Materials and Methods

Search Strategy

In order to identify eligible studies, the main search was conducted in 3 electronic databases, namely PubMed, Cochrane Library, and Embase (the last search was conducted on October 20, 2016). Combinations of the key terms "leptin," "resistin," "adiponectin," "adipokine*," and "psoriasis" were used. The procedure was concluded by (i) the perusal of the reference sections of all relevant studies and (ii) a manual search of key journals and abstracts from the major annual meetings in the field of dermatology. The main search was completed independently by two investigators (A.K. and A.P.). Any discrepancy was solved by consultation with an investigator not involved in the initial procedure (D.G.G.).

Study Selection

Criteria for inclusion/exclusion of studies were established prior to the literature search. Eligible for the systematic review and meta-analysis were studies that have assessed leptin, resistin, or adiponectin (adipokines) concentrations in patients with psoriasis (cases) and a reference group (controls). Reviews and studies published in a language other than English were excluded from the systematic review and meta-analysis, as well as nonhuman studies, nonoriginal studies, studies with insufficient information on circulating adipokine concentrations, studies exclusively focused on patients with psoriatic arthritis, genetic variation studies on adipokines, and studies reporting the expression of adipokines only on skin/tissue specimens (not in plasma or serum). In the case of multiple reports from the same sample, only the most complete or the most recent study was enrolled.

Data Extraction

To minimize bias, screening of titles, abstracts, and full-text articles was completed independently by two investigators (A.K. and A.P.). The following data were extracted from the included studies: title, first author, year of publication, study location, number and characteristics of cases and controls (age, gender, BMI, Psoriasis Area and Severity Index

(PASI), assay methods, and plasma/serum concentrations of leptin, adiponectin, and resistin). Initially, each investigator collected the above-mentioned data in a standardized data extraction form, and the forms were then cross-checked for any potential differences. Where appropriate, the data set was completed through communication with the authors. To retrieve any missing data, the corresponding authors of the primary studies were contacted. Specifically, an e-mail was sent and, when no answer was received, a second one followed after a 2-week interval. Any discrepancy was solved by consultation with a third investigator (D.G.G.).

Quality Assessment

In order to assess the quality of the included studies, the RTI item bank tool for observational studies was used [52]. The assessment was performed independently by two investigators (A.K. and D.G.G.). All studies were examined with the appropriate tool questions in order to detect different types of bias, namely selection, performance, detection, attrition, and reporting bias. Any disagreements were adjudicated by consensus.

Statistical Analysis

Mean differences and 95% confidence intervals were calculated for the main outcome and secondary study outcomes for all eligible studies for the meta-analyses [53]. Heterogeneity between the results of different studies was quantified by the I^2 test [54]. Significant heterogeneity was explored by means of sensitivity analysis, meta-regression, and publication bias. For the latter, funnel plots were constructed and their symmetry was checked by the Egger test ($p > 0.1$ indicating absence of publication bias). Meta-analysis including meta-regression was conducted using R Studio for Mac (version 1.0.44; RStudio, Inc.). The report was carried out in adherence with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) group standards for reporting meta-analysis of observational studies [55].