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## Head-to-head comparison of fluticasone propionate and fluticasone furoate in allergic rhinitis & chronic rhinosinusitis with nasal polyposis: A meta-analysis

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### Abstract

**Background:** Allergic rhinitis (AR) and chronic rhinosinusitis with nasal polyposis (CRSwNP) are highly prevalent inflammatory disorders of the upper airway. Intranasal corticosteroids (INCS) represent the first-line treatment for both conditions; however, head-to-head comparisons between fluticasone propionate (FP) and fluticasone furoate (FF) are scarce. FF possesses higher glucocorticoid receptor affinity and extended mucosal retention, potentially translating into faster and superior symptom control compared to FP. Nonetheless, the comparative efficacy and safety of these agents in AR and CRSwNP remain unclear.

**Objective:** To perform a simulated head-to-head meta-analysis comparing FP and FF in the management of AR and CRSwNP, evaluating clinical efficacy, rapidity of symptom relief, patient preference and polyp size reduction-surgery avoidance, and safety (epistaxis incidence).

**Methodology:** Hypothetical but realistic data were derived from four AR trials (total N=1,200), two CRSwNP trials (N=350), and five studies evaluating epistaxis risk (N=1,500). Outcomes included mean differences (MD) in reflective Total Nasal Symptom Score (rTNSS), time to symptom onset (days), patient preference (%), change in endoscopic polyp score, surgery avoidance rate (%), and relative risk (RR) for epistaxis. Standard meta-analytic techniques (fixed/random effects), estimation of heterogeneity ( $I^2$ ), and calculation of pooled effect sizes were employed. Published clinical and pharmacologic studies served as reference anchors.

**Results:** In AR, FF reduced rTNSS by a pooled mean difference of  $-0.25 (\pm 0.10; P=0.01; I^2=45\%)$  and expedited symptom relief by approximately 0.8 days ( $P=0.005; I^2=30\%$ ) compared to FP. Patient preference favored FF significantly, with 58% opting for FF versus 27% for FP (difference  $+28 \pm 6\%; p<0.001; I^2=20\%$ ). In CRSwNP, both agents showed comparable efficacy: polyp score change was negligible (MD  $+0.02; P=0.80; I^2=0\%$ ), and surgery avoidance exhibited a minor, non-significant preference for FP ( $\Delta +5\%; P=0.45; I^2=10\%$ ). Safety profiles were largely similar, with epistaxis risk ratio at  $1.10 (\pm 0.05; P=0.15; I^2=25\%)$ .

**Conclusion:** Our simulated meta-analysis supports that FF offers modest but statistically significant benefits in AR including quicker symptom relief and stronger patient preference likely attributable to its pharmacologic profile and sensory advantages. In CRSwNP, FF and FP perform similarly in reducing polyp burden and avoiding surgery. Safety profiles overlap, with no appreciable difference in the risk of epistaxis. These findings suggest FF may be favored in AR for its patient-centered advantages, while either agent may be appropriate in CRSwNP. However, these modeled results should be confirmed by real-world, well-powered, head-to-head randomized trials with extended follow-up and quality-of-life and economic evaluations.

**Keywords:** Allergic rhinitis, chronic rhinosinusitis with nasal polyposis, fluticasone furoate, fluticasone propionate, intranasal corticosteroids

### Introduction

Inhaled and intranasal corticosteroids, particularly fluticasone esters, are foundational in managing asthma and allergic rhinitis. Two key formulations fluticasone furoate (FF) and fluticasone propionate (FP) exhibit distinct pharmacokinetic and pharmacodynamic characteristics [1].

Despite a shared corticosteroid backbone, FF and FP differ in Glucocorticoid receptor affinity and lipophilicity, with FF showing higher binding and extended tissue retention [2, 3]; Dosing regimens, as FF is often prescribed once daily, compared to twice-daily dosing for FP. [3]; Onset of action, sensory experience, and adherence, with studies reporting that patients prefer FF's nasal formulation in terms of scent and aftertaste relief [4].

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These differences suggest potential clinical advantages for FF. However, the extent to which these translate into superior patient outcomes is still under investigation. Key comparative studies include A model-based meta-analysis (14 RCTs; N=6,640), which reported similar FEV<sub>1</sub> improvement by Week 2 for both drugs, although FF showed a plateau only at higher doses <sup>[1]</sup>; Two RCTs in seasonal allergic rhinitis (SAR), (Okubo *et al.*, 2009; Meltzer *et al.*, 2010) demonstrated comparable nasal and ocular symptom relief between FF and FP; FF onset was faster (day 1 vs. day 2) and exhibited better patient preference regarding sensory attributes <sup>[4, 5]</sup>. Despite these findings, a comprehensive synthesis covering efficacy, onset of action, safety, tolerability, and dosing adherence across both conditions has yet to be performed.

Objectives of This meta-analysis aims to rigorously compare FF and FP by evaluating the Efficacy [pooled measures of lung function (FEV<sub>1</sub> for asthma) and symptom scores (nasal/ocular in rhinitis)]; Onset of effect [time to therapeutic response]; Safety and tolerability [adverse events and patient preference]; Adherence implications [impact of once-daily dosing on compliance].

By providing a unified synthesis, this study will clarify whether pharmacologic differences between FF and FP result in meaningful clinical benefits or if FP remains an equally effective option.

## Materials and Methods

The review will adhere to PRISMA 2020 standards and be registered on PROSPERO before data extraction begins. Eligibility Criteria (PICOS).

### Adolescents and adults (≥ 12 years) diagnosed with

- Allergic rhinitis (seasonal or perennial)
- Chronic rhinosinusitis (with or without nasal polyps, CRS/CRSwNP)

### Outcomes to be measured

- **Rhinitis:** Total Nasal Symptom Score (TNSS), Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ), onset of action
- **CRS:** Patient-reported symptom scores (e.g., VAS), endoscopic polyp scores, need for surgery, quality of life
- **Study types:** Randomized controlled trials (parallel or crossover), with follow-up ≥ 4 weeks in rhinitis and ≥ 12 weeks in CRS.

Outcome	Number of Trials	N (Total)	FF vs FP Effect (Mean Difference ±SE)	P-Value	I <sup>2</sup> (Heterogeneity)
Seasonal AR (rTNSS change)	4	1200	-0.25±0.10 (FF favored)	0.01	45%
Onset of action (days)	3	700	-0.8±0.3 (FF faster)	0.005	30%
Patient preference (% favoring FF)	3	900	+28±6 %	<0.001	20%
CRSwNP polyp score reduction	2	350	+0.02± 0.08 (NS)	0.80	0%
CRSwNP surgery avoidance (%)	2	300	+5±7 % (FP favored slightly)	0.45	10%
Epistaxis incidence (RR)	5	1500	1.10±0.05	0.15	25%

## Discussion

Our simulated meta-analysis indicates that Fluticasone Furoate (FF) offers a modest but statistically significant advantage over Fluticasone Propionate (FP) in the management of Allergic Rhinitis (AR). Specifically, FF demonstrated a mean reduction in total nasal symptom scores of approximately -0.25 points and an accelerated onset of action by roughly 0.8 days. This outcome aligns

Study selection process is by dual independent screening of titles/abstracts, followed by full-text reviews, Conflicts resolved by consensus or a third reviewer, data extraction variables include Study details, Population, diagnosis (e.g., SAR, perennial AR, CRS w/ or w/o NP), age, sample size, Intervention/comparator: Dose, regimen, duration and Outcomes like AR: TNSS, RQLQ, onset time (e.g., day of first symptom improvement), CRS: VAS symptom scores, endoscopic grading, CT scores, surgical intervention rates; Adverse events: Epistaxis, local irritation, Risk of bias (assessed by Cochrane Risk of Bias Tool).

Statistical analysis is by pairwise meta-analysis of continuous outcomes (e.g., TNSS, endoscopic scores): Mean difference (MD) + 95% CI; Dichotomous outcomes (e.g., surgery avoidance): Risk ratio (RR) + 95% CI. Sensitivity analyses Excluding high risk-of-bias studies and short-duration trials and Publication bias: Funnel plots and Egger's test (if ≥ 10 studies) using Software & Tools like Analyses: R (packages: Meta, metafor), RevMan 5.4 and Network meta-analysis: if indirect comparisons exist (e.g., including exhalation delivery system steroid for CRS).

This methodology ensures a rigorous, transparent, and clinically relevant synthesis of FF vs FP in both allergic rhinitis and chronic rhinosinusitis.

## Results

In patients with seasonal Allergic Rhinitis based on the crossover study where both FF and FP improved symptoms, but FF had a slightly larger reduction in rTNSS (-0.8 vs. -0.6), Onset of Action FF showed effect from day 1, versus day 2 for FP, Patient Preference.

In that study, approximately 58 % preferred FF vs 27 % for FP; CRSwNP Polyp Score: Scale of 0-3 endoscopic, RCTs show no significant difference; Surgery Avoidance

Some evidence shows FP drops reduce the need for surgery; Epistaxis Risk in higher doses of intranasal steroids moderately increase bleeding risk .Our results showed that in patients with allergic rhinitis FF offers a modest but significant improvement in symptoms and faster onset, along with better patient preference, likely due to once-daily dosing and better sensory profile in Chronic Rhinosinusitis with Nasal Polyposis (CRSwNP)

Both FP and FF show comparable efficacy in reducing polyp size. FP may slightly edge out in reducing need for surgery, but this is not statistically significant and when it comes to side effects like Epistaxis no meaningful difference in bleeding risk between FF and FP.

with pharmacodynamic studies showing FF's enhanced glucocorticoid receptor affinity and extended retention in target tissues, which fosters more sustained anti-inflammatory effects compared to FP <sup>[6]</sup>.

In terms of patient-reported outcomes, our simulation found that approximately 58% of participants favored FF over 27% for FP. This preference likely stems from sensory advantages such as finer mist, lack of aftertaste, and a gentle

spray as well as once-daily dosing convenience, which together enhance adherence and perceived relief. These findings are consistent with crossover trials showcasing FF's favourable user experience in seasonal AR [17].

When examining chronic rhinosinusitis with nasal polyposis (CRSwNP), our analysis revealed comparable efficacy between FF and FP in reducing polyp scores, with no statistically significant difference in surgical avoidance rates. This is in concordance with broader intranasal corticosteroid reviews, which report similar effectiveness across different formulations in CRSwNP management [18]. Additionally, although FP nasal drops have been historically investigated for polyp size reduction, our simulated trend favoring FP in surgery avoidance did not reach significance, likely due to limited sample sizes and variability in study protocols [19]. Regarding safety, both FF and FP exhibited a modestly elevated epistaxis risk ( $RR \approx 1.10$ ), but this was not statistically significant. Intranasal corticosteroids, in general, have a known association with mild nasal bleeding; however, comparative meta-analyses do not indicate a particular steroid as significantly safer or riskier than others [10].

Collectively, these results suggest that FF may be preferable for allergic rhinitis, particularly when rapid symptom relief and improved patient adherence are priorities. In CRSwNP, therapeutic decisions can hinge more on practical considerations such as cost, availability, patient familiarity with a delivery device since clinical effectiveness is similar. Importantly, both FF and FP maintain strong safety profiles, with no major differences in epistaxis risk.

However, several limitations must be acknowledged. Our findings are based on simulated data and thus require confirmation in real-world, head-to-head randomized controlled trials (RCTs). The small number of studies, variation in dosing schedules (spray versus drop), and treatment duration across trials may introduce heterogeneity. Moreover, long-term patient outcomes such as recurrence rates, corticosteroid tolerance, quality of life, and cost-effectiveness were not evaluated. Future research should focus on robust RCTs comparing FF and FP across both AR and CRSwNP, with a focus on patient-centered outcomes and economic analyses.

## Conclusion

Our simulated meta-analysis suggests that Fluticasone Furoate (FF) provides a modest but clinically meaningful edge over Fluticasone Propionate (FP) in Allergic Rhinitis (AR), delivering faster relief of symptoms and earning higher patient preference. This advantage is likely due to FF's greater glucocorticoid receptor affinity and prolonged tissue retention, which enhance anti-inflammatory efficacy.

In contrast, chronic rhinosinusitis with nasal polyposis (CRSwNP) appears to respond similarly to both FF and FP, with negligible differences in polyp size reduction or avoidance of surgery. While FP nasal drops have a documented role in reducing polyp burden, the simulated slight trend favoring FP did not reach significance, likely due to variations in dosing and small sample sizes.

Regarding safety, both steroids have comparable low risk for epistaxis, consistent with known side effect profiles of intranasal corticosteroids.

## Conflict of Interest

Not available

## Financial Support

Not available

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