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REVIEW ARTICLE

Medication adherence, sensory attributes, and adverse effects of intranasal corticosteroids in allergic rhinitis patients: A systematic review and meta-analysis

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Abstract

Background: Intranasal corticosteroid (INCS) remains the primary treatment for allergic rhinitis (AR). Understanding adherence, safety concerns and sensory preferences is crucial for optimal care.

Objective: This review aims to determine medication adherence, sensory attributes and adverse effects of INCS in AR patients.

Methods: A systematic search of PubMed, Web of Science, Scopus, and Cochrane database was conducted for English articles published from 2004 to 2023. Eligibility includes clinical trials and observational studies with adult patients (18 years old or older) receiving INCS for AR (both intermittent and persistent).

Results: Thirty-one studies with 10,582 patients, comprising 10 cross-sectional studies and 21 randomized controlled trials (RCT) were included. Adherence rates ranged from 28% to 87%, with an average of 55.8%. Forgetfulness was the primary reason for non-adherence (63.1-77.8%), followed by adverse events (26.4-61.5%) and fear of adverse events (3.8-31.5%). Scent (38%), taste (28.5%), or aftertaste (24.3%) were the main differentiators for sensory attribute, with varying levels of intensity and preferences for each INCS. Common adverse events encompass epistaxis, nasal dryness/irritation, headache and nasopharyngitis. A meta-analysis of eight RCT detected no significant difference in adverse events between the INCS and control groups (risk ratio 1.05; 95% confidence interval, 0.88-1.24; $p = 0.61$).

Conclusion: The findings of this review indicate that medication adherence to INCS is not optimal, with non-adherence mostly attributed to forgetfulness, preferences for sensory attributes, and unpleasant effects associated with INCS. The underlying factors should be addressed as part of a multimodal strategy to improve adherence.

Key words: allergic rhinitis, intranasal corticosteroids, medication adherence, patient preference, adverse effects

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Introduction

Allergic rhinitis (AR) represents a global health issue affecting 10% to 40% of the population.[1] It arises from an immune response mediated by immunoglobulin E to environmental allergens,[2,3] leading to symptoms encompassing nasal congestion, runny nose, red and itchy eyes, and postnasal drip.[4] When uncontrolled, these symptoms significantly impact quality of life, work productivity,

sleep quality, the ability to perform daily activities, and medical costs.[5] Intranasal corticosteroid (INCS) proves to be the most effective medication in managing AR symptoms due to their ability to modulate the pathophysiology of the condition.[3,6] According to the current guidelines on Allergic Rhinitis and its Impact on Asthma, INCS are the preferred treatment for moderate-to-severe AR, especially when nasal congestion is the predominant symptom.[1,5,7] Continuous use of intranasal corticosteroid is recommended and more efficacious than intermittent use to achieve maximum benefit and relief,[8] while using them only symptomatically may result in suboptimal relief and potential nonadherence.[9]

Patient adherence is crucial for the successful treatment of any disease, as improved health outcomes depend on proper medication use.[9] Failure to adhere to prescribed medication regimens presents a substantial risk of reduced therapeutic efficacy, regardless of the disease or patient attributes.[10] Several factors, particularly those related to the patient, may influence medication adherence. Various barriers, such as safety concerns and undesirable sensations related to intranasal administration, can hinder the use of INCS,[5] and all those factors usually interact. Patient beliefs and concerns about adverse effects may lead to non-adherence.[11] This non-adherence may stem from patient perceptions and worries about experiencing adverse reactions. Patients may develop a fear of potential complications from continuing to take their medications due to experiences with unfavorable effects from past medication use or witnessing friends or family members taking them. Consequently, patients may hesitate to adhere to their prescribed medication regimen, either by delaying or reducing their dosage frequency. It should be highlighted that most of the safety data for INCS are derived from a carefully selected group that received medication under controlled and monitored conditions in clinical studies. As a result, the safety information might not entirely reflect observations in routine clinical practice.

As a primary treatment option for AR, INCS comes in various formulations and brands. Unlike oral medications, INCS act locally in the nasal passages, making sensory experiences more immediate and pronounced. The sensory attributes of these formulations, including smell, taste, and feel upon administration, play a crucial role in determining patient acceptance and adherence.[12] The olfactory experience of using INCS prominently influences a patient's willingness to adhere to the prescribed treatment. Unpleasant or strong odors may discourage consistent use. Additionally, the taste of INCS is another critical factor affecting adherence. Bitter or unpleasant tastes can create aversions, making it challenging for children and adults to comply with the prescribed regimen. Moreover, the sensations experienced during and after INCS administration, such as the texture and potential post-nasal drip, can impact its use. Formulations that provide a comfortable application experience may contribute to increased acceptance and consistent use. Given that INCSs are equally effective, safety and sensory characteristics are crucial when tailoring therapies to the specific requirements of each patient.[5,13]

The objective of this review is to determine medication adherence (primary outcome) and investigate secondary outcomes such as sensory attributes and adverse effects of INCS in AR patients.

Methods

Protocol and registration

This systematic review adhered to the guidelines set forth by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[14] and conducted according to the protocol registered in PROSPERO (CRD42024523556). Ethical approval was not deemed necessary since the study exclusively utilized aggregated public sources with no individually identifying information.

Eligibility criteria

All studies involving adult patients (age 18 years old or older) receiving INCS for AR (with or without bronchial asthma) with documentation of medication adherence, sensory attributes of INCS or adverse events were eligible. Included were randomized clinical trials (RCT), non-RCT and observational studies on AR, both intermittent and persistent. Exclusion criteria encompassed non-English papers, review papers of previously published data, meeting proceedings, non-human studies, case series, case reports and studies which enrolled only pediatric participants.

Search strategy

A thorough examination of the English-language literature was conducted to identify published studies using the following databases: PubMed, Web of Science, Scopus, and Cochrane. The search was conducted on 5 October 2023, including records published from 2004 up to September 2023. Adhering to the population, intervention, comparator, and outcome (PICO) format, the search terms were: (allergic rhinitis) AND (intranasal corticosteroid* OR intranasal steroid* OR nasal steroid*) AND (adheren* OR complian* OR preference OR adverse effect* OR side effect* OR safety). The collated records were managed using EndNote 21,[15] with removal of duplicates through EndNote 21 and manual author review.

Study selection

A preliminary screening of titles and abstracts, focusing on studies involving human subjects, was conducted. Full texts of selected articles were retrieved and independently reviewed. Further sources were identified from the bibliographies of pertinent journal articles. Eligibility was independently evaluated, and rationales for exclusion were provided. Studies that did not report outcome data were excluded. Duplicate articles and those failing to meet the study criteria after the full review were excluded. Any disagreements among the reviewers were discussed and resolved by all authors. The study's authors were contacted if additional information was required.

Data extraction

A data extraction form was developed using a Microsoft Excel® spreadsheet, containing information on study characteristics such as study design, sample size, age, measurement tool, medication adherence rate, reasons for non-adherence, sensory attribute preference, and adverse events. Data extraction was performed by two authors.

Outcome measures

Medication adherence refers to the extent to which a patient adheres to the specified treatment plan, including taking medications as directed.[16] Adherence entails consistently using INCS at the recommended dosage, frequency, and duration of use. Sensory attribute preferences towards INCS refer to individual preferences or reactions related to the sensory aspects of using these nasal medications.[17] The sensory attributes encompass various elements that influence the user experience, including taste, smell, and overall sensation during and after administration. Adverse effects are the negative experiences or unwanted effects reported by individuals using INCS.[18] These were primarily treatment-emergent adverse event (TEAE) defined as adverse events which commenced or intensified in severity after the initial administration of study drug.[19]

Risk-of-bias analysis

Quality assessment and risk of bias evaluations for each included study were independently conducted by two authors using the relevant Joanna Briggs Institute critical appraisal tool checklist.[20] All authors participated in the discussion to resolve any discrepancies. Studies were classified as low-quality (high risk of bias) if the overall score was ≤ 50%.

Statistical analysis

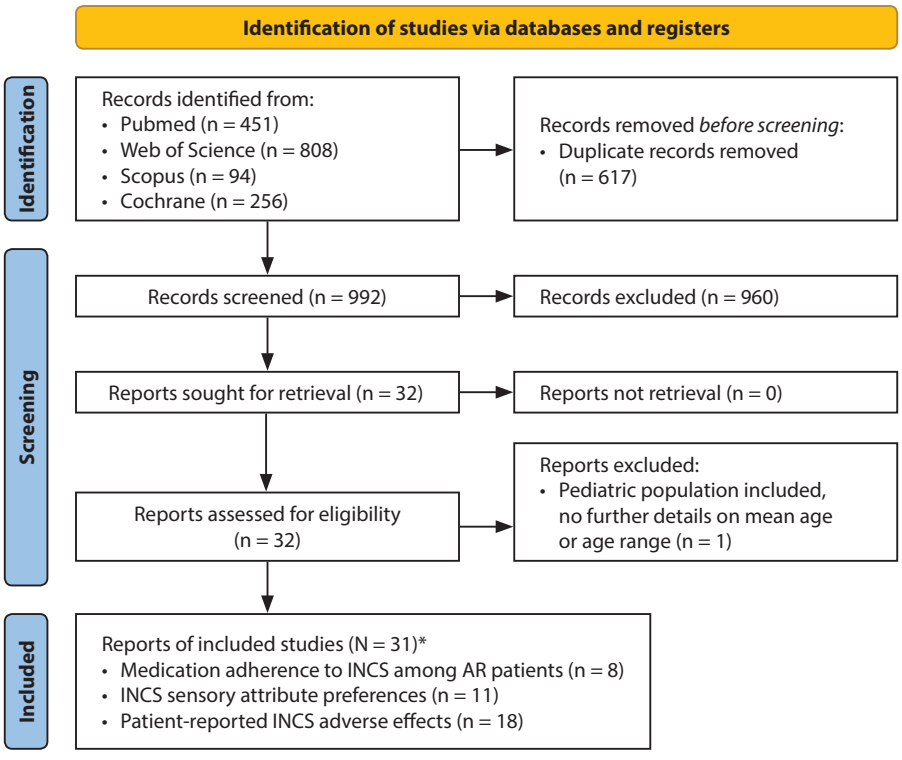
Descriptive statistics, including means, standard deviations, medians, and interquartile ranges were calculated as appropriate. The results of data synthesis were presented in tables. A qualitative comparison of results from all studies was also performed. Meta-analysis was done when applicable, using data from RCT only. Results of interest lacking sufficient reported data to complete a meta-analysis (medication adherence, and sensory attribute preferences) are reported qualitatively.

Utilizing Review Manager 5.3 software, a random effects model was employed to analyze the data. Heterogeneity was assessed using I^2 statistics with the following definitions: 0% to 40% non-significant, 30% to 60% moderate, 50% to 90% substantial, and 75% to 100% considerable.[21] A forest plot was illustrated to generate the relative risk (RR) of the adverse effect using a 95% confidence interval. A p-value of 0.05 was considered significant.

Results

Study selection

A search in the selected databases identified 1,609 records. These records were imported into EndNote 21, and 617 duplicates were removed prior to screening. Among the 992 records screened, 32 records were deemed relevant, and full articles were retrieved to access eligibility. One article was subsequently omitted due to the inclusion of pediatric population without further details on the mean age or age range of the participants. Eventually, 31 studies with 10,582 patients with AR in total were selected.[11-13,22-49] The selection process is shown in **Figure 1**.



*The studies considered for inclusion may present multiple study outcomes.

Figure 1. Flow diagram of study selection.

Table 1. Characteristics of included studies.

Study	Study design	No. of patients	Age, mean ± SD or mean (range), years	Measurement tool	Type of INCS	Adherence, %	Reasons for non-adherence, %	Intensity of sensory attribute, %	Sensory attribute with type of INCS or preference, %	Adverse events, %
Almutairi et al (2020)[23]	Cross-sectional	375	34.4 ± 10.84	Questionnaire-based survey	NR	71.5	Fear of adverse effects (26.4) INCS not effective (7.7) INCS not helpful (6.9) Other reasons (33.9)	NR	NR	Headache (29.6) URTI (8.3) Epistaxis (5.3) Nasopharyngitis (4) Cough (4)
Hankin et al (2012)[27]	Cross-sectional	390	12 and above	Medication possession ratio (MPR)	BDP (Beconase®) BUD (Rhinocort®) TCA (Nasocort®)	34.7	INCS not effective (percentage NR)	NR	NR	NR
Lee et al (2021)[22]	Cross-sectional	65	39	Questionnaire-based survey (frequency of use, technique of spraying, frequency of missed-dose due to forgetfulness, sensory attributes, and side effects experienced)	1. FF (Avamys®) 2. MF (Nasonex®) 3. TCA (Nasocort®)	63.1	Forgetfulness (63.1) Experience of AE (61.5) Sensory attributes of INCS (47.7)	Throat rundown (29.2) Aftertaste (21.5) Immediate taste (20.0) Scent/odor (16.9) Dripping out (13.8) Urge to sneeze (16.9)	Unfavorable attributes TCA (83.3) MF (65.2) FF (28.6)	Rebound effect (33.8) Dependency (23.1) Dryness of throat, nose, and mouth (20) Sneezing (13.8) Headache (12.3) Epistaxis (7.7) Nausea (4.6)
Loh et al (2004)[24]	Cross-sectional	53 AR, 10 non-AR	29 (15-68)	Self-report adherence Weight of medication consumed	TCA (Nasocort®)	87 (as reported by patients) 65 (by weight of medication consumed)	Forgetfulness (77.8)	NR	NR	NR
Mahadevia et al (2004)[12]	Cross-sectional	120	39	Frequency of INCS use Classification of adherence on a scale (1 to 10)	NR	48	NR, evaluated based on sensory attributes of INCS	NR	NR	NR
Manjit Singh et al (2022)[11]	Cross-sectional	185	37.9 (18-74)	Adherence evaluation by "drug diary" Barriers to adherence assessed by Brief Medication Questionnaire (BMQ)	BUD MF FF	59.5	Symptoms improved (41) Symptoms not bothering (30.8) Busy schedule (9.2) Fear of adverse effects (3.8) Ran out of supply (2.7) INCS not effective (0.5)	NR	NR	NR
Ocak et al (2017)[25]	Cross-sectional	59	32.5 (21-52)	Turkish- validated (Morisky Medication Adherence Scale) MMAS-8 questionnaire	MF	45.5* *MMAS-8 score = 3.64 (max score: 8, higher scores = less adherence to treatment)	Number of dependent children (40) Symptoms improved (36)	NR	NR	NR

Table 1. (Continued)

Study	Study design	No. of patients	Age, mean ± SD or mean (range), years	Measurement tool	Type of INCS	Adherence, %	Reasons for non-adherence, %	Intensity of sensory attribute, %	Sensory attribute with type of INCS or preference, %	Adverse events, %
Wang et al (2014)[26]	RCT	19	31.0 ± 10.88	Self-reported adherence	BUD (Rhinocort®)	28	Forgetfulness (63.2) Symptoms improved (36.8) Fear of adverse effects (31.5) INCS not effective (10.5) Troublesome to use (5.3) Other reasons, NR (10.5)	NR	NR	NR
Berger et al (2013)[28]	RCT	294	36.6 ± 14.75	ARTSP questionnaire	CIC MF	NR	NR	CIC vs MF: Nasal irritation (48 vs 52, NS) ¥Dislike scent/odour (37 vs 63, $p < 0.001$) ¥Dislike taste (32 vs 68, $p < 0.001$) ¥Throat rundown (15 vs 85, $p < 0.001$) ¥Dripping out (13 vs 87, $p < 0.001$) ¥Scores were inverted to indicated bothersomeness	Overall preference CIC vs MF (68.1 vs 31.7, $p < 0.001$)	NR
Khanna et al (2005)[29]	RCT	114	18-40	Nasal Spray Evaluation Questionnaire	BDP (Beclate®) BUD (Budenase®) FP (Flomist®) MF (Metaspray®)	NR	NR	MF vs BUD vs FP vs BDP: ¥Overall discomfort (31 vs 38 vs 45 vs 43) Odor strength* (44 vs 38 vs 79 vs 58) ¥Dislike scent/odour* (29 vs 48 vs 60 vs 56) ¥Drying feeling* (25 vs 42 vs 37 vs 57) Immediate taste (18 vs 28 vs 22 vs 36) Nasal irritation* (17 vs 38 vs 43 vs 31) Dripping out (11 vs 15 vs 16 vs 18) Throat rundown (8 vs 10 vs 13 vs 19) Bitter taste (8 vs 11 vs 8 vs 10) Aftertaste* (7 vs 22 vs 19 vs 27) Urge to sneeze (5 vs 6 vs 6 vs 5) ¥Scores were inverted to indicate bothersomeness *Significant difference detected	Overall liking of product MF (68) BUD (43) FP (31) BDP (23) MF > BUD ($p < 0.05$) MF > FP ($p < 0.01$) MF > BDP ($p < 0.01$)	NR

Table 1. (Continued)

Study	Study design	No. of patients	Age, mean ± SD or mean (range), years	Measurement tool	Type of INCS	Adherence, %	Reasons for non-adherence, %	Intensity of sensory attribute, %	Sensory attribute with type of INCS or preference, %	Adverse events, %
Meltzer et al (2005)[31]	RCT	100 (ITT)	39.7 for treatment sequence MF/FP 37.6 for treatment sequence FP/MF Range: 18-65	Product attribute questionnaire Overall preference questionnaire	MF (Nasonex®) FP (Flonase®)	NR	NR	MF vs FP: Scent/odor (56 vs 24, $p = 0.0005$) Immediate taste (46 vs 21, $p = 0.005$) Aftertaste (45 vs 21, $p = 0.005$) Throat rundown (41 vs 26, NS) Nasal irritation (41 vs 24, NS) Dripping out (39 vs 29, NS) Soothing sensation (32 vs 34, NS) Urge to sneeze (28 vs 12, $p = 0.01$)	Overall preference MF vs FP (53 vs 34, $p < 0.05$)	NR
Meltzer et al (2008)[30]	RCT	120	39.7 ± 14.05	Patient-rated sensory attributes and product attributes questionnaires	FF (Veramyst™, also known as Avamys®) FP	NR	NR	FF vs FP: Scent/odor (64 vs 29, $p < 0.001$) Dripping out (49 vs 19, $p < 0.001$) Taste (47 vs 21, $p < 0.001$) Aftertaste (44 vs 22, $p = 0.002$) Throat rundown (43 vs 27, $p = 0.037$)	Overall preference FF vs FP (60 vs 33, $p = 0.003$)	NR
Meltzer et al (2010)[32]	RCT	360	38.3	Product attributes questionnaires	FF FP FF matched placebo FP matched placebo	NR	NR	FF vs FP: Aftertaste (60 vs 18, $p < 0.001$) Throat rundown (59 vs 21, $p < 0.001$) Scent/odor (58 vs 27, $p < 0.001$) Nasal irritation (57 vs 26, $p < 0.001$)	NR	FF vs FP: Any events (12 vs 21) Headache (4 vs 9) Back pain (< 1 vs 1) Sinus headache (< 1 vs 1) Unilateral deafness (< 1) Myalgia (< 1 vs 0) Pharyngolaryngeal pain (0 vs 2)
Naclerio et al (2007)[33]	Cross-sectional	2500	NR	Patient survey through phone interview	All type of INCS nasal spray	NR	NR	Drying feeling (47) Throat rundown (41) Immediate taste (32) Nasal irritation (17)	NR	Drowsiness (37) Headache (16)

Table 1. (Continued)

Study	Study design	No. of patients	Age, mean ± SD or mean (range), years	Measurement tool	Type of INCS	Adherence, %	Reasons for non-adherence, %	Intensity of sensory attribute, %	Sensory attribute with type of INCS or preference, %	Adverse events, %
Stokes et al (2004)[13]	RCT	215	36.2	Nasal spray evaluation questionnaire (NSEQ) Overall NSEQ	TCA FP MF	NR	NR	TCA vs FP vs MF: ¥Drying feeling (40 vs 44.2 vs 44.2, $p = 0.011$) ¥Dislike scent/odor (26.8 vs 48 vs 48.6, $p < 0.001$) Dripping out (26.8 vs 25.6 vs 27.3) Nasal irritation (15.3 vs 16.6 vs 21.9) Odor strength (14.8 vs 54.3 vs 53.2, $p < 0.001$) Immediate taste (14.3 vs 20.5 vs 26.1, $p < 0.001$) Aftertaste (12.8 vs 18.9 vs 21.1, $p < 0.001$) Urge to sneeze (8.9 vs 9.3 vs 11.4, NS) Bitter taste (8.1 vs 9.2 vs 13.7, $p = 0.003$) ¥Scores were inverted to indicate bothersomeness	Overall preference TCA vs FP (50 vs 25, $p < 0.05$) TCA vs MF (50 vs 25, $p < 0.001$)	NR
Varshney et al (2012)[34]	RCT	74	32 (IQR 25-41)	Sensory attributes questionnaire	CIC (Cinase) FP (Fluticone)	NR	NR	FP vs CIC: Soothing sensation (56.7 vs 20.3, $p < 0.001$) Scent/odor (50 vs 8.1, $p < 0.001$) Nasal irritation (1.4 vs 28.4, $p = 0.002$) Urge to sneeze (1.4 vs 13.5, NS)	Overall preference FP vs CIC (55.4 vs 25.7, $p = 0.007$)	NR

Table 1. (Continued)

Study	Study design	No. of patients	Age, mean ± SD or mean (range), years	Measurement tool	Type of INCS	Adherence, %	Reasons for non-adherence, %	Intensity of sensory attribute, %	Sensory attribute with type of INCS or preference, %	Adverse events, %
Yanez et al (2016)[35]	RCT	276	40 (17-65)	Overall preference questionnaire Immediate attributes questionnaire Delayed attributes questionnaire	FF (Avamys®) MF (Nasonex®)	NR	NR	FF vs MF Throat rundown (38 vs 18) Aftertaste (25 vs 18) Immediate taste (23 vs 18) Scent/odor (28 vs 20) Dripping out (35 vs 22) Less irritation (40 vs 15) Urge to sneeze (15 vs 13)	Overall preference FF vs MF (56 vs 32, $p < 0.001$)	FF vs MF: Any events (2 vs 4) Rhinorrhoea (< 1 vs 1) Nasal discomfort (< 1) Cough (0 vs 1) Nasal pruritus (< 1) Sneezing (< 1) Upper respiratory tract congestion (< 1) Oropharyngeal pain (0 vs < 1) Throat irritation (0 vs < 1) Dysphagia (0 vs < 1) Dysgeusia (0 vs < 1) Pruritus (< 1 vs 0)
Yonezaki et al (2015)[36]	RCT	40	51.7 ± 13.5	Japanese Rhinoconjunctivitis Quality of Life Questionnaire (JRQLQ) Product attributes questionnaire	FF MF	NR	NR	FF vs MF Throat rundown (12 vs 22.7) Immediate taste (9.8 vs 20.6) Dripping out (13.1 vs 29.2) Nasal irritation (12.2 vs 24.3) Urge to sneeze (7.8 vs 16.8) Inducing rhinorrhea (11.8 vs 25.3)	Overall preference FF vs MF (52.5 vs 22.5)	NR
Antila et al (2016)[37]	RCT	387	Study: 27.74 ± 12.51 Control: 31.04 ± 14.41	Drug diary	2 different formulations of MF (Eurofarma, study vs Nasonex, control)	NR	NR	NR	NR	Nasonex (62.3) Eurofarma (59.2) • More frequent backpain/myalgia and epistaxis in Nasonex • More frequent ECG abnormality in Eurofarma
Benninger et al (2008)[38]	Cross-sectional	226	NR	Self-reported epistaxis	NR	NR	NR	NR	NR	Epistaxis (2.7)
Given et al (2010)[39]	RCT	315	Study: 38.1 ± 14.2 Control: 39.3 ± 15.1	NR	FF	NR	NR	NR	NR	FF: Any events (> 3%) Epistaxis (15%) Nasopharyngitis (5%)

Table 1. (Continued)

Study	Study design	No. of patients	Age, mean ± SD or mean (range), years	Measurement tool	Type of INCS	Adherence, %	Reasons for non-adherence, %	Intensity of sensory attribute, %	Sensory attribute with type of INCS or preference, %	Adverse events, %
Jacobs et al (2009)[40]	RCT	302	Study: 37.0 ± 13.9 Control: 38.1 ± 13.60	AE monitoring, clinical examination, 12-lead ECG monitoring and clinical laboratory tests	FF	NR	NR	NR	NR	FF: Any events (22) Headache (5) Epistaxis (3) Nasopharyngitis (2) Nausea (1) Pharyngolaryngeal pain (1) Sinus headache (1)
Karaulov et al (2019)[41]	RCT	260	TCA: 33.3 ± 8.5 FP: 31.8 ± 8.47	NR	TCA (Nasacort®) FP (Flixonase®)	NR	NR	NR	NR	TCA vs FP: Any TEAEs (19.4 vs 16.8) Headache (9.3 vs 4.6) Nasal dryness (2.3 vs 3.1) Application site pain (2.3 vs 0) Nasal discomfort (0.8 vs 2.3) Upper abdominal pain (0 vs 2.3)
LaForce et al (2013)[42]	RCT	548 (ITT)	Study: 37 (12-70) Control: 38 (12-65)	Ophthalmic examinations, vital signs, nasal examinations, AE monitoring, clinical laboratory tests	FF (Veramyst™, also known as Avamys®)	NR	NR	NR	NR	FF: Any TEAEs (34) Epistaxis (28) Nasal ulcer (7) Nasal septum ulceration (5) Nasal discomfort (3)
Meltzer et al (2012)[43]	RCT	574	Study: 36.8 ± 14.5 (12-82) Control: 37.2 ± 13.7 (12-71)	Physical examinations, ECG, clinical laboratory tests	BDP	NR	NR	NR	NR	BDP: Any events (20.3) BDP (TEAE): Nasal discomfort (5.9) Epistaxis (1.7) Headache (1.3) URTI (1.3) Sinus headache (1.3) Oropharyngeal pain (0.8)
Pitsios et al (2006)[44]	RCT	61	MF: 30.1 ± 10.9 (12-50) Nedocromil: 29.5 ± 11.2 (14-57)	Diary card	MF	NR	NR	NR	NR	MF: Burning nose (13) Bad taste (9) Insomnia (6) Epistaxis (6) Headache (3) Somnolence (3)
Raphael et al (2013)[45]	RCT	486 (ITT)	38.5 ± 14.5 (12-78)	AE monitoring, physical examinations, vital sign measurements, ENT examinations	BDP (80 µg, 160 µg, 320 µg)	NR	NR	NR	NR	BDP 80 vs 160 vs 360 µg (TEAE): Nasal discomfort (2.5 vs 4.1 vs 3.3) Epistaxis (5.1 vs 2.4 vs 2.5) Headache (0 vs 1.6 vs 4.1) URTI (0.8 vs 0.8 vs 0.8) Pyrexia (0 vs 1.6 vs 0.8)

Table 1. (Continued)

Study	Study design	No. of patients	Age, mean ± SD or mean (range), years	Measurement tool	Type of INCS	Adherence, %	Reasons for non-adherence, %	Intensity of sensory attribute, %	Sensory attribute with type of INCS or preference, %	Adverse events, %
Rosenblut et al (2007)[46]	RCT	806 (ITT)	32.4 ± 14.38	Diary cards and interviews at each visit	FF	NR	NR	NR	NR	FF: Any events (77) Headache (31) Nasopharyngitis (26) Epistaxis (20) Pharyngolaryngeal pain (9) Back pain (6) URTI (6) Cough (5) Influenza (5) Toothache (5) Upper abdominal pain (4) Dysmenorrhea (4) Septal ulceration (3) Pyrexia (3) Nasal dryness (3) Ear pain (2) Scab (2) Rhinitis (2) Rhinorrhea (2) Nasal oedema (<1) Nasal discomfort (<1)
van Bavel et al (2012)[47]	RCT	338	39.3 ± 13.4 (12-68)	TEAE monitoring, physical examination, vital signs measurements, ENT assessments	BDP	NR	NR	NR	NR	BDP: Any TEAEs (13.8) Nasal discomfort (6.6) Headache (1.8) Epistaxis (1.2) Nausea (1.2) Urticaria (1.2) Nasopharyngitis (0.6)
Weber et al (2006)[48]	Cross-sectional	396	31.9 (12-69)	Daily diary card, physical examination, vital signs, laboratory measurements	TCA	NR	NR	NR	NR	TCA: Any TEAEs (43.7) Nasal irritation (22.5) Sneezing (20.7) Epistaxis (19.4) Dry mucous membrane (4) Nasosinus congestion (1.3) Pharyngitis (0.8)
Weinstein et al (2014)[49]	RCT	524 (ITT)	BDP: 37.4 ± 13.6 (12-74) Placebo: 35.7 ± 12.9 (12-67)	TEAE monitoring, physical examination, vital sign measurements, ENT evaluation	BDP	NR	NR	NR	NR	BDP: Any TEAEs (68.2) Nasopharyngitis (16.1) Epistaxis (10.6) URTI (10.4) Sinusitis (8.2) Headache (6.7) Acute sinusitis (2.2)

Abbreviations: AE, adverse event; ARTSP, Allergic Rhinitis Treatment Satisfaction and Preference instrument; BDP, beclomethesone dipropionate; BUD, budesonide; CIC, ciclesonide; ECG, electrocardiogram; ENT, ear, nose, throat; FF, fluticasone furoate; FP, fluticasone propionate; INCS, intranasal corticosteroids; ITT, intention-to-treat; MF, mometasone furoate; MMAS-8, eight-item Morisky Medication Adherence Scale; NR, not reported; NS, not significant; RCT, randomized controlled trial; TEAE, treatment-emergent adverse event; TCA, triamcinolone acetonide; URTI, upper respiratory tract infection.

Characteristics of included studies

Table 1 outlines the characteristics of included studies, such as study design, sample size, age, measurement tool, type of INCS, and outcome measures like adherence rate, sensory attribute preference, and adverse events. The studies analyzed in this research encompassed 10 cross-sectional studies and 21 RCT, involving an average sample size of 250 participants (ranging from 19 to 574), excluding those conducted by Naclerio et al. (n = 2,500)[33] and Rosenblut et al. (n = 806).[46] These studies were published between 2004 to 2023. Beclomethasone dipropionate, budesonide, ciclesonide, mometasone furoate, fluticasone propionate, and triamcinolone acetonide were among the INCS that were investigated.

Primary outcome: Medication adherence to intranasal corticosteroids

Eight studies reporting medication adherence to INCS met the inclusion criteria.[11,12,22-27] Subjective approaches such as questionnaire-based surveys, drug diaries, or patient self-reports were used for the evaluations, while the objective method was based on the weight of medication used. With the exception of one study (Loh et al.)[24] that included subjective and objective assessments, all of the other studies employed subjective measures to determine adherence. The adherence rate was reported as a percentage in almost all studies (**Table 1**). Only one study[25] reported it as a score using Morisky Medication Adherence Scale questionnaire. The range of the adherence rate was 28-87%, with an average of 55.8% (calculated by averaging the individual rate provided in the studies).

Forgetfulness was the largest contributor to non-adherence (range 63.1-77.8%),[22,24,26] followed by adverse events (range 26.4-61.5%)[22,23] and fear of adverse events (range 3.8-31.5%).[11,26] Disliking the sensory attributes was reported as a reason for non-adherence by 47.7% of participants.[22] Additionally, improvements in symptoms contributed to non-adherence in 36-41% of participants.[11,25,26] Some participants (30.8%) felt that their symptoms were not bothersome, resulting in non-adherence.[11]

A minority of participants were non-adherent due to perceived ineffectiveness (range 0.5-10.5%)[11,23,26] or reported it as not helpful (6.9%).[23] Some also cited logistic issues, such as number of dependent children (40%),[25] a busy schedule (9.2%),[11] troublesome to use (5.3%),[26] or running out of supply (2.7%).[11]

Secondary outcome 1: Sensory attribute preferences

Eleven satisfied the inclusion criteria regarding sensory attribute preferences, assessed through either questionnaires or phone interviews.[13,22,28-36] The main attributes resulting in significantly greater sensory attribute preference or intensity included scent (38%), immediate taste (28.5%), or aftertaste (24.3%) of the INCS.

Among the included studies, the study by Khanna et al. is the only study that compared sensory attribute preferences to four types of INCS: mometasone furoate stood out with the highest overall liking by 68% of participants when compared with budesonide (43%), fluticasone propionate (31%) and beclomethasone dipropionate (23%).[29]

Meltzer et al. conducted a series of RCTs comparing mometasone furoate, fluticasone propionate, and fluticasone furoate.[30-32] An overall preference for mometasone furoate over fluticasone propionate was observed (53% vs 34%), especially concerning the immediate taste (46% vs 21%), aftertaste (45% vs 21%), and urge to sneeze (28% vs 12%).[31] A separate study (N = 120) reported an overall preference for fluticasone furoate over fluticasone propionate (60% vs 33%).[30] This trial (N = 360) was repeated to include matched placebo, and both studies were in favor of fluticasone furoate for its scent, aftertaste, and throat rundown.[30,32]

Triamcinolone acetonide is preferred over fluticasone propionate (50% vs 25%) and mometasone furoate (50% vs 25%). An overall treatment difference was seen in several sensory attributes, including drying feeling, scent, immediate taste, aftertaste, and bitter taste.[13] Conversely, another study found that majority of participants reporting unfavorable sensory attributes were on triamcinolone acetonide (83.3%), followed by mometasone furoate (65.2%) and fluticasone furoate (28.6%).[22]

Despite having equivalent efficacy in symptomatic alleviation, circlesonide was preferred over mometasone furoate (68.1% vs 31.7%), which was largely due to better scent and taste profiles with fewer throat rundown and dripping complaints.[28] However, when comparing fluticasone propionate to ciclesonide, the former was preferred (55.4% vs 25.7%) due to its soothing sensation (56.7% vs 20.3%) and scent (50% vs 8.1%).[34]

Two different studies concluded that fluticasone furoate is preferred over mometasone furoate, as reported by Yanez et al. (56% vs 32%)[35] and Yonezaki et al. (52.5% vs 22.5%).[36] Meanwhile, Naclerio et al. enrolled 2,500 adults with AR, found that the most bothersome attribute was drying feeling (47%), followed by throat rundown (41%), immediate taste (32%), and nasal irritation (17%).[33] Based on a comparison of the top three INCS sensory traits (aftertaste, scent, and taste) among Asians, Americans, and mixed populations, no discernible differences in preferences were found (**Table 2**).

Table 2. Comparison of sensory attributes across different demographics.

Population	Study, country	Sensory attributes of INCS		
		Aftertaste (%)	Taste (%)	Scent (%)
Asian	Lee et al (2021), Singapore[22]	21.5	20	16.9
	Khanna et al (2005), India[29]	7-27	18-36	38-79
	Vashney et al (2012), India[34]	8.1 vs 16.2	16.2 vs 23	8.1 vs 50
USA	Berger et al (2013)[28]	NR	32-68	37-63
	Meltzer et al (2005)[31]	21-45	21-46	24-56
	Meltzer et al (2008)[30]	22-44	21-47	29-64
	Meltzer et al (2010)[32]	18-60	NR	27-58
	Naclerio et al (2007)[33]	NR	32	NR
	Stokes et al (2004)[13]	12.8-21.1	14.3-26.1	14.8-54.3
Mixed	Yanez et al (2016), Argentina, Australia, Russia, South Korea[35]	18-25	18-23	20-28

Abbreviation: NR, not reported.

Secondary outcome 2: Adverse events

Eighteen studies reported adverse events and TEAE related to the use of INCS.[22,23,32,33,35,37-49] Studies on fluticasone furoate and mometasone furoate showed a wide range of frequencies for adverse events, ranging from 2% to 77% for fluticasone furoate[32,35,39,40,46] and 4% to 62.3% for mometasone furoate.[35,37] Fluticasone propionate contributed to 21% adverse events,[32] while beclomethasone dipropionate reported 20.3%.[43]

TEAEs were observed in 13.8% to 68.2% of participants using beclomethasone dipropionate,[47,49] 19.4% to 43.7% using triamcinolone acetonide,[41,48] 34% using fluticasone furoate,[42] and 16.8% using fluticasone propionate.[41]

Common local adverse events include epistaxis,[22,23,37-40,42-49] nasal dryness,[41,46] nasal discomfort,[35,41-43,45-47] and nasal irritation,[13,28,29,31-36,48] while systemic adverse events comprise headache,[22,23,32,33,40,41,43-47,49] nasopharyngitis,[23,39,40,46,47,49] and pharyngolaryngeal pain.[40,46] The frequency of adverse events from each study were summarized in **Table 1**.

Eight placebo-controlled RCTs[39,40,42,43,45-47,49] included for meta-analysis has detected no significant difference in risk of adverse events between the INCS and control groups (RR 1.05; 95%CI, 0.88-1.24; p = 0.61; high certainty evidence) (**Figure 2**).

Risk-of-bias assessment

Table 3 and 4 outline the quality assessment of the RCTs and cross-sectional studies, respectively. There was a low risk of bias in 17 studies (54.8%), a moderate risk in 10 studies (32.3%), and a high risk in 4 studies (12.9%) (**Tables 3 and 4**). Only three (33.3%) of the nine cross-sectional studies implemented objective standard criteria for measuring the outcome, another three (33.3%) identified confounding factors, and two (22.2%) described strategies that mitigate confounding factors. Only 10 of the 21 RCTs (47.6%) utilized true randomization to assign individuals to treatment groups, while six studies (28.6%) employed personnel delivering the treatment blindly to treatment groups.

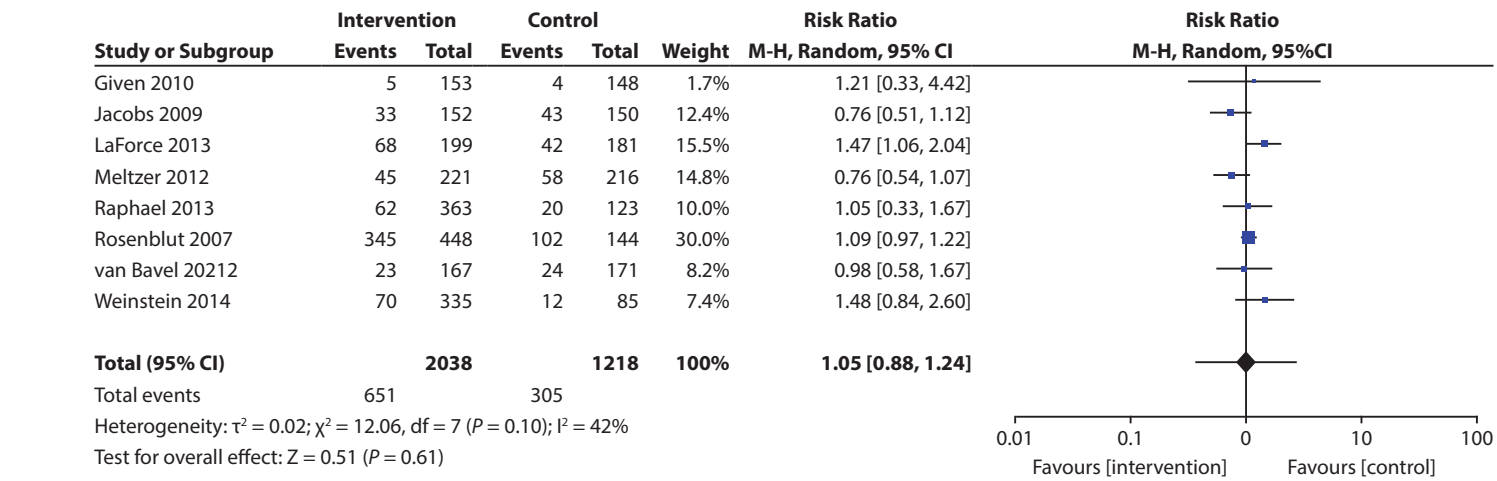


Figure 2. Adverse effects of intranasal corticosteroids versus control.

Table 3. Quality assessment of RCTs.

Study	Questions													Score (%)	Risk of bias
	1	2	3	4	5	6	7	8	9	10	11	12	13		
Antila et al (2016)	Yes	No	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	69.2	Moderate
Berger et al (2013)	No	No	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	61.5	Moderate
Given et al (2010)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	92.3	Low
Jacobs et al (2009)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	92.3	Low
Karaulov et al (2019)	No	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	69.2	Moderate
Khanna et al (2005)	No	No	Unclear	No	No	Yes	No	Yes	No	Yes	Yes	Unclear	No	36.4	High
LaForce et al (2013)	No	No	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	61.5	Moderate
Meltzer et al (2005)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	92.3	Low
Metlzer et al (2008)	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	84.6	Low
Metlzer et al (2010)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	84.6	Low
Meltzer et al (2012)	No	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	69.2	Moderate
Pitsios et al (2006)	No	No	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	53.8	Moderate
Raphael et al (2013)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	84.6	Low
Rosenblut et al (2007)	No	Yes	Yes	Yes	No	Yes	No	No	No	No	No	No	Yes	38.5	High
Stokes et al (2004)	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	76.9	Low
Van Bavel et al (2012)	No	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	76.9	Low
Varshney et al (2012)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	76.9	Low
Wang et al (2014)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100	Low
Weinstein et al (2014)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	84.6	Low
Yenes et al (2016)	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	92.3	Low
Yonezaki et al (2015)	No	No	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes	No	38.5	High

Questions: 1. Was true randomization used for assignment of participants to treatment groups? 2. Was allocation to treatment groups concealed? 3. Were treatment groups similar at the baseline? 4. Were participants blind to treatment assignment? 5. Were those delivering the treatment blind to treatment assignment? 6. Were treatment groups treated identically other than the intervention of interest? 7. Were outcome assessors blind to treatment assignment? 8. Were outcomes measured in the same way for treatment groups? 9. Were outcomes measured in a reliable way? 10. Was follow-up complete and if not, were differences between groups in terms of their follow-up adequately described and analyzed? 11. Were participants analyzed in the groups to which they were randomized? 12. Was appropriate statistical analysis used? 13. Was the trial design appropriate and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?

Table 4. Quality assessment of cross-sectional studies.

Study	Questions								Score (%)	Risk of bias
	1	2	3	4	5	6	7	8		
Alumuitairi et al (2020)	Yes	Yes	No	No	No	No	Yes	Yes	50	Moderate
Beniger et al (2008)	Yes	Yes	Yes	No	No	No	No	Yes	50	Moderate
Hankin et al (2012)	Yes	Yes	No	No	No	No	Yes	Yes	50	Moderate
Lee et al (2021)	Yes	Yes	Yes	No	Yes	No	Yes	Yes	75	Low
Loh et al (2004)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	75	Low
Mahadevia et al (2004)	Yes	Yes	No	No	No	No	No	Yes	37.5	High
Naclerio et al (2007)	Yes	Yes	No	Yes	No	No	No	Yes	50	Moderate
Ocak et al (2017)	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	87.5	Low
Manjit Singh et al (2022)	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	87.5	Low
Weber et al (2006)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	75	Low

Questions: 1. Were the criteria for inclusion in the sample clearly defined? 2. Were the study subjects and the setting described in detail? 3. Was the exposure measured in a valid and reliable way? 4. Were objective, standard criteria used for measurement of the condition? 5. Were the confounding factors identified? 6. Were strategies to deal with confounding factors stated? 7. Were the outcomes measured in a valid and reliable way? 8. Was appropriate statistical analysis used?

Discussion

To the best of our knowledge, this review is the first to evaluate medication adherence to INCS while considering the significance of adverse events and preferences for sensory attributes as contributory factors.

An average adherence rate of 55.8% was reported from eight studies on medication adherence to INCS,[11,12,22-27] which corresponds to the reported adherence rate of 50% for chronic treatments according to a report by the World Health Organization.[50] The significant variance in adherence rates (28-87%) between the studies may be due to the use of non-standardized subjective evaluations that incorporate self-reports and assessments from clinicians,[11,12,22-27] which are frequently used in clinical settings because of their affordability and practicality but have drawbacks of their own.[51] These assessments have low sensitivity and specificity due to the likelihood of inaccurate data input by patients or faulty communication skills and queries, casting doubt on their reliability, and can only provide a rough estimate of medication adherence.[51] But it's also important to note that a study on the medication adherence of chronic medical conditions discovered that a direct interview showed a strong correlation with pill counts, correctly identifying 75% of patients who were following their treatment plan.[52]

Medication adherence needs to be at least 80% when expressed as a proportion of days covered.[53] Consequently, 55.8% of adherence is deemed to be suboptimal. It is worth noting that a review found that patients with respiratory disease have lower medication adherence (range 51-55%) than patients with cardiovascular disease, infectious disease, cancer, fertility, psychiatry, epilepsy, and general medical disorders (range 70-80%).[54] One of the reasons reported for this mismatch is patients' impression of their medical state. Patients with respiratory diseases may perceive their symptoms as less severe than those of other illnesses, which may reduce their motivation to follow treatment recommendations.[55]

The current review identified forgetfulness, adverse effects, and sensory characteristics as contributing factors to non-adherence. Forgetfulness is a major contributing factor to medication non-adherence in an assortment of medical diseases. Claxton et al. observed that forgetfulness was one of the most common reasons for non-adherence to INCS among patients with AR.[54] Similarly, another study by Manjit Singh et al. highlighted forgetfulness as a prevalent factor contributing to non-adherence to INCS.[11] Among patients with AR, forgetfulness was reported to be a major cause of non-adherence by Bousquet et al., coupled with worries about adverse effects and a lack of perceived efficacy.[56] Forgetfulness can stem from various factors, including busy lifestyles, cognitive impairment, lack of routine, or simply not prioritizing medication intake.[57] Moreover, forgetfulness may be compounded by the asymptomatic nature of AR during periods of remission or low allergen exposure, leading patients to underestimate the importance of adhering to their medication schedules.[11] This lack of perceived immediate benefit can further contribute to non-adherence behaviors.

Addressing forgetfulness requires strategies that are tailored to individual needs and circumstances. The use of reminders can be an effective way to combat forgetfulness. This could include setting alarms on smartphones or using medication reminder applications. Studies have shown that electronic reminders significantly improve medication adherence.[58] Innovative technologies, such as smart pill bottles or electronic monitoring devices, can provide real-time feedback and reminders to promote adherence. These technologies can be beneficial for individuals who struggle with forgetfulness. Syncing medication schedules with daily routines or other habitual activities can help

reinforce adherence. For example, taking medications at mealtimes or associating medication administration with brushing teeth can serve as reminders. Involving family members or caregivers in medication management can provide additional support and reminders. This could involve having a family member help set up pill organizers or providing verbal reminders. Providing education about the importance of medication adherence and the potential consequences of non-adherence can improve understanding and motivation. Behavioral interventions, such as motivational interviewing or cognitive-behavioral therapy, can help address underlying reasons for forgetfulness and enhance motivation and self-efficacy for medication adherence.

The primary attributes influencing preference for INCS include scent, immediate taste, aftertaste, and throat sensation, along with factors like the urge to sneeze, dryness, and dripping. Sensory attributes play a critical role in determining patient preference and maximizing the effectiveness of INCS while ensuring adherence to therapy.[31] Previous studies have shown that higher intensity of unfavorable sensory attributes leads to reduced adherence to INCS.[22] When drugs in the same class have similar safety and efficacy profiles, other characteristics become pivotal in product acceptance.[30] In the face of sensory intolerance to the usage of INCS, different strategies can be implemented. For instance, it is essential to correct misunderstandings and concerns about INCS therapy, as well as to educate patients about the possible sensory characteristics they might experience and provide reassurance that these effects are usually temporal. Choosing an INCS formulation with desirable sensory properties, such as minimal odor and taste, may help to avoid this problem in the first place, as newer generation INCS formulations may have better sensory profiles than earlier formulations.[29] Hence, selecting the INCS that align with a patient's sensory preferences can improves adherence to INCS therapy.[30]

Variations in sensory attributes may exist among different populations. A meta-analysis of olfactory impairment in COVID-19 patients from various populations revealed a lower frequency in Asians compared to Europeans and North Americans.[59] This may suggest that, in addition to variations in case reporting between countries, there exist disparities in the perceptions of olfactory anomalies among different populations. When evaluated amongst different populations, the sensory attributes of INCS in Asian countries and the United States are relatively comparable (**Table 2**). Although there are variations in rates even across the same groups, the rates appear to be consistent when the top three sensory attributes (aftertaste, taste, and scent) were considered for comparison. Remarkably, a mixed population with individuals from South Korea, Australia, Argentina, and Russia exhibited the exact same predisposition. This implies that sensory preferences are a worldwide concern rather than a population-specific phenomenon.

Adverse events linked to INCS[22,23] and the fear of experiencing such events[11,26] were among the leading causes of non-adherence. These events commonly include epistaxis, nasal dryness, nasal irritation, headache, nasopharyngitis and pharyngolaryngeal pain. These effects can cause discomfort and inconvenience for patients, potentially leading to discontinuation or reduced adherence to treatment. Furthermore, these consequences have the potential to reduce patients' quality of life and satisfaction with their therapy. The negative impact on quality of life may lead to decreased adherence as patients weigh the perceived benefits of treatment against its adverse effects. A meta-analysis of all the RCTs found that there does not seem to be a significant variation in the risk of adverse reactions between the INCS and the control groups. This could indicate that perception, rather than fact, is the primary force at play. Given that RCTs or observational studies on adverse events may not fully reflect real-world occurrence because of stringent patient selection criteria and brief trial durations,[60] it is important to address patients' concerns and perceptions about possible adverse reactions of medications.[61] Unresolved fears and concerns may prompt treatment discontinuation, imposing unnecessary financial burden and compromising quality of life.[23]

The impact of additional therapies on INCS compliance varies based on the type of therapy, the patient's health, and their perspectives and experiences with the treatments. Additional therapies can have an impact on INCS compliance, both positively and negatively. Combining INCS with other medications, such as antihistamines or leukotriene receptor antagonists, may enhance symptom management, resulting in higher patient satisfaction and compliance.[7] That said, increasing the number of drugs prescribed might make a patient's treatment plan more complicated, which can cause confusion and lower adherence.[11] Patients who are taking other drugs in addition to INCS may find it difficult to adhere to the regimen regularly. This can be particularly challenging for elderly patients or those with cognitive impairments. New adverse reactions from additional treatments could discourage patients from utilizing INCS. Patients may mistakenly link the negative effects from other medications to INCS and discontinue their use. Educating patients about the importance of INCS and how they work in conjunction with additional treatments can improve compliance. Patients need to understand the benefits and the role of each medication in their treatment plan. Clear instructions on how to use INCS, potential adverse effects, and the importance of adherence can empower patients to follow their regimen more closely. Where possible, simplifying treatment regimens can enhance compliance. Using combination products that include INCS and other medications in a single formulation can reduce the pill burden and improve adherence. Regular follow-ups and reassessments of the treatment plan can help in making necessary adjustments to keep the regimen manageable for the patient.

A multifaceted strategy to enhance medication adherence should prioritize understanding patients' immediate concerns while considering long-term treatment goals.[61] It is crucial to reiterate the chronic nature of AR and the relevance of regular medical treatment.[23] Aside from that, patients should receive thorough training and regular reviews on proper INCS administration techniques to optimize efficacy and minimize side effects.[22,23] Effective communication between physicians and patients is key for aligning treatment expectations and addressing concerns about adverse effects.[61] Involving patients in the decision-making process regarding INCS selection allows them to weigh the risk and benefit, fostering greater commitment from patients.[61]

Several strengths of the present review include a well-defined research question, an extensive search of electronic databases, and a rigorous assessment of the quality of studies. The exclusion of non-English articles is one of the constraints, albeit it had little effect because there were not many non-English articles discovered. Significant clinical and methodological heterogeneity was also demonstrated by the included studies, particularly related to the type and severity of AR, and assessment of the outcomes. Furthermore, the quality of the review may be impacted by the fact that almost half of the studies were classified as high- or moderate-risk, raising concerns about the robustness of the evidence.

Conclusion

This review provides a comprehensive overview of medication adherence, sensory attribute preferences, and adverse effects related to INCS use in AR patients. The insights gained contribute to a holistic understanding of interplay between sensory attribute preferences, adverse events, and treatment adherence. This review observed that medication adherence to INCS is far from optimal, with non-adherence mostly driven by forgetfulness, sensory attribute preferences, and INCS-related adverse effects. A multimodal strategy for improving medication adherence should include measures to address the contributing factors. Fostering efficient communication between physicians and patients, as well as incorporating patients in treatment decision-making processes, can help to empower them and strengthen their commitment to therapy.

Conflicts of Interest

BA, FDZ and AH declare no conflict of interest regarding the publication of this article. SH declares receipt of speaker fees from Sanofi and Abbott.

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- Conceptualisation, BA, FDZ, AH and SH
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- Formal analysis, BA, FDZ and AH
- Funding acquisition, BA
- Investigation, BA, FDZ, AH
- Writing – original draft, BA, FDZ, AH and SH
- Writing – review and editing, BA, FDZ, AH, SH

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Supplementary Material

Supplement 1. Full search strategy.
PICO keywords:

	Concepts
Population	Allergic rhinitis
Intervention	Intranasal corticosteroid*, intranasal steroid*, nasal steroid*
Comparators	-
Outcomes	Adheren*, complian*, preference, adverse effect*, side effect*, safety

(allergic rhinitis) AND (intranasal corticosteroid* OR intranasal steroid* OR nasal steroid*) AND (adheren* OR complian* OR preference OR adverse effect* OR side effect* OR safety)

Filter: 1 Jan 2004 – 20 Sep 2023, English, Human
Seach: title/abstract/keywords

PubMed
Search – All fields

History and Search Details

Download Delete

Search	Actions	Details	Query	Results	Time
#7	•••	›	Search: **(allergic rhinitis) AND (intranasal corticosteroid* OR intranasal steroid* OR nasal steroid*) AND (adheren* OR complian* OR preference OR adverse effect* OR side effect* OR safety)** Filters: **Humans, English, from 2004/1/1 - 2023/9/30**	451	21:22:49
#6	•••	›	Search: **(allergic rhinitis) AND (intranasal corticosteroid* OR intranasal steroid* OR nasal steroid*) AND (adheren* OR complian* OR preference OR adverse effect* OR side effect* OR safety)** Filters: **Humans, from 2004/1/1 - 2023/9/30**	484	21:22:44
#5	•••	›	Search: **(allergic rhinitis) AND (intranasal corticosteroid* OR intranasal steroid* OR nasal steroid*) AND (adheren* OR complian* OR preference OR adverse effect* OR side effect* OR safety)** Filters: **from 2004/1/1 - 2023/9/30**	576	21:22:35
#4	•••	›	Search: **(allergic rhinitis) AND (intranasal corticosteroid* OR intranasal steroid* OR nasal steroid*) AND (adheren* OR complian* OR preference OR adverse effect* OR side effect* OR safety)**	871	21:22:09

PubMed search result: 451 articles

Web of Science
Search – Topic (title, abstract, indexing)

Web of Science Search Strategy (v0.1)

Database: All Databases

Entitlements:

- WOS: 1970 to 2023
- DIIDW: 2007 to 2023
- KJD: 1980 to 2023
- PPRN: 1991 to 2023
- PQDT: 1637 to 2023
- SCIELO: 2002 to 2023

Searches:

1: (allergic rhinitis) AND (intranasal corticosteroid* OR intranasal steroid* OR nasal steroid*) AND (adheren* OR complian* OR preference OR adverse effect* OR side effect* OR safety) (Topic) and Preprint Citation Index (Exclude – Database) Date Run: Thu Oct 05 2023 09:28:20 GMT+0800 (Malaysia Time) Results: 1273

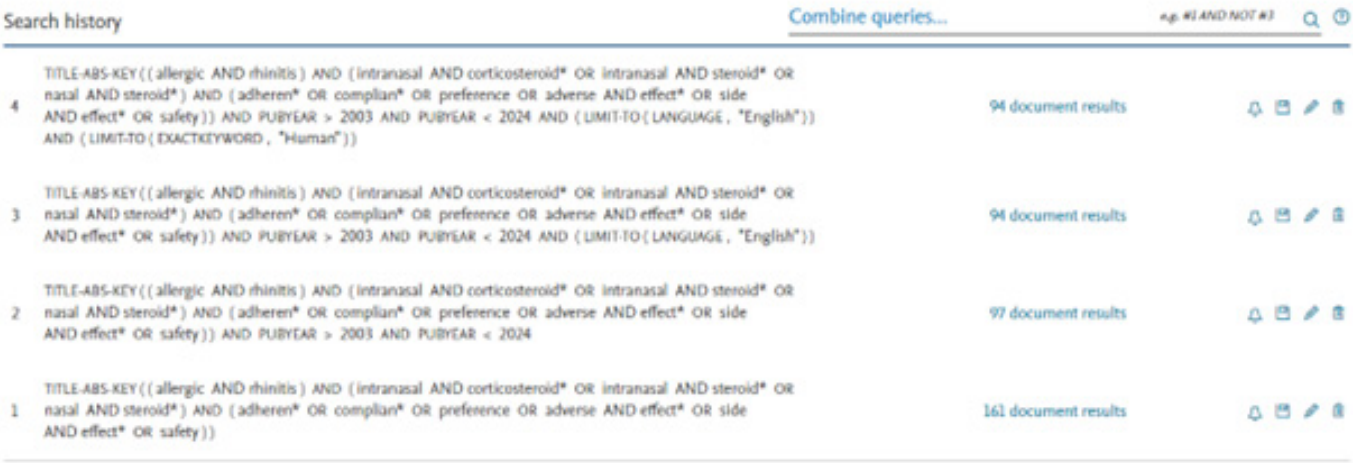
2: (allergic rhinitis) AND (intranasal corticosteroid* OR intranasal steroid* OR nasal steroid*) AND (adheren* OR complian* OR preference OR adverse effect* OR side effect* OR safety) (Topic) and Preprint Citation Index (Exclude – Database) Timespan: 2004-01-01 to 2023-09-30 Date Run: Thu Oct 05 2023 09:28:59 GMT+0800 (Malaysia Time) Results: 836

3: (allergic rhinitis) AND (intranasal corticosteroid* OR intranasal steroid* OR nasal steroid*) AND (adheren* OR complian* OR preference OR adverse effect* OR side effect* OR safety) (Topic) Timespan: 2004-01-01 to 2023-09-30 Date Run: Thu Oct 05 2023 09:29:04 GMT+0800 (Malaysia Time) Results: 836

4: (allergic rhinitis) AND (intranasal corticosteroid* OR intranasal steroid* OR nasal steroid*) AND (adheren* OR complian* OR preference OR adverse effect* OR side effect* OR safety) (Topic) and English (Languages) Timespan: 2004-01-01 to 2023-09-30 Date Run: Thu Oct 05 2023 09:30:15 GMT+0800 (Malaysia Time) Results: 808

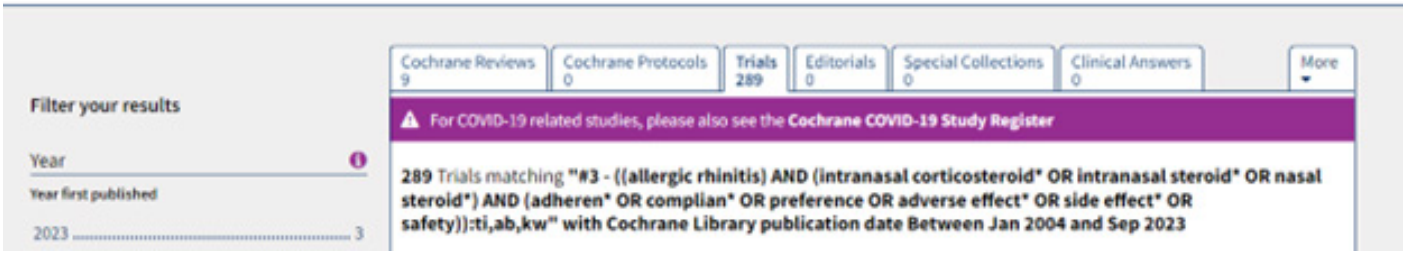
Web of Science search result: 808 articles

Scopus
Search – title/abstract/keywords



Scopus search result: 94 articles

Cochrane Central
Search – title/abstract/keyword



Cochrane search result: 277 articles; manually removed 21 titles (published outside timeline)
Final search result: 256 articles