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Title Page

Title: A systematic review of the use of quality of life instruments in randomised controlled trials of psoriasis

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Running head: Systematic review on the use of QoL Instruments in RCTs of psoriasis

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Conflicts of Interest

AYF is joint copyright owner of the DLQI and Cardiff University receives some income from the use of the DLQI. AYF has had paid consultancies or advisory boards with Novartis, Napp Pharmaceuticals, Pfizer, Sanofi, and Galderma. VP has received educational and/or research grants from Abbvie, Cellgene, Novartis, J&J.

SS has received educational and/or research grants from Sanofi, Novartis, BMS, Pfizer & Sevier.

FA, AC, JV, AA declare no conflicts of interest.

What's already known about this topic?

- Psoriasis significantly impacts quality of life (QoL) in patients.
- Generic, skin-specific and disease-specific instruments are used in psoriasis interventional studies.
- In psoriasis randomized controlled trials (RCTs), biologics are the most researched interventions that report QoL.

What does this study add?

- The most commonly used QoL instruments in psoriasis RCTs are the DLQI, SF-36 & EQ-5D.

- There is an increasing use of QoL instruments in RCTs in psoriasis.
- Minimal clinically important difference of QoL measure scores is under-reported
- There is inconsistent reporting of QoL data and a need for guidelines when reporting.

Keywords: Psoriasis, systematic review, quality of life, treatment, DLQI

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Abstract

Background

Planners of interventional studies in psoriasis face the dilemma of selecting suitable quality of life (QoL) measures. Systematic reviews (SR) have the potential of identifying psychometrically sound measures in a given therapeutic area, whilst guiding the development of practice guidelines.

Objectives

The aim of this SR was to generate evidence of the use of QoL instruments in randomised controlled trials (RCTs) for interventions in psoriasis.

Methods

The methodology followed PRISMA guidelines. Six databases were searched with 388 search terms. Abstracts of articles were reviewed independently by two assessors, a third adjudicator resolved any opinion differences. Risk of bias was assessed using the *JADAD scale*.

Results

Of 3646 screened publications, 99 articles (100 trials) met eligibility criteria for inclusion, describing research on 33,215 subjects. 33 trials tested topical therapy, 18 systemic, 39 biologics, 9 phototherapy and 10 tested other interventions.

The Dermatology Life Quality Index (DLQI) was the most commonly used QoL instrument (number of studies=83, 83%), followed by the Short Form-36 (SF-36) (31, 31%), EuroQoL (EQ-5D) (15, 15%), Psoriasis Disability Index (PDI) (14, 14%) and Skindex (5, 5%). There was widespread inconsistency in the way that QoL data was reported. Of the 100 trials identified, 37 reported Minimal Clinically Important Difference (MCID); 32 were for DLQI, 10 for SF-36 and six for EQ-5D.

Conclusions

QoL measurement is increasingly being reported in RCTs of psoriasis. Formal guidelines are needed for assessment and publishing of QoL data. Researchers should consider whether MCID information is available, and development of MCID data should be encouraged.

Introduction

From the psoriasis patient's perspective, quality of life (QoL) improvement is as important as improvement in clinical signs ¹. Health-related QoL (HRQoL) instruments are increasingly used as outcome measures ²⁻⁵ in assessing interventions ^{6,7}. Types of HRQoL instruments used include generic, speciality-specific and disease-specific; specific tools are perceived as more relevant and thus preferred by patients ⁸.

Previous reviews have examined the impact of psoriasis interventions on QoL ⁹⁻¹². De Korte et al. ⁹ reviewed QoL data with clinical and demographic correlations. Kitchen et al. ¹³ carried out a systematic review (SR) of patient-reported outcome measures and evidence of their validation in psoriasis. These reviews underscored the value of QoL measurement in psoriasis. However we need to understand how QoL has been reported in previous trials; a comprehensive review is needed of the use of QoL instruments in randomized controlled trials (RCTs) for interventions in psoriasis.

The aims of this SR were to identify RCTs of therapies in psoriasis that have assessed QoL and to evaluate patterns of utility and reporting of QoL data. This SR should reveal how QoL instruments have been used across therapeutic trials, including consideration of the minimal clinically important difference (MCID), frequency of measurement and sensitivity to change. The review may be useful for those who wish to understand the patterns of use in interventional trials for psoriasis.

Materials and Methods

Data sources

We searched six computerized bibliographical databases up to November 2014: Cochrane Library CENTRAL, MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, EMBASE, WEB OF SCIENCE Core Collection, SCOPUS. The search was restricted to publications in English and was conducted using PRISMA guidelines (Prospero registration no: CRD42015009193).

Keywords were formulated using Scottish Intercollegiate Guidelines Network (SIGN) and COCHRANE search filters for RCTs and SCHARR search filters for QoL. Keywords for psoriasis treatments were developed through a pilot search of other SRs on psoriasis treatments and of the British National Formulary. 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 RCTs of any psoriasis treatment using at least one QoL instrument in adults (aged 18 and over) with psoriasis of either sex and of any ethnicity, including all psoriasis subtypes of psoriasis. Psoriatic arthritis trials were only included if a

skin-specific QoL instrument was used to differentiate QoL impairment for arthritis from that of psoriasis.

Exclusion criteria

The exclusion criteria for the systematic review were as follows; psoriatic arthritis studies where it was not possible to differentiate data on QoL impact of arthritis from QoL impact of psoriasis, studies which included any patient less than 18 years of age, and articles where the change in QoL values cannot be reliably calculated (including graphical representation). For consistency, QoL data only presented as sub-scales, where total scores are usually calculated, were excluded. Abstracts and posters where further data is not available upon contacting the author were also excluded.

Outcome measures extracted

Primary Outcome

Data recorded included QoL instrument used and scores at baseline, treatment and follow-up endpoints and change in QoL attributed to treatment. For studies with an open label extension, the data was only extracted for the period of the study while it was randomised and controlled. For cross-over trials, the data was extracted prior to the crossover.

Secondary Outcomes

Psoriasis Area and Severity Index (PASI) score or any other psoriasis severity scale (PSS) used.

Data extraction and synthesis

Two reviewers (FA and AC) extracted data independently from all eligible published studies, discussed any disagreements and, if necessary involved a third reviewer (AA) for resolution. We adapted a form, which included the Cochrane Risk of Bias tool, for recording data ¹⁴ that included study design, details of administration, methodological quality and duration of treatment and follow-up. Article quality was quantitatively rated using the JADAD score ¹⁵.

We recorded PASI or any other PSS and all QoL data including the baseline, treatment and follow-up endpoint scores and whether the studies detailed QoL percentage change, full scores, graphs or MCID.

Results

Of 3646 screened records, 99 articles met the inclusion criteria, describing 100 RCTs and 33,215 patients (Fig. 1). Some trials were reported in more than one publication: all relevant references are given in Table 1. Sixty-three studies were placebo-controlled, 33 head-to-head trials and 36 tested a single drug in different dosage regimens or formulations (total >99 as studies fulfilled more than one criterion). Although JADAD scores ¹⁵ were not integral to the inclusion criteria, Table 1 ranks interventions from low to high methodological quality.

Of the 100 trials that measured QoL, 33 tested topical, 18 systemic, 39 biologics, 9 phototherapy, and 10 tested other interventions including educational treatments, diet, writing exercises, balneotherapy, auriculotherapy, relaxation therapies and interdisciplinary care (Table 1, Fig. 2 and Fig. 5). The number of studies reporting each topical intervention were: calcipotriol (13 trials), calcipotriol/bethametasone (7), clobetasol (4) and dithranol (4). Systemic medications trials included: methotrexate (7), ciclosporin (3) and voclosporin (2). Biologic trials included etanercept (14), ustekinumab (8), adalimumab (7), infliximab (6) and alefacept (4). Quality of life was evaluated in nine phototherapy trials. In the category of “other interventions” QoL was used most commonly in educational (3) and diet (3) studies.

The mean JADAD score was 3.34 (range 1-5, Table 1). QoL was tested a range of 2-6 times for topical, 2-25 times for systemic and 2-12 times for biologic interventions. Sixteen trials lasted >12 weeks, 49 from 12 to 24 weeks and 35 >24 weeks. The subject number ranged from 20¹⁶ to 2546¹⁷ patients, with a mean male:female ratio of 1.7:1 per study arm. Mean PASI at baseline ranged from 1.7 to 33.1. The range of mean QoL scores at baseline were: Dermatology Life Quality Index (DLQI) 1.7-20.1 (Minimum-maximum for this measure = 0-30); Short Form 36 (SF-36) physical component summary (PCS) 32.7-56.2 (0-100) and mental component summary (MCS) 35.7-52.4 (0-100); EuroQoL (EQ-5D) Component I 0.48-0.74 (0 to 1), EuroQoL Component II 55.3-76.4 (0-100); and Psoriasis Disability Index (PDI) 7.6-52.6 (0-90).

Instruments used

Thirteen instruments were used to measure QoL; some studies used more than one. Five generic instruments were used: the SF-36¹⁸; EQ-5D¹⁹; General Health Questionnaire (GHQ-12)^{20,21}; Quality of Life Index (QLI)²²; and Sickness Impact Profile (SIP)^{23,24}. In addition, four dermatology specific instruments, three specific to psoriasis and one for scalp dermatitis were used: DLQI²⁵; Skindex²⁶; Dermatology Quality of Life Scales (DQOLS)²⁷; Freiburg Life Quality Assessment (FLQA-d)²⁸; PDI²⁴; 12-Item Psoriasis Quality of Life Questionnaire (PQOL-12)²⁹; Psoriatic Arthritis Quality of Life measure (PsAQoL)³⁰; and SCALPDEX³¹. Of these, the DLQI was the most commonly used QoL instrument (number of studies=83, 83%), followed by the SF-36 (31, 31%), EQ-5D (15, 15%), PDI (14, 14%) and Skindex (5, 5%).

Minimal Clinically Important Difference (MCID) and Statistical Reporting

Of the 100 trials identified, 37 reported MCID; 32 were for DLQI, 10 for SF-36 and six for EQ-5D. The DLQI MCID was considered to be a score change of five³² but is now reported as four³³. Of the 83 RCTs that utilised the DLQI, 32 trials reported the MCID. Change in mean DLQI scores from baseline to treatment end ranged from -14.4³⁴ to +3.0³⁵. Where DLQI score changes were reported, 115 of 142 ‘study arms’ met the 4-point MCID³³. Biologic interventions usually attained DLQI MCID: 91.2% (83 of 91 study arms) met the 4-point MCID. The MCID was attained by 77.8% (14 of 18) of topical, and 52.4% (11 of 21) of systemic treatment arms. One RCT of infliximab measuring QoL at 100 weeks³⁵ reported 3 points worsening of DLQI. However, this study ended prematurely and had a low JADAD score of only 2.

Another trial, with a high JADAD score of 5³⁶ demonstrated mean DLQI score increasing by 0.4 after folic acid was added to methotrexate. The MCID was not met for any study arm.

The SF-36 MCID is a change of three in the total score³⁷. The SF-36 was used in 31 trials and MCID reported in 10. The mean SF-36 change from baseline to treatment end ranged from PCS -7.4³⁵ to +10.1^{38,39} MCS from -0.3⁴⁰ to +12.2³⁹. Where extracting change in SF-36 MCS scores was possible, 52.2% (24 of 46) 'study arms' met the 3-point MCID: 58.3% (21 of 36) of biologic interventions met this. For PCS scores, 50% (24 of 48) of 'study arms' met the MCID as did 60.5% (23 of 38) of biologic interventions. Only 25% (1 of 4) of systemic and no topical treatments met the MCID for both MCS and PCS domains.

The EQ-5D was used in 15 trials, 6 reported the MCID which is 0.05^{41,42}. The PDI was used in 14 trials: the MCID is not known. Skindex was used in five RCTs; MCIDs for Skindex versions have not been published.

Fig. 3 shows correlation between PASI and absolute DLQI ($R^2=0.494$) and percentage ($R^2=0.641$) score changes, where available. In some cases the correlation was weak⁴³, possibly attributed to non-optimal endpoint measurement for QoL where maximum effect may be missed⁴⁴. Furthermore some interventions may have a psychological impact not captured by clinical parameters.

Table 1 gives the studies included that documented full QoL data and statistical significance for intervention versus comparator. Significant changes were reached in 52 trials for the DLQI, 19 for the SF-36, 5 for both the EQ-5D and PDI and 2 for the Skindex. Conversely there was no statistical improvement in 19 trials for the DLQI, 6 for the SF-36, 3 for the EQ-5D, 6 for the PDI and 3 for Skindex. Twelve trials did not report statistical significance for the DLQI, 6 for the SF-36, 4 for the EQ-5D and 2 for the PDI.

The first two studies identified, that fulfilled inclusion criteria, were published in 1998^{45,46}. Since then, reports of psoriasis interventions that fulfilled inclusion criteria have gradually increased over time: 1998-2004 = 12, 2005-2009 = 33, and 2010-2014 = 55 (Fig. 4).

Discussion

QoL assessment is a frequent component in assessing psoriasis treatment efficacy⁴⁷. This SR has identified therapeutic RCTs that demonstrated extractable QoL data, inevitably with heterogeneity in design, disease severity and QoL reporting. Many trials were excluded because of inconsistent reporting and analysis of QoL (Fig. 1)⁴⁸. Baseline and end-of-treatment values were not always provided. Often QoL scores were presented as percentage or value changes without pre or post-intervention scores. Mean values were most commonly reported, though median values are preferable with ordinal data⁴⁷. Standard deviation, *p*-values or confidence intervals were sometimes omitted and intention-to-treat (ITT) numbers were sometimes omitted from the QoL data set. This presented challenges for synthesizing data.

The MCID is the minimal change in score that is considered of clinical relevance⁴⁹.

Of the 13 QoL instruments used, only the DLQI, SF-36 and EQ-5D have MCID values reported in the literature. Although interventions may result in statistically significant QoL improvement, this does not necessarily correlate with clinically important change. MCID values enhance the clinical meaningfulness of QoL scores, particularly if data is correlated with clinical efficacy. Thirty-seven trials reported consideration of MCID, with the DLQI and SF-36 being the most commonly used instruments with known MCID. The EQ-5D was the only other used instrument with known MCID: this data is not reported as numbers were so low.

The MCID of QoL measures may be determined using several methodologies, and at least nine approaches have been reported⁵⁰. These may be categorised into two main groups: anchor-based and distribution based approaches. Whereas the former incorporates patient perspective, the latter determines MCID using statistical significance. The anchor-based method is the most commonly used for determining the MCID, as used in the case of the DLQI³³.

Each methodology has its limitations, for example, anchor-based methods have often been criticised for unequal changes required for deterioration versus improvement of a condition⁵¹. Several factors may influence MCID scores, including patient baseline status, disease group and severity, treatment and patient demographics. Furthermore, it is important to note that MCID values may differ significantly within the same population depending on the methodology chosen⁵². Therefore interpreting MCID scores should be considered in the context of these limitations.

More generic QoL instruments were used (n=5) than specialty (n=4) or condition specific questionnaires (n=3). The DLQI was the most commonly used instrument; possibly because of the simplicity of reporting a single summary score, the ease of completion in 2 minutes⁵³, its widespread use in national psoriasis guidelines⁵⁴ amongst other reasons⁵⁵. The frequency of QoL measurement varied across studies depending on intervention type and trial duration. The UK guidelines, that recommend DLQI measurement at 10 to 16 weeks depending on the biologic, may not capture the best DLQI responses for biologic therapies⁴⁴.

Several reviews have explored the effects of biologic treatment on QoL^{10,11,56,57}, Other SRs have explored QoL in psoriasis; the review by De Korte *et al.*⁹ was not limited to RCTs and this provided difficulties in interpreting the dataset. This SR investigates the patterns of use of QoL instruments as well as the reporting of the outcomes. We employed strict entry criteria allowing for robust comparison across interventions per QoL instrument. We only included data from the double-blind controlled phases of each trial. Nevertheless, the lack of adequate guidelines on QoL data reporting still rendered data analysis problematic.

Kitchen *et al.*¹³ reviewed the ability of psoriasis-specific instruments to adequately capture domains relating to psoriasis: no existing psoriasis specific patient reported outcome (PRO) instrument has sufficient evidence on validity, reliability and sensitivity to change, but both DLQI⁵⁸ and Skindex demonstrated content validity. However, this SR demonstrates that several generic and disease/specialty-specific instruments were sensitive to change with positive QoL outcomes.

The DLQI and SF-36 are the most frequently used instruments across psoriasis RCTs. A European S3 guidelines report on psoriasis systemic treatment⁵⁹ described

the DLQI as an ‘important’ variable in assessment of treatment efficacy. However the DLQI has limitations, including previous criticisms of its uni-dimensionality and low representation of emotional aspects ⁶⁰. There is diverse practice in monitoring therapeutic effect on QoL and questionnaire preference. We rejected 113 RCTs because of inextricable QoL data. The European Academy of Dermatology and Venereology Task Force provides recommendations for use of QoL measures ⁶¹. Currently there is great variation in the quality of reporting of QoL data ^{62,63}, creating difficulties in cross-interventional meta-analyses. This SR emphasizes the need for guidelines concerning appropriate reporting of QoL data.

This review has several limitations. Only English language literature was examined and only studies with extractable QoL data were included. There was too little comparative data from other QoL instruments to be included. Several studies were excluded due to inadequate QoL data reporting. Collating data across studies other than RCTs was not possible due to the wide variation in methodologies. Although an author (AYF) is joint DLQI copyright holder, bias was countered by two independent principal reviewers conducting data search, extraction and synthesis, with a third independent adjudicator reviewer.

We recommend improvement of QoL reporting to include baseline, treatment and follow-up endpoint absolute median scores with interquartile range. Patient numbers should always be reported as well as whether intention to treat was implemented, as previously suggested ^{62,63}. If a graphical representation of QoL is published, it should be accompanied by numerical data. Authors should not submit only percentage and/or graphical data to represent study outcomes as this data cannot be used in meta-analysis and systematic reviews. Journals should furthermore implement such criteria prior to accepting publications. The MCID and validated band descriptors where available should be used to interpret data as this holds greater clinical value than statistical significance alone. Researchers should consider the availability of MCID when choosing QoL instruments, and be encouraged to publish MCID information. Whilst there are numerous approaches for calculating MCID scores, there is a need for consensus on new or improved methodological approaches towards calculating MCID. Existing methodologies should be cautiously taken into account by clinicians and researchers alike to facilitate the interpretation of results. Though minimal change is clinically important, the question arises of whether intervention endpoints should target perfect quality of life, rather than demonstrating a measurable improvement.

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Tables

Table 1. Included studies: Jadad score, treatment duration, sample characteristics, QoL instruments and main psoriasis severity scale used

Main QoL article, Year (salami publications used to derive non-QoL data)	J A D A D	Interventions (Grouped per intervention, ranked by increasing JADAD score)	Treat ment End point (Weeks) Unless specified	Number of Subjects	QoL instruments used * Significant improvement vs comparator † No significant improvement vs comparator ° No significance data provided	Psoriasis severity scale used (Primary)
BIOLOGICS						
Asahina 2010 ⁶⁴	3	Adalimumab vs Placebo	24	169	DLQI*, SF-36*	PASI
Genovese 2007 ⁶⁵	4	Adalimumab vs Placebo	12	100	DLQI*, HAQ-DI*, SF-36* (PCS ONLY), FACIT F†	PGA
Mease 2005 ⁶⁶	4	Adalimumab vs Placebo	24	313	DLQI*, HAQ-DI*, SF-36* (PCS ONLY)	PASI

Shikiar 2007 ⁶⁷ (Gordon 2006 ⁶⁸ , Menter 2010 ⁶⁹)	4	Adalimumab vs Placebo	12	148	DLQI*, EQ-5D*, SF-36* (EXCEPT FOR PCS IN 40 MG EOW ARM)	PASI
Revicki 2007 ⁷⁰ (Kimball 2011 ⁷¹ , Menter 2008 ⁷² , ⁷³ Revicki 2008 ⁷³ ,)	5	Adalimumab vs Placebo	16	1212	DLQI*, SF-36*	PASI
Revicki 2008 ⁷⁴ (Saurat 2008 ⁷⁵ , Navarini 2014 ⁷⁶ , Saurat 2011 ⁷⁷)	5	Adalimumab vs MTX	16	271	DLQI*, EQ-5D*	PASI
Thaci 2010 ⁷⁸ , Paul 2012 ⁷⁹	5	Adalimumab + CAL/BD vs Adalimumab + Vehicle	16	730	DLQI [†]	PASI
Lui 2012 ⁸⁰	2	Alefacept vs nUVB	16	98	DLQI [†]	PASI
Ellis 2003 ⁸¹ (Ellis 2001 ⁸²)	4	Alefacept vs Placebo	12	205	DLQI ⁰ , SF-36 ⁰ , DQOLS ⁰	PASI
Finlay 2003 ⁸³ (Lebwohl 2003 ⁸⁴)	4	Alefacept vs Placebo	12	507	DLQI [†] , DQOLS* (15 MG ARM ONLY), SF-36* (PCS ONLY)	PASI
Yan 2011 ⁸⁵	4	Alefacept vs MTX	12	212	DLQI [†] , SF-36 [†]	PASI
Papp 2014 ⁸⁶ (Gordon 2012 ⁸⁷)	5	Briakinumab vs Placebo	12-40	2209	DLQI*, SF-36*	PASI
Gordon 2014 ⁸⁸ (Papp 2012 ⁸⁹)	5	Brodalumab vs Placebo	12	198	DLQI*, SF-36* (140 MG ARM ONLY, AND MCS FOR 210 MG ARM)	PASI
Gladman 2014 ⁹⁰ (Mease 2013 ⁹¹)	3	Certolizumab vs Placebo	24	409	DLQI*, SF-36*, PSAQOL*, HAQ-DI*	PASI

Reich 2012 ⁹²	5	Certolizumab vs Placebo	12	176	DLQI ⁰	PASI
Dubertret 2006 ³⁸ (Ortonne 2005 ³⁹)	4	Efalizumab vs Placebo	12	793	DLQI [*] , SF-36 [*]	PASI
Gordon 2003 ³ (Menter 2005 ⁹³)	5	Efalizumab vs Placebo	12	556	DLQI [*] , PSA [*]	PASI
Cassano 2006 ⁹⁴	1	Etanercept (Dose-comparison)	12	108	DLQI [†]	PASI
Dauden 2009 ⁹⁵ (Ortonne 2008 ⁹⁶ , Luger 2009 ⁹⁷)	1	Etanercept (Continuous vs Intermittent)	54	720	DLQI [*] , EQ-5D [†] , SF-36 [†]	PASI
Gelfand 2008 ¹⁷ (Moore 2007 ⁹⁸)	2	Etanercept (Continuous vs Intermittent)	24	2546	DLQI ⁰ , EQ-5D ⁰ (EuroQoL-FT), SF-36 ⁰	PASI
Gniadecki 2012 ⁹⁹ (Sterry 2010 ¹⁰⁰)	3	Etanercept (Dose-comparison)	12	752	DLQI [*] , EQ-5D [†] , HAQ-DI [†]	PASI
Lynde 2012 ¹⁰¹	3	Etanercept vs Etanercept + nUVB	12	75	DLQI [†]	PASI
Ortonne 2013 ¹⁰²	3	Etanercept (Dose-comparison)	24	72	DLQI ⁰	PASI
Thaci 2014 ⁵ (Strohal 2013 ¹⁰³)	3	Etanercept (Dose-comparison)	12	273	DLQI [*]	PASI
Zachariae 2008 ¹⁰⁴	3	Etanercept + MTX (Tapered vs Continued)	24	59	DLQI [*] , EQ-5D [†]	PASI
Krueger 2005 ¹⁰⁵ (Papp 2005 ¹⁰⁶)	4	Etanercept vs Placebo	12	583	DLQI [*] , SF-36 [*]	PASI
Feldman 2005 ¹⁰⁷ (Leonardi 2003 ¹⁰⁸)	5	Etanercept vs Placebo	12	652	DLQI [*]	PASI
Gottlieb 2003 ¹⁰⁹	5	Etanercept vs Placebo	24	112	DLQI [*]	PASI

Reich 2009 ¹¹⁰ (Van de Kerkhof 2008 ¹¹¹)	5	Etanercept vs Placebo	12	142	DLQI*, SF-36*	PASI
Tyring 2007 ¹¹² (Tyring 2006 ¹¹³)	5	Etanercept vs Placebo	12	618	DLQI*	PASI
Reich 2013 ³⁵ , extension of trial Barker 2011 ¹¹⁴)	2	Infliximab (Continuous vs Intermittent)	100	441	DLQI ⁰ , SF-36 ⁰	PASI
Yang 2012 ¹¹⁵	2	Infliximab vs Placebo	10	129	DLQI*	PASI
Barker 2011 ¹¹⁴	3	Infliximab vs MTX	16	868	DLQI*, SF-36* (PCS ONLY), EQ-5D*	PASI
Feldman 2008 ¹¹⁶ (Menter 2007 ¹¹⁷)	4	Infliximab vs Placebo	10	1430	DLQI*, SF-36*	PASI
Torii 2010 ¹¹⁸	4	Infliximab vs Placebo	14	54	DLQI*	PASI
Bissonnette 2011 ¹¹⁹	5	Infliximab vs Placebo	14	24	DLQI [†]	m- PPPASI
Feldman 2005 ¹²⁰ (Gottlieb 2004 ¹²¹)	5	Infliximab vs Placebo	10	249	DLQI*	PASI
Reich 2006 ¹²² (Reich 2005 ¹²³)	5	Infliximab vs Placebo	24	378	DLQI*, SF-36*	PASI
Krupashankar 2014 ¹²⁴	4	Itolizumab (Loading dose vs. Non-loading dose)	12	225	DLQI ⁰ , SF-36 ⁰	PASI
Leonardi 2012 ¹²⁵	5	Ixekizumab vs Placebo	8	142	DLQI*	PASI
Langley 2014 ¹²⁶	4	Secukinumab vs Etanercept vs Placebo	12	2044	DLQI* (VS PLACEBO ONLY)	PASI

Mamolo 2014 ¹²⁷	4	Tofacitinib vs Placebo	12	197	DLQI*, SF-36*	PASI
Paul 2014 ¹²⁸ (Reich 2014 ¹²⁹)	2	Ustekinumab + MTX (Gradual vs. Immediate withdrawal)	16	489	DLQI ⁰ , EQ-5D ⁰ , VAS ⁰	PASI
Nakagawa 2012 ¹³⁰ (Igarashi 2012 ¹³¹)	3	Ustekinumab vs Placebo	12	158	DLQI*, SF-36* (PCS ONLY), PDI*	PASI
Kimball 2012 ¹³² (Leonardi 2008 ¹³³ , Lebwohl 2010 ¹³⁴ , Kimball 2013 ¹³⁵)	3	Ustekinumab vs Placebo	12	766	DLQI*, SF-36 ⁰	PASI
Zhu 2013 ¹³⁶	3	Ustekinumab vs Placebo	12	322	DLQI*	PASI
Langley 2010 ¹³⁷ (Papp 2008 ^{138,139})	4	Ustekinumab vs Placebo	12	1230	DLQI*	PASI
McInnes 2013 ¹⁴⁰	4	Ustekinumab vs Placebo	24	615	DLQI*, HAQ-DI*, SF-36* (EXCEPT MCS IN 45 MG ARM)	PASI
Kavanaugh 2010 ¹⁴¹ (Gottlieb 2009 ¹⁴²)	5	Ustekinumab vs Placebo	12	146	DLQI*, HAQ-DI*	PASI
Tsai 2012 ¹⁴³ (Tsai 2011 ¹⁴⁴)	5	Ustekinumab vs Placebo	12	121	DLQI*	PASI
SYSTEMICS						
Strand 2013 ¹⁴⁵ (Papp 2012 ¹⁴⁶)	5	Apremilast vs Placebo	16	352	DLQI* (EXCEPT 10 MG ARM), SF 36* (MCS ONLY)	PASI

Möller 2010 ¹⁴⁷	4	Chondroitin Sulphate vs Placebo	12	116	DLQI [†] , SF-36 [†]	PASI
Beissert 2009 ¹⁴⁸	3	Ciclosporin vs Mycophenolate Mofetil	12	54	PDI [†]	PASI
Thaci 2002 ¹⁴⁹	4	Ciclosporin (Body-weight dependent dose vs Independent dose)	12	212	PDI ⁰	PASI
Roberti 2014 ⁴³	4	Cytokines (low dose)	12	41	DLQI [*]	PASI
Bagel 1998 ⁴⁶	2	DAB389IL02 vs Placebo	4	70	DLQI ⁰	PASI
Greenberger 2012 ¹⁵⁰	3	Dunaliella bardawil (9-cis b-carotene) vs Placebo	12	44	DLQI [*]	PASI
Salim 2006 ³⁶	5	MTX + Folic acid vs MTX	12	22	DLQI [†]	PASI
Kaltwasser 2004 ¹⁵¹ (Nash 2006 ¹⁵²)	5	Leflunomide vs Placebo	24	190	DLQI [*] , HAQ [*]	PASI
Faurschou 2014 ¹⁶	4	Liraglutide vs Placebo	8	20	DLQI [†]	PASI
Flytström 2008 ¹⁵³	3	MTX vs Ciclosporin	12	84	DLQI [†] , SF-36 [*] (PCS ONLY)	PASI
Asawanonda 2006 ¹⁵⁴	4	MTX + nUVB vs MTX + Placebo	24	24	DLQI [†]	PASI
Ho 2010 ¹⁵⁵	2	Traditional Chinese Medicine vs MTX	24	61	PDI [*] (FOR MTX VS PLACEBO)	PASI
Gupta 2008 ¹⁵⁶	3	Voclosporin vs Placebo	12	201	DLQI ⁰ , PDI ⁰	PASI
Kunynetz 2011 ¹⁵⁷ (Papp 2008 ¹³⁹)	5	Voclosporin vs Placebo	12	451	DLQI [*] (FOR 0.3 AND 0.4 MG ARMS), PDI [*] (FOR 0.3 AND 0.4 MG ARMS)	PASI

Drouin 2008 ¹⁵⁸	5	XP-828L (Dermylex) vs Placebo	8	26	DLQI*	PASI
PHOTOTHERAPY						
Koek 2009 ¹⁵⁹ (Koek 2006 ¹⁶⁰)	2	Home UVB (TL-01) vs Outpatient UVB (TL-01)	'46 irradiation s'	196	PDI†, SF-36 ⁰ , EQ-5D ⁰	PASI
Gahalaut 2014 ¹⁶¹	2	PUVASol + Isotretinoin vs PUVASol	12	40	DLQI*	PASI
Klein 2011 ¹⁶²	2	Synchronous balneophototherapy vs nUVB monotherapy	'35 sessions'	367	PDI†, SIP*, FLQA-d*(PHYSICAL COMPLAINTS AND GLOBAL HEALTH ONLY)	PASI
TOPICALS						
Choonhakarn 2010 ¹⁶³	4	Aloe Vera vs Triamcinolone Acetonide	8	75	DLQI†	PASI
Ortonne 2014 ¹⁶⁴	5	Betamethasone valerate dressing vs CAL/BD ointment	4	324	DLQI*	TSS-4
Wall 1998 ⁴⁵	1	CAL vs Dithranol	12	306	PDI†, SIP†	IGA
Ortonne 2009 ¹⁶⁵ (Kragballe 2009 ¹⁶⁶)	2	CAL/BD scalp formulation vs CAL scalp solution	8	312	SF-36†, Skindex-16*	TSS

Saraceno 2007 ¹⁶⁷	2	CAL/BD vs CAL	4	150	Skindex-29*	PASI
Zheng 2011 ¹⁶⁸	2	CAL/BD vs CAL	4	320	DLQI*	VAS
De Korte 2008 ⁴⁰ (Van De Kerkhof 2006 ¹⁶⁹)	3	CAL vs Dithranol	12	106	Skindex-29 [†] , SF-36 [†]	Modified PASI
Menter 2013 ¹⁷⁰	4	CAL/BD vs BD vs CAL vs Vehicle	8	1152	DLQI* (EXCEPT VS CAL GROUP)	PASI
Van De Kerkhof 2004 ¹⁷¹	4	CAL/BD vs CAL vs Placebo	4	828	EQ-5D*, PDI [†]	PASI
Woo 2003 ¹⁷²	5	CAL + nUVB vs CAL vs Vehicle	20 sessions	50	PDI [†]	PASI
Hutchinson 2000 ¹⁷³	1	Calcitriol vs Dithranol	8	114	PDI*	PASI
Bergstrom 2003 ¹⁷⁴	1	Clobetasol (Foam vs Cream/Solution)	2	32	DLQI [†] , EQ-5D*	PASI
Menter 2009 ⁴	1	Clobetasol propionate vs Calcipotriene + Betamethasone dipropionate	4	93	PQOLS [†]	ODS
Mraz 2008 ¹⁷⁵	1	Clobetasol propionate (Spray vs Foam)	2-4	77	DLQI*	IGS
Sofen 2011 ¹⁷⁶	2	Clobetasol propionate spray vs Vehicle	4	81	Scalpdex*	GSS
Prins 2005 ¹⁷⁷	2	Dithranol (Short contact) + nUVB vs Dithranol (Inpatient)	8-12	238	SIP*, PDI*	PASI

Alora-Palli 2010 ¹⁷⁸	2	Liquor Carbonis Distillate (LCD) Solution vs Calcipotriene cream	12	60	DLQI [†]	Modified PASI
Bernstein 2006 ¹⁷⁹	2	M. Aquifolium vs Placebo	12	200	QLI [*]	PASI
Tiplica 2009 ¹⁸⁰	3	Mometasone furoate 0.1% + Salicylic acid 5% vs Mometasone furoate 0.1%	1	359	DLQI ⁰	PASI
Galvez 2012 ¹⁸¹	3	Sulphurous Mineral Waters Spray vs Distilled Water Spray	2	39	DLQI [†]	PASI
OTHERS						
Lu 2012 ¹⁸²	2	Auricular therapy + Yinxieling formula vs Yinxieling formula	8	84	DLQI [†]	PASI
Schmitt 2014 ¹⁸³	3	Interdisciplinary dermatological and psychiatric care for psoriasis vs Dermatological care for psoriasis	24	47	DLQI [†]	PASI
Ersser 2012 ¹⁸⁴	2	Educational nursing intervention vs No education intervention	6	64	DLQI [†]	PASI
Bostoen 2012 ¹⁸⁵	4	Educational programme vs No educational intervention	12	29	DLQI [*] , PDI [*] , Skindex-29 [†]	PASI
Vedhara 2007 ¹⁸⁶	2	Emotional disclosure vs Standard control writing intervention	0.5	59	DLQI ⁰	PASI
Guida 2014 ³⁴	2	Patients on immunosuppressives: Energy-restricted diet vs Usual diet	24	44	DLQI [*]	PASI

Jensen 2013 ¹⁸⁷	2	Low energy diet vs Standard routine dietary guidance	16	60	DLQI*	PASI
Fordham 2014 ¹⁸⁸	2	MCBT vs Usual treatment	8	29	DLQI*	SAPASI
Chambers 2012 ¹⁸⁹	2	Online Healthcare Delivery vs In-Office Care	16	64	DLQI ⁰ , EQ-5D ⁰	PASI
Tabolli 2012 ¹⁹⁰	2	Writing exercise (Pennebaker) vs Educational intervention	0.5	202	Skindex-29 [†] , SF-36 [†] , GHQ [†]	PASI

MTX – Methotrexate

nUVB – Narrowband UVB

MCBT - Mindfulness-based cognitive therapy

CALC – Calipotriol

BD – Betamethasone dipropionate

* Indicates significant improvement versus comparator(s)

† Indicates no significant improvement versus comparator(s)

⁰ Indicates no significance data was provided

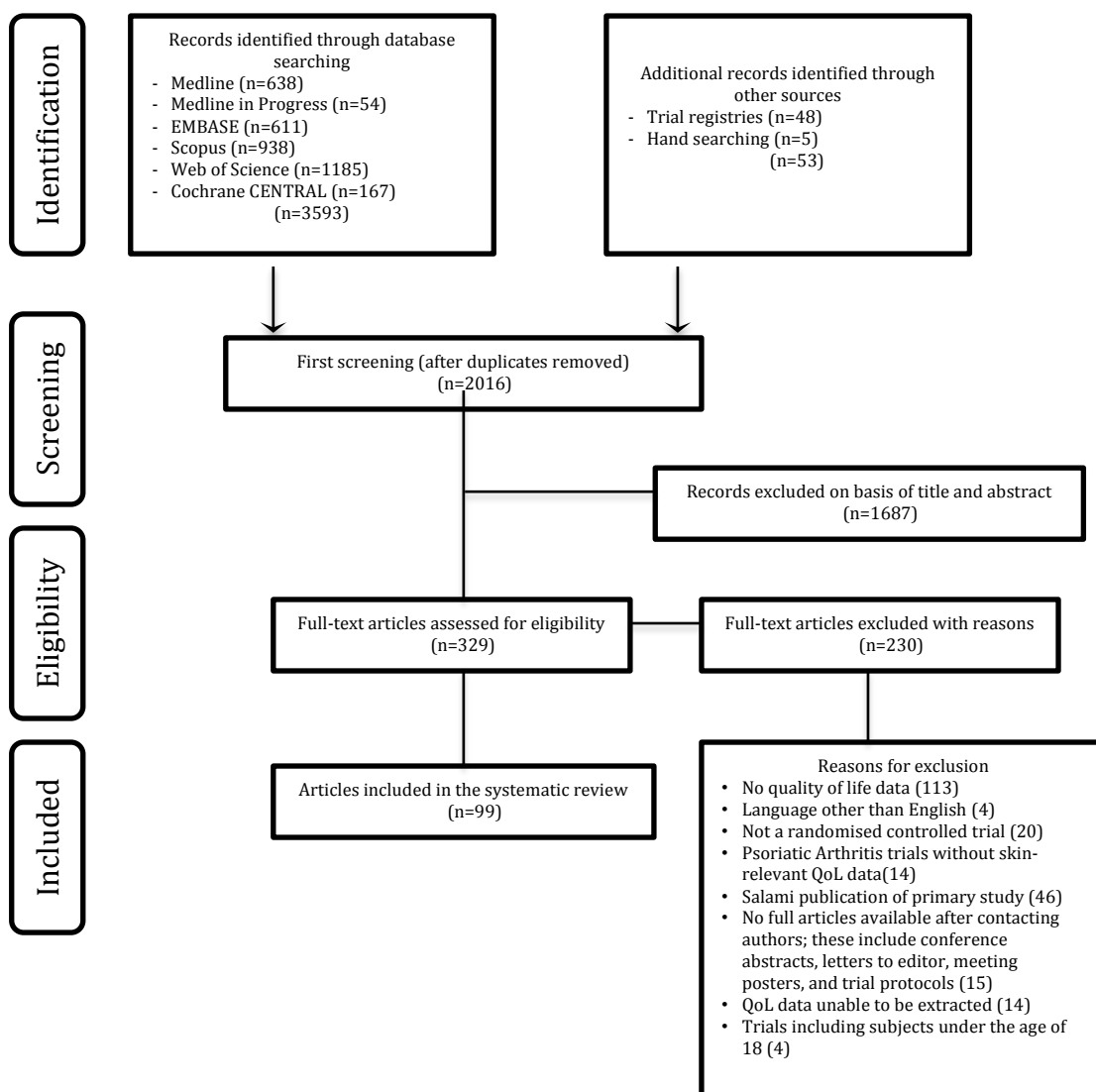


Figure 1. Flow diagram of article selection

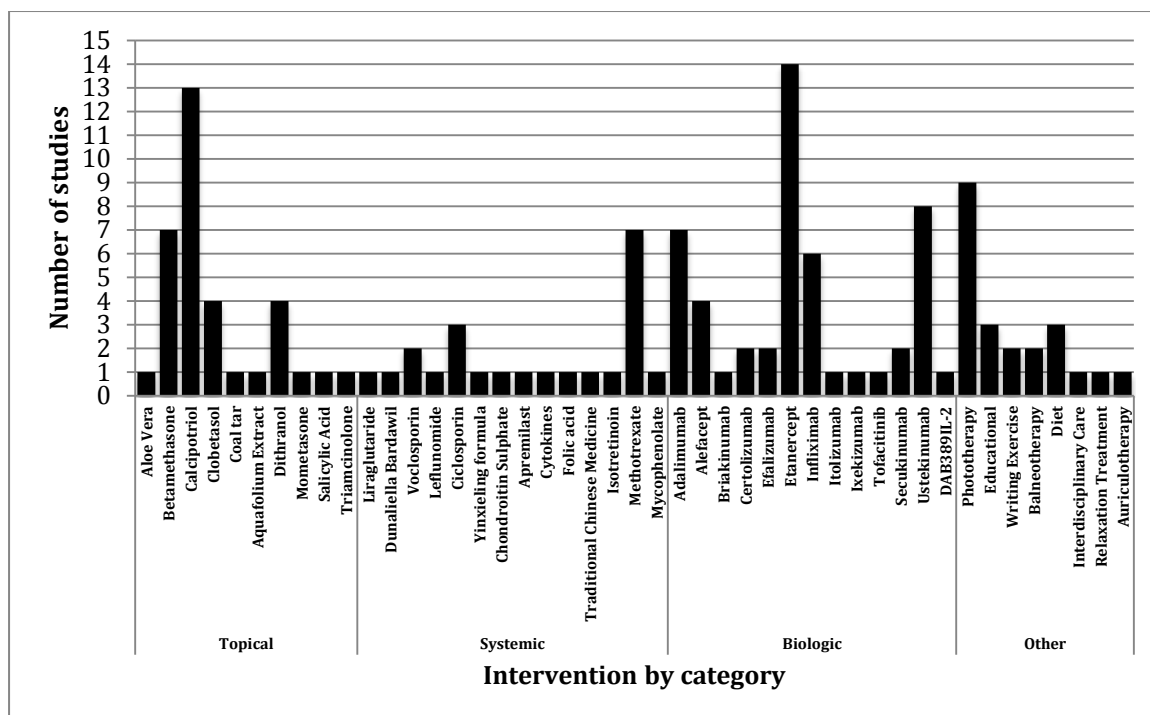


Figure 2. Number of randomised controlled trials of each intervention that measured HRQoL

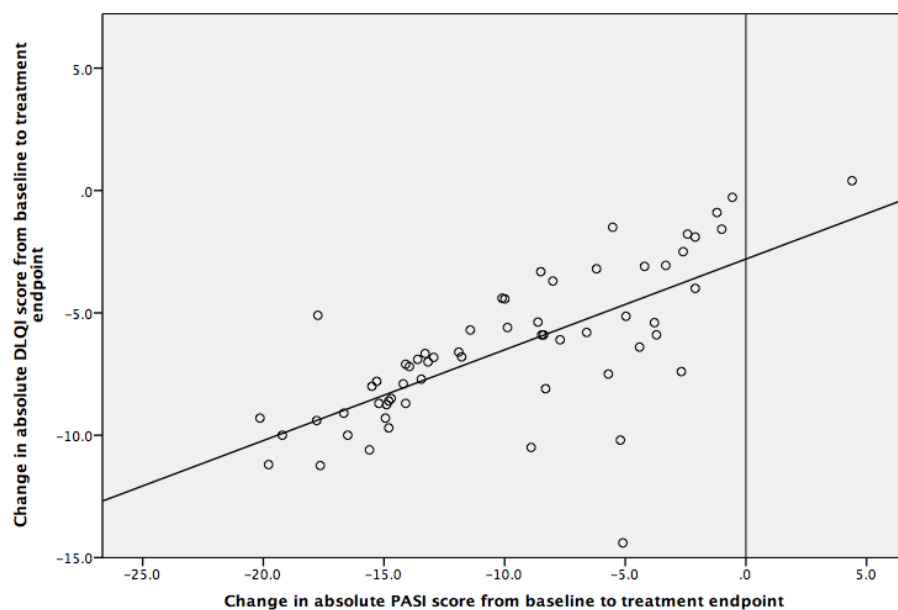


Figure 3(a)

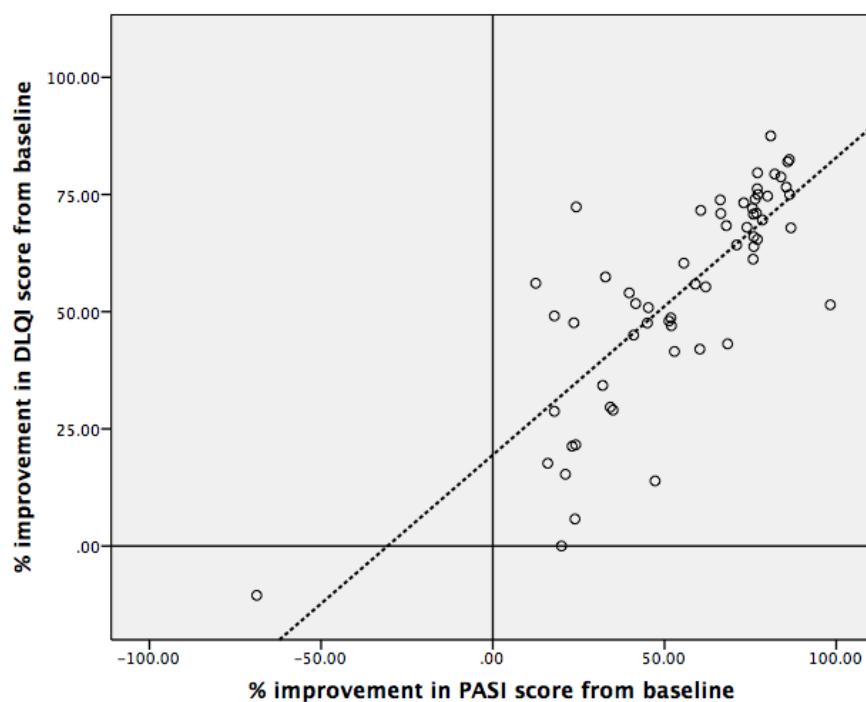


Figure 3(b)

Figure 3. Correlation of (a) absolute change in DLQI scores with absolute change in PASI scores ($R^2 = 0.494$) (b) percentage improvement in DLQI scores with percentage improvement in PASI scores ($R^2 = 0.641$)

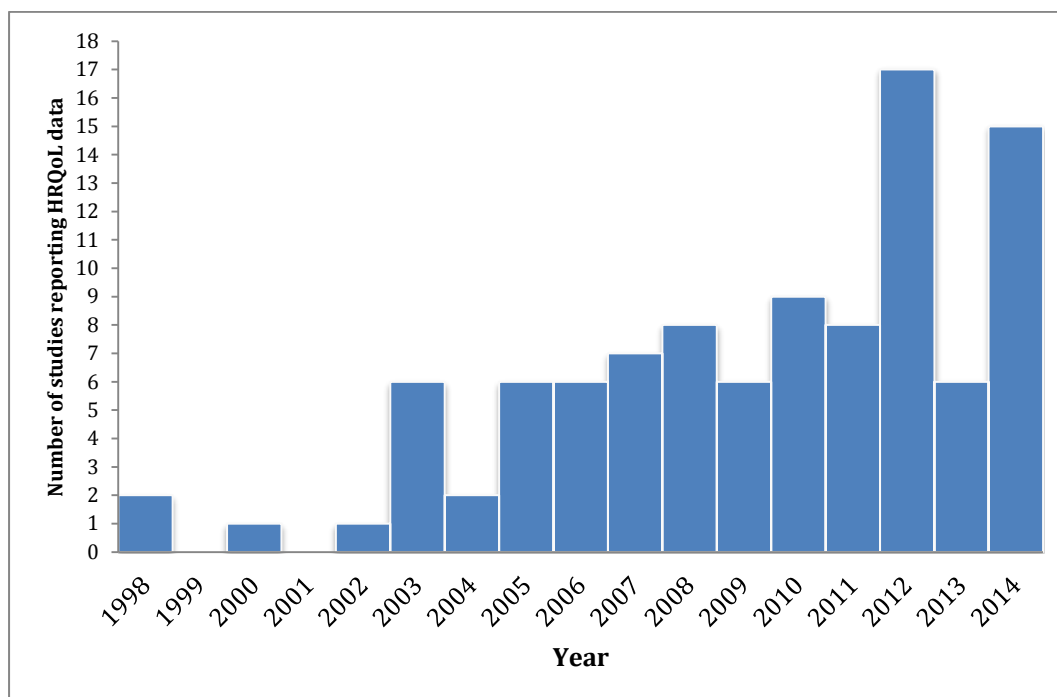


Figure 4. Increasing use of QoL instruments in included psoriasis studies since 1998 (n=100)

Example search strategy

Medline OVID search strategy

- 1.psoriasis.mp.orexpPsoriasis/
- 2.psoria*.mp.
- 3.erythrodermicpsoriasis.mp.
- 4.guttatepsoriasis.mp.
- 5.pustularpsoriasis.mp.
- 6.palmoplantarpsoriasis.mp.
- 7.psoriasisvulgaris.mp.
- 8.plaquepsoriasis.mp.
- 9.localisedpustularpsoriasis.mp.
- 10.localizedpustularpsoriasis.mp.
- 11.inversepsoriasis.mp.
- 12.scalppсориаз.mp.
- 13.nailpsoriasis.mp.
- 14.inflammatorypsoriasis.mp.
- 15.or/1-14
- 16.intervention*.mp.
- 17.treatment*.mp.
- 18.topical.mp.
- 19.systemic.mp.
- 20.immunosuppressivedrug.mp.
- 21.ImmunosuppressiveAgents/
- 22.NonprescriptionDrugs/
- 23.over-the-counter.mp.
- 24.otc.mp.
- 25.expTars/
- 26.(tarortars).tw.
- 27.expSteroids/
- 28.expRetinoids/
- 29.retinoid*.tw.

- 30.steroid*.tw.
- 31.expemollientagent/
- 32.emollient*.tw.
- 33.expTacrolimus/
- 34.tacrolimus.tw.
- 35.topicalimmunemodulator*.tw.
- 36.(topicaladj3therap*).tw.
- 37.(topicaladj3treatment*).tw.
- 38.(topicaladj3agent*).tw.
- 39.vitaminDanalogues.mp.
- 40.calcipotriol.mp.
- 41.dovonex.tw.
- 42.dovobet.tw.
- 43.xamiol.tw.
- 44.calcipotriene.mp.
- 45.taclonex.tw.
- 46.Calcitriol/orcalcitriol.mp.
- 47.silkis.tw.
- 48.tacalcitol.mp.
- 49.curatoderm.tw.
- 50.vitaminD.tw.
- 51.tars.mp.orTars/
- 52.(calamineandcoaltarointment).mp.
- 53.coaltar.mp.
- 54.calamine.mp.
- 55.(coaltarandsalicylicacidointment).mp.
- 56.coaltarpaste.mp.
- 57.(zincandcoaltarpaste).mp.
- 58.zincoxide.mp.
- 59.alphosyl.mp.
- 60.crudecoaltar.mp.
- 61.dithranol.mp.
- 62.anthralin.mp.orAnthralin/

- 63.dithrocream.tw.
- 64.micanol.tw.
- 65.psorin.tw.
- 66.zithranol.tw.
- 67.topicalretinoids.mp.
- 68.tazarotene.mp.
- 69.zorac.tw.
- 70.tazorac.tw.
- 71.corticosteroid.mp.
- 72.hydrocortisone.mp.orHydrocortisone/
- 73.dioderm.tw.
- 74.mildison.tw.
- 75.alphaderm.tw.
- 76.calmuridHC.tw.
- 77.eurax-hydrocortisone.tw.
- 78.canestenHC.tw.
- 79.daktacort.tw.
- 80.fucidinH.tw.
- 81.nystaform-HC.tw.
- 82.timodine.tw.
- 83.hydrocortisonebutyrate.mp.
- 84.locoid.tw.
- 85.locoidcrelo.tw.
- 86.alclometasonedipropionate.mp.
- 87.modrasone.tw.
- 88.betamethasoneesters.mp.
- 89.betamethasonevalerate.tw.
- 90.betacap.tw.
- 91.betesil.tw.
- 92.betnovate.tw.
- 93.betnovate-rd.tw.
- 94.bettamousse.tw.
- 95.diprosone.tw.

- 96.diprosalic.tw.
- 97.betnovate-c.tw.
- 98.betnovate-n.tw.
- 99.fucibet.tw.
- 100.lotriderm.tw.
- 101.clobetasolpropionate.mp.
- 102.clarelux.tw.
- 103.dermovate.tw.
- 104.etrivex.tw.
- 105.dermovate-nn.tw.
- 106.clobetasonebutyrate.mp.
- 107.eumovate.tw.
- 108.diffucortolonevalerate.mp.
- 109.nerisone.tw.
- 110.nerisoneforte.tw.
- 111.fludroxycortide.mp.
- 112.flurandrenolone.tw.
- 113.haelan.tw.
- 114.fluocinoloneacetoneide.mp.orFluocinoloneAcetoneide/
- 115.synalar1in4dilution.tw.
- 116.synalar1in10dilution.tw.
- 117.synalarc.tw.
- 118.synalarn.tw.
- 119.fluocinonide.mp.orFluocinonide/
- 120.metosyn.tw.
- 121.fluocortolone.mp.orFluocortolone/
- 122.ultralanumplain.tw.
- 123.fluticasonepropionate.mp.
- 124.cutivate.tw.
- 125.mometasonefuroate.mp.
- 126.elocon.tw.
- 127.triamcinoloneacetoneide.mp.orTriamcinoloneAcetoneide/
- 128.aureocort.tw.

- 129.KeratolyticAgents/orkeratolytic.mp.
- 130.salicylicacid.mp.orSalicylicAcid/
- 131.zinc.mp.andsalicylicacidpaste.tw.
- 132.Sulfur/orsulphur.mp.
- 133.expUltravioletRays/
- 134.expUltravioletTherapy/
- 135.ultraviolet*.tw.
- 136.(uvorUVBorUVA).tw.
- 137.phototherapy.mp.orPhototherapy/
- 138.ultravioletb.mp.
- 139.UVB.mp.
- 140.narrowbandUVB.mp.
- 141.narrow-bandUVB.mp.
- 142.narrowbandUVBtherapy.mp.
- 143.broadbandlighttherapy.mp.
- 144.ultravioletlight.mp.
- 145.UVlight.mp.
- 146.naturallight.mp.
- 147.combinationlighttherapy.mp.
- 148.photochemotherapy.mp.orPhotochemotherapy/
- 149.psoralen.mp.
- 150.PUVA.mp.
- 151.oralretinoids.mp.
- 152.acitretin.mp.orAcitretin/
- 153.neotigason.tw.
- 154.cyclosporin.mp.orCyclosporine/
- 155.ciclosporin.mp.
- 156.deximune.tw.
- 157.neoral.tw.
- 158.sandimmune.tw.
- 159.hydroxycarbamide.mp.
- 160.hydrea.tw.
- 161.hydroxyurea.mp.orHydroxyurea/

- 162.methotrexate.mp.orMethotrexate/
- 163.metoject.tw.
- 164.cytokinemodulators.mp.
- 165.etanercept.mp.
- 166.enbrel.tw.
- 167.adalimumab.mp.
- 168.humira.tw.
- 169.infliximab.mp.
- 170.remicade.tw.
- 171.ustekinumab.mp.
- 172.stelara.tw.
- 173.efalizumab.mp.
- 174.raptiva.tw.
- 175.biologic*.mp.
- 176.Psychotherapy/
- 177.(psycho*adj3therap*).tw.
- 178.psychotherap*.tw.
- 179.expCognitiveTherapy/
- 180.(cognit*adj3therap*).tw.
- 181.((behaviourorbehavior)adj3therap*).tw.
- 182.psyoeducation.tw.
- 183.CBT.tw.
- 184.expPeerGroup/
- 185.expSelf-HelpGroups/
- 186.(peeradj3group*).tw.
- 187.((supportorself-helporselfhelp)adj3group*).tw.
- 188.alternativetherapy.mp.
- 189.homeopathy.mp.orHomeopathy/
- 190.Relaxation/orrelaxation.mp.
- 191.oreganooil.mp.
- 192.traditionaltreatment*.mp.
- 193.oatextracts.mp.
- 194.coldwaterfishoils.mp.

- 195.eveningprimroseoil.mp.
- 196.teatreeoil.mp.or"TeaTreeOil"/
- 197.aloevera.mp.orAloe/
- 198.taichi.mp.
- 199.yoga.mp.orYoga/
- 200.laser.mp.
- 201.herbalmedication.mp.
- 202.petroleumjelly.mp.
- 203.massage*.mp.
- 204.sharkcartilageextract.mp.
- 205.meditation.mp.orMeditation/
- 206.complementarytherapy.mp.orComplementaryTherapies/
- 207.hypnotherapy.mp.
- 208.milkthistle.mp.orMilkThistle/
- 209.expMotorActivity/
- 210.(physicaladj3activit\$).tw.
- 211.expExercise/
- 212.expExerciseTherapy/
- 213.exercis\$.tw.
- 214.expLifeStyle/
- 215.lifestyle\$.tw.
- 216.(lifeadj3style\$).tw.
- 217.expHealthBehavior/
- 218.(healthadj3(behavior\$orbehaviour\$)).tw.
- 219.expDiet/
- 220.expDietarySupplements/
- 221.diet\$.tw.
- 222.nutrition\$.tw.
- 223.expObesity/
- 224.expBodyWeight/
- 225.obes\$.tw.
- 226.weight\$.tw.
- 227.expSmoking/

- 228.(smokingorsmoker*).tw.
- 229.expAlcohol-RelatedDisorders/
- 230.expAlcoholicBeverages/
- 231.alcohol*.tw.
- 232.drinking.tw.
- 233.expEmployment/
- 234.expOccupations/
- 235.(employment*oroccupation*orwork).tw.
- 236.goeckermantherapy.mp.
- 237.excimertherapy.mp.
- 238.scalelifters.mp.
- 239.non-biologicalmedications.mp.
- 240.FishOils/orfishoil*.mp.
- 241.vitamins.mp.orVitamins/
- 242.vitaminE.mp.orVitaminE/
- 243.VitaminA/orvitaminA.mp.
- 244.mineral*.mp.
- 245.selenium.mp.orSelenium/
- 246.Antimetabolites/orantimetabolite*.mp.
- 247.thioguanine.mp.orThioguanine/
- 248.tioguanine.mp.
- 249.miscellaneous.mp.
- 250.immunomodulatoragents.mp.
- 251.immunomodulatordrugs.mp.
- 252.calcineurininhibitors.mp.
- 253.anti-itch.mp.
- 254.e45cream.mp.
- 255.fumaricacidesters.mp.
- 256.fumaricacidesters.mp.
- 257.FAE.mp.
- 258.sorbelene.mp.
- 259.anti-fungal.mp.
- 260.skinbiopsy.mp.

261.alefacept.mp.
262.amevive.tw.
263.or/16-262
264.QOL.mp.
265.qualityoflife.mp.or"QualityofLife"/
266.healthrelatedqualityoflife.mp.
267.HRQOL.mp.
268.EQ5D.mp.
269.nationalpsoriasisfoundation.mp.
270.skindex.mp.
271.DLQI.mp.
272.dermatologylifequalityindex.mp.
273.burdenofskindisease.mp.
274.patientreportedoutcomemeasure.mp.
275.qualityoflifeimpairment.mp.
276.outcomemeasurement.mp.
277."OutcomeAssessment(HealthCare)"/oroutcomeassessment.mp.
278.QOLtools.mp.
279.patientreportedoutcome.mp.
280.PRO.mp.
281.NHP.mp.
282.WHO-QOL.mp.
283.psoriasisdisabilityindex.mp.
284.PDI.mp.
285.salfordpsoriasisindex.mp.
286.SPI.mp.
287.FDLQI.mp.
288.PFI.mp.
289.skindex-16.mp.
290.skindex-29.mp.
291.skindex-teen.mp.
292.childrensdermatologylifequalityindex.mp.
293.CDLQI.mp.

294.familydermatologylifequalityindex.mp.
295.psoriasis-specificmeasureofqualityoflife.mp.
296.PSORIQoL.mp.
297.USPSORIQoL.mp.
298.skindex-17.mp.
299.DQOLS.mp.
300.dermatologyqualityoflifescal.es.mp.
301.shortform-36.mp.
302.KMPI.mp.
303.PDI.mp.
304.nationalpsoriasisfoundationpsoriasisscore.mp.
305.NPF-PS.mp.
306.physicianstaticglobalassessment.mp.
307.PSGA.mp.
308.overalllesionassessment.mp.
309.OLA.mp.
310.physiciandynamicglobalassessment.mp.
311.physiciandynamicglobalassessment.mp.
312.PDGA.mp.
313.latticesystemglobalpsoriasisscore.mp.
314.LS-GPS.mp.
315.PsAQoL.mp.
316.dermatologyindexofdiseaseseverity.mp.
317.DIDS.mp.
318.psoriasislifestressinventory.mp.
319.PLSI.mp.
320.WHOQOL-26.mp.
321.WHOQOL-100.mp.
322.patientgeneralindex.mp.
323.PGI.mp.
324.DIELH.mp.
325.VQ-dermato.mp.
326.impactofchronicskindiseaseondailylife.mp.

- 327.ISDL.mp.
- 328.freiberglifequalityassessment.mp.
- 329.FLQA.mp.
- 330.SF-29.mp.
- 331.valueoflife/
- 332.qualityadjustedlifeyear/
- 333.qualityadjustedlife.tw.
- 334.(qaly\$orqald\$orqale\$orqtime\$).tw.
- 335.disabilityadjustedlife.tw.
- 336.daly\$.tw.
- 337.healthstatusindicators/
- 338.(sf36orsf36orshortform36orshortform36orsfthirtysixorsfthirtysixorshortformthirtysixorshortformthirtysixorshortformthirtysixorshortformthirtysix).tw.
- 339.(sf6orsf6orshortform6orshortform6orsfsixorsfsixorshortformsixorshortformsix).tw.
- 340.(sf12orsf12orshortform12orshortform12orsftwelveorsftwelveorshortformtwelveorshortformtwelve).tw.
- 341.(sf16orsf16orshortform16orshortform16orsfsixteenorsfsixteenorshortformsixteenorshortformsixteen).tw.
- 342.(sf20orsf20orshortform20orshortform20orsftwentyorsftwentyorshortformtwentyorshortformtwenty).tw.
- 343.(euroqoloreuroqoloreq5doreq5d).tw.
- 344.(hqlorhqolorhqolorhrqolorhrqol).tw.
- 345.(hyeorhyes).tw.
- 346.health\$year\$equivalent\$.tw.
- 347.healthutilit\$.tw.
- 348.(huiorhui1orhui2orhui3).tw.
- 349.disutili\$.tw.
- 350.rosser.tw.
- 351.qualityofwellbeing.tw.
- 352.qwb.tw.
- 353.willingnesstopay.tw.
- 354.standardgamble\$.tw.

355.timetradeoff.tw.
 356.timetradeoff.tw.
 357.tto.tw.
 358.or/264-357
 359.RandomizedControlledTrialsasTopic/
 360.Randomi?edcontrolledtrial/
 361.RandomAllocation/
 362.DoubleBlindMethod/
 363.SingleBlindMethod/
 364.clinicaltrial/
 365.clinicaltrial,phasei.pt.
 366.clinicaltrial,phaseii.pt.
 367.clinicaltrial,phaseiii.pt.
 368.clinicaltrial,phaseiv.pt.
 369.controlledclinicaltrial.pt.
 370.randomi?edcontrolledtrial.pt.
 371.multicenterstudy.pt.
 372.clinicaltrial.pt.
 373.expClinicalTrialsastopic/
 374.randomly.ab.
 375.trial.ab.
 376.groups.ab.
 377.or/359-376
 378.(clinicaladjtrial\$).tw.
 379.((singl\$ordoubl\$ortreb\$ortripl\$)adj(blind\$3ormask\$3)).tw.
 380.PLACEBOS/
 381.placebo\$.tw.
 382.randomlyallocated.tw.
 383.(allocatedadj2random\$).tw.
 384.or/378-383
 385.377or384
 386.casereport.tw.
 387.letter/

388.historicalarticle/

389.or/386-388

390.385not389

391.15and263and358and390

