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## Diet and Psoriasis: Part I. Impact of Weight Loss Interventions

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### Abstract

One of the most frequently asked questions by patients with psoriasis is whether dietary changes can improve their condition. Included in this discussion is whether dietary weight loss can benefit their skin disease. Obesity has been associated with a pro-inflammatory state and several studies have demonstrated a relationship between body mass index (BMI) and psoriasis severity.

However, the question of whether weight loss interventions can impact psoriasis outcome is less clear. Here, we review the literature to examine the efficacy of weight loss interventions, both dietary and surgical, on psoriasis disease course.

### Keywords

psoriasis; diet; nutrition; BMI; obesity; gastric bypass; weight loss

### Abbreviations and Acronyms

BMI; BSA; HAQ; MDA; PASI; PGA; WC; WHR

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## Introduction

Psoriasis is a chronic inflammatory disease that affects 2.6% of the U.S. population.<sup>1</sup> The disease is characterized by erythematous, well-demarcated, cutaneous scaly plaques that can be disfiguring and disabling.<sup>2</sup> Beyond the skin, psoriasis is associated with a systemic inflammatory state that has been linked to obesity, type 2 diabetes, and cardiovascular diseases. Although a correlative relationship between obesity and psoriasis has been well recognized, the mechanistic link between these conditions is not fully understood. Adipocytes produce a variety of pro-inflammatory cytokines including TNF-alpha, MCP-1, and IL-6.<sup>3</sup> Moreover, the key psoriasis cytokines IL-17 and IL-23 have been found to be elevated in obese women compared to lean women.<sup>4</sup> These cytokines may potentially serve to worsen existing psoriasis or trigger the development of new psoriasis.

Given the negative impact of psoriasis on quality of life,<sup>5</sup> patients often seek information about dietary and lifestyle modifications to assist in clearing their skin lesions. Modifying diet is an accessible and self-empowering method that patients are eager to embrace in treating their disease. With increasing awareness that psoriasis is associated with cardiovascular disease and metabolic syndrome, patients may also seek to improve diet to prevent these co-morbidities.

Here, we review the relationship between body mass index and psoriasis incidence, severity, and response to medications. We also review whether weight loss regimens have a beneficial effect in the treatment of psoriasis. These regimens include weight loss through a low-calorie diet or through gastric bypass surgery.

## Methods

We performed a literature review in June 2013 by searching the electronic MEDLINE database via PubMed. Search terms included combinations of the terms “psoriasis”, “PASI”, and “psoriasis severity” with “diet”, “nutrition”, “obesity”, and “BMI”. In addition, abstracts containing the keywords “alternative therapies” and “nonstandard treatment” were reviewed. Results were reviewed independently by two investigators, M.D. and J.M., and this was adjudicated by W.L. We limited our search to articles available in English and those published between 1960 and 2013. Manual searches of bibliographies of the articles were also performed to identify additional studies. Overall, the quality of the identified studies was moderate. Studies describing the relationship between BMI and psoriasis incidence, severity, or response to therapy were typically large (n>200) cohort, cross-sectional, or case-control studies, as well as post-hoc analyses of large phase III clinical trials. Studies of the impact of dietary weight loss in psoriasis (n=7) were primarily prospective, controlled trials, though the size the trials was generally small (n<100). Studies of the impact of weight loss surgeries in psoriasis consisted of retrospective case series and case reports.

## Results

### Observational Studies of Body Mass Index and Psoriasis

**Effect of Body Mass Index on Psoriasis**—Several studies have been conducted to explore the association between obesity and psoriasis incidence and severity. A case-control study of 373 psoriasis patients and matched healthy controls showed that there was a two-fold increased risk for psoriasis development in the setting of obesity as compared to normal body weight. In addition, for each unit increment increase in BMI, there was a 9% higher risk for psoriasis onset and a 7% higher risk for increased PASI (Psoriasis Area Severity Index).<sup>6</sup> Similarly, the Nurses Health Study prospectively followed 67,300 female nurses over a 12-year period and found a graded positive association between BMI and risk of developing psoriasis. The multivariate relative risk of incident psoriasis for BMI 35.0 was 1.63 (95% CI, 1.58–2.61) as compared to the reference group with BMI from 18.5 to 24.9. Moreover, there was a graded association found between the amount of weight gained since age 18 and incident psoriasis. The prospective longitudinal data from incident case analysis implies that increased BMI precedes the onset of psoriasis.<sup>7</sup>

In a study by Murray et al., 88 pairs of same-gender full siblings were compared to explore the association of psoriasis severity and BMI. They found a positive correlation between Physician's Global Assessment (PGA) and BMI ( $p=0.007$ ).<sup>8</sup> Additionally, a cross-sectional study of 399 patients found that there was a linear trend for increasing psoriasis severity across increasing BMI categories ( $p=0.004$ ) after adjusting for age, gender, cigarette smoking and disease duration. They found this relationship to be greater in men than women ( $p=0.03$ ).<sup>9</sup>

More recently, a cross-sectional study involving 296 psoriatic patients compared measures of adiposity to patients' PASI scores. In patients with BMI scores of <25, 25–30, and >30, median PASI scores were 3.9, 6.0, and 7.0, respectively ( $P < 0.01$ ). In fact, the study showed that all three measures of excess weight—BMI, waist circumference (WC) and waist-to-hip ratio (WHR)—are directly correlated to PASI-measured severity, suggesting that excess adiposity may be a risk factor for disease severity.<sup>10</sup>

Regarding pediatric psoriasis populations, Paller et al. published a multicenter, cross-sectional study of 409 children across nine countries. Data showed that “excess adiposity”—defined as overweight or obese with a BMI 85<sup>th</sup> percentile—was present in 37.9% of psoriatic children vs 20.5% of controls. Additionally, children with severe psoriasis had a higher odds ratio (OR 4.92) of being obese than children with moderate psoriasis (OR 3.60), suggesting that increased BMI, measured as BMI > 30 kg/m<sup>2</sup>, may correlate with increased incidence and severity of psoriasis.<sup>4</sup>

**Effect of Body Mass Index on Psoriasis Pharmacologic Therapy**—Several studies have explored the possible effect of BMI on the effectiveness of psoriasis therapies, including biologic treatments. In a recent analysis by Edson-Heredia et al.<sup>11</sup> examining which demographic or clinical factors are associated with response to biologic therapy in psoriasis, it was found that BMI had the strongest effect across studies. A phase III trial of ustekinumab for psoriasis found that higher body weight was an independent predictor of

response to ustekinumab at week 28 ( $p < 0.0001$ ).<sup>12</sup> Indeed, the rationale for offering two weight-based dosing regimens for ustekinumab came from the observation that for patients over 100 kg, there was a significant difference in PASI 75 response to 90 mg vs 45 mg dosing (PASI 75: 74.2% and 54.6%, respectively), whereas no such difference was observed for patients under 100 kg.<sup>13</sup> Similarly, post hoc analyses of the adalimumab phase III trial REVEAL showed that overweight and obese patients were less likely to achieve PASI 75 by week 16 ( $p < 0.001$ ).<sup>14</sup> In another study of 144 psoriasis and psoriatic arthritis patients receiving adalimumab, PASI 50 response was observed more frequently in patients with BMI less than 30 as compared to greater than 30 (79% vs 58%,  $p = 0.02$ ).<sup>15</sup> Data from the Psocare project, a nationwide outcome study conducted in Italy, showed that PASI improvement was inversely correlated with BMI among patients using any systemic treatment, including phototherapy, oral medications and biologics.<sup>16</sup> The results showed that the proportion of patients achieving PASI 75 steadily decreased with higher BMI scores at both 8 and 16 weeks into the study. The adjusted odds ratio for achieving PASI 75 in obese compared to normal-weight patients was 0.73 at 8 weeks and 0.62 at 16 weeks.

Weight loss during the course of biologic therapy may also affect outcomes. In an observational study of 33 patients on various biologics including etanercept, adalimumab, infliximab, and efalizumab, Bardazzi et al. reported that by 4 months, patients who gained weight did not achieve PASI 50, those who kept their weight stable had variable responses, and all seven patients who lost weight achieved PASI 90 or PASI 75.<sup>17</sup>

Conversely, several studies found no association between BMI and response to biologic treatment. For etanercept, pooled clinical trial data from three studies on etanercept totaling 1,187 patients,<sup>18</sup> a three-year registry of 118 etanercept patients in the Netherlands,<sup>19</sup> a retrospective study involving 77 patients on etanercept,<sup>20</sup> and a study of 100 psoriasis patients taking etanercept in Italy<sup>21</sup> did not show any evidence that BMI was associated with etanercept efficacy.

Overall, there is suggestive evidence that a BMI  $> 30 \text{ kg/m}^2$  may potentially play a role in patients' abilities to achieve the full therapeutic effect of psoriasis therapy, although this finding may in part depend on the specific therapy being studied.

**Effect of Body Mass Index on Psoriatic Arthritis**—In a population study of 75,395 patients with psoriasis, obesity was found to be a risk factor for the development of psoriatic arthritis.<sup>22</sup> A few recent studies have also examined whether obesity may affect response to therapy in psoriatic arthritis. A prospective study compared the response to TNF- $\alpha$  inhibitors in 135 obese psoriatic arthritis patients versus 135 normal-weight psoriatic arthritis patients. At 12-months, the prevalence of obesity was significantly higher in patients who failed to achieve Minimal Disease Activity (MDA) than in those who achieved MDA (64.0% vs 25.5%,  $p < 0.001$ ). Furthermore, among subjects who had achieved MDA at the 12-month follow-up, the presence of obesity predicted a poor probability of sustained MDA at the 24-month follow-up.<sup>23</sup> On the other hand, a recent retrospective study of 135 patients with active psoriatic arthritis treated with various biologics showed that BMI did not correlate with disease activity and did not predict disease remission or changes in Health Assessment Questionnaire (HAQ) score following anti-TNF- $\alpha$  therapy.<sup>24</sup> These conflicting conclusions

illustrate the need for further study of how obesity may affect the incidence, severity, and response to therapy in psoriatic arthritis.

### Impact of Weight Loss Interventions on Psoriasis and Psoriatic Arthritis

**Low-Calorie Diet**—Seven prospective trials have been conducted to examine the effect of combining a low-calorie diet with other therapies for the treatment of psoriasis (Table 1). Jensen et al. performed a randomized, controlled trial comparing a low energy diet (LED) (800–1000 kcal/day) to a routine diet for psoriasis patients with plaque psoriasis and BMI>27. During the trial, patients were allowed to continue their baseline anti-psoriatic treatment which had been unchanged for 3 months prior, with approximately 20% of the patients on systemic psoriasis treatments. The LED group lost significantly more weight than the routine diet group ( $p<0.001$ ). Moreover, the LED group achieved a greater reduction in PASI ( $p=0.06$ ) and greater improvement in the Dermatology Life Quality Index ( $p=0.02$ ) than the control group.

Another study was performed examining the efficacy of combining a low-calorie diet with cyclosporine. In this randomized, investigator-blinded trial, 61 moderate-to-severe psoriasis patients with BMI > 30 kg/m<sup>2</sup> were given either a low dose of cyclosporine (2.5 mg/kg/day) or low dose of cyclosporine (2.5 mg/kg/day) in combination with a low-calorie diet for 24 weeks. The group that followed a low-calorie diet reduced their body weight by 5% to 10% and reached a significantly greater percentage of PASI 75 than the control group that received cyclosporine alone.<sup>25</sup>

In a Croatian study, 42 patients hospitalized with moderate psoriasis were treated with topical steroids twice daily plus calorie restriction for four weeks while the control group of 40 patients was treated with topical steroids alone. Although there was no significant change in body weight between the two groups, the calorie restriction group saw a more significant decrease in psoriasis severity and in serum triglycerides, total cholesterol and LDL compared to the control group. The degree of improvement in serum lipids correlated significantly with improvement in psoriasis.<sup>26</sup>

A small study of 30 psoriasis patients with BMI>25 randomized to Ornish, South Beach, or control diets while receiving narrowband UVB phototherapy did not show any statistically significant difference in PASI improvement,<sup>27</sup> while an uncontrolled trial of 10 plaque psoriasis patients with BMI 30 receiving a low calorie diet and topical steroids resulted in average weight loss of 9.6% at 12 weeks and a PASI 50 response rate of 50%.<sup>28</sup>

The impact of a hypocaloric diet on maintenance of psoriasis remission has also been examined. Del Giglio et al. studied 42 obese psoriasis patients who had achieved psoriasis remission after 12 weeks of methotrexate therapy. The methotrexate was discontinued and 22 patients were randomized to a hypocaloric diet for 24 weeks and the other 20 patients randomized to no dietary guidance. Although the two groups did not show a statistically significant difference in maintenance of psoriasis remission, the hypocaloric group displayed a trend towards slower rebound of their disease.<sup>29</sup>

With regard to psoriatic arthritis, Di Minno et al. studied whether dietary intervention could influence response to TNF- $\alpha$  blockers in patients with psoriatic arthritis. They prospectively followed 138 overweight/obese patients with psoriatic arthritis starting TNF- $\alpha$  blockers who were randomized into a hypocaloric diet or free-managed diet. They found that regardless of type of diet, weight loss  $\geq 5\%$  of baseline was significantly associated with a higher rate of achievement of minimal disease activity (MDA).<sup>30</sup>

**Gastric Bypass Surgery**—Gastric bypass is a surgical option for losing weight and achieving a lower BMI. We identified one retrospective study and five case studies evaluating clinical psoriasis improvement following gastric bypass surgery.<sup>31–36</sup>

Recently, Hossler et al. conducted a retrospective study on 34 patients with psoriasis that had undergone weight loss surgery. 62% reported improvement in psoriasis after surgery, 9% reported no change, and 12% reported worsening of their psoriasis. Additionally, it seemed that patients tended to decrease their need for more aggressive psoriasis therapies. Four patients tolerated a decrease from systemic to topical therapy, seven patients were decreased from topical to no therapy, while two patients reported escalation of therapy. Interestingly, it seems those who worsened following bypass surgery tended to be younger (mean age 38.5 years old) whereas those improved tended to be older (mean age 52.7 years old).<sup>36</sup>

A case series was performed of 10 patients with BMI  $38.8 \pm 5.2$  kg/m<sup>2</sup> who underwent either laparoscopic Roux-en-Y gastric bypass or laparoscopic sleeve gastrectomy between 2008 and 2011.<sup>32</sup> Six months after the procedure, 7 of the 10 patients experienced complete lesion resolution, while 2 remained stable and 1 reported increased lesions. At long-term follow up to 2.5 years after the procedure, 4 of the 7 patients who were in remission for the first 6 months reported some new development of lesions, but these were much fewer and smaller than their lesions prior to surgery. Additionally, 3 of the 4 patients who were previously on systemic treatment regimens were able to discontinue medication.<sup>32</sup>

Hossler et al. reported 2 patients with severe plaque psoriasis who also experienced significant lesion improvement following gastric bypass surgery.<sup>31</sup> The first patient experienced a reduction in affected body surface area from 75% to less than 5%. She also went from requiring superpotent topical steroids and phototherapy to using intermittent topical steroid therapy and experienced no psoriasis rebound for at least 6 years after surgery. The second patient had psoriasis involving 25% of her body and required several medications including topical steroids, methotrexate, and UVB phototherapy. Six months after her procedure, her psoriasis was limited to 9% of her body surface area and lesions displayed decreased erythema and thickness. She experienced no rebound for at least 13 months following her surgery. Recently, Faurschou et al. proposed that the clinical psoriasis improvement associated with gastric bypass surgery may not necessarily be due to the resulting decrease in weight, but perhaps due to the hypersecretion of gut incretin hormone glucagon-like peptide-1 (GLP-1) that occurs following surgery.<sup>37</sup> Interestingly, while GLP-1 has been shown to reduce appetite and gastrointestinal motility, it may also have anti-inflammatory effects that could contribute to psoriasis improvement following gastric

bypass surgery. This could explain improvement in psoriasis that is seen immediately after surgery and before substantial weight loss is achieved.

In summary, although gastric bypass is not typically used as a first-line treatment for psoriasis alone, patients who undergo gastric bypass surgery for other indications may experience psoriasis improvement. The exact mechanism of this improvement has yet to be determined.

## Discussion

The effects of weight loss on psoriasis are of great interest to physicians and patients alike. This review of the literature indicates elevated BMI is associated with increased psoriasis incidence and severity and diminished therapeutic effect of certain medications. Interestingly, the effects of BMI on psoriasis may depend on a person's genetics: a recent study by Li et al. found that the risk of developing psoriasis was influenced by the interaction of BMI with two variants in the IL12B and IL23R genes. This suggests that a gene-environment interaction could play an important role in the development of psoriasis.<sup>38</sup>

Based on the studies cited, a BMI > 30 kg/m<sup>2</sup> may potentially play a role in patients' abilities to achieve the full therapeutic effect of psoriasis therapy. This could be for two possible reasons: it may be a consequence of decreased drug distribution into the body due to increased body mass, or it may be a consequence of increased pro-inflammatory cytokine release as a result of increased adipocyte count. Given the potential correlation between elevated BMI with increasing psoriasis severity, weight loss has been considered as a potential adjunct to other psoriasis therapies.

We found several prospective, controlled studies examining the impact of weight loss on psoriasis or psoriatic arthritis. Weight loss in overweight or obese subjects, through decreased caloric intake, appears to have an added beneficial effect on psoriasis or psoriatic arthritis when used in conjunction with other prescription medications. Interestingly, studies have shown that caloric restriction in obese subjects lowers the level of circulating inflammatory cytokines.<sup>24, 39</sup> This may contribute to the observed beneficial effect in psoriatic disease. Dietary weight loss may certainly be recommended as a lifestyle change by dermatologists for overweight and obese patients with psoriasis. The evidence to support this is currently graded as level IB, signifying evidence from at least one randomized controlled trial (Table 1).

In addition, gastric bypass surgery is emerging as an intriguing treatment option and may be secondarily beneficial for psoriasis when performed for other medical conditions. Decreased need for treatment and general improvement of patients' psoriasis have been reported in several case studies and a recent retrospective study.<sup>31-36</sup> Similar to a hypocaloric diet, it is an illustrative example of how weight loss may lead to psoriasis improvement.

## Conclusion

A number of studies suggest that weight loss may be a useful preventative and adjunctive therapy for the treatment of psoriasis or psoriatic arthritis. Gastric bypass surgery appears to



be beneficial in select patients. However, additional larger, prospective clinical studies are needed to further delineate the efficacy of diet and weight loss interventions in psoriasis improvement. Given the vast body of popular literature available to patients, it is important for clinical providers to familiarize themselves with the evidence supporting various dietary plans. By doing so, they will be able to engage their patients and partner with them to maximize the impact of pharmacologic and non-pharmacologic interventions.

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Table I

Interventional studies of dietary weight loss in psoriatic disease

Study	Study Design	Intervention	Size	Inclusion Criteria	Key Results
Jensen et al, 2013	Prospective, randomized controlled trial	Low energy diet (LED) (800–1000 kcal/day) vs. routine diet, all subjects continued their baseline anti-psoriatic treatment throughout the trial	LED (n=30) Control (n=30)	Plaque psoriasis, BMI>27	At week 16, the LED group lost on average 15.4 kg more in weight than control group (p<0.001). The LED group achieved a greater reduction in Psoriasis Area and Severity Index (p=0.06) and greater improvement in the Dermatology Life Quality Index (p=0.02) than the control group.
Gisondi et al, 2008	Prospective, randomized, investigator-blinded controlled trial	Cyclosporine (2.5 mg/kg/day) plus low calorie diet vs. cyclosporine alone	Diet (n=30) Control (n=31)	Plaque psoriasis with BSA 10%, PASI 10, BMI>30	At week 24, mean reduction in body weight was 7% in the diet group vs 0.2% in the control (p<0.001). PASI 75 was 66.7% in the diet group vs 29% in the control (p<0.001).
Rucevic et al, 2003	Prospective, controlled trial in hospitalized patients	Low energy diet (LED) (855 kcal/day) vs. standard hospital diet (2,100 kcal/day)	LED (n=42) Control (n=40)	Plaque psoriasis for greater than 10 years, BSA 30%	At week 4, there was no significant difference in weight loss between two groups; however, the LED group showed a greater reduction in total cholesterol, LDL cholesterol, and triglycerides compared to the control group (p<0.01 for all). Improvement in psoriasis (graded as minimal, moderate, significant) was associated with reduction in LDL cholesterol and triglycerides (p<0.05).
Kimball et al, 2012	Prospective, randomized, investigator-blinded controlled trial	Ornish diet vs South Beach diet vs no dietary intervention with all subjects receiving nbUVB phototherapy 3x/wk	Ornish (n=10) South Beach (n=10) Control (n=10)	Plaque psoriasis with PASI 10, BMI>25	At week 12, Ornish and South Beach diets lost an average of 8% and 7% of initial body weight, respectively vs 0% in controls (p<0.05). No significant difference in mean PASI improvement in Ornish (78%) vs South Beach (72%) vs control (71%) groups.
Roongpisuthipong et al, 2013	Prospective, uncontrolled trial	Low-calorie diet with low- or mid-potency topical corticosteroids	Diet (n=10)	Plaque psoriasis, BMI 30, metabolic syndrome	At week 12, the mean reduction in body weight was 9.6%. There was a significant reduction compared to baseline in LDL cholesterol and triglycerides (p<0.05). Number of subjects achieving PASI 50 was 50%. Mean improvement in Dermatology Life Quality Index was 62.5%.
Giglio et al, 2012	Prospective, randomized, investigator-blinded controlled trial	Low-calorie diet (1200–1600 kcal/day) vs routine diet in previous methotrexate (MTX) responders (PASI 75); MTX discontinued during diet	Diet (n=22) Control (n=20)	Plaque psoriasis, BMI 30	At weeks 12 and 24, BMI was significantly reduced in the diet group but not controls (p<0.05). There was no significant difference in maintenance of methotrexate-induced remission in the diet vs control group, although there was a trend towards slower rebound in the diet group.
Di Minno et al, 2012	Prospective, randomized, investigator-blinded controlled trial	Low-calorie diet (1500 kcal/day) vs free diet in subjects starting TNF-alpha inhibitor	Diet (n=63) Control (n=63)	Psoriatic arthritis per CASPAR criteria; failed DMARDs	After 24 weeks, more low-calorie diet subjects achieved 5% weight loss compared to controls (p<0.001). Low-calorie diet subjects had greater reduction in ESR and VAS than controls (p<0.005). MDA was achieved by 42.9% of low-calorie subjects and 34.9% of controls (p<0.05). Regardless of diet, subjects with 5% weight loss achieved higher rate of MDA.

**Abbreviations:** BSA: body surface area affected; BMI: body mass index, kg/m<sup>2</sup>; ESR: erythrocyte sedimentation rate; MDA: minimal disease activity; PASI: psoriasis area and severity index; PASI 75: 75% or greater reduction in psoriasis area and severity index; PASI 50: 50% or greater reduction in psoriasis area and severity index; VAS: Visual Analog Scale for pain