OVERVIEW OF CHARACTERISTICS OF ADHERENCE TO TREATMENT OF ALLERGIC RHINITIS

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ABSTRACT

Objective: Overview of characteristics of treatment adherence in Allergic Rhinitis. **Methods:** A scoping review. **Results:** Of the 51 relevant articles, 5 articles that met the selection criteria were included in the study. These studies were conducted in many different countries, all showing the complex characteristics of adherence to treatment of allergic rhinitis in real-life contexts, thereby providing initial suggestions for more effective, patient-centered intervention strategies to improve clinical outcomes and quality of life for patients. **Conclusion:** Treatment adherence in allergic rhinitis patients is not a single issue of willpower, but a multifactorial challenge, reflecting the complexity of the disease and human behavior in real-life settings.

Keywords: Treatment adherence, Allergic rhinitis.

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1. Overview

Allergic rhinitis (AR) is a common condition that causes a significant disease burden and reduced quality of life globally [1, 2]. Allergen-specific immunotherapy (AIT), including subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT), is considered the only treatment with the potential to alter the natural history of allergic disease [1, 3]. However, despite proven efficacy in controlling symptoms and improving quality of life [1], adherence is a major barrier to optimal treatment outcomes [1]. Conventional immunotherapies (SCIT/SLIT) often face low adherence rates due to the long treatment duration (usually 3–5 years to achieve long-term benefits) and potential side effects [1, 2]. In fact, many patients discontinue treatment within the first year [1, 2].

Research has shown that missed doses are the main cause of non-adherence to SLIT [1]. Although overall adherence rates may be high in some patient groups or regimens, barriers remain [1]. However, some studies have reported high adherence rates in specific immunotherapies, such as SCIT in children with IBD in Indonesia, where significant local and systemic side effects did not hinder the treatment or efficacy of SCIT [3]. This suggests that managing side effects and patient satisfaction can significantly promote adherence [1]. Furthermore, actual patient behavior is often “as needed” rather than regular use, especially with intranasal corticosteroids (INCS) [4, 5]. This leads to the need for flexible treatment strategies that are tailored to patient behavior [4].

By synthesizing and analyzing arguments from various research sources, this study will provide a more comprehensive and in-depth look at the complex characteristics of AR treatment adherence in real-life contexts, thereby providing initial suggestions for more effective, patient-centered intervention strategies to improve clinical outcomes and quality of life for patients.

2. The research subject and method

1.1. Research subject

The research subjects are scientific articles and documents related to the characteristics of treatment adherence in Allergic Rhinitis

Selection criteria: Studies on the subject of treatment adherence of patients with Allergic Rhinitis; Location: Worldwide; Language: English; Publication: 2015-2025.

Exclusion criteria: Articles do not provide original data; Articles do not have full-text articles; Articles are not freely available.

2.2 Method search strategies and data sources

- Research design: A scoping review.
- Database sources and search strategies: We systematically searched the PubMed,

Sciencedirect, Cochrane databases with the English keywords: “adherence, patients allergic rhinitis”.

- All original articles are reviewed: Research title, research abstract, full text, independently evaluated by at least 2 authors.

2.3. Research selection

Two researchers will independently perform 2 steps:

Step 1: Abstracts of found articles will be deduplicated and entered into Endnote X7 document management software. Researchers will carefully read the title and abstract. Articles that meet the criteria will be selected, articles that do not meet the criteria will be excluded.

Step 2: Studies with suitable titles and abstracts will be read in full text, if determined to be suitable for the research objectives, they will be selected and information collected.

In these 2 steps, if there is a conflict between the two researchers, both will discuss and reach a consensus.

2.4. Data Extraction

Author, year of publication, location, study design, study subjects, main results and research conclusions of the study.

3. Results

The number of documents found with PubMed, Sciencedirect, Cochrane, Scholar databases was 51. After removing duplicate cases using EndNotex7 software, reviewing titles and abstracts, analyzing full-text articles, 5 qualified scientific articles were included in the study (diagram below).

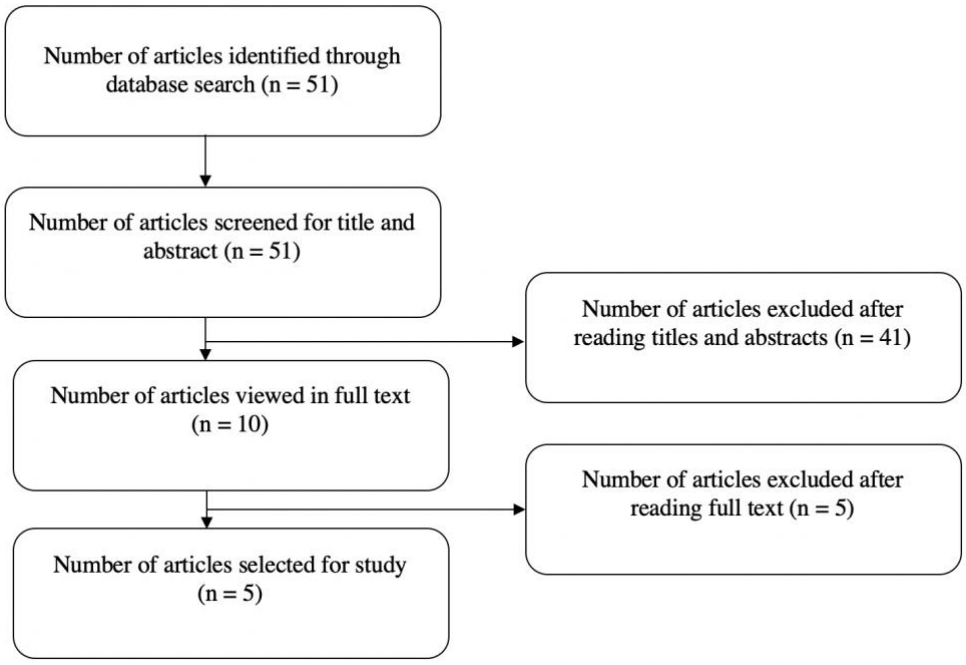

Table 1. Main results from eligible articles

Author(s), year	Location	Subjects	Study design	Main results	Main conclusions
Sara Garrido-Fernández et al, 2018 [1]	Spain	859 patients ≥ 5 years old with Allergic Rhinitis (AR) due to house dust mites and/or pollen, uncontrolled by symptomatic treatment, currently receiving Sublingual Immunotherapy (SLIT)	Multicenter descriptive epidemiological study, retrospective cross-sectional data	The majority of patients adhered to SLIT. The main cause of non-adherence was forgetting. High adherence rates were reported: 58.9% (Morisky-Green), 91.3% (Haynes-Sackett), 86.6% (self-reported).	SLIT is a rapidly effective treatment for moderate to severe AR symptoms and asthma. The issue of forgetting needs to be addressed to enhance adherence. The quick onset of action of Allergen Immunotherapy (AIT) is associated with adherence in SLIT.
Bernardo Sousa-Pinto et al, 05/21/2015 to 12/31/2022 [2]	Europe	1361 Regular users of the MASK-air application in Europe self-reporting AR and using Oral Antihistamines (OAH), Intranasal Corticosteroids (INCS), or azelastine-fluticasone	Observational study using long-term real-life data from the MASK-air mobile health application	Adherence levels (medication use > 80% of days) for specific medications ranged from 31.7% (azelastine-fluticasone) to 38.5% (OAH). The percentage of uncontrolled symptomatic days was higher during weeks with higher adherence. 41.2% of AR medication days during fully adherent weeks involved co-administration of other medications.	High adherence was found in patients who reported frequent use of MASK-air, potentially related to selection bias due to application adherence. Rhinitis control decreased as adherence increased, suggesting patients often only use medication when symptoms occur.
Junyan Zhang et al,	China	80 patients (40 active, 40 placebo), aged 18-55 with	Randomized, double-blind, placebo-	Primary endpoints (TNSS and DTNSS) significantly improved	Intratonsillar Immunotherapy (ITIT) with HDM extract is safe

07/2018 to 10/2019 [3]		moderate to severe AR due to house dust mites and/or pollen	controlled clinical trial	after 3 months of treatment compared to placebo. Most side effects were local reactions (sore throat, throat irritation), mild and self-limiting; no systemic reactions were observed.	and effective in AR patients. Efficacy may gradually decline over time; optimization of the protocol and allergen formulation is needed to maintain effectiveness.
Anang Endaryanto and Ricardo Adrian Nugraha, 2015 to 2020 [4]	Indonesia	1098 SCIT patients matched with 1098 control patients (total 2196), children with AR due to house dust mites and/or pollen, with or without asthma, who received Subcutaneous Immunotherapy (SCIT) with high adherence rates	Retrospective cohort study	25.87% of SCIT patients experienced side effects (SE); SE occurred in 2.27% of total SCIT injections. Local SE: 17.9% of patients; Systemic SE: 8.38% of patients. SCIT improved nasal, ocular, lung symptoms, and Total Symptom Score, reduced skin prick test diameter, and spHDM IgE levels. Medication scores significantly decreased in the SCIT group.	HDM SCIT is safe in children with AR. Despite significant SE, they did not affect the AR treatment process or the efficacy of SCITin these highly adherent patients.
Phinyo, P. et al, May 2021[5]	Systematic review including studies from Canada, Saudi Arabia, Netherlan	5 eligible RCTs (total 436 patients); 4 studies with sufficient data for quantitative analysis (total 286 patients), AR patients of all ages	Systematic review and meta-analysis of Randomized Controlled Trials (RCTs)	The change in TNSS for as-needed INCS was not significantly differentcompared to regular use after 4 and 6 weeks. Most individual nasal symptom scores and Quality of Life (QoL)	The efficacy of as-needed INCS with a corticosteroid exposure level equal to or greater than 50% is equivalent to regular use in improving nasal symptoms and QoL. As-needed use has the potential to reduce the

	ds, Thailand			scores were not significantly different. Treatment efficacy was less sustained with as-needed INCS. As-needed use with an INCS dose equal to or greater than 50% of the regular dose provided similar efficacy.	cumulative dose of INCS. This suggests that as-needed use may be more practical and effective in clinical practice if patients are permitted to reduce the dose.

The main results show that AR is a common condition that causes significant burden and impairment in quality of life. Although allergen-specific immunotherapy (AIT), including SCIT and SLIT, is considered the only treatment with the potential to alter the natural history of the disease, adherence is a major barrier to optimal outcomes. Traditional immunotherapies often face low adherence rates due to the long treatment duration (typically 3-5 years) and potential side effects, leading many patients to discontinue treatment within the first year. The main reason for non-adherence to SLIT is “forgetfulness”.

4. Discussion

4.1. Characteristics of time and location of the study:

Studies on adherence to AR treatment have been conducted in many different geographical areas with diverse time frames, providing a comprehensive view of the complex characteristics of this issue. Specifically, the study by Sara Garrido-Fernández et al [1] was conducted in Spain in 2018, providing cross-sectional data on adherence to sublingual immunotherapy (SLIT). Meanwhile, Anang Endaryanto and Ricardo Adrian Nugraha [3] conducted a long-term retrospective cohort study from 2015 to 2020 in Indonesia, focusing on the safety and efficacy of subcutaneous immunotherapy (SCIT) in children with high adherence rates. The scope of the study was significantly extended by Bernardo Sousa-Pinto et al [4] by analyzing real-world data from the MASK-air mobile application collected from 21/05/2015 to 31/12/20224 across Europe, highlighting the role of technology in monitoring adherence. A randomized clinical trial was conducted by Junyan Zhang et al [2] in China, with patient recruitment from 07/2018 to 10/20196, examining intratonsillar immunotherapy (ITIT). Finally, a systematic review by Phinyo, P.

et al [5] synthesized studies from several countries including Canada, Saudi Arabia, the Netherlands, and Thailand, with a literature search up to May 2021, evaluating the efficacy of intranasal corticosteroid sprays (INCS) used "as needed" versus regularly. These characteristics of study location and time demonstrate a diversity of approaches, from country-specific surveys to global systematic reviews and studies using mobile technology to collect longitudinal data in real-world settings. This has important implications for future research in Vietnam. To improve adherence to AR treatment, Vietnam needs to take advantage of diverse research methods, including conducting longitudinal cohort studies to understand the adherence behavior of Vietnamese patients over time, especially with long-term maintenance therapies such as AIT. At the same time, flexible treatment strategies, such as "as needed" INCS regimens, need to be explored and adapted to the medication use behavior of Vietnamese patients. More importantly, the implementation and evaluation of the effectiveness of mobile technology (mHealth) solutions in monitoring and supporting adherence, especially in addressing the issue of missed doses, would be a potential direction, learning from the European experience. Finally, research in Vietnam should also consider studying new and convenient therapies to shorten treatment time or reduce side effects to optimize adherence.

4.2. Subject characteristics, sample size and research methods:

Studies on adherence to treatment of AR have used a variety of subjects, sample sizes and designs, reflecting the multifaceted nature of this issue. Specifically, the study by Sara Garrido-Fernández et al [1] in Spain focused on 859 adult and pediatric patients aged 5 years and older with AR who were using sublingual immunotherapy (SLIT) in a multicenter, retrospective cross-sectional epidemiological study. In contrast, Bernardo Sousa-Pinto et al [4] analyzed long-term real-world data from 1361 regular users of the MASK-air app in Europe, including those who self-reported AR and used oral antihistamines (OAH) or intranasal corticosteroids (INCS), with an observational study design. In China, Junyan Zhang et al [2] conducted a randomized, double-blind, placebo-controlled clinical trial in 80 patients (40 active, 40 placebo) with moderate to severe IBD, aged 18–55 years, to evaluate intratonsillar immunotherapy (ITIT). Anang Endaryanto and Ricardo Adrian Nugraha [3] conducted a retrospective cohort study in Indonesia in 2196 children (1098 SCIT group and 1098 control group) with IBD, with or without asthma, who received subcutaneous immunotherapy

(SCIT). Finally, the systematic review by Phinyo, P. et al [5] synthesized the results from five eligible randomized clinical trials (RCTs) with a total of 436 patients (and 286 patients with sufficient data for quantitative analysis) with AR of all ages, evaluating the effectiveness of INCS used "as needed" versus regularly.

The diversity of subjects (from children to adults, patients using different drugs and therapies), sample sizes (from tens to thousands), and study designs (cross-sectional, real-world observational, randomized clinical trials, retrospective cohorts, systematic reviews) provides a comprehensive picture of approaches to studying AR treatment adherence. This has profound implications for future studies in Vietnam. To improve adherence to treatment of AR, Vietnam needs to combine diverse research methods, including conducting randomized clinical trials to evaluate the effectiveness of new therapies or optimal regimens on specific target groups. At the same time, long-term cohort studies are needed to monitor the actual adherence behavior of Vietnamese patients, especially with therapies that require persistence. Exploiting real-world data from mobile applications or available health systems with large sample sizes will also provide insights into factors affecting adherence in the real-life context of Vietnam. Finally, it is necessary to consider the unique characteristics of Vietnamese patients (such as medication use habits, access to health care, culture) to customize research subjects and designs to provide the most effective adherence intervention strategies.

4.3. Key findings and conclusions of the study:

The studies have provided important results and conclusions on adherence to AR treatment, thereby shaping the direction for future intervention strategies. Sara Garrido-Fernández et al [1] showed that although the majority of patients adhered to sublingual immunotherapy (SLIT), the leading cause of non-adherence was missed doses. This study also suggested that the rapid onset of action of specific immunotherapy (AIT) may be a factor promoting adherence. More broadly, real-world data from the MASK-air application analyzed by Bernardo Sousa-Pinto et al [4] in Europe showed low adherence rates for specific medications (ranging from 31.7% to 38.5%), and particularly highlighted the tendency for patients to use medications "as-needed" rather than regularly. In contrast, Anang Endaryanto and Ricardo Adrian Nugraha [3] reported high compliance rates to subcutaneous immunotherapy (SCIT) in children with IBD in Indonesia, and despite significant local and systemic side effects, they did not affect the treatment or efficacy of SCIT in

this highly compliant patient group6, suggesting that side effect management and patient satisfaction may play an important role in promoting compliance. Regarding novel therapies, Junyan Zhang et al [2] demonstrated that intratonsillar immunotherapy (ITIT) is safe and effective in improving IBD symptoms, although the effect may wane over time and regimen optimization is needed to maintain efficacy. Finally, a systematic review by Phinyo, P. et al [5] concluded that "as needed" intranasal corticosteroids (INCS) with cumulative doses of 50% or more were as effective as regular use in improving symptoms and quality of life, and had the potential to reduce cumulative doses of INCS, reinforcing the need for flexible treatment strategies that are tailored to patient behavior.

To optimize clinical outcomes and improve quality of life for patients with AR in Vietnam, future studies should prioritize addressing the issue of missed doses through practical interventions such as automated reminder systems from mobile applications (mHealth), learning from the experience of MASK-air. At the same time, flexible and effective treatment regimens, especially "as needed" medication strategies for INCS, should be explored and applied, as this reflects common medication use behaviors and may improve adherence among Vietnamese patients. Research and evaluation of new, more convenient therapies such as ITIT that shorten treatment duration and reduce systemic side effects are also potential directions to optimize adherence, but attention must be paid to maintaining long-term efficacy. Finally, attention to side effect management and patient satisfaction will be key, especially for long-term therapies such as AIT, to encourage patients to continue treatment, even when experiencing mild side effects. A comprehensive, patient-centered approach, incorporating digital technology and education, is needed to improve adherence and improve clinical outcomes for patients with AR in Vietnam.

5. Conclusions

Patient adherence to treatment for IBD is a major challenge, particularly given that patients often miss doses and tend to take their medications "on demand" rather than consistently following a regimen. To optimize clinical outcomes and enhance quality of life, improving adherence requires a multifaceted approach that incorporates flexible treatment strategies, effective use of digital technologies, enhanced patient education, and the development of new therapies that deliver rapid and significant results.

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