Title: Correlating the DLQI with psychiatric measures: a systematic review

Faraz M Ali[1*] (MBChB MRCP), Nutjaree Johns[1,2] (PharmD PhD), Sam Salek[3,4](PhD), Andrew Y Finlay[1*] (MBBS FRCP (Lond & Glasg))

[1]Department of Dermatology and Academic Wound Healing, Division of Infection and Immunity, School of Medicine, Cardiff University, Cardiff, UK

[2]Faculty of Pharmaceutical Sciences and Melatonin Research Group, Khon Kaen University, Thailand.

[3]School of Life and Medical Sciences, University of Hertfordshire, Hatfield, UK

[4]Institute for Medicines Development, Cardiff, UK.

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*Correspondence:

- Dr Faraz Ali, Department of Dermatology, Division of Infection and Immunity, School of Medicine, Cardiff University, 3rd Floor Glamorgan House, Heath Park, Cardiff CF14 4XN, UK
  email: AliFM@cardiff.ac.uk, tel: 02920 744721
- Prof A.Y. Finlay, Department of Dermatology, Division of Infection and Immunity, School of Medicine, Cardiff University, 3rd Floor Glamorgan House, Heath Park, Cardiff CF14 4XN, UK email:
  FinlayAY@cardiff.ac.uk

Funding: none

Conflicts of Interest

AYF is joint copyright owner of the DLQI and Cardiff University and AYF receive royalties.

FA, NJ, SS declare no conflicts of interest.

Keywords: DLQI, HADS, psychiatric measures, systematic review

Manuscript word count: 1737 (excluding abstract)

Manuscript table count: 2

Manuscript figure count: 2

ORCID Numbers:

Faraz Ali: 0000-0002-4184-2023

Nutjaree Johns: 0000-0002-7890-1402

Sam Salek: 0000-0002-4612-5699

Andrew Finlay: 0000-0003-2143-1646

Abstract (195 words)

Skin conditions may have a major impact on the psychological well-being of patients, ranging from depression to anxiety. The Dermatology Life Quality Index (DLQI) is the most commonly used quality of life tool in dermatology, though it has yet to be correlated with psychiatric measures used in clinical therapeutic trials.

We conducted a systematic review to determine whether there is any correlation between the DLQI and psychiatric measure scores, potentially allowing the DLQI to be used as a surrogate measure for depression or psychiatric screening. Six databases were searched using the keywords: 'DLQI', 'Dermatology Life Quality Index', 'Psych*', 'depression', 'anxiety', 'stress' and 'trial*'. All randomised trials where full DLQI and psychiatric scores were provided were included. PRISMA guidelines were followed.

462 records were screened but only seven met inclusion criteria. Hospital Anxiety and Depression Scale (HADS) was the most commonly used psychiatric measure; the 'depression' component score changes correlated strongly with the DLQI (r=0.715).

There needs to be guidance on psychiatric measurement and reporting in clinical trials. Though the DLQI correlated well with the 'depression' domain of the HADS scale, interviews and screening for depression are still vital for full assessment of patient psychological well-being.

Introduction

Skin conditions may have significant implications on a patient's quality of life (QoL), affecting various aspects of their day-to-day living.[1] This includes routine activities, household chores, social interactions, and relationships. There is a well-documented impact on psychological well-being, often manifesting in psychiatric problems that may range from depression to anxiety.[2] Several studies have examined the relationship between psychiatric morbidity and skin diseases.[3-7] For example, psoriasis is associated with psychologic disorders with sexual and sleep complaints being the most prevalent.[3] Anxiety and depression are strongly correlated in such conditions as alopecia areata,[4] vitiligo,[5] rosacea,[6] and hirsutism.[7]

The Dermatology Life Quality Index[8] (DLQI, score range 0-3) has been used in many skin conditions and across a wide range of disease severities.[9,10] It is a dermatology-specific tool that assesses the QoL impairment in the past week for those aged 16 and above. It has 10 questions and evaluates 6 parameters: symptoms and feelings, daily activities, leisure, work/school, personal relationships, and treatment. The total possible score ranges from 0 to 30 where a higher score signifies a larger impairment in the patient's QoL caused by the skin disease. The minimal clinically important difference (MCID), i.e. the minimum change in score that has clinical relevance, is 4 [11] and score ranges have also been banded to aid interpretation of QoL severity. [12] It has high patient acceptability,[13] short completion time of around two

minutes [14] and extensive validation,[9] resulting in its widespread use in both clinical settings and clinical therapeutic research trials globally.[15] The DLQI is also integral to several national registries and guidelines, for example the National Institute for Health and Clinical Excellence (NICE) guidelines for biologics in the treatment of psoriasis. [10] The psychosocial aspects captured by the DLQI are well documented.[10] Despite this, the DLQI has yet to be compared and correlated with other psychiatric morbidity measures in randomized controlled trials.

We have conducted a systematic review to identify the various validated psychiatric measures that have been utilized in conjunction with the DLQI in randomized controlled trials (RCTs). This might also reveal whether there is any correlation between the scores that would potentially allow the DLQI to be used as a surrogate measure for depression or psychiatric screening.

Materials and Methods

Data sources

Six computerized bibliographic databases were searched up to 19 May 2016: OVID MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, EMBASE, WEB OF SCIENCE Core Collection, SCOPUS and PsycInfo. The search was not restricted by language and was conducted using PRISMA guidelines.

Keywords used were: ‘DLQI’, ‘Dermatology Life Quality Index’, ‘Psych*’, ‘depression’, ‘anxiety’, ‘stress’ and ‘trial*’.

Search filters are given in the Supplementary Material. We ran supplementary searches and reviewed trial registers and grey literature. Reference lists of all included studies and of recent reviews were also assessed. Electronic publications in advance of print were also included.

Selection criteria

We included all randomized controlled trials for any condition where the DLQI was used. This included cross-over trials and trials with open-label extensions, in all languages studying the adult population (aged 18 and over) of either sex and of any ethnicity. Only papers where the absolute scores or change in scores for the DLQI and for psychiatric measures were provided were included.

Exclusion criteria

The exclusion criteria for the systematic review were as follows: studies which included any patient less than 18 years of age, and presentations where the change in scores could not be reliably calculated for the DLQI or any psychiatric morbidity scale (including graphical representation). Abstracts and posters were excluded where further data were not available after contacting the author.

Outcome measures extracted

Primary Outcome

Data recorded included DLQI scores and those psychiatric morbidity scale being utilized. Scores for these measures were recorded at baseline, treatment, and follow-up endpoints, as well as the change in these scores attributed to treatment. For studies with an open label extension, the data were only extracted for the period of the study randomized and controlled.

Secondary Outcomes

Correlation between the sensitivity of the DLQI and psychiatric measures to change.

Data extraction and synthesis

Two reviewers (FA and NJ) extracted data independently from all eligible published studies, discussed any disagreements and, if necessary involved a third reviewer (Dr. Jui Vyas, Cardiff University) for resolution. We adapted a form, which included the Cochrane Risk of Bias tool, for recording data[16] that included study design, details of administration, methodologic quality and duration of treatment and follow-up. The quality of each presentation was quantitatively rated using the JADAD score.[17]

Results

Characteristics and attributes of the studies selected

462 records were screened from the initial database search, of which only seven interventional RCTs met the inclusion criteria; six studies were for psoriasis and one for atopic dermatitis. One study, for which results were available, was identified by searching trial registries (Fig. 1). The data described results from 5578 adult patients, with an average age of 45 years. Approximately 63.8% of the study population were men. Table 1 contains the studies identified by the systematic review.

The most common psychiatric tools used alongside the DLQI were: Beck Depression Inventory (BDI, 2 studies) and the Hospital Anxiety and Depression Scale (HADS, 5 studies). The BDI, published in 1961,[25] is a 21-item patient reported outcome measure (score range 0-63) and is commonly used in studies to assess the severity of depression. The inventory covers various aspects of mental health and depression as well as physical symptoms and relationships. The HADS scale was developed in 1983 [26] as a screening tool and consists of 14 items (score range 0-21). The questions encapsulate two domains: anxiety (HADS-A) and depression (HADS-D), each containing seven questions with a four-level response system. Scores ranging from 0-7 are considered ‘normal’, 8-10 ‘borderline abnormal’ and 11-21 ‘abnormal’.

DLQI and the psychiatric measures scores

Mean scores at baseline ranged from 6.6-13.8 for the DLQI, 8.1-12.3 for the BDI, 5.0-6.6 for HADS-D and 6.8-8.3 for the HADS-A. At treatment endpoint, the scores ranged from 2.6-6.1 for the DLQI, 5.8-10.5 for BDI, 3.1-5.00 for HADS-D, 4.3-6.1 for HADS-A (Table 2) In five studies, the DLQI was measured more frequently than the psychiatric scores throughout the study duration; however, only measurement scores for simultaneous assessment points of the two measures (i.e. DLQI, HADS or BDI) were examined.

Relationships between the DLQI and psychiatric measures

Change in score for these measures at treatment endpoint were recorded, or calculated where needed from the absolute data provided. As the HADS was the most commonly used tool (5 out of 7 studies), DLQI scores were correlated with this measure (Figure 2a and 2b). Both domains of the HADS were strongly correlated to the DLQI (HADS-D index: R^2=0.715, and HADS-A index: R^2=0.423).

Relevance of accumulative change of scores for the DLQI and HAD Scale

Table 2 demonstrates a mean baseline HADS-D score across all studies of 5.8 (‘normal’ according to the HADS-D scoring index[26]) and a mean baseline

HADS-A score of 7.4 (‘borderline abnormal’). The expected DLQI score change per HADS-D point is 4.59 and 4.29 for the HADS-A. This suggests that there is a relationship between the two scales, where improvement in DLQI scores may indicate incremental changes in HADS scores.

Discussion

Depression and other psychiatric issues continue to be significant problems experienced by dermatology patients, potentially affecting treatment compliance, leading to premature treatment discontinuation and alteration of the disease course.[27] The implications extend beyond QoL for concerned individuals, with concurrent economic repercussions through lost productivity and sick leave.[28, 29] Researchers often administer QoL tools which encompass a psychological component alongside psychiatric measures where appropriate to gather holistic efficacy data, though these are predominantly cited as secondary outcomes. This systematic review highlights the need for more frequent psychiatric assessment in RCTs, particularly where quality of life is measured; several studies had to be excluded from this review as a result. Full scores for psychiatric measures are not always provided, with researchers favoring clinical data. While primary outcomes are centered around these clinical parameters, psychiatric morbidity should not be sidelined, given its prevalence in this population.[2-7]

Although the HADS is commonly used to assess symptoms of depression and anxiety, it is most appropriate as a screening tool with routine clinical

psychiatric assessment considered as the primary diagnostic method.[30] The DLQI contains questions on various aspects of quality of life, including 'embarrassment' and 'self-consciousness,' but it does not overtly record data on depression or anxiety.[8] The total DLQI score correlates well with score changes in the Depression component of the HADS, though not as well as with the Anxiety component (Figures 2a/b). It may be possible to consider depression and anxiety in patients using DLQI scores, especially in the absence of an appropriate psychiatric measure; a DLQI score change of 4.59 and 4.29 results in a point change for the HADS-D and HADS-A respectively. However, a significant limitation of this systematic review is that there was very little data in interventional trials where both DLQI and HADS values were provided, thereby necessitating further work on more expansive datasets for more accurate and refined correlation values.

Several studies used inappropriate or non-validated scales to assess psychiatric morbidity, which led to their exclusion in this systematic review. The frequency at which this data was recorded compared to quality of life also varied across studies, despite majority of the identified studies belonging to the same intervention group. Generic and disease-specific QoL questionnaires may capture elements of depression and other mental health disorders, though these have not been validated as such for their primary purpose. Where psychiatric scores were provided, on occasion, the authors omitted commenting on the results and therefore deducing worthwhile conclusions. We suggest guidelines to ensure routine and correct measurement of psychiatric symptoms using appropriate measures, alongside

QoL assessment. The diverse and inconsistent nature of the data-reporting limits the potential to analyse and compare data between trials, whilst potentially missing cases of depression or other significant mental health issues. Almost all the studies identified in this review assessed psoriasis, a condition commonly linked with psychological distress.[31] In such cases, psychotherapy may be a significant adjuvant to traditional topical and systemic dermatological treatment, further highlighting the need for full and accurate reporting of psychological data.

There are several limitations to this review. Though the focus was primarily on interventional studies, to capture more extensive correlation data, observational studies could also have been included. We only studied DLQI data given its widespread implementation[15;] further research correlating other QoL measures may highlight other patterns of data reporting. The mean baseline HADS-D score of 5.8 is rated 'normal' according to the screening cut-off [26] and 7.4 'borderline abnormal' for the HADS-A. This highlights that mostly patients without, or with minimal, psychiatric morbidity were recruited, emphasizing the limited availability of such data in trials. Perhaps, if data with patients suffering with more significant psychiatric morbidity were available for RCTs, we might see higher score changes in the HAD scale, and subsequently more sensitive DLQI correlation values (Table 2).

Conclusions

The results of this systematic review echo our recent calls for guidance on the reporting of QoL scores[15]; we extend these suggestions for psychiatric morbidity reporting. Given the widespread adoption of the DLQI by healthcare policy makers, it is important that clinicians understand its potential value in informing routine decision-making. [32] Chronic skin conditions are associated with impaired QoL and morbidity rather than mortality, and thus such questionnaires are perceived to be more relevant by patients. This in turn encourages patients to be more actively involved in their healthcare decisions. [33] Though skin disease are assessed using clinical parameters, their visible nature means patients often suffer with depression and suicidal ideation. [30] If appropriate measures such as the HADS are not administered, these potentially-serious symptoms may be missed, perhaps leading to avoidable detrimental consequences.

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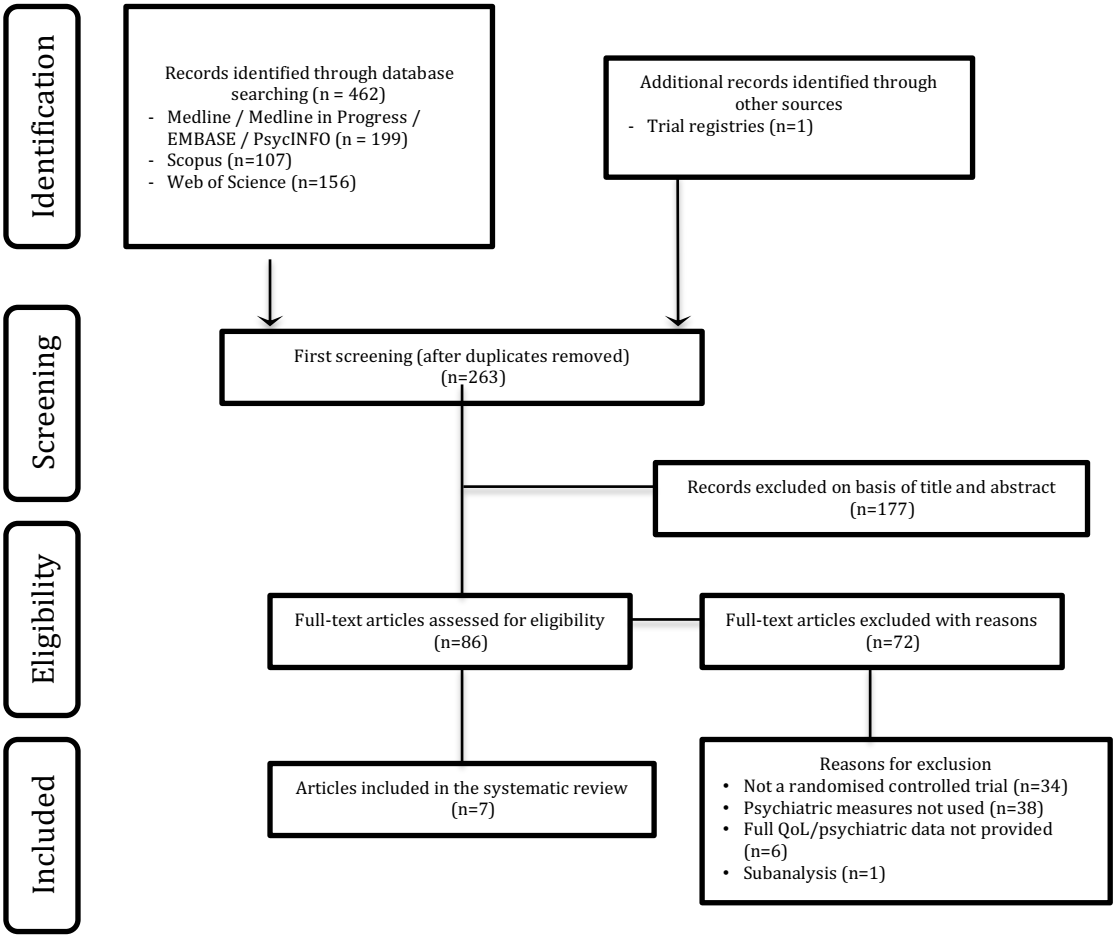
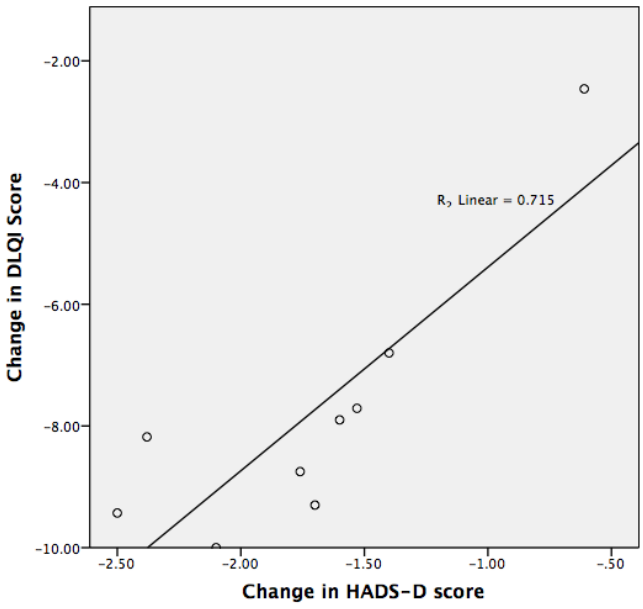
Figure 1 Flow diagram of publication selection



Figures 2a & b

a) Correlation between change in DLQI scores and HADS-D scores
b) Correlation between change in DLQI scores and HADS-A scores



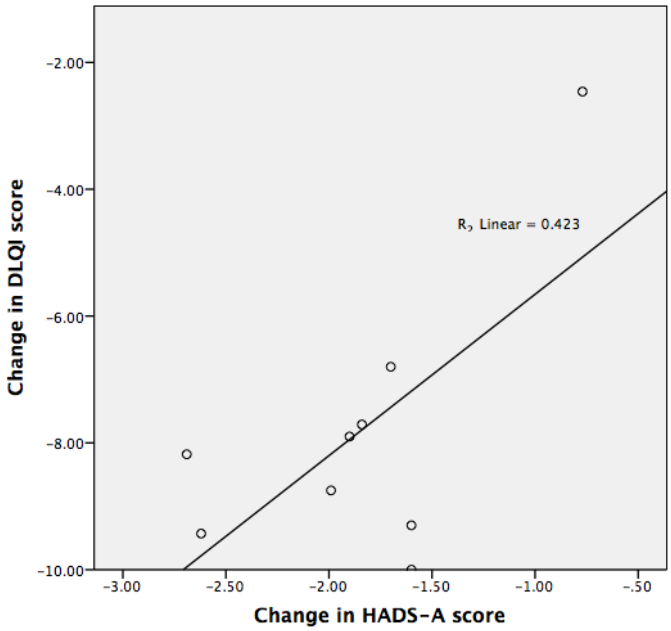


Table 1 Table of included studies, basic demographic information, and psychiatric measures used

Author, Year	JADAD score	Interventional study arm	Condition	Study duration (weeks)	Average participant age	Total no. of study participants	Psychiatric measure used
Bostoen 2012[18]	4	Educational Programme	Atopic dermatitis	12	38.5	16	BDI
Bundy 2013[19]	2	eTIPS*	Psoriasis	6	45.8	61	HADS
Dauden 2009[20]	1	Etanercept (Continuous)	Psoriasis	54	44.8	352	HADS
		Etanercept (Paused)			45.2	359	
Gelfand 2008[21]	1	Etanercept (Continuous)	Psoriasis	12	45.8	1272	BDI
		Etanercept (Interrupted)			44.9	1274	
Gniadecki 2012[22]	3	Etanercept BIW†	Psoriasis	12	46.1	379	HADS
		Etanercept QW††			46.9	373	
Langley 2010[23]	4	Ustekinumab 45 mg	Psoriasis	52	45.1	409	HADS
		Ustekinumab 90 mg			46.6	411	
Trial No: NCT01309737[24]	N/A	CP-690,550 5 mg	Psoriasis	52	45.9	331	HADS
		CP-690,550 10 mg			44.3	341	

* eTIPS, electronic Targeted Intervention for Psoriasis
† BIW, twice weekly
†† QW, once weekly

Table 2 Baseline scores and change in scores after treatment as reported in each study

Author, Year	Interventional study arm	Baseline score HADS-D	Baseline score HADS-A	Baseline score DLQI	Change in score HADS-D	Change in score HADS-A	Change in score DLQI	Expected DLQI score change for 1 HADS-D point	Expected DLQI score change for 1 HADS-A point
Bundy 2013[19]	eTIPS*	5.0	7.6	6.6	-0.6	-0.8	-2.5	4.0	3.2
Dauden 2009[20]	Etanercept (Continuous)	5.7	7.2	12.8	-1.8	-2.0	-8.8	5.0	4.4
	Etanercept (Paused)	6.2	7.7	13.8	-1.5	-1.8	-7.7	5.0	4.2
Gniadecki 2012[22]	Etanercept BIW†	6.6	8.3	12.3	-1.6	-1.9	-7.9	4.9	4.2
	Etanercept QW††	6.4	8.0	12.3	-1.4	-1.7	-6.8	4.9	4.0
Langley 2010[23]	Ustekinumab 45 mg	4.9	6.8	12.2	-1.7	-1.6	-9.3	5.4	5.8
	Ustekinumab 90 mg	5.4	6.9	12.6	-2.1	-1.6	-10.0	4.8	6.3
Trial No: NCT01309737[24]	CP-690,550 5 mg	6.0	7.1	13.2	-2.4	-2.7	-8.2	3.4	3.0
	CP-690,550 10 mg	5.6	6.9	12.7	-2.5	-2.6	-9.4	3.8	3.6
Mean (SD)		5.8 (0.6)	7.4 (0.5)	11.1 (2.2)	-1.7 (0.6)	-1.9 (0.6)	-7.8	4.6	4.3
Range		4.9 to 6.6	6.8 to 8.3	6.6 to 13.8	-2.5 to -0.6	-2.7 to -0.8	-10.0 to -2.5	3.4 to 5.5	3.0 to 6.3

* eTIPS, electronic Targeted Intervention for Psoriasis

† BIW, twice weekly

†† QW, once weekly