

Appendix S1

SUPPLEMENTARY METHODS

Data sources and searches

The main systematic literature searches were unrestricted and carried out using the online bibliographic databases PubMed, Embase, CINAHL, PsycINFO and Scopus for papers published between 1995 (the date of introduction of the first paediatric dermatology-specific HRQOL questionnaire (25)) and January 2016. Additional searches for studies published from January until July 2016 were undertaken to ensure that recently published articles were considered. Keywords were established by means of a pilot search, and included the following combinations of keywords and (when possible) MeSH (Medical Subject Headings) terms: "quality of life" AND "psoriasis" AND "children" OR "adolescents". In addition, alternative conceptualizations of the latter 2 keywords were utilized when relevant (i.e. paediatric, juvenile, childhood). In addition to the main literature searches, www.clinicaltrials.gov was searched to identify unpublished studies. Furthermore, a backward search (snowballing) was conducted using reference lists of identified papers and earlier reviews, together with a forward search (citation tracking), until no additional relevant papers were found.

Study selection

Studies were considered eligible if they: (i) reported data on HRQOL in children or adolescents 4–18 years of age with psoriasis; and (ii) used a quantitative approach to measure HRQOL by either generic, dermatology, or disease-specific self-report questionnaires. Studies restricted to only 1 aspect of quality of life, or related constructs, such as health status, depression, or anxiety, were excluded.

Due to the scarcity of studies examining HRQOL in children and adolescents, we included both controlled and uncontrolled studies, as well as published conference proceedings (i.e. "grey literature"). Papers published in English, German, or Scandinavian languages were included. Case studies describing special cases seen in the clinic or studies with sample sizes <5 were excluded (26–28). In case of missing data, authors were contacted by e-mail and asked to forward relevant data. Authors of papers presenting data on mixed populations of patients with various skin diseases that did not present separate data for their paediatric patients with psoriasis were also contacted. Studies were excluded if authors did not respond or were unable to provide the data. Study selection was conducted by 2 independent authors (HR, TT). Disagreements between reviewers were resolved by discussion. A third author (RZ) was consulted if initial agreement could not be reached.

Quality assessment

To assess the quality of the included studies, we used a revised version of the 5 appraisal-criteria developed by van der Linden and colleagues to assess quality of HRQOL-measurement in studies of HRQOL in patients with cutaneous rosacea (29), together with 9 additional criteria developed specifically for the present study. To adapt van der Linden et al.'s criteria to our population of interest, we replaced the word "rosacea" with "psoriasis", redefined the sample size cut-offs with categories corresponding to the ability to detect small, medium, and large effect sizes (Cohen's *d*) with 80% statistical power (30), and expanded criterion 4 (comparison with persons with other skin diseases or healthy controls) by differentiating between healthy control groups (4a) and comparison groups with other skin or chronic diseases (4b). The 5 revised criteria and their scoring were as follows: 1) sample size ($n < 27$: 0, $n \geq 27$: 1, $n \geq 84$: 2, or $n \geq 795$: 3), 2) grading of clinical disease severity (no: 0, yes: 1), 3) classification into subtypes of psoriasis

(no: 0, yes: 1), 4a) comparison with healthy controls (s) (no: 0, yes: 1), 4b) comparison with patients with other diseases (no: 0, yes: 1), and 5) the specificity of the applied HRQOL instrument (generic: 0, dermatology: 1, or psoriasis-specific: 2).

The following 9 additional criteria were specifically developed for the present study: 6) eligibility criteria well-defined (no: 0, partly: 1, yes: 2), 7) description of recruitment setting and time frame (no: 0, partly: 1, yes: 2), 8) confirmation of psoriasis diagnosis (no: 0, by non-dermatologist physician or not specified: 1, by dermatologist/specialist: 2), 9) reported whether patients were in treatment (no: 0, yes: 1), 10) relevant demographic characteristics of study participants provided (no: 0, partly: 1, yes: 2), 11) relevant clinical characteristics provided (no: 1, partly: 1, yes: 2), 12) use of HRQOL instrument with age-appropriate versions separating between children and adolescents (no: 0, yes: 1), 13) data analysed within clearly defined age-groups (i.e. children vs. adolescents; no: 0, yes: 1), and 14) response rate reported (no: 0, yes: 1).

A total quality score was obtained by summing the scores of items 1 to 14, yielding a total score ranging from 0 to 23. The strength of agreement between reviewers was evaluated with the between-rater total score correlation. Quality ratings were not used as weights in main analyses, as this is generally discouraged (31). Instead, associations between weighted means HRQOL and study quality were explored using meta-regression, and a detailed overview of study quality assessment was provided.

Data extraction

Data extraction was conducted independently by 2 authors (HR, TT) and included: (i) first author and year of publication, (ii) study design, recruitment setting, and country, (iii) comparison groups, (iv) primary objectives, (v) psoriasis patient characteristics (number of patients; clinical subtype; age; boys/girls-ratio; disease duration; age at onset), (vi) clinical disease severity (e.g. Psoriasis Area and Severity Index (PASI); body surface area (BSA)), and (vii) HRQOL-scores. When summary data (means, SDs) were unavailable, other descriptive statistics (e.g. medians and range) were extracted and converted into the desirable format (32). For studies reporting data from independent subgroups of participants (e.g. children and adolescents), the original subgroups were maintained in our analyses to provide the richest datasets possible (33, 34). If data from more than one instrument was available in a single study, e.g. the Pediatric Quality of Life Inventory (PedsQL) and the Children's Dermatology Quality of Life Index (CDLQI) (34,35), we extracted data for both instruments and used these data in separate analyses.

Analytical strategy

To enable between-study comparisons, studies were grouped according to the specific HRQOL instrument used. Separate random-effects meta-analyses were conducted based on these groupings. Independency was ensured by only combining and comparing studies with independent samples within each analysis. The impact of psoriasis on HRQOL was explored by combining the inverse variance weighted mean results from the included studies, thereby taking the precision of each study into consideration. When interpreting the mean score on the CDLQI/DLQI instrument, we relied on stratification bands developed for the CDLQI from a UK sample: no effect (0–1 points), small effect (2–6 points), moderate effect (7–12) very large effect (13–18 points) and extremely large effect (19–30 points) (36). Interpretation of the PedsQL was based on weighted mean total scores only, as norms across other diseases and healthy populations are available online (www.pedsq.org).

When available for ≥ 3 studies for any HRQOL instrument, the following clinical and demographic characteristics of study participants were explored as possible moderators of HRQOL im-

pairment using meta-regression: (i) percentage girls, (ii) age, (iii) clinical disease severity, (iv) age at onset, (v) duration, (vi) region (Western vs. other), and (vii) study quality. Prior to running the meta-regression analyses, we tested whether any of the proposed moderators were correlated. Highly correlated variables ($r < 0.70$) were entered as covariates in the relevant meta-regression models.

Heterogeneity was assessed using Q , I^2 , and T^2 statistics. Heterogeneity tests are aimed at determining whether results are likely to reflect genuine differences (heterogeneity), or whether the variation is more likely to be due to sampling error (homogeneity) (37). In accordance with recommendations, due to the often low statistical power of heterogeneity tests (38), a p -value ≤ 0.10 was used to indicate statistically significant heterogeneity. The I^2 quantity provides a measure of the degree of inconsistency by estimating the amount of total variance that can be accounted for by heterogeneity in the sample of studies (39). I^2 values of 25, 50, and 75% are considered low, moderate, and high, respectively.

T^2 is the variance of the true effects, and was used to calculate prediction intervals. The prediction interval represents the region in which results of comparable, future studies are expected to be found (40).

Publication bias is a widespread problem when conducting meta-analyses (41). Publication bias was evaluated using funnel plots and Egger's method (42, 43). A funnel plot is a graphic illustration of study results in relation to study size or precision. Egger's test provides a statistic for the skewness of results (44). If the results were suggestive of publication bias, an adjusted point estimate was calculated using Duval and Tweedie's trim and fill method (45), which imputes estimates of missing studies and recalculates it accordingly.

Data were pooled with a random-effects model using Comprehensive Meta-Analysis, version 3. Additional calculations were performed using SPSS version 22 or various formulas in Microsoft Excel.

Appendix S2

Design/not-representative sample:

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Full-text article not retrievable:

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Table SI. Overview of included studies

Author, year (ref.)	Publication type	Country	Study design	Recruitment setting	Primary objective (s)	Instru- ment (s)	Patients, N ^b	Boys/girls ratio	Age range, years (mean)	Mean (SD) PASI disease severity ^d	Mean (SD) HRQOL
Balci et al., 2007 (63)	Published article	Turkey	Observational study	Dermatology clinic	To assess the validity and reliability of the CDLQI the Turkish version of the CDLQI	CDLQI	6	NA	5-16 (NA)	NA	7.76 (4.08)
Beattie & Lewis-Jones, 2006 (64)	Published article	UK	Observational study	Dermatology clinic	a) To cross-validate a new generic HRQOL proxy instrument (Children's Life Quality Index, CLQI) b) To compare skin disease with other common chronic childhood diseases	CDLQI	29	11/18	5-16 (10.2)	NA	9.17 (7.83)
Bigic et al., 2010a (33)	Published article ^a	Turkey	Observational study (child group)	Dermatology clinic	To examine the symptoms of depression and anxiety and HRQOL in children and adolescents with psoriasis vs. healthy controls	PedsQL	22		8-12 (10.1)	6.4 (7.0)	72.83 (13.20)
Bigic et al., 2010b (33)	Published article ^a	Turkey	Observational study (adolescent group)	Dermatology clinic	To examine the symptoms of depression and anxiety and HRQOL in children and adolescents with psoriasis vs. healthy controls	PedsQL	26	17/31 (combined sample)	13-18 (15.3)	9.8 (10.5)	75.33 (14.93)
Chang et al., 2010 (67)	Conference abstract and poster	Malaysia	Observational study	Dermatology clinics (n = 13)	To study the socio-demographic characteristics, clinical manifestation, comorbidities, treatment, outcome, and HRQOL issues of patients with psoriasis	DLQI	180	NA	NA	NA	7.50 (6.52)
de Jager et al., 2011 (61)	Published article (Brief report)	The Netherlands	Observational study	General population database	Pilot study to explore the physical, emotional, and social limitations that children with psoriasis have to cope with	CDLQI	15	4/11	3-17.6 (12.8)	Mostly mild psoriasis	2.90 (2.90)
Gånemo et al., 2011 (50)	Published article ^a	Sweden	Observational study	Dermatology clinics (n = 2)	a) To assess Quality-of-Life in children and parents b) To examine relations between clinical data and QoL	CDLQI	42	17/28	5-16 (12.9)	4.9 (3.2)	5.05 (5.00)
van Geel et al., 2016 (60)	Published article	The Netherlands	Observational study	Dermatology clinic	To compare DLQI and CDLQI scores in patients with psoriasis aged 16-17 years	CDLQI	56	24/32	16-17 (16.6)	NA	CDLQI: 6.61 (5.74) DLQI: 5.41 (5.20)
Khawaja et al., 2015 (48)	Published article ^a	Pakistan	Observational study	Dermatology clinics (n = 3)	To explore the severity of psoriasis, dermatology-related quality of life, and psychiatric health of the patients with reference to sociodemographic, lifestyle, and clinical characteristics	DLQI	8	7/1	13-18 (15.5)	8.0 (10.3)	9.49 (9.17)
Landells et al., 2015 (63)	Published article	Canada and Europe	Intervention study	Dermatology clinics (n = 36)	To evaluate treatment effect in adolescents with moderate-to-severe psoriasis	CDLQI	101	54/65 ^c	12-17 (15.2)	21.1 (8.9)	9.60 (6.50)
Langley et al., 2011a (34)	Published article	USA and Canada	Intervention study (treatment group)	Dermatology clinics (n = 42)	To evaluate efficacy and safety of treatment	CDLQI and PedsQL	CLDQI: 100 PedsQL: 104	55/51	4-17 (12.2)	18.5 (6.7)	CDLQI: 8.90 (6.00) PedsQL: 74.80 (17.80)
Langley et al., 2011b (34)	Published article	USA and Canada	Intervention study (placebo group)	Dermatology clinics (n = 42)	To evaluate efficacy and safety of treatment	CDLQI and PedsQL	CDLQI: 102 PedsQL: 104	53/52	4-17 (11.7)	18.6 (6.8)	CDLQI: 10.00 (6.40) PedsQL: 76.10 (16.90)
Lewis-Jones & Finlay, 1995 (25)	Published article	UK	Observational study	Dermatology clinic	To develop and initially validate the CDLQI instrument	CDLQI	25	7/18	4-16 (10.4)	NA	5.40 (5.00)
Manzoni et al., 2012 (65)	Published article	Brazil	Observational study	Dermatology clinics (n = 3)	a) To compare quality of life across paediatric patients with atopic dermatitis, psoriasis and vitiligo b) To correlate the findings with clinical findings	CDLQI	25	NA	5-16 (NA)	BSA total: mdn: 6 (range: 2-37) BSA exposed, mdn: 4 (range: 1-6.5)	7.90 (3.20)
Matusiewicz et al., 2013 (66)	Published article	Germany	Observational study	Online survey	To characterize the health-care situation and quality of life in children and adolescents with psoriasis	CDLQI	84	27/57	5-16 (NA)	NA	7.60 (3.50)

Table SI. Contd.

Matterne & Apfelbacher, 2016 (46)	Published article	Germany	Observational study	Randomly selected from local population registries across the county	To describe HRQOL in paediatric psoriasis compared with psoriasis-free children and adolescents	KINDL-R	108	NA	11-17 (NA)	NA	69.85
Oostveen et al., 2012 (49)	Published article	The Netherlands	Observational study	Dermatology clinic	To assess the CDLQI in a cohort of patients with juvenile psoriasis and to evaluate the influence of treatments in daily clinical practice on CDLQI	CDLQI	125	46/79	3-17 (10.7)	7.0 (5.8)	6.50 (5.00)
Papp et al., 2014 (35)	Conference abstract	Multi-site international study	Intervention study	Dermatology clinics (NA)	To report baseline characteristics of an ongoing intervention study	CDLQI and PedsQL	114	49/65	4-18 (13.0)	18.3 (8.8)	CDLQI: 11.30 (6.79) PedsQL: 73.10 (17.44)
Smidt et al., 2010 (47)	Published article	USA	Observational study	Dermatology clinic	To develop and validate a quality-of-life instrument (Skindex-Teen) for adolescents with skin-disease	Skindex-Teen	11	NA	12-17 (NA)	NA	21.20 (10.30)

^aAdditional unpublished data provided on request. ^bTotal N for patients with psoriasis enrolled in HRQOL aim. ^cNo separate data on patients enrolled in HRQOL aim available, the ratio reported relates to total sample of paediatric patients ($n=119$). ^dMeasured by Psoriasis Area and Severity Index (PASI) unless otherwise specified. CDLQI: Children's Dermatology Quality of Life Index; DLQI: Dermatology Quality of Life Index; PedsQL: The Pediatric Quality of Life Inventory; PASI: Psoriasis Area Severity Index; BSA: body surface area; NA: not available; Mdn: median.

Table SII. Study quality ratings

Author, year (ref.)	1. Sample size	2. Grading of disease severity	3. Classification of subtypes	4a. Comparison group (s): healthy controls	4b. Comparison group (s): other disease	5. Specificity of HRQOL instrument	6. Well-defined eligibility criteria	7. Recruitment setting and time frame reported	8. Confirmation of diagnosis	9. Reported whether patients were in treatment	10. Demographic characteristics	11. Clinical characteristics	12. Age-sensitive HRQOL measurement	13. Data analysed within clearly defined age groups	14. Response rate reported	Total, sum	Percent (23=100%)
Balci et al., 2007 (63)	0	1	0	0	1	1	1	2	2	0	0	0	0	0	0	8	34.8
Beattie & Lewis-Jones, 2006 (64)	1	0	0	0	1	1	1	2	2	0	2	0	0	0	0	10	43.5
Bilgic et al., 2010 (33)	1	1	0	1	0	0	2	1	2	0	2	2	1	1	1	15	65.2
Chang et al., 2008 (67)	2	0	0	0	0	1	1	2	2	1	0	0	0	0	0	9	39.1
de Jager et al., 2011 (61)	0	1	0	0	0	1	1	1	0	0	2	1	0	0	0	7	30.4
Gånemo et al., 2011 (50)	1	1	1	0	0	1	2	2	2	1	2	2	0	1	0	16	69.6
van Geel et al., 2016 (60)	1	0	0	0	0	1	2	1	2	1	2	0	1	1	1	13	56.5
Khawaja et al., 2015 (48)	0	1	1	0	0	1	2	2	2	0	2	2	0	0	0	13	56.5
Landells et al., 2015 (62)	2	1	1	0	0	1	2	2	2	0	2	2	0	0	0	15	65.2
Langley et al., 2011 (34)	2	1	1	1	1	1	2	2	2	0	2	1	1	0	1	18	72.3
Lewis-Jones & Finlay, 1995 (25)	0	0	0	1	1	1	1	1	2	0	2	0	0	0	1	10	43.5
Manzoni et al., 2012 (65)	0	1	0	0	1	1	2	2	2	0	0	0	0	0	0	9	39.1
Matusiewicz et al., 2013 (66)	2	0	0	0	0	1	1	2	0	1	2	1	0	0	1	11	47.8
Matterne & Apfelbacher, 2016 (46)	2	0	0	1	0	0	2	2	0	0	0	0	1	0	1	9	39.1
Oostveen et al., 2012 (49)	2	1	0	0	0	1	2	2	2	1	2	2	0	1	0	16	69.6
Papp et al., 2014 (35)	2	1	1	0	0	1	2	1	2	0	2	1	1	0	0	14	60.9
Smidt et al., 2010 (47)	0	0	0	0	1	1	2	1	2	0	0	0	1	0	1	9	39.1

Study quality criteria and scoring: 1) sample size, k (number of studies) <27: 0 k ≥27 1 k ≥84: 2 k ≥795: 3, 2) grading of clinical disease severity, no: 0 yes: 1, 3) classification of subtypes, no: 0 yes: 1, 4a) comparison with healthy controls, no: 0 yes: 1, 4b) comparison with other disease, no: 0 yes: 1, 5) specificity of HRQOL instrument, generic: 0, dermatology-specific: 1, psoriasis-specific: 2, 6) well-defined eligibility criteria, no: 0 partly: 1 yes: 2, 7) recruitment setting and period, no: 0 partly: 1 yes: 2, 8) confirmation of diagnosis, no: 0, by non-dermatologist physician or not specified: 1, by dermatologist/specialist 2, 9) reports whether patients are in treatment, no: 0 yes: 1, 10) demographic characteristics, no: 0, partly: 1, yes: 2, 11) background clinical characteristics, no: 0, partly: 1, yes: 2, 12) age-sensitive HRQOL measurement (use of instrument with age-appropriate versions separating between children and adolescents), no: 0 yes: 1, 13) data analysed within clearly defined age groups (children vs. adolescents), no: 0 yes: 1, 14) response rate reported, no: 0 yes: 1.