

# Adherence in the Treatment of Psoriasis: A Systematic Review

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## Key Words

Psoriasis outcome · Medication adherence · Treatment compliance · Quality of life

## Abstract

**Background:** Medication adherence and compliance are essential for disease management and can significantly improve outcomes and quality of patient care. The literature suggests that up to 40% of patients do not use their medication as intended. **Objective:** To elucidate current knowledge on adherence/compliance in psoriasis. In particular, methods of adherence/compliance evaluation and influencing factors were to be identified. **Methods:** Systematic literature review based on a protocol-rooted search in online databases, followed by a structured critical appraisal and consecutive descriptive report. **Results:** Thirty-five original publications on adherence/compliance in psoriasis were identified, addressing the extent and quality of adherence/compliance in topical, systemic and UV treatments. Estimates of compliance varied considerably between 27 and 97%. Age, sex, psychosocial, disease-specific and treatment-specific factors were identified as predictors of adherence/compliance. **Conclusion:** A better understanding of the determinants of adherence can improve the outcomes of psoriasis treatment and lead to higher patient satisfaction and quality of care.

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## Introduction

With a prevalence of 2–3% [1–3] in western industrial countries, psoriasis vulgaris is an important chronic, recurrent skin disease which is now categorized as a systemic inflammatory reaction [4, 5]. The incidence and disease burden of psoriasis result in a high need for care [6]. There is also a demand for the treatment of comorbidity, such as arthritis, depression, cardiovascular and metabolic diseases or chronic inflammatory autoimmune diseases [7–10]. Accordingly, psoriasis patients are at an increased risk for the development of atherosclerosis and cardiovascular morbidity [11] and in most cases may require early drug treatment. The high consecutive costs – which increase with the severity of the disease – constitute the great socio-economic relevance of psoriasis from a health-political perspective [12–15]. From the patient's perspective, psoriasis represents a huge burden because of the marked decrease in quality of life, the often refractory course and also the considerable side effects of therapy [16–20].

Motivation to follow the instructions for treatment can be poor particularly in patients who have been suffering for many years, the consequence being a reduction in compliance and adherence [21]. Patient behaviour which leads to following the doctor's instructions is called compliance [22]. By contrast, adherence means sticking to the therapeutic goals set mutually by patient and doctor with reference to the individual needs of the patient

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and any factors which make it difficult for the patient to achieve these goals [23]. The need for this construct arose from the fact that consideration only of compliance fails to take due account of the perspective, right of self-determination and competence of the informed and autonomous patient. The World Health Organization recognizes adherence in chronic diseases such as psoriasis as one of the most important factors contributing to efficient therapy [24]. Thus, poor adherence and subsequently suboptimum therapeutic results can lead to increased costs due to additional office visits and treatments as well as a negative impact on work and productivity. Consequently, any intervention which leads to improved adherence is beneficial. An objective and valid measurement of the two parameters compliance and adherence is difficult because they are both modes of patient behaviour which, in most cases, are difficult to objectify. An approximation can, however, be achieved by the use of established research methods.

The aims of the present paper were to (1) identify and assess suitable methods for the evaluation of adherence in psoriasis patients; (2) determine the extent of adherence in psoriasis patients within different therapeutic procedures; (3) characterize factors influencing adherence on the basis of a systematic literature search.

## Methods

### *Methodology of Adherence Evaluation*

In the first step, publications on the methodology of assessments for adherence were identified from the literature by a PubMed research using the following terms: Adherence OR Compliance AND (measurement OR evaluation OR assessment) AND (methodology OR methods).

### *Adherence and Compliance in Psoriasis*

In the second step, systematic literature searches were performed in the databases PubMed and Cochrane library in May 2010. The first search was conducted in PubMed with the search terms (Psoriasis AND Compliance) and (Psoriasis AND Adherence). In order to specifically identify publications on adherence in systemic therapy, the following search terms were used: [(Fumar\* OR Methotrexate OR Cyclosporine OR Acitretin\* OR Infliximab OR Etanercept OR Adalimumab) AND (compliance OR adherence) AND psoriasis] in the title or abstract. The Cochrane search included the search terms (Psoriasis AND/OR Adherence AND/OR Compliance). In addition, further publications that had not shown up in the databank searches were selected from the bibliographies of the publications identified in the PubMed search.

The searches covered all languages and dates of publication. The abstracts had to meet the following criteria for inclusion of the publication in the later evaluation: (1) compliance or adher-

ence in the therapy of psoriasis or other dermatological diseases as a main criterion; (2) factors influencing compliance as a main criterion; (3) a description of the particular methods used to measure compliance; (4) influencing factors with indirect effects on compliance as a main conclusion of the publication; (5) up-to-date information on the management of psoriasis.

## Results

### *Methodology of Adherence Evaluation*

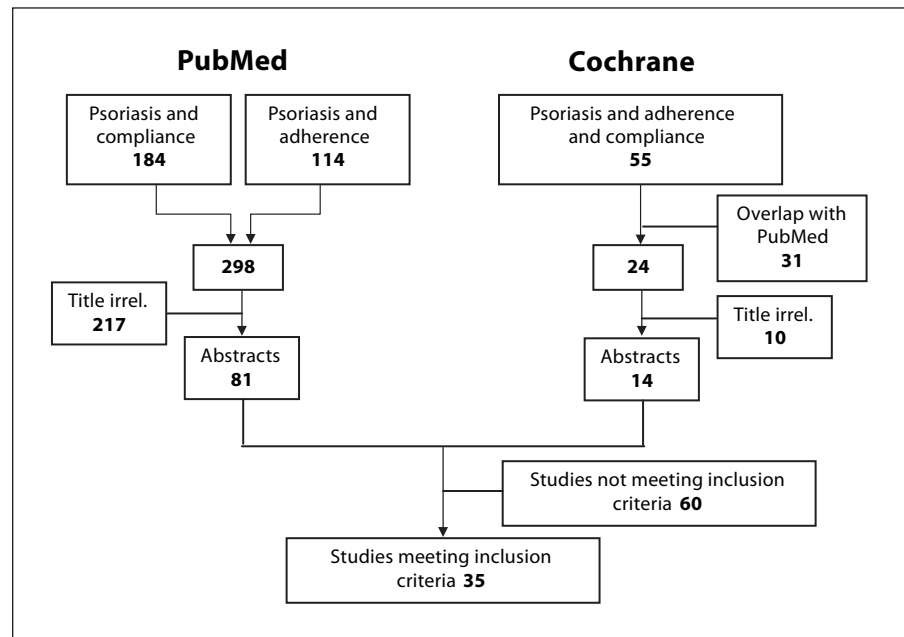
The methodology for determining compliance in clinical and health care studies involved primarily questioning of the patient by means of various questionnaires or self-reporting by the patient. Major results can be summarized as follows below.

### *Self-Reporting*

In the procedure of patient questioning, compliance is documented either during an interview by the physician or by the patient himself on previously compiled questionnaires. A particular advantage of written documentation by the patient is that it offers the possibility of anonymous data acquisition, which increases the probability of obtaining truthful answers [25]. The questions can be adapted to each individual study and formulated openly or provided with possible responses. Because the quality of results is greatly dependent on the wording of the questions [26], validated instruments such as the Mirosky Scale [27] and the Medication Adherence Report Scale [28, 29] are preferable to non-validated methods. Direct questioning by interview tends to show low concordance with the more objective methods described below [30] and, consequently, can be recommended for the determination of adherence only with reservations. In conclusion, there is no gold standard of self-reporting techniques for adherence evaluation.

### *Pharmacy Records of Drug Consumption*

These data are based on a comparison of the theoretical number of days a prescription should last and the actual frequency with which prescriptions are redeemed. Differences between this parameter and the actual adherence arise when a patient visits several pharmacies or redeems his prescription but does not take the medication. Moreover, this method does not provide any indication of the regularity of use [31]. The adherence determined in this way nevertheless showed acceptable correlation with the 'cumulative' adherence determined with the Medication Event Monitoring System (MEMS) [32] and tends



**Fig. 1.** Methodology of the literature search.

less to overestimation of adherence than direct questioning [33].

#### *Counting/Weighing of Unused Medication*

Counting (in the case of separable forms of presentation) or weighing unused medication returned after the end of treatment is a way of measuring adherence which is independent of information from the patient. Overestimation of the actual adherence is however possible even with this method if – intentionally or unintentionally – the patient does not return all the unused medication [26].

#### *Clinicochemical Parameters*

In the case of systemic therapy, the determination of clinicochemical parameters, e.g. blood level measurements, can be important and lead to an estimation of adherence.

#### *Electronic Measuring Systems (MEMS Cap)*

The MEMS consists of a standard bottle with a screw cap housing a microprocessor. The time, date and time elapsed since the bottle was last opened is recorded every time the cap is unscrewed. Provided the pharmaceutical formulation is suitable, the bottles can be used not only for solid and liquid, but also for semisolid presentation forms [34]. This monitoring system tends to furnish lower adherence values than the patient interview [35, 36] or

the determination of medication usage [32] and, consequently, is often regarded as today's reference standard despite the costs and limited usage.

#### *Adherence and Compliance in Psoriasis*

The search term combination (Psoriasis AND Compliance) produced 184 hits in PubMed, while the combination (Psoriasis AND Adherence) achieved 114 hits. Of these, 81 abstracts were viewed in addition to 14 abstracts from the Cochrane search, which produced 55 hits, 31 of which overlapped with the results of the PubMed search. In total, 35 publications were chosen for this literature study on the basis of the inclusion criteria (fig. 1).

The main topic in 8 studies was compliance in psoriasis treatment, while 4 studies examined the influencing factors and 15 the concomitant circumstances which, in turn, affect compliance.

#### *Studies with the Primary Criterion 'Compliance' or 'Adherence'*

In an anonymous questionnaire survey of 120 patients at a specialized psoriasis clinic in Great Britain in 1999, 61% of the patients with psoriasis said that they were 'always' compliant, while the other 39% ticked 'sometimes' or 'never' [37]. Another similar survey in the USA in 2006 involving 53 patients under topical corticosteroid treat-

ment had a comparable compliance rate, with 40% non-adherent patients [38]. Higher compliance values were reported in a study conducted in Turkey in 2008 in which 103 outpatients were surveyed at the end of 8 weeks of treatment. The questionnaire employed elicited data on the doses used, the relationship of which to the doses prescribed (= 100%) allowed a mean medication adherence score of 75% to be calculated [39]. In contrast, 73% of 1,281 active members of several psoriasis patient organizations in France, the UK, Belgium, Germany and the Netherlands stated in a patient questionnaire to determine compliance in their psoriasis treatment that they had not adhered strictly to the instructions in the last 3 days and over the previous weekend [40].

The results of objectively measured and subjectively reported compliance can differ substantially from each other, as a study with 201 outpatients conducted in Great Britain in 2004 has shown: the mean medication adherence measured objectively by counting or weighing the unused medication was 60.6%, while the patients had an adherence score of 92.0% in the questionnaire survey [41]. A comparison of the data of a MEMS cap with the corresponding patient diaries in 2003 showed a discrepancy of the same magnitude for patients in the USA: the mean compliance was 67% according to the diaries and 92% according to the MEMS [35]. Another MEMS assessment conducted in 2004 in a US clinical study of 29 patients showed a mean adherence of 55% – a figure similar to that obtained from determination of unused medication or the use of anonymous questionnaires. The continuous data recording also showed that adherence in the case of the twice daily application of salicylic acid gel was significantly higher on the days close to office visits ( $\pm 2$  days) than on the other days of the 8-week observation period [42]. When the correlation between adherence and the therapeutic result was examined in 24 patients of the same study, it was found that a decrease in adherence of 10% was associated with a deterioration of the psoriasis of 1 point on a 9-point scale [43]. A further study conducted in the USA examined adherence in 27 patients under combined therapy consisting of acitretin and UV phototherapy which was to be performed at home. Tablet ingestion was determined with a MEMS cap, irradiation with data loggers for the UV lamps. Over the 12-week observation period, acitretin ingestion decreased continuously from around 94 to 54%, while adherence to phototherapy remained constant [44]. A survey performed in 2006 also showed that adherence is greater under therapy with biologicals than under other psoriasis treatments [45].

While the aim of most studies is to determine medication adherence, that of a study conducted in Denmark in 2008 was primary adherence, i.e. 322 outpatients of a dermatology clinic were followed up to determine how many redeemed their prescription. The survey was made possible by an electronic register so far established only in Denmark. Almost 45% of psoriasis patients failed to redeem their prescriptions – a percentage for primary adherence much lower than in patients with some other skin diseases [46]. Table 1 provides an overview of the measuring methods used in the individual studies together with an assessment of the results by the authors of the individual publications.

#### *Sociodemographic Factors with an Influence on Compliance*

The main sociodemographic factors examined to date are sex, age and marital status. A study by Zaghoul and Goodfield [41] found that adherence was higher in the women, the study of primary adherence by Storm et al. [46] showed that it was higher in the men, while Gokdemir et al. [39] were unable to establish any association between sex and adherence. With regard to age, Storm et al. [46] and Richards et al. [37] both reported that older patients tended to be more compliant than younger ones. Zaghoul and Goodfield [41] and Gokdemir et al. [39] disagreed as regards the influence of marital status, employment and smoking habits. In the study by Zaghoul and Goodfield, adherence was higher in married, employed and non-smoking patients, while Gokdemir et al. found higher adherence in single patients and no influence on adherence for employment and smoking habits. Gokdemir et al. also observed a positive association between higher educational level and adherence, and Zaghoul and Goodfield reported a negative association between increased alcohol consumption and adherence. An overview of these findings is presented in table 2.

#### *Treatment-Specific Factors Influencing Compliance*

Evaluation of the patient questionnaires completed by 1,281 members of several psoriasis patient organizations in Europe shows that the main reasons for non-compliance were low efficacy, poor cosmetic properties, time-consuming use and the occurrence of side effects [40]. The results of a questionnaire survey of 567 patients provide information about the preferred forms of presentation. Distinct differences were found in the satisfaction with the mode of administration – injectable agents were preferred to oral and oral to topical treatments. Moreover, satisfaction increased with the length of treatment in

**Table 1.** Studies of topical and systemic psoriasis therapy with the primary criterion ‘compliance’ or ‘adherence’

First author, year	Method	Perspective/rater	Compliance	Authors' conclusions
Richards [37], 1999	Topical, systemic, photo- or combined therapy; anonymous patient questioning; subdivision into ‘compliers’ (always compliant) and ‘non-compliers’ (sometimes or never compliant)	Patient	61%	None
Zaghloul [41], 2004	Topical or oral therapy; determination of ‘medication adherence’ from theoretical and actual use by weighing/counting unused medication (objective method) and patient interview for comparison purposes (subjective method)	Investigator Patient	61% 92%	The resultant Medication Adherence Score furnishes objective data; the result – a percentage – is preferred to the subdivision into ‘compliers’ and ‘non-compliers’ based on a cut-off limit
Carroll [36], 2004	Topical therapy; MEMS cap; on salicylic acid gel in contralateral comparison salicylic acid gel + tacrolimus ointment versus salicylic acid gel + base → indirect adherence measurement for tacrolimus ointment	Investigator	60%	Suitable method for objective determination of adherence, as the patients were not informed about the nature of the adherence measurement
Carroll [36], 2004	Topical therapy; patient diary versus MEMS with salicylic acid gel versus weighing of unused medication	Investigator Patient	From 85 to 51% (after 8 weeks) 90%	Only the MEMS is a suitable measuring method, but not diaries or weighing of unused medication because of extreme variability of the results
Balkrishnan [35], 2003	Topical therapy; patient diary versus MEMS with salicylic acid gel	Patient Investigator	92% 67%	Electronic determination is more reliable than questioning
Fouéré [40], 2005	Topical or combined therapy; patient questionnaire; compliance defined as strict adherence to instructions in the last 3 days and on the previous weekend	Patient	27%	The compliance determined is lower than in other studies because of different definition and measuring instruments; errors or bias are inevitable with this kind of data generation
Brown [38], 2006	Topical cortisone therapy; anonymous patient questionnaire (inclusion criterion: at least 1 cortisone therapy in the previous 12 months)	Patient	60%	This type of data generation poses the risk of memory errors or gaps; however, the results agree with those of other adherence studies
Storm [46], 2008	A new (not further described) therapy for the patient; electronic register: 4 weeks after the visit, check on whether the prescription was redeemed (‘primary adherence’)	Investigator	55%	Method for the objective determination of ‘primary adherence’ (once in Denmark)
Gokdemir [39], 2008	Oral, topical, photo- or combined therapy; patient questionnaires: daily record of drug use (actual consumption) and determination of the adherence score by established method from theoretical and actual consumption	Patient	75%	Adherence rates are often overestimated when – as in this case – they are based on patients' reports
Yentzer [44], 2008	Oral and phototherapy; MEMS cap (acitretin), data loggers (UV lamps)	Investigator	From 94 to 54% after 12 weeks (acitretin)	Both methods determine adherence objectively; the loggers are validated for recording UV irradiation
Bhosle [45], 2006	Systemic therapy; drug consumption data from the pharmacy for patients for whom biologicals (inter alia) were prescribed	Investigator	66% (biologicals) and 36% (other)	The adherence scores are higher for biologicals than for other psoriasis therapies
Van de Kerkhof [47], 2000	Topical, photo(chemo)- or systemic therapy; patient questionnaires, sent to subscribers to <i>Psoriasis</i> (magazine of the Dutch Psoriasis Patient Organization)	Patient	Compliance relating to frequency of use: 51% (topical therapy); 90% photo(chemo)therapy; 97% systemic therapy	Selection bias possible by contact made via <i>Psoriasis</i> subscription → overestimation of compliance possible because of greater interest in or worry about the disease

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