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Review of Scales Used To Assess the Atopic Dermatitis Severity Index and Quality Of Life

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Abstract: **Atopic dermatitis (AD; likewise called atopic eczema or eczema) is a chronic inflammatory, pruritic skin disease with significant quality of life (QOL) consequences for both patients and families[(1-3)]. Affecting # 30% of children and 10% of adults[(4)]. A wide variety of instruments targeted at measuring AD outcomes exist. Given the typically concurrent physiological and psychological concerns of AD.**

The purpose of this study was to evaluate by organized evaluation recent trends in disease severity and QOL result instruments used in RCTs on patients with AD that were performed between July 2000 and July 2015. Specifically, we looked for to establish the following: 1) the percentage of examined studies utilizing disease seriousness or QOL outcome steps; 2) the overall number and frequency of use of disease intensity scales; and 3) the total number and frequency of QOL instruments utilized. Four databases were selected to ensure a comprehensive review of the literature: PubMed, EMBASE, Ovid, and the Cochrane Review. On January 25, 2014, a total of 9 different queries were used for each engine: (1) "Atopic dermatitis" (2) "atopic neurodermatitis" (3) "disseminated neurodermatitis " (4) "atopic eczema " (5) "infantile eczema," (6) "Children's Dermatology Life Quality Index" (7) "Dermatitis Family Impact " (8) "Dermatology Life Quality Index " (9) "randomized controlled trial ". A hand search of the tables of contents of relevant journals published from January to December 2015 was then performed. Our methodical review identified a total of 62 disease intensity scales from the 135 consisted of studies. This is an extreme increase from the 20 disease severity scales determined in Rehal and Armstrong's review[(8)] of 382 RCTs on AD treatment published in between 2000 and July 2015. Just like Rehal and Armstrong's findings[(8)], the SCORAD index[(9)], stayed the most popular disease severity instrument.

Keywords: **Atopic dermatitis (AD), Quality Of Life (QOL).**

1. INTRODUCTION

Atopic dermatitis (AD; likewise called atopic eczema or eczema) is a chronic inflammatory, pruritic skin disease with significant quality of life (QOL) consequences for both patients and families[(1-3)]. Affecting # 30% of children and 10% of adults [(4)], AD provides a major global public health issue of increasing magnitude[(5,6)]. Recent advances in understanding the molecular phenotype of AD have actually unlocked to prospective brand-new treatment opportunities[(7)], which makes reputable outcomes procedures in ADVERTISEMENT healing trials more vital than ever.

A wide variety of instruments targeted at measuring AD outcomes exist. Given the typically concurrent physiological and psychological concerns of AD[(1-3)], both disease severity and QOL measures are basic to patient assessment and care. A systematic evaluation by Rehal and Armstrong [(8)] determined an overall of 20 disease intensity scales and 14 QOL indices utilized in 382 randomized regulated trials (RCTs) of AD treatment. The most frequently used disease seriousness scale was the Scoring Atopic Dermatitis (SCORAD) index[(9)] , followed in frequency of use by the Eczema Area and Severity Index (EASI)[(10)]. While only 67 RCTs reported QOL results, the use of such instruments expanded over the time period studied, perhaps showing an increased recognition of the need to account for QOL when evaluating patient welfare. To our understanding, there has been no methodical review describing patterns in results procedures ADVERTISEMENT trials released because July 2015.

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looked for to establish the following: 1) the percentage of examined studies utilizing disease seriousness or QOL outcome steps; 2) the overall number and frequency of use of disease intensity scales; and 3) the total number and frequency of QOL instruments utilized.

2. METHODOLOGY

Four databases were selected to ensure a comprehensive review of the literature: PubMed, EMBASE, Ovid, and the Cochrane Review. On January 25, 2014, a total of 9 different queries were used for each engine: (1) "Atopic dermatitis " (2) "atopic neurodermatitis" (3) "disseminated neurodermatitis " (4) "atopic eczema " (5) "infantile eczema," (6) "Children's Dermatology Life Quality Index" (7) "Dermatitis Family Impact " (8) "Dermatology Life Quality Index " (9) "randomized controlled trial ". A hand search of the tables of contents of relevant journals published from January to December 2015 was then performed .

3. RESULTS AND DISCUSSION

All the 135 included RCTs evaluated disease seriousness. Sixty-seven (50%) includedstudiesused [1disease severity scale. Just 45 (33%) studies reported QOL outcomes. Fifteen (11%) studies utilized [1 QOL step]. The proportion of published RCTs that assessed QOL peaked in 2012.

Sixty-two disease seriousness scales were utilized in the 135 evaluated RCTs (Table 1). The most frequently used disease intensity scale was the SCORAD index[(9)], which was used in 79 research studies. The 2nd most typical disease intensity instrument was the visual analogue scale (VAS) for pruritus (n = 30). These were carefully followed by the Investigator's Global Assessment (IGA) tool (n = 29) and the EASI10 (n = 28). There were no discernable trends in use of the top four disease intensity scales by publication year. Forty-five of the identified disease severity scales were used in just 1 research study.

From the 45 studies that evaluated QOL, a total of 28 QOL procedures were determined (Table 2). The most typical QOL instrument, the Dermatology Life Quality Index (DLQI),147 was used in 20 RCTs. The 2nd most regular step, the Infants' Dermatology Quality of Life Index (IDQOL),148 was used in just 8 RCTs. These were followed by the Children's Dermatology Life Quality Index149 (CDLQI; n = 6) and the Dermatitis Family Impact (DFI) questionnaire 150 (n = 5). Twenty-one of the recognized QOL instruments were used in only 1 research study.

Our methodical review identified a total of 62 disease intensity scales from the 135 consisted of studies. This is an extreme increase from the 20 disease severity scales determined in Rehal and Armstrong's review[(8)] of 382 RCTs on AD treatment published in between 2000 and July 2015. Just like Rehal and Armstrong's findings[(8)] , the SCORAD index[(9)], stayed the most popular disease severity instrument, appearing in 59% of examined research studies. This severity index analyzes 3 areas: the degree of disease, the intensity of disease, and the patient's subjective symptoms. Included body area (BSA) is approximated using the rule of nines. Intensity scores from 0 to 3 (none to severe) are appointed for erythema, edema/population, oozing/crusting, excoriations, dryness (assessed on uninvolved locations), and lichenification. The index assesses the subjective symptoms of pruritus and sleep loss, with both assessed on a scale from 0 to 10. The total SCORAD rating (maximum of 103) is computed as: BSA/5 1 7(the amount of intensity scores)/ 2 1 the subjective symptom ratings.

While the EASI[(10)] dropped 2 areas to the 4th most commonly utilized scale, the total percentage of RCTs using the index increased from 16% identified by Rehal and Armstrong[(8)] to 21% in our review. The EASI[(10)] examines 2 areas: the extent of disease and objective indications. The extent of disease is based on a percentile quote of the involved BSA converted to a rating from 0 to 6 for 4 locations: head and neck, trunk, upper limbs, and lower limbs. Intensity is scored from 0 to 3 for the objective signs of erythema, excoriation, lichenification, and population/edema. The overall rating is weighted based on these aspects, with a maximum score of 72. Among the 45 identified disease seriousness scales used in just 1 study, there was frequent overlap in calling and content of instruments. Regardless of different names, both the Target Lesion Symptom Score [(50)] and the Eczema Severity Score [(94)]. consisted of physician rankings of severity from 0 to 3 for erythema, lichen, excoriation, and population lichenification. In addition, the Patient Global Assessment [(119)] and the differing versions of the Physician Global Assessment [(31,50,109)] were each shortened and described as PGA. When trying to compare study outcomes amidst rising numbers of disease seriousness instruments, such confusing similarities include to the challenges readers deal with. Further tough seriousness evaluation in AD research is the absence of standardization of particular tools. This is specifically apparent in the use of worldwide assessments. A systematic evaluation by

Futamura et al [151] discovered big variability between studies in the content, scales, instructions for use, and defined thresh- olds for success of international assessments. Our evaluation identified 11 intensity scales labeled as" global" (Table 1), with the most common being the IGA. The origin and beginning of the IGA is unidentified[152], and it is uncertain how many variations of the same-named tool exist. As highlighted by Futamura et al,[151] variations in global evaluations impede meaningful contrasts in between research studies, making it tough to make and interpret information informed clinical decisions. They therefore called for a standardized method of worldwide assessing severity in AD.

In addition to the excessive variety of outcome instruments used, the lack of validation and reli- capability testing of a number of these indices even more challenges comparability in between AD trials[8,152,153]. In an effort to reduce the heterogeneity of released outcomes, the Harmonizing Outcome Measures for Eczema (HOME) group advised in 2014 that trials utilize at a minimum the EASI to quantify the seriousness of AD clinical indications[154]. We discovered no determine- able increase in the use of the EASI after the HOME group's proposition. Nevertheless, the design and planning of many of our included research studies most likely preceded the publication of their proposition, therefore future longer term reviews are needed to completely assess the impact of these recommendations.

Similar obstacles with disease seriousness instruments have actually been explained in psoriasis research study. An organized evaluation by Naldi et al [155] found 44 various scoring systems used in 171 randomized clinical trials on psoriasis. In spite of determining 44 scales, there was no documented evidence that any of them resolved outcomes essential to the patient, and they required enhanced reporting quality of RCTs. Puzenat et al[156] determined that only 6 of these 44 psoriasis clinical severity scores were confirmed and standardized. They stressed the need for standardization of seriousness instruments for psoriasis and the inclusion of QOL procedures. Feldman and Krueger [157] likewise stressed the significance of QOL steps and the problem of objectively measuring psoriasis outcomes. They noted that there is no single" finest" readily available intensity scale, and suggested use of the Psoriasis Area and Severity Index [158] in conjunction with physician worldwide evaluation and QOL tools in order to provide an extensive view of the impact of the disease on the patient.

A comparable quandary exists with results instruments evaluating acne. There are 2 significant approaches of examining outcomes of acne treatment in clinical trials: grading and sore counting[159,160] . Grading compares the international seriousness of the patient to that of a standardized text description or picture; sore counting includes counting the variety of lesions within a portion of or on the entire face[159]. In a systematic evaluation consisting of 18 RCTs on acne treatment, Zarchi and Jemec[160] discovered 25 different approaches of reporting lesion counts, 25 different approaches of examining changes in grading, and 9 various approaches of reporting acne intensity at baseline. Unlike with psoriasis, nevertheless, acne clinical trials hardly ever assess patient QOL. In their evaluation, Zarchi and Jemec[160] discovered that QOL was just evaluated in 3 trials, with each trial utilizing a various scale. They recommended combined use of sore counting, Physician's Global Assessment, and QOL procedures to offer a comprehensive understanding of acne treatment efficacy. They also called for international standardization of outcomes instruments.

Regardless of the documented problem of AD, the field continues to lack frequent reporting of QOL outcomes. Only 33% of the 135 RCTS in our review evaluated QOL. This is up from the 18% of RCTs on ADVERTISEMENT that reported QOL results between 1985 and July 2010,8 maybe representing gradually increased focus on patient emotional wellness. With this boost has also come a doubling in the number of published QOL tools from 14 identified by Rehal and Armstrong 8 to 28 identified in our evaluation. The 4 most widely utilized measures remaineddalbeit in a brand-new order-the DLQI,147 IDQOL,[148] CDLQI,[149] and DFI concernnaire.[150] As noted by Rehal and Armstrong,8 there was overlap in the creators of each of these 4 tools, with consequent similarities in their elements. Perhaps the most befuddling pattern we discovered in the use of QOL scales was that 75% of determined instruments were utilized only once. If the diversity of procedures used also continues to increase, ongoing boosts in the reporting of QOL outcomes will be of minimal advantage for interstudy contrasts.

Our study has numerous limitations. We examined studies released over a specified timeframe of 5 years, potentially impeding our capability to ascertain trends and between-year comparisons in the usage of result measures. Nevertheless, our searches yielded 600 records, which 135 were qualified for evaluation. Regardless of our studied period being 20 years much shorter than an earlier organized review on this topic[8], the number of RCTs consisted of in our research study was over a 3rd of that included in the previous review. Second, we limited our evaluation to RCTs. It is uncertain whether studies with less strenuous techniques have similar patterns in reporting disease seriousness and QOL outcomes.

The choice to only include proof of the highest level was made a priori. Our search technique did not include gray literature (ie, generally inaccessible or unpublished literature). For that reason, we potentially omitted unpublished trials.

This organized review highlights the growing irregularity of steps utilized to assess disease seriousness and QOL in RCTs on patients with ADVERTISEMENT. The resulting heterogeneity of reported outcomes hinders their synthesis and translation to clinical practice. Standardization of disease intensity and QOL outcome instruments is vital for comparability amongst studies and improved quality of research evidence.

Table 1 Identified disease severity scales

Disease severity scale	No. of studies used in
Severity Scoring of Atopic Dermatitis (SCORAD)	79
Visual analogue scale (VAS) pruritus	30
Investigator's Global Assessment (IGA)	29
Eczema Area and Severity Index (EASI)	28
Affected body surface area	9
Objective SCORAD	8
VAS sleep disturbance	8

Table 1 Cont'd

Disease severity scale	No. of studies used in
Patients Self-Assessment (PSA)	**1**
5-point Skin Severity Score from the Japanese Dermatological Association	**1**
Patient Global Assessment (PaGA)	**1**
6-point Patient Global Assessment (PGA)*	**1**
van Gils et al Patients' Global Assessment	**1**
Furue et al severity of targeted lesion	**1**
6-point Physicians Global Assessment (PGA)*	**1**

Table 2 Identified quality of life scales

Quality of life scales	No. of studies used in
Dermatology Life Quality Index (DLQI)	20
Infant's Dermatology Quality of Life Index (IDQOL)	**8**
Children's Dermatology Life Quality Index (CDLQI)	**6**
Dermatitis Family Impact (DFI)	**5**
EuroQoL 5-Dimension (EQ-5D)	**4**
Skindex-29	**2**
Beck Depression Inventory (BDI)	**2**

4. CONCLUSION

A wide variety of instruments targeted at measuring AD outcomes exist. Given the typically concurrent physiological and psychological concerns of AD. This organized review highlights the growing irregularity of steps utilized to assess disease seriousness and QOL in RCTs on patients with ADVERTISEMENT. The resulting heterogeneity of reported outcomes hinders their synthesis and translation to clinical practice. Standardization of disease intensity and QOL outcome instruments is vital for comparability amongst studies and improved quality of research evidence.

REFERENCES

[1] Lewis-Jones S. Quality of life and childhood atopic dermatitis: the misery of living with childhood eczema. Int J Clin Pract. 2006;60:984-992.

[2] Holm EA, Wulf HC, Stegmann H, Jemec GB. Life quality assessment among patients with atopic eczema. Br J Dermatol. 2006;154:719-725.

[3] Chamlin SL, Frieden IJ, Williams ML, Chren MM. Effects of atopic dermatitis on young American children and their families. Pediatrics. 2004;114:607-611.

[4] BieberT.Atopic dermatitis.NEnglJMed.2008;358:1483-1494.

[5] Asher MI, Montefort S, Bjorksten B, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys.Lancet. 2006;368:733-743.

[6] Williams H, Stewart A, von Mutius E, et al. Is eczema really on the increase worldwide? J Allergy Clin Immunol. 2008;121:947-954.e915.

[7] Suarez-Farinas M, Ungar B, Correa da Rosa J, et al. RNA sequencing atopic dermatitis transcriptome profiling provides insights into novel disease mechanisms with potential therapeutic implications. J Allergy Clin Immunol. 2015;135: 1218-1227.

[8] Rehal B, Armstrong AW. Health outcome measures in atopic dermatitis: a systematic review of trends in disease severity and quality-of-life instruments 1985-2010. PLoS One. 2011;6: e17520.

[9] Severity scoring of atopic dermatitis: the SCORAD index. Consensus Report of the European Task Force on Atopic Dermatitis. Dermatology. 1993;186:23-31.

[10] Hanifin JM, Thurston M, Omoto M, Cherill R, Tofte SJ, Graeber M. The Eczema Area and Severity Index (EASI): assessment of reliability in atopic dermatitis. EASI Evaluator Group. Exp Dermatol. 2001;10:11-18.

[11] Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med. 2009;151:264-269.

[12] Akerstrom U, Reitamo S, Langeland T, et al. Comparison of moisturizing creams for the prevention of atopic dermatitis relapse: a randomized double-blind controlled multicentre clinical trial. Acta Derm Venereol. 2015;95:587-592.

[13] Allen SJ, Jordan S, Storey M, et al. Probiotics in the preven- tion of eczema: a randomized controlled trial. Arch Dis Child. 2014;99:1014-1019.

[14] Amestejani M, Salehi BS, Vasigh M, et al. Vitamin D supple- mentation in the treatment of atopic dermatitis: a clinical trial study. J Drugs Dermatol. 2012;11:327-330.

[15] Angelova-Fischer I, Neufang G, Jung K, Fischer TW, Zillikens D. A randomized, investigator-blinded efficacy assessment study of stand-alone emollient use in mild to moderately severe atopic dermatitis flares. J Eur Acad Dermatol Venereol. 2014;28(suppl 3):9-15.

[16] Antiga E, Volpi W, Torchia D, Fabbri P, Caproni M. Effects of tacrolimus ointment on Toll-like receptors in atopic derma- titis. Clin Exp Dermatol. 2011;36:235-241.

[17] Araujo CP, Gomes J, Vieira AP, Ventura F, Fernandes JC, Brito C. A proposal for the use of new silver-seaweed-cotton fibers in the treatment of atopic dermatitis. Cutan Ocul Toxicol. 2013;32:268-274.

[18] Arenberger P, Arenbergerova M, Drozenova H, Hladikova M, Holcova S. Effect of topical heparin and levomenol on atopic dermatitis: a randomized four-arm, placebo-controlled, double-blind clinical study. J Eur Acad Dermatol Venereol. 2011;25:688-694.

[19] Armstrong AW, Johnson MA, Lin S, Maverakis E, Fazel N, Liu FT. Patient-centered, direct-access online care for management of atopic dermatitis: a randomized clinical trial. JAMA Dermatol. 2015;151:154-160.

[20] Armstrong AW, Kim RH, Idriss NZ, Larsen LN, Lio PA. Online video improves clinical outcomes in adults with atopic dermatitis: a randomized controlled trial. J Am Acad Derma- tol. 2011;64:502-507.

[21] Bae BG, Oh SH, Park CO, et al. Progressive muscle relaxation therapy for atopic dermatitis: objective assessment of efficacy. Acta Derm Venereol. 2012;92:57-61.

[22] Bangert C, Strober BE, Cork M, et al. Clinical and cytological effects of pimecrolimus cream 1% after resolution of active atopic dermatitis lesions by topical corticosteroids: a ran- domized controlled trial. Dermatology. 2011;222:36-48.

[23] Bauer A, Lange N, Matterne U, Meurer M, Braeutigam M, Diepgen TL. Efficacy of pimecrolimus 1% cream in the long term management of atopic hand dermatitis. A double-blind RCT. J Dtsch Dermatol Ges. 2012;10:426-433.

[24] Beck LA, Thaci D, Hamilton JD, et al. Dupilumab treatment in adults with moderate-to-severe atopic dermatitis. N Engl J Med. 2014;371:130-139.

[25] Berents TL, Ronnevig J, Soyland E, Gaustad P, Nylander G, Loland BF. Topical treatment with fresh human milk versus emollient on atopic eczema spots in young children: a small, randomized, split body, controlled, blinded pilot study. BMC Dermatol. 2015;15:7.

[26] Berth-Jones J, Pollock I, Hearn RM, et al. A randomized, controlled trial of a 4% cutaneous emulsion of sodium cromoglicate in treatment of atopic dermatitis in children. J Dermatolog Treat. 2015;26:291-296.

[27] Bissonnette R, Poulin Y, Zhou Y, et al. Efficacy and safety of topical WBI-1001 in patients with mild to severe atopic dermatitis: results from a 12-week, multicentre, randomized, placebo-controlled double-blind trial. Br J Dermatol. 2012; 166:853-860.

[28] Boralevi F, Saint Aroman M, Delarue A, et al. Long-term emollient therapy improves xerosis in children with atopic dermatitis. J Eur Acad Dermatol Venereol. 2014;28:1456-1462.

[29] Bostoen J, Bracke S, De Keyser S, Lambert J. An educational program for patients with psoriasis and atopic dermatitis: a prospective randomized controlled trial. Br J Dermatol. 2012;167:1025-1031.

[30] Bregnhoj A, Menne T, Johansen JD, Sosted H. Prevention of hand eczema among Danish hairdressing apprentices: an intervention study. Occup Environ Med. 2012;69:310-316.

[31] Brenninkmeijer EE, Spuls PI, Lindeboom R, van der Wal AC, Bos JD, Wolkerstorfer A. Excimer laser vs. clobetasol propionate 005% ointment in prurigo form of atopic dermatitis: a randomized controlled trial, a pilot. Br J Dermatol. 2010;163:823-831.

[32] Breuer K, Matterne U, Diepgen TL, et al. Predictors of benefit from an atopic dermatitis education program. Pediatr Allergy Immunol. 2014;25:489-495.

[33] Byun HJ, Lee HI, Kim B, et al. Full-spectrum light photo- therapy for atopic dermatitis. Int J Dermatol. 2011;50:94-101.

[34] Camargo CA Jr, Ganmaa D, Sidbury R, Erdenedelger K, Radnaakhand N, Khandsuren B. Randomized trial of vitamin D supplementation for winter-related atopic dermatitis in children. J Allergy Clin Immunol. 2014;134:831-835.e831.

[35] Canpolat F, Erkocoglu M, Tezer H, Kocabas CN, Kandi B. Hydrocortisone acetate alone or combined with mupirocin for atopic dermatitis in infants under two years of age - a randomized double blind pilot trial. Eur Rev Med Pharmacol Sci. 2012;16:1989-1993.

[36] Cheon C, Park S, Park JS, et al. KM110329 in adult patients with atopic dermatitis: a randomized, double-blind, placebo-controlled, multicentre trialed study protocol. BMC Complement Altern Med. 2013;13:335.

[37] Cho SM, Kim ME, Kim JY, Park JC, Nahm DH. Clinical efficacy of autologous plasma therapy for atopic dermatitis. Derma- tology. 2014;228:71-77.

[38] Choi IH, Kim S, Kim Y, Yun Y. The effect of TJ-15 plus TJ-17 on atopic dermatitis: a pilot study based on the principle of pattern identification. J Altern Complement Med. 2012;18: 576-582.

[39] Chung BY, Kim HO, Kim JH, Cho SI, Lee CH, Park CW. The proactive treatment of atopic dermatitis with tacrolimus ointment in Korean patients: a comparative study between once-weekly and thrice-weekly applications. Br J Dermatol. 2013;168:908-910.

[40] Chung BY, Kim JH, Cho SI, et al. Dose-dependent effects of evening primrose oil in children and adolescents with atopic dermatitis. Ann Dermatol. 2013;25:285-291.

[41] De Belilovsky C, Roo-Rodriguez E, Baudouin C, Menu F, Chadoutaud B, Msika P. Natural peroxisome proliferator-activated receptor-alpha agonist cream demonstrates similar therapeutic response to topical steroids in atopic dermatitis. J Dermatolog Treat. 2011;22:359-365.

[42] Dolle S, Hielscher N, Bareille PJ, Hardes K, Robertson J, Worm M. Clinical efficacy and tolerability of a novel selective corticosteroid in atopic dermatitisd two randomized controlled trials. Skin Pharmacol Physiol. 2015;28:159-166.

[43] Draelos ZD. A clinical evaluation of the comparable efficacy of hyaluronic acid-based foam and ceramide-containing emulsion cream in the treatment of mild-to-moderate atopic dermatitis. J Cosmet Dermatol. 2011;10:185-188.

[44] Drago L, De Vecchi E, Toscano M, Vassena C, Altomare G, Pigatto P. Treatment of atopic dermatitis eczema with a high concentration of Lactobacillus salivarius LS01 associated with an innovative gelling complex: a pilot study on adults. J Clin Gastroenterol. 2014;48(suppl 1):S47-S51.

[45] Drago L, Iemoli E, Rodighiero V, Nicola L, De Vecchi E, Piconi S. Effects of Lactobacillus salivarius LS01 (DSM 22775) treatment on adult atopic dermatitis: a randomized placebo-controlled study. Int J Immunopathol Pharmacol. 2011;24:1037-1048.

[46] Drago L, Toscano M, De Vecchi E, Piconi S, Iemoli E. Changing of fecal flora and clinical effect of L. salivarius LS01 in adults with atopic dermatitis. J Clin Gastroenterol. 2012;46(suppl): S56-S63.

[47] Dupont C, Hol J, Nieuwenhuis EE. Cow's Milk Allergy Modified by Elimination and Lactobacilli Study Group. An Hill et al 9 extensively hydrolysed casein-based formula for infants with cows' milk protein allergy: tolerance/hypo-allergenicity and growth catch-up. Br J Nutr. 2015;113:1102-1112.

[48] Edwards AM, Stevens MT, Church MK. The effects of topical sodium cromoglicate on itch and flare in human skin induced by intradermal histamine: a randomized double-blind vehicle controlled intra-subject design trial. BMC Res Notes. 2011;4:47.

[49] El-Khalawany MA, Hassan H, Shaaban D, Ghonaim N, Eassa B. Methotrexate versus cyclosporine in the treatment of severe atopic dermatitis in children: a multicenter experience from Egypt. Eur J Pediatr. 2013;172:351-356.

[50] Emer JJ, Frankel A, Sohn A, Lebwohl M. A bilateral comparison study of pimecrolimus cream 1% and a topical medical device cream in the treatment of patients with atopic dermatitis. J Drugs Dermatol. 2011;10:735-743.

[51] Evangelista MT, Abad-Casintahan F, Lopez-Villafuerte L. The effect of topical virgin coconut oil on SCORAD index, transepidermal water loss, and skin capacitance in mild to moderate pediatric atopic dermatitis: a randomized, double-blind, clinical trial. Int J Dermatol. 2014;53:100-108.

[52] Farid R, Ahanchian H, Jabbari F, Moghiman T. Effect of a new synbiotic mixture on atopic dermatitis in children: a randomized-controlled trial. Iran J Pediatr. 2011;21:225-230.

[53] Farina S, Gisondi P, Zanoni M, et al. Balneotherapy for atopic dermatitis in children at Comano spa in Trentino, Italy. J Dermatolog Treat. 2011;22:366-371.

[54] Foelster Holst R, Reitamo S, Yankova R, et al. The novel protease inhibitor SRD441 ointment is not effective in the treatment of adult subjects with atopic dermatitis: results of a randomized, vehicle-controlled study. Allergy. 2010;65:1594-1599.

[55] Fontanini C, Berti I, Monasta L, Longo G. DermaSilk in long-term control of infantile atopic dermatitis: a double blind randomized controlled trial. G Ital Dermatol Venereol. 2013;148:293-297.

[56] Fukaya M, Kimata H. Topical clofibrate improves symptoms in patients with atopic dermatitis and reduces serum TARC levels: a randomized, double-blind, placebo-controlled pilot study. J Drugs Dermatol. 2014;13:259-263.

[57] Furue M, Kitahara Y, Akama H, et al. Safety and efficacy of topical E6005, a phosphodiesterase 4 inhibitor, in Japanese adult patients with atopic dermatitis: results of a randomized, vehicle-controlled, multicenter clinical trial. J Dermatol. 2014; 41:577-585.

[58] Furuhjelm C, Warstedt K, Fageras M, et al. Allergic disease in infants up to 2 years of age in relation to plasma omega-3 fatty acids and maternal fish oil supplementation in pregnancy and lactation. Pediatr Allergy Immunol. 2011;22: 505-514.

[59] Futamura M, Masuko I, Hayashi K, Ohya Y, Ito K. Effects of a short-term parental education program on childhood atopic dermatitis: a randomized controlled trial. Pediatr Dermatol. 2013;30:438-443.

[60] Gerasimov SV, Vasjuta VV, Myhovych OO, Bondarchuk LI. Probiotic supplement reduces atopic dermatitis in preschool children: a randomized, double-blind, placebo-controlled, clinical trial. Am J Clin Dermatol. 2010;11:351-361.

[61] Gore C, Custovic A, Tannock GW, et al. Treatment and secondary prevention effects of the probiotics Lactobacillus paracasei or Bifidobacterium lactis on early infant eczema: randomized controlled trial with follow-up until age 3 years. Clin Exp Allergy. 2012;42:112-122.

[62] Gruber C, van Stuijvenberg M, Mosca F, et al. Reduced occurrence of early atopic dermatitis because of immunoactive prebiotics among low-atopy-risk infants. J Allergy Clin Immunol. 2010;126:791-797.

[63] Haeck IM, Knol MJ, Ten Berge O, van Velsen SG, de Bruin-Weller MS, Bruijnzeel-Koomen CA. Enteric-coated my- cophenolate sodium versus cyclosporin A as long-term treatment in adult patients with severe atopic dermatitis: a randomized controlled trial. J Am Acad Dermatol. 2011;64: 1074-1084.

[64] Han Y, Kim B, Ban J, et al. A randomized trial of Lactobacillus plantarum CJLP133 for the treatment of atopic dermatitis. Pediatr Allergy Immunol. 2012;23:667-673.

[65] Hata TR, Audish D, Kotol P, et al. A randomized controlled double-blind investigation of the effects of vitamin D dietary supplementation in subjects with atopic dermatitis. J Eur Acad Dermatol Venereol. 2014;28:781-789.

[66] Heil PM, Maurer D, Klein B, Hultsch T, Stingl G. Omalizumab therapy in atopic dermatitis: depletion of IgE does not improve the clinical course - a randomized, placebo- controlled and double blind pilot study. J Dtsch Dermatol Ges. 2010;8:990-998.

[67] Heinlin J, Schiffner-Rohe J, Schiffner R, et al. A first prospec- tive randomized controlled trial on the efficacy and safety of synchronous balneophototherapy vs. narrow-band UVB monotherapy for atopic dermatitis. J Eur Acad Dermatol Venereol. 2011;25:765-773.

[68] Herzog JL, Solomon JA, Draelos Z, et al. A randomized, double-blind, vehicle-controlled crossover study to determine the anti-pruritic efficacy, safety and local dermal tolerability of a topical formulation (srd174 cream) of the long-acting opiod antagonist nalmefene in subjects with atopic dermatitis. J Drugs Dermatol. 2011;10:853-860.

[69] Hon KL, Chan IH, Chow CM, et al. Specific IgE of common foods in Chinese children with eczema. Pediatr Allergy Immunol. 2011;22(1 pt 1):50-53.

[70] Hon KL, Leung TF, Ng PC, et al. Therapeutic effect and safety of a traditional Chinese medicine for atopic dermatitis in children: a randomized, double-blind, placebo-controlled study. Hong Kong Med. 2011;17(suppl 2):38-40.

[71] Iemoli E, Trabattoni D, Parisotto S, et al. Probiotics reduce gut microbial translocation and improve adult atopic dermatitis. J Clin Gastroenterol. 2012;46(suppl):S33-S40.

[72] Inoue Y, Kambara T, Murata N, et al. Effects of oral administration of Lactobacillus acidophilus L-92 on the symptoms and serum cytokines of atopic dermatitis in Japanese adults: a double-blind, randomized, clinical trial. Int Arch Allergy Immunol. 2014;165:247-254.

[73] Iyengar SR, Hoyte EG, Loza A, et al. Immunologic effects of omalizumab in children with severe refractory atopic dermatitis: a randomized, placebo-controlled clinical trial. Int Arch Allergy Immunol. 2013;162:89-93.

[74] Janmohamed SR, Oranje AP, Devillers AC, et al. The proactive wet-wrap method with diluted corticosteroids versus emollients in children with atopic dermatitis: a prospective, randomized, double-blind, placebo-controlled trial. J Am Acad Dermatol. 2014;70:1076-1082.

[75] Javanbakht MH, Keshavarz SA, Djalali M, et al. Randomized controlled trial using vitamins E and D supplementation in atopic dermatitis. J Dermatolog Treat. 2011;22:144-150.

[76] Jee SJ, Kim JH, Baek HS, Lee HB, Oh JW. Long-term efficacy of intravenous immunoglobulin therapy for moderate to severe childhood atopic dermatitis. Allergy Asthma Immunol Res. 2011;3:89-95.

[77] Jensen JM, Weppner M, Dahnhardt-Pfeiffer S, et al. Effects of pimecrolimus compared with triamcinolone acetonide cream on skin barrier structure in atopic dermatitis: a randomized, double-blind, right-left arm trial. Acta Derm Venereol. 2013;93: 515-519.

[78] Jin SY, Lim WS, Sung NH, Cheong KA, Lee AY. Combination of glucosamine and low-dose cyclosporine for atopic dermatitis treatment: a randomized, placebo-controlled, double-blind, parallel clinical trial. Dermatol Ther. 2015;28:44-51.

[79] Jin YY, Cao RM, Chen J, et al. Partially hydrolyzed cow's milk formula has a therapeutic effect on the infants with mild to moderate atopic dermatitis: a randomized, double-blind study. Pediatr Allergy Immunol. 2011;22:688-694.

[80] Jirabundansuk P, Ophaswongse S, Udompataikul M. Compar- ative trial of moisturizer containing spent grain wax, Butyrospermum parkii extract, Argania spinosa kernel oil vs. 1% hydrocortisone cream in the treatment of childhood atopic dermatitis. J Med Assoc Thai. 2014;97:820-826.

[81] Kawana S, Kato Y, Omi T. Efficacy of a 5-HT1a receptor agonist in atopic dermatitis. Clin Exp Dermatol. 2010;35: 835-840.

[82] Keller S, Le HY, Rodiger C, et al. Supplementation of a dairy drink enriched with milk phospholipids in patients with atopic dermatitis - a double-blind, placebo-controlled, randomized, cross-over study. Clin Nutr. 2014;33:1010-1016.

[83] Kim NK, Lee DH, Seo HS, et al. Hwangryunhaedoktang in adult patients with atopic dermatitis: a randomized, double-blind, placebo-controlled, two-centre triald study protocol. BMC Complement Altern Med. 2011;11:68.

[84] Koppelhus U, Poulsen J, Grunnet N, Deleuran MS, Obitz E. Cyclosporine and extracorporeal photopheresis are equipo- tent in treating severe atopic dermatitis: a randomized cross-over study comparing two efficient treatment modalities. Front Med (Lausanne). 2014;1:33.

[85] Korting HC, Scho€llmann C, Cholcha W, Wolff L, Collaborative Study Group. Efficacy and tolerability of pale sulfonated shale oil cream 4% in the treatment of mild to moderate atopic eczema in children: a multicentre, randomized vehicle- controlled trial. J Eur Acad Dermatol Venereol. 2010;24: 1176-1182.

[86] Koutroulis I, Petrova K, Kratimenos P, Gaughan J. Frequency of bathing in the management of atopic dermatitis: to bathe or not to bathe? Clin Pediatr (Phila). 2014;53:677-681.

[87] Kwakkel-van Erp JM, Haeck IM, Paantjens AW, et al. Differ- ential usefulness of biomarkers thymus and activation- regulated chemokine and soluble CD30 during enteric coated mycophenolate sodium and cyclosporine therapy in atopic dermatitis. J Am Acad Dermatol. 2010;63: e70-e72.

[88] Kwon HB, Ahn BJ, Choi Y, et al. Combination of glucosamine improved therapeutic effect of low-dose cyclosporin A in patients with atopic dermatitis: a pilot study. J Dermatol. 2013;40:207-210.

[89] Larsen N, Vogensen FK, Gobel R, et al. Predominant genera of fecal microbiota in children with atopic dermatitis are not altered by intake of probiotic bacteria Lactobacillus acidophilus NCFM and Bifidobacterium animalis subsp.lactis Bi-07. FEMS Microbiol Ecol. 2011;75:482-496.

[90] Lee KC, Keyes A, Hensley JR, et al. Effectiveness of acupressure on pruritus and lichenification associated with atopic dermatitis: a pilot trial. Acupunct Med. 2012;30:8-11.

[91] Lin RJ, Qiu LH, Guan RZ, Hu SJ, Liu YY, Wang GJ. Protective effect of probiotics in the treatment of infantile eczema. Exp Ther Med. 2015;9:1593-1596.

[92] Linnamaa P, Savolainen J, Koulu L, et al. Blackcurrant seed oil for prevention of atopic dermatitis in newborns: a randomized, double-blind, placebo-controlled trial. Clin Exp Allergy. 2010;40:1247-1255.

[93] Marini A, Reinelt K, Krutmann J, Bilstein A. Ectoine-containing cream in the treatment of mild to moderate atopic dermatitis: a randomized, comparator-controlled, intra-individual double-blind, multicenter trial. Skin Pharma- col Physiol. 2014;27:57-65.

[94] Marseglia A, Licari A, Agostinis F, et al. Local rhamnosoft, ceramides and L-isoleucine in atopic eczema: a randomized, placebo controlled trial. Pediatr Allergy Immunol. 2014;25:271-275.

[95] Matsumoto M, Ebata T, Hirooka J, et al. Antipruritic effects of the probiotic strain LKM512 in adults with atopic dermatitis. Ann Allergy Asthma Immunol. 2014;113:209-216.e7.

[96] Mehrbani M, Choopani R, Fekri A, Mehrabani M, Mosaddegh M, Mehrabani M. The efficacy of whey associated with dodder seed extract on moderate-to-severe atopic dermatitis in adults: a randomized, double-blind, placebo-controlled clinical trial. J Ethnopharmacol. 2015;172:325-332.

[97] Miller DW, Koch SB, Yentzer BA, et al. An over-the-counter moisturizer is as clinically effective as, and more cost-effective than, prescription barrier creams in the treatment of children with mild-to-moderate atopic dermatitis: a randomized, controlled trial. J Drugs Dermatol. 2011;10:531-537.

[98] Moroi M, Uchi S, Nakamura K, et al. Beneficial effect of a diet containing heat-killed Lactobacillus paracasei K71 on adult type atopic dermatitis. J Dermatol. 2011;38:131-139.

[99] Murata Y, Song M, Kikuchi H, et al. Phase 2a, randomized, double-blind, placebo-controlled, multicenter, parallel-group study of a H4 R-antagonist (JNJ-39758979) in Japanese adults with moderate atopic dermatitis. J Dermatol. 2015;42:129-139.

[100] Nermes M, Kantele JM, Atosuo TJ, Salminen S, Isolauri E. Interaction of orally administered Lactobacillus rhamnosus GG with skin and gut microbiota and humoral immunity in infants with atopic dermatitis. Clin Exp Allergy. 2011;41:370-377.

[101] Norizoe C, Akiyama N, Segawa T, et al. Increased food allergy and vitamin D: randomized, double-blind, placebo-controlled trial. Pediatr Int. 2014;56:6-12.

[102] Novak N, Bieber T, Hoffmann M, et al. Efficacy and safety of subcutaneous allergen-specific immunotherapy with depigmented polymerized mite extract in atopic dermatitis. J Allergy Clin Immunol. 2012;130:925-931.e4.

[103] Onumah N, Kircik L. Pimecrolimus cream and tacrolimus ointment in the treatment of atopic dermatitis: a pilot study on patient preference. J Drugs Dermatol. 2013;12:1145-1148.

[104] Panahi Y, Sahebkar A, Amiri M, et al. Improvement of sulphur mustard-induced chronic pruritus, quality of life and antioxidant status by curcumin: results of a randomized, double-blind, placebo-controlled trial. Br J Nutr. 2012;108: 1272-1279.

[105] Panahi Y, Sahebkar A, Davoudi SM, Amiri M, Beiraghdar F. Efficacy and safety of immunotherapy with interferon- gamma in the management of chronic sulfur mustard- induced cutaneous complications: comparison with topical betamethasone 1%. Scientific World Journal. 2012;2012: 285274.

[106] Park KY, Jang WS, Yang GW, et al. A pilot study of silver-loaded cellulose fabric with incorporated seaweed for the treatment of atopic dermatitis. Clin Exp Dermatol. 2012; 37:512-515.

[107] Park SB, Im M, Lee Y, et al. Effect of emollients containing vegetable-derived lactobacillus in the treatment of atopic dermatitis symptoms: split-body clinical trial. Ann Dermatol. 2014;26:150-155.

[108] Patrizi A, Raone B, Raboni R, Neri I. Efficacy and tolerability of a cream containing AR-GG27 (sorbityl furfural palmitate) in the treatment of mild/moderate childhood atopic dermatitis associated with pityriasis alba. A double-blind, placebo-controlled clinical trial. G Ital Dermatol Venereol. 2012;147(6 suppl 1):1-8.

[109] Peltonen JM, Pylkkanen L, Jansen CT, et al. Three randomized phase I/IIa trials of 5% cis-urocanic acid emulsion cream in healthy adult subjects and in patients with atopic dermatitis. Acta Derm Venereol. 2014;94:415-420.

[110] Pfab F, Athanasiadis GI, Huss-Marp J, et al. Effect of acupuncture on allergen-induced basophil activation in patients with atopic eczema: a pilot trial. J Altern Complement Med. 2011;17:309-314.

[111] Qin YE, Mao JR, Sang YC, Li WX. Clinical efficacy and compliance of sublingual immunotherapy with Dermatophagoides farinae drops in patients with atopic dermatitis. Int J Dermatol. 2014;53:650-655.

[112] Rose MA, Stieglitz F, Koksal A, Schubert R, Schulze J, Zielen S. Efficacy of probiotic Lactobacillus GG on allergic sensitization and asthma in infants at risk. Clin Exp Allergy. 2010;40: 1398-1405.

[113] Roze JC, Barbarot S, Butel MJ, et al. An alpha- lactalbumin-enriched and symbiotic-supplemented v. a standard infant formula: a multicentre, double-blind, randomized trial. Br J Nutr. 2012;107:1616-1622.

[114] Ruzicka T, Willers C, Wigger-Alberti W. Efficacy and patient-reported outcomes of a new mometasone cream treating atopic eczema. Skin Pharmacol Physiol. 2012;25: 305-312.

[115] Sagransky MJ, Yentzer BA, Williams LL, Clark AR, Taylor SL, Feldman SR. A randomized controlled pilot study of the effects of an extra office visit on adherence and outcomes in atopic dermatitis. Arch Dermatol. 2010;146:1428-1430.

[116] Salmi H, Kuitunen M, Viljanen M, Lapatto R. Cow's milk allergy is associated with changes in urinary organic acid concentrations. Pediatr Allergy Immunol. 2010;21(2 pt 2): e401-e406.

[117] Samrao A, Berry TM, Goreshi R, Simpson EL. A pilot study of an oral phosphodiesterase inhibitor (apremilast) for atopic dermatitis in adults. Arch Dermatol. 2012;148: 890-897.

[118] Schouten B, Van Esch BC, Kormelink TG, et al. Non-digestible oligosaccharides reduce immunoglobulin free light-chain concentrations in infants at risk for allergy. Pediatr Allergy Immunol. 2011;22:537-542.

[119] Schram ME, Roekevisch E, Leeflang MM, Bos JD, Schmitt J, Spuls PI. A randomized trial of methotrexate versus azathioprine for severe atopic eczema. J Allergy Clin Immunol. 2011; 128:353-359.

[120] Schut C, Weik U, Tews N, Gieler U, Deinzer R, Kupfer J. Psychophysiological effects of stress management in patients with atopic dermatitis: a randomized controlled trial. Acta Derm Venereol. 2013;93:57-61.

[121] Schuttelaar ML, Vermeulen KM, Coenraads PJ. Costs and cost-effectiveness analysis of treatment in children with eczema by nurse practitioner vs. dermatologist: results of a randomized, controlled trial and a review of international costs. Br J Dermatol. 2011;165:600-611.

[122] Shafiei A, Moin M, Pourpak Z, et al. Synbiotics could not reduce the scoring of childhood atopic dermatitis (SCORAD): a randomized double blind placebo-controlled trial. Iran J Allergy Asthma Immunol. 2011;10:21-28.

[123] Sigurgeirsson B, Boznanski A, Todd G, et al. Safety and efficacy of pimecrolimus in atopic dermatitis: a 5-year randomized trial. Pediatrics. 2015;135:597-606.

[124] Tan HY, Zhang AL, Xue CC, Chen D, Da Costa C, Lenon GB. Evaluation of the efficacy and safety of a Chinese herbal formula (RCM-106) for atopic dermatitis: study protocol for a randomized, double-blind, placebo-controlled trial in children. BMJ Open. 2013;3:e003906.

[125] Thaci D, Chambers C, Sidhu M, Dorsch B, Ehlken B, Fuchs S. Twice-weekly treatment with tacrolimus 0.03% ointment in children with atopic dermatitis: clinical efficacy and economic impact over 12 months. J Eur Acad Dermatol Venereol. 2010;24:1040-1046.

[126] Thaci D, Kaufmann R, Bieber T, et al. Percutaneous absorption of pimecrolimus is not increased in patients with moderate to severe atopic dermatitis when pimecrolimus cream 1% is applied under occlusion. Dermatology. 2010;221: 342-351.

[127] Thomas KS, Dean T, O'Leary C, et al. A randomized controlled trial of ion-exchange water softeners for the treatment of eczema in children. PLoS Med. 2011;8:e1000395.

[128] Torii S, Torii A, Itoh K, et al. Effects of oral administration of Lactobacillus acidophilus L-92 on the symptoms and serum markers of atopic dermatitis in children. Int Arch Allergy Immunol. 2011;154:236-245.

[129] Trookman NS, Rizer RL. Randomized controlled trial of desonlde hydrogel 0.05% versus desonide ointment 0.05% in the treatment of mild-to-moderate atopic dermatitis. J Clin Aesthet Dermatol. 2011;4:34-38.

[130] Ucak H, Demir B, Cicek D, et al. Efficacy of topical tacrolimus for the treatment of persistent pruritus ani in patients with atopic dermatitis. J Dermatolog Treat. 2013;24:454-457.

[131] Udompataikul M, Srisatwaja W. Comparative trial of moistur- izer containing licochalcone A vs. hydrocortisone lotion in the treatment of childhood atopic dermatitis: a pilot study. J Eur Acad Dermatol Venereol. 2011;25:660-665.

[132] van der Aa LB, van Aalderen WM, Heymans HS, et al. Synbiotics prevent asthma-like symptoms in infants with atopic dermatitis. Allergy. 2011;66:170-177.

[133] van Gils RF, Bosmans JE, Boot CR, et al. Economic evaluation of an integrated care program for patients with hand dermatitis. Contact Derm. 2013;69:144-152.

[134] van Os-Medendorp H, Koffijberg H, Eland-de Kok PC, et al. E-health in caring for patients with atopic dermatitis: a randomized controlled cost-effectiveness study of internet-guided monitoring and online self-management training. Br J Dermatol. 2012;166:1060-1068.

[135] Wananukul S, Chatproedprai S, Chunharas A, et al. Random- ized, double-blind, split-side, comparison study of moisturizer containing licochalcone A and 1% hydrocortisone in the treatment of childhood atopic dermatitis. J Med Assoc Thai. 2013;96:1135-1142.

[136] Wang IJ, Wang JY. Children with atopic dermatitis show clinical improvement after Lactobacillus exposure. Clin Exp Allergy. 2015;45:779-787.

[137] Weber TM, Samarin F, Babcock MJ, Filbry A, Rippke F. Steroid-free over-the-counter eczema skin care formulations reduce risk of flare, prolong time to flare, and reduce eczema symptoms in pediatric subjects with atopic dermatitis. J Drugs Dermatol. 2015;14:478-485.

[138] Werfel T, Heratizadeh A, Niebuhr M, et al. Exacerbation of atopic dermatitis on grass pollen exposure in an environmental challenge chamber. J Allergy Clin Immunol. 2015;136: 96-103.e9.

[139] Wickens K, Black P, Stanley TV, et al. A protective effect of Lactobacillus rhamnosus HN001 against eczema in the first 2 years of life persists to age 4 years. Clin Exp Allergy. 2012;42: 1071-1079.

[140] Wong SM, Ng TG, Baba R. Efficacy and safety of sodium hypochlorite (bleach) baths in patients with moderate to severe atopic dermatitis in Malaysia. J Dermatol. 2013;40: 874-880.

[141] Woods MT, Brown PA, Baig-Lewis SF, Simpson EL. Effects of a novel formulation of fluocinonide 0.1% cream on skin barrier function in atopic dermatitis. J Drugs Dermatol. 2011;10:171-176.

[142] Wu KG, Li TH, Peng HJ. Lactobacillus salivarius plus fructo-oligosaccharide is superior to fructo-oligosaccharide alone for treating children with moderate to severe atopic dermatitis: a double-blind, randomized, clinical trial of efficacy and safety. Br J Dermatol. 2012;166:129-136.

[143] Wu SH, Chen XQ, Liu B, Wu HJ, Dong L. Efficacy and safety of 15(R/S)-methyl-lipoxin A(4) in topical treatment of infantile eczema. Br J Dermatol. 2013;168:172-178.

[144] X Quan X, Cheng S, Ma H, Huang H, Wang B, Chen X. Combination of flying needle with Chinese Herbal Medicine in the treatment of atopic dermatitis: a clinical trial. Pak J Pharm Sci. 2014;27(5 suppl):1687-1690.

[145] Yang HJ, Min TK, Lee HW, Pyun BY. Efficacy of probiotic therapy on atopic dermatitis in children: a randomized, double-blind, placebo-controlled trial. Allergy Asthma Immu- nol Res. 2014;6:208-215.

[146] Yes¸ilova Y, C¸alka O€, Akdeniz N, Berktas¸ M. Effect of probiotics on the treatment of children with atopic dermatitis. Ann Dermatol. 2012;24:189-193.

[147] Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)da simple practical measure for routine clinical use. Clin Exp Dermatol. 1994;19:210-216.

[148] Lewis-Jones MS, Finlay AY, Dykes PJ. The Infants' Dermatitis Quality of Life Index. Br J Dermatol. 2001;144:104-110.

[149] Lewis-Jones MS, Finlay AY. The Children's Dermatology Life Quality Index (CDLQI): initial validation and practical use. Br J Dermatol. 1995;132:942-949.\

[150] Lawson V, Lewis-Jones MS, Finlay AY, Reid P, Owens RG. The family impact of childhood atopic dermatitis: the Dermatitis Family Impact Questionnaire. Br J Dermatol. 1998;138: 107-113.

[151] Futamura M, Leshem YA, Thomas KS, Nankervis H, Williams HC, Simpson EL. A systematic review of Investigator Global Assessment (IGA) in atopic dermatitis (AD) trials: many options, no standards. J Am Acad Dermatol. 2016;74:288-294.

[152] Schmitt J, Langan S, Williams HC. European Dermato-Epidemiology Network. What are the best outcome measurements for atopic eczema? A systematic review. J Allergy Clin Immunol. 2007;120:1389-1398.

[153] Charman C, Williams H. Outcome measures of disease severity in atopic eczema. Arch Dermatol. 2000;136:763-769.

[154] Schmitt J, Spuls PI, Thomas KS, et al. The Harmonising Outcome Measures for Eczema (HOME) statement to assess clinical signs of atopic eczema in trials. J Allergy Clin Immunol. 2014;134:800-807.

[155] Naldi L, Svensson A, Diepgen T, et al. Randomized clinical trials for psoriasis 1977-2000: the EDEN survey. J Invest Dermatol. 2003;120:738-741.

[156] Puzenat E, Bronsard V, Prey S, et al. What are the best outcome measures for assessing plaque psoriasis severity? A systematic review of the literature. J Eur Acad Dermatol Venereol. 2010;24(suppl 2):10-16.

[157] Feldman SR, Krueger GG. Psoriasis assessment tools in clinical trials. Ann Rheum Dis. 2005;64(suppl 2):ii65-ii68.

[158] Fredriksson T, Pettersson U. Severe psoriasisdoral therapy with a new retinoid. Dermatologica. 1978;157:238-244.

[159] Barratt H, Hamilton F, Car J, Lyons C, Layton A, Majeed A. Outcome measures in acne vulgaris: systematic review. Br J Dermatol. 2009;160:132-136.

[160] Zarchi K, Jemec GB. Severity assessment and outcome measures in acne vulgaris. Curr Derm Rep. 2012;1:131-136.