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Low-calorie diet improves PASI score in psoriasis patients with obesity: An evidence-based case report

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Abstract

Background: The association between psoriasis and metabolic syndrome is appealing as the two may share a similar cross-linking systemic inflammation process. The inflammation processes occurring in obesity and psoriasis may aggravate one another. This raised the question of whether a low-calorie diet would possibly reverse the aforementioned process. This study aims to determine whether calorie restriction reduces psoriasis area and severity index (PASI) in obese patients with moderate-to-severe psoriasis receiving conventional treatment compared to no calorie restriction.

Methods: We searched Pubmed/Pubmed Central, ScienceDirect, Cochrane library, EBSCOhost, and Scopus databases using keywords derived from our clinical question. The inclusion criteria were randomized clinical trial (RCT) or systematic review, published in English, and available in full-text.

Results: We obtained 2 systematic reviews with meta-analyses by Ko et al. and Upala et al. Ko et al. included 6 RCTs which found that the inclusion of a low-calorie diet shows significant improvement in PASI 75 compared to standard therapy (RR 1.66; 95%CI 1.07, 2.58). Upala et al. also found significant improvement in PASI 75 in a meta-analysis of 7 RCTs (Pooled OR 2.92; 95%CI 1.39, 6.13), but shows moderately high heterogeneity between studies. Other secondary outcomes have also shown significant improvements, such as quality of life and metabolic parameters.

Conclusion: The intervention of a low-calorie diet may significantly reduce PASI, improve quality of life and reduce comorbidities in obese patients with moderate-to-severe psoriasis, and thus can be recommended in psoriasis management.

Keywords: *low-calorie diet, obesity, PASI, psoriasis*

Background

Psoriasis is a chronic, systemic, hyper-proliferative, immune-mediated inflammatory entity. Psoriasis is recognized for its potential threat in causing a negative impact on patients' quality of life—which can be immense. According to the WHO¹, the reported prevalence of psoriasis ranges between 0.09% and 11.43% across countries. Its systemic immune-mediated entity has drawn interest in researchers to uncover the true connection between psoriasis and other systemic diseases in the last decades. This is especially true towards the idea of whether metabolic syndrome may predispose while at the same time aggravating

the clinical manifestation of psoriasis.^{2,3} Currently, our world is faced with an alarming incidence of obesity. The epidemiology suggests a doubled prevalence during the past four decades worldwide.⁴

The association between psoriasis and obesity is observed in both epidemiological reports and underlying pathological processes. A study by Neimann et al.⁵ in 2006 showed a positive correlation between the increase of body mass index (BMI) and the severity of psoriasis area and severity index (PASI) score. A meta-analysis by Armstrong et al.⁶ in 2012 determined a higher prevalence of obesity in psoriasis patients with high

PASI scores. In 2015, a meta-analysis by Fleming et al.⁷ showed a greater reduction of PASI in patients achieving weight loss reduction due to non-pharmacological interventions compared with controls. These epidemiological data are further studied and explained through possible underlying pathological processes. Kong et al.⁸ has comprehensively reviewed these correlations by exploring the many effects of adipokines, a type of cytokine synthesized and secreted by adipocytes, which contributes to both up-regulation of pro-inflammatory factors (i.e., leptin, chemerin, and visfatin) and down-regulation of anti-inflammatory factors (i.e., adiponectin and omentin) in overweight or obese patients.

This evidence then raised the question of whether a low-calorie diet would possibly reverse the aforementioned process by aiding the reduction of pro-inflammatory response and consequently increase anti-inflammatory response. This evidence-based case report aims to explore current evidence regarding the implementation of a low-calorie diet for moderate, to severe psoriasis and to study their impacts in treating psoriasis patients.

Case Illustration

A 45-year-old woman came to the dermatology clinic with a pruritic scaly patch a month ago. She was first diagnosed with psoriasis vulgaris in 2010. She had received narrowband ultraviolet B (NBUVB) phototherapy treatment with the dose of 200 mJ/cm², 2 days before the visit. The patient complained of dizziness and fever. Joint pain was not present. In 2012, the patient received phototherapy, but only underwent five sessions and stopped her visits as the condition improved. In 2014, the patient was diagnosed with diabetes mellitus (DM) type II and hypertension grade I. She had gained 15 kg body weight within 4 years. At that time, the patient's BMI was 34.2. The patient did not do routine check-ups and sometimes consumed her medicine, metformin, and acarbose, without prescription.

In March 2017, she went for a check-up at the outpatient clinic in the Dermato-venereology Department of RSCM, due to relapse. She was treated with methotrexate once per week and folic acid for one month. The patient showed poor

compliance. Methotrexate was then replaced with cyclosporine from April until October 2017 (the dose of the drug was not recalled). Patients also went to Internal Medicine Clinic for diabetes mellitus and hypertension. An abdominal ultrasound was performed, and the results showed evidence of fatty liver, hence cyclosporine was discontinued. She received amlodipine 10 mg daily for her hypertension, NBUVB phototherapy three times a week, and petrolatum.

In December 2019, the patient had a more severe complaint of red and itchy scaly patches. According to the patient, this condition arises as she was having stress due to her work. The patient did not have hypertension.

The physical examination revealed generalized, multiple erythematous plaques, confluence, circumscribed, with white, thick, layered scales on top. Body surface area (BSA): 90%, PASI: 43,20. Waist circumference was 96 cm with a BMI of 30 kg/m² (obese). We assessed severe psoriasis vulgaris with metabolic syndrome. Due to this, we were considering adding diet restrictions to the conventional treatment for this patient.

Based on the case illustration, the formulated clinical question is "Will a low-calorie diet reduce PASI in obese patients with moderate-to-severe psoriasis receiving conventional treatment compared to no calorie restriction?"

Methods

Literature searching was conducted in April 2020 from five databases (Cochrane, EBSCO, Scopus, Science Direct, and PubMed). Keywords used in the search are shown in table 1. The studies obtained were screened by title and abstract. From 161 studies, 17 were selected according to our inclusion criteria. Relevant articles were then studied thoroughly in full text. The searching strategy and result are shown in figure 1. Inclusion criteria in our study include studies published in English; available in full text; RCT or systematic review or meta-analysis of RCTs; overweight or obese adult participants; and low-calorie diet intervention for weight loss. We excluded review studies, case reports, letters, commentaries, and abstracts. Studies with participants who were already on diet or receiving medication to reduce weight were excluded from our study.

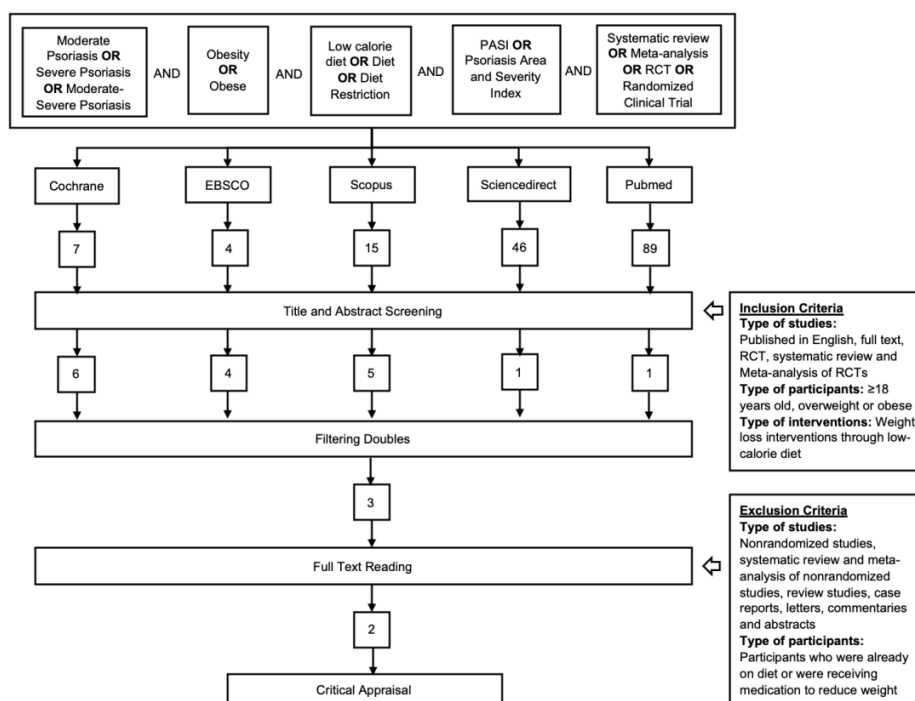


Figure 1. Literature Searching Procedure

Results

Two relevant studies (Upala et al.² and Ko et al.⁹) were included in our evidence-based case report. The summary of the two systematic review and meta-analysis studies is shown in table 2. We critically appraised the studies in this paper, according to the Centre for Evidence-Based Medicine appraisal tools for systematic review and meta-analysis. The validity of the studies is shown in table 3.

Ko et al.⁹ analyzed three comparisons to the control, which are dietary intervention (strict caloric restriction), dietary intervention with exercise, and education program. Then, several outcomes were measured. Dietary intervention versus control was proven to be significant in association with lower severity of psoriasis and better adherence to the intervention. Moreover, this finding shows a specific association between dietary intervention and lower psoriasis severity, which is similar to our clinical question. The goal of therapy was measured by PASI 75 (the proportion of participants achieving at least 75% improvement from baseline of the Psoriasis Area and Severity Index), considering that a European consensus proposed PASI 75 as a treatment goal for

psoriasis. Participants were followed up for 24 weeks. The included studies on dietary intervention were Al-Mutairi (2014); Del Giglio (2012); Gisondi (2008); Guida (2014); Jensen (2013); Kimball (2012). However, there were only two studies, conducted by Gisondi and Al-Mutairi, which reported the outcome with PASI 75 and match the criteria of 24 weeks follow-up. The study shows pooled PASI 75 (RR 1.66;95%CI 1.07, 2.58) with moderate heterogeneity ($I^2=56.6\%$; $P=0.13$). On the other side, four included trials on dietary intervention provided data on the number of participants who completed the trials, which were used for calculating the outcome 'adherence to the intervention' which were study conducted by Kimball (2012); Gisondi (2008); Guida (2014); Jensen (2013). Only two of the study reported the outcomes for 24-week measurement which were studies from Gisondi (2008) and Guida (2014). Adherence to the intervention RR 1.26 (95% CI 0.76, 2.09) with high heterogeneity ($I^2=79.78\%$, $P=0.03$).

From the study conducted by Upala et al.² (2015), dietary and lifestyle weight-loss interventions were measured into two groups: PASI 75 and mean change in PASI. There are 4 studies analyzed in each group. The PASI 75 group analyzed studies from Gisondi (2008), Kimball (2012), Mutairi

(2014), Naldi (2014) with OR 4.89 [95%CI:1.65-14.47], 3.33 (95%CI 0.56, 19.95), 4.27 (95%CI 2.32, 7.83), 1.38 (95%CI 0.80, 2.38), respectively. Total events in this group were 180 participants in the intervention group and 119 participants in the control group. The pooled risk ratio of the four RCTs was significant (OR 2.92; 95%CI 1.3, 6.13). The other group with mean change in PASI consisted of studies from Gisondi (2008), Guida (2014), Jensen (2013), Naldi (2014) and had mean differences (MD) of -6.00 (95%CI -9.99, -3.21), -4.00 (95%CI -6.91, -1.09), -2.00 (95%CI -2.35, -1.65), and -0.90 (95%CI -1.92, 0.12), respectively. The pooled MD of the four RCTs was significant (MD -2.49; 95%CI 1.39, 6.13).

Both studies had similar subjects to our case. The studies demonstrated that dietary and lifestyle weight loss intervention may reduce the severity of psoriasis and improve quality of life in obese patients more than standard care alone. The combination of dietary intervention and exercise programs was proven to be significant along with the medication therapy for psoriatic patients.^{2,9}

Discussion

Severity of Psoriasis

Obesity and metabolic syndrome have been associated interdependently with psoriasis severity. The association is a reciprocal cause and effect aggravating each other, often described as a vicious cycle of psoriasis and metabolic syndrome. One study found that obesity was found in 20.7% of patients with severe psoriasis compared to 13.2% of those without.¹⁰ There is also a significant correlation between BMI and psoriasis severity measured in PASI.¹¹ Both obesity and psoriasis are correlated with systemic inflammation. In obesity, plasma levels of interleukin-1 (IL-1), IL-6, TNF- α , and acute-phase proteins such as C-reactive proteins increase. This may be explained by the inflammatory activity of adipocytes which are abundant in obesity. Adipose tissue normally secretes adipokines to communicate with other parts of the body; these adipokines include the previously mentioned IL-6, TNF- α , as well as leptin, and plasminogen activation inhibitor-1.^{12,13} An increase of IL-1, IL-6, and TNF- α is also a characteristic of chronic inflammatory diseases, including psoriasis.¹³

Anti-inflammatory cytokine adiponectin has also been observed to decrease in obesity. Adiponectin has been shown to inhibit IL-6 and TNF- α production and is tied to the pathogenesis of insulin resistance.^{12,13} Meanwhile, leptin, another pro-

inflammatory adipokine associated with regulating feeding behavior in the central nervous system, has also shown an effect of increased keratinocyte proliferation and thus is thought to also contribute to the pathogenesis of psoriasis.¹³

A low-calorie diet has been shown to reduce levels of pro-inflammatory cytokines in obesity, although it is not fully understood whether it is through a decrease in the number of adipocytes or direct intervention in the inflammatory process.^{14,15} This is shown through the meta-analysis by Ko et al.⁹ The study shows a significant reduction of psoriasis severity through a low-calorie diet (RR = 1.66, 95% CI = 1.07 – 2.58). In this meta-analysis, a significant primary outcome is expressed through PASI 75 as it is associated with significant quality of life (QoL) improvement.^{9,16} Similar results with greater effect are demonstrated in the meta-analysis by Upala et al.² (RR = 2.92, 95% CI = 1.39 – 6.13). Effect size might be reflected more towards Ko et al.⁹ as opposed to Upala et al.², as Upala et al.² included studies with special dietary intervention or diet intervention mixed with exercise in the meta-analysis and shows substantial heterogeneity compared to Ko et al.⁹ Ko et al.⁹ also specify such significant results in studies with 24 weeks follow-up. Both meta-analyses also included predominantly non-Asian populations, therefore might not be fully applicable to the case as Asians have different body compositions from Europeans in general.^{2,9,17}

Adherence to Intervention

Ko et al.⁹ only included four trials on dietary intervention in their meta-analysis, which provided data on the number of participants who completed the trials. These data were used for analyzing adherence to the intervention. There was no significant difference in adherence to the trial intervention between the dietary intervention and control groups every week, from week 12 to 24. The meta-analysis was conducted only on week 24. On week 24, there is an increase, though not significant, in adherence to intervention (RR 1.26, 95%CI 0.76, 2.09; $I^2=80\%$; 2 trials, 60 participants in total; low-quality evidence). However, high statistical heterogeneity in two studies has been observed and the study did not carry out a subgroup analysis due to a limited number of studies.⁹

There is no clear difference in adherence to intervention between those receiving the intervention (i.e., combined dietary intervention) and those on education programs only. However, most participants in the studies generally adhered

well to the lifestyle interventions compared to standard treatment alone. Moreover, the increase in adherence to intervention can be explained by the improvement of severity of psoriasis by the combination of dietary intervention and the standard treatment, as well as with the increment of the QoL.⁹ For instance, Gisondi et al.¹⁸ reported that 10 out of 14 participants who dropped out from the control group are unsatisfied with the efficacy of the treatment they received, the 4 others dropped out due to adverse effects of treatment. Previously, another systematic review focusing on adherence in the treatment of psoriasis identified treatment-specific factors as predictors, as well as sex, psychosocial, and disease-specific factors.¹⁹

Quality of Life (QoL)

Psoriasis greatly hampers QoL by decreasing patients' productivity, increasing individual absence from work, increasing maladaptive defense mechanisms, increasing problems regarding self-esteem and self-perception of body image. Embarrassment to appear in public and fear of public judgment would also further hamper patients' QoL.²⁰ Ko et al.⁹ in their meta-analysis of two trials showed a significantly higher improvement of DLQI score in the dietary intervention group compared to the control group, provided with the greater reduction of DLQI at both weeks 16 (MD -2.00; 95%CI -3.66, -0.34; 1 trial) and month 6 (MD -12.20, 95%CI = -13.92, -10.48; 1 trial).

Reduction of Comorbidities

The correlation between severe psoriasis and metabolic syndrome has been widely studied.²¹⁻³⁰ Metabolic syndrome^{22,23} and coronary plaque¹⁷ are found twice as often in psoriasis patients. In the study by Ko et al.⁹, reduction of obesity was found significantly more prominent in the dietary-intervention group. The reductions were recorded either through calculating changes in body weights, BMI, or waist circumference, both at weeks 16 and 24. Changes in body lipids were also assessed. There is also a significant reduction in total cholesterol and serum levels of triglyceride in the dietary-intervention group.

The relationship between these comorbidities and psoriasis impacts both directions. Psoriasis worsens the comorbidities and vice versa. Studies showed an increase in psoriasis incidence, higher psoriasis severity, and reduced response to conventional psoriasis treatment in patients with obesity.³¹⁻³⁴ Moreover, a systematic review including 25 studies found a higher prevalence rate

of dyslipidemia in psoriasis patients with higher PASI scores.³⁵ This may be explained by the systemic inflammation that may contribute to both the development of psoriasis and lipid disturbance. IL-1, IL-6, and TNF- α , which are upregulated in psoriasis patients, also play important roles in the dysregulation and disturbance of serum lipids. The aforementioned cytokines may also be involved in the decrease of triglyceride clearance, the elevation of lipid levels, and the stimulation of free fatty acid (FFA) production.³⁶ Adiponectin which decreased in obesity has also been shown to be negatively correlated with PASI ($r=-0.34$, $p<0.05$).^{37,38}

Conclusion

The inclusion of a low-calorie diet may significantly reduce psoriasis severity, improve quality of life and reduce comorbidities in obese patients with moderate-to-severe psoriasis, and thus can be recommended to be included in psoriasis management. Further RCTs should be performed to provide higher quality evidence, especially for Asian populations.

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Table 1. Searching Strategy

Database	Searching Strategy	Hits	Selected
Pubmed & Pubmed Central	("Moderate Psoriasis" OR "Severe Psoriasis" OR "Moderate-Severe Psoriasis" OR) AND ("Obesity") AND ("Low calorie diet" OR "Diet" OR "Diet Restriction") AND ("PASI" OR "Psoriasis Area and Severity Index") AND ("Systematic review" OR "Meta-analysis" OR "RCT" OR "Randomized Clinical Trial")	89	1
Sciencedirect	(Obesity OR Obese) AND (Psoriasis OR Psoriatic) AND ("low calorie diet" OR "calorie restriction" OR "weight reduction") AND (PASI OR "Psoriasis Area Severity Index")	46	1
Cochrane	([mh Obesity] OR Obesity OR Obese) AND ([mh "Caloric Restriction"] OR "low calorie diet" OR "calorie restriction") AND [mh Psoriasis] AND ("Psoriasis Area Severity Index" OR PASI)	7	6
Scopus	(Obesity OR Obese) AND (Psoriasis OR Psoriatic) AND ("low calorie diet" OR "calorie restriction" OR "weight reduction") AND (PASI OR "Psoriasis Area Severity Index")	15	5
EBSCOhost	(Psoriasis) AND Obesity AND (Low-calorie diet OR Diet) AND (PASI OR Psoriasis Area and Severity Index) AND (systematic review OR Meta-analysis OR Randomized Clinical Trial OR RCT)	4	4

Table 2. Summary of studies focusing on weight loss intervention through dietary changes

Upala et al.² (2015)

Databases: Cochrane Library, PubMed and EMBASE

Time frame: Up to 1 August 2014

Type, Recruitment Interventions	Measurement	Study Characteristics	Clinical Outcomes
<p>Type of studies RCTs examining weight loss intervention through diet or exercise or both</p> <p>Type of participants <u>Inclusion criteria</u> 1) Overweight or obese patients (BMI \geq 25kg/m²) 2) At least 18 years of age 3) Any type of psoriasis</p> <p><u>Exclusion criteria</u> Participants who were already on diet or were receiving medication to reduce weight</p> <p>Type of interventions and comparisons 1) Studies involving lifestyle interventions (i.e., dieting, calorie restrictions, physical activity, exercise or behavioral therapy) 2) Studies with control participants receiving usual care or not receiving weight loss intervention</p>	<p>Primary outcome measure Disease severity of psoriasis as measured by the PASI score: 100, 75 and 50% reductions in the PASI score (PASI 100, PASI 75 and PASI 50, respectively)</p> <p>Secondary outcome measures Quality of life and minimal disease activity in patients with psoriasis</p>	<p>7 RCTs with a total of 878 participants were included in the systematic review.</p> <p>One study was excluded from the meta-analysis because there was no report of the PASI score.</p> <p>Interventions include: 1) weight loss intervention by with low-calorie diet (5 studies) 2) omega-3-rich diet (1 study) 3) exercise and diet (1 study)</p>	<p>Primary outcome Greater reduction in PASI score as well as a higher proportion achieving PASI 100, PASI 75 and PASI 50 were found in those who received weight loss intervention compared with the control group.</p> <p>The pooled odds ratio (OR) of achieving PASI 75 in participants receiving weight loss intervention vs. controls in four studies was 2.92 (95% CI 1.39, 6.13; P=0.005; I²=62%).</p> <p>The pooled mean difference among three studies in the reduction of the PASI score was significantly greater toward weight loss intervention (MD - 2.49; 95% CI - 3.90, - 1.08; P=0.004; I²=77%).</p> <p>Secondary outcome Patients who received the intervention tended to have better assessment outcomes in accordance to their DLQI score, visual analog scale (VAS) score and minimal disease activity.</p>

Ko et al.⁹ (2019)

Databases: Cochrane Skin Specialised Register, CENTRAL, MEDLINE, Embase, LILACS, the China National Knowledge Infrastructure, the Airiti Library, and four trial registries

Time frame: Up to July 2018

Type, Recruitment Interventions	Measurement	Study Characteristics	Clinical Outcomes
<p>Type of studies <u>Inclusion criteria</u> 1) RCTs which examined lifestyle changes intervention (either alone or in combination), regardless of language or publication status (published, un-published, in press, or in-progress)</p> <p>Type of participants <u>Inclusion criteria</u> People with psoriasis diagnosed by a healthcare professional. No limitations on the severity of psoriasis or the age of the participants</p> <p>Type of interventions and comparisons 1) Studies involving lifestyle interventions (e.g., weight reduction, alcohol abstinence, smoking cessation, dietary modification, exercise; and other lifestyle change interventions), alone or combined 2) Treatment had to be given for at least 12 weeks 3) Studies with control participants receiving no lifestyle changes or another active intervention</p>	<p>Primary outcome measure 1) Severity of psoriasis (PASI 75 or other validated assessment tools for psoriasis) 2) Adherence to the intervention</p> <p>Secondary outcome measures 1) Quality of life (DLQI or other validated tools) 2) Time to relapse 3) Reduction in comorbidities (i.e. diseases associated with psoriasis, for example, reduction in obesity)</p>	<p>10 RCTs with 1163 participants, which interventions include: 1) dietary intervention i.e., low-calorie diet (6 studies) 2) combined dietary-exercise programme (1 study) 3) walking exercise and continuous health education (one study) 4) education programs promoting a healthy lifestyle (two study)</p> <p>Interventions ranged from 12 weeks and three years</p>	<p>Primary outcome 1) Improvements of PASI 75 was greater in dietary intervention (strict caloric restriction) group, compared to usual care (RR = 1.66, 95% CI = 1.07 to 2.58; 2 trials, 323 participants; low-quality evidence). 2) Adherence found to be greater in the intervention group compared to usual care, although 95% CI indicating little or no difference towards this founding (RR 1.26, 95% CI 0.76 to 2.09; 2 trials, 105 participants; low-quality evidence)</p> <p>Secondary outcome 1) Dietary intervention achieves a greater improvement of DLQI score compared to usual care, provided with the greater reduction of DLQI at both week 16 (Mean Difference/ MD = -2.00, 95% CI = -3.66 to -0.34; 1 trial, 60 participants) and month 6 (MD = -12.20, 95% CI = -13.92 to -10.48; 1 trial, 36 participants) 2) None of the trials assessed the time of relapse 3) Significant reductions of body weight, BMI, or waist circumference were found at both week 16 (MD = -15.40, -5.00, -11.50) and week 24 (MD = -10.04, -4.65, -12.00), in the dietary-intervention groups, compared to control groups.</p>

Table 3. Validity of the included studies

Question	Ko et al. ⁹ 2019	Upala et al. ² 2015
What question (PICO) did the systematic review address?	"Does lifestyle changes including weight reduction, alcohol abstinence, smoking cessation, dietary modification, exercise, and other lifestyle change interventions ameliorate severity of psoriasis and adherence to the intervention in obese psoriatic patient?"	"Does effect of dietary and lifestyle weight loss intervention show improvement in psoriasis severity in overweight and obese patients with psoriasis?"
Is it unlikely that important, relevant studies were missed?	Yes. Five databases were used (Cochrane Skin Specialised Register, CENTRAL, MEDLINE, Embase, and LILACS). This study also searched the China National Knowledge Infrastructure, the Airtiti Library, and five other trials registers (ISRCTN registry, ClinicalTrials.gov, ANZCTR, the World Health Organization ICTRP, the EU Clinical Trials Register). The review also reported searching other resources such as references from included trial and unpublished literature. Search strategy of each database and other resources are written separately in the appendix of the study.	Unclear. Two reviewers searched independently from three databases (CENTRAL in The Cochrane Library, MEDLINE, EMBASE). A manual search for references from selected article was also performed. The search strategy is not stated in the article.
Were the criteria used to select articles for inclusion appropriate?	Yes. The review included randomized studies of lifestyle changes (either alone or in combination) for treating psoriasis in people diagnosed by a healthcare professional, and did not impose any limitation on the severity of psoriasis. The treatment had to be given for at least 12 weeks, including weight reduction, alcohol abstinence, smoking cessation, dietary modification, exercises, and other lifestyle change interventions. The eligibility criteria for the comparisons were no lifestyle changes or other active interventions.	Yes. The review included published and unpublished RCTs on weight loss intervention by dieting or exercise or both in overweight and obese patients (defined as those with aBMI of ≥ 25 kg/m ²) of min 18 y.o. with any type of psoriasis. Participants who were already receiving medication or on a diet to reduce weight were excluded.
Were the included studies sufficiently valid for the type of question asked?	Yes. Six studies were assessed using the Cochrane's tool for assessing risk of bias in RCTs. Each study was evaluated in the following domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other bias: Concerns of any bias were not addressed in the other domains. Most common items that we judged at high risk of bias were blinding of participants and personnel, and incomplete outcome data. Moreover, only 6 out of 10 studies were analysed quantitatively, and the included study was based on moderate-quality evidence.	Unclear. A total of seven RCTs and cohort studies were assessed using the Bias Assessment Tool. Nevertheless, the name of the tool is not mentioned in the article. Three out of 7 studies were reported having high or unclear risk of bias.
Were the results similar from study to study?	Yes. Six RCTs were included in meta-analysis with the outcome of greater improvement from baseline in the PASI 75, adherence to the intervention, and dermatology life quality index (DLQI). The study shows PASI 75 (RR 1.66; 95%CI 1.07, 2.58) with moderate heterogeneity ($I^2=56.6\%$; $P=0.13$) and overall effect ($Z=2.26$; $P=0.02$), adherence to the intervention (RR 1.26; 95%CI 0.76, 2.09) with high heterogeneity ($I^2=79.78\%$, $P=0.03$) and overall effect ($Z=0.9$, $P=0.37$), and DLQI (MD -12.20; 95%CI -13.92, -10.48) with not applicable for heterogeneity and overall effect ($Z=13.91$, $P < 0,0001$)	Yes. Seven RCTs were included in the meta-analysis of PASI 75 and mean change in PASI. Each analysis included 4 of 7 included studies. The PASI 75 analysis shows pooled OR 2.92 (95%CI: 1.39-6.13) with moderately high heterogeneity ($I^2=67\%$, $P=0.03$) and overall effect ($Z=2.82$, $P=0.005$). Besides, the MD in PASI analysis shows pooled -2.49 (95%CI: -3.90 - -1.08) with significant heterogeneity ($I^2=77\%$, $P=0.004$), with overall effect ($Z=3.45$, $P=0.0006$).
Conclusion	The study is valid	The study is valid, but unclear