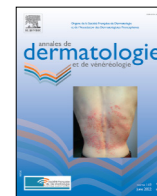




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Review

Barriers and suggestions for improving the implementation of guidelines in the systemic treatment of moderate to severe psoriasis: A literature review



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ARTICLE INFO

Article history:

Received 14 August 2023

Accepted 2 April 2024

Available online 22 May 2024

Keywords:

Psoriasis

Guidelines

Biologics

Adhesion

Barrier to care

Quality of care

ABSTRACT

Background: Despite the availability of a wide range of therapies for the systemic treatment of moderate to severe psoriasis, many psoriasis patients do not receive adequate treatment, suggesting that guidelines may not be correctly applied by physicians.

Objectives: The aim of this study was to analyze data on physicians' implementation of, and reasons for noncompliance with, guidelines for the systemic treatment of moderate to severe psoriasis.

Methods: We conducted a systematic literature review according to the Preferred Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We searched the PubMed and Embase databases for studies on guideline adherence in the systemic treatment of moderate to severe psoriasis. All eligible articles were retrieved in full text and the relevant references of retrieved articles were included.

Results: A total of 20 studies were selected. Four studies investigated knowledge of the guidelines, six studies examined their application, and five studies focused on the various barriers to implementation. Finally, five studies discussed ways to improve implementation. Several studies on the quality of psoriasis care have revealed discrepancies between the reality and the optimal care described in national and international guidelines.

Conclusion: Various barriers to implementation of recommendations exist, such as economic barriers, lack of dermatologic orientation towards, lack of knowledge of recommendations by other specialists, lack of applicability, and country- and practice-specific features (e.g., different benefit/risk ratios, different reimbursement rates and conditions). This review can help the everyday practitioner to better understand these barriers, which will have a direct impact on improving the quality of life of psoriasis patients.

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1. Introduction

Psoriasis is a common chronic inflammatory skin disease affecting 2–3% of the European population [1]. As a systemic inflammatory disease, it is associated with comorbidities such as psoriatic arthritis, inflammatory bowel disease, cardiovascular disease, and neuropsychological disorders. Psoriasis can have a negative impact

on patients socially, physically or emotionally, and can severely affect their quality of life [2].

Since the development of modern biologics, the treatment of patients with psoriasis has undergone a fundamental change. Four classes of biologic therapies targeting tumor necrosis factor α (TNF α), interleukin (IL)-12/23, IL-17 and IL-23 are currently approved in France for the treatment of psoriasis [3]. This wide

Abbreviations used: AAD, American Academy of Dermatology; AGREE, Appraisal of Guidelines REsearch and Evaluation; DLQI, Dermatology Life Quality Index; GRPso, French Psoriasis Research Group; IL-12/23, Interleukin 12/23; IL-17, Interleukin 17; IL-23, Interleukin 23; NICE, National Institute for Health and Care Excellence; PASI, Psoriasis Area and Severity Index; PRISMA, Preferred Items for Systematic Reviews and Meta-Analyses; TNF α , Tumor necrosis factor α ; UK, United Kingdom; US, United States.

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<https://doi.org/10.1016/j.annder.2024.103280>

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range of therapies allows dermatologists to offer a treatment tailored to the profile of each patient. Guidelines based on a high level of scientific evidence would seem to be necessary for our clinical practice.

The French guidelines on the systemic treatment of psoriasis were published in 2019. Their aim was to determine the criteria for initiating systemic treatment, to outline therapeutic objectives, and to rank the available therapies. Only three years after their publication, they are already outdated as they do not consider the class of IL-23 inhibitors [4]. The most recent European guidelines were published in two parts (2020 and 2021). Their key objectives were to provide an update by including new biologic treatments and to develop a treatment algorithm that includes all systemic treatments.

If they are to be known and applied, guidelines must be effectively communicated to all physicians concerned. Knowledge of national guidelines in Europe is high (100% in the UK, 98% in Germany and 94% in Spain), and while awareness of the European guidelines is acceptable (54%), it is particularly high in countries that have recently implemented their national guidelines [5].

Given the number of available therapies and guidelines, the undertreatment of moderate to severe psoriasis is currently too great to ignore. A 2015 multinational study by Van de Kerkhof *et al.* found that 75% of patients with moderate to severe psoriasis were treated with topical treatments (either alone or in combination with another treatment), 20% with systemic treatments, and 20% with biotherapies [6]. The same finding in a 2016 study in the US by Armstrong *et al.* reported that only 40.9% of the 1.7 million eligible US patients were receiving treatment for moderate to severe psoriasis [7]. To improve psoriasis care, it is imperative to investigate the barriers to prescribing effective, guideline-concordant treatments for moderate to severe psoriasis. The aim of this publication is therefore to describe the barriers to guideline adherence and to suggest tools for improvement.

2. Methods

A systematic literature search was conducted for clinical and epidemiologic studies focusing on the implementation of guidelines in the systemic treatment of moderate to severe psoriasis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [8]. No protocol was submitted, and thus no ethics review was required. We searched the PubMed and Embase databases for all articles using various combinations of the following keywords: "Guideline adherence" [Mesh] OR "Protocol compliance" OR "Guidelines applicability" AND "Psoriasis" [Mesh]. We limited the literature search to articles on human subjects written in English or French. No restrictions on publication date were applied.

In addition, further publications were selected from the references in articles identified in the PubMed and Embase searches. The additional search results were checked to avoid duplication of the original searches and then selected for inclusion.

Relevant studies were selected by first reviewing the title and abstract, excluding manuscripts that did not address the topics of interest, and then reading the full article for the remaining studies. Exclusion criteria were non-relevant studies, reviews and case studies, non-dermatological guidelines, and psoriatic arthritis studies.

For each article, the following data were extracted: author, year of publication, study design, country, inclusion period, guidelines and years of publication, patient and physician characteristics, number of psoriasis patients, severity at baseline, treatment duration, method of measuring compliance, implementation rate,

reasons for noncompliance, and actions to improve compliance (see Table 1).

3. Results (Table 1)

Initially, 96 publications ($n = 30$ in Medline database, $n = 56$ in Embase, 9 from references) were included. After identifying duplicates, reading the titles and abstracts, and the full text, 20 articles met the inclusion criteria (Fig. 1).

The studies were published between 2007 and 2021 and examined 8 guidelines published between 2005 and 2019 (the UK (NICE) [9,10], Germany (S3 guidelines) [11–16], Europe (European S3 guidelines) [5,17], the USA (AAD) [18,19], Spain [20], Brazil [21], the Netherlands [22,23], and France [5,24]). Six of these studies were conducted by a German team [11–16]. Four studies examined knowledge of the guidelines [5,22,23,25], six examined their application [9,10,12,17,20,26], and five focused on external factors as barriers to implementation [11,19,21,24,27]. Finally, five studies discussed methods to improve implementation [13–16,18]. Numerous studies on the quality of psoriasis care have shown discrepancies between reality and optimal care as described in national and European guidelines [10,11,19,21].

3.1. Knowledge of the guidelines

In 2008, a Dutch practice self-assessment survey investigated awareness of the guidelines among practitioners: 46% of dermatologists surveyed responded, of whom 96% were aware of the guidelines, and 75% used them in their daily practice [23]. Two studies looked specifically at the use of methotrexate: one found that the guidelines were known in 83% of cases while the other showed that half of the patients were maintained on their treatment despite an inadequate therapeutic response [22,25].

3.2. Application of the guidelines

An English study conducted by Wade *et al.* showed that 65.5% of patients with a DLQI > 5 had not been seen by a dermatologist within the previous year [9]. Significant differences in prescribing behavior were also observed. A study by Augustin *et al.* before the advent of biologics showed a significant use of systemic corticosteroids in psoriasis, with 52% of prescribers being general practitioners, 35% internists, and 11% dermatologists [12]. Finally, weaknesses in the applicability of the guidelines have been highlighted by two international studies conducted by Tan *et al.* [17] and Nast *et al.* [26] using the Appraisal of Guidelines Research and Evaluation (AGREE) tool. One of the most common weaknesses was the applicability of the guidelines to clinical practice.

3.3. Barriers related to external factors

Several studies have identified external factors as barriers to guideline adherence [11,19,21,24,27]. An international multicenter study by Nast *et al.* [24] investigated the different barriers to prescribing systemic treatments for psoriasis in 6 countries and showed that the perception of barriers varies according to the country and practice context. The analysis of national data showed a "national tradition" in prescribing habits; the perception of the safety of a given treatment differs from country to country. The benefit/risk ratio of certain therapies varies between countries and may limit their prescription, e.g., 49% of Canadian dermatologists consider cyclosporine as having an inappropriate benefit/risk profile compared to 12% in the UK [24]. The use of biologics for psoriasis in some Central and Eastern European countries is not

Table 1

Summary of articles included in the literature review.

Article	Date	DOI	Countries	Results
Knowledge of guidelines National and multinational guidelines in Europe... (5)	03.13	https://doi.org/10.1007/s00403-013-1341-x	Europe	Knowledge is high (100% in the UK, 98% in Germany and 94% in Spain) and awareness of European directives is acceptable (54%), but particularly high in countries in which the national directives have recently been implemented.
Dermatologists' Adherence to ... (22)	02.07	https://doi.org/10.1159/000102033	Netherlands	Use of methotrexate: guidelines were known in 83% of cases.
Knowledge, attitudes and use ... (23)	04.08	https://doi.org/10.1111/j.1365-2133.2008.08692.x	Netherlands	46% of dermatologists surveyed responded, 96% were aware of the guidelines and 75% used them in their daily practice.
Methotrexate Management in Psoriasis ... (25)	11.17	https://doi.org/10.2340/00015555-2857	Europe	Use of methotrexate: half of patients continued treatment despite an inadequate response.
Application of the guidelines Severity and management of psoriasis ... (9)	10.16	https://doi.org/10.1186/s12875-016-0544-6	U.K (NICE)	65.5% of patients with a DLQI > 5 were not referred to a dermatologist, despite the indication.
Current application of National Institute ... (10)	08.11	https://doi.org/10.1111/j.1365-2230.2010.04011.x	U.K (NICE)	Adherence to indications, but no interruption of treatment. Frequent review of recommendations is necessary to allow adjustment.
Systemic treatment with corticosteroids ... (12)	04.11	https://doi.org/10.1111/j.1610-0387.2011.07713.x	Germany	Significant use of systemic corticosteroids for psoriasis, with 52% of prescribers being general practitioners, 35% internists, and 11% dermatologists.
Critical Appraisal of Quality of Clinical ... (17)	06.10	https://doi.org/10.1038/jid.2010.164	Europe	Use of the Appraisal of Guidelines Research and Evaluation (AGREE) tool. One of the most common weaknesses was the applicability of the guidelines to clinical practice.
AndA critical appraisal of evidence-based ... (26)	12.08	https://doi.org/10.1111/j.1468-3083.2009.03166.x		
Expert Report on Psoriasis: Spanish ... (20)	10.12	https://doi.org/10.1016/j.adengl.2013.04.003	Spain	The percentage of patients with moderate to severe psoriasis treated with traditional systemic therapies or biologics ranged from 61% to 73% in most regions of Spain.
Barriers related to external factors Guideline compliant prescription ... (11)	06.19	https://doi.org/10.1111/jdv.14811	Germany	The use of biologics is based more on economic reasons (cost of products, inadequate reimbursement for dermatologists, insufficient consultation time to initiate systemic treatment in private practice) than on medical reasons.
Are patients with psoriasis undertreated? ... (19)	06.07	https://doi.org/10.1016/j.jaad.2007.06.042	US (AAD)	40% of people with moderate to severe psoriasis receive no treatment. For severe psoriasis: 26% receive systemic treatment, 39% receive no treatment, and 35% receive only medication.
Adherence to guidelines ... (21)	01.14	https://doi.org/10.1136/bmjopen-2013-004179	Brazil	14.2% of dermatologists fully comply with the recommendations.
Barriers to the prescription of systemic ... (24)	06.13	https://doi.org/10.1007/s00403-013-1372-3	Canada, Germany, Spain, France, Italy, UK	The benefit/risk ratio of certain therapies varies between countries and may limit their prescription, e.g., 49% of Canadian dermatologists consider cyclosporine to have an inappropriate benefit/risk profile compared to 12% in the UK.
Use of biologics for psoriasis in Central ... (27)	05.15	https://doi.org/10.1111/jdv.13222	Central and Eastern Europe	Use of biologics is not hindered by the high cost of biologics, but rather by restrictive eligibility criteria, with stricter reimbursement conditions (e.g., DLQI > 20). 0.25% of all psoriasis patients are treated with biologics.
Improved patient care and compliance with guidelines Do guidelines change the way we treat? ... (13)	06.09	https://doi.org/10.1007/s00403-009-0978-y	Germany	Most private dermatologists (80% of 49) participating in a German practice study reported that the guidelines had led to changes in their treatment decisions.
Quality of psoriasis care in Germany ... (14)	02.21	https://doi.org/10.1111/jdv.17220	Germany	In 12 years, PASI score > 20 decreased from 17.8 to 7.3%, DLQI score > 10 fell from 34% to 21.4%, and the rate of patients treated with systemic therapy increased from 32.9% to 57.6%.
Translating psoriasis treatment ... (15)	10.07	https://doi.org/10.1111/j.1365-2753.2008.00971.x	Germany	20% of dermatologists have heard of the guidelines, 20% have studied them, 25% have never heard of them. 79% of dermatologists believe that the guidelines help with the use of systemic medications.
Evaluation of Quality of Care and ... (16)	02.09	https://doi.org/10.1159/000218161	Germany	The presented set of key indicators of quality of care provides a sound method for describing changes in health care, which has become increasingly relevant in recent years.
Translating psoriasis guidelines ... (18)	11.15	https://doi.org/10.1016/j.jaad.2015.11.045	US (AAD)	Most participating dermatologists (67.7%) felt that these sessions had a strong impact on their practice, and 80% would recommend them to their colleagues.

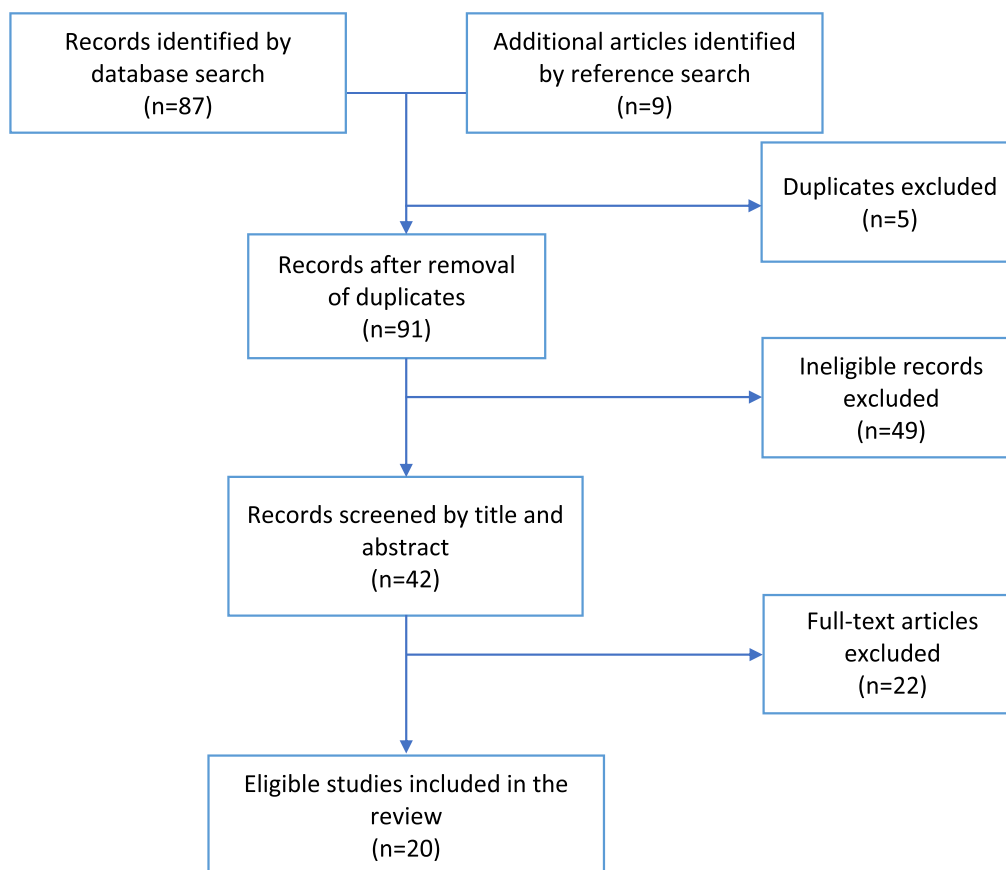


Fig. 1. Study flow chart.

hindered by the high cost of biologics, but rather by restrictive eligibility criteria, with stricter reimbursement conditions (e.g., DLQI > 20). A mean 0.25% of all psoriatic patients in these countries are treated with biologics [27].

3.4. Improved patient care and adherence to guidelines

Three prospective German studies showed that the introduction of their national guidelines resulted in increased use of systemic treatments [13–15]. Most private dermatologists (80% of 49) participating in a German practice study stated that the guidelines had led to changes in their treatment decisions [13]. A study by Langenbruch *et al.* [14] compared the quality of care for psoriasis patients between 2016/2017 and 2004/2005 to determine the evolution of care over time and thus the effectiveness of the health programs implemented. Within 12 years, PASI score > 20 decreased from 17.8 to 7.3%, the DLQI score > 10 fell from 34% to 21.4%, and the rate of patients treated with systemic therapy increased from 32.9% to 57.6% [14]. In addition, patients treated with biologics experienced greater therapeutic benefit and satisfaction with their treatment. A prospective US survey by Bhushan *et al.* investigated the value of guideline implementation sessions for practice improvement. Most participating dermatologists (67.7%) felt that these sessions had a strong impact on their practice and 80% said they would recommend them to their colleagues [18]. The same result was seen in the German prospective observational study by Nast *et al.* [15].

4. Discussion

According to the literature, there is a significant gap between the daily clinical practice of dermatologists and the guidelines for the systemic treatment of moderate to severe psoriasis. The reasons for this gap are multiple and vary between countries.

Despite the availability of many effective treatments on the international market and evidence-based guidelines, a significant proportion of psoriasis patients are not treated according to the guidelines [7]. This leads to a lower quality of life for patients as well as significant costs for the health care system (e.g., sick leave, repeated hospitalizations). It is thus vital to identify the barriers to optimal treatment.

The systemic therapy guidelines for psoriasis appear to be well known among practitioners, subject to selection bias, as most studies on awareness of the guidelines are practice surveys, and it is assumed that respondents are very interested in the topic. Barriers to guideline implementation focus on three categories of barriers, namely the patient, the physician, and various external factors, among which the health care system is prominent (Fig. 2). In certain countries, physician decisions regarding the use of biologics are based more on economic grounds (cost of products, insufficient remuneration of dermatologists, insufficient consultation time to initiate systemic treatment in 'private practice') than on medical grounds [11,24]. One might suppose that the introduction of international guidelines would help break national prescribing habits and achieve higher standards of care for psoriatic patients, but there are many differences between countries (e.g., health and

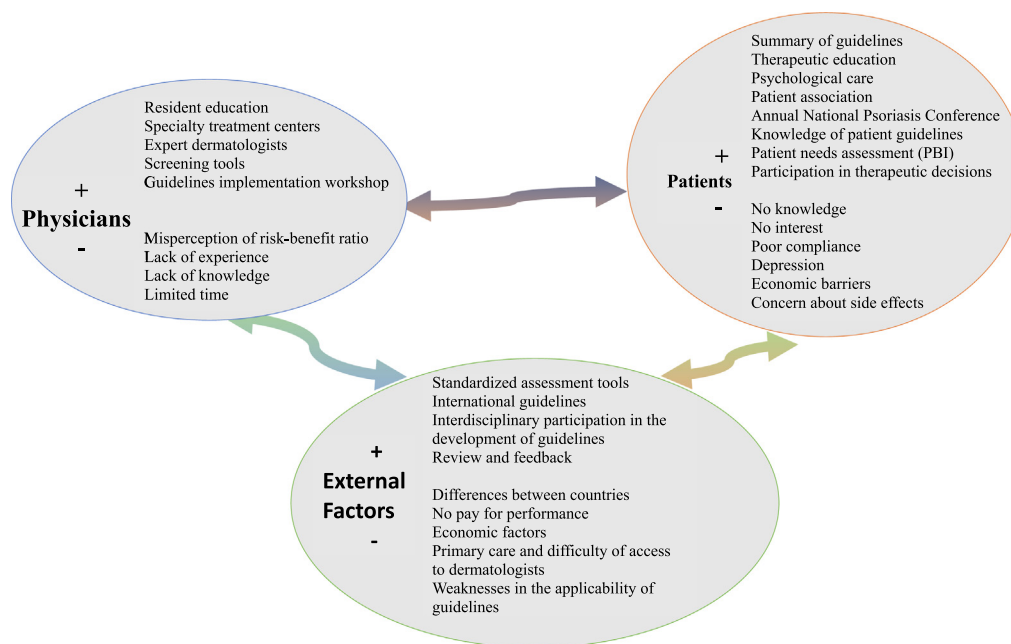


Fig. 2. Barriers and facilitators to psoriasis guidelines adherence inspired by Augustin et al. [28].

health insurance systems, access to therapies) that make these studies non-comparable and may prevent standardization.

Some improvements have been tested in the various studies and deserve to be developed: the establishment of specialized treatment centers for psoriasis patients or, alternatively, creation of networks between specialized clinics and private practices, could help to ensure that the guidelines are applied continuously and consistently [13]. In Germany, a national program has been developed in collaboration with dermatologists and patients to define new guidelines, create regional networks, reach a consensus on more patient-centered treatment goals, set up an annual National Psoriasis Conference, increase the use of innovative medicines, and define national health care goals for psoriasis [28]. While dermatologists provide most of the care for psoriasis patients, the extension of these national health programs to other groups of practitioners, such as general practitioners, would be a significant step forward in the management of these patients. Psoriasis guidelines are often not developed among other specialists and therefore awareness in these populations is likely to be low [12]. A better understanding of psoriasis and its guidelines among other specialists therefore seems necessary (the UK for instance has developed guidelines for general practitioners [29]).

In France, it is the mission of the Psoriasis Research Group (GRPso) to develop clinical and therapeutic research projects, to organize an annual psoriasis meeting, and to participate in the international network of national psoriasis research groups; it also provides patient information sheets and collects and shares news about psoriasis on its website [30].

As with all systematic reviews, our review has some limitations. The literature search may not have identified all relevant studies; however, the two most relevant media databases were searched. Only a small number of studies were included. The age of the publications and the predominance of German publications on this topic also constitute limitations of this study. In addition, we were not able to compare the data from the different studies because the discrepancy in characteristics studied from one study to another. The strengths of our study are the extended period selected and the analysis of studies from different countries.

To our knowledge this is the first literature review that examines the various barriers and suggestions for improving the imple-

mentation of guidelines in the systemic treatment of moderate to severe psoriasis in a multinational setting.

In conclusion, the barriers to implementation of the recommendations are diverse: economic, lack of referral to dermatology, lack of knowledge of the recommendations by other specialists, lack of applicability, while others are specific to the individual country and practice, e.g., different risk-benefit ratios, different reimbursement rates and conditions. This review contributes to a better understanding of the reasons preventing implementation in clinical practice and provides tools to improve guideline-based management of psoriasis patients. Better management of psoriasis patients involving treatment according to disease activity and guidelines will improve their quality of life.

Funding sources

None.

Conflicts of interest

None to declare.

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