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REVIEW ARTICLE

# Meta-analysis and cost-effectiveness analysis of intranasal corticosteroid treatment in allergic rhinitis with ocular symptoms

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## Abstract

**Background:** Intranasal corticosteroid (INCS) has a beneficial effect on ocular symptoms in allergic rhinitis (AR). To our knowledge, the cost-effectiveness of available INCS for AR with ocular symptoms is yet to be demonstrated.

**Objective:** To evaluate the cost-effectiveness of INCSs including Budesonide (BANS), Mometasone furoate (MFNS), Triamcinolone (TANS), and Fluticasone furoate (FFNS) on ocular symptoms associated with AR in the Thai context.

**Methods:** The percentage of effectiveness in improving total ocular symptoms score (TOSS) was derived from the result of a meta-analysis that estimated the SMD of each INCS treatment compared to placebo as clinical input parameters. A cost-effectiveness analysis based on a decision-tree model to assess one-year costs and outcomes from a Thai societal perspective. The outcomes were to compare incremental cost-effectiveness ratio (ICER). Probabilistic sensitivity analyses (PSA) were also conducted to capture parameter uncertainties.

**Results:** 13 eligible RCTs with a total of 3,722 patients with SAR were included in the analysis. The percentage of effectiveness of FFNS, MFNS, TANS, and BANS was 59.89%, 45.60%, 24.89%, and 16.00%, respectively. The ICER of FFNS, MFNS, and TANS is THB -6,539.92, 4,593.83, and 1,401.24 compared to BANS. CECA result showed the probability of using FFNS is considered cost-effective in 87.50% of cases from zero value followed by MFNS (0.80%), TANS (5.40%), and BANS (6.30%). With a threshold greater than THB 20,000, FFNS is considered a cost-effective strategy.

**Conclusion:** FFNS is a cost-effective option compared to alternative INCSs in Thailand for treating AR with ocular symptoms.

**Key words:** allergic rhinitis, ocular symptom, intranasal corticosteroids, cost-effectiveness, economic evaluation

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**Abbreviations:**

| | |
|---|---|
| AR | Allergic rhinitis |
| AC | Allergic conjunctivitis |
| ARC | Allergic rhino-conjunctivitis |
| BUD | Budesonide |
| BANS | Budesonide aqueous nasal spray |
| CECA | Cost-effectiveness acceptability curves |
| CSMBS | Civil Servant Medical Benefit Scheme |
| FF | Fluticasone furoate |

**Abbreviations (Continued):**

| | |
|---|---|
| FFNS | Fluticasone furoate nasal spray |
| FPNS | Fluticasone propionate nasal spray |
| INCS | Intranasal corticosteroid |
| MF | Mometasone furoate |
| MFNS | Mometasone furoate nasal spray |
| NLEM | National List of Essential Medicine |
| PAR | Perennial allergic rhinitis |
| PSA | Probabilistic sensitivity analysis |
| QoL | Quality of life |
| RCT | Randomized controlled trial |
| SAR | Seasonal allergic rhinitis |
| SD | Standard deviation |
| SMD | Standardized mean difference |
| SSS | Social Security Scheme |
| SLR | Systematic Literature Review |
| TA | Triamcinolone acetonide |
| TANS | Triamcinolone acetonide nasal spray |
| TOSS | Total ocular symptom score |
| UCS | Universal Coverage Scheme |
| OPD | Outpatient department |

## Introduction

The prevalence of allergic rhinitis (AR) has been growing worldwide in the last decade. AR was found in over 400 million people[1] and affected up to 40% of the general population.[2] The prevalence of AR in Thailand is up to 44.2% which is considered a common disease in the Thai people.[3] Allergic rhinitis significantly affects patients' quality of life (QoL) and constitutes economic burden.[2,3] Allergic rhinitis is a systemic disease with immunoglobulin E-mediated inflammation of nasal mucosa.[4] In terms of systemic allergic disease, AR has significantly associated with numerous comorbidities, including asthma, atopic dermatitis, conjunctivitis, sinusitis, middle ear problems, laryngeal problems, sleep, and behavioral problems.[4] Allergic conjunctivitis (AC) is considered a conjunctival reaction generally associated with AR, which is found in up to 70% of patients.[4,5] The ocular symptoms are characterized by watery, red, and itchy eyes,[5] and it is more commonly occurs in seasonal allergic rhinitis (SAR) than in perennial allergic rhinitis (PAR).[6] The involvement of ocular symptoms in AR is associated with exposure to allergens through the nose and naso-ocular reflexes.[4] The extent of co-occurrence conjunctivitis in AR significantly affects patients' quality of life, loss of daily productivity, impaired school performance, and utilizes higher healthcare costs.[7,8]

AR management aims to control symptoms, reduce persistent inflammation and improve patients' QOL.[9,10] The common management is allergen avoidance and pharmacotherapy such as antihistamines, intranasal corticosteroids (INCS), or leukotriene receptor antagonists[5] and allergen immunotherapy in more severe cases. INCS is recommended as a pharmacological treatment choice for patients with AR.[9] Furthermore, some INCSs are also shown efficacy in treating ocular symptoms in AR, and Fluticasone furoate nasal spray (FFNS) had shown consistent efficacy in treating ocular symptoms in AR.[11] In addition, only FFNS has approved indications for treating nasal and ocular symptoms of SAR.[12] Apart from allergen avoidance and treating AR, the available pharmacological options for AC treatment include oral antihistamines/ mast cell stabilizers, topical ocular antihistamines, topical ocular decongestants, lubricants, and topical steroids which the ophthalmologists commonly use based on severity.[10]

There were many INCSs available as an option in Thailand, including FFNS, Mometasone Furoate nasal spray (MFNS), Triamcinolone nasal spray (TANS), and Budesonide nasal spray (BANS). The cost-effectiveness of comparing each available INCS for AR with ocular symptoms has yet to be globally identified in terms of selecting the optimal options for health decision-making. Therefore, this study aims to inform both physicians and payers to help decision-making about the relative cost-effectiveness of INCS and the budget allocation in treating AR with ocular symptoms from a Thai societal perspective.

## Methods

### *Model description*

This is a meta-analysis and cost-effectiveness analysis of INCSs in SAR patients aged ≥ 12 years with ocular symptoms. The study included the available INCSs in the Thai health system by the end of November 2022, which are FFNS, MFNS, TANS, and BANS. The pairwise meta-analysis was performed as an input effectiveness parameter for each INCS in the Cost-effectiveness model. This Cost-effectiveness model was constructed using a 1-year time frame (12 months).

The cost-effectiveness analysis included the estimation of clinical benefits (improvement of ocular symptoms) and the costs of the different treatments. A decision tree model was developed to evaluate the cost-effectiveness of INCS in AR with ocular symptoms from a Thai healthcare system societal perspective (**Figure. 1**). One-year cost was captured in the analysis. A hypothetical cohort population of any aged of SAR patient with ocular symptoms, caused by a variety of aeroallergens, and treated with a single intranasal corticosteroid treatment was used for symptom relief.

### *Meta-analysis of INCS effectiveness for allergic rhinitis with ocular symptoms*

The systematic literature review (SLR) and meta-analysis methods and reporting were in accordance with the Cochrane Collaboration and the preferred meta-analyses statement. The evaluation followed the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) guidelines.

The eligibility criteria for the SLR on which the meta-analysis was conducted included the published Randomized (parallel group) placebo-controlled trials, any age, confirmed diagnosis of allergic rhinitis by the clinical history or the allergen identified, and sensitivity proven by positive skin prick test, included any ocular outcome measurement: reflective TOSS (rTOSS) with average score of AM + PM, instant TOSS (iTOSS); predose 24 hr, Total Ocular symptoms scores, and using recommended dose for each INCS. The exclusion criteria were non-English, not available full article access, and cross-over designs trials with other co-interventions were excluded.

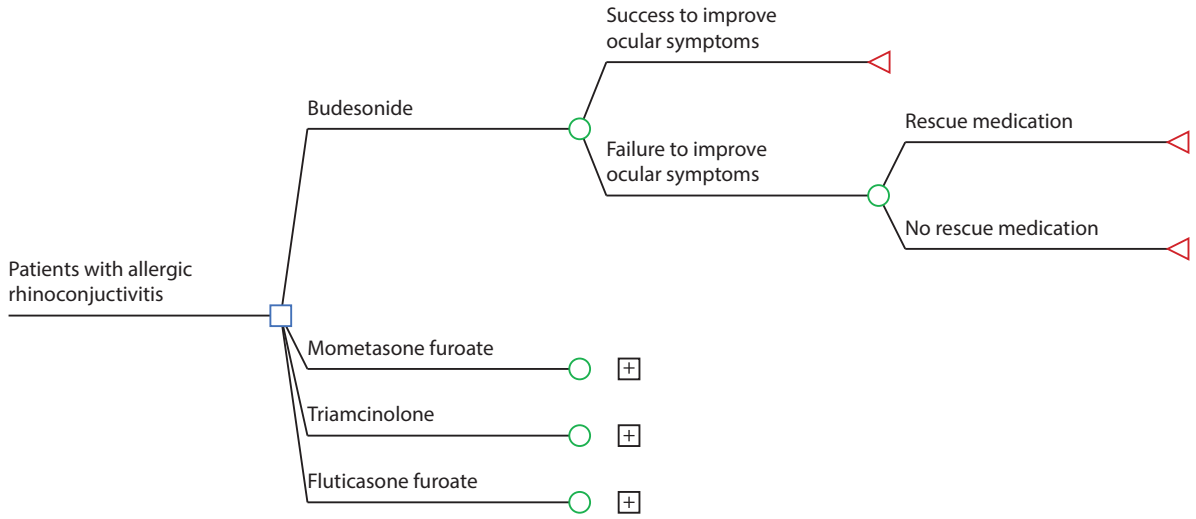


**Figure 1. A one-year decision tree model for allergic rhino-conjunctivitis patients.**

We search all eligible published studies in MEDLINE, SCOPUS, and Cochrane library from 1970-2022 using the search term of allergic rhinitis and INCS comparators names as "Rhinitis, Allergic"[tw] OR "Rhinitis, Allergic, Perennial"[tw] OR "Rhinitis, Allergic, Seasonal"[tw] AND "Fluticasone Furoate"[tw] OR "Mometasone Furoate"[tw] OR "Triamcinolone Acetonide"[tw] OR "Budesonide"[tw] following the PRISMA-P guidance.

Two review authors (CY, TB) independently reviewed the titles and abstracts and obtained full-text articles that appeared to fulfil the eligibility criteria. We independently evaluated the trial's eligibility and documented the reasons for exclusion. Duplicates will be omitted using EndNote software Duplicates will be omitted using EndNote software (Version X9.0). All disagreements between review authors were resolved through discussion. The Cochrane risk of bias 2 (RoB 2) instrument was used to evaluate the quality of the final included trials by assessing the risk of bias for each study.[13]

To estimate the treatment effectiveness of each INCS, we calculated the standardized mean difference (SMD) using Hedges' adjusted g for the eligible studies reporting TOSS improvement of each INCS in the study compared to the placebo from random effect model pairwise meta-analysis. All eligible studies were included in the quantitative analysis. To measure the treatment effect, the SMD using Hedges' adjusted g between the INCS and placebo group was calculated for each study. The quantitative analysis was performed by using the review manager (Revman version 5.4; Cochrane, London, UK). Heterogeneity, as measured by the I-squared statistic (I2), was interpreted as follows: 0–40% may not be important; 30–60% may indicate moderate heterogeneity; 50–90% may indicate substantial heterogeneity; and 75–100% would indicate considerable heterogeneity.[13] To calculate common SD from the eligible studies, we perform SD calculation following the Cochrane Handbook for Systematic Reviews of Interventions.[14]

To calculate the percentage of clinical improvement for each INCS which will reflect as INCS effectiveness, the method was used with the following equation.

$$\text{Significant improvement} = \frac{\sum \text{Mean difference}}{\sum \text{Standardized mean difference}} \times \text{Pooled standardized mean difference}$$

***Cost-effectiveness analysis of INCS efficacy for allergic rhinitis with ocular symptoms***

The analysis was performed from the Thai societal perspective, so direct medical costs and direct non-medical costs were included in the model. The analysis assumed that there are no differences in the number and severity of adverse events.

The following assumptions were included in the model; the management of rhinitis requires an initial visit and follow-up visits, the prescription of nasal corticosteroids, and follow-up visits during the following 12 months. The cost of laboratory and radiodiagnosis were not included based on Thai practice by expert panel consultation. The drug cost for the model was calculated as the expected day of the treatment per year (365 days) multiplied by the daily wholesale acquisition cost. The drug cost inputs in the model were from the medical price database from the national drug information[15] and direct non-medical cost per day for Outpatient department (OPD) visits was referred to the Standard Cost Lists for Health Technology Assessment database.[16]

In the case of therapeutic failure, the experts (Allergists) were asked additional OPD visits of patients requiring consultations, rescue treatment, and duration of rescue treatment in days. The cost of the rescue treatment was calculated based on unit cost of oral antihistamines and antihistamine eye drops to cover eight weeks period. Subsequently, the acquisition costs of the initial intranasal corticosteroids and the costs originating from the therapeutic failure of these drugs (use of oral antihistamines and antihistamine eye drops, skin prick test, and additional visit of OPD visit for medical consultant) were evaluated for two months, according to an estimate by Thai clinical experts.

We performed the decision tree model for four decision pathways of INCS selection using TreeAge Pro 2022, R1. (TreeAge Software, Williamstown, MA) (**Figure 1**) and calculated the incremental cost-effectiveness ratio (ICER) of each intranasal corticosteroid using following formulas.

$$\text{ICER} = \frac{\text{Intervention cost} - \text{control cost}}{\text{Intervention effectivenss} - \text{control effectiveness}}$$

Key input parameters were varied through plausible ranges to assess the robustness of the cost-effectiveness analysis results. The varied parameters included the effectiveness of INCSs which derived from the meta-analysis result, the drug costs, cost of OPD visits. Cost per day of INCS was varied within the range of ±20% and hospitalization costs were varied using the standard deviation. All probabilities were varied within the range of ±10%. To calculate cost per OPD consultation in terms of direct non-medical costs, we included travel costs, food costs, and cost for time spent in OPD per day. The cost of time spent in OPD per day calculate using the income per capita per year in 2022 which is 253,169 THB (USD 7233.40).[17] The input parameters both effectiveness and cost were shown as variables in **Table 1**.

***Sensitivity analysis***

A probabilistic sensitivity analysis (PSA) was performed to examine the effect of all parameter uncertainty by allowing all input parameter values to vary simultaneously over their respective feasible ranges within the model. A Monte Carlo simulation was performed (1,000 iterations) based on variable-specific distributions. For the Monte-Carlo simulation, fixed distributions were selected, and the parameters of each distribution were estimated based on the primary data of the clinical outcome analysis. A log-normal distribution was assigned for costs, a normal distribution for resource use, and a beta distribution for model probabilities based on the variability described in the studies. The result of the PSA is presented graphically as a scatterplot of cost-effective dispersion and cost-effectiveness acceptability curve (CEAC).

**Table 1. Parameter input in the model and Deterministic results of the cost-effectiveness analysis of Budesonide compared to Fluticasone furoate, Mometasone furoate, and Triamcinolone nasal spray in the treatment of AR with ocular symptoms.**

| Parameters | Base value | Range | Distribution | Reference |
|---|---|---|---|---|
| **Probability of improvement in Ocular Symptoms** | | | | |
| Efficacy of FFNS | 0.59 | 0.53-0.65 | Beta | Meta-analysis calculation |
| Efficacy of MFNS | 0.46 | 0.41-0.50 | Beta | Meta-analysis calculation |
| Efficacy of TANS | 0.25 | 0.23-0.28 | Beta | Meta-analysis calculation |
| Efficacy of BANS | 0.16 | 0.14-0.18 | Beta | Meta-analysis calculation |
| **Cost parameters** | | | | |
| Drug costs per day, THB | | | | |
| Cost of FFNS | 8.03 | 6.42-9.64 | Gamma | NDI (2016) [15] |
| Cost of MFNS | 16.11 | 12.89-19.33 | Gamma | NDI (2016) [15] |
| Cost of TANS | 7.06 | 5.65-8.47 | Gamma | NDI (2016) [15] |
| Cost of BANS | 4.83 | 3.86-5.80 | Gamma | NDI (2016) [15] |
| Cost of diagnostic tests, THB | | | Gamma | HITAP (2009) [16] |
| Skin prick test | 1,100 | 880-1320 | Gamma | |
| Cost per OPD consultation (first/second level), THB | 816.21 | 652.07-979.45 | Gamma | HITAP (2009) [16] |
| Travel | 151 | 120.80-181.20 | Gamma | HITAP (2009) [16] |
| Food | 55 | 44-66 | Gamma | HITAP (2009) [16] |
| Time spent in OPD per day, minutes | 361 | - | - | HITAP (2009) [16] |
| The income per capita per year (2021), THB | 253,169 | - | - | World Bank [17] |
| **Health Care Resource Use** | | | | |
| Number of OPD visits per patient per year for success to improve ocular symptoms | 4 | 2-5 | Uniform | Expert consultation |
| Number of OPD visits per patient per year for failure to improve ocular symptoms | 6 | 4-7 | Uniform | Expert consultation |

**Table 1. (Continued)**

| Deterministic results of the cost-effectiveness analysis | | | | | | |
|---|---|---|---|---|---|---|
| **INCS option** | **Costs (THB)** | **Incremental Cost** | **Effectiveness** | **Incremental Effectiveness** | **Cost/Effect Average** | **ICER compared to BANS (THB)** |
| BANS | 10,495.87 | - | 0.16 | - | 65,599.22 | - |
| FFNS | 7,690.90 | -2,804.97 | 0.59 | 0.43 | 13,059.77 | -6,539.92 |
| MFNS | 11,855.65 | 1,359.77 | 0.46 | 0.30 | 25,999.23 | 4,593.83 |
| TANS | 10,620.49 | 124.62 | 0.25 | 0.09 | 42,664.19 | 1,401.24 |

FFNS = Fluticasone furoate nasal spray, MFNS = Mometasone furoate nasal spray, TANS = triamcinolone acetonide nasal spray, BANS = Budesonide aqueous nasal spray

## Results

### *Meta-analysis of TOSS compares INCS vs placebo*

Thirteen eligible RCTs with a total of 3,722 SAR patients were included in the analysis. The analysis for the FFNS case included 6 studies and had an n = 1,107 for treatment and n = 1,112 for placebo. In the case of MFNS, 4 studies were included with n = 479 for MFNS and n = 460 for placebo. For TANS there were two eligible studies included with n = 185 for treatment and n = 177 for placebo. In the case of BANS, only one study was included with n = 102 for treatment and n = 100 for placebo.

The meta-analysis result was shown as a forest plot in **Figure 2**. The TOSS changes of each INCS were significantly different from the placebo, including FFNS (SMD -0.32 [95%CI: -0.40 to -0.24], $p < 0.001$), MFNS (SMD -0.27 [95%CI: -0.40 to -0.13], $p < 0.001$) $p < 0.001$), TANS (SMD -0.24 [95%CI: -0.44 to -0.03], $p = 0.02$), and BANS (SMD -0.21 [95%CI: -0.49 to 0.006], $p = 0.13$).

From the results of the meta-analysis, the probabilities of achieving an improvement in ocular symptom of AR for the different options analyzed were estimated as INCS effectiveness in put for CEA. The estimated INCS effectiveness of FFNS, MFNS, TANS, and BANS was 59.89%, 45.60%, 24.89%, and 16.00% which showed as 0.59, 0.45, 0.25, and 0.16, respectively in **Table 1**.

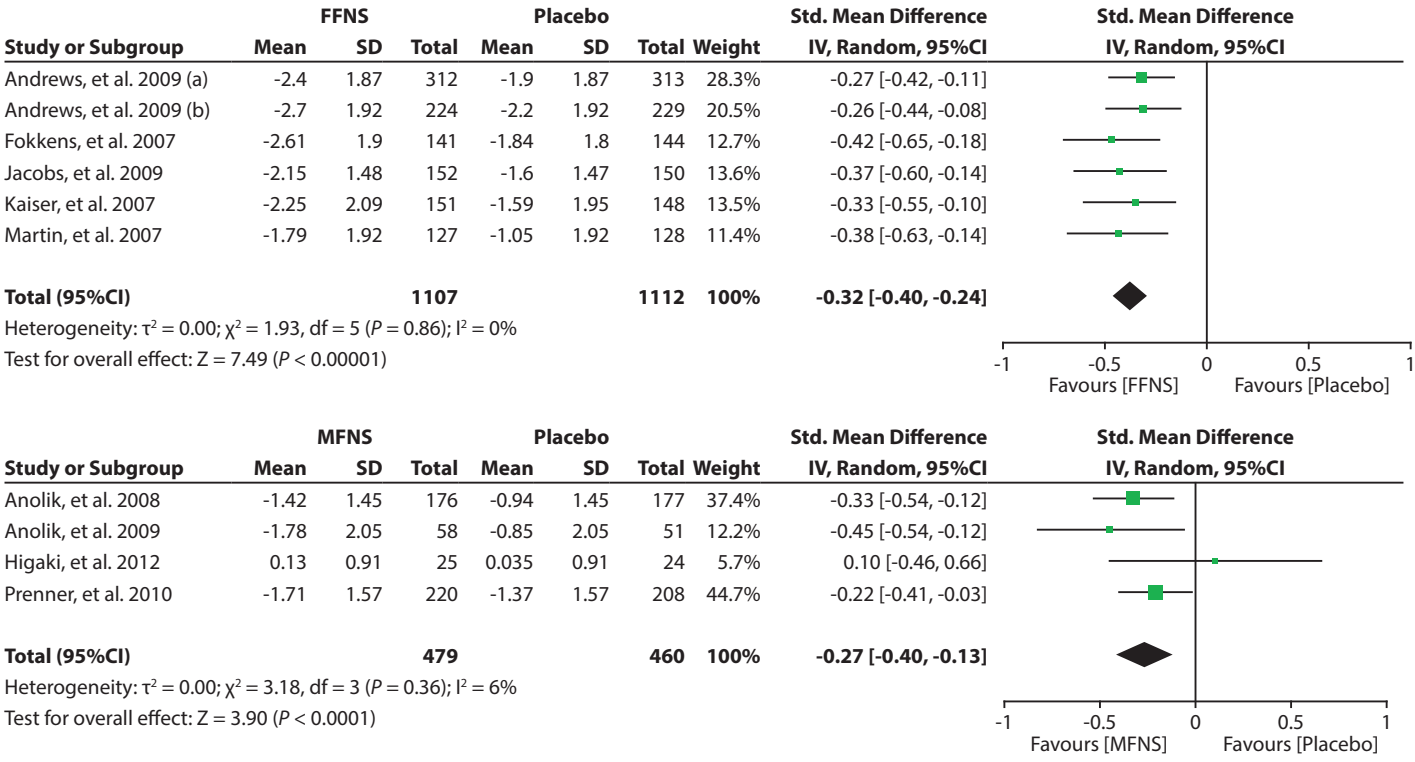


**Figure 2. Results of the analysis of intranasal corticosteroids in the improvement of the ocular.**

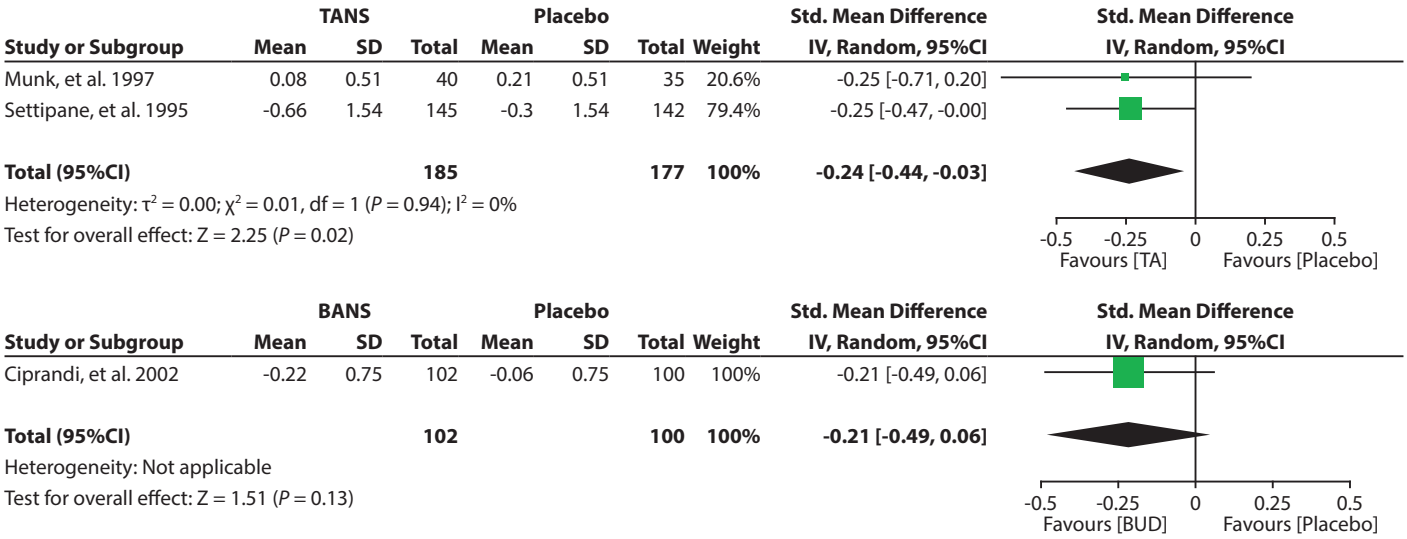


**Figure 2. (Continued)**

### *Cost-effectiveness analysis*

**Table 1** describes the results of the cost-effectiveness analysis of BANS compared to FFNS, MFNS, and TANS in the treatment of AR with ocular symptoms as a deterministic analysis. The total annual cost of FFNS, MFNS, TANS, and BANS was THB 7,690.90 (USD 213.64), 11,855.65 (USD 329.32), 10,620.49 (USD 295.01), and 10,495.87 (USD 291.55), respectively. Regarding the total cost of treatment, FFNS was the least expensive (THB 7,690.90; USD 213.64), which makes it the dominant alternative in this comparison (**Table 1**, **Figure 3**).

The ICER (Cost/Symptom improvement) of FFNS, MFNS, TANS, and FFNS compared to BANS were THB -6,539.92 (USD -181.66), 4,593.83 (USD 127.61), and 1,401.24 (USD 38.92) THB per effectiveness gained (**Table 1**). From the cost-effectiveness (CE) plane of deterministic analysis, the result of ICER in the CE plane demonstrated that FFNS is more effective and less costly when compared with BANS with the ICER of THB -6,539.92 (USD -181.66) in the right lower quadrant of the CE plane while MFNS is considered more effective but more costly when compared with BANS

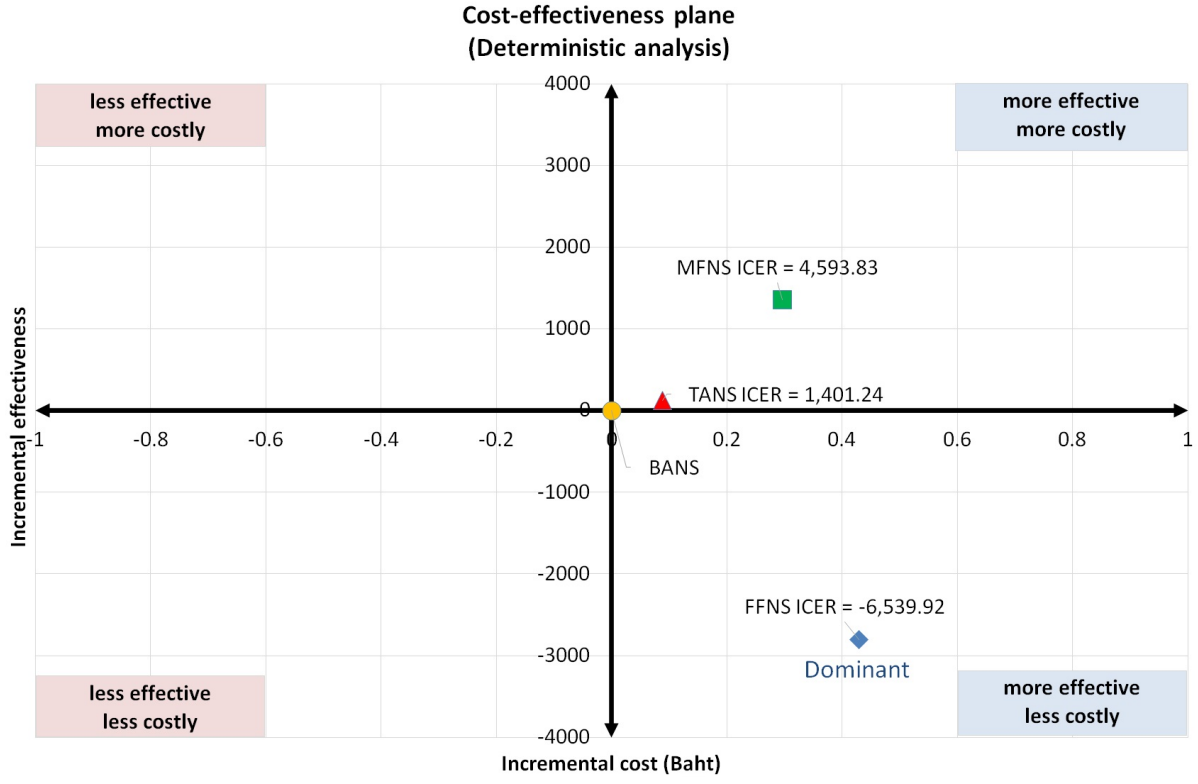


**Figure 3. Cost-effectiveness plane (Deterministic analysis).**

(ICER = THB 4,593.83; USD 127.61) showed in right upper quadrant. The result of the ICER of TANS is considered more costly when compared with BANS (ICER = THB 1,401.24; USD 38.92). From the CE plane of deterministic analysis, FFNS was considered the dominant INCS option in Thai healthcare societal perspective (**Figure 3**).

***Probabilistic sensitivity analysis***

A probabilistic sensitivity analysis was performed to compare BANS with FFNS, MFNS, and TANS. The results of the PSA based on 1,000 Monte Carlo simulations are presented as a scatter plot of Cost Effectiveness Dispersion (**Figure 4A**), Cost-effectiveness plane (Probabilistic sensitivity analysis) (**Figure 4B**), and Cost-effectiveness Acceptability curve (CECA) of INCS in the treatment of ocular symptoms of AR (**Figure 5**).

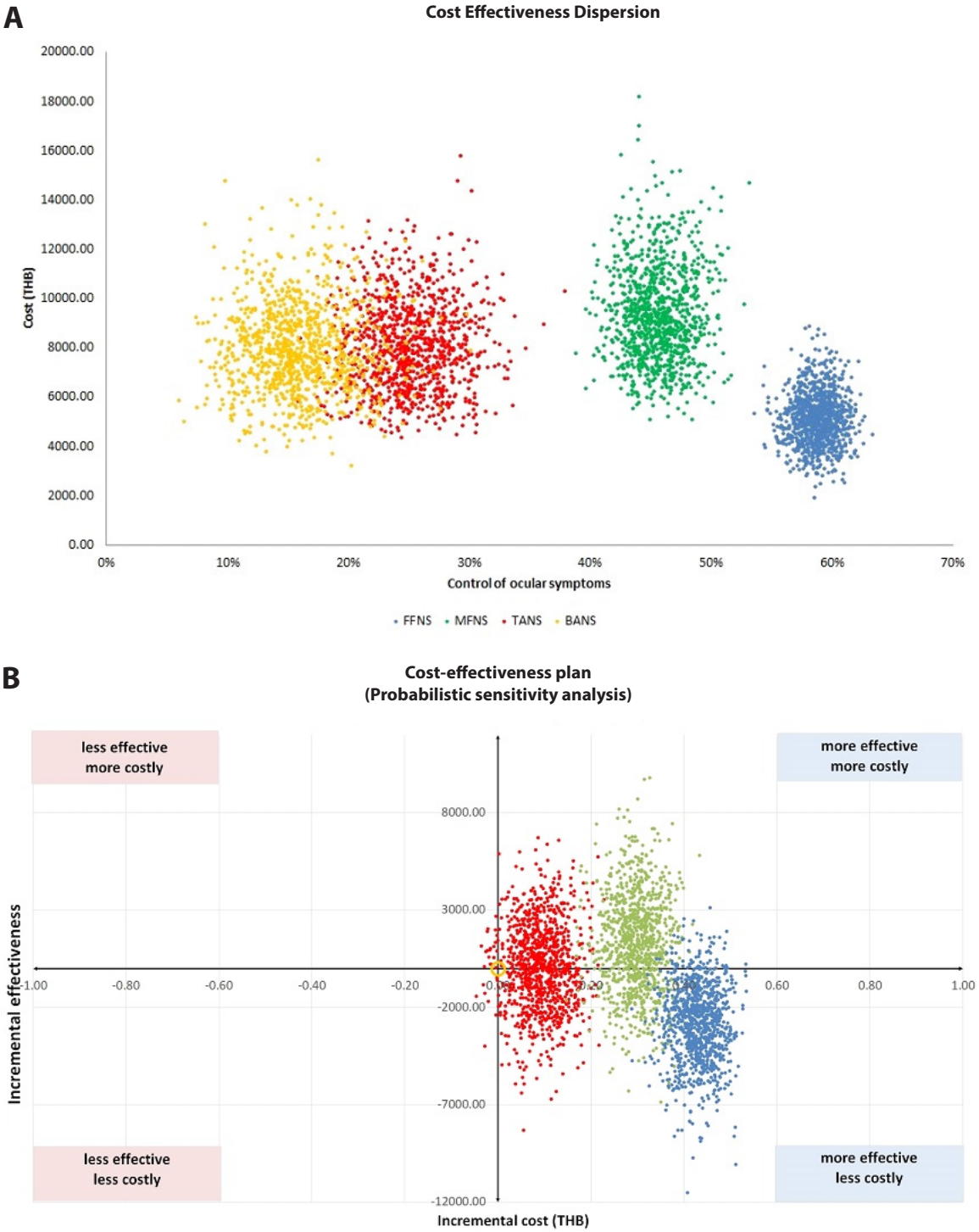


**Figure 4.**
**A) Cost Effectiveness Dispersion (Probabilistic sensitivity analysis)**
**B) Cost-effectiveness plane (Probabilistic sensitivity analysis)**

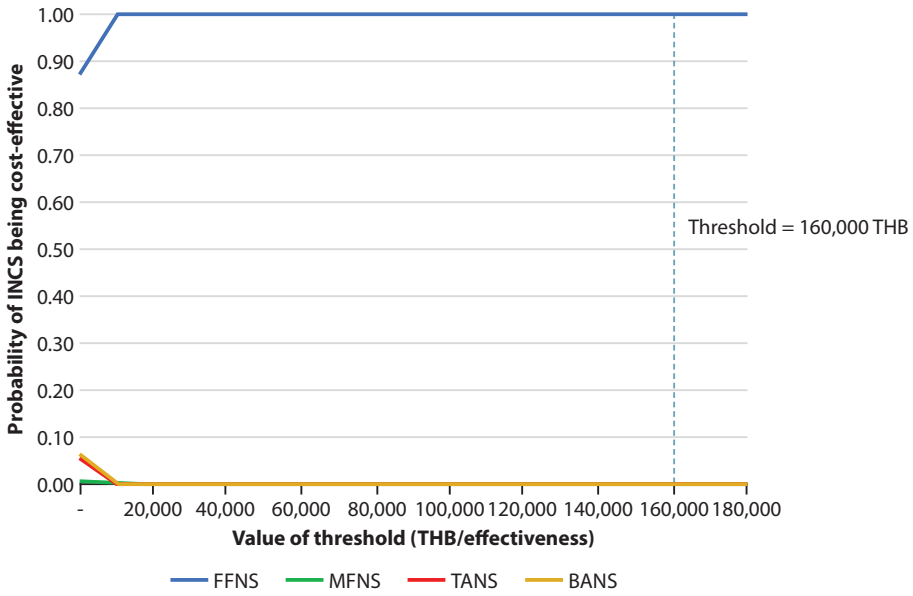


**Figure 5. Cost-effectiveness Acceptability curve of Intranasal corticosteroid in the treatment of ocular symptoms of allergic rhinitis.**

**Figure 4B** shows that FFNS ICERs of the 1,000 simulations fell mostly in the right lower quadrant, which indicates that treatment with FFNS incurred a lower cost and yielded better effectiveness than BANS. Moreover, the overall PSA result of BANS vs FFNS in terms of incremental cost and effectiveness showed that FFNS in 1,000 iterations reflect the increase in effectiveness with decrease in incremental cost. While TANS and MFNS ICERs fell in the right upper quadrant indicated more effective but higher cost than BANS (**Figure 4B**).

The CEACs for the effectiveness of the four INCS were shown in **Figure 5**. At a value threshold of zero value, FFNS demonstrated an 87.50% cost-effectiveness strategy, while the cost-effectiveness of MFNS, and TANS, BANS, were 0.80%, 5.40%, and 6.30%, respectively. At a threshold of 20,000 THB and above, FFNS demonstrated a 100.00% cost-effectiveness strategy. The results of the CECA showed a consistent increase in effectiveness, while the savings from using FFNS as a substitute for BANS are presented in 87.50% of the simulations performed. Using FFNS is considered a cost-effective strategy in 100% of cases, given the local national threshold of 160,000 THB.

## Discussion

This study demonstrates the differences in cost-effectiveness of different INCS options that are used in the management of ocular symptoms in AR in the Thai health context. Our pairwise meta-analysis results showed that FFNS had the highest effectiveness (59.89%), based on the effect size of TOSS improvement of each INCS from 6 RCTs,[18-22] and this was followed by MFNS (45.60%) from 4 RCTs,[23-26] TANS (24.89%) from 2 RCTs[27,28] and BANS which had the lowest effectiveness in percentage (16.00%). There was a single study in the analysis for BANS vs placebo which showed a total effect size of -0.21 (95%CI -0.49 to -0.06) which was not statistically significant ($p$ = 0.13) at 5 weeks in a clinical trial.[29]

Several potential pathways for allergic rhinitis-related ocular symptoms includes the nasal-ocular reflex and allergen exposure to the ocular via the nasolacrimal duct.[30] According to the severity of the ocular symptoms in both types of AR, patients with PAR tend to exhibit milder ocular symptoms than those with SAR, and ocular involvement was more prevalent in SAR.[31]

The most effective treatment for allergic rhinitis symptoms for nasal symptoms is INCS, which has also demonstrated significant ocular symptom efficacy.[30] However, the findings of the available research were not consistent for all INCSs.[32] In spite of various allergy seasons and geographic locations, Maspero, J. F. et al. (2010) found that FFNS, 110 micrograms, once daily reliably alleviated all nasal and ocular symptoms of SAR. According to Baroody et al. (2011), FFNS showed a significant decrease in all ocular symptoms following an allergen challenge. Additionally, only FFNS has a valid indication for treating SAR with ocular symptoms.[12] Previous studies on the use of FFNS in ocular symptoms revealed that SAR demonstrated a greater improvement in TOSS score than PAR, indicating a difference in the severity of the AR phenotype.[33] In our study, we analyzed solely the SAR phenotype and the showed ocular effectiveness consistent with the meta-analysis of Rodrigo et al. 2010 for FFNS at a once-daily dosage of 110 mcg in SAR.

To the best of the authors' knowledge, this is the first study to compare the different INCSs available in Thailand and worldwide for treating patients of AR with accompanying ocular symptoms, in terms of cost-effectiveness. Previous cost comparison study of the INCS, Reissman et al 2004 determined the relative cost for the treatment with the INCSs, Fluticasone propionate nasal spray (FPNS), MFNS, TANS, BANS using the IMS National Disease and Therapeutic Index database at 120 metered-dose sprays which aimed to compare economic differences resulting from these prescribing behaviors, the result showed that

BANS offered the most days of therapy (44 days) per prescription filled and the lowest cost per day compared to FPNS, MFNS, and TANS.[34] However, this study did not mention the efficacy comparison of each INCS with only cost comparison is mentioned and there is no FFNS comparison in this study (early year from FFNS found in the market).

In an analysis of clinical trial data comparing BANS, FPNS, and placebo for the treatment of PAR in Canada, Ståhl et al. (2000) compared the direct medical costs of BANS, 256 mcg q.d., and FPNS, 200 mcg q.d. BANS was found to be more cost-effective than FPNS in the treatment of PAR, with an average 12-month cost that was 23.3% cheaper for BANS than for FPNS.[35,36] Our study has no FPNS comparison and BANS was found to be less cost effectiveness option for Thai context comparing with leading four INCS available in Thailand.

With respect to the cost-effective analysis comparing the four INCS, FFNS was dominant as a cost-effective option compared to MFNS, TANS, and BANS. Thus, ICER result showed that FFNS is the cost-effective strategy in Thailand for managing patients of allergic rhinitis with ocular symptoms.

From the literature review, none of the studies indicates the result of a cost-effective analysis of INCS in treating allergic rhinitis with ocular symptoms. There are four INCSs available in Thailand which showed in this study. Cost-effectiveness analysis comparing BANS with FFNS, MFNS, and TANS suggested that FFNS is a dominant option. FFNS in the treatment of AR is a cost-effective option (more effective at a lower cost) in the treatment of ocular symptoms associated with AR in the Thai context.

In 2002, the Thai government initiated the Universal Health Coverage (UHC) scheme (30 Baht scheme), which assures that even the poorest residents have equitable access to health care.[37,38] This protection covered inpatient and outpatient treatment, accidents, emergencies, and all medications on the National List of Essential Medicines (NLEM).[39] In Thailand, universal healthcare is provided and reimbursed through three government schemes including 9% from Civil Servant Medical Benefit Scheme (CSMBS), 16% from Social Security Scheme (SSS), and the majority of Thai people (75%) were coverage by Universal Coverage Scheme (UCS),[40] and direct medical costs and specifically drug costs are an important consideration when prescribing medication. For UCS population, there were two INCSs in NLEM, notably BANS and FFNS; therefore, the results of our study would aid in the selection of medication for patients covered by UCS based on effectiveness and cost-effectiveness comparisons between BANS and FFNS as well as the safety perspective which is the high systemic absorption of BANS.

Our research has a few limitations. We extracted data from available published data, which may vary by RCT population and region in terms of disease severity and TOSS of SAR patients. We overcame this limitation through sensitivity analysis. To reflect the application of the model in a Thai context, we aimed to incorporate local national data and Thai-based costs into the model. This study's findings may limit the applicability of our findings to countries with different healthcare systems.

The results of this study will potentially support the daily clinical decision-making process of choosing between a range of options for patients with AR in Thailand. When choosing the most efficient therapy for managing AR, it is possible to positively impact on the significant morbidity and economic burden associated with the disease.

## Conclusion

Fluticasone furoate nasal spray is a cost-effective option for allergic rhinitis with ocular symptoms among other currently available intranasal steroid options for the Thai AR patients. This cost-effectiveness data could be used by both physicians and payers to make informed decisions about the budget allocation for allergic rhinitis patient care in Thailand.

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## Conflict of interests

- CY, TB, BM, MV, AP, and BA are employees of GSK.
- PP did not receive any fee and has no conflicts of interest to declare.
- There are no other conflicts of interest to declare.

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## Author contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agreed to be accountable for all aspects of the work.

## Ethics approval

Ethics approval was considered exempt due to the nature of the systematic review, meta-analysis, and economic evaluation model.

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