itch, and pain symptom scale: 0–100; DLQI scale: 0–30; EQ-VAS scale: 0–100; WPAI scale: 0–10.

All models adjusted a priori for age, gender, psoriasis duration, and body mass index at registry enrollment.

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In IGA models, mild, moderate, and severe psoriasis categories were significantly associated with worse outcomes for the WPAI domain of "daily activities impaired" compared with clear/almost clear (all $P < 0.05$). Compared with the mild psoriasis category, moderate and severe psoriasis categories were significantly associated with poorer outcomes in the domains of "work hours missed," "impairment while working," and "work hours affected" (all $P < 0.05$).

Sensitivity Analysis

Ordinal regression modeling was performed as a sensitivity analysis to confirm the results of the linear regression; results confirmed a consistent trend, with increasing severity of disease associated with worsening QoL and greater impairment in work productivity and activity. Results of the proportional odds models for BSA and IGA disease severity categories are shown in **Supplementary Table 1**.

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DISCUSSION

In this cross-sectional analysis of the Corrona Psoriasis Registry, multivariable linear regression models showed patient-reported symptoms, QoL, and work productivity worsened with increasing disease severity, as measured by BSA and IGA. The results were statistically significant across all levels of psoriasis severity for patient-reported pain, itch, and fatigue; DLQI overall scores; EQ-VAS; and the "daily activities impaired" domain of the WPAI questionnaire. For the WPAI domains "work hours missed," "impairment while working," and "work hours affected" outcomes were significantly worse for patients with the highest severity of psoriasis (BSA = very severe, IGA = severe). Findings were overall consistent between the BSA and IGA results.

To the authors' knowledge, the present study was the first to explore the link between IGA and PROs in a real-world setting. Physician's Global Assessment has been used previously in real-world settings in both postmarketing safety studies[15,16] and patient registries.[16-19] A multicenter, prospective study conducted in Spain found psoriasis severity was the primary factor affecting QoL. Although PGA data were collected in that study, PASI was ultimately used for the multivariate modeling.[20]

Of note, the BSA and IGA categories as defined in the present study differ somewhat from those used in prior research. The present study used the 5-point mod 2011 scale, which differs from the 6-point scales used in some clinical trials of biologic treatments for psoriasis[9] in that the "almost clear" category is more narrowly defined compared with the "minimal" category in PGA and the other IGA versions.[9] The category cutoff points for BSA used in the present study (ie, mild: 0%–5%, moderate: >5%–10%, severe: >10%–15%, and very severe: >15%) also differed from those that have been used in certain studies and referred to in guidelines and expert consensus

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statements (eg, mild 0%–<3%, moderate 3%–<10%, and severe ≥10%;[5] moderate to severe >10%[21], no/little <1%, mild 1%–2%, severe ≥3% [8]). The addition of the "very severe" category in the present study may shed light on specific unmet medical needs in this segment of the population with psoriasis. Further research is required to fully understand how differences in BSA categorization may impact results across clinical trials and observational studies.

In a prior study by Korman *et al* of psoriasis severity and PROs, severity of symptoms, EQ-5D, DLQI, and WPAI domains were assessed using BSA category (mild, moderate, or severe as determined by a physician).[4] Although the categorization of psoriasis severity differed, the results are generally consistent with the findings of the present study, for which severity of fatigue, itching, and pain; DLQI total scores; and WPAI domains worsened with increasing disease severity.[4] In addition, lower EQ-5D summary scores were reported with increasing disease severity,[4] similar to the lower EQ-VAS scores observed in the present study.

Although the present study demonstrates the association between increased psoriasis severity and worsened PROs, future research may clarify this relationship. The present analysis did not address the potential for the outcomes of interest to be highly correlated with one another. For instance, previous research by Lewis-Beck *et al.* found an inverse relationship between itching, pain, and scaling severity and work productivity.[22] Further research may investigate how QoL and work productivity measures may interact with one another in the context of psoriasis severity. In addition, due to the cross-sectional study design, the results represent psoriasis severity and PROs at one timepoint. Future research using longitudinal data could show how changes in psoriasis severity may relate to changes over time in QoL and work productivity. In addition, particularly for a longitudinal study, the combination and interaction of BSA and IGA as a single measure of severity could prove informative.

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The results of this study must be interpreted in the context of the source of the data, study design, and analysis methods. First, this study was a cross-sectional analysis, which does not allow for causal inferences regarding psoriasis severity and the outcomes of interest. Second, the patients enrolled in the registry were recruited from specific dermatology practices, which may have been more focused on psoriasis therapy and, therefore, may not be representative of the general US psoriasis population. The linear regression model was robust to the non-normal distribution of the data; however, estimates at the extreme lower and upper levels of severity may have been over- or underestimated.

CONCLUSIONS

Increased psoriasis severity as measured by both BSA and IGA categories was associated with worsened PROs in this US-based psoriasis registry study. Future research is warranted to understand the potential interrelationships between PROs and to understand whether longitudinal improvements in psoriasis severity are associated with improvements in PROs.

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FOOTNOTES

Contributors: BS interpreted the results, critically reviewed the manuscript, and agreed to be accountable for all aspects of the manuscript. JDG helped design the study, acquired the data, critically reviewed the manuscript, and agreed to be accountable for all aspects of the manuscript. CK helped design the study, interpreted the results, and critically reviewed the manuscript. MM helped design the study, collected the data, undertook the data analysis, interpreted the results, and critically reviewed the manuscript. NG undertook the data analysis, interpreted the results, and critically reviewed the manuscript. PH helped design the study, interpreted the results, and critically reviewed the manuscript. YZ helped design the study, interpreted the results, and critically reviewed the manuscript. VH interpreted the results and critically reviewed the manuscript. FL helped design the study, interpreted the results, and critically reviewed the manuscript. ML helped design the study, acquired the data, and critically reviewed the manuscript.

Funding: This study was sponsored by Corrona, LLC and the analysis was funded by Novartis. Access to study data was limited to Corrona and Corrona statisticians completed all of the analysis; all authors contributed to the interpretation of the results. Corrona has been supported through contracted subscriptions in the last 2 years by AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Crescendo, Eli Lilly and Company, Genentech, Gilead, GSK, Janssen, Momenta Pharmaceuticals, Novartis, Pfizer Inc., Regeneron, Roche, Merck, UCB, and Valeant.

Parts of this manuscript were presented as a poster March 3–7, 2017 at 75th Annual Meeting of the American Academy of Dermatology in Orlando, Florida, USA.

Competing interests: BS has served as a consultant for AbbVie, Almirall, Amgen, AstraZeneca, Boehringer Ingelheim, Celgene, Dermira, Galderma, GlaxoSmithKline, Eli Lilly, Janssen, LEO

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Pharma, Medac, Meiji Seika Pharma, Menlo Therapeutics, Novartis, Ortho Dermatologics/Valeant, Pfizer, Regeneron, Sanofi-Genzyme, Sun Pharma, UCB Pharma; as Co-scientific Director of the Corrona Psoriasis Registry; and has received grant support for the University of Connecticut fellowship program from AbbVie and Janssen. ML is an employee of Mount Sinai and receives research funds from: Abbvie, Boehringer Ingelheim, Celgene, Eli Lilly, Incyte, Janssen/Johnson & Johnson, Leo Pharmaceuticals, Medimmune/Astra Zeneca, Novartis, Pfizer, Sciderm, Valeant, and ViDac. ML is also a consultant for Allergan, Aqua, Boehringer Ingelheim, Corrona, LEO Pharma, Menlo, and Promius. JDG is an employee and shareholder of Corrona, LLC, and has been a consultant to Genentech, Janssen, Novartis, Pfizer, and Eli Lilly. MM is an employee of Corrona, LLC, and at the time of the study, was a member of the University of Delaware, Dept. of Behavioral Health and Nutrition Affiliate Faculty (non-remunerative position). NG is an employee of Corrona, LLC, and CK was an employee of Corrona, LLC, at the time of the study. VH and PH are employees of Novartis, and YZ and FL were employees of Novartis at the time of the study.

Patient consent: All patients were required to provide written, informed consent prior to participating.

Ethics approval: All participating investigators were required to obtain full board approval for research involving human subjects through a central institutional review board (IntegReview). For academic investigative sites that did not receive a waiver to use the central IRB, full board approval was obtained for the respective governing IRB, and documentation of approval was submitted to the sponsor prior to initiating any study procedures.

Data sharing statement: No additional data are available.

Acknowledgments

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Access to study data was limited to Corrona, and Corrona statisticians completed all of the analysis; all authors contributed to the interpretation of the results. Corrona has been supported through contracted subscriptions in the last 2 years by AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Crescendo, Eli Lilly and Company, Genentech, Gilead, GSK, Janssen, Merck, Momenta Pharmaceuticals, Novartis, Pfizer, Regeneron, Roche, UCB, and Valeant. Novartis participated in the interpretation of data, review, and approval of the manuscript.

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REFERENCES

1 Rachakonda TD, Schupp CW, Armstrong AW. Psoriasis prevalence among adults in the United States. *J Am Acad Dermatol* 2014;**70**:512–6.

2 Bhosle MJ, Kulkarni A, Feldman SR, et al. Quality of life in patients with psoriasis. *Health Qual Life Outcomes* 2006;**4**:35.

3 Gelfand JM, Feldman SR, Stern RS, et al. Determinants of quality of life in patients with psoriasis: A study from the US population. *J Am Acad Dermatol* 2004;**51**:704–8.

4 Korman NJ, Zhao Y, Pike J, *et al*. Relationship between psoriasis severity, clinical symptoms, quality of life and work productivity among patients in the USA. *Clin Exp Dermatol* 2016;**41**:514–21.

5 Armstrong AW, Schupp C, Wu J, *et al.* Quality of life and work productivity impairment among psoriasis patients: findings from the National Psoriasis Foundation survey data 2003-2011. *PLoS One* 2012;**7**:e52935.

6 Menter A, Gottlieb A, Feldman SR*, et al*. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 1. Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. *J Am Acad Dermatol* 2008;**58**:826–850.

7 Armstrong AW, Siegel MP, Bagel J*, et al.* From the Medical Board of the National Psoriasis Foundation: Treatment targets for plaque psoriasis. *J Am Acad Dermatol* 2017;**76**:290–8.

8 Helmick CG, Lee-Han H, Hirsch SC, *et al*. Prevalence of psoriasis among adults in the U.S.: 2003-2006 and 2009-2010 National Health and Nutrition Examination Surveys. *Am J Prev Med* 2014;**47**:37–45.

9 Langley RG, Feldman SR, Nyirady J, *et al.* The 5-point Investigator's Global Assessment (IGA) Scale: a modified tool for evaluating plaque psoriasis severity in clinical trials. *J Dermatolog Treat* 2015;**26**:23–31.

For peer review only

10 Feldman SR, Krueger GG. Psoriasis assessment tools in clinical trials. *Ann Rheum Dis* 2005; **64 Suppl 2**:ii65–8;discussion ii69–73.

11 Duffin KC, Papp KA, Bagel J, et al. Evaluation of the Physician Global Assessment and Body Surface Area Composite Tool for assessing psoriasis response to apremilast therapy: results from ESTEEM 1 and ESTEEM 2. *J Drugs Dermatol* 2017;**16**:147–53.

12 Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)—a simple practical measure for routine clinical use. *Clin Exp Dermatol* 1994;**19**:210–6.

13 EuroQol Group. EuroQol—a new facility for the measurement of health-related quality of life. *Health Policy* 1990;**16**:199–208.

14 Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. *Pharmacoeconomics* 1993;**4**:353–65.

15 Kimball AB, Pariser D, Yamauchi PS, *et al*. OBSERVE-5 interim analysis: An observational postmarketing safety registry of etanercept for the treatment of psoriasis. *J Am Acad Dermatol* 2013;**68**:756–64.

16 Menter A, Thaci D, Papp KA, *et al.* Five-year analysis from the ESPRIT 10-year postmarketing surveillance registry of adalimumab treatment for moderate to severe psoriasis. *J Am Acad Dermatol* 2015;**73**:410–9,e416.

17 Strober BE, Bissonnette R, Fiorentino D, *et al*. Comparative effectiveness of biologic agents for the treatment of psoriasis in a real-world setting: results from a large, prospective, observational study (Psoriasis Longitudinal Assessment and Registry [PSOLAR]). *J Am Acad Dermatol* 2016;**74**:851-861,e854.

18 Huynh DH, Boyd TA, Etzel CJ, *et al*. Persistence of low disease activity after tumour necrosis factor inhibitor (TNFi) discontinuation in patients with psoriatic arthritis. *RMD Open* 2017;**3**:e000395.

For peer review only

19 Lindstrom Egholm C, Krogh NS, Pincus T, *et al.* Discordance of global assessments by patient and physician is higher in female than in male patients regardless of the physician's sex: data on patients with rheumatoid arthritis, axial spondyloarthritis, and psoriatic arthritis from the DANBIO registry. *J Rheumatol* 2015;**42**:1781–5.

20 Daudén E, Pujol RM, Sanchez-Carazo JL, *et al.* Demographic characteristics and health-related quality of life of patients with moderate-to-severe psoriasis: the VACAP study. *Actas Dermosifiliogr* 2013;**104**:807–14.

21 Mrowietz U, Kragballe K, Reich K, *et al.* Definition of treatment goals for moderate to severe psoriasis: a European consensus. *Arch Dermatol Res* 2011;**303**:1–10.

22 Lewis-Beck C, Abouzaid S, Xie L, *et al.* Analysis of the relationship between psoriasis symptom severity and quality of life, work productivity, and activity impairment among patients with moderate-to-severe psoriasis using structural equation modeling. *Patient Prefer Adherence* 2013;**7**:199–205.

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FIGURES

Figure 1A and 1B. Patient-reported Symptoms by BSA Severity Group (A) and IGA Severity Group (B)

Fatigue, itch, and pain symptom scale: 0–100.

BSA, Body surface area; IGA, Investigator's Global Assessment; VAS, visual analogue scale.

Figure 2A and 2B. DLQI Scores by BSA Severity Group (A) and IGA Severity Group (B)

DLQI scale: 0–30.

DLQI, Dermatology Life Quality Index; BSA, body surface area; IGA, Investigator's Global Assessment.

Figure 3A and 3B. EQ-VAS by BSA Severity Group (A) and IGA Severity Group (B)

EQ-VAS scale: 0–100.

EQ-VAS, EuroQoL visual analog scale; BSA, body surface area; IGA, Investigator's Global Assessment; VAS, visual analog scale.

Figure 4A and 4B. WPAI Domains by BSA Severity Group (A) and IGA Severity Group (B)

WPAI, Work Productivity and Activity Impairment; BSA, body surface area; IGA, Investigator's Global Assessment.

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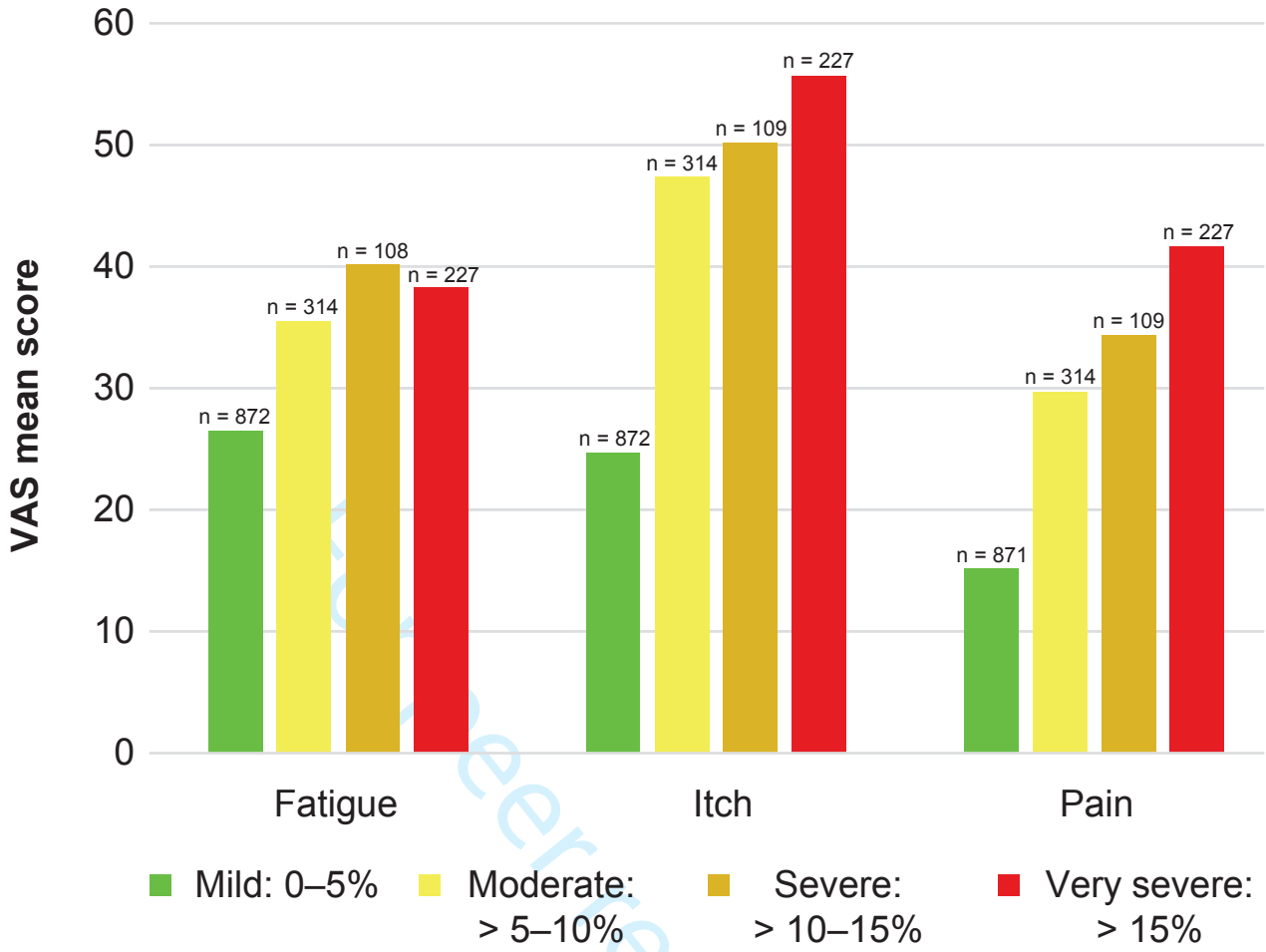

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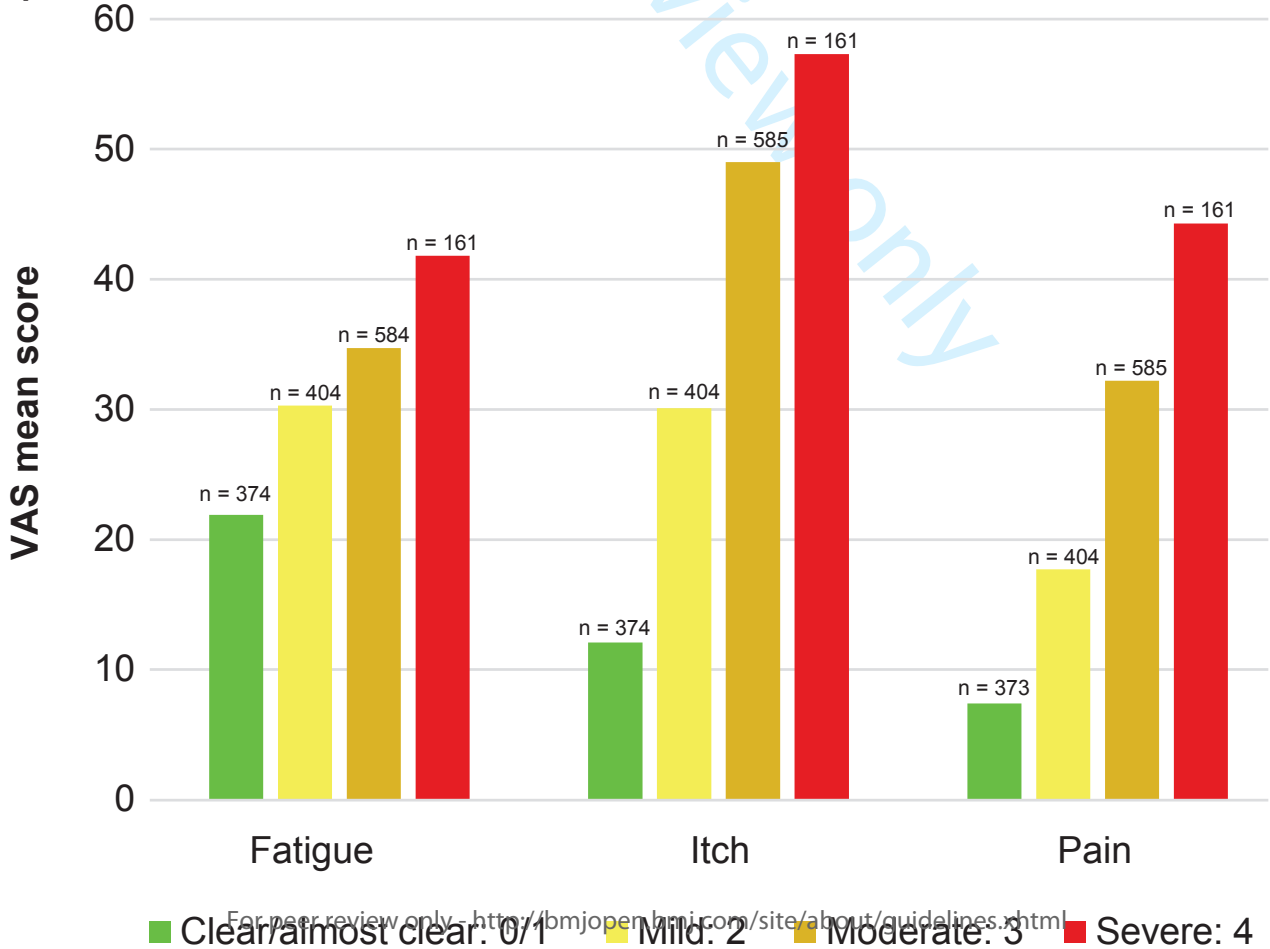

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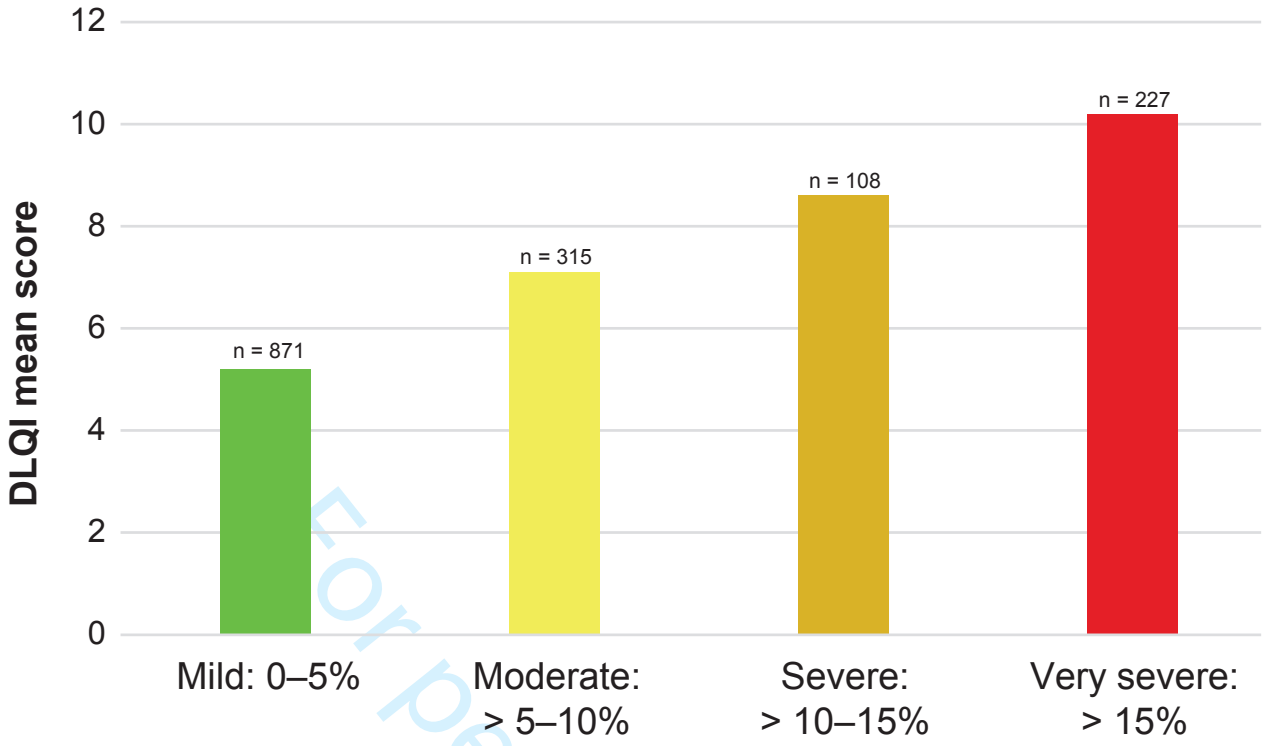

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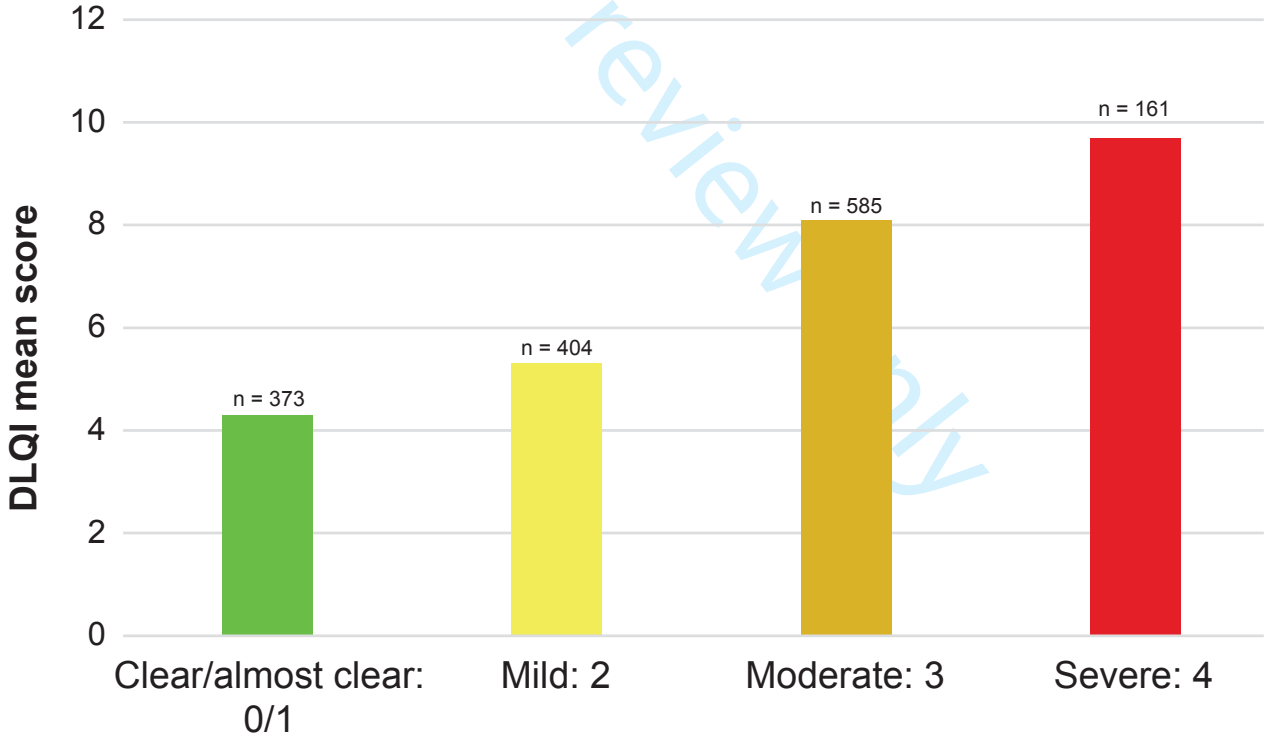

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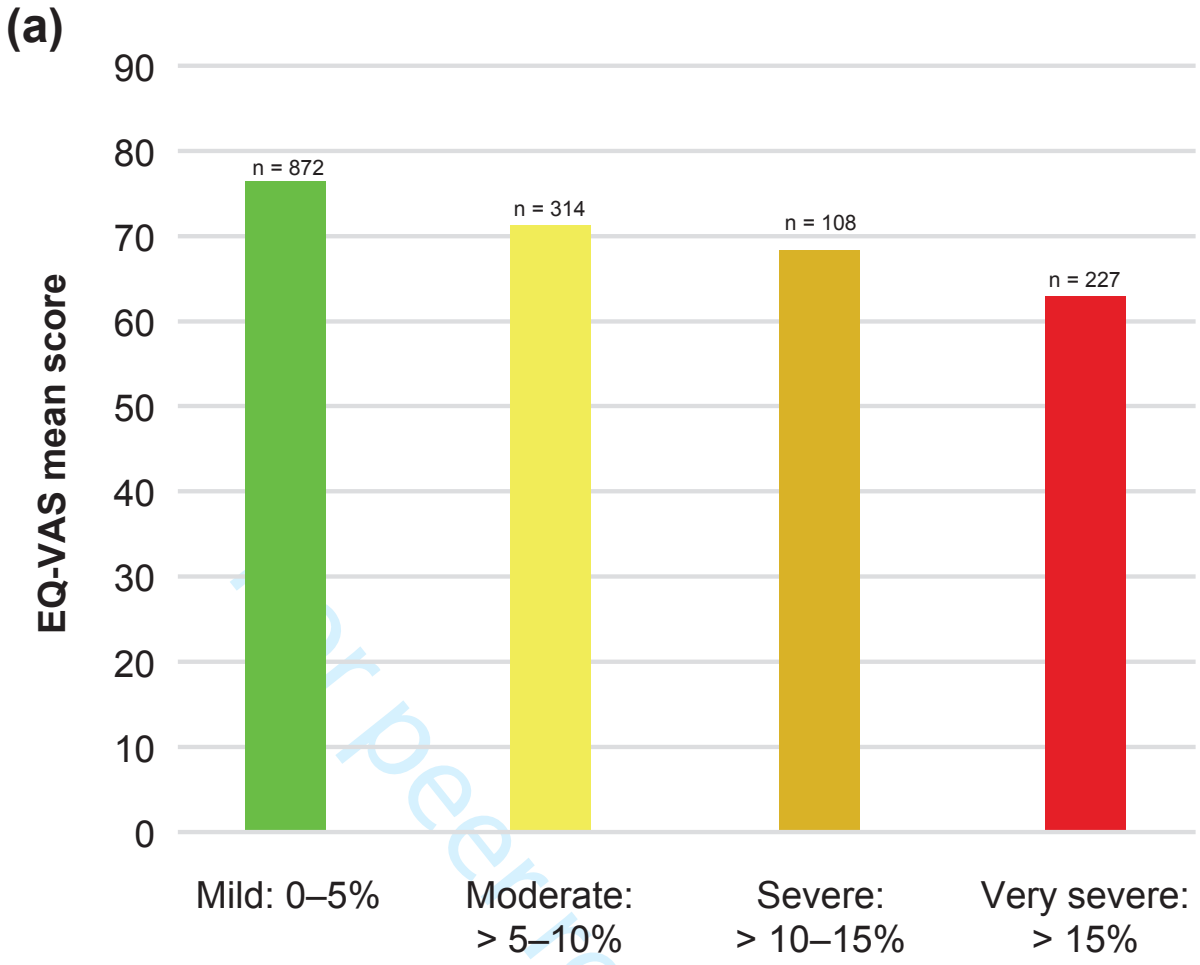

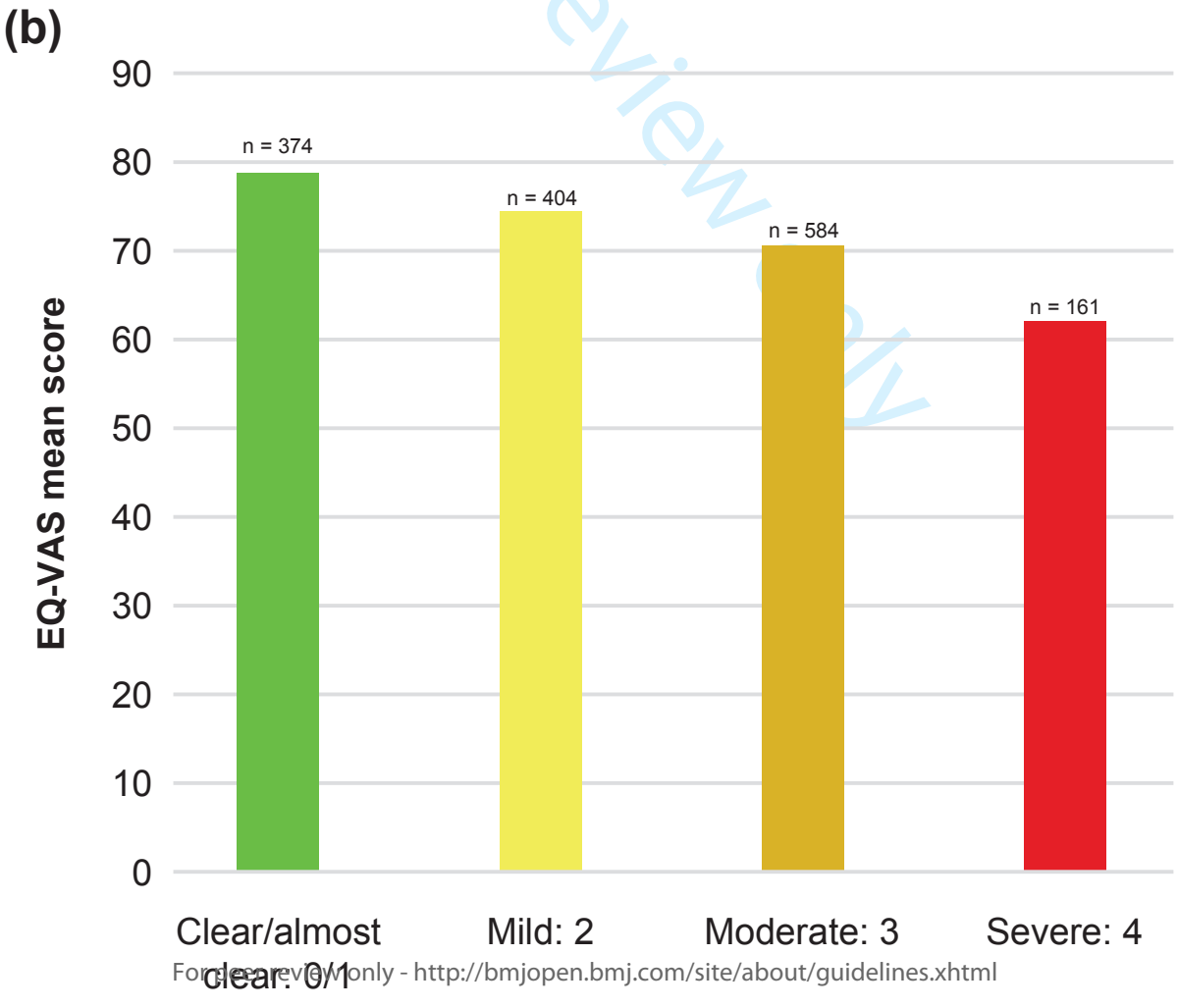

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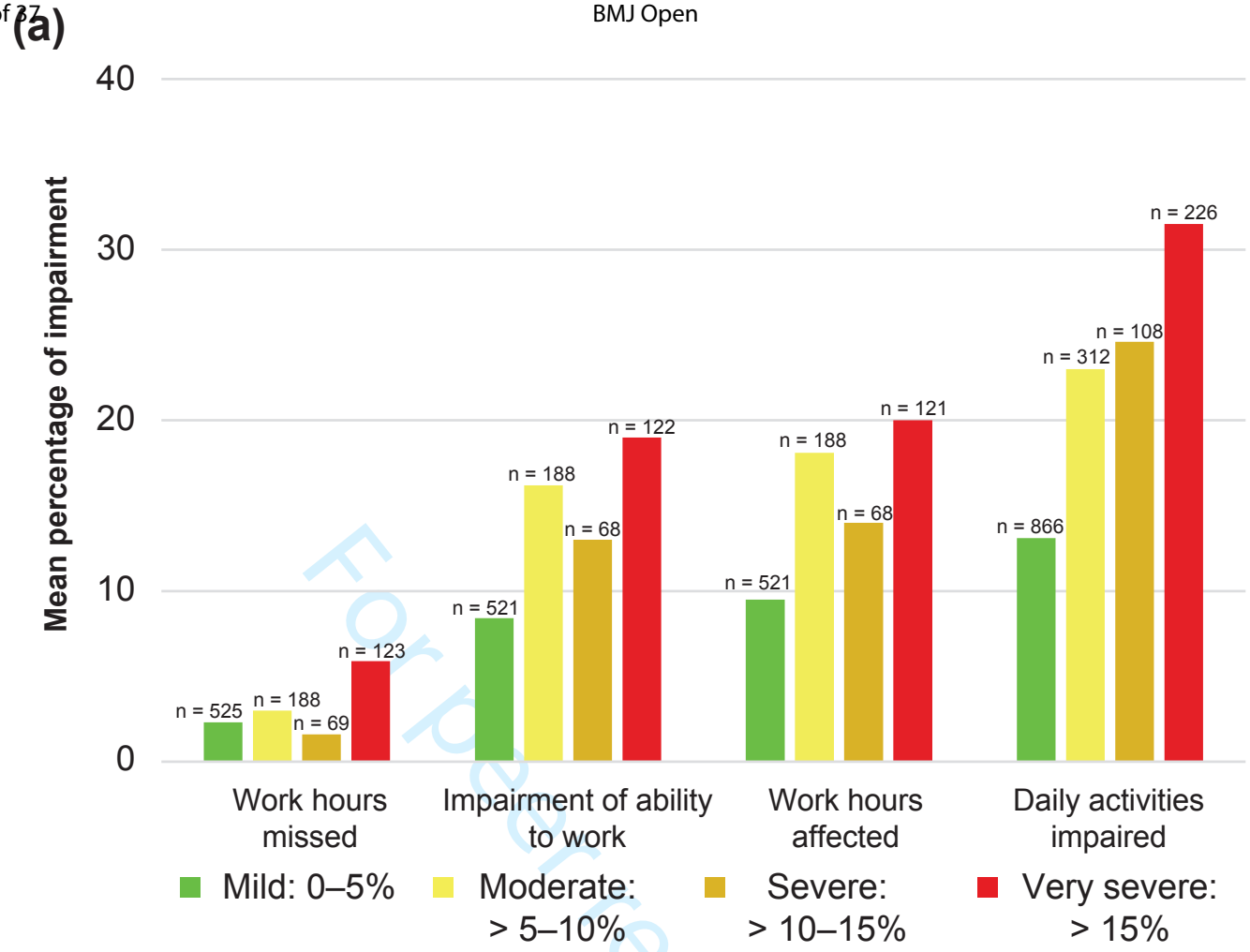

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Supplementary Table 1. Proportional odds model results for specific PROs by BSA and IGA severity covariates

	Severity measured by BSA	Severity measured by IGA
Odds Ratio (95% CI)		
Symptoms		
Fatigue		
None vs (Mild, Moderate, Severe, Very Severe)	1.01 (1.00, 1.02)	1.19 (1.07, 1.33)
(None, Mild) vs (Moderate, Severe, Very Severe)	1.02 (1.01, 1.03)	1.44 (1.31, 1.58)
(None, Mild, Moderate) vs (Severe, Very Severe)	1.03 (1.02, 1.04)	1.46 (1.33, 1.61)
(None, Mild, Moderate, Severe) vs Very Severe	1.02 (1.02, 1.03)	1.43 (1.27, 1.61)
Itch		
None vs (Mild, Moderate, Severe, Very Severe)	1.10 (1.07, 1.13)	2.69 (2.45, 2.95)*
(None, Mild) vs (Moderate, Severe, Very Severe)	1.09 (1.07, 1.11)	
(None, Mild, Moderate) vs (Severe, Very Severe)	1.06 (1.04, 1.07)	
(None, Mild, Moderate, Severe) vs Very Severe	1.05 (1.04, 1.06)	
Pain		
None vs (Mild, Moderate, Severe, Very Severe)	1.06 (1.04, 1.07)	1.89 (1.71, 2.10)
(None, Mild) vs (Moderate, Severe, Very Severe)	1.06 (1.05, 1.08)	2.21 (1.99, 2.46)
(None, Mild, Moderate) vs (Severe, Very Severe)	1.06 (1.05, 1.07)	2.44 (2.15, 2.77)
(None, Mild, Moderate, Severe) vs Very Severe	1.04 (1.03, 1.05)	2.48 (2.11, 2.91)
DLQI		
None vs (Small, Moderate, Very Large, Extremely Large)	1.09 (1.07, 1.12)	2.24 (1.99, 2.52)
(None, Small) vs (Moderate, Very Large, Extremely Large)	1.06 (1.05, 1.08)	1.85 (1.66, 2.06)
(None, Small, Moderate) vs (Very Large, Extremely Large)	1.04 (1.03, 1.05)	1.57 (1.40, 1.77)
(None, Small, Moderate, Very Large) vs Extremely Large	1.03 (1.01, 1.04)	1.27 (1.01, 1.59)
EQ-VAS	0.97 (0.97, 0.98)*	0.71 (0.66, 1.78)*
WPAI questionnaire		
Work time missed†	1.02 (1.00, 1.03)	1.45 (1.21, 1.75)
Impairment while working†	1.03 (1.02, 1.04)	1.51 (1.34, 1.71)
Working hours affected†	1.03 (1.02, 1.04)	1.51 (1.33, 1.70)
Daily activities affected		
None vs (A Little, A Lot)	1.04 (1.03, 1.04)*	1.55 (1.41, 1.70)
(None, A Little) vs A Lot		1.95 (1.68, 2.25)

*Proportional odds assumption was not violated.

†Logistic regression model.

Fatigue outcome levels (0–100 VAS): 0 = None (0), 1 = Mild (>0 to ≤12), 2 = Moderate (>12 to ≤32), Severe = (>32 to ≤59), Very Severe (>59 to ≤100).

Itch outcome levels (0–100 VAS): 0 = None (0), 1 = Mild (>0 to ≤9), 2 = Moderate (>9 to ≤34), 3 = Severe (>34 to ≤69), Very Severe (>69 to ≤100).

Pain outcome levels (0–100 VAS): 0 = None (0), 1 = Mild (>0 to ≤7), 2 = Moderate (>7 to ≤24), 3 = Severe (>24 to ≤59), Very Severe (>59 to ≤100).

DLQI outcome levels: 0 = None, 1 = Small, 2 = Moderate, 3 = Very Large, 4 = Extremely Large.

EQ-VAS outcome levels: 0 = Poor Health (≥0 to ≤20), 1 = Fair Health (<20 to ≤40), 2 = Good Health (<40 to ≤60), 3 = Very Good Health (<60 to ≤80), 4 = Excellent Health (>80 to ≤100).

WPAI outcome levels for work time missed due to psoriasis, impairment while working due to psoriasis, and working hours affected by psoriasis: 0 = None, 1 = Some (>0 to ≤100).

WPAI outcome levels for daily activities affected by psoriasis: 0 = None (0), 1 = A Little (>0 to <50), 2 = A Lot (≥50 to ≤100).

BSA, body surface area; CI, confidence interval; DLQI, Dermatology Life Quality Index; EQ-VAS, EuroQoL visual analog scale; IGA, Investigator's Global Assessment, VAS, visual analog scale; WPAI, Work Productivity and Activity Impairment.

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract *The abstract describes the study as a "cross-sectional analysis". Page 1.*
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found *The abstract describes the methods and key findings. Pages 3-4.*
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported *The background and rationale are described in paragraphs 1-6 of the Introduction. Pages 4-6.*
Objectives	3	State specific objectives, including any prespecified hypotheses *The specific aims of the study are stated in paragraph 7 of the Introduction. Page 6.*
Methods		
Study design	4	Present key elements of study design early in the paper *The study design is described in paragraphs 1-4 and 8-10 of the Methods. Pages 6-10.*
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection *The setting and patient enrollment are described in paragraph 2 of the Methods. Pages 6-7.*
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants *The selection of the sample is described in paragraph 3 of the Methods. Pages 6-7.*
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable *Outcomes and exposures are described in the Study Measures subsection, paragraphs 4-7 of the Methods. Pages 7-8.*
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group *The source of the data is reported in paragraph 3 of the Methods. Pages 6-7.*
Bias	9	Describe any efforts to address potential sources of bias *Multivariable regression modeling provided a method to address potential confounding variables, described in paragraph 9 of the Methods. Page 9.*

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Study size	10	Explain how the study size was arrived at *Not applicable; because this was a secondary analysis, study size was dependent on enrollment in the original registry study that was the source of the data*
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why *Quantitative variables, including categories for categorical variables and ranges for continuous variables, are described in paragraphs 3-7 of the Methods. Pages 6-8.*
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding *Statistical methods are described in the Statistical Analysis subsection (paragraphs 8-10 of the Methods). Page 9.*
		(*b*) Describe any methods used to examine subgroups and interactions *Not applicable*
		(*c*) Explain how missing data were addressed *There were virtually no missing data in the dataset because variables of interest were specified as "required" during data collection. This is described in paragraph 10 of the Methods. Page 9.*
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy *Not applicable; this was a secondary analysis of registry data*
		(*e*) Describe any sensitivity analyses *Sensitivity analysis is described in paragraph 9 of the Methods. Page 9.*
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed *The number of eligible patients is reported in paragraph 1 of the Results. Because this is a secondary analysis, details of the numbers of patients at each stage of the study is described in a previous publication. Page 10.*
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders *Descriptive data are presented in paragraphs 1-2 of the Results and in Table 1. Pages 10-15.*
		(b) Indicate number of participants with missing data for each variable of interest *The number of participants with complete data is reported in paragraph 1 of the Results. Page 10.*
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures *Patient-reported outcome measures ranges, stratified by disease severity, are reported in subsection Patient-Reported Outcomes Descriptive Analysis Results (paragraph 3 of the*

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		Results). Page 15.
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included *Confounder-adjusted estimates with 95% confidence intervals are reported in the subsection Multivariable Linear Regression Model (paragraphs 4-5 of the Results) and Table 2. Pages 16-19.*
		(*b*) Report category boundaries when continuous variables were categorized *Category boundaries for independent variables are reported in paragraph 4 of the Methods. Dependent variables were continuous. Page 7.*
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period *Not applicable*
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses *The sensitivity analysis is described in the Sensitivity Analysis subsection, paragraph 7 of the Results. Page 19.*
Discussion		
Key results	18	Summarise key results with reference to study objectives *Key results are summarized in paragraph 1 of the Discussion. Page 20.*
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias *Study limitations are discussed in paragraphs 4-5 of the Discussion. Page 22.*
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence *Interpretation of the results in the context of similar studies is discussed in paragraphs 2-3 of the Discussion. Pages 20-21.*
Generalisability	21	Discuss the generalisability (external validity) of the study results *External validity of the study results is discussed in paragraph 5 of the Discussion. Page 22.*
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based *Study funding is reported in the Footnotes section at the end of the manuscript. Page 23.*

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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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

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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

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Conflict of interest disclosure

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Running head: Psoriasis Severity and Quality of Life

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ABSTRACT

Objectives: This analysis examined the association between psoriasis severity, assessed by body surface area (BSA) and the Investigator's Global Assessment (IGA; previously used only in clinical trials) and patient-reported outcomes (PROs) in a real-world setting.

Design: Cross-sectional analysis within the Corrona Psoriasis Registry, an independent, prospective registry

Setting: 70 dermatology practices in the United States by May 31, 2016

Participants: 1529 adult patients with psoriasis being treated with biologic or nonbiologic systemic psoriasis treatment by May 31, 2016

Primary and secondary outcome measures: Psoriasis severity was assessed by percentage of affected BSA (mild [0–5%], moderate [>5–10%], severe [>10–15%], very severe [>15%]), and IGA scores (clear/almost clear [0–1], mild [2], moderate [3], severe [4]). PROs (pain, itch, fatigue; Dermatology Life Quality Index [DLQI]; EuroQoL Visual Analog Scale [EQ-VAS]; Work Productivity and Activity Impairment [WPAI]) were compared across BSA and IGA levels using ANOVA and chi-square tests. The association between psoriasis severity and PROs was examined using multivariable regression models.

Results: The mean age was 50.6 years and 47% of patients were female. Consistently with more severe psoriasis, symptoms worsened, DLQI scores increased ($P < 0.05$ for each level of BSA and IGA), EQ-VAS decreased ($P < 0.05$ for each level of BSA and IGA), and WPAI scores increased. By BSA score, moderate to very severe psoriasis was associated with poorer outcomes for the "impairment while working" and "daily activities impaired" WPAI domains (all $P < 0.05$ vs mild psoriasis). Very severe psoriasis was associated with increased "work hours missed" and "work hours affected" (both $P < 0.05$ vs mild psoriasis) Findings were similar by IGA. Results were confirmed by multivariable regression analyses.

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Conclusions: In a real-world setting, more severe psoriasis, assessed by BSA and IGA, was consistently associated with worse PROs.

Strengths and limitations of this study

- This is the first study to explore the link between psoriasis severity measured by the Investigator's Global Assessment (IGA) and patient reported outcomes (PROs) in a real-world setting
- Due to the cross-sectional study design, causal inferences regarding the relationship between psoriasis severity and PROs cannot be made, and changes in psoriasis severity or PROs over time were not measured
- Patients were recruited from specific dermatology practices, which may have been more focused on psoriasis therapy and, therefore, may not be representative of the general US psoriasis population

Keywords: Psoriasis – Disease Severity – Health-related Quality of Life – Patient-reported Outcomes – Work Productivity

INTRODUCTION

Psoriasis is a chronic, immune-mediated, systemic, inflammatory, and often debilitating skin disease, affecting 2.6%–3.7% of the population in the United States (US).[1] With itching, pain, and scaling as its key symptoms, psoriasis can have a significant impact on patients' health-related quality of life (QoL) and work productivity, depending on disease severity.[2–4]

A growing body of real-world evidence has shown greater psoriasis severity is associated with worse QoL and higher impairments in work productivity.[4,5] Survey data from the National Psoriasis Foundation in the US revealed patients with severe psoriasis had a greater likelihood of

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being unemployed than those having mild disease.[5] In another US survey, Korman and colleagues found increased psoriasis severity was associated with more itching, pain, and scaling; poorer QoL; and greater productivity impairment.[4]

However, methods of measuring psoriasis severity are not used consistently across studies. Affected body surface area (BSA) is a widely known and used measure of psoriasis severity in clinical practice,[6,7] and dermatologists prefer this tool for evaluating patient outcomes.[7] Although BSA has been used in studies of psoriasis-associated QoL, BSA-defined disease severity varies across studies (eg, no/little <1%, mild 1%–2%, severe ≥3%, as used by the National Health and Nutrition Examination Survey[8] vs mild 0%–<3%, moderate 3%–<10%, severe ≥10%, as used by the National Psoriasis Foundation[5]). In addition, using BSA alone does not capture information regarding disease location or symptoms.[7]

Several other severity measures exist, with their respective strengths and limitations. The Psoriasis Area and Severity Index (PASI) score is the most widely used and most thoroughly validated severity measure as a primary endpoint in clinical trials. However, it has not been employed routinely in clinical practice and tends to be poorly understood by clinicians and patients.[6,9,10] In addition, it shows low sensitivity to changes in disease severity in cases with low BSA involvement (ie, <10%).[6] The physician's global assessment (PGA) has been described as being easier to understand compared with the PASI and more similar to assessments of disease used in clinical practice.[10] However, definitions and criteria for points within the PGA values lack standardization, and expert consensus has not yet been reached.[9] Further, a large discordance may exist between PGA and BSA, resulting in either an over- or underestimate of true disease severity.[11]

The 5-point investigator's global assessment (IGA) modified (mod) 2011 scale is typically used in clinical trials and gauges psoriasis severity according to the patient's degree of skin redness,

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thickening, and scaling. Its advantage over other tools (6-point IGA and PGA) is that it more narrowly defines the lowest level of disease severity.[9] However, the IGA mod 2011 scale has not been examined in real-world studies of psoriasis-associated QoL.

Although the IGA mod 2011 scale provides a useful framework for the assessment of disease features, use of this scale alone and without accounting for BSA may not accurately reflect disease severity. In clinical practice, physicians may use a combination of objective assessments of psoriasis severity, such as the IGA mod 2011 scale, BSA, and symptoms, and more subjective measures, such as the emotional impact of psoriasis on the patient.[6]

This analysis aims to define the relationship between psoriasis severity and symptom severity, QoL, and work productivity among US patients with psoriasis in a real-world setting. Separate analyses were conducted, with psoriasis severity defined using both BSA and IGA.

METHODS

Study Design

A cross-sectional study was conducted using the enrollment data from the Corrona Psoriasis Registry to identify associations between disease severity and patient-reported outcomes (PROs).

Patient and Public Involvement

Patients were not involved in determining the design, the recruitment to, or the conduct of this study. All patients enrolled in the Corrona Psoriasis Registry receive a patient newsletter that shares study results twice per year.

Data Source

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The Corrona Psoriasis Registry is an independent, prospective observational cohort launched in April 2015 in collaboration with the National Psoriasis Foundation, with a target enrollment of 10,000 patients with psoriasis from 200 sites throughout the US. The study inclusion criteria matched those for registry enrollment: Patients must be at least 18 years old, must have been given a psoriasis diagnosis by a dermatologist, and had to have begun treatment with a qualifying biologic or nonbiologic systemic psoriasis treatment either within the 12 months preceding or on the day of the enrollment visit. Data collected from the registry launch date (April 2015) through May 31, 2016 were analyzed for the study.

Study Measures

Data related to demographics, disease severity (BSA and IGA scores), disease duration, prior and current use of systemic treatments for psoriasis, physician-reported medical history (eg, cardiovascular disease, diabetes mellitus, cardiovascular disease and diabetes risk factors, lymphoma/malignancy, Crohn's disease, anxiety/depression), and PROs collected at registry enrollment were examined. Patients reported their levels of pain, itching, and fatigue on a visual analog scale (VAS) of 0 (none) to 100 (very severe) and completed 2 validated and commonly used health-related quality-of-life (HRQoL) assessment instruments: the Dermatology Life Quality Index (DLQI)[12] and the visual analog component of the EuroQoL Five Dimensions Questionnaire VAS (EQ-VAS).[13] In addition, the patients completed the Work Productivity and Activity Impairment (WPAI) questionnaire.[14] Dermatologists assessed disease severity in terms of the percentage of total BSA affected and/or the IGA mod 2011 scale score. BSA percentages were categorized as mild (0–5%), moderate (>5–10%), severe (>10–15%), and very severe (>15%). The 5-point IGA was used to categorize levels of skin induration, scaling, and redness as clear/almost clear (0–1), mild (2), moderate (3), and severe (4).

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Dermatology Life Quality Index

The DLQI, which is a dermatology-specific tool to measure HRQoL, requires respondents to answer 10 questions classified within 6 domains: symptoms and feelings, daily activities, leisure activities, work and school, personal relationships, and treatment. Respondents indicate the degree to which they experienced problems for a recall period of 1 week, and responses are assessed with a 4-point Likert scale: 0 (not at all/not relevant), 1 (a little), 2 (a lot), and 3 (very much). Responses are calculated for the total DLQI score, which is 0–30. Higher scores indicate worse HRQoL.

EuroQol Visual Analog Scale

The EuroQol Visual Analog Scale (EQ-VAS) is a non-disease–specific HRQoL assessment tool in which respondents indicate their state of health on the day of assessment on a scale of 0–100, with 100 being the best imaginable state of health and 0 being the worst imaginable state of health.

Work Productivity and Activity Impairment

The WPAI questionnaire measures impairment in work hours missed, work productivity and impairment, and daily activities. Based on a scale of 1 (no effect) to 10 (completely prevented patient from working/participating), respondents report the following domains for the previous week: work hours missed, work hours affected, impairment while working, and daily activities impaired. Daily activities include housework, shopping, exercise, and studying. Responses for all domains, except for daily activities, are valid only if the respondent is employed.

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Statistical Analysis

Data regarding patient characteristics, disease characteristics, comorbidities, treatment history, and PROs collected at registry enrollment were reported for the overall study population and by BSA and IGA disease severity groups. Frequency counts and percentages were reported for all categorical variables (sex, employment status, disability status, psoriatic arthritis diagnosis, treatment history, and history of comorbidities). Means and standard deviations (SDs) were reported for all continuous variables (age, body mass index [BMI], psoriasis duration, BSA, and IGA). Significance testing with analysis of variance (ANOVA) was used for continuous variables, and chi-square tests of association were employed for categorical variables to investigate if any differences in values were present across the levels of BSA and IGA disease severity.

Multivariable linear regression was used to model the association between disease severity levels and PROs. To address potential confounding, the model adjusted a priori for age, gender, disease duration, and BMI at enrollment. IGA and BSA were modeled separately. Ordinal regression modeling was performed as a confirmatory sensitivity analysis.

Statistical analyses included patients who had complete data on analysis variables at enrollment. To minimize the potential impact of missing data, variables of interest were specified as "required" during data collection; therefore, no statistical techniques were needed to account for missing data. All analyses were performed using STATA (StataCorp LP 2015, Stata Statistical Software: Release 14, Version 2, College Station, TX) with significance set at the $P < 0.05$ level.

Protection of Patients

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The study used blinded data to maintain patient confidentiality. The Corrona Psoriasis Registry was approved by both local and central review boards at the participating sites. All patients provided written informed consent prior to their enrollments in the registry.

RESULTS

Study Sample Characteristics

As of May 31, 2016, 1529 patients were enrolled in the registry; the mean age was 50 years and 47% were female. Among these patients, 1525 had complete BSA data and 1527 had complete IGA data, and the BSA and IGA patients were similar in age and gender types. No patients were omitted from the analysis, but some did not have complete data sets.

Similar proportions of patients were biologic experienced and had prior nonbiologic systemic therapy across disease severity groups (BSA and IGA). The proportion of patients who were biologic experienced ranged from 53%–59% across BSA categories and 53%–57% across IGA categories. Proportions of patients who had been treated with nonbiologic systemic therapies ranged from 45%–49% across BSA categories, and 42%–54% across IGA categories. The disease severity groups also had similar disease durations (**Table 1**).

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Table 1. Baseline patient characteristics by BSA and IGA severity categories

	BSA Severity Groups (n = 1525)				IGA Severity Groups (n = 1527)			
	Mild: 0–5% (n = 873)	**Moderate: >5–10% (n = 316)**	**Severe: >10–15% (n = 109)**	**Very Severe: >15% (n = 227)**	**Clear/ almost clear: 0/1 (n = 375)**	**Mild: 2 (n = 404)**	**Moderate: 3 (n = 586)**	**Severe: 4 (n = 162)**
Patient characteristics								
Female, n (%)	439 (50)	136 (43)	53 (49)	88 (39)	186 (50)	205 (51)	262 (45)	64 (40)
Age (years), mean (SD)	50.6 (14.4)	50.8 (13.9)	49.8 (14.8)	50.4 (14.9)	50 (14.3)	51.5 (14.8)	50.7 (14.1)	49.5 (14.9)
Body weight (kg), mean (SD)	87.5 (22.2)	88.7 (24.8)	92.3 (23.8)	95.4 (27.3)	85.6 (19.6)	89.6 (24.3)	90.0 (25.3)	94.1 (24.9)
Body mass index (kg/m^2), mean (SD)	30.1 (6.8)	30.2 (7.3)	32.0 (8.1)	32.2 (8.4)	29.2 (5.7)	31.0 (7.6)	30.8 (7.7)	32.0 (8.0)
Employed, n (%)	575 (66)	209 (67)	72 (66)	137 (61)	261 (70)	258 (64)	374 (64)	101 (63)

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Disabled, n (%)	59 (7)	28 (9)	8 (7)	31 (14)	20 (5)	22 (5)	60 (10)	24 (15)
Disease characteristics								
Psoriasis duration (years), mean (SD)	15.6 (13.8)	15.1 (12.9)	15.7 (13.7)	17.2 (13.4)	15.8 (13.2)	17.0 (14.8)	15.2 (13.2)	14.1 (12.4)
Psoriatic arthritis diagnosis, n (%)	369 (42)	120 (38)	37 (34)	90 (40)	152 (41)	165 (41)	223 (38)	78 (48)
Treatment history								
Biologic naïve, n (%)	410 (47)	148 (47)	48 (44)	93 (41)	165 (44)	188 (47)	277 (47)	70 (43)
Biologic experienced, n (%)	463 (53)	168 (53)	61 (56)	134 (59)	210 (56)	216 (53)	309 (53)	92 (57)
Nonbiologic systemic therapy, n (%)	389 (45)	141 (45)	52 (48)	111 (49)	169 (45)	170 (42)	268 (46)	88 (54)
Psoriasis severity								
BSA (%), mean (SD)	2.2 (1.7)	8.3 (1.6)	13.4 (1.5)	34.8 (18.8)	1.3 (3.3)	5.7 (8.5)	11.7 (12.1)	26.6 (21.9)
IGA, mean (SD)	1.7 (1.1)	2.8 (0.6)	3.1 (0.5)	3.3 (0.7)	0.6 (0.5)	2.0 (0.0)	3.0 (0.0)	4.0 (0.0)

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History of comorbidities								
Cardiovascular disease, n (%)	103 (12)	35 (11)	13 (12)	30 (13)	48 (13)	52 (13)	66 (11)	16 (10)
Coronary artery disease, n (%)	25 (3)	4 (1)	2 (2)	12 (5)	9 (2)	16 (4)	12 (2)	6 (4)
Congestive heart failure, n (%)	7 (1)	9 (3)	0 (0)	5 (2)	3 (1)	5 (1)	11 (2)	2 (1)
Stroke, n (%)	15 (2)	3 (1)	2 (2)	1 (0)	6 (2)	8 (2)	6 (1)	1 (1)
Cardiovascular disease/diabetes risk factors, n (%)	413 (47)	159 (50)	51 (47)	113 (50)	167 (45)	190 (47)	296 (51)	84 (52)
Hypertension, n (%)	327 (38)	126 (40)	45 (41)	95 (42)	139 (37)	152 (38)	239 (41)	64 (40)
Hyperlipidemia, n (%)	253 (29)	97 (31)	23 (21)	60 (26)	96 (26)	123 (31)	168 (29)	46 (28)
Metabolic syndrome, n (%)	13 (1)	3 (1)	3 (3)	7 (3)	5 (1)	8 (2)	7 (1)	6 (4)
Diabetes mellitus, n (%)	111 (13)	50 (16)	17 (16)	38 (17)	40 (11)	55 (14)	92 (16)	29 (18)

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Lymphoma/malignancy, n (%)	40 (5)	20 (6)	5 (5)	9 (4)	18 (5)	17 (4)	34 (6)	5 (3)
Crohn's disease, n (%)	4 (0)	3 (1)	0 (0)	1 (0)	2 (1)	3 (1)	2 (0)	1 (1)
Depression, n (%)	161 (18)	58 (18)	24 (22)	48 (21)	56 (15)	79 (20)	120 (20)	36 (22)
Anxiety, n (%)	154 (18)	52 (16)	25 (23)	44 (19)	69 (18)	75 (19)	98 (17)	33 (20)

BSA, body surface area; IGA, Investigator's Global Assessment; SD, standard deviation.

History of comorbidities/medical history: cardiovascular disease: combined histories of myocardial infarction, acute coronary syndrome, coronary artery disease, congestive heart failure, peripheral artery disease, cardiac revascularization procedure, ventricular arrhythmia, cardiac arrest, unstable angina, stroke, transient ischemic attack, pulmonary embolism, carotid artery disease, deep vein thrombosis or other cardiovascular event; cardiovascular/diabetes risk factors: hypertension, hyperlipidemia, or metabolic syndrome; lymphoma/malignancy: lymphoma, breast, lung, skin (excluding nonmelanoma skin cancer), or other.

Prior use of biologics: adalimumab, alefacept, certolizumab, efalizumab, etanercept, golimumab, infliximab, ixekizumab, secukinumab, ustekinumab, investigational drugs, and other patient-specified biologics.

Prior use of nonbiologics: acitretin, apremilast, cyclosporine, hydroxyurea, methotrexate, mycophenolate, mofetil, sulfasalazine, tofacitinib, 6-thioguanine, and other patient-specified nonbiologics.

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The most common comorbidities were hypertension (BSA range: 38%–42%; IGA range: 37%–41%), hyperlipidemia (BSA range: 21%–31%; IGA range: 26%–31%), depression (BSA range 18%–22%; IGA range 15%–22%), and anxiety (BSA range: 16%–23%; IGA range: 17%–20%; **Table 1**). Across BSA and IGA groups, at least 60% of patients worked full-time or part-time. Increasing proportions of patients were disabled as severity increased according to BSA (range: 7%–14%) and IGA (range: 5%–15%; **Table 1**).

Patient-Reported Outcomes Descriptive Analysis Results

Fatigue, itching, and pain VAS scores worsened with disease severity as assessed by both BSA and IGA (**Figures 1A and 1B**). Across BSA categories, mean fatigue scores ranged from 26.5–40.2, itching was 24.7–55.7, and pain was 15.2–41.7. Among IGA categories, mean fatigue scores ranged from 21.9–41.8, itching was 12.1–57.3, and pain was 7.4–44.3.

DLQI scores worsened and EQ-VAS health status decreased with increasing disease severity (**Figures 2A and 2B** and **Figures 3A and 3B**). Across BSA and IGA categories, mean DLQI scores ranged from 5.2–10.2 and 4.3–9.7, respectively. Mean EQ-VAS scores ranged from 62.9 (very severe) to 76.4 (mild) across BSA categories and 62.1 (severe) to 78.8 (clear/almost clear) across IGA categories, with higher scores indicating better health. Work productivity impairment also increased with greater disease severity (**Figures 4A and 4B).** By BSA category, the "work hours missed" domain was 2.3%–5.9%, "impairment while working" was 8.4%–19.0%, "work hours affected" was 9.5%–20.0%, and "daily activities impaired" was 13.1%–31.5%. By IGA category, the "work hours missed" domain was 1.2%–4.2%, "impairment while working" was 5.5%–19.9%, "work hours affected" was 6.0%–20.9%, and "daily activities impaired" was 8.2%–34.1%.

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Multivariable Linear Regression Model

The multivariable linear regression models confirmed the overall pattern in the descriptive results, demonstrating an association between greater disease severity when assessed by BSA and IGA, and worsening symptoms, worse QoL, and greater work productivity and activity impairment. Worsening itch, pain, and fatigue were significantly associated with increases in BSA and IGA levels: $P < 0.001$ for moderate, severe, and very severe BSA (reference: mild) and for mild, moderate, and severe IGA (reference: clear/almost clear). Overall DLQI and EQ-VAS scores also worsened with disease severity ($P < 0.05$ for each level of BSA and IGA) (**Table 2**).

In BSA models, the moderate, severe, and very severe psoriasis categories were significantly associated with poorer outcomes in the WPAI domains of "impairment while working" and "daily activities impaired" compared with mild severity (all $P < 0.05$) (**Table 2**). Very severe disease was significantly associated with increased "work hours missed" ($P < 0.05$), and moderate and very severe disease were associated with increased "work hours affected" (both $P < 0.05$) compared with mild disease.

Table 2. Linear regression results by BSA and IGA severity

	BSA Severity Groups (reference = mild: 0–5%)			**IGA Severity Groups (reference = clear/almost clear: 0/1)**		
Parameter, coefficient (95% CI)	**Moderate: >5–10%**	**Severe: >10–15%**	**Very severe: >15%**	**Mild: 2**	**Moderate: 3**	**Severe: 4**
Symptoms						

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Fatigue	9.50 (5.87, 13.14)*	13.13 (7.49, 18.76)*	12.67 (8.52, 16.82)*	7.52 (3.55, 11.49)*	12.45 (8.79, 16.11)*	19.69 (14.48, 24.91)*
Itch	23.17 (19.27, 27.06)*	25.42 (19.40, 31.44)*	32.10 (27.66, 36.54)*	18.27 (14.21, 22.33)*	37.15 (33.41, 40.90)*	45.70 (40.36, 51.04)*
Pain	15.09 (11.46, 18.71)*	19.37 (13.76, 24.97)*	27.68 (23.55, 31.82)*	10.36 (6.48, 14.24)*	25.15 (21.57, 28.72)*	37.37 (32.27, 42.47)*
DLQI	1.91 (1.17, 2.66)*	3.40 (2.25, 4.56)*	5.26 (4.41, 6.11)*	0.85 (0.04, 1.67)*	3.76 (3.01, 4.52)*	5.47 (4.40, 6.55)*
EQ-VAS	–5.14 (–7.91, –2.36)*	–7.34 (–11.64, –3.04)*	–12.98 (–16.14, –9.81)*	–3.47 (-6.51, –0.43)*	–7.35 (–10.16, –4.55)*	–15.15 (–19.15, –11.55)*
WPAI questionnaire						
Work time missed	0.58 (–1.38, 2.55)	–0.71 (-3.68, 2.26)	3.50 (1.17, 5.82)*	1.13 (–1.01, 3.27)	2.96 (1.01, 4.92)*	2.87 (0.01, 5.73)*
Impairment while working	8.00 (4.58, 11.39)*	5.22 (0.06, 10.39)*	11.52 (7.49, 15.55)*	2.87 (–0.78, 6.53)	11.56 (8.22, 14.91)*	15.14 (10.29, 20.00)*

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Working hours affected	8.79 (5.20, 12.37)*	5.17 (–0.27, 10.61)	11.44 (7.19, 15.70)*	3.49 (–0.35, 7.33)*	13.05 (9.54, 16.55)*	15.65 (10.54, 20.77)*
Daily activities affected	10.28 (7.01, 13.54)*	11.54 (6.50, 16.59)*	19.69 (15.97, 23.40)*	7.88 (4.34, 11.42)*	15.04 (11.78, 18.31)*	26.36 (21.70, 31.01)*

*Significant at $P < 0.05$.

BSA, body surface area; CI, confidence interval; DLQI, Dermatology Life Quality Index; EQ-VAS, EuroQoL visual analog scale; IGA, Investigator's Global Assessment, WPAI, Work Productivity and Activity Impairment.

Fatigue, itch, and pain symptom scale: 0–100; DLQI scale: 0–30; EQ-VAS scale: 0–100; WPAI scale: 0–10.

All models adjusted a priori for age, gender, psoriasis duration, and body mass index at registry enrollment.

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In IGA models, mild, moderate, and severe psoriasis categories were significantly associated with worse outcomes for the WPAI domain of "daily activities impaired" compared with clear/almost clear (all $P < 0.05$). Compared with the mild psoriasis category, moderate and severe psoriasis categories were significantly associated with poorer outcomes in the domains of "work hours missed," "impairment while working," and "work hours affected" (all $P < 0.05$).

Sensitivity Analysis

Ordinal regression modeling was performed as a sensitivity analysis to confirm the results of the linear regression; results confirmed a consistent trend, with increasing severity of disease associated with worsening QoL and greater impairment in work productivity and activity. Results of the proportional odds models for BSA and IGA disease severity categories are shown in **Supplementary Table 1**.

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DISCUSSION

In this cross-sectional analysis of the Corrona Psoriasis Registry, multivariable linear regression models showed patient-reported symptoms, QoL, and work productivity worsened with increasing disease severity, as measured by BSA and IGA. The results were statistically significant across all levels of psoriasis severity for patient-reported pain, itch, and fatigue; DLQI overall scores; EQ-VAS; and the "daily activities impaired" domain of the WPAI questionnaire. For the WPAI domains "work hours missed," "impairment while working," and "work hours affected" outcomes were significantly worse for patients with the highest severity of psoriasis (BSA = very severe, IGA = severe). Findings were overall consistent between the BSA and IGA results.

To the authors' knowledge, the present study was the first to explore the link between IGA and PROs in a real-world setting. Physician's Global Assessment has been used previously in real-world settings in both postmarketing safety studies[15,16] and patient registries.[16-19] A multicenter, prospective study conducted in Spain found psoriasis severity was the primary factor affecting QoL. Although PGA data were collected in that study, PASI was ultimately used for the multivariate modeling.[20]

Of note, the BSA and IGA categories as defined in the present study differ somewhat from those used in prior research. The present study used the 5-point mod 2011 scale, which differs from the 6-point scales used in some clinical trials of biologic treatments for psoriasis[9] in that the "almost clear" category is more narrowly defined compared with the "minimal" category in PGA and the other IGA versions.[9] The category cutoff points for BSA used in the present study (ie, mild: 0%–5%, moderate: >5%–10%, severe: >10%–15%, and very severe: >15%) also differed from those that have been used in certain studies and referred to in guidelines and expert consensus

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statements (eg, mild 0%–<3%, moderate 3%–<10%, and severe ≥10%;[5] moderate to severe >10%[21], no/little <1%, mild 1%–2%, severe ≥3% [8]). The addition of the "very severe" category in the present study may shed light on specific unmet medical needs in this segment of the population with psoriasis. Further research is required to fully understand how differences in BSA categorization may impact results across clinical trials and observational studies.

In a prior study by Korman *et al* of psoriasis severity and PROs, severity of symptoms, EQ-5D, DLQI, and WPAI domains were assessed using BSA category (mild, moderate, or severe as determined by a physician).[4] Although the categorization of psoriasis severity differed, the results are generally consistent with the findings of the present study, for which severity of fatigue, itching, and pain; DLQI total scores; and WPAI domains worsened with increasing disease severity.[4] In addition, lower EQ-5D summary scores were reported with increasing disease severity,[4] similar to the lower EQ-VAS scores observed in the present study.

Although the present study demonstrates the association between increased psoriasis severity and worsened PROs, future research may clarify this relationship. The present analysis did not address the potential for the outcomes of interest to be highly correlated with one another. For instance, previous research by Lewis-Beck *et al.* found an inverse relationship between itching, pain, and scaling severity and work productivity.[22] Further research may investigate how QoL and work productivity measures may interact with one another in the context of psoriasis severity. In addition, due to the cross-sectional study design, the results represent psoriasis severity and PROs at one timepoint. Future research using longitudinal data could show how changes in psoriasis severity may relate to changes over time in QoL and work productivity. In addition, particularly for a longitudinal study, the combination and interaction of BSA and IGA as a single measure of severity could prove informative.

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The results of this study must be interpreted in the context of the source of the data, study design, and analysis methods. First, this study was a cross-sectional analysis, which does not allow for causal inferences regarding psoriasis severity and the outcomes of interest. Second, the patients enrolled in the registry were recruited from specific dermatology practices, which may have been more focused on psoriasis therapy and, therefore, may not be representative of the general US psoriasis population. The linear regression model was robust to the non-normal distribution of the data; however, estimates at the extreme lower and upper levels of severity may have been over- or underestimated.

CONCLUSIONS

Increased psoriasis severity as measured by both BSA and IGA categories was associated with worsened PROs in this US-based psoriasis registry study. Future research is warranted to understand the potential interrelationships between PROs and to understand whether longitudinal improvements in psoriasis severity are associated with improvements in PROs.

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FOOTNOTES

Contributors: BS interpreted the results, critically reviewed the manuscript, and agreed to be accountable for all aspects of the manuscript. JDG helped design the study, acquired the data, critically reviewed the manuscript, and agreed to be accountable for all aspects of the manuscript. CK helped design the study, interpreted the results, and critically reviewed the manuscript. MM helped design the study, collected the data, undertook the data analysis, interpreted the results, and critically reviewed the manuscript. NG undertook the data analysis, interpreted the results, and critically reviewed the manuscript. PH helped design the study, interpreted the results, and critically reviewed the manuscript. YZ helped design the study, interpreted the results, and critically reviewed the manuscript. VH interpreted the results and critically reviewed the manuscript. FL helped design the study, interpreted the results, and critically reviewed the manuscript. ML helped design the study, acquired the data, and critically reviewed the manuscript.

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Competing interests: BS has served as a consultant for AbbVie, Almirall, Amgen, AstraZeneca, Boehringer Ingelheim, Celgene, Dermira, Galderma, GlaxoSmithKline, Eli Lilly, Janssen, LEO

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Pharma, Medac, Meiji Seika Pharma, Menlo Therapeutics, Novartis, Ortho Dermatologics/Valeant, Pfizer, Regeneron, Sanofi-Genzyme, Sun Pharma, UCB Pharma; as Co-scientific Director of the Corrona Psoriasis Registry; and has received grant support for the University of Connecticut fellowship program from AbbVie and Janssen. ML is an employee of Mount Sinai and receives research funds from: Abbvie, Boehringer Ingelheim, Celgene, Eli Lilly, Incyte, Janssen/Johnson & Johnson, Leo Pharmaceuticals, Medimmune/Astra Zeneca, Novartis, Pfizer, Sciderm, Valeant, and ViDac. ML is also a consultant for Allergan, Aqua, Boehringer Ingelheim, Corrona, LEO Pharma, Menlo, and Promius. JDG is an employee and shareholder of Corrona, LLC, and has been a consultant to Genentech, Janssen, Novartis, Pfizer, and Eli Lilly. MM is an employee of Corrona, LLC, and at the time of the study, was a member of the University of Delaware, Dept. of Behavioral Health and Nutrition Affiliate Faculty (non-remunerative position). NG is an employee of Corrona, LLC, and CK was an employee of Corrona, LLC, at the time of the study. VH and PH are employees of Novartis, and YZ and FL were employees of Novartis at the time of the study.

Patient consent: All patients were required to provide written, informed consent prior to participating.

Ethics approval: All participating investigators were required to obtain full board approval for research involving human subjects through a central institutional review board (IntegReview). For academic investigative sites that did not receive a waiver to use the central IRB, full board approval was obtained for the respective governing IRB, and documentation of approval was submitted to the sponsor prior to initiating any study procedures.

Data sharing statement: No additional data are available.

Acknowledgments

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Access to study data was limited to Corrona, and Corrona statisticians completed all of the analysis; all authors contributed to the interpretation of the results. Corrona has been supported through contracted subscriptions in the last 2 years by AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Crescendo, Eli Lilly and Company, Genentech, Gilead, GSK, Janssen, Merck, Momenta Pharmaceuticals, Novartis, Pfizer, Regeneron, Roche, UCB, and Valeant. Novartis participated in the interpretation of data, review, and approval of the manuscript.

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REFERENCES

1 Rachakonda TD, Schupp CW, Armstrong AW. Psoriasis prevalence among adults in the United States. *J Am Acad Dermatol* 2014;**70**:512–6.

2 Bhosle MJ, Kulkarni A, Feldman SR, et al. Quality of life in patients with psoriasis. *Health Qual Life Outcomes* 2006;**4**:35.

3 Gelfand JM, Feldman SR, Stern RS, et al. Determinants of quality of life in patients with psoriasis: A study from the US population. *J Am Acad Dermatol* 2004;**51**:704–8.

4 Korman NJ, Zhao Y, Pike J, *et al*. Relationship between psoriasis severity, clinical symptoms, quality of life and work productivity among patients in the USA. *Clin Exp Dermatol* 2016;**41**:514–21.

5 Armstrong AW, Schupp C, Wu J, *et al.* Quality of life and work productivity impairment among psoriasis patients: findings from the National Psoriasis Foundation survey data 2003-2011. *PLoS One* 2012;**7**:e52935.

6 Menter A, Gottlieb A, Feldman SR*, et al*. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 1. Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. *J Am Acad Dermatol* 2008;**58**:826–850.

7 Armstrong AW, Siegel MP, Bagel J*, et al.* From the Medical Board of the National Psoriasis Foundation: Treatment targets for plaque psoriasis. *J Am Acad Dermatol* 2017;**76**:290–8.

8 Helmick CG, Lee-Han H, Hirsch SC, *et al*. Prevalence of psoriasis among adults in the U.S.: 2003-2006 and 2009-2010 National Health and Nutrition Examination Surveys. *Am J Prev Med* 2014;**47**:37–45.

9 Langley RG, Feldman SR, Nyirady J, *et al.* The 5-point Investigator's Global Assessment (IGA) Scale: a modified tool for evaluating plaque psoriasis severity in clinical trials. *J Dermatolog Treat* 2015;**26**:23–31.

For peer review only

10 Feldman SR, Krueger GG. Psoriasis assessment tools in clinical trials. *Ann Rheum Dis* 2005; **64 Suppl 2**:ii65–8;discussion ii69–73.

11 Duffin KC, Papp KA, Bagel J, et al. Evaluation of the Physician Global Assessment and Body Surface Area Composite Tool for assessing psoriasis response to apremilast therapy: results from ESTEEM 1 and ESTEEM 2. *J Drugs Dermatol* 2017;**16**:147–53.

12 Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)—a simple practical measure for routine clinical use. *Clin Exp Dermatol* 1994;**19**:210–6.

13 EuroQol Group. EuroQol—a new facility for the measurement of health-related quality of life. *Health Policy* 1990;**16**:199–208.

14 Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. *Pharmacoeconomics* 1993;**4**:353–65.

15 Kimball AB, Pariser D, Yamauchi PS, *et al*. OBSERVE-5 interim analysis: An observational postmarketing safety registry of etanercept for the treatment of psoriasis. *J Am Acad Dermatol* 2013;**68**:756–64.

16 Menter A, Thaci D, Papp KA, *et al.* Five-year analysis from the ESPRIT 10-year postmarketing surveillance registry of adalimumab treatment for moderate to severe psoriasis. *J Am Acad Dermatol* 2015;**73**:410–9,e416.

17 Strober BE, Bissonnette R, Fiorentino D, *et al*. Comparative effectiveness of biologic agents for the treatment of psoriasis in a real-world setting: results from a large, prospective, observational study (Psoriasis Longitudinal Assessment and Registry [PSOLAR]). *J Am Acad Dermatol* 2016;**74**:851-861,e854.

18 Huynh DH, Boyd TA, Etzel CJ, *et al*. Persistence of low disease activity after tumour necrosis factor inhibitor (TNFi) discontinuation in patients with psoriatic arthritis. *RMD Open* 2017;**3**:e000395.

For peer review only

19 Lindstrom Egholm C, Krogh NS, Pincus T, *et al.* Discordance of global assessments by patient and physician is higher in female than in male patients regardless of the physician's sex: data on patients with rheumatoid arthritis, axial spondyloarthritis, and psoriatic arthritis from the DANBIO registry. *J Rheumatol* 2015;**42**:1781–5.

20 Daudén E, Pujol RM, Sanchez-Carazo JL, *et al.* Demographic characteristics and health-related quality of life of patients with moderate-to-severe psoriasis: the VACAP study. *Actas Dermosifiliogr* 2013;**104**:807–14.

21 Mrowietz U, Kragballe K, Reich K, *et al.* Definition of treatment goals for moderate to severe psoriasis: a European consensus. *Arch Dermatol Res* 2011;**303**:1–10.

22 Lewis-Beck C, Abouzaid S, Xie L, *et al.* Analysis of the relationship between psoriasis symptom severity and quality of life, work productivity, and activity impairment among patients with moderate-to-severe psoriasis using structural equation modeling. *Patient Prefer Adherence* 2013;**7**:199–205.

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FIGURES

Figure 1A and 1B. Patient-reported Symptoms by BSA Severity Group (A) and IGA Severity Group (B)

Fatigue, itch, and pain symptom scale: 0–100.

BSA, Body surface area; IGA, Investigator's Global Assessment; VAS, visual analogue scale.

Figure 2A and 2B. DLQI Scores by BSA Severity Group (A) and IGA Severity Group (B)

DLQI scale: 0–30.

DLQI, Dermatology Life Quality Index; BSA, body surface area; IGA, Investigator's Global Assessment.

Figure 3A and 3B. EQ-VAS by BSA Severity Group (A) and IGA Severity Group (B)

EQ-VAS scale: 0–100.

EQ-VAS, EuroQoL visual analog scale; BSA, body surface area; IGA, Investigator's Global Assessment; VAS, visual analog scale.

Figure 4A and 4B. WPAI Domains by BSA Severity Group (A) and IGA Severity Group (B)

WPAI, Work Productivity and Activity Impairment; BSA, body surface area; IGA, Investigator's Global Assessment.

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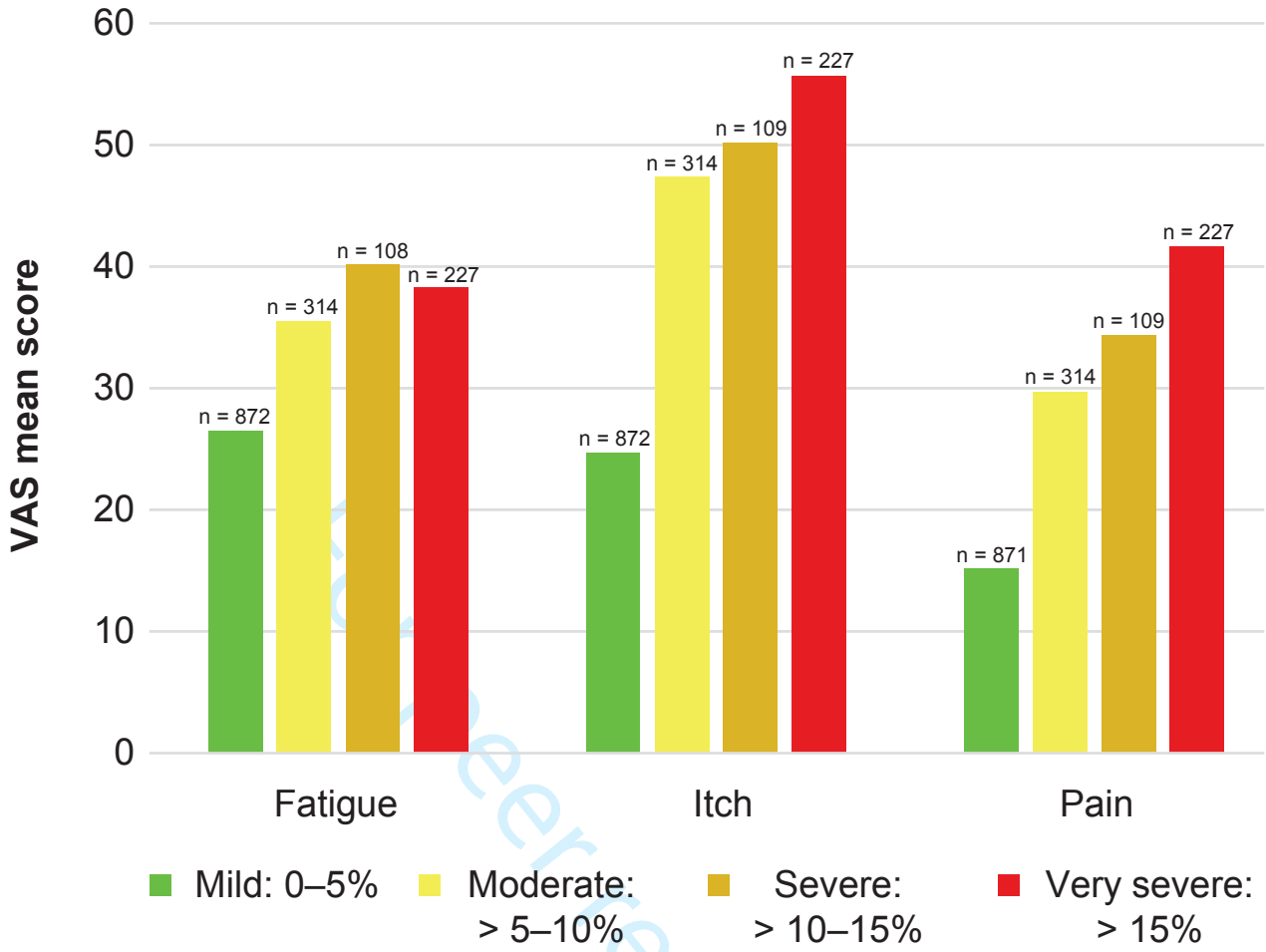

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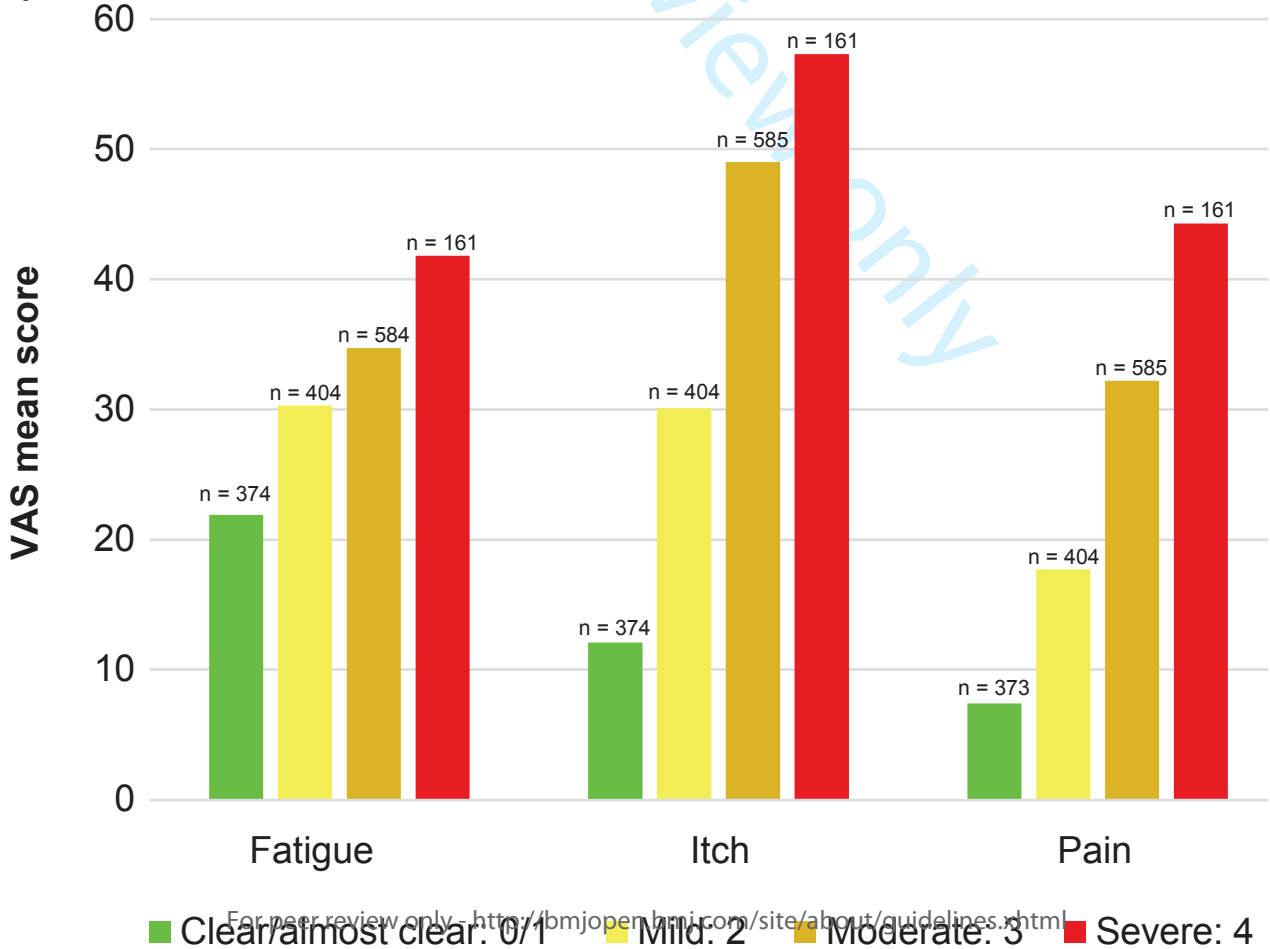

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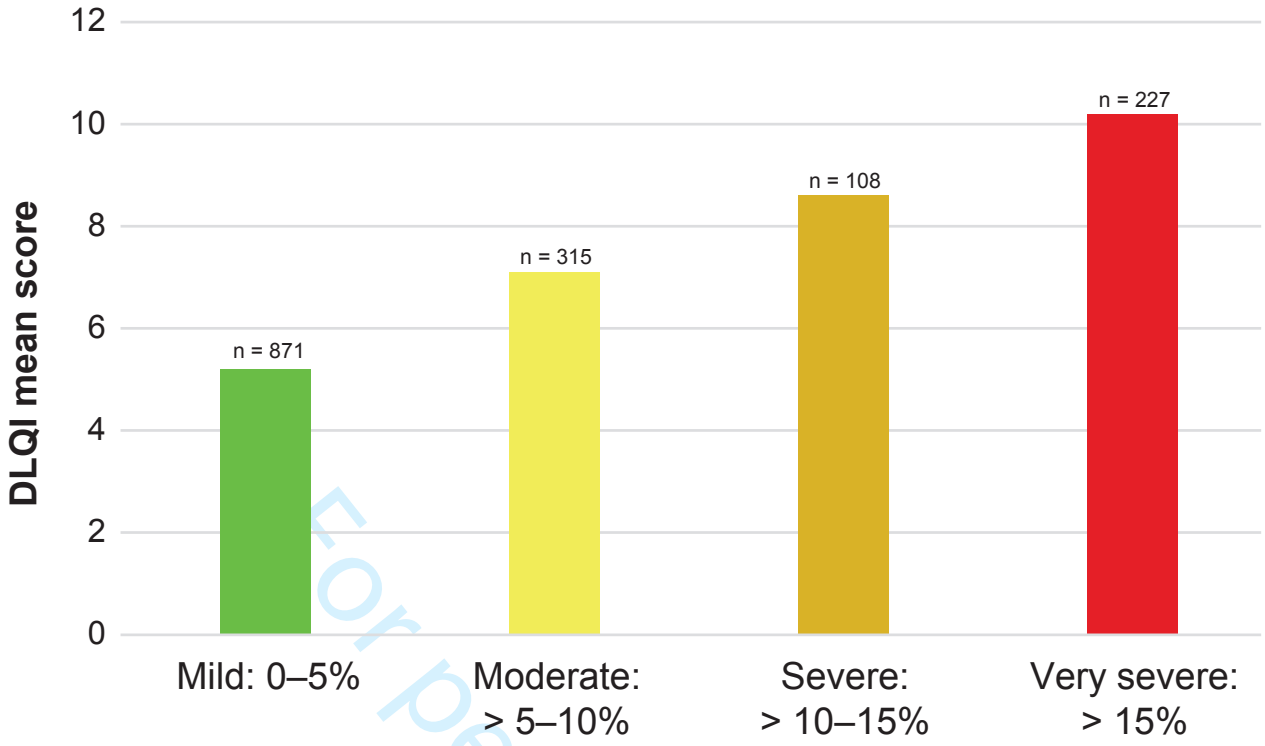

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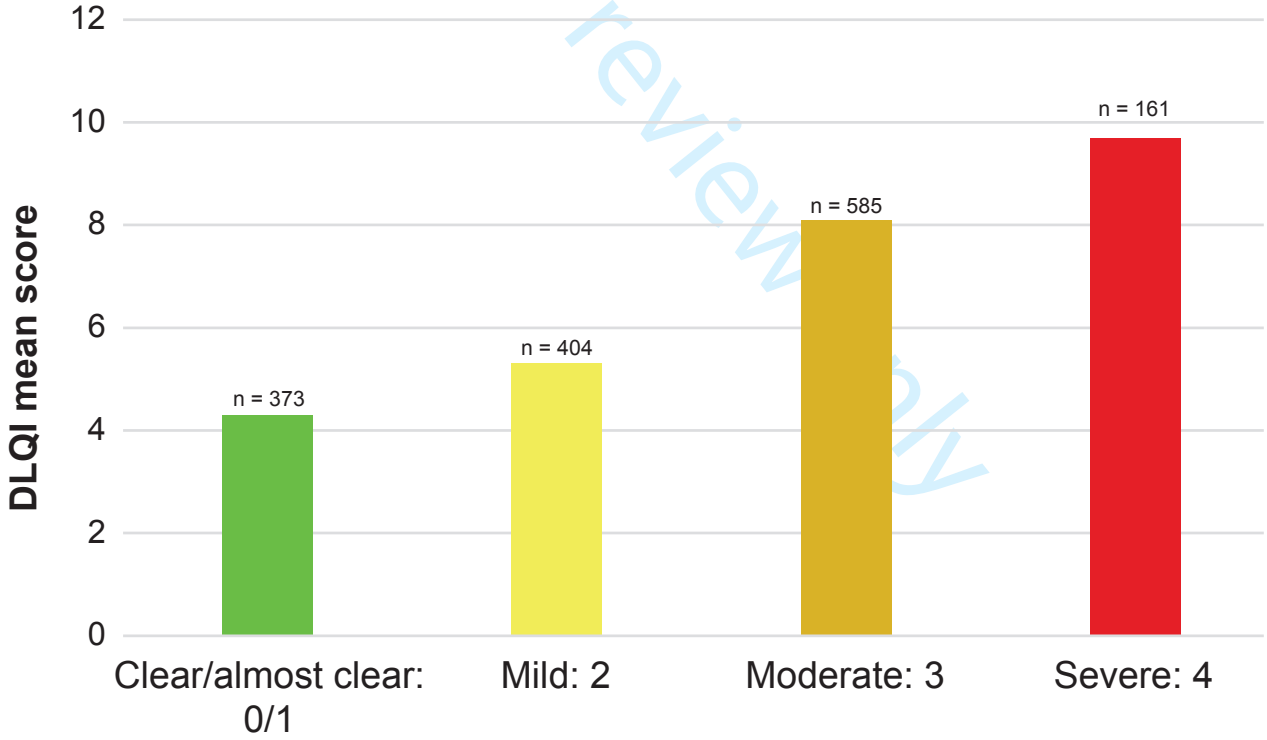

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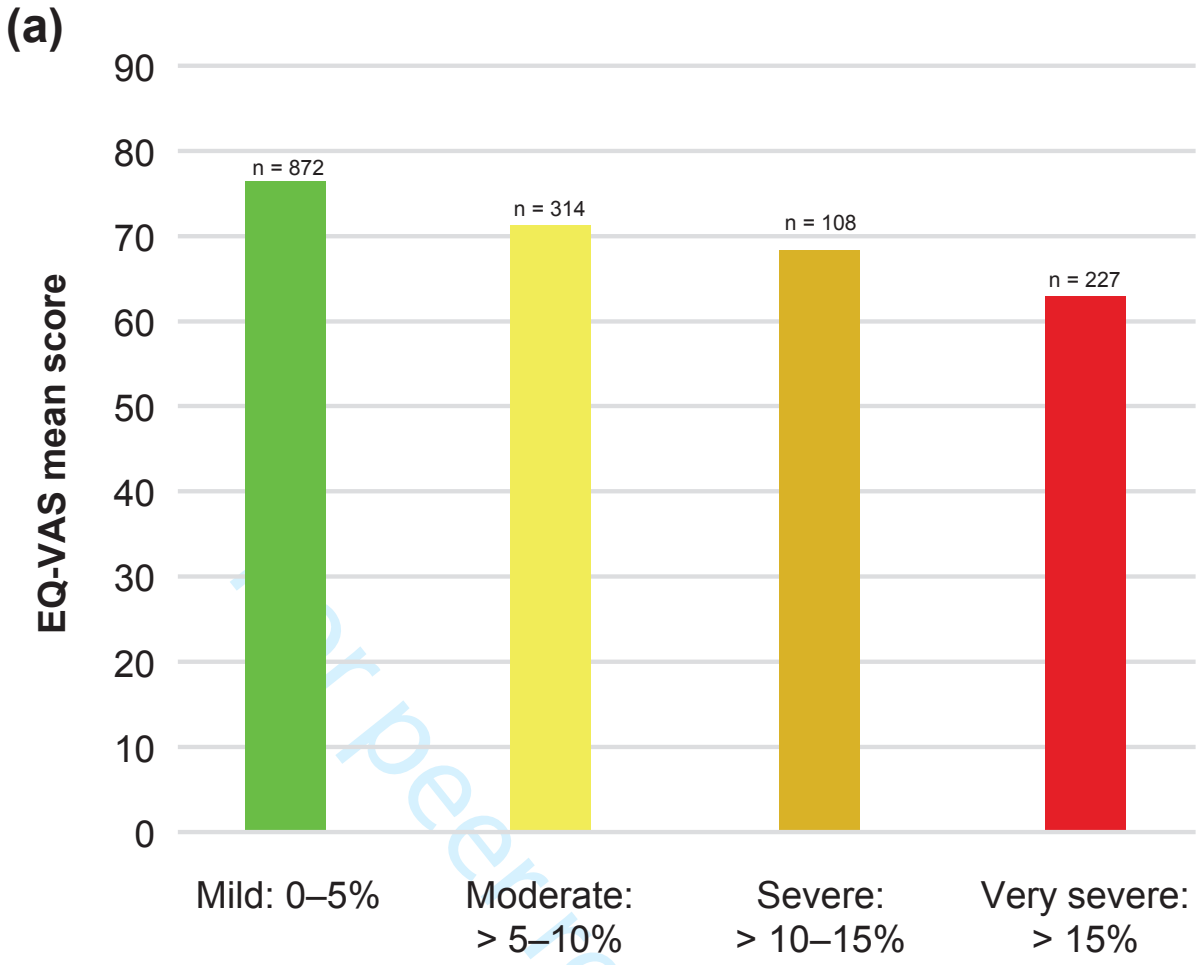

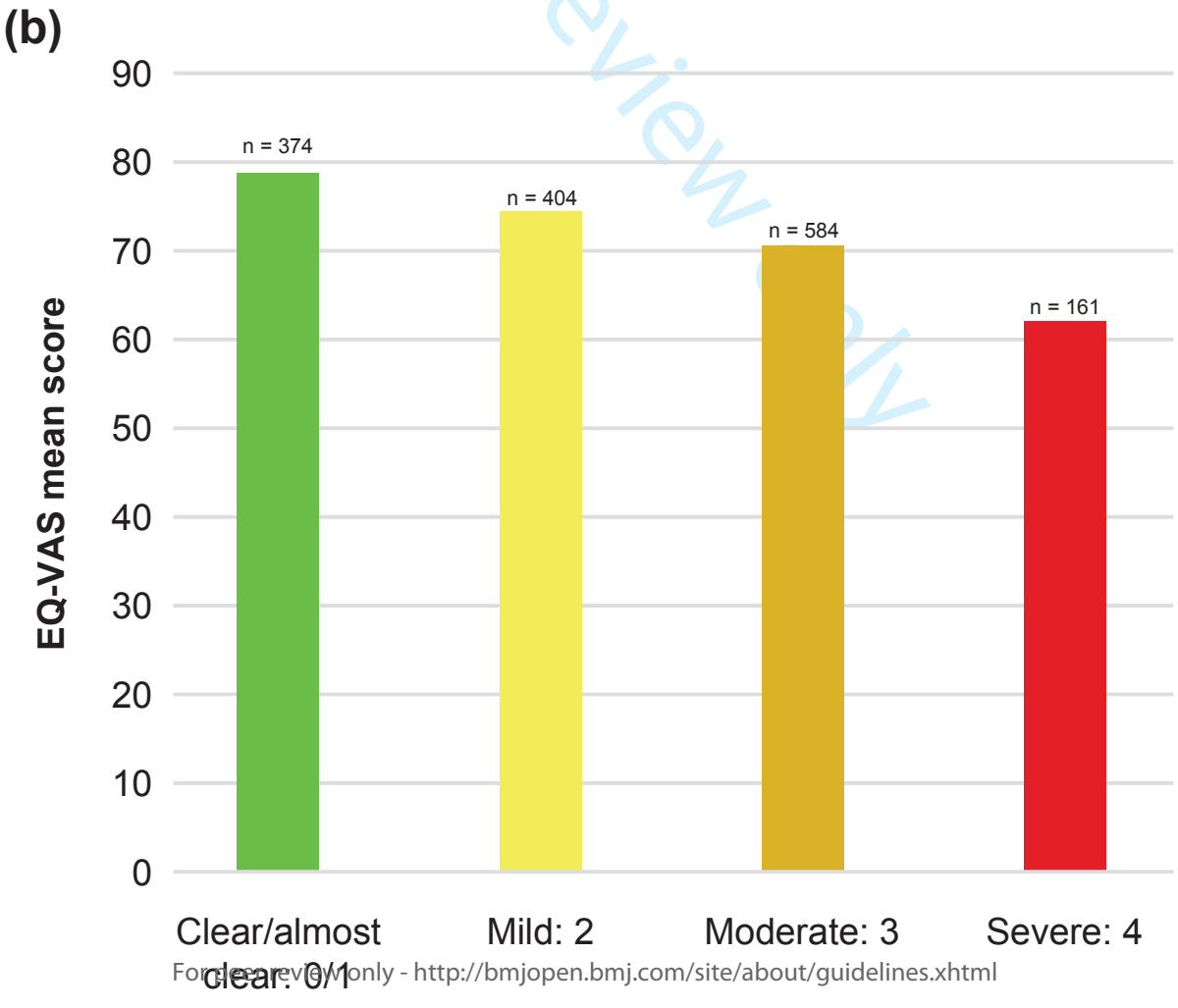

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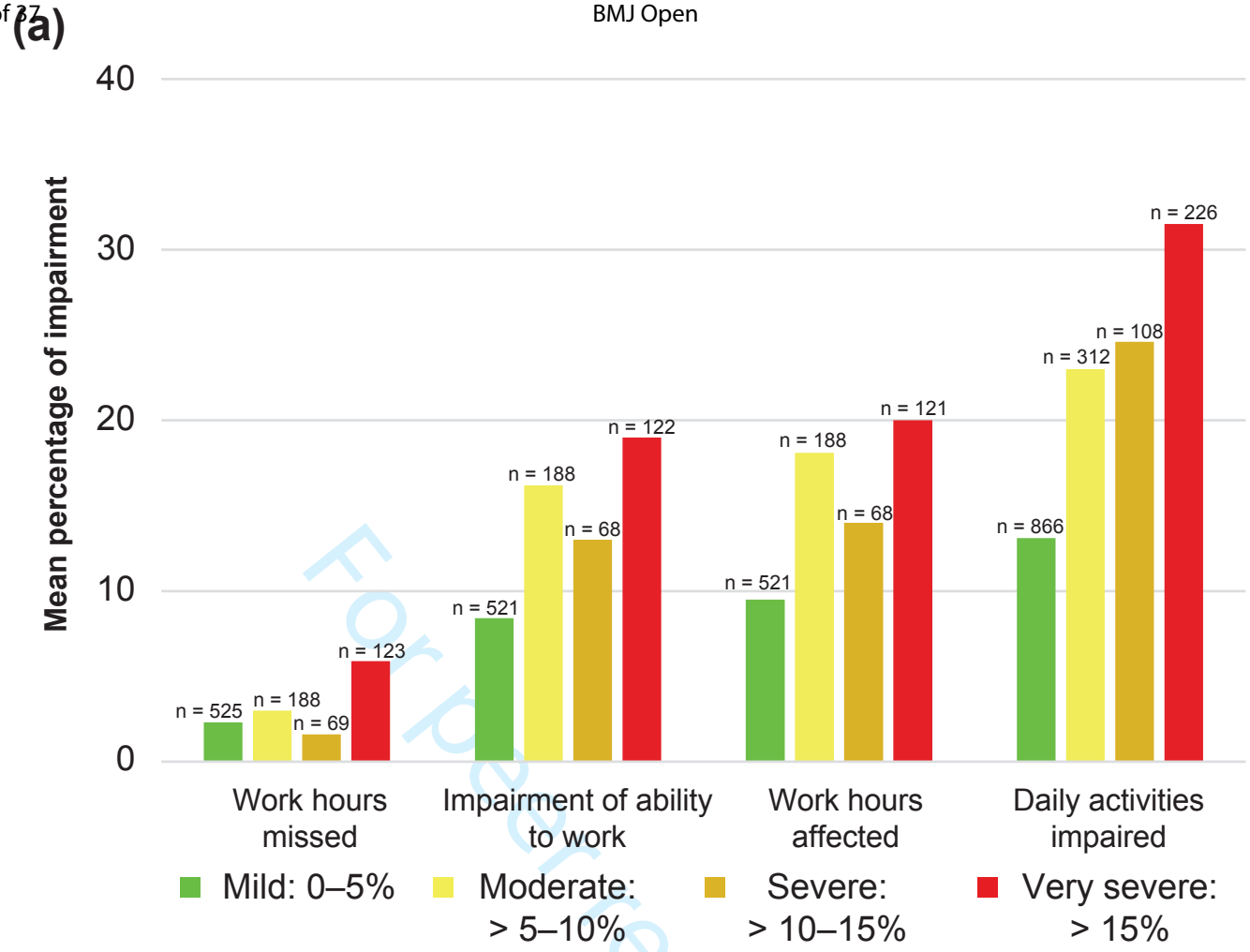

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Supplementary Table 1. Proportional odds model results for specific PROs by BSA and IGA severity covariates

	Severity measured by BSA	Severity measured by IGA
Odds Ratio (95% CI)		
Symptoms		
Fatigue		
None vs (Mild, Moderate, Severe, Very Severe)	1.01 (1.00, 1.02)	1.19 (1.07, 1.33)
(None, Mild) vs (Moderate, Severe, Very Severe)	1.02 (1.01, 1.03)	1.44 (1.31, 1.58)
(None, Mild, Moderate) vs (Severe, Very Severe)	1.03 (1.02, 1.04)	1.46 (1.33, 1.61)
(None, Mild, Moderate, Severe) vs Very Severe	1.02 (1.02, 1.03)	1.43 (1.27, 1.61)
Itch		
None vs (Mild, Moderate, Severe, Very Severe)	1.10 (1.07, 1.13)	2.69 (2.45, 2.95)*
(None, Mild) vs (Moderate, Severe, Very Severe)	1.09 (1.07, 1.11)	
(None, Mild, Moderate) vs (Severe, Very Severe)	1.06 (1.04, 1.07)	
(None, Mild, Moderate, Severe) vs Very Severe	1.05 (1.04, 1.06)	
Pain		
None vs (Mild, Moderate, Severe, Very Severe)	1.06 (1.04, 1.07)	1.89 (1.71, 2.10)
(None, Mild) vs (Moderate, Severe, Very Severe)	1.06 (1.05, 1.08)	2.21 (1.99, 2.46)
(None, Mild, Moderate) vs (Severe, Very Severe)	1.06 (1.05, 1.07)	2.44 (2.15, 2.77)
(None, Mild, Moderate, Severe) vs Very Severe	1.04 (1.03, 1.05)	2.48 (2.11, 2.91)
DLQI		
None vs (Small, Moderate, Very Large, Extremely Large)	1.09 (1.07, 1.12)	2.24 (1.99, 2.52)
(None, Small) vs (Moderate, Very Large, Extremely Large)	1.06 (1.05, 1.08)	1.85 (1.66, 2.06)
(None, Small, Moderate) vs (Very Large, Extremely Large)	1.04 (1.03, 1.05)	1.57 (1.40, 1.77)
(None, Small, Moderate, Very Large) vs Extremely Large	1.03 (1.01, 1.04)	1.27 (1.01, 1.59)
EQ-VAS	0.97 (0.97, 0.98)*	0.71 (0.66, 1.78)*
WPAI questionnaire		
Work time missed†	1.02 (1.00, 1.03)	1.45 (1.21, 1.75)
Impairment while working†	1.03 (1.02, 1.04)	1.51 (1.34, 1.71)
Working hours affected†	1.03 (1.02, 1.04)	1.51 (1.33, 1.70)
Daily activities affected		
None vs (A Little, A Lot)	1.04 (1.03, 1.04)*	1.55 (1.41, 1.70)
(None, A Little) vs A Lot		1.95 (1.68, 2.25)

*Proportional odds assumption was not violated.
†Logistic regression model.
Each “vs” comparison implies the "0 vs 1” structure of a traditional logistic regression. The 0 group is the reference.
Fatigue outcome levels (0–100 VAS): 0 = None (0), 1 = Mild (>0 to ≤12), 2 = Moderate (>12 to ≤32), Severe = (>32 to ≤59), Very Severe (>59 to ≤100).
Itch outcome levels (0–100 VAS): 0 = None (0), 1 = Mild (>0 to ≤9), 2 = Moderate (>9 to ≤34), 3 = Severe (>34 to ≤69), Very Severe (>69 to ≤100).
Pain outcome levels (0–100 VAS): 0 = None (0), 1 = Mild (>0 to ≤7), 2 = Moderate (>7 to ≤24), 3 = Severe (>24 to ≤59), Very Severe (>59 to ≤100).
DLQI outcome levels: 0 = None, 1 = Small, 2 = Moderate, 3 = Very Large, 4 = Extremely Large.
EQ-VAS outcome levels: 0 = Poor Health (≥0 to ≤20), 1 = Fair Health (<20 to ≤40), 2 = Good Health (<40 to ≤60), 3 = Very Good Health (<60 to ≤80), 4 = Excellent Health (>80 to ≤100).
WPAI outcome levels for work time missed due to psoriasis, impairment while working due to psoriasis, and working hours affected by psoriasis: 0 = None, 1 = Some (>0 to ≤100).
WPAI outcome levels for daily activities affected by psoriasis: 0 = None (0), 1 = A Little (>0 to <50), 2 = A Lot (≥50 to ≤100).
BSA, body surface area; CI, confidence interval; DLQI, Dermatology Life Quality Index; EQ-VAS, EuroQoL visual analog scale; IGA, Investigator’s Global Assessment, VAS, visual analog scale; WPAI, Work Productivity and Activity Impairment.

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract *The abstract describes the study as a "cross-sectional analysis". Page 1.*
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found *The abstract describes the methods and key findings. Pages 3-4.*
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported *The background and rationale are described in paragraphs 1-6 of the Introduction. Pages 4-6.*
Objectives	3	State specific objectives, including any prespecified hypotheses *The specific aims of the study are stated in paragraph 7 of the Introduction. Page 6.*
Methods		
Study design	4	Present key elements of study design early in the paper *The study design is described in paragraphs 1-4 and 8-10 of the Methods. Pages 6-10.*
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection *The setting and patient enrollment are described in paragraph 2 of the Methods. Pages 6-7.*
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants *The selection of the sample is described in paragraph 3 of the Methods. Pages 6-7.*
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable *Outcomes and exposures are described in the Study Measures subsection, paragraphs 4-7 of the Methods. Pages 7-8.*
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group *The source of the data is reported in paragraph 3 of the Methods. Pages 6-7.*
Bias	9	Describe any efforts to address potential sources of bias *Multivariable regression modeling provided a method to address potential confounding variables, described in paragraph 9 of the Methods. Page 9.*

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Study size	10	Explain how the study size was arrived at *Not applicable; because this was a secondary analysis, study size was dependent on enrollment in the original registry study that was the source of the data*
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why *Quantitative variables, including categories for categorical variables and ranges for continuous variables, are described in paragraphs 3-7 of the Methods. Pages 6-8.*
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding *Statistical methods are described in the Statistical Analysis subsection (paragraphs 8-10 of the Methods). Page 9.*
		(*b*) Describe any methods used to examine subgroups and interactions *Not applicable*
		(*c*) Explain how missing data were addressed *There were virtually no missing data in the dataset because variables of interest were specified as "required" during data collection. This is described in paragraph 10 of the Methods. Page 9.*
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy *Not applicable; this was a secondary analysis of registry data*
		(*e*) Describe any sensitivity analyses *Sensitivity analysis is described in paragraph 9 of the Methods. Page 9.*
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed *The number of eligible patients is reported in paragraph 1 of the Results. Because this is a secondary analysis, details of the numbers of patients at each stage of the study is described in a previous publication. Page 10.*
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders *Descriptive data are presented in paragraphs 1-2 of the Results and in Table 1. Pages 10-15.*
		(b) Indicate number of participants with missing data for each variable of interest *The number of participants with complete data is reported in paragraph 1 of the Results. Page 10.*
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures *Patient-reported outcome measures ranges, stratified by disease severity, are reported in subsection Patient-Reported Outcomes Descriptive Analysis Results (paragraph 3 of the*

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		Results). Page 15.
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included *Confounder-adjusted estimates with 95% confidence intervals are reported in the subsection Multivariable Linear Regression Model (paragraphs 4-5 of the Results) and Table 2. Pages 16-19.*
		(*b*) Report category boundaries when continuous variables were categorized *Category boundaries for independent variables are reported in paragraph 4 of the Methods. Dependent variables were continuous. Page 7.*
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period *Not applicable*
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses *The sensitivity analysis is described in the Sensitivity Analysis subsection, paragraph 7 of the Results. Page 19.*
Discussion		
Key results	18	Summarise key results with reference to study objectives *Key results are summarized in paragraph 1 of the Discussion. Page 20.*
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias *Study limitations are discussed in paragraphs 4-5 of the Discussion. Page 22.*
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence *Interpretation of the results in the context of similar studies is discussed in paragraphs 2-3 of the Discussion. Pages 20-21.*
Generalisability	21	Discuss the generalisability (external validity) of the study results *External validity of the study results is discussed in paragraph 5 of the Discussion. Page 22.*
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based *Study funding is reported in the Footnotes section at the end of the manuscript. Page 23.*

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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