

Health-related Quality of Life of Patients with Rosacea: A Systematic Review and Meta-analysis of Real-world Data

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Patients with rosacea commonly experience stigmatization, which induces stress and thereby exacerbates their symptoms. Given the strong effects of rosacea on health-related quality of life (HRQoL), addressing the physical and psychosocial aspects of rosacea is essential. To examine the effects of rosacea on HRQoL, we conducted a systematic review and meta-analysis involving real-world data. PubMed, EMBASE, and the Cochrane Library were searched, and randomized controlled trials (RCTs), cross-sectional studies, and case series evaluating the HRQoL of patients with rosacea were included. HRQoL assessment tools such as the Dermatology Life Quality Index (DLQI) and Rosacea-Specific Quality-of-Life Questionnaire (RosaQoL) were used. Data on 13,453 patients were retrieved from 52 eligible studies: 4 RCTs, 15 case series, and 33 cross-sectional studies. Compared with healthy controls, patients with rosacea had significantly lower DLQI scores (standardized mean difference [SMD] = -1.09, 95% confidence interval [CI] = -0.81 to -1.37). The DLQI scores after treatment were higher than those before treatment (SMD = -1.451, 95% CI = -1.091 to -1.810). The pooled estimates for the overall DLQI and RosaQoL scores were 8.61 and 3.06, respectively. In conclusion, patients with rosacea have lower HRQoL compared with healthy individuals, and treatment for rosacea improves their HRQoL.

Key words: quality of life; real-world; rosacea.

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Rosacea is a common inflammatory skin disorder characterized by flushing, facial erythema, phymatous changes, papules, pustules, telangiectasia, and ocular involvement. According to the National Rosacea Society Expert Committee, these signs can be classified into 4 main clinical subtypes: erythematotelangiectatic, papulopustular, rhinophymatous, and ocular (1). Patients with rosacea may exhibit symptoms from multiple subtypes and may progress from one subtype to another (2). According to a meta-analysis published in 2018, which

SIGNIFICANCE

Patients with rosacea and low health-related quality of life and emotional stress may experience rosacea relapse and exacerbation, leading to a more severe psychosocial burden. Therefore, holistic care including health-related quality of life assessment is essential. We examined rosacea's effect on health-related quality of life by comprehensively reviewing real-world data on 13,453 patients across 52 studies. Using established assessment tools, we discovered significantly lower health-related quality of life in patients with rosacea compared with healthy controls. Treatment improved health-related quality of life, indicating the importance of early intervention. These results provide valuable insights that emphasize the importance of health-related quality of life assessment in managing the complex interplay between rosacea, perceived stigmatization, and overall well-being.

included studies from multiple continents, the prevalence of rosacea in the general population ranges from 0.09% to 22.41%, with a pooled proportion of 5.46% (3, 4).

Many patients with skin disorders perceive stigmatization, which substantially contributes to their stress and psychological burden, particularly for those with rosacea (5). Rosacea can lead to anxiety, depression, lack of confidence, and low self-esteem, which may exacerbate psychological stress and thereby worsen the physical symptoms of rosacea (6).

Health-related quality of life (HRQoL) is an assessment of mental and physical well-being and is widely used to evaluate the effect of rosacea on patients (7). Low HRQoL not only reflects poor confidence in disease regression from the patient's perspective but also reduces the rate of regression as a result of high stress. Therefore, understanding HRQoL may help physicians manage rosacea. In the field of dermatology, the Dermatology Life Quality Index (DLQI) (8), Rosacea-Specific Quality-of-Life Questionnaire (RosaQoL) (9), Skindex-29 (10), and Skindex-16 (11) are commonly used quality of life (QoL) questionnaires specific to patients with rosacea.

Several clinical trials have examined the effects of rosacea and its treatment on HRQoL (12, 13). In their systematic review, van Zuuren et al. (14) summarized 11 randomized controlled trials (RCTs) comparing HRQoL

changes when various rosacea interventions were applied (14). They indicated that because HRQoL is a comprehensive assessment tool for understanding patients' perceptions of rosacea, studies involving real-world epidemiological data should be considered. In another systematic review, van der Linden et al. (15) analysed 12 studies on HRQoL in patients with rosacea and reported that rosacea had a significant negative effect on HRQoL (15). However, the studies included were not sufficient to provide conclusive evidence with minimal heterogeneity or to enable a further meta-analysis.

To the best of our knowledge, no studies have yet synthesized real-world data from around the world to examine the effect of rosacea on HRQoL. In addition, multiple observational studies and clinical trials have been conducted since the publication of the aforementioned systematic reviews. Therefore, in this systematic review and meta-analysis, we used real-world data to examine the effect of rosacea on HRQoL and determine the levels of HRQoL before and after rosacea treatment. Our goal was to determine the effect of rosacea and its treatment on HRQoL to better guide clinicians in managing rosacea from the QoL perspective.

MATERIALS AND METHODS

This meta-analysis was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (16). This systematic review was registered on the online PROSPERO international prospective register of systematic reviews (National Institute for Health Research, CRD42023447947).

Search strategy and study selection

Studies were identified by searching for keywords in PubMed, Embase, and the Cochrane Library. The following terms and Boolean operators were used in MeSH and free-text searches: ("rosacea" AND "quality of life"). Table S1 lists the search terms used in this study. We employed the "related articles" feature in PubMed to expand our search. No language restrictions were applied. A comprehensive search was conducted in September 2023. We reviewed the reference sections of relevant articles and consulted known experts in the field. Unpublished studies were also searched for using the ClinicalTrials.gov registry.

Selection criteria

RCTs, cross-sectional studies, and case series evaluating HRQoL scores in patients with rosacea were included. Studies meeting the following criteria were included: (1) evaluating patients with rosacea, (2) including at least 5 patients, and (3) evaluating HRQoL. If a study included only a subset of patients meeting these criteria, only eligible patients were considered in the analysis. Studies meeting any of the following criteria were excluded: (1) being a review article, guideline, or protocol; (2) not evaluating HRQoL; (3) measuring HRQoL in conditions other than rosacea; (4) involving HRQoL assessment in both rosacea and other diseases but not presenting or discussing the results for rosacea separately; or (5) involving duplicate reporting of patient cohorts.

Primary outcomes

The primary outcome for this study was the HRQoL scores of patients with rosacea, specifically their DLQI and RosaQoL scores.

Methodological quality appraisal

Two reviewers, Ching-Wen Chiu and Yu-Chen Huang, independently appraised the methodological quality of each included study by using various tools to critically evaluate their risk of bias (ROB). For cross-sectional studies in which HRQoL scores were obtained for both patients with rosacea and healthy controls, the Newcastle–Ottawa Scale (NOS) was used, which involves 6 variables, with scores ranging from 0 to 9 points (17). Studies scoring 0–4 points were considered as having a high ROB, studies scoring 5 or 6 points were considered as having a moderate ROB, and studies scoring 7–9 points were considered as having a low ROB. The included RCTs were evaluated using the revised Cochrane Risk of Bias (RoB 2.0) tool, covering domains such as selection, performance, detection, attrition, reporting, and overall bias. For case series, we used the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool to evaluate their quality and internal validity (18, 19). This tool consists of 7 methodological domains and categorizes ROB as low, moderate, serious, or critical. The overall ROB was determined by the most severe RoB 2.0 or ROBINS-I level observed in any domain. For cross-sectional studies without a comparison, we used the Agency for Healthcare Research and Quality (AHRQ) (20), which contains 11 items, each contributing to an overall score. For each item, 1 point is awarded if the quality of the study meets the methodological standard. Scores of 0 to 4 indicate a high ROB, scores of 5 to 7 indicate a moderate ROB, and scores of 8 to 11 indicate a low ROB.

Data extraction

Two reviewers, Ching-Wen Chiu and Yu-Chen Huang, independently extracted the following details from the included studies: population characteristics, HRQoL assessment results, and HRQoL scores. Discrepancies between the reviewers were resolved by a third reviewer, Jerry Tsai. The main HRQoL assessment tools included the DLQI and RosaQoL. The DLQI consists of 10 questions related to symptoms, feelings, daily activities, leisure activities, work or school patterns, personal relationships, and treatment side effects. Higher scores indicate poorer HRQoL. The RosaQoL consists of 3 domains: emotion, symptom, and function domains. In this study, the scores of each domain formed part of our outcomes. In studies evaluating HRQoL not only with the DLQI or RosaQoL but also with other assessment tools, only the DLQI or RosaQoL scores were extracted for statistical analysis.

Statistical analysis

Differences in HRQoL scores were estimated between patients with rosacea and healthy controls, between patients with and without rosacea treatment, and between before and after treatment. Continuous data are presented as a standardized mean difference (SMD) with a 95% confidence interval (CI) to account for the varied and non-standardized outcomes across the studies. A pooled estimate of HRQoL scores was calculated using the DerSimonian and Laird random-effects model (21). Statistical heterogeneity was evaluated using the I^2 test, which quantifies the proportion of total outcome variability due to variability among studies. To evaluate publication bias, the funnel plot technique and Egger's test were employed for scenarios involving more than 10 studies. Visual inspection of plot symmetry was used to determine potential bias. All statistical analyses were conducted using Review Manager

version 5.4 and Comprehensive Meta-Analysis version 3 (Biostat, Englewood, NJ, USA).

RESULTS

Study characteristics

Fig. 1 depicts the study selection process. Our initial search yielded 1,646 studies, of which 426 were duplicates. After the titles and abstracts were screened, 1,075 studies were deemed ineligible and excluded. Subsequently, the full texts of the 145 remaining studies were retrieved for further review. Of these articles, 93 were excluded for the following reasons: 16 articles reported irrelevant outcomes, 27 articles were ongoing clinical protocols, 18 articles were review articles, 31 articles were conference abstracts, and 1 article reported duplicate cohorts. The remaining 52 eligible studies were included in our analysis.

Table I lists the characteristics of the studies included (12, 13, 22–71). These studies were published between 2001 and 2023 and had sample sizes ranging from 8 to 973 patients, with a total of 13,453 patients. Of these studies, 3 were cross-sectional studies comparing HRQoL in patients with rosacea and healthy controls, 4 were RCTs comparing HRQoL in treatment versus nontreatment groups, and 15 were case series comparing HRQoL in patients before and after treatment. The remaining 30 studies were cross-sectional studies that only provided HRQoL scores for patients with rosacea. In total, 20 studies were from Asia, 20 studies were from Europe, and 12 studies were from North America. HRQoL in patients with rosacea was analysed (Tables SII–SV).

Methodological appraisal

Tables SVI and SVII and Figs. S1 and S2 summarize the methodological quality (ROB 2.0, NOS, ROBINS-I,

and AHRQ scores) of the included studies. All 3 studies involving healthy controls, which were evaluated using the NOS, received 6 or more points, indicating a low-to-moderate ROB. Three of the 4 RCTs had low concern in the ROB 2.0 quality assessment. Only 1 of the case series had a severe ROB according to their ROBINS-I score, with the remaining 14 having a low-to-moderate ROB. Of the cross-sectional studies without healthy controls, 13 (43%) had a low ROB, whereas 11 (37%) had a moderate ROB.

Overall HRQoL score in patients with rosacea

A total of 37 studies (22–32, 34, 36–39, 41, 45, 47, 49–52, 55–59, 61, 62, 64, 65, 67–71) examined the overall DLQI scores in 8,629 patients, reporting scores ranging from 2.00 to 22.25. As shown in **Fig. 2**, the pooled estimate for the overall DLQI score was 8.00 (95% CI=7.37–8.63). Visual inspection of the funnel plot for the overall DLQI scores in patients with rosacea indicated an asymmetrical distribution of studies. Therefore, publication bias was evaluated using Egger's regression test, which confirmed significant publication bias ($p<0.001$). In response, a trim-and-fill analysis was conducted (**Fig. S3**). After 3 additional studies were adjusted for, the adjusted overall DLQI score was calculated to be 8.61 (95% CI=7.06–10.16). Three studies (13, 35, 60) examined the overall RosaQoL score in patients with rosacea, with scores ranging from 2.56 to 3.48. As shown in **Fig. S4a**, the pooled estimate for the overall RosaQoL score was 3.06 (95% CI=2.734–3.375). The pooled estimates for the overall RosaQoL scores in the symptom, emotion, and function domains were 3.21 (95% CI=2.960–3.458), 3.42 (95% CI=3.368–3.475), and 2.45 (95% CI=2.191–2.708), respectively (**Figs. S4b–d**).

Comparison of HRQoL scores in patients with rosacea vs healthy controls

Three studies (41, 42, 58) compared the HRQoL scores of 375 patients with rosacea vs 360 healthy controls. These studies reported that the healthy controls had significantly higher QoL (95% CI=4.60–6.42, $p<0.0001$, **Fig. 3**), with a difference of 5.51 points in the DLQI score. However, moderate heterogeneity among the included studies was determined ($I^2=63\%$).

Comparison of mean HRQoL scores in patients with rosacea before vs after treatment

A total of 12 studies reported DLQI scores before and after treatment in 820 patients with rosacea (13, 25, 29, 31, 32, 45, 47, 49, 51, 52, 61, 68). Random-effects model analysis revealed a significant difference between the pre-treatment and post-treatment scores (95% CI=–2.991 to –4.058, $p<0.0001$, **Fig. 4**), with a difference of 3.53

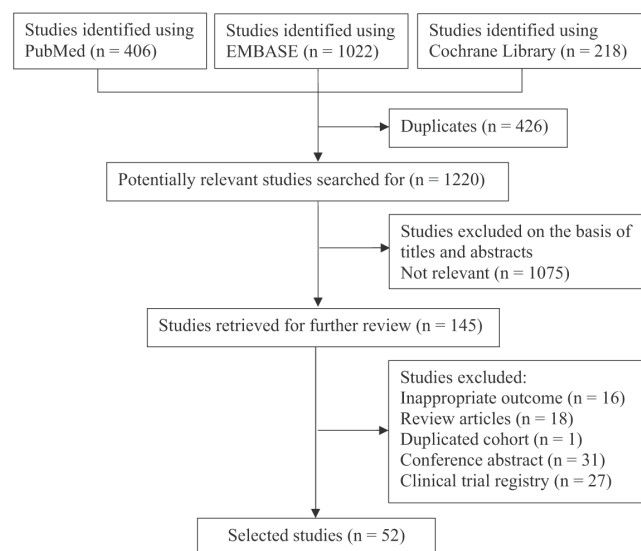


Fig. 1. Flowchart of the studies included.

Table I. Baseline characteristics of the studies included

Study name (year)	Study design	Country	Sample size, n	Female, n (%)	Age, year (SD)	Duration of rosacea diagnosis, year, mean (SD)	HRQoL assessment
Rosacea with healthy control							
Ozcan 2023	Cross-sectional	Turkey	R: 134 C: 120	R: 105 (78.4) C: 60 (48.4)	Nil	8.4 (9.5)	DLQI
Wu 2018	Cross-sectional	China	R: 201 C: 196	R: 137 (68.2) C: 119 (60.7)	Nil	Nil	DLQI
Salamon 2009	Cross-sectional	Poland	R: 40 C: 40	R: 31 (77.5) C: 31 (77.5)	R: 50.71 (10.36)	Nil	SF-36
Rosacea patients without control							
Treatment vs non-treatment							
Sbidian 2016	RCT	France	156	100 (64.1)	47.5 (20.9–80.7) ^a	5 ^a	Skindex score
Tyring 2016	RCT	USA	961	702 (73.0)	51.5 (19–92) ^b	Nil	DLQI, RosaQoL, EQ-5D-5L
Bribeche 2015	RCT	Ukraine	65	33 (50.76)	43.04 (11.2)	Nil	DLQI
Luger 2015	RCT	Germany	61	48 (78.69)	51.76 (10.66)	Nil	RosaQoL
Pre-treatment vs post-treatment							
Yang 2022	Case series	China	16	16 (100)	30 (13)	Nil	DLQI
Wang 2021	Case series	China	34	32 (94.12)	28 (21–50)	3.5 (2–20)	DLQI
Wang 2020	Case series	China	30	6 (20.0)	26.8 (2.8)	4.2 (2.6)	DLQI
Campos 2019	Case series*	Portugal	27	17 (62.96)	52.9±15.9	Nil	DLQI
Friedman 2019	Case series	Israel	16	16 (100)	41.5 (12.4)	7.44 (4.16)	DLQI
Baskan 2018	Case series	Turkey	14	9 (64.29)	45.36 (8.93)	21.64 (14.25)	Questionnaire on life quality
Schaller 2016	Case series*	Germany	161	Nil	Nil	Nil	EQ-5D, DLQI
Taieb 2016	Case series*	USA	962	Nil	Nil	Nil	EQ-5D
Shim 2013	Case series	UK	20	11 (55)	42 (7.75)	Nil	DLQI
Aksoy 2010	Case series	Turkey	308	221 (71.8)	42.7 (14.0)	6.44 (8.73)	DLQI
Menezes 2009	Case series	Portugal	22	15 (68.2)	52.6	5.5	DLQI
Trumbore 2009	Case series	USA	8	2 (25)	58.3 (42–77) ^b	Nil	RosaQoL
Weissenbacher 2008	Case series*	Germany	40	15 (37.5)	58 (36–76): mean	Nil	DLQI
Fleischer 2005	Case series	USA	583	448 (76.8)	50.9 (14.35)	Nil	RosaQoL
Tan 2005	Case series	USA	16	14 (87.5)	48.2 (7.7)	12.9	DLQI
Provided only the total life of quality score in rosacea patients							
Augustin 2023	Cross-sectional	Germany	475	380 (79.9)	56.3 (12.5)	8.8 (8.2)	DLQI
Azrumelashvili 2023	Cross-sectional	Georgia	138	113 (81.88)	ET: 45.25 (12.81) PP: 42.96 (10.72) PH: 62.08 (13.07) Ocular: 58.00 (20.15)	Nil	DLQI
Kulaklı 2023	Cross-sectional	Turkey	R: 94 C: 87	R: 77 (81.9) C: 72 (82.8)	R: 40.90 (14.42) C: 41.06 (13.73)	T: 2 (1–5.25) ^a	DLQI, RosaQoL
Yang 2023	Cross-sectional**	China	41	34 (83)	34 (28–45) ^a	24 (12–48) ^a	RosaQoL
Huang 2022	Cross-sectional	China	973	83 (9.0)	32.4 (11.1)	< 2: 265 (28.8) ≥ 2: 537 (58.3)	DLQI
Wang 2022	Cross-sectional	China	R: 160 C: 100	R: 58 (36.3)	R: 37 (6.64) C: 36 (18–60) ^c	Nil	DLQI
Wang 2021	Cross-sectional	China	58	50 (86.2)	Group 1: 32.7 (10.0) Group 2: 34.8 (11.2)	Nil	RosaQoL
Yamasaki 2022	Cross-sectional	Japan	130	107 (82.3)	47.8 (13.0)	4.7 (6.8)	DLQI, Skindex-16, EQ-5D-5L
Yang 2022	Cross-sectional	China	469	392 (83.6)	36.6 (10.6)	< 5: 343 5–10: 85 ≥ 10: 41	DLQI, RosQoL
Acar 2021	Cross-sectional	Turkey	100	100 (100)	43.21 (10.1)	54.8 (5.9)	DLQI
Chen 2021	Cross-sectional	China	774	699 (90.3)	33.01 (11.13)	Nil	DLQI
Yang 2021	Cross-sectional	Taiwan	31	28 (90.3)	35.2 (9.4)	Nil	DLQI, SF-36
Karabay 2020	Cross-sectional	Turkey	85	85 (100)	33 (20–47) ^c	24 (1–144) ^b	DLQI
Wienholtz 2020	Cross-sectional	Denmark	309	203 (67.7)	51 (43.0–61.0) ^a	Nil	DLQI
Baldwin 2019	Cross-sectional	USA	708	588 (83.1)	52.4 (14.7)	Nil	IA-RFR, DLQI
Kubanov 2019	Cross-sectional	Russia	120	68 (56.66)	42.7 (12.93)	Nil	DLQI
Tan 2019	Cross-sectional	Global	710	467 (65.8)	44.5 (13.8)	Nil	DLQI
Williamson 2019	Cross-sectional	USA	54	49 (90.7)	48.1 (9.4)	Nil	DLQI
Harper J 2018	Cross-sectional	USA	409	277 (67.7)	53.1 (13.47)	Nil	SF-36
Williamson 2018	Cross-sectional	USA	122	96 (78.7)	59.38 (14.06)	Nil	DLQI
Zeichner 2018	Cross-sectional	USA	600	400 (66.7)	51.69	Nil	RosaQoL, SF-36
Thomas 2017	Cross-sectional***	Australia	54	43 (79.6)	49.3 (11.8)	Nil	Skindex-16 score
van der Linden 2017	Cross-sectional**	Netherlands	80	59 (74)	46 (3.33)	5 (1.33)	RosaQoL
Li 2016	Cross-sectional	China	76	60 (78.94)	36.0 (10.7)	4.5 (4.7)	DLQI, RosaQoL
Beikert 2013	Cross-sectional	Germany	475	370 (79.9)	55.8 (11.9)	8.8 (8.2)	DLQI
Böhm 2013	Cross-sectional	Germany	168	88 (52.38)	56	nil	DLQI
Langenbruch 2011	Cross-sectional	Germany	475	370 (79.9)	56.3 (12.5)	8.8 (8.2)	DLQI, EQ-VAS
Baldwin 2010	Cross-sectional	USA	966	684 (70.8)	50.6 (18–87) ^b	5.2	RosaQoL
Kini 2009	Cross-sectional	USA	135	99 (73.3)	56.6 (14.2)	> 5: 47 (34.8)	RosaQoL
Hiltscher 2001	Cross-sectional	Germany	46	Rosacea: 23 (67) Rhino: 0 (0)	Rosacea: 48.8 (15.3) Rhino: 62.3 (9.9)	Rosacea: 2.5 (3.2) Rhino: 11.1 (8.7)	DLQI

^aMedian (interquartile range [IQR]). ^bMean (range). ^cMedian (range).

*Although the original study was an RCT, this study is reported as a case series because only the pre-treatment and post-treatment QoL data of patients with rosacea were extracted. **Although the original study was an RCT, this study is reported as a cross-sectional study because only the QoL scores of patients with rosacea were extracted.

***Although the original study was a case series, this study is reported as a cross-sectional study because only the baseline QoL scores of patients with rosacea were extracted. C: control group; DLQI: Dermatology Life Quality Index; EQ-5D: EuroQol Five-Dimension Scale; EQ-5D-5L: EuroQol Five-Dimension Five-Level Scale; EQ-VAS: EuroQol Visual Analog Scale; ET: erythematotelangiectatic; HRQoL: health-related quality of life; IA-RFR: Impact Assessment for Rosacea Facial Redness; PH: phymatous; PP: papulopustular; QoL: quality of life; R: rosacea group; RosaQoL: Rosacea-Specific Quality-of-Life Questionnaire; SF-36: 36-Item Short Form Health Survey; T: total.

points in DLQI score. However, substantial heterogeneity among the included studies was discovered ($I^2=90.92\%$). The funnel plot for DLQI scores before versus after treatment was asymmetric, with Egger's regression test confirming significant publication bias ($p<0.001$). After 2 additional studies were adjusted for, trim-and-fill analysis revealed higher QoL after treatment (95% CI=-0.680 to -1.777, Fig. S5).

The scores in 3 domains of the RosaQoL were reported in 4 studies (12, 13, 31, 49). Regarding the function domain, random-effects model analysis revealed improved QoL after treatment for rosacea (SMD=-0.323, 95% CI=-0.026 to 0.672, $p=0.07$, Fig. S6a). Regarding the symptom and emotion domains, treatment for rosacea significantly improved the QoL of patients with rosacea (symptom domain: SMD=1.877, 95% CI=0.521-1.967, $p=0.01$; emotion domain: SMD=1.455, 95% CI=0.587-2.324, $p=0.001$; Fig. S6b and c). However, substantial heterogeneity among the included studies was discovered for the function, symptom, and emotion domains, with $I^2=78\%$, 96% , and 93% , respectively.

DISCUSSION

In this systematic review, we established the levels of HRQoL in patients with rosacea. Specifically, we obtained an overall DLQI score of 8.61 in patients with rosacea. We also discovered that rosacea treatment improved the DLQI score and RosaQoL scores in 3 domains and that patients with rosacea had significantly lower HRQoL compared with healthy controls.

Although holistic care is currently gaining attention in the field of healthcare, no comprehensive studies on QoL and the psychological effects of chronic skin disorders have yet been conducted. The majority of physicians manage chronic skin disorders such as rosacea on the basis of the disorders' objective severity, but low HRQoL and emotional stress may trigger relapse and exacerbation of rosacea (72), further increasing the psychosocial burden (73). Therefore, recognizing and addressing potential discrepancies between the clinician-assessed severity of rosacea and patient-reported HRQoL is essential. Even when rosacea is assessed as being well controlled through objective criteria, patients

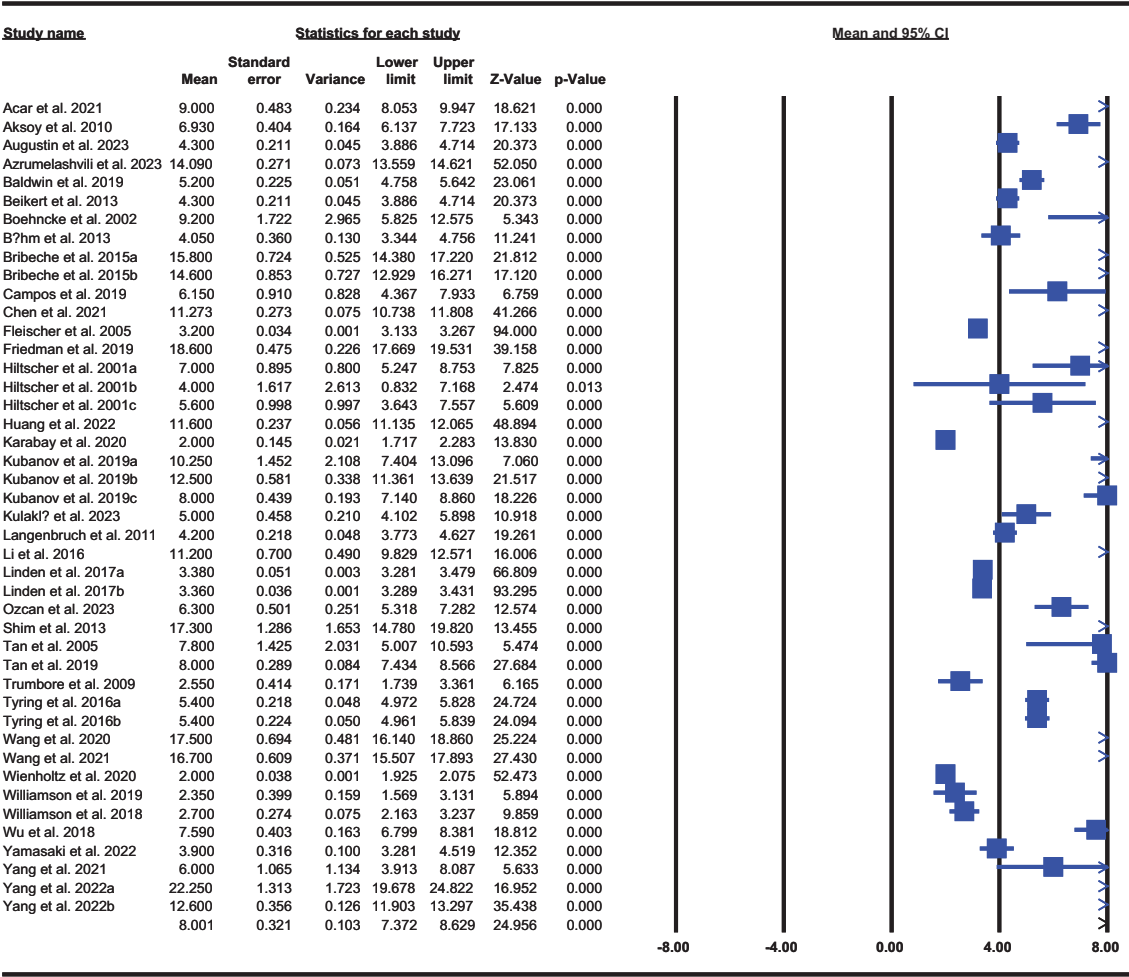


Fig. 2. Mean Dermatology Life Quality Index (DLQI) scores in patients with rosacea.^a ^aStudies with quality of life scores other than those of the DLQI or RosaQoL were excluded.

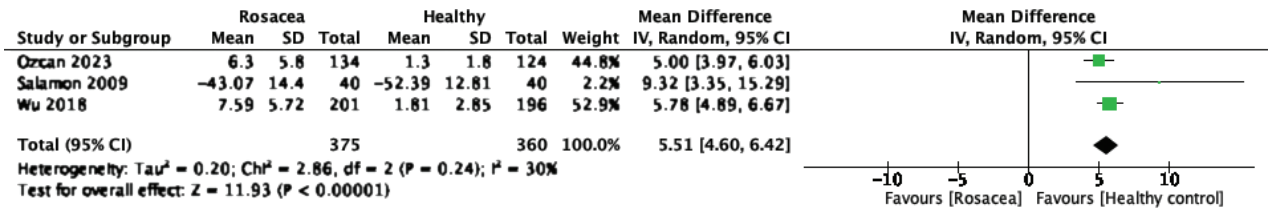


Fig. 3. Mean Dermatology Life Quality Index (DLQI) scores in patients with rosacea and healthy controls.

may continue to experience major psychosocial distress because of their condition. In addition, the effect of rosacea on HRQoL can vary greatly between individuals. Therefore, physicians should provide comprehensive care that addresses both the physical and psychosocial aspects of rosacea and ultimately improves patient outcomes and satisfaction.

Given the subjective nature of HRQoL, assessments involving HRQoL may increase the difficulty of disease management for physicians. Providing dermatologists with access to HRQoL scores derived from real-world data can help them effectively manage rosacea by comparing these scores with those of individual patients. Thus, establishing the levels of rosacea-related HRQoL is regarded as a primary goal for dermatologists.

Rosacea has a major effect on HRQoL. In a study included in this meta-analysis, the authors examined the psychosocial effect of chronic facial dermatoses on adults and reported significantly higher DLQI scores in patients with rosacea than in healthy controls (41). The HRQoL scores of patients with rosacea were lower than those of the healthy population. Although our findings are consistent with those of previous studies, our study involved a larger sample and a broader compilation of related articles.

Various tools have been used to examine rosacea-related HRQoL, such as the DLQI established in 1994 (8) and the RosaQoL established in 2004 (10). Multiple

studies have examined the effects of rosacea treatment by utilizing HRQoL assessment tools. However, no definitive conclusions have yet been drawn because of the heterogeneity in these assessment tools. Van Zuuren et al. (14) systematically reviewed 11 studies examining HRQoL changes after treatment for rosacea up to July 2014, but many relevant studies have since been published and should be included in a systematic review (43, 60). In addition, although van Zuuren et al. (14) examined improvements in HRQoL and symptoms after treatment for rosacea, they did not report the real-world effectiveness of such treatment. Therefore, in this study, we conducted a comprehensive systematic review and meta-analysis to determine the effect of treatment on HRQoL in patients with rosacea by analysing real-world data. We discovered that patients with rosacea who received treatment had higher HRQoL scores compared with those who did not. Therefore, we concluded that treatment for rosacea has positive effects on HRQoL.

Compared with other skin disorders, rosacea may be associated with lower HRQoL. Cresce et al. (74) reported DLQI scores ranging from 2.0 to 17.7 for acne and from 4.3 to 17.3 for rosacea. Although our findings are somewhat similar, we obtained DLQI scores ranging from 2.00 to 22.25 in patients with rosacea, a wider range than that for acne reported in a previous study. Given that our study involved real-world data collected up to 2023, recent research findings may account for discrepancies with

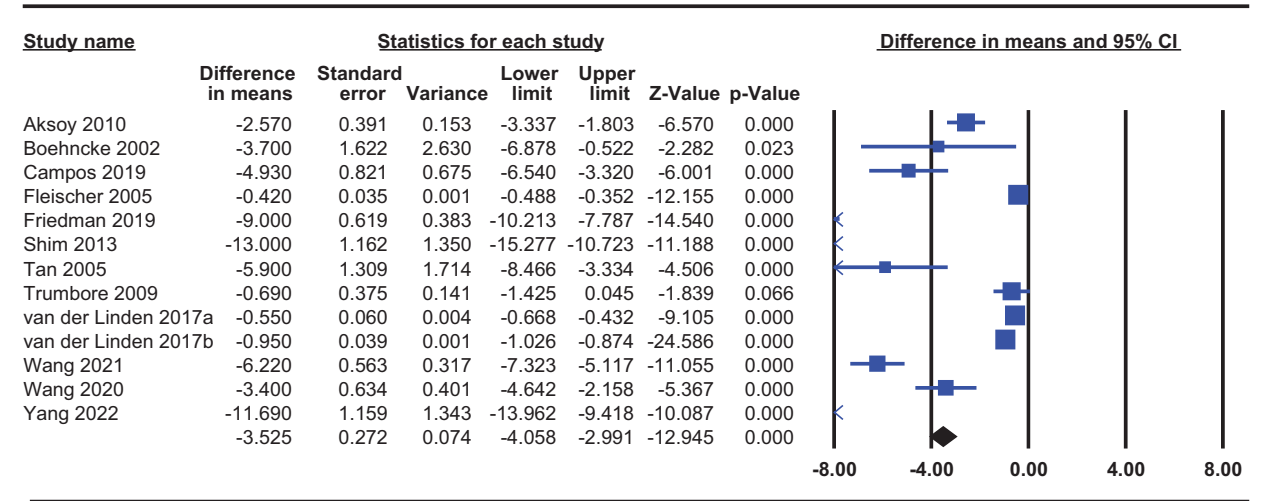


Fig. 4. Mean Dermatology Life Quality Index (DLQI) scores in patients with rosacea before and after treatment.

other studies. These discrepancies may be due to changes in methodology or patients' changing perceptions of HRQoL. In this study, we discovered that treatment for rosacea significantly improved HRQoL, consistent with previous findings regarding atopic dermatitis (75). Overall, rosacea, acne vulgaris, and atopic dermatitis can be concluded to have major effects on patients' HRQoL and psychological well-being.

Limitations

This study has several limitations. First, moderate-to-severe heterogeneity was discovered. Second, some HRQoL assessment tools were not included in our analysis because of value incompatibility. Nevertheless, our findings indicate that physicians should incorporate HRQoL into their future evaluations of rosacea. Third, research letters and unpublished studies were not included in our analysis. Fourth, the improvement discovered in the emotion domain of the RosaQoL after treatment for rosacea may have been due to placebo, particularly in the non-RCT studies. The included studies that exhibited moderate heterogeneity presumably did so for the following reasons. First, the treatments for rosacea were diverse, and the number of articles examining the effectiveness of each treatment technique was insufficient to conduct a subgroup analysis. Second, multiple HRQoL assessment tools have been developed and modified depending on patients' demographics, resulting in discrepancies in criteria and values. Third, major variations existed in the baseline characteristics of patients, including disease duration, rosacea clinical subtype, and disease severity. Finally, various study types were included in our analysis: 4 RCTs, 15 case series, and 33 cross-sectional studies.

Conclusion

Treatment improves the HRQoL of patients with rosacea. Patients with rosacea have lower HRQoL compared with healthy individuals; their overall HRQoL score was found to be 8.61. To reduce the severity of rosacea and interrupt the detrimental cycle of low HRQoL, psychological stress, and disease progression, we strongly recommend incorporating HRQoL assessment into the management of rosacea. Future studies should explore the HRQoL outcomes of rosacea and other skin disorders to further emphasize the role of HRQoL assessment in clinical practice.

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REFERENCES

1. Wilkin J, Dahl M, Detmar M, Drake L, Feinstein A, Odom R, et al. Standard classification of rosacea: Report of the National Rosacea Society Expert Committee on the Classification and Staging of Rosacea. *J Am Acad Dermatol* 2002; 46: 584–587.
2. Tan J, Blume-Peytavi U, Ortonne JP, Wilhelm K, Marticou L, Baltas E, et al. An observational cross-sectional survey of rosacea: clinical associations and progression between subtypes. *Br J Dermatol* 2013; 169: 555–562.
3. Tan J, Berg M. Rosacea: current state of epidemiology. *J Am Acad Dermatol* 2013; 69: S27–S35.
4. Gether L, Overgaard LK, Egeberg A, Thyssen JP. Incidence and prevalence of rosacea: a systematic review and meta-analysis. *Br J Dermatol* 2018; 179: 282–289.
5. Van Beugen S, Schut C, Kupfer J, Bewley AP, Finlay AY, Gierler U, et al. Perceived stigmatization among dermatological outpatients compared with controls: an observational multi-centre study in 17 European countries. *Acta Derm Venereol* 2023; 103: adv6485.
6. Chang HC, Huang YC, Lien YJ, Chang YS. Association of rosacea with depression and anxiety: a systematic review and meta-analysis. *J Affect Disord* 2022; 299: 239–245.
7. van Zuuren EJ, Graber MA, Hollis S, Chaudhry M, Gupta AK, Gover M. Interventions for rosacea. *Cochrane Database Syst Rev* 2005; Cd003262.
8. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI): a simple practical measure for routine clinical use. *Clin Exp Dermatol* 1994; 19: 210–216.
9. Nicholson K, Abramova L, Chren MM, Yeung J, Chon SY, Chen SC. A pilot quality-of-life instrument for acne rosacea. *J Am Acad Dermatol* 2007; 57: 213–221.
10. Renzi C, Tabolli S, Picardi A, Abeni D, Puddu P, Braga M. Effects of patient satisfaction with care on health-related quality of life: a prospective study. *J Eur Acad Dermatol Venereol* 2005; 19: 712–718.
11. Chren MM, Lasek RJ, Sahay AP, Sands LP. Measurement properties of Skindex-16: a brief quality-of-life measure for patients with skin diseases. *J Cutan Med Surg* 2001; 5: 105–110.
12. Luger T, Peukert N, Rother M. A multicentre, randomized, placebo-controlled trial establishing the treatment effect of TDT 068, a topical formulation containing drug-free ultra-deformable phospholipid vesicles, on the primary features of erythematotelangiectatic rosacea. *J Eur Acad Dermatol Venereol* 2015; 29: 283–290.
13. van der Linden MMD, van Ratingen AR, van Rappard DC, Nieuwenburg SA, Spuls PI. DOMINO, doxycycline 40 mg vs. minocycline 100 mg in the treatment of rosacea: a randomized, single-blinded, noninferiority trial, comparing efficacy and safety. *Br J Dermatol* 2017; 176: 1465–1474.
14. van Zuuren EJ, Fedorowicz Z, Carter B, van der Linden MM, Charland L. Interventions for rosacea. *Cochrane Database Syst Rev* 2015; 2015: Cd003262.
15. van der Linden MM, van Rappard DC, Daams JG, Sprangers MA, Spuls PI, de Korte J. Health-related quality of life in patients with cutaneous rosacea: a systematic review. *Acta Derm Venereol* 2015; 95: 395–400.
16. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol* 2009; 62: e1–34.
17. Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle–Ottawa Scale (NOS) for Assessing the Quality of Non-Randomized Studies in Meta-Analysis. Ottawa Hospital Research Institute; 2000.
18. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA, editors. *Cochrane handbook for systematic reviews of interventions version 6.4 (updated August 2023)*. Cochrane; 2023. Available from www.training.cochrane.org/handbook.
19. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of

- bias in non-randomised studies of interventions. *BMJ* 2016; 355: i4919.
20. Rostom A, Dubé C, Cranney A, Saloojee N, Sy R, Garritty C, et al. Celiac disease. Rockville (MD): Agency for Healthcare Research and Quality (US); 2004 Sep. (evidence Reports/Technology assessments, no. 104). Appendix D: quality assessment forms; 2014.
 21. DerSimonian R, Laird N. Meta-analysis in clinical trials revisited. *Contemp Clin Trials* 2015; 45: 139–145.
 22. Acar EM, Kaya Erdoğan H, Şaş S, Acer E. Evaluation of fibromyalgia syndrome in patients with rosacea. *Arch Rheumatol* 2021; 36: 252–257.
 23. Augustin M, Sommer R, Blome C, Kirsten N, Langenbruch A. Development of a specific variant of Patient Benefit Index (PBI) assessing patient needs, goals and benefits in rosacea treatment. *Patient Prefer Adherence* 2023; 17: 1335–1345.
 24. Azumelashvili S, Kituashvili T. Quality of life and disease coping strategies in patients with rosacea. *Georgian Med News* 2023; 336: 66–72.
 25. Boehncke WH, Ochsendorf F, Paeslack I, Kaufmann R, Zollner TM. Decorative cosmetics improve the quality of life in patients with disfiguring skin diseases. *Eur J Dermatol* 2002; 12: 577–580.
 26. Böhm D, Schwanitz P, Stock Gissendanner S, Schmid-Ott G, Schulz W. Symptom severity and psychological sequelae in rosacea: results of a survey. *Psychol Health Med* 2014; 19: 586–591.
 27. Bribeche MR, Fedotov VP, Gladichev VV, Pukhalskaya DM, Kolitcheva NL. Clinical and experimental assessment of the effects of a new topical treatment with praziquantel in the management of rosacea. *Int J Dermatol* 2015; 54: 481–487.
 28. Bulbul Baskan E, Akin Belli A. Evaluation of long-term efficacy, safety, and effect on life quality of pulsed dye laser in rosacea patients. *J Cosmet Laser Ther* 2019; 21: 185–189.
 29. Campos MA, Sousa AC, Varela P, Baptista A, Menezes N. Comparative effectiveness of purpuragenic 595 nm pulsed dye laser versus sequential emission of 595 nm pulsed dye laser and 1,064 nm Nd:YAG laser: a double-blind randomized controlled study. *Acta Dermatovenereol Alp Pannonica Adriat* 2019; 28: 1–5.
 30. Chen M, Deng Z, Huang Y, Li J. Prevalence and risk factors of anxiety and depression in rosacea patients: a cross-sectional study in China. *Front Psychiatry* 2021; 12: 659171.
 31. Fleischer A, Suephy C. The face and mind evaluation study: an examination of the efficacy of rosacea treatment using physician ratings and patients' self-reported quality of life. *J Drugs Dermatol* 2005; 4: 585–590.
 32. Friedman O, Koren A, Niv R, Mehrabi JN, Artzi O. The toxic edge: a novel treatment for refractory erythema and flushing of rosacea. *Lasers Surg Med* 2019; 51: 325–331.
 33. Harper J, Del Rosso JQ, Ferrusi IL. Cross-sectional survey of the burden of illness of rosacea by erythema severity. *J Drugs Dermatol* 2018; 17: 150–158.
 34. Huang Y, Yan S, Xie H, Wang B, Zhao Z, Huang Y, et al. Health related quality of life of rosacea patients in China assessed by dermatology life quality index and willingness to pay. *Patient Prefer Adherence* 2022; 16: 659–670.
 35. Kini SP, Nicholson K, DeLong LK, Dannemann T, Estaris J, Foster J, et al. A pilot study in discrepancies in quality of life among three cutaneous types of rosacea. *J Am Acad Dermatol* 2010; 62: 1069–1071.
 36. Kubanov A, Gallyamova Y, Kravchenko A. Clinical picture, diagnosis and treatment of rosacea, complicated by Demodex mites. *Dermatol Reports* 2019; 11: 7675.
 37. Kulaklı S, Oğuz ID, Sari IF, Sengul I, Kulaklı F, Akşan B, et al. "Zooming" in the association between rosacea and fibromyalgia syndrome: is it worth mentioning? *Rev Assoc Med Bras* (1992) 2023; 69: e20230256.
 38. Langenbruch AK, Beket E, Augustin M. Quality of health care of rosacea in Germany from the patient's perspective: results of the national health care study Rosareal 2009. *Dermatology* 2011; 223: 124–130.
 39. Li J, Li M, Chen Q, Fu J, Zhang M, Hao F. Quality of life among patients with rosacea: an investigation of patients in China using two structured questionnaires. *J Eur Acad Dermatol Venereol* 2016; 30: e98–e99.
 40. Menezes N, Moreira A, Mota G, Baptista A. Quality of life and rosacea: pulsed dye laser impact. *J Cosmet Laser Ther* 2009; 11: 139–141.
 41. Ozcan Y, Sungur MA, Ozcan BY, Eyup Y, Ozlu E. The psychosocial impact of chronic facial dermatoses in adults. *Dermatol Pract Concept* 2023; 13: e2023029.
 42. Salamon M, Chodkiewicz J, Sysa-Jedrzejowska A, Wozniacka A. [Quality of life in patients with rosacea]. *Przegl Lek* 2008; 65: 385–389 (in Polish).
 43. Sbidian E, Vicaute É, Chidiack H, Anselin E, Cribier B, Dréno B, et al. A randomized-controlled trial of oral low-dose isotretinoin for difficult-to-treat papulopustular rosacea. *J Invest Dermatol* 2016; 136: 1124–1129.
 44. Schaller M, Dirschka T, Kemény L, Briantais P, Jacovella J. Superior efficacy with ivermectin 1% cream compared to metronidazole 0.75% cream contributes to a better quality of life in patients with severe papulopustular rosacea: a subanalysis of the randomized, investigator-blinded ATTRACT study. *Dermatol Ther (Heidelb)* 2016; 6: 427–436.
 45. Shim TN, Abdullah A. The effect of pulsed dye laser on the dermatology life quality index in erythematotelangiectatic rosacea patients: an assessment. *J Clin Aesthet Dermatol* 2013; 6: 30–32.
 46. Taieb A, Passeron T, Ruzicka T, Berth-Jones J, Jacovella J, Huang MY, et al. Ivermectin cream improves health-related quality of life in patients with rosacea: data from a randomized trial. *Br J Dermatol* 2016; 175: 1366–1368.
 47. Tan SR, Tope WD. Pulsed dye laser treatment of rosacea improves erythema, symptomatology, and quality of life. *J Am Acad Dermatol* 2004; 51: 592–599.
 48. Thomas CL, Kim B, Lam J, Richards S, See A, Kalouche S, et al. Objective severity does not capture the impact of rosacea, acne scarring and photoaging in patients seeking laser therapy. *J Eur Acad Dermatol Venereol* 2017; 31: 361–366.
 49. Trumbore MW, Goldstein JA, Gurge RM. Treatment of papulopustular rosacea with sodium sulfacetamide 10%/sulfur 5% emollient foam. *J Drugs Dermatol* 2009; 8: 299–304.
 50. Tyring S, Solomon JA, Staedtler G, Lott JP, Nkulikiyinka R, Shakery K. Patient-reported outcomes of azelaic acid foam 15% for patients with papulopustular rosacea: secondary efficacy results from a randomized, controlled, double-blind, phase 3 trial. *Cutis* 2016; 98: 269–275.
 51. Wang B, Deng YX, Li PY, Yan S, Xie HF, Li J, et al. Efficacy and safety of non-insulated fractional microneedle radiofrequency for treating difficult-to-treat rosacea: a 48-week, prospective, observational study. *Arch Dermatol Res* 2022; 314: 643–650.
 52. Wang B, Deng YX, Yan S, Xie HF, Li J, Jian D. Efficacy of non-ablative fractional 1440-nm laser therapy for treatment of facial acne scars in patients with rosacea: a prospective, interventional study. *Lasers Med Sci* 2021; 36: 649–655.
 53. Wang T, Liu F, Jia X, Tan J, Qi B, Guo J, et al. Serum level of brain-derived neurotrophic factor (BDNF) associated with depression in patients with rosacea: a candidate predictive biomarker. *Clin Cosmet Investig Dermatol* 2022; 15: 1029–1036.
 54. Weissenbacher S, Merkl J, Hildebrandt B, Wollenberg A, Braeutigam M, Ring J, et al. Pimecrolimus cream 1% for papulopustular rosacea: a randomized vehicle-controlled double-blind trial. *Br J Dermatol* 2007; 156: 728–732.
 55. Wienholtz NKF, Christensen CE, Haugaard JH, Zhang DG, Ashina M, Thyssen JP, et al. Cohort profile: COpenhagen ROsacea COhort (COROCO) and COpenhagen Mlgraine COhort (COMICO). *BMJ Open* 2020; 10: e039445.
 56. Williamson T, Cameron J, McLeod K, Turner B, Quillen A, LaRose A, et al. Concerns and treatment satisfaction in patients being treated with azelaic acid foam for rosacea. *J Drugs Dermatol* 2019; 18: 381–386.
 57. Williamson T, Cheng WY, McCormick N, Vekeman F. Patient preferences and therapeutic satisfaction with topical agents for rosacea: a survey-based study. *Am Health Drug Benefits* 2018; 11: 97–106.
 58. Wu Y, Fu C, Zhang W, Li C, Zhang J. The dermatology life quality index (DLQI) and the hospital anxiety and depression (HADS) in Chinese rosacea patients. *Psychol Health Med*

- 2018;23: 369–374.
59. Yang F, Zhang Q, Song D, Liu X, Wang L, Jiang X. A cross-sectional study on the relationship between rosacea severity and quality of life or psychological state. *Clin Cosmet Investig Dermatol* 2022; 15: 2807–2816.
 60. Yang J, Liu X, Cao Y, Wang P, Zhang H, Chen Q, et al. 5-aminolevulinic acid photodynamic therapy versus minocycline for moderate to severe rosacea: a single-center, randomized, evaluator-blind controlled study. *J Am Acad Dermatol* 2023; 89: 711–718.
 61. Yang R, Liu C, Liu W, Luo J, Cheng S, Mu X. Botulinum toxin A alleviates persistent erythema and flushing in patients with erythema telangiectasia rosacea. *Dermatol Ther (Heidelb)* 2022; 12: 2285–2294.
 62. Yang TT, Lan CE. Impacts of skin disorders associated with facial discoloration on quality of life: novel insights explaining discordance between life quality scores and willingness to pay. *J Cosmet Dermatol* 2022; 21: 3053–3058.
 63. Zeichner JA, Eichenfield LF, Feldman SR, Kasteler JS, Ferrusi IL. Quality of life in individuals with erythematotelangiectatic and papulopustular rosacea: findings from a web-based survey. *J Clin Aesthet Dermatol* 2018; 11: 47–52.
 64. Hiltcher D, Boslet WT, Fuchslocher M, Sinkgraven R, Rzany B. Quality of life in patients with rosacea and rhinophyma. *Aktuelle Derm* 2001; 27: 391–394.
 65. Tan J, Steinhoff M, Bewley A, Gieler U, Rives V. Characterizing high-burden rosacea subjects: a multivariate risk factor analysis from a global survey. *J Dermatol Treat* 2020; 31: 168–174.
 66. Wang B, Yuan X, Huang X, Tang Y, Zhao Z, Yang B, et al. Efficacy and safety of hydroxychloroquine for treatment of patients with rosacea: a multicenter, randomized, double-blind, double-dummy, pilot study. *J Am Acad Dermatol* 2021; 84: 543–545.
 67. Yamasaki K, Miyachi Y. Perspectives on rosacea patient characteristics and quality of life using baseline data from a phase 3 clinical study conducted in Japan. *J Dermatol* 2022; 49: 1221–1227.
 68. Aksoy B, Altaykan-Hapa A, Egemen D, Karagöz F, Atakan N. The impact of rosacea on quality of life: effects of demographic and clinical characteristics and various treatment modalities. *Br J Dermatol* 2010; 163: 719–725.
 69. Aktaş Karabay E, Karşıyakalı N, Karabay E. Evaluation of sexual functions in female rosacea patients: a prospective, case-control study. *Int J Impot Res* 2020; 32: 628–634.
 70. Baldwin HE, Harper J, Baradaran S, Patel V. Erythema of rosacea affects health-related quality of life: results of a survey conducted in collaboration with the National Rosacea Society. *Dermatol Ther* 2019; 9: 725–734.
 71. Beikert FC, Langenbruch AK, Radtke MA, Augustin M. Willingness to pay and quality of life in patients with rosacea. *J Eur Acad Dermatol Venereol* 2013; 27: 734–738.
 72. Woo YR, Lim JH, Cho DH, Park HJ. Rosacea: molecular mechanisms and management of a chronic cutaneous inflammatory condition. *Int J Mol Sci* 2016; 17: 1562.
 73. Bewley A, Fowler J, Schöfer H, Kerrouche N, Rives V. Erythema of rosacea impairs health-related quality of life: results of a meta-analysis. *Dermatol Ther (Heidelb)* 2016; 6: 237–247.
 74. Cresce ND, Davis SA, Huang WW, Feldman SR. The quality of life impact of acne and rosacea compared to other major medical conditions. *J Drugs Dermatol* 2014; 13: 692–697.
 75. Yepes-Núñez JJ, Guyatt GH, Gómez-Escobar LG, Péres-Herrera LC, Chu AWL, Ceccaci R, et al. Allergen immunotherapy for atopic dermatitis: systematic review and meta-analysis of benefits and harms. *J Allergy Clin Immunol* 2023; 151: 147–158.