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"HEAD-TO-HEAD COMPARISON:FLUTICASONE/FORMOTEROL VS BUDESONIDE/FORMOTEROL IN MILD–MODERATE ASTHMA"

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ABSTRACT

Introduction: The chronic inflammatory respiratory condition known as bronchial asthma affects millions of people all over the world and has an important impact on the quality of life of those affected. The most effective method for managing asthma is the combination of inhaled corticosteroids (ICSs) and long-acting beta-agonists (LABAs). However, there has been a relatively limited amount of research conducted on the safety and effectiveness of fluticasone and formoterol (FFF) and budesonide and formoterol (BFF) in patients who have mild to moderate asthma.

Aims and Objectives: The primary objective is to compare the improvement in "FEV1/FVC ratio" and health status among both groups. FEV1/FVC ratio and FEV1 values will be assessed using spirometry at baseline, weeks 2, 4 and 8 weeks. Secondary objective is to compare the adverse effects among both the groups

Methodology: This institution-based, prospective, randomized, observational, open-labeled study was conducted at the Pulmonary Medicine Outpatients Department of "Sree Balaji Medical College and Hospital, Chennai", over one year. Eighty adult patients were randomized into two groups: Group 1 (FFF) and Group 2 (BFF), receiving respective treatments twice daily. Spirometry were recorded at baseline, Weeks 2, 4, and 8. Adverse effects were also monitored.

Results: Both treatment groups showed significant improvement in lung function and symptom control. However, FFF demonstrated greater improvement in spirometry values at Weeks 2, 4, and 8 ($p < 0.05$). Additionally, the FFF group exhibited better tolerability, with fewer adverse effects reported at Weeks 2 and 4.

Conclusion: While both treatment regimens effectively managed asthma symptoms, the FFF combination exhibited superior efficacy and safety. It proved to be a more effective option for asthma management, ensuring better pulmonary function and symptom relief with fewer adverse effects.

KEYWORDS: Budesonide/formoterol; Fluticasone/formoterol; Asthma; Comparative analysis.

INTRODUCTION

The respiratory condition known as bronchial asthma is a chronic inflammatory condition that affects a number of cells and biological components. Mast cells, macrophages, neutrophils, eosinophils, T-lymphocytes, and epithelial cells are the specific cells that are immune cells (1). Because of this inflammation, certain individuals are more likely to experience recurrent episodes of coughing, chest tightness, wheezing, and dyspnoea, particularly throughout the night or in the early morning during the night (2). Despite this, it is not frequently simple to separate asthma from other respiratory problems due to the fact that these symptoms are so similar to those of other respiratory conditions. In order to achieve a precise diagnosis of asthma, it is important to have persistent respiratory symptoms as well as the identification of variable expiratory airflow obstruction that is recorded on spirometry (3). It become mandatory to prioritise symptom management and prevent recurrent exacerbations by using individualised

treatment plans that use a step-by-step approach and consider the frequency, intensity, and possible hazards of the symptoms (4).

Asthma is among the major non-communicable diseases, and many patients suffer a significant decrease in quality of life. Asthma ranks 28th in terms of illness burden and 16th in terms of years lived with disability based on disability-adjusted life years. The global prevalence of asthma exceeds 300million individuals, and it is anticipated that an additional 100 million individuals will be affected by the disease by 2025 (5). The prevalence, severity, and mortality of asthma vary significantly among different regions. Although asthma is more common in high-income nations, three-quarters of asthma-related deaths occur in low- and middle-income nations (6). According to earlier research, the incidence of asthma in Indian children and adults ranges from 2% to 23%. Significant differences in India's geography, culture, ethnicity, and socioeconomic profile, as well as different research approaches, might account for this wide variety in prevalence (7).

The Global Burden of Disease (GBD) 2019 report estimates that India contributes to 13.09% of global asthma cases, with approximately 34.3 million individuals affected. Despite this, asthma-related deaths and DALYS in India are significantly higher than global averages—nearly threefold and over twofold, respectively. These figures likely reflect systemic challenges such as late diagnosis, underrecognition, and insufficient access to timely and effective treatment.(8)

The 2024 Global Initiative for Asthma (GINA) update reflects a significant shift in the global approach to asthma management. It now recommends that all adults and adolescents with asthma be treated with inhaled corticosteroid (ICS)-containing medications, moving away from the traditional reliance on short-acting beta-agonists (SABAs) alone. To guide treatment decisions, GINA outlines two main **pathways**. The preferred **Pathway 1** involves the use of a low-dose ICS–formoterol combination taken as needed, providing both symptom relief and anti-inflammatory action. **Pathway 2**, on the other hand, involves a SABA used as a reliever alongside a separate ICS inhaler for maintenance. In addition to pharmacological guidance, the update emphasizes the importance of individualized care—recommending that every patient be provided with a written asthma action plan and a treatment approach tailored to their specific needs. These strategies are aimed at reducing the risk of severe exacerbations, hospitalizations, and asthma-related deaths, while promoting more effective long-term disease control.

ICSs are the mainstay of treatment for asthma symptoms, reducing inflammation-related risks going forward. When ICSs alone are unable to completely manage asthma symptoms, LABAs are administered (7,9). Because formoterol is both a fast-acting and long-acting bronchodilator, “budesonide/formoterol (BUD/FOR)” might serve as a controller and a rescue drug. This process is known as single maintenance and reliever treatment (SMART). According to earlier research, individuals with asthma who received SMART therapy experienced fewer acute exacerbations, had better symptom management, and needed fewer ICS doses (10). In the present study, the FEV1/FVC ratio is utilized as a vital measure to assess lung function in patients diagnosed with mild to moderate bronchial asthma. Initially, this ratio is used to confirm both the presence and severity of airflow obstruction among participants. Subsequent measurements taken at Weeks 2, 4, and 8 allow for a clear, objective evaluation of how each treatment—Fluticasone-Formoterol (FFF) and Budesonide-Formoterol (BFF)—impacts pulmonary function over time. As bronchial asthma is characterized by reversible airway obstruction, an increase in the FEV1/FVC ratio following therapy serves as strong evidence of treatment efficacy and helps validate the therapeutic response in both groups.(11)

METHODOLOGY

STUDY DESIGN:

This is an Institution-based prospective, randomized, observational, open-labeled study conducted to compare the effects of combination of Fluticasone and Formoterol with Budesonide and Formoterol.

STUDY AREA:

This study involved patients who visited the Pulmonary Medicine Outpatient Department at Sree Balaji Medical College and Hospital in Chrompet, Chennai.

STUDY POPULATION:

This study involved all adult patients of both sexes attending the Pulmonary Medicine OPD at "Sree Balaji Medical College and Hospital, Chrompet, Chennai".

STUDY DURATION:

This study was conducted for 1 year from October 2023 to October 2024.

STUDY GROUPS:

This study involved 2 study groups Group 1 and Group 2.

- Group 1: Fluticasone + Formoterol (FFF 125/6 – MDI) (mcg)/ 2puff /twice daily.
- Group 2: Budesonide + Formoterol (BFF 200/6 - MDI) (mcg) / 2puff /twice daily.

(As per physician advice)(38,39)

SAMPLE SIZE:

$n = 2[Z \sigma / E]2 = 2[1.96*12.8/5]2 = 34$

Total Sample Size (N) = 2[34] + 10% (Loss to follow up) = 75

Therefore n= 80 (Dropout rate for 10%)

Group A (FFF) = 40

Group B (BFF) = 40

SAMPLING METHOD:

Simple random sampling was the sampling method used for selection of study participants for this study.

INCLUSION CRITERIA

- Males and females (aged 18 to 65)
- Non–smoking subjects with asthma stable for 8 weeks before screening and baseline
- FEV1 60-80 %.

EXCLUSION CRITERIA

- Patients with age < 18 years and > 65years.
- Pregnant and/or nursing mothers
- Smoking/alcohol/ substance abuse.
- sensitivities or contraindications to any of the medications under trial.
- Patient with severe asthma
- Patient with COPD
- Subjects with significant pulmonary diseases, and recent respiratory tract infections.
- Patients with Renal impairment, and cardiovascular disease.
- Undergone surgeries that include lobectomy or bronchoscopic lung volume reduction.
- Patients with autoimmune diseases and on chronic immunosuppression.
- Patients contraindicated for performing spirometry(9,50).

WITHDRAWAL CRITERIA

- Treatment failure
- Subject's unwillingness/dropouts
- Serious adverse event endangering life/ disability/ prolonged hospitalization.
- Noncompliance of the patient.

STUDY PROCEDURE:

This study had been performed "To compare the safety & efficacy of Fluticasone + Formoterol vs Budesonide + Formoterol therapy in mild to moderate asthma patients in a tertiary care hospital" by strictly adhering to the research protocol after approval from the Institutional Ethics Committee with the approval letter with reference number:002/SBMCH/IHEC/2023/2019 of "Sree Balaji Medical College and Hospital, Chrompet, Chennai". Written informed consent (in the language they understand) was obtained from all the study participants in compliance with the "International Council For Harmonisation/ Good Clinical Practice" regulations.

FOLLOW-UP PERIOD:

Following the selection of the participants, they were assessed for baseline data and any adverse reactions. Following this they were followed up on 2nd week, 4th week, and 8th week.

STUDY PROTOCOL:

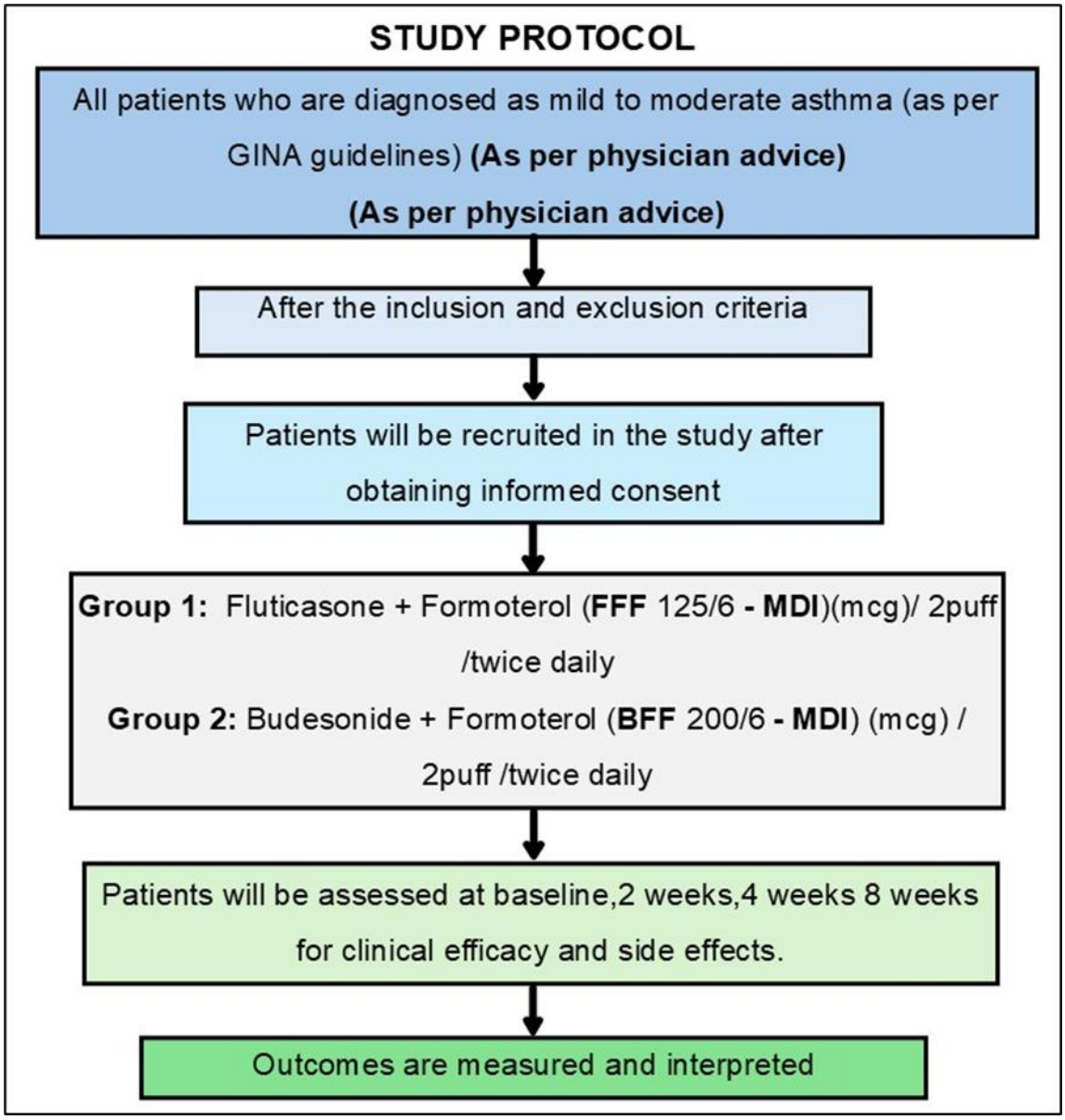

FIGURE 1: STUDY PROTOCOL

SCREENING:

Screening of the patients before selection was as per the study protocol. All the asthma patients attending the respiratory medicine OPD were undergone routine examination and screening. It

comprised an elaborate medical history of present complaints and co-morbidities, medication for chronic diseases or drugs that interact with the study drugs, a complete physical examination of the study participants, and a wide range of laboratory investigations.(51,52).

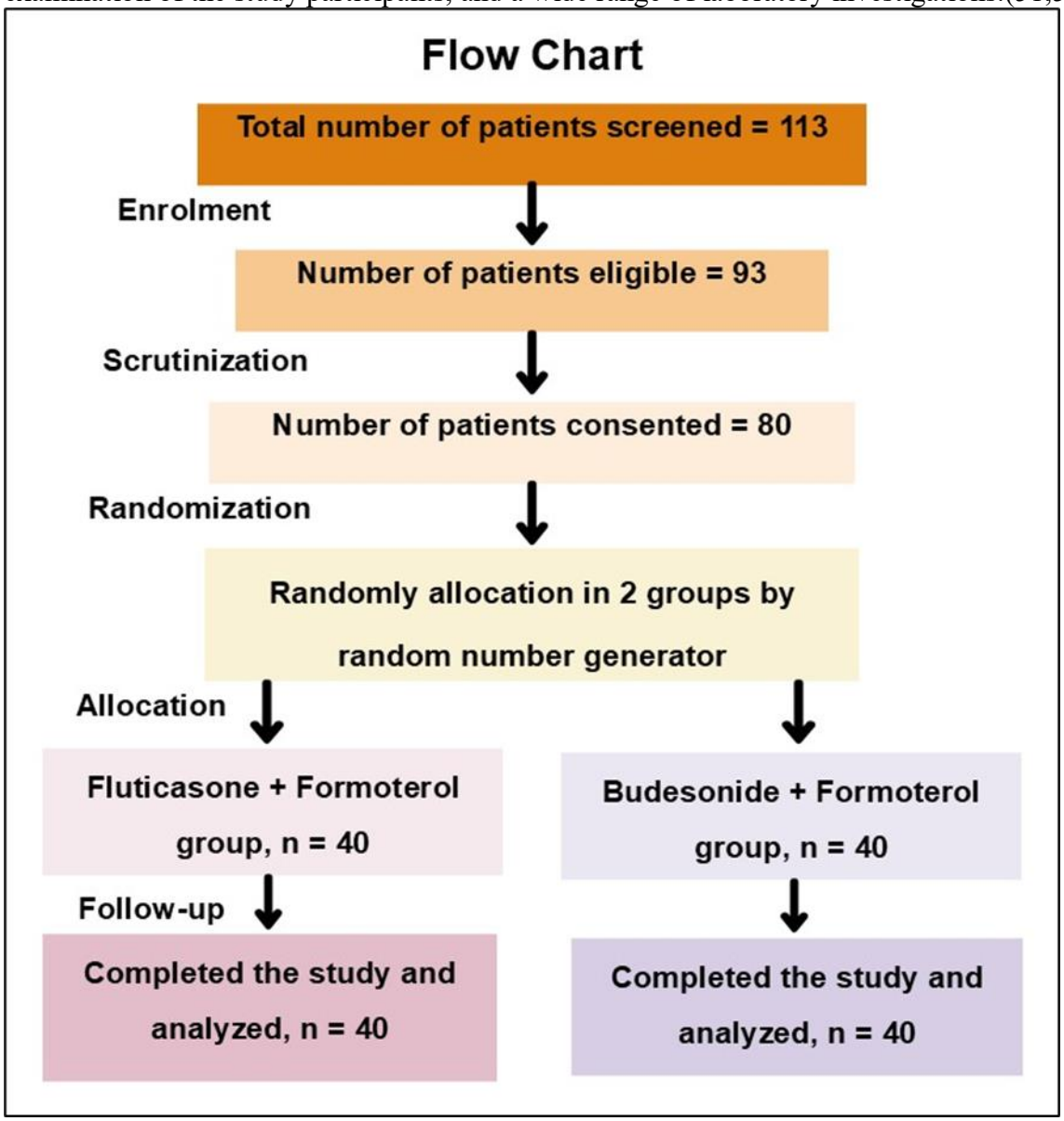

FIGURE 2: STUDY FLOWCHART

Present Complaints:

• Patients came in with symptoms like cough, phlegm, fever, loss of appetite, chest pain, breathlessness, and sometimes even coughing up blood. Their medical history, medication use, family background, and lifestyle were noted, followed by a complete physical check-up—including vital signs and system-wise examination. Tests such as chest X-rays, spirometry, and kidney and liver function tests were done, and only those with normal results were included in the study.

One hundred thirteen patients with mild to moderate asthma were screened at study onset. Among them, 93 patients were enrolled who met the inclusion as well as exclusion criteria. Finally, participants were selected for the study after approaching 80 participants who were ready to provide written informed consent. The chosen participants were educated about the significance of the study as well as its significance within the community to enhance results in asthma patients. They were also informed of the possible risks and benefits of the combination

therapy. They were assured that their identity would not be revealed their participation was out of their own interest and confidentiality would be maintained. The participants were also assured that they could withdraw anytime they wanted and they would not be forced to continue against their consent.

RANDOMIZATION:

Out of all participants, 80 were chosen and placed in either of the two groups (Group 1, Group 2). They were allocated to each group at random by using the Block randomization method with a system-generated random number generator. 40 participants were assigned to Group 1 and the remaining 40 to Group 2, with a total sample size of 44 determined for this study. All the selected 80 participants completed the full study with follow-up till 8 weeks.

GROUP ALLOCATION WITH DOSAGE:

- Group 1: Patients treated with Fluticasone + Formoterol (FFF 125/6 - MDI) (mcg) / 2puff /twice daily for the 40 participants.
- Group 2: Patients treated with Budesonide + Formoterol (BFF 200/6 - MDI) (mcg) / 2puff /twice daily for the 40 participants.

EVALUATIONS:

All the selected participants after randomization were allocated to a specific group. After allocation in the designated groups, all the participants' screening reports were considered as baseline investigation. Following this, all the participants were provided with either Fluticasone + Formoterol (FFF 125/6 - MDI) (mcg) or Budesonide + Formoterol (BFF 200/6 - MDI) (mcg) based on the allotted group.

All the individuals were explained about the proper technique of administering the given medication and the time when to take medications. They were also instructed to come for a review on completion of 2 weeks, 4 weeks, and 8 weeks following initiation of treatment. During the follow-up visit, they were asked to undergo the routine investigation done at the baseline.(53,54)

INVESTIGATIONS:

Spirometry:

"Spirometry is one of the most readily available and useful tests for pulmonary function. It measures the volume of air exhaled at specific time points during complete exhalation by force, which is preceded by a maximal inhalation.". Spirometry is a non-invasive gold standard test for objective assessment of lung function. The device employed to compute airflow and lung volumes is called a spirometer. During the study, ATS/ERS guidelines on pulmonary function tests were followed. We recorded the spirometry on an electronic portable spirometer.

We used a large three-litre syringe to calibrate the spirometer.(55,56). The following lung function parameters had been observed for analysis:

- "Forced vital capacity (FVC) – the volume of air in liters that is maximally forcefully exhaled after a full inspiration.
- Forced expiratory volume at one second (FEV1) – the volume of air in liters that is forcefully exhaled in one second after a full inspiration.
- Ratio of FEV1 to FVC (FEV1/FVC), expressed as percentage (%).
- Forced expiratory flow at 25-75% (FEF25-75%) or maximal mid-expiratory flow rate (MMEF), which is the average expiration flow rate during the middle 50% of the FVC.
- Peak expiratory flow rate (PEFR) – the peak flow rate during expiration." (55)

Data Collection Methods:

This is a hospital-based prospective observational study carried out in a "tertiary care hospital" in Chrompet, Chennai during the period October 2023 to October 2024. Those participants willing and satisfying the inclusion criteria were selected for the research after obtaining

informed consent. The patients were reviewed by Pulmonary Medicine out-patients department consultants on the first visit following selection, 2, 4, and 8 weeks at "Sree Balaji Medical College and Hospital". The data was collected, entered in MS Excel, verified for any wrong entry, and statistically analyzed.

STATISTICAL ANALYSIS

Statistical analysis had been carried out by employing SPSS version 21. The collected data was obtained as Microsoft EXCEL and verified for errors in reporting. The finalized master chart was uploaded in the SPSS version 21 and analyzed.

Continuous variables are described with mean and standard deviation. Statistical significance had been evaluated by performing a T-test with a p-value <0.05. All categorical variables were described as frequency and proportion. The test of significance was performed using Chi-square test/ Fischer's test with a statistical significance of p-value <0.05. The results were presented as tables, charts, and figures.

RESULTS

Age in years	Group				Total		P value
	FFF		BFF				
	n=40	%	n=40	%	n=80	%	
<20	1	2.5%	1	2.5%	2	2.5%	0.925
20-40	18	45.0%	15	37.5%	33	41.3%	
40-60	14	35.0%	16	40.0%	30	37.5%	
>60	7	17.5%	8	20.0%	15	18.8%	

Table 1: AGE DISTRIBUTION OF STUDY PARTICIPANTS

In Table 1, the age distribution of study participants was depicted. In FFF group, 18 (45%) had an age within 20-40 years, and 14 (35%) had an age within 40-60 years. In BFF group, 16 (40%) had an age within 40-60 years and 15 (37.5%) had an age within 20-40 years. A small proportion of participants had an age less than 20 and greater than 60 years in both groups. No statistically significant difference between groups (P=0.925).

Gender	Group				Total		P value
	FFF		BFF				
	n=40	%	n=40	%	n=80	%	
Male	30	75.0%	32	80.0%	62	77.5%	0.592
Female	10	25.0%	8	20.0%	18	22.5%	

Table 2 : GENDER DISTRIBUTION OF STUDY PARTICIPANTS

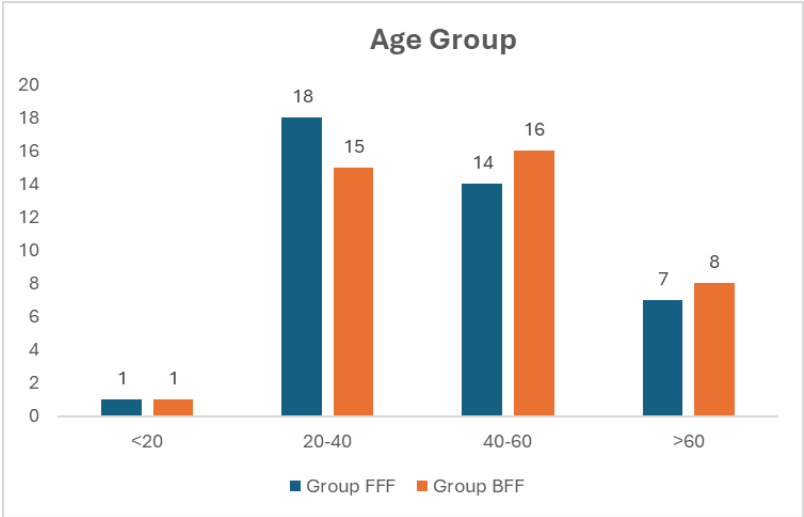

Figure 3: AGE DISTRIBUTION OF STUDY PARTICIPANTS

Table 2 shows the gender distribution of study participants. In FFF group, 30 (75%) were male and 10 (25%) were female. In BFF group, 32 (80%) were male and 8 (20%) were female. The P-value=0.592, indicating no significant difference between the groups.

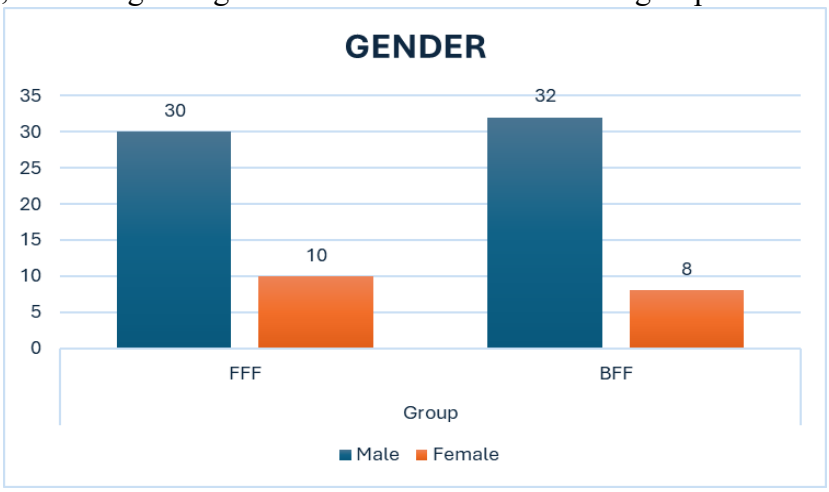

Figure 4: GENDER DISTRIBUTION OF STUDY PARTICIPANTS

Table 3: BMI distribution of study participants

BMI	Group				Total		P value
	FFF		BFF				
	n=40	%	n=40	%	n=80	%	
Underweight	17	42.5%	15	37.5%	32	80.0%	0.564
Normal	23	57.5%	24	60.0%	47	17.5%	
Overweight	0	0.0%	1	2.5%	1	2.5%	

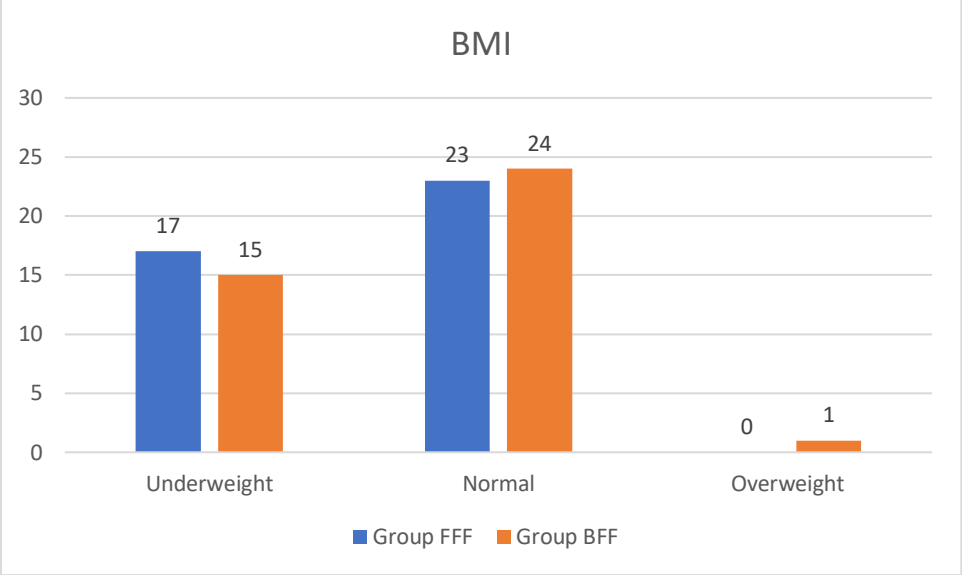

Figure 4: BMI DISTRIBUTION OF STUDY PARTICIPANTS

Table 3 shows the BMI distribution of study participants. Among the participants, 17 (42.5%) of the FFF group and 15 (37.5%) of the BFF group were classified as underweight. In the normal weight category, 23 (57.5%) of FFF and 24 (60.0%) of BFF participants were represented. Notably, only 2.5% of participants were classified as overweight, with no overweight individuals in the FFF group. BMI: P value 0.564, indicating no statistically significant difference in BMI distribution between the two groups.

Table 4: Distribution of study participants according to present complaints

Present complaints		Group				Total		P value
		FFF		BFF				
		n=40	%	n=40	%	n=80	%	
Cough	No	7	17.5%	6	15.0%	13	16.3%	0.762
	Yes	33	82.5%	34	85.0%	67	83.8%	
Expectoration	No	11	27.5%	16	40.0%	27	33.8%	0.237
	Yes	29	72.5%	24	60.0%	53	66.3%	
Fever	No	16	40.0%	17	42.5%	33	41.3%	0.82
	Yes	24	60.0%	23	57.5%	47	58.8%	
Loss of appetite	No	18	45.0%	23	57.5%	41	51.3%	0.263
	Yes	22	55.0%	17	42.5%	39	48.8%	
Chest pain	No	20	50.0%	23	57.5%	43	53.8%	0.501
	Yes	20	50.0%	17	42.5%	37	46.3%	
Breathlessness	No	20	50.0%	16	40.0%	36	45.0%	0.369
	Yes	20	50.0%	24	60.0%	44	55.0%	
Haemoptysis	No	29	72.5%	28	70.0%	57	71.3%	0.805
	Yes	11	27.5%	12	30.0%	23	28.8%	

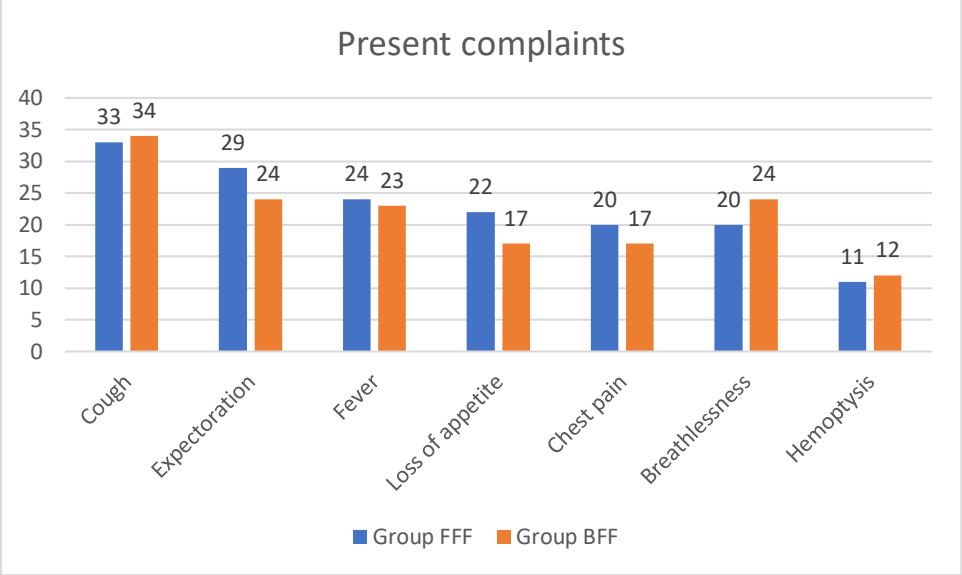

Figure 5: DISTRIBUTION OF STUDY PARTICIPANTS ACCORDING TO PRESENT COMPLAINTS

The distribution of study participants according to present complaints is revealed in Table 4. The majority of participants in both FFF 33 (82.5%) and BFF 34(85.0%) groups report experiencing cough. In terms of expectoration, 29 (72.5%) participants in FFF and 24 (60.0%) in BFF were reported. Regarding fever, 24 (60.0%) in FFF and 23 (57.5%) reported. For loss of appetite, 22 (55.0%) in FFF and 17 (42.5%) in BFF were reported. Lastly, both groups reported similar rates of hemoptysis, with 11 (27.5%) in FFF and 12 (30.0%) in BFF. P values for each of the complaints were all >0.05; thus, no statistically significant differences were noted between the groups.

Table 5: Comparison of BP parameters between groups

BP parameters		**Mean**	**Std. Deviation**	**P value**
SBP	FFF	124.3	9.0	0.724
	BFF	125.0	9.9	
DBP	FFF	80.8	8.0	0.885
	BFF	81.0	7.4	
Respiratory rate	FFF	16.4	2.6	0.061
	BFF	15.3	2.6	
Spo2	FFF	95.7	2.8	0.2
	BFF	96.5	2.6	

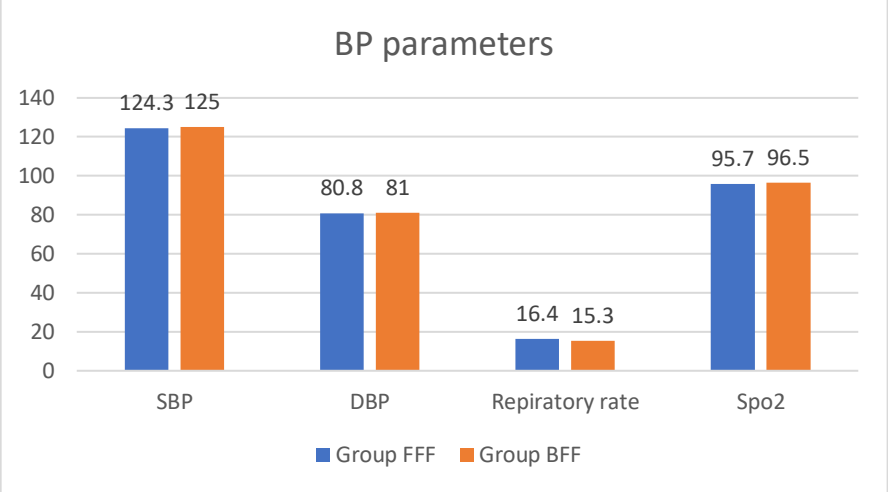

Figure 6: COMPARISON OF BP PARAMETERS BETWEEN GROUPS

Table 5 reveals the comparison of BP parameters between groups. The mean "systolic blood pressure (SBP)" was 124.3mmHg (SD = 9.0) among participants in the FFF group and 125.0 mmHg (SD = 9.9) among those in the BFF group (P = 0.724). For DBP, the mean value for the FFF group was 80.8 mmHg, while for the BFF group, it was 81.0 mmHg (P = 0.885). This difference is approximately 1 maximal breath (where the last digits of the last two numbers suffer a value difference of almost 0.11 ± 20.16%), which is significantly different (P = 0.061, FS = 0.02). Finally, the mean oxygen saturation (SpO2) in the FFF group was 95.7% (SD = 2.8) versus 96.5% (SD = 2.6) in the BFF group (P = 0.2), and this is not statistically different.

Table 6: Comparison of FEV 1 between groups

FEV1		**Mean**	**Std. Deviation**	**P value**
Baseline	FFF	61.9	8	0.572
	BFF	62.9	8.5	
2 weeks	FFF	68	8.8	0.023*
	BFF	63.5	8.6	
4 weeks	FFF	74.8	9.7	<0.001*
	BFF	64.2	8.7	
8 weeks	FFF	82.3	10.7	<0.001*
	BFF	64.8	8.8	

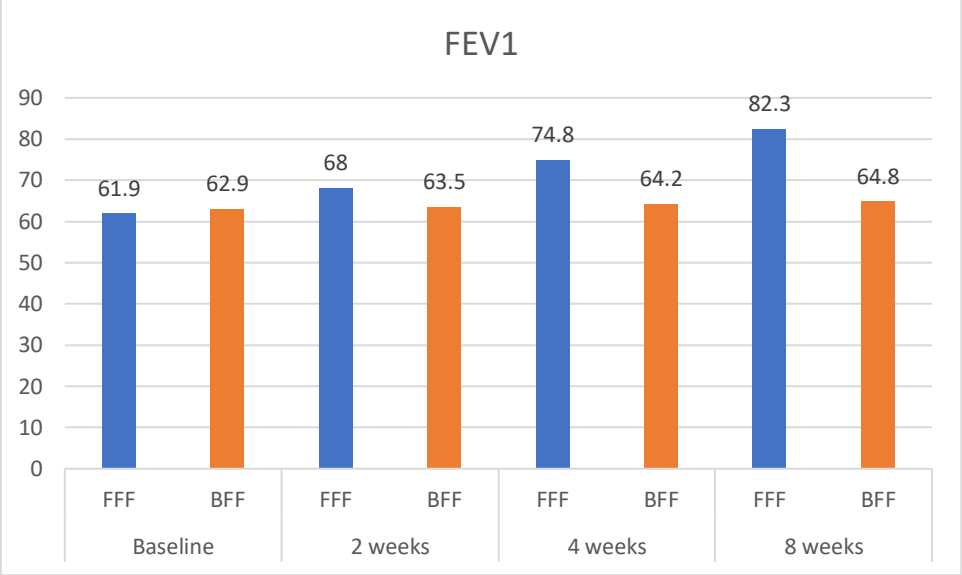

Figure 7: COMPARISON OF FEV 1 BETWEEN GROUPS

FEV1 is shown in Table 6. The FFF group had a mean FEV1 of 61.9 (SD = 8), P=0.572 baseline compared to BFF (mean 62.9; SD = 8.5). However, at 2 weeks (FFF 68 (SD = 8.8) vs. 63.5 (SD = 8.6); P = 0.023), a statistically significant difference was found between the FFF group and the BFF group. At 4 weeks, the FFF group had a mean FEV1 of 74.8 (SD = 9.7) and 64.2 (SD = 8.7) for the BFF group, with a P value <0.001, which shows that this difference is statistically significant. The FEV1 in the FFF group at 8 weeks was 82.3 (SD = 10.7) while 64.8 (SD = 8.8) in the BFF, with a P value <0.001, demonstrating a significant difference between the groups.

Table 7: Comparison of FVC between groups

FVC		**Mean**	**Std. Deviation**	**P value**
Baseline	FFF	77.4	8.7	0.872
	BFF	77.1	9.3	
2 weeks	FFF	69.7	7.9	<0.001*
	BFF	54	6.5	
4 weeks	FFF	62.9	7.2	<0.001*
	BFF	54	6.5	
8 weeks	FFF	44	5.1	<0.001*
	BFF	48.6	5.8	

Table 7 shows the comparison of FVC. The mean FVC was 77.4 (SD = 8.7) for the FFF group and 77.1 (SD = 9.3) for the BFF group at baseline, with a P value of 0.872, performed with no difference. However, at the 2-week mark, the FFF group had a mean FVC of 69.7 (SD = 7.9) vs. 54 (SD = 6.5) in the BFF group, and a P value of less than 0.001, which can be deemed statistically significant. The base difference in FVC between the FFF and BFF groups at 4 weeks was mean (SD) 62.9 (7.2) vs. 54 (6.5)—the P value < 0.001 showing statistical significance. At 8 weeks, mean FVC was 44 (SD = 5.1) in the FFF group and 48.6 (SD = 5.8)

in the BFF group, with a P value <0.001 demonstrating that there was a statistically significant difference between groups.

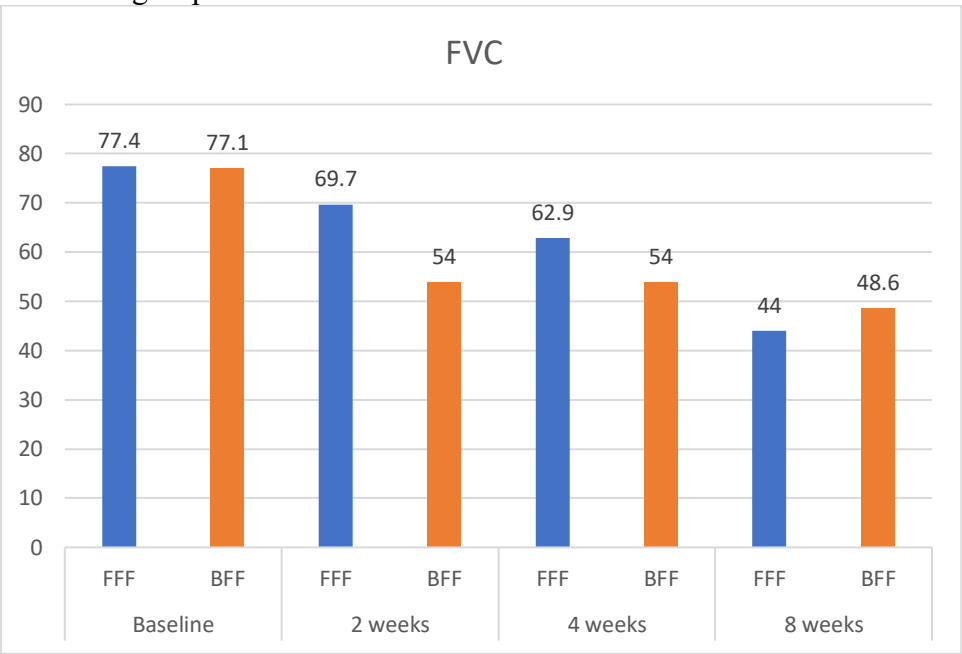

Figure 8: COMPARISON OF FVC BETWEEN GROUPS

Table 8: Comparison of FEV1/FVC ratio between groups

FEV1/FVC		Mean	Std. Deviation	P value
Baseline	FFF	0.8	0.2	0.652
	BFF	0.8	0.1	
2 weeks	FFF	1	0.2	<0.001*
	BFF	1.2	0.2	
4 weeks	FFF	1.8	0.2	<0.001*
	BFF	1.2	0.2	
8 weeks	FFF	1.9	0.4	<0.001*
	BFF	1.4	0.2	

The FEV1/FVC ratio comparison between FFF and BFF groups is shown in Table 9. The mean FEV1/FVC was 0.8 (SD = 0.2) for the FFF group and 0.8 (SD = 0.1) for the BFF group at baseline (P value = 0.652). Despite the statistically significant difference at the 2-week mark, the FFF group had a 1.0 (SD = 0.2) mean FEV1/FVC while the BFF group had a 1.2 (SD = 0.2), P-value < 0.001. As reported by Diab et al (5), at week 4, the mean FEV1/FVC was 1.8 (SD = 0.2) in the FFF group and 1.2 (SD = 0.2) for the BFF group, with a P < 0.001, thus confirming a significant difference between the groups. At 8 weeks, mean FEV1/FVC (SD) in the FFF group was 1.9 (0.4), and in the BFF group was 1.4 (0.2), with P < 0.001.

Table 9: Comparison of adverse effects between groups

Adverse effects	Group				Total		P value
	FFF		BFF				
	n=40	%	n=40	%	n=80	%	

Week 2	NIL	36	90.0%	25	62.5%	61	76.3%	0.038*
	Dyspnoea	1	2.5%	5	12.5%	6	7.5%	
	Infection	2	5.0%	7	17.5%	9	11.3%	
	Oral candidiasis	1	2.5%	3	7.5%	4	5.0%	
Week 4	NIL	38	95.0%	29	72.5%	67	83.8%	0.044*
	Dyspnoea	1	2.5%	2	5.0%	3	3.8%	
	Infection	1	2.5%	6	15.0%	7	8.8%	
	Oral candidiasis	0	0.0%	3	7.5%	3	3.8%	
Week 8	NIL	40	100.0%	34	85.0%	74	92.5%	0.09
	Dyspnoea	0	0.0%	1	2.5%	1	1.3%	
	Infection	1	100.0%	4	10.0%	4	5.0%	
	Oral candidiasis	2	200.0%	1	2.5%	1	1.3%	

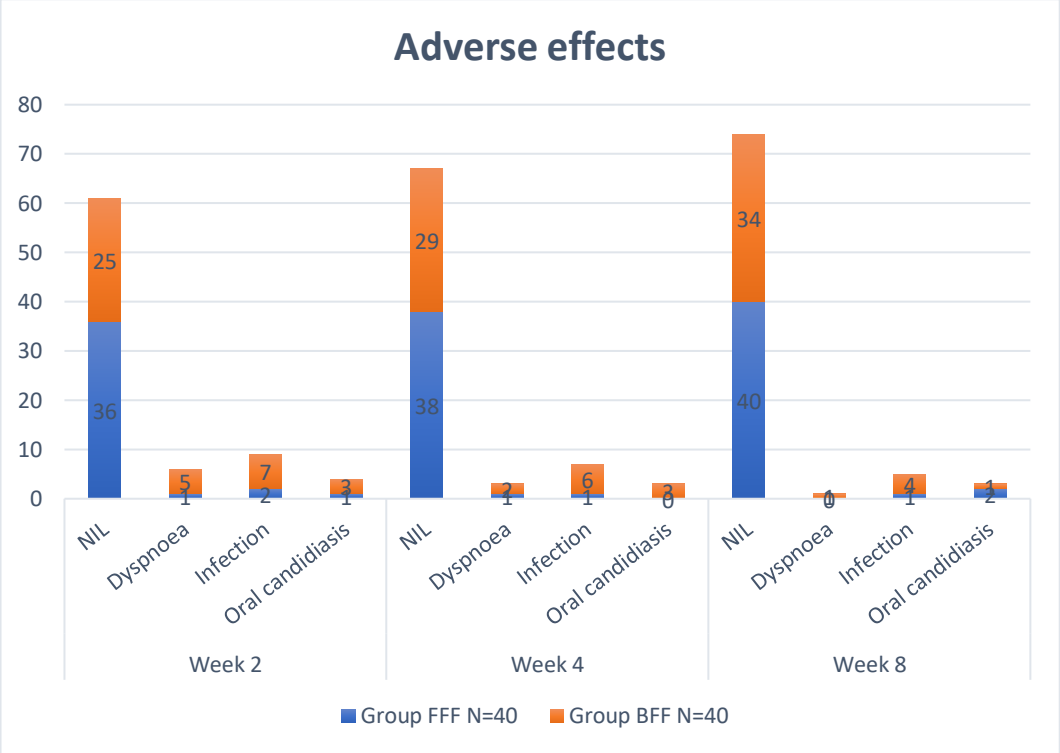

Figure 10: COMPARISON OF ADVERSE EFFECTS BETWEEN GROUPS

The comparison of adverse effects between the FFF and BFF groups, as shown in Table 10, revealed that at Week 2, 90.0% of the FFF group reported no adverse effects compared to 62.5% in the BFF group, with a P value of 0.038, that indicate a significant difference. At Week 4, 95.0% of the FFF group reported no adverse effects versus 72.5% in the BFF group, with a P value of 0.044, also significant. By Week 8, 100.0% of the FFF group reported no adverse effects compared to 85.0% in the BFF group, but the P value of 0.09 indicated no significant difference between the groups.

DISCUSSION

The chronic inflammatory airway illness known as asthma is defined by inflammation that results in airway hyperreactivity and blockage, which produces coughing, chest tightness, wheezing, and shortness of breath. It is a major world health problem that affects millions and importantly impacts quality of life. Data on ICS + LABA therapy as regular use in asthma management are used to reduce chronic inflammation and improve lung function (Oct 2023).. As asthma has a multifactorial etiology, early diagnosis and appropriate medication selection are crucial for achieving optimal disease control and reducing long-term complications.

In summary, data from our study suggests that the majority of participants were aged between 20 and 60 years in both the Fluticasone-Formoterol and Budesonide-Formoterol categories, with a very low percentage of people aged below and above these ranges. In the Fluticasone-Formoterol group, for instance, 45% of participants were aged 20-40 years, and 35% were aged 40-60 years. In the BFF group, 37.5% of participants were aged 20-40 years, and 40% were aged 40-60 years. These findings are consistent with previous studies. For example, Cukier et al. reported an average age of 35.1 years, with 19.9% of participants being adolescents (12–18 years), indicating a younger cohort.(57). Balki et al. and Lukaszyk AB et al. found a mean age of 41 years (±13.42 years) and 43 years (±14.42 years), which aligns closely with our study's dominant age group (20-60 years)(49,58).

In terms of gender, the Fluticasone-Formoterol group had 75% males while in Budesonide-Formoterol group had 80% males. Compared to other studies, Cukier et al. reported a predominantly female population (74.5%), which contrasts with our findings. Balki et al. found that 59% of male participants, aligned more closely with our study.(57,58). Our study findings regarding age and gender distribution are largely consistent with previous research, particularly in terms of mean age and male predominance. However, variations exist due to differences in study populations, geographic locations, and inclusion criteria.

The BMI distribution among participants in our study indicates that the majority were classified as underweight or normal weight, with very few in the overweight category. Specifically, the mean BMI was 23.4 ± 4.31 in the Fluticasone-Formoterol group and 24.13 ± 4.19 in the BFF group. Huang W et al. reported a higher mean BMI (25.7 vs. 24.2 kg/m², $p = 0.039$) in the Fluticasone-Formoterol group compared to the Budesonide-Formoterol group, indicating a slightly greater tendency toward overweight participants in their study.(10). Lukaszyk AB et al. found even higher BMI values (27.1 ± 5.31 vs. 27.43 ± 5.79), suggesting that their study population had a greater proportion of overweight or obese participants compared to our study.(49). These differences could be attributed to variations in study populations, lifestyle, or regional factors, emphasizing the need for further research on BMI-related impacts in asthma management.

Our study analyzed the distribution of presenting complaints among participants in the Fluticasone-Formoterol and Budesonide-Formoterol groups. Cough was the most commonly reported symptom in both groups followed by Expectoration, Fever, Loss of appetite, and Hemoptysis had a similar distribution. Huang W et al. reported dyspnea as the most common symptom, followed by cough, which aligns with our findings where cough was predominant but does not highlight dyspnea.(10). Kumar S et al. and Boulet et al. found breathlessness as the most frequent symptom, followed by cough. This differs from our study, where cough was the primary symptom rather than dyspnea.(14,59). Rhinitis (20.4%) was noted in Huang W et al., a symptom not prominently observed in our study. While cough remains a primary symptom across studies, differences in the prevalence of dyspnea, expectoration, and systemic symptoms highlight potential variations in disease presentation, population characteristics, or treatment response.

In our study, at baseline, the mean Spirometry values (FEV1, FVC, and FEV1/FVC) showed no significant difference. By 2 weeks, 4 weeks, and 8 weeks, the Fluticasone/Formoterol group

had significantly improved spirometry measurements compared to the Budesonide/Formoterol group. Compared with similar studies, Cukier A et al. observed a statistically significant increase in lung parameters by spirometry in the Fluticasone/Formoterol group from baseline to weeks, whereas the Budesonide/Formoterol group showed no significant improvement.(57). This aligns with our study. Balki A. et al. found that Fluticasone/Formoterol was non-inferior to Budesonide/Formoterol in terms of mean spirometry value change at week 12, with no significant difference between groups, which contrasts with our study.(58). Lukaszyk et al. also confirmed the non-inferiority of Fluticasone/Formoterol to Budesonide/Formoterol, showing similar spirometry improvements at weeks 2, 6, and 12(13). This finding is different from our study, where Fluticasone/Formoterol exhibited superior improvement over Budesonide/Formoterol as early as week 2. These studies suggest that Fluticasone-Formoterol provides superior spirometry improvement compared to Budesonide-Formoterol, with statistically significant differences emerging early and persisting over time.

In our study, at baseline, there was no significant difference while at week 2, week 4, and week 8, the Fluticasone-Formoterol group demonstrated superior symptom improvement compared to the Budesonide-Formoterol group confirming a highly significant difference between the two treatments. In comparison with Previous Studies, Furuhashi K et al. and Huang W K et al. reported no significant difference in ACQ-5 scores between Fluticasone-Formoterol and Budesonide-Formoterol, contradicting our findings, where the Fluticasone-Formoterol group demonstrated superior improvement over Budesonide-Formoterol group from Week 2 onward(10,60). Differences could be related to differences between patients (demographics or asthma severity), adherence to treatment, or length of study. However, long-term studies are needed to confirm that there was no difference, as previous studies indicate no difference; thus, the clinical impact of these findings is limited.

Our study suggests that the Fluticasone-Formoterol group has a better tolerability profile than the Budesonide-Formoterol group, with significantly fewer adverse effects at Weeks 2 and 4 and a trend toward fewer side effects at Week 8. The lack of significant difference by Week 8 may indicate that over time, patients in both groups adapted to treatment or that adverse effects naturally resolved. Lasserson TJ et al., Cukier A et al., and Balki A et al. reported no significant differences in the profile of adverse events between the Fluticasone-Formoterol group and Budesonide-Formoterol group, which differs from our results. (57,58,61). This discrepancy may be because of differences in study design, patient populations, duration of follow-up, or definitions of adverse events. Hence it can be suggested that the Fluticasone-Formoterol group is better tolerated than the Budesonide-Formoterol group especially in the early weeks of treatment, with fewer reported adverse effects. However, the results of the studies mentioned here are not completely consistent, thus additional study is required to validate these findings, particularly large-scale and long-term investigations.

CONCLUSION

The study revealed that both Fluticasone + Formoterol (FFF) and Budesonide + Formoterol (BFF) combinations effectively improved pulmonary function and symptom control in patients. However, on comparison, the FFF combination demonstrated a greater improvement in spirometry values over 2, 4, and 8 weeks, indicating superior clinical efficacy. Additionally, the FFF group exhibited a lower incidence of adverse effects at weeks 2 and 4 compared to the BFF group, highlighting better tolerability. To conclude, the Fluticasone + Formoterol (FFF) combination serves as the more effective option for achieving improved respiratory function, symptom relief, and safety in asthma patients.

REFERENCES

1. Asthma - Causes and Triggers | NHLBI, NIH [Internet]. [cited 2024 Oct 13]. Available from: https://www.nhlbi.nih.gov/health/asthma/causes
2. Papi A, Brightling C, Pedersen SE, Reddel HK. Asthma. Lancet (London, England) [Internet]. 2018 Feb 24 [cited 2024 Dec 28];391(10122):783–800. Available from: https://pubmed.ncbi.nlm.nih.gov/29273246/
3. Sockrider M, Fussner L. What Is Asthma? Am J Respir Crit Care Med [Internet]. 2020 Nov 1 [cited 2024 Dec 28];202(9):P25–6. Available from: https://pubmed.ncbi.nlm.nih.gov/33124914/
4. Chetta A, Calzetta L. Bronchial asthma: an update. Minerva Med [Internet]. 2022 Feb 1 [cited 2024 Dec 28];113(1):1–3. Available from: https://pubmed.ncbi.nlm.nih.gov/34913639/
5. Subbarao P, Mandhane PJ, Sears MR. Asthma: epidemiology, etiology and risk factors. C Can Med Assoc J [Internet]. 2009 Oct 10 [cited 2024 Oct 13];181(9):E181. Available from: /pmc/articles/PMC2764772/
6. Lugogo NL, Kraft M. Epidemiology of asthma. Clin Chest Med. 2006 Mar;27(1):1–15.
7. Miller RL, Grayson MH, Strothman K. Advances in asthma: New understandings of asthma's natural history, risk factors, underlying mechanisms, and clinical management. J Allergy Clin Immunol [Internet]. 2021 Dec 1 [cited 2024 Dec 28];148(6):1430–41. Available from: https://pubmed.ncbi.nlm.nih.gov/34655640/
8. Singh S, Salvi S, Mangal DK, Singh M, Awasthi S, Mahesh PA, *et al*. Prevalence, time trends and treatment practices of asthma in India: The Global Asthma Network study. ERJ Open Res 2022;8:00528-2021.
9) Dubin S, Patak P, Jung D. Update on Asthma Management Guidelines. Mo Med. 2024 Sep-Oct;121(5):364-367. PMID: 39421468; PMCID: PMC11482852.

10. Huang WC, Cheng WC, Chen CY, Liao WC, Wu BR, Chen WC, et al. Comparison of Budesonide/formoterol versus Fluticasone furoate/vilanterol as maintenance and reliever therapy for asthma control: a real-world observational study. BMC Pulm Med [Internet]. 2024 Dec 1 [cited 2024 Oct 12];24(1):1–10. Available from: https://bmcpulmmed.biomedcentral.com/articles/10.1186/s12890-024-03190-8
11. David S, Goldin J, Edwards CW. Forced Expiratory Volume. [Updated 2024 Oct 14]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK540970/

12. Papadopoulos NG, Miligkos M, Xepapadaki P. A Current Perspective of Allergic Asthma: From Mechanisms to Management. Handb Exp Pharmacol [Internet]. 2022 [cited 2024 Dec 28];268:69–93. Available from: https://pubmed.ncbi.nlm.nih.gov/34085124/
13. Bodzenta-Lukaszyk A, Buhl R, Balint B, Lomax M, Spooner K, Dissanayake S. Fluticasone/formoterol combination therapy versus budesonide/formoterol for the treatment of asthma: a randomized, controlled, non-inferiority trial of efficacy and safety. J Asthma [Internet]. 2012 Dec [cited 2024 Oct 12];49(10):1060–70. Available from: https://pubmed.ncbi.nlm.nih.gov/23102189/
14. Kumar S, Singh DP, Rath RS, Kushwaha G, Ansari S, Rai DK, et al. Clinical Profile of Adult Bronchial Asthma Patients Presenting at a Tertiary Care Teaching Institute in Northern

India. Cureus [Internet]. 2023 May 22 [cited 2024 Oct 12];15(5). Available from: /pmc/articles/PMC10282159/
15. Troeger C, Blacker B, Khalil IA, Rao PC, Cao J, Zimsen SRM, et al. Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory infections in 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Infect Dis [Internet]. 2018 Nov 1 [cited 2025 Jan 2];18(11):1191–210. Available from: https://pubmed.ncbi.nlm.nih.gov/30243584/
16. Safiri S, Mahmoodpoor A, Kolahi AA, Nejadghaderi SA, Sullman MJM, Mansournia MA, et al. Global burden of lower respiratory infections during the last three decades. Front public Heal [Internet]. 2023 Jan 9 [cited 2025 Jan 2];10. Available from: https://pubmed.ncbi.nlm.nih.gov/36699876/
17. Shi T, Denouel A, Tietjen AK, Campbell I, Moran E, Li X, et al. Global Disease Burden Estimates of Respiratory Syncytial Virus-Associated Acute Respiratory Infection in Older Adults in 2015: A Systematic Review and Meta-Analysis. J Infect Dis [Internet]. 2020 [cited 2025 Jan 2];222(Suppl 7):S577–83. Available from: https://pubmed.ncbi.nlm.nih.gov/30880339/
18. Hashmi MF, Tariq M, Cataletto ME. Asthma. StatPearls [Internet] [Internet]. 2024 May 3 [cited 2024 Oct 12]; Available from: https://www.ncbi.nlm.nih.gov/books/NBK430901/
19. Kwah JH, Peters AT. Asthma in adults: Principles of treatment. Allergy asthma Proc [Internet]. 2019 Nov 1 [cited 2024 Dec 28];40(6):396–402. Available from: https://pubmed.ncbi.nlm.nih.gov/31690379/
20. Asthma [Internet]. [cited 2024 Oct 13]. Available from: https://www.who.int/news-room/fact-sheets/detail/asthma/?gad_source=1&gclid=CjwKCAjw3624BhBAEiwAkxgTOqFvozN4zUek9vC2JszPaqgrqAQKC8R3oSGCWJ-ix5OGKP1kAIQNWhoClAkQAvD_BwE
21. Risk factors for asthma - UpToDate [Internet]. [cited 2024 Oct 13]. Available from: https://www.uptodate.com/contents/risk-factors-for-asthma
22. Guan SY, Zheng JX, Feng XY, Zhang SX, Xu SZ, Wang P, et al. Global burden due to modifiable risk factors for autoimmune diseases, 1990-2021: Temporal trends and socio-demographic inequalities. Autoimmun Rev [Internet]. 2024 Dec 1 [cited 2025 Jan 2];23(12). Available from: https://pubmed.ncbi.nlm.nih.gov/39461487/
23. Sharpe R, Thornton CR, Osborne NJ. Modifiable factors governing indoor fungal diversity and risk of asthma. Clin Exp Allergy [Internet]. 2014 [cited 2025 Jan 2];44(5):631–41. Available from: https://pubmed.ncbi.nlm.nih.gov/24471926/
24. Valencia-Hernández CA, Fabiola Del Greco M, Sundaram V, Portas L, Minelli C, Bloom CI. Asthma and incident coronary heart disease: an observational and Mendelian randomisation study. Eur Respir J [Internet]. 2023 [cited 2025 Jan 2];62(5). Available from: https://pubmed.ncbi.nlm.nih.gov/37945032/
25. Melén E, Zar HJ, Siroux V, Shaw D, Saglani S, Koppelman GH, et al. Asthma Inception: Epidemiologic Risk Factors and Natural History Across the Life Course. Am J Respir Crit Care Med [Internet]. 2024 Sep 15 [cited 2025 Jan 2];210(6). Available from: https://pubmed.ncbi.nlm.nih.gov/38981012/
26. Ntontsi P, Photiades A, Zervas E, Xanthou G, Samitas K. Genetics and Epigenetics in Asthma. Int J Mol Sci [Internet]. 2021 Mar 1 [cited 2024 Dec 28];22(5):1–14. Available from: https://pubmed.ncbi.nlm.nih.gov/33673725/
27. Willemsen G, Van Beijsterveldt TCEM, Van Baal CGCM, Postma D, Boomsma DI. Heritability of self-reported asthma and allergy: a study in adult Dutch twins, siblings and parents. Twin Res Hum Genet [Internet]. 2008 Apr [cited 2024 Oct 13];11(2):132–42. Available from: https://pubmed.ncbi.nlm.nih.gov/18361713/

28. Kaur R, Chupp G. Phenotypes and endotypes of adult asthma: Moving toward precision medicine. J Allergy Clin Immunol [Internet]. 2019 Jul 1 [cited 2024 Dec 28];144(1):1–12. Available from: https://pubmed.ncbi.nlm.nih.gov/31277742/
29. Corominas JM, Rabasa M. Fluticasone. Arch Otolaryngol Head Neck Surg [Internet]. 1997 [cited 2025 Jan 2];123(4):248–51. Available from: https://pubmed.ncbi.nlm.nih.gov/9109799/
30. Couillard S, Pavord ID. Fluticasone furoate: CAPTAIN of fluticasones in type 2 inflammatory asthma. Respirology [Internet]. 2022 Mar 1 [cited 2025 Jan 2];27(3):184–6. Available from: https://pubmed.ncbi.nlm.nih.gov/35104914/
31. Sutariya V, Kelly SJ, Weigel RG, Tur J, Halasz K, Sharma NS, et al. Nanoparticle drug delivery characterization for fluticasone propionate and in vitro testing 1. Can J Physiol Pharmacol [Internet]. 2019 [cited 2025 Jan 2];97(7):675–84. Available from: https://pubmed.ncbi.nlm.nih.gov/31100204/
32. McCarthy MW. Fluticasone propionate as a potential treatment for COVID-19. Drugs Today (Barc) [Internet]. 2022 May 1 [cited 2025 Jan 2];58(5):241–7. Available from: https://pubmed.ncbi.nlm.nih.gov/35535815/
33. Aschenbrenner DS. New Combination Asthma Drug. Am J Nurs [Internet]. 2023 May 1 [cited 2025 Jan 2];123(5):22. Available from: https://pubmed.ncbi.nlm.nih.gov/37077014/
34. López-Sanromán A, Clofent J, Garcia-Planella E, Menchén L, Nos P, Rodríguez-Lago I, et al. Reviewing the therapeutic role of budesonide in Crohn's disease. Gastroenterol Hepatol [Internet]. 2018 Aug 1 [cited 2025 Jan 2];41(7):458–71. Available from: https://pubmed.ncbi.nlm.nih.gov/30007787/
35. Barratt J, Kristensen J, Pedersen C, Jerling M. Insights on Nefecon®, a Targeted-Release Formulation of Budesonide and Its Selective Immunomodulatory Effects in Patients with IgA Nephropathy. Drug Des Devel Ther [Internet]. 2024 [cited 2025 Jan 2];18:3415–28. Available from: https://pubmed.ncbi.nlm.nih.gov/39100224/
36. Bafadhel M, Peterson S, De Blas MA, Calverley PM, Rennard SI, Richter K, et al. Predictors of exacerbation risk and response to budesonide in patients with chronic obstructive pulmonary disease: a post-hoc analysis of three randomised trials. Lancet Respir Med [Internet]. 2018 Feb 1 [cited 2025 Jan 2];6(2):117–26. Available from: https://pubmed.ncbi.nlm.nih.gov/29331313/
37. Lipworth B, Kuo CRW, Stewart K, Chan R. Budesonide/Formoterol or Budesonide/Albuterol as Anti-Inflammatory Reliever Therapy for Asthma. J allergy Clin Immunol Pract [Internet]. 2024 Apr 1 [cited 2025 Jan 2];12(4):889–93. Available from: https://pubmed.ncbi.nlm.nih.gov/38346474/
38. Tunceli O, Williams SA, Kern DM, Elhefni H, Pethick N, Wessman C, et al. Comparative Effectiveness of Budesonide-Formoterol Combination and Fluticasone-Salmeterol Combination for Asthma Management: A United States Retrospective Database Analysis. J Allergy Clin Immunol Pract. 2014 Nov 1;2(6):719-726.e6.
39. O'Byrne PM, FitzGerald JM, Bateman ED, Barnes PJ, Zhong N, Keen C, et al. Inhaled Combined Budesonide-Formoterol as Needed in Mild Asthma. N Engl J Med [Internet]. 2018 May 17 [cited 2025 Jan 2];378(20):1865–76. Available from: https://pubmed.ncbi.nlm.nih.gov/29768149/
40. Beasley R, Bruce P, Houghton C, Hatter L. The ICS/Formoterol Reliever Therapy Regimen in Asthma: A Review. J allergy Clin Immunol Pract [Internet]. 2023 Mar 1 [cited 2025 Jan 2];11(3):762-772.e1. Available from: https://pubmed.ncbi.nlm.nih.gov/36639054/
41. Krishnan JA, Buhl R. As-needed ICS/formoterol or as-needed SABA in mild asthma? Eur Respir J [Internet]. 2024 [cited 2025 Jan 2];63(4). Available from: https://pubmed.ncbi.nlm.nih.gov/38575166/

42. Reddel HK, Bateman ED, Schatz M, Krishnan JA, Cloutier MM. A Practical Guide to Implementing SMART in Asthma Management. J allergy Clin Immunol Pract [Internet]. 2022 Jan 1 [cited 2025 Jan 2];10(1S):S31–8. Available from: https://pubmed.ncbi.nlm.nih.gov/34666208/
43. Jacobson GA, Raidal S, Hostrup M, Calzetta L, Wood-Baker R, Farber MO, et al. Long-Acting β2-Agonists in Asthma: Enantioselective Safety Studies are Needed. Drug Saf [Internet]. 2018 May 1 [cited 2025 Jan 2];41(5):441–9. Available from: https://pubmed.ncbi.nlm.nih.gov/29332144/
44. Mostafa MM, Rider CF, Wathugala ND, Leigh R, Giembycz MA, Newton R. Transcriptome-Level Interactions between Budesonide and Formoterol Provide Insight into the Mechanism of Action of Inhaled Corticosteroid/Long-Acting β 2-Adrenoceptor Agonist Combination Therapy in Asthma. Mol Pharmacol [Internet]. 2021 [cited 2025 Jan 2];99(3):197–216. Available from: https://pubmed.ncbi.nlm.nih.gov/33376135/
45. Busse WW, Castro M, Casale TB. Asthma Management in Adults. J allergy Clin Immunol Pract [Internet]. 2023 Jan 1 [cited 2025 Jan 2];11(1):21–33. Available from: https://pubmed.ncbi.nlm.nih.gov/36283607/
46. Christopher DJ, Oommen AM, George K, Shankar D, Agrawal A, Thangakunam B. Prevalence of Airflow Obstruction as Measured by Spirometry, in Rural Southern Indian Adults. COPD [Internet]. 2020 Mar 3 [cited 2022 Sep 21];17(2):128–35. Available from: https://pubmed.ncbi.nlm.nih.gov/32020813/
47. Papi A, Blasi F, Canonica GW, Morandi L, Richeldi L, Rossi A. Treatment strategies for asthma: reshaping the concept of asthma management. Allergy Asthma Clin Immunol [Internet]. 2020 Aug 15 [cited 2025 Feb 11];16(1):75. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC7491342/
48. O'Keefe A, Connors L, Ling L, Kim H. Asthma. Allergy, Asthma Clin Immunol 2025 203 [Internet]. 2025 Feb 10 [cited 2025 Feb 11];20(3):1–16. Available from: https://aacijournal.biomedcentral.com/articles/10.1186/s13223-025-00949-4
49. Bodzenta-Lukaszyk A, Buhl R, Balint B, Lomax M, Spooner K, Dissanayake S. Fluticasone/formoterol combination therapy versus budesonide/formoterol for the treatment of asthma: a randomized, controlled, non-inferiority trial of efficacy and safety. J Asthma [Internet]. 2012 Dec [cited 2025 Feb 7];49(10):1060–70. Available from: https://pubmed.ncbi.nlm.nih.gov/23102189/
50. ATS/ACCP Statement on Cardiopulmonary Exercise Testing. Am J Respir Crit Care Med. 2003;167(2):211–77.
51. Asthma - Diagnosis | NHLBI, NIH [Internet]. [cited 2025 Feb 11]. Available from: https://www.nhlbi.nih.gov/health/asthma/diagnosis
52. National Institute of Health and Care Excellence, The British Thoracic Society, Scottish Intercollegiate Guideline Network. Asthma: diagnosis, monitoring and chronic asthma management. Gid-Ng10186 [Internet]. 2021 Mar 22 [cited 2025 Feb 11];(March 2021). Available from: https://www.ncbi.nlm.nih.gov/books/NBK560178/
53. PAVORD ID, PETERS AT, PORSBJERG C, CASTRO M, VIRCHOW JC, COUILLARD S, et al. ASSESSING THE IMPACT OF ASTHMA CONTROL QUESTIONNAIRE SCORE CUTOFFS WITHIN THE MULTICOMPONENT CLINICAL REMISSION ENDPOINT ON CLINICAL OUTCOMES: TRAVERSE OPEN-LABEL STUDY. Chest [Internet]. 2024 Oct 1 [cited 2025 Feb 11];166(4):A4797–800. Available from: http://journal.chestnet.org/article/S001236922403664X/fulltext
54. Rhee H, Love T, Mammen J. Comparing Asthma Control Questionnaire (ACQ) and National Asthma Education and Prevention Program (NAEPP) Asthma Control Criteria. Ann

Allergy Asthma Immunol [Internet]. 2018 Jan 1 [cited 2025 Feb 11];122(1):58. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC6309658/
55. Lamb K, Theodore D, Bhutta BS. Spirometry. StatPearls [Internet]. 2022 Jul 18 [cited 2022 Sep 20]; Available from: https://www.ncbi.nlm.nih.gov/books/NBK560526/
56. GOLD. Pocket guide to COPD diagnosis, management and prevention: a guide for health care professionals. Glob Initiat Chronic Obstr Lung Dis Inc [Internet]. 2018;1(1):3–14. Available from: http://goldcopd.org/wp-content/uploads/2018/02/WMS-GOLD-2018-Feb-Final-to-print-v2.pdf
57. Cukier A, Jacob CMA, Rosario Filho NA, Fiterman J, Vianna EO, Hetzel JL, et al. Fluticasone/formoterol dry powder versus budesonide/formoterol in adults and adolescents with uncontrolled or partly controlled asthma. Respir Med. 2013 Sep 1;107(9):1330–8.
58. Balki A, Balamurugan S, Bardapurkar S, Dalal S, Singh A, Singh BP, et al. Comparison of fluticasone/formoterol with budesonide/formoterol pMDI in adults with moderate to severe persistent asthma: Results from a 12-week randomized controlled trial. Pulm Pharmacol Ther [Internet]. 2018 Feb 1 [cited 2025 Feb 7];48:28–36. Available from: https://pubmed.ncbi.nlm.nih.gov/28890299/
59. Boulet LP, Boulay MÈ. Asthma-related comorbidities. Expert Rev Respir Med [Internet]. 2011 [cited 2024 Dec 28];5(3):377–93. Available from: https://pubmed.ncbi.nlm.nih.gov/21702660/
60. Furuhashi K, Fujisawa T, Hashimoto D, Kamiya Y, Yasui H, Karayama M, et al. Once-daily fluticasone furoate/vilanterol combination versus twice-daily budesonide/formoterol combination in the treatment of controlled stable asthma: a randomized crossover trial. J Asthma Allergy [Internet]. 2019 [cited 2025 Feb 11];12:253–61. Available from: https://pubmed.ncbi.nlm.nih.gov/31571932/
61. Lasserson TJ, Ferrara G, Casali L. Combination fluticasone and salmeterol versus fixed dose combination budesonide and formoterol for chronic asthma in adults and children. Cochrane database Syst Rev [Internet]. 2011 Dec 7 [cited 2025 Feb 7];2011(12). Available from: https://pubmed.ncbi.nlm.nih.gov/22161385/