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Article details

Chernyshov P.V., Tomas-Aragones L., Manolache L., Svensson A., Marron S.E., Evers A.W.M., Bettoli V., Jemec G.B. & Szepietowski J.C. (2018), Which acne treatment has the best influence on health-related quality of life? Literature review by the European Academy of Dermatology and Venereology Task Force on Quality of Life and Patient Oriented Outcomes, *Journal of the European Academy of Dermatology and Venereology* 32(9): 1410-1419.

Doi: 10.1111/jdv.15048

REVIEW ARTICLE

Which acne treatment has the best influence on health-related quality of life? Literature review by the European Academy of Dermatology and Venereology Task Force on Quality of Life and Patient Oriented Outcomes

P.V. Chernyshov,^{1,*} L. Tomas-Aragones,² L. Manolache,³ A. Svensson,⁴ S.E. Marron,⁵ A.W.M. Evers,⁶ V. Bettoli,⁷ G.B. Jemec,⁸ J.C. Szepietowski⁹

¹Department of Dermatology and Venereology, National Medical University, Kiev, Ukraine

²Department of Psychology, Aragon Health Sciences Institute (IACS), University of Zaragoza, Zaragoza, Spain

³Dermatology, Dali Medical, Bucharest, Romania

⁴Department of Dermatology and Venereology, Skane University Hospital, Malmö, Sweden

⁵Department of Dermatology, Royo Villanova Hospital, Aragon Health Sciences Institute (IACS), Zaragoza, Spain

⁶Health, Medical, and Neuropsychology unit, Leiden University, Leiden, The Netherlands

⁷Department of Medical Sciences, Section of Dermatology, University of Ferrara, Ferrara, Italy

⁸Department of Dermatology, Zealand University Hospital, Roskilde, Denmark

⁹Department of Dermatology, Venereology and Allergology, Wrocław Medical University, Wrocław, Poland

*Correspondence: P. Chernyshov. E-mail: chernyshovpavel@ukr.net

Abstract

According to results of a recent literature search performed by the European Academy of Dermatology and Venereology (EADV) Task Forces (TF) on Quality of Life and Patient Oriented Outcomes (QoL and PO) and Acne, Rosacea and Hidradenitis Suppurativa (ARHS), most of the publications where health-related (HR) QoL of acne patients was studied were clinical trials. Members of the EADV TF on QoL and PO decided to detect which acne treatment has the best influence on HRQoL of acne patients. A new literature search was organized to find publications on acne treatment where the HRQoL of patients was assessed as an outcome measure. From 186 papers with HRQoL assessment, 37 papers were included for further analysis. Our results revealed that oral isotretinoin had the best influence on HRQoL of acne patients. Several other treatment methods also showed good effects on the HRQoL of acne patients. Oral isotretinoin and norethindrone acetate/ethinyl estradiol, topical clindamycin phosphate/benzoyl peroxide and adapalene/benzoyl peroxide showed significantly better effect on HRQoL than placebo. There is limited number of the high-quality studies on acne treatment where HRQoL was assessed. Dermatology-specific and acne-specific instruments showed much better sensitivity to successful therapeutic intervention than generic HRQoL instruments. The most frequently used HRQoL instrument was the Dermatology Life Quality Index questionnaire.

Received: 23 November 2017; Accepted: 13 April 2018

Conflicts of interest

GBJ has received consulting fees from AbbVie, AstraZeneca, MSD, LEO Pharma, Novartis, Pfizer, InflaRx and UCB; lecture fees from AbbVie, Galderma and Roche; grant support from AbbVie, Novartis and LEO Pharma; equipment on loan from Michelson Diagnostics. GBJ is a joint copyright owner of the AKQOL and SCQOL. JCS served as a consultant and advisor for AbbVie, Celgene, Dignity Sciences, Leo Pharma, Novartis, Pierre-Fabre and Sandoz; investigator for AbbVie, Actelion, Amgen, GSK, Janssen, Merck, Novartis, Regeneron and Trevi; and speaker for AbbVie, Actavis, Astellas, Janssen, Leo Pharma, Novartis, SunFarm, Sandoz and Eli Lilly.

Funding source

None.

Introduction

The treatment of acne is comparatively well established and has been made the subject of several guidelines by e.g. European Dermatology Forum, American Academy of Dermatology and numerous other national organizations.¹⁻⁴ Guidelines generally describe a systematic treatment escalation based on disease severity and treatment response; starting with topical treatments using e.g. benzoyl peroxide or retinoids, progressing over systemic therapies with antibiotics to isotretinoin.

Health-related quality of life (HRQoL) assessment in patients with acne is recommended by several national guidelines.⁵ The European Dermatology Forum S3-Guideline for the Treatment of Acne recommended adopting a QoL measure as an integral part of acne management.¹ There are many reasons to measure HRQoL in clinical practice,⁶ but according to a recent literature search performed by the European Academy of Dermatology and Venereology (EADV) Task Forces (TF) on Quality of Life and Patient Oriented Outcomes (QoL and PO) and Acne, Rosacea and Hidradenitis Suppurativa (ARHS), most of the publications where the HRQoL of acne patients was studied were clinical trials.⁷ Generic, dermatology- and disease-specific QoL instruments were used as an outcome measures to assess the efficacy of different treatment methods. The highest number of studies identified was those concerning isotretinoin and benzoyl peroxide. Members of the EADV TF on QoL and PO decided to detect which acne treatment has the best influence on HRQoL of acne patients.

Methods

Based on the results of the Position Paper of the EADV TFs on QoL and PO and ARHS on QoL measurement in acne,⁴ 186 papers with HRQoL assessment in acne patients were found. A new literature search was organized to find publications on acne treatment where HRQoL of patients was assessed as an outcome measure. Authors of the Position Paper on QoL measurement in acne were invited to participate. All those who volunteered were allocated a section of the identified articles to review.

Inclusion criteria:

- Study participants diagnosed with established acne by healthcare practitioner.
- Information on acne treatment:
 - Treatment method.
 - Duration of the treatment.
 - Frequency of the treatment.
- Information on QoL assessment:
 - QoL assessed by validated instrument.
 - QoL assessment data before and after the treatment.

All publications were independently assessed by two coauthors. The assessments were compared and discrepancies discussed and resolved. The remaining publications were analysed in detail, and the HRQoL instruments used in studies on acne treatment were listed.

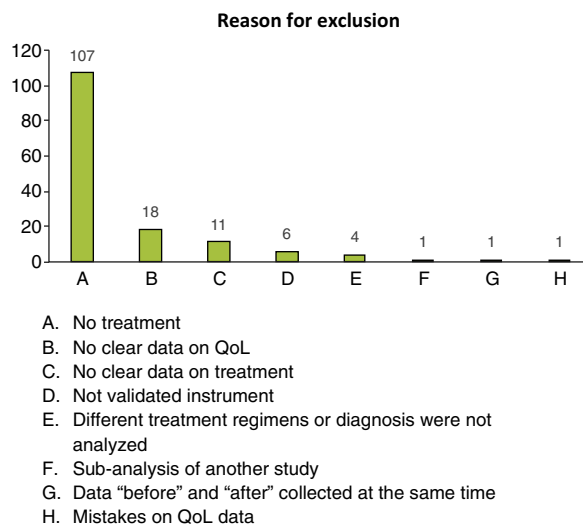


Figure 1 Reasons for exclusion.

Different QoL instruments often have dissimilar minimal and maximal total scores or have domain scores only. It was decided by coauthors to present mean change of HRQoL impairment from baseline in percentage for all acne treatment methods from included articles. Mean total scores were calculated even for instruments that normally have only separate domains' scores (sum of domain scores in percentage divided by the number of domains). We acknowledge that there is no validated method of direct comparison of the scores of different HRQoL instruments. However, the use of the mean change of HRQoL impairment in percentage after the treatment makes it possible *de facto* to detect which acne treatment method had the best effect on patients' HRQoL.

The new word 'quimp', meaning quality of life impairment, was recently proposed.⁸ The EADV TF on QoL and PO recommends the word 'quimp' for routine clinical and research use.⁹

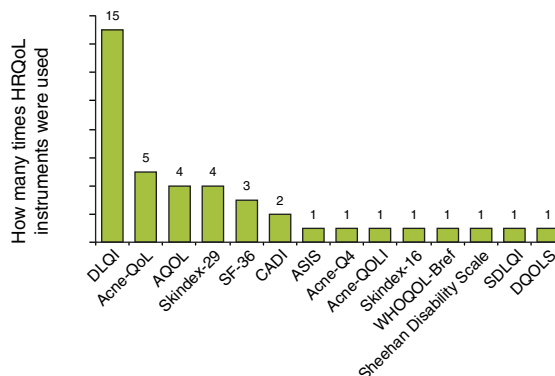


Figure 2 Frequency of health-related quality of life instruments use.

Table 1 Information on treatment methods, duration, health-related quality of life (QoL) instruments, number of patients, strength of recommendation and level of evidence for included double-blind, randomized comparative studies

Treatment	Duration of the study	QoL instrument	Number of patients	% of QoL change	Reference	Strength of recommendation	Level of evidence
Isotretinoin 5 mg capsules (once daily)	16 weeks	DLQI	29	72.92	15	A	I, II
Emulsion containing licochalcone A, L-carnitine and 1,2-decanediol	8 weeks	DLQI	25	40	42	–	–
Clindamycin phosphate 1.2% and benzoyl peroxide 2.5%	12 weeks	Acne-Q4	797	59	31	A	I
Adapalene 0.1% gel and Sébium Global cream	8 weeks	CADI	55	54	23	A†	I, II†
Adapalene 0.1% gel and vehicle cream	8 weeks	CADI	56	31.2	23	A†	I, II†
Norethindrone acetate/ethinyl estradiol oral contraceptive pill combining low-dose phasic ethinyl estradiol (20, 30 and 35 µg for 5, 7 and 9 days, respectively) with a constant 1 mg dose of norethindrone acetate	6 months	Acne-QoL	296	48.18	19	A	I
Clindamycin phosphate 1.2%–benzoyl peroxide 2.5% combination	12 weeks	Acne-QoL	?	48	26	A	I
Oral doxycycline 100 mg once daily and fixed-dose combination gel of adapalene 0.1% and benzoyl peroxide 2.5%	12 weeks	Acne-QoL	216	42.63	22	A	I, II
Oral doxycycline 100 mg once daily and gel vehicle	12 weeks	Acne-QoL	204	34.11	22	A‡	I, II‡
Salicylic acid 0.5% gel	12 weeks	Acne-QoL	33	17.5	30	B	II
Adapalene 0.1% and benzoyl peroxide 2.5% fixed-dose combination gel	24 weeks	Acne-QoL	113	5.29	22	A	I, II

†For adapalene. ‡For doxycycline. ?Exact number is absent in cited article. CADI, Cardiff Acne Disability Index; DLQI, Dermatology Life Quality Index.

Table 2 Information on treatment methods, duration, health-related quality of life (QoL) instruments, number of patients, strength of recommendation and level of evidence for included single-blind, randomized, parallel-group studies

Treatment	Duration	QoL instrument	Number of patients	% of QoL change	Reference	Strength of recommendation	Level of evidence
Tretinoin 0.05% cream and clindamycin phosphate 1% lotion twice daily	12 weeks	AQOL	23	54.5	28	A	I, II
3% salicylic acid and clindamycin phosphate 1% lotion twice daily	12 weeks	AQOL	23	51.28	28	B† and A‡	II† and I, II‡
Adapalene 0.1% gel once daily for 9 months	9 months	DLQI	11	46.7	21	A	I, II
Adapalene 0.1% gel once daily	12 weeks	DLQI	48	45.82	24	A	I, II
Azelaic acid 15% gel twice daily for 3 months followed by a 6-month observational phase	9 months	DLQI	16	41.09	21	A	I
Tretinoin 0.025% gel once daily	12 weeks	DLQI	46	34.70	24	A	I, II
Azelaic acid 15% gel twice daily for 9 months	9 months	DLQI	11	33.87	21	A	I
Benzoyl peroxide 5% and clindamycin 1%	12 weeks	Skindex-29	83	40.96	35	A	I, II
Adapalene 0.1%	12 weeks	Skindex-29	85	13.47	35	A	I, II

†For salicylic acid. ‡For clindamycin phosphate. AQOL, Acne Quality of Life Scale; DLQI, Dermatology Life Quality Index.

Guidelines of care for the management of acne vulgaris developed by the American Academy of Dermatology were used to show strength of recommendation and level of evidence. Evidence was graded using a 3-point scale based on the quality of methodology as follows: I – good-quality patient-oriented evidence and II – limited-quality patient-oriented

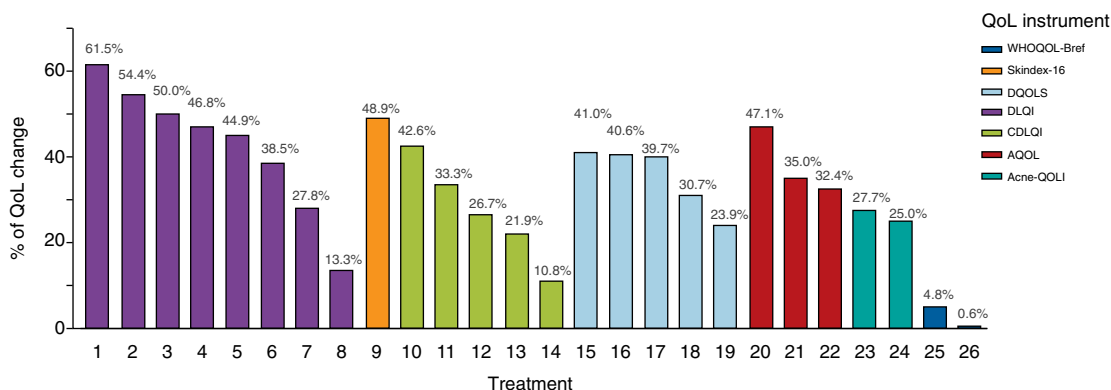
evidence. Clinical recommendations were developed on the best available evidence. The strength of recommendation was ranked as follows: A. recommendation based on consistent and good-quality patient-oriented evidence and B. recommendation based on inconsistent or limited-quality patient-oriented evidence.²

Results

From 186 papers with HRQoL assessment in acne patients, 149 were excluded during the literature search. The reasons for exclusion are presented in Fig. 1. The remaining 37 papers were included for further analysis. Generic, dermatology-specific, acne-specific HRQoL instruments and even instrument originally created for HRQoL assessment in patients with mental problems were used. How frequently these HRQoL instruments

were used is presented in Fig. 2. Almost half of the studies were funded by pharmaceutical companies, 16 papers have no information about funding, authors of two studies reported no industrial support, and one study was supported by non-commercial organization.

Information on treatment methods and duration of treatment, HRQoL instruments, number of patients, percentage of HRQoL changes from baseline, strength of recommendation



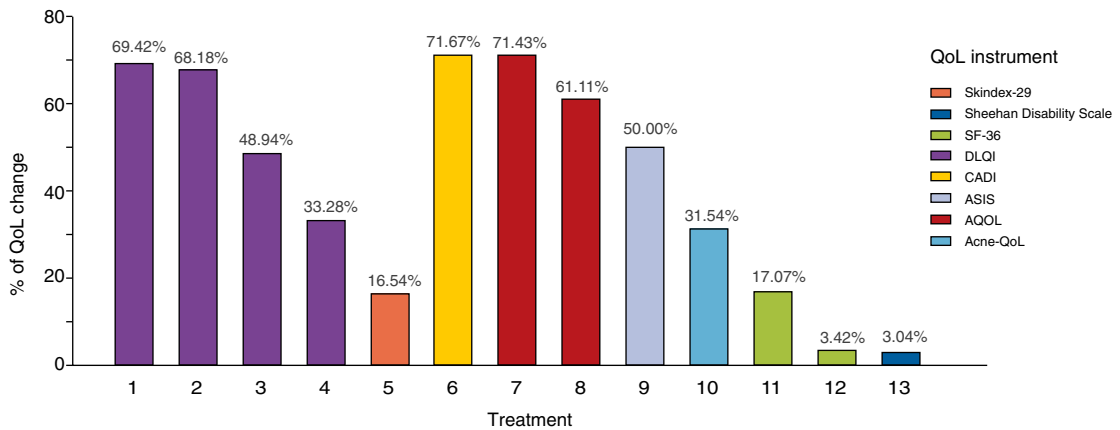
1. Oral isotretinoin 1 mg/kg/day, in two divided doses¹⁶
2. Minocycline 100 mg orally once daily²⁰
3. Oral tetracycline hydrochloride (500 mg twice daily) and topical adapalene 0.1% gel once a day¹⁶
4. Isotretinoin 0.5–0.8 mg/kg/d in two divided doses for at least 20 weeks, ensuring that the cumulative dose was 100 mg/kg¹⁷
5. 3% erythromycin and 5% benzoyl peroxide twice a day²⁰
6. Topical 2% erythromycin once-daily and topical 5% benzoyl peroxide once-daily²⁰
7. Oxytetracycline 500 mg orally twice daily²⁰
8. 5% benzoyl peroxide twice a day²⁰
9. Combination of 0.1% topically applied adapalene gel, once daily in the evening and 1% clindamycin phosphate topical gel, twice daily in the morning and evening²⁵
10. 5% benzoyl peroxide twice a day²⁰
11. Minocycline 100 mg orally once daily²⁰
12. 3% erythromycin and 5% benzoyl peroxide twice a day²⁰
13. Topical 2% erythromycin once-daily and topical 5% benzoyl peroxide once-daily²⁰
14. Oxytetracycline 500 mg orally twice daily²⁰
15. 3% erythromycin and 5% benzoyl peroxide twice a day²⁰
16. Minocycline 100 mg orally once daily²⁰
17. Topical 2% erythromycin once-daily and topical 5% benzoyl peroxide once-daily²⁰
18. Oxytetracycline 500 mg orally twice daily²⁰
19. 5% benzoyl peroxide twice a day²⁰
20. Clindamycin phosphate gel 10 mg/ml once daily²⁷
21. Benzoyl peroxide gel 50 mg/ml once daily²⁷
22. Clindamycin phosphate 10 mg/ml and benzoyl peroxide 50 mg/ml combination gel once daily²⁷
23. Tretinoin Gel Microsphere 0.04%²⁹
24. Tretinoin Gel Microsphere 0.1%²⁹
25. Isotretinoin 0.5mg/kg/day for the first two weeks, followed by 1mg/kg/day until a cumulative dose of 120mg/kg was obtained¹⁸
26. Lymecycline 408mg daily (or minocycline 100mg daily if lymecycline was previously ineffective or unacceptable), plus adapalene cream¹⁸

Figure 3 Percentage of quality of life changes in open-label multiple-group studies.

and level of evidence for double-blind, randomized comparative trials and single-blind, randomized, parallel-group trials are presented in Tables 1 and 2, respectively. The percentage of QoL changes in open-label multiple-group studies and open-label single-group studies are presented in Figs 3 and 4. The strength of recommendation for treatment methods presented in Figs 3 and 4 is 'A' and the level of evidence – I or II. Available data on QoL change at weeks 8, 12 and 24 are presented in Figs 5–7. Studies on acupuncture,¹⁰ clay jojoba oil facial mask,¹¹ photodynamic¹² and blue light therapy¹³ and pilot study on subcutaneous injections of afamelanotide¹⁴ showed QoL improvement, but limited data exist regarding the safety and efficacy of these agents to recommend their use in acne by established guidelines.^{1,2}

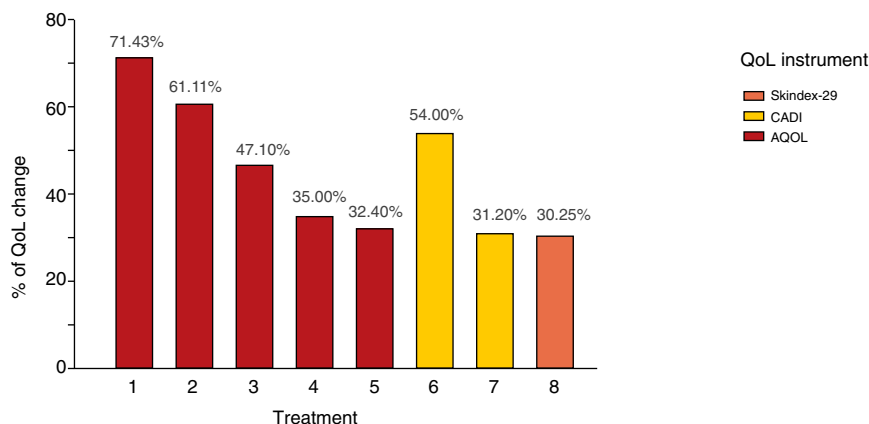
Studies with direct comparison of different treatments with the same duration and HRQoL instrument are important to define treatment options with the best effect on patients' HRQoL. There were highly significant differences ($P < 0.0001$) in the Dermatology Life Quality Index (DLQI) scores after

16 weeks of oral isotretinoin, compared to placebo in the study by Rademaker *et al.*¹⁵ No significant differences in changes of the DLQI scores between oral isotretinoin 1 mg/kg/day group and oral tetracycline hydrochloride 500 mg twice daily and topical adapalene once a day group were reported by Oprica *et al.*¹⁶ In the study by Kaymak *et al.*¹⁷ at the end of the second and fourth months, HRQoL assessed by the DLQI was more impaired in the topical treatment group (topical treatment consisted of either topical antibiotics or topical retinoids) compared to the isotretinoin group ($P < 0.05$). In another study, improving of social QoL of the generic WHOQOL-BREF questionnaire was significantly greater in the isotretinoin group than the antibiotic group ($P < 0.05$).¹⁸ Norethindrone acetate/ethinyl estradiol-treated subjects experienced greater (statistically significant) improvements in all four domains of the Acne-QoL when compared with placebo-treated subjects at cycle 3. These treatment advantages continued to increase until the end of the study (cycle 6).¹⁹ The improvement in total DLQI score for the 5% benzoyl peroxide twice a day group was significantly less than



1.	Isotretinoin 0.5mg/kg/d ⁴³
2.	Isotretinoin a total cumulative dose of 120 mg/kg was given for 30 week ⁴⁴
3.	Azelaic acid 15% gel ⁴⁵
4.	Oral roxithromycin 300 mg daily for 2–4 weeks ⁴⁶
5.	Oral roxithromycin 300 mg daily for 2–4 weeks ⁴⁶
6.	The initial isotretinoin dosage was 0.5 mg/ kg for the first month and then 1 mg/ kg until a cumulative dose of 130–150 mg/ kg had been completed ³²
7.	Benzoyl peroxide/ clindamycin topical gel twice daily ³³
8.	Benzoyl peroxide/clindamycin gel twice daily ⁴⁷
9.	Dapsone gel 5% twice a day ³⁴
10.	Azithromycin, 500 mg, orally thrice weekly and 0.1% topical adapalene (gel or cream) to apply to the affected areas of the face and trunk once daily in the evening, and benzoyl peroxide (gel) to apply to inflammatory lesions of the face and trunk once daily in the morning ⁴⁸
11.	Isotretinoin at 0.5-1.0 mg/kg/day orally for 6 months to reach a cumulative dose of 120 mg/kg ⁴⁹
12.	Isotretinoin (0.5–1 mg/ kg/ day for average 24 weeks) ⁵⁰
13.	Isotretinoin 0.5–1.0 mg/kg/day orally during 6 months to reach a cumulative dose of 120 mg/kg ⁵¹

Figure 4 Percentage of quality of life changes in open-label single-group studies

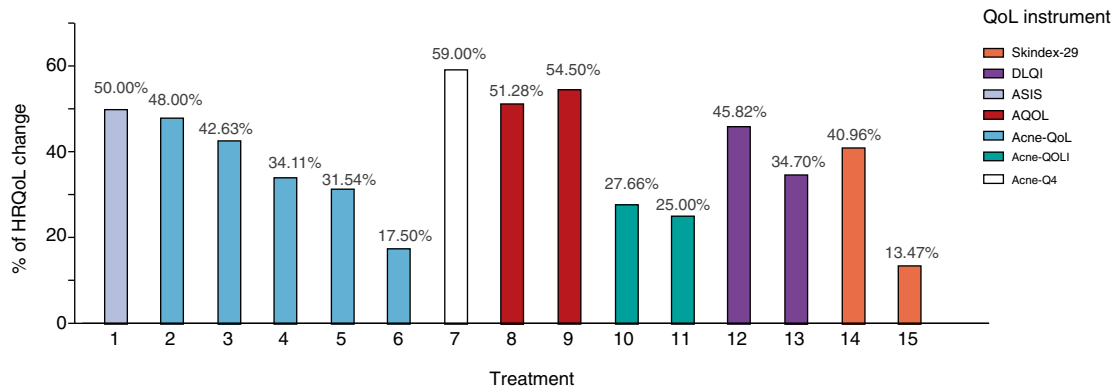


1.	Benzoyl peroxide/ clindamycin topical gel twice daily ³³
2.	Benzoyl peroxide/clindamycin gel twice daily ⁴⁷
3.	Clindamycin phosphate gel 10 mg/ml once daily ²⁷
4.	Benzoyl peroxide gel 50 mg/ml once daily ²⁷
5.	Clindamycin phosphate 10 mg/ml and benzoyl peroxide 50 mg/ml combination gel once daily ²⁷
6.	Adapalene 0.1% gel and Sébium Global cream ²³
7.	Adapalene 0.1% gel and vehicle cream ²³
8.	For the first two weeks: clindamycin 1%/benzoyl peroxide 5% (and adapalene 0.1%/benzoyl peroxide 2.5% gel in a bilateral split-face fashion (allocation to the left or right side of the face was randomized). For the remaining six weeks, subjects applied clindamycin 1%/benzoyl peroxide 5% to the entire face, in an open-label, full-face fashion. ⁵²

Figure 5 Quality of life change at week 8.

for all the other groups (oxytetracycline 500 mg orally twice daily; minocycline 100 mg orally once daily; 3% erythromycin and 5% benzoyl peroxide twice a day; topical 2% erythromycin once daily; and topical 5% benzoyl peroxide once daily).²⁰ There were no significant differences in changes of the DLQI scores between groups of patients that were treated by azelaic acid 15% for 9 months, azelaic acid 15% gel for 3 months followed by a 6-month observational phase or adapalene 0.1% gel for 9 months.²¹ The acne symptoms domain of the Acne-QoL showed a statistically significantly greater improvement ($P = 0.002$) for patients using adapalene 0.1% and benzoyl peroxide 2.5% fixed-dose combination gel and oral doxycycline compared to patients using the gel vehicle and oral doxycycline. The mean differences in scores between the adapalene 0.1% and benzoyl peroxide 2.5% fixed-dose combination gel and vehicle-treated patients at week 36 were statistically significant in all four Acne-QoL domains ($P = 0.001$).²² Adapalene 0.1% gel and skin care product Sébium Global cream showed significantly better improvement of the Cardiff Acne Disability Index (CADI) in comparison with adapalene 0.1% gel and vehicle cream ($P < 0.005$).²³ Responses to individual DLQI questions were significantly lower in the adapalene group than the tretinoin group at week one for items related to close contacts and skin

symptoms and at week 12 for social interactions and skin symptoms.²⁴ There were no significant differences in the total mean Skindex-16 scores and mean scores of all three Skindex-16 domains between the once-daily adapalene treatment group and once-daily adapalene on 2 days per week groups at 4 and 8 weeks of the study.²⁵ Participants treated with clindamycin phosphate 1.2%/benzoyl peroxide 2.5% had significantly greater improvements in all four Acne-QoL domains compared with participants treated with each individual active ingredient and vehicle ($P < 0.001$) in the study by Webster *et al.*²⁶ Meanwhile, there was no significant difference in the Acne Quality of Life Scale (AQOL) scores of acne patients treated by clindamycin phosphate 10 mg/mL and benzoyl peroxide 50 mg/mL combination gel and acne patients treated by clindamycin phosphate gel 10 mg/mL or benzoyl peroxide gel 50 mg/mL in the study by Stinco *et al.*²⁷ There were no significant differences in AQOL between 3% salicylic acid and clindamycin phosphate 1% lotion twice daily (first group) and tretinoin 0.05% cream and clindamycin phosphate 1% lotion twice daily (second group) at baseline and at the end of the study by Babayeva *et al.*²⁸ No difference between two different tretinoin concentrations according to the Acne-QOLI scores was found in the study on tretinoin pump.²⁹ The average self-perception and role-social scores of



1.	Dapsone gel 5% twice a day ²⁴
2.	Clindamycin phosphate 1.2% - benzoyl peroxide 2.5% ²⁶
3.	Oral doxycycline 100 mg once daily and fixed-dose combination gel of adapalene 0.1% and benzoyl peroxide 2.5% ²²
4.	Oral doxycycline 100 mg once daily and gel vehicle ²²
5.	Azithromycin, 500 mg, orally thrice weekly and 0.1% topical adapalene (gel or cream) once daily in the evening, and benzoyl peroxide (gel) once daily in the morning ⁴⁸
6.	Salicylic acid 0.5% gel ³⁰
7.	Clindamycin phosphate 1.2% - benzoyl peroxide 2.5% ³¹
8.	3% salicylic acid and clindamycin phosphate 1% lotion twice daily ²⁸
9.	Tretinoin 0.05% cream and clindamycin phosphate 1% lotion twice daily ²⁸
10.	Tretinoin Gel Microsphere 0.04% ²⁹
11.	Tretinoin Gel Microsphere 0.1% ²⁹
12.	Adapalene 0.1% gel once daily ²⁴
13.	Tretinoin 0.025% gel once daily ²⁴
14.	Benzoyl peroxide 5% and clindamycin 1% ³⁵
15.	Adapalene 0.1% ³⁵

Figure 6 Quality of life change at week 12.

Acne-QoL in salicylic acid 0.5% group increased significantly higher than in vehicle group ($P < 0.05$).³⁰

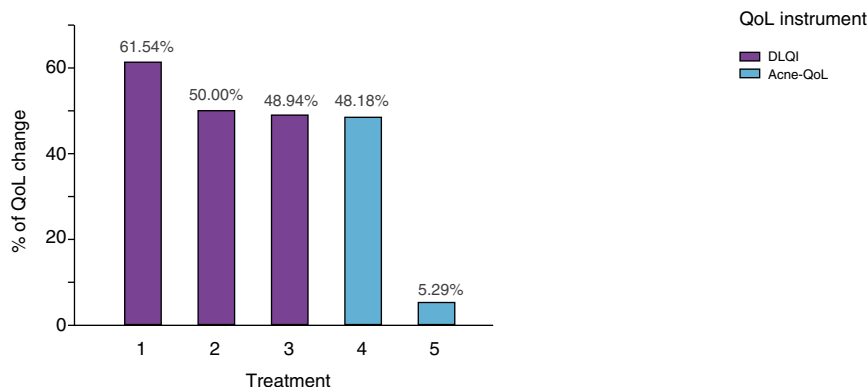
Discussion

In theory, all instruments that were appropriately validated to measure HRQoL in the same disease should reflect all aspect of QoL impairment related to that condition. Nevertheless, there is no evidence that a direct comparison of the scores of different HRQoL instruments is possible. The study by Ozilins *et al.*²⁰ showed that the percentage of HRQoL changes in the same patients assessed simultaneously by different instruments were not equal. However, the use of the mean change of HRQoL impairment after the treatment makes it possible *de facto* to detect which acne treatment method had the best effect on HRQoL. The main limitation of such an approach is a theoretical possibility to obtain different results (lower or higher) in the case of assessment by other HRQoL instruments. A comparison of the impact of different treatment methods on HRQoL of patients assessed by the same instrument is considered to be a

more methodologically reliable approach, but in the case of high diversity of instruments and a lack of well-designed studies, it also leads to significant limitations.

We can speculate that percentage changes of HRQoL assessed by dermatology-specific and acne-specific questionnaires look comparable. In contrast, percentage changes of generic instruments scores are much lower in comparison with other types of the instruments. We analysed separately *de facto* mean changes of HRQoL after the treatment that were assessed by different instruments in groups of studies with common design and same treatment duration. Also, we analysed the HRQoL changes after the treatment in different studies where the same HRQoL instruments were used.

According to the results of double-blind, randomized comparative studies, the highest changes of HRQoL from baseline were reported with regard to patients treated with isotretinoin (measured by the DLQI)¹⁵ and benzoyl peroxide/clindamycin topical gel (measured by the Acne-Q4).³¹ Clindamycin phosphate 1% lotion and tretinoin 0.05% cream showed the highest change of



- | | |
|----|--|
| 1. | Oral isotretinoin, 1 mg/ kg/day, in two divided doses (isotretinoin-treated females were independently given oral contraceptives) ¹⁶ |
| 2. | Oral tetracycline hydrochloride (500 mg twice daily) and topical adapalene 0.1% gel once a day in a thin film on the affected area ¹⁶ |
| 3. | Azelaic acid 15% gel ⁴⁵ |
| 4. | Estrostep (norethindrone acetate/ethinyl estradiol) oral contraceptive pill combining low-dose phasic ethinyl estradiol (20, 30, and 35 µg for 5, 7, and 9 days, respectively) with a constant 1 mg dose of norethindrone acetate. ¹⁹ |
| 5. | Adapalene 0.1% and benzoyl peroxide 2.5% fixed-dose combination gel ²² |

Figure 7 Quality of life change at week 24.

HRQoL from baseline (measured by AQOL)²⁸ in single-blind, randomized, parallel-group studies. Oral isotretinoin showed the highest HRQoL change (measured by the DLQI)¹⁶ in open-label multiple-group studies. Patients treated with oral isotretinoin³² and topical benzoyl peroxide/clindamycin gel³³ showed the highest dynamics of HRQoL in open-label single-group studies (measured by the CADI and the AQOL, respectively). After 8 weeks of treatment, the highest changes of HRQoL from the baseline were shown by patients treated with benzoyl peroxide/clindamycin gel (measured by the AQOL).³³ After 12 weeks of treatment, the highest changes of HRQoL were in patients treated with clindamycin phosphate 1.2% - benzoyl peroxide 2.5% (measured by Acne-Q4)³¹ and tretinoin 0.05% cream and clindamycin phosphate 1% lotion (measured by the AQOL).²⁸ After 24 weeks of treatment, the best influence on HRQoL (measured by the DLQI) had oral isotretinoin.¹⁶ Oral isotretinoin,¹⁵ oral norethindrone acetate/ethinyl estradiol,¹⁹ topical clindamycin phosphate 1.2%/benzoyl peroxide 2.5%²⁶ and adapalene 0.1%/benzoyl peroxide 2.5% fixed-dose combination gel²² showed significantly better effect on HRQoL than placebo.

Good changes of quimp of acne patients were reported in studies supported by pharmaceutical companies and those with no industrial support. However, bias may be a potential concern, especially in studies with no information on funding sources.

The most frequently used HRQoL instrument was dermatology-specific questionnaire the DLQI. According to the DLQI changes, isotretinoin was the best treatment option.¹⁵

Another dermatology-specific instrument Skindex-29, acne-specific questionnaires Acne-Specific Quality of Life

Questionnaire (Acne-QoL), AQOL, CADI and generic instrument Short Form 36 Item Health Survey (SF-36) were used more than once. Generic HRQoL instruments SF-36 and World Health Organization Quality of Life (WHOQOL)-BREF showed much lower sensitivity to successful therapeutic intervention than dermatology-specific and acne-specific instruments. It is confirmed by Ozolins *et al.*²⁰ in the study where generic instrument SF-36 was used in parallel with three other dermatology-specific instruments: the DLQI, Children's DLQI (CDLQI) and Dermatology Quality of Life Scales (DQOLS). According to the Skindex-29 and AQOL, topical clindamycin phosphate/benzoyl peroxide had the best influence on HRQoL.^{33,35} According to the Acne-QoL questionnaire, the biggest changes in HRQoL were reported after the treatment with the use of the oral contraceptive pill¹⁹ and clindamycin phosphate/benzoyl peroxide.²⁶ Oral isotretinoin caused the most prominent improvement of acne impact in the studies where HRQoL was measured by the CADI.³² The absence of clear numeric data on HRQoL before and after treatment was the most frequent reason for exclusion of publications on acne treatment. Authors often reported only baseline data and changes without clear numeric data after the treatment. The absence of any data on separate items of HRQoL questionnaires in selected papers makes it impossible to analyse effects of the treatment on different aspects of HRQoL.

Our study has some limitations. There is a lack of well-organized studies with a high number of patients. Few studies with the common design used the same HRQoL instruments. Our

results show that the use of HRQoL instruments, except the DLQI, was infrequent.

Included studies had different duration and number of patients. Participants of included studies may have different acne severity and baseline HRQoL scores. Some used HRQoL instruments have no total score, and several domain scores are used instead. We calculated mean total scores using domain scores for this study. Such ‘artificial’ calculation of total scores may be considered methodologically incorrect. However, it helped us to include instruments with no total scores. As stated above, this method makes it possible *de facto* to detect which acne treatment method had the best effect on HRQoL. The main limitation of this approach is theoretically poor reproducibility of the results in the case of selection of other HRQoL instruments. Meanwhile, acne-specific instruments may assess HRQoL in both children and young adults,³⁶ and dermatology-specific instruments have established age limits except the family DLQI.^{37,38} However, we decided not to exclude publications where HRQoL instruments were used out of their validated age limits in some participants if other inclusion criteria were met.

Conclusions

Our results revealed that oral isotretinoin had the best influence on HRQoL of acne patients. It is confirmed both by the results of the studies where the DLQI, the most frequently used HRQoL instrument, was applied and by the comparison of the mean percentage changes in the scores of different HRQoL instruments. Several other treatment methods also showed good effects on HRQoL of acne patients. Our results are in line with current European and US guidelines.^{1,2} There is limited number of the high-quality studies on acne treatment where HRQoL was assessed. No high-quality studies on acne treatment with <8 weeks duration were found. Dermatology-specific and acne-specific instruments showed much better sensitivity to successful therapeutic intervention than generic HRQoL instruments. The EADV TF on QoL and PO recommends to present numeric data on HRQoL before and after treatment in all studies where HRQoL instrument are used as an outcome measures. Recommendations on choice and appropriate use of HRQoL instruments were presented in previous publications of our TF.^{6,7,36, 39–41}

Acknowledgement

We thank Dr. R. Styles (UK) for language editing.

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