

# Clinical pharmacist-led intervention improves anxiety, depression and inhaler technique in budesonide/glycopyrronium/formoterol-using patients: A single-center prospective randomized cohort study

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**Abstract: Background:** Chronic respiratory disease (CRD) patients using budesonide/glycopyrronium/formoterol (BGF) inhalers often face anxiety, depression and incorrect inhaler technique, which impair treatment outcomes. **Objectives:** This study aimed to evaluate the effects of clinical pharmacist-led intervention on anxiety, depression, inhaler technique, adverse drug reactions (ADR) and body mass index (BMI) in BGF users. **Methods:** A prospective randomized cohort study enrolled 100 BGF users from July 2023 to December 2023 at a public tertiary hospital and randomized them 1:1 to either the experimental or control group. Among these, 48 experimental patients and 45 control patients completed this study, which comprised an initial and three follow-up visits. The control group received routine care, whereas the experimental group received supplementary care led by a clinical pharmacist alongside conventional treatment. Outcomes included Self-Rating Anxiety Scale (SAS), the Self-Rating Depression Scale (SDS), Inhaler technique scores, Adverse drug reaction (ADR) and Body mass index (BMI) were assessed at 1-, 3- and 6-months post-intervention. **Results:** The experimental group had lower SAS scores at 3/6 months ( $p < 0.05$ ), lower moderate-to-severe anxiety rate at 6 months (68.75% vs. 93.33%,  $p < 0.05$ ) and lower SDS scores at 3/6 months ( $p < 0.05$ ). Inhaler technique scores were higher in the experimental group at all follow-ups ( $p < 0.05$ ). ADR incidence was lower (2 vs. 5 cases) and BMI slightly increased ( $p = 0.312$ ). **Conclusions:** Pharmacist-led intervention alleviates anxiety/depression, improves inhaler technique and reduces ADR in BGF users. These findings support the adoption of pharmacist-led integration into comprehensive BGF management.

**Keywords:** Anxiety; Budesonide/glycopyrronium/formoterol (BGF); Clinical pharmacist; Depression; Inhaler technique proficiency

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## INTRODUCTION

Chronic respiratory diseases (CRDs), primarily encompassing chronic obstructive pulmonary disease (COPD) and asthma, constitute a leading cause of global morbidity and mortality (Xiong *et al.*, 2023), long-term follow-up and observation of the impact of CRD is still ongoing (Grana-Castro *et al.*, 2024; Zhai *et al.*, 2025). Inhaled medications serving as the cornerstone of CRD pharmacological management due to their targeted action and favorable safety profile, first-line treatments include long-acting muscarinic antagonists (LAMA) and long-acting  $\beta_2$ -agonists (LABA) and inhaled corticosteroids (ICS) (Mannino *et al.*, 2025). The available evidence suggests that triple therapy may reduce rates of exacerbation and result in an improvement in health-related quality of life compared to combination LABA/LAMA inhalers (van Geffen *et al.*, 2023).

Budesonide/glycopyrronium/formoterol (BGF) is a fixed-dose combination of ICS, LAMA and LABA, which is approved for the maintenance treatment of chronic

respiratory disease (Heo, 2021; Takahashi *et al.*, 2024). BGF was launched in China on December 18, 2019. The availability and consumption of BGF were significantly greater than those of other inhalers from 2020 to 2022 (Li *et al.*, 2025). Although BGF has a greater deposition profile across each therapeutic component, including the total lung and large and small airway deposition profiles (Dorinsky *et al.*, 2020; Singh *et al.*, 2025), but BGF is a pressurized metered-dose inhaler (pMDI) which 92% of patients made at least one potentially important error (Perumal *et al.*, 2020). Incorrect inhaler technique is considered a practical barrier to adherence and proper use of BGF devices is essential for achieving compliance. Studies on clinical pharmacist interventions for patients using BGF remain limited.

However, the clinical efficacy of inhalers is not solely determined by drug formulation or device type; accumulating evidence indicates that comorbid psychological states, particularly anxiety and depression, significantly undermine treatment outcomes (M. Chen *et al.*, 2026). Patients with CRDs frequently exhibit anxiety and depressive symptoms and anxiety and depression are

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commonly observed in patients with COPD, with prevalence rates ranging from 10% to 65% (Wu et al., 2025), reducing inhaler technique proficiency and increasing the risk of readmission for diseases (Martinez-Gestoso et al., 2022). Anxiety-induced hyperventilation can alter airway responsiveness, while depressive symptoms correlate with poor inhaler use, directly reducing drug deposition in the lower respiratory tract. Furthermore, anxiety and depression can contribute to reduced adherence to treatment, fewer positive health behaviors and higher medical costs (Abbas et al., 2023). These psychological burdens further erode patients' willingness to take medication and their confidence in treatment, establishing a vicious cycle of "clinical deterioration → escalating distress → declining adherence → further exacerbations" that undermines the consistency and effectiveness of care.

Current strategies to mitigate anxiety and depression primarily include non-pharmacological approaches such as physical exercise, cognitive-behavioral therapy and complementary interventions like inhalation aromatherapy (Cui et al., 2022). Notably, a critical gap exists in the literature regarding the role of clinical pharmacists—key providers of medication therapy management in CRD care—in addressing these psychological comorbidities. Clinical pharmacists are uniquely positioned to optimize inhaler use through device training and deliver patient-centered education. Emerging evidence supports pharmacist-led mental health interventions in community settings (Taylor et al., 2024), which improve outcomes in patients with depressive and anxiety disorders (Cabasag et al., 2025; Sarwar et al., 2025). However, very limited studies are available to evaluate whether pharmacist-driven interventions targeting anxiety and depression can enhance inhaler efficacy and subsequent treatment outcomes.

Given these challenges, the traditional physician-dominated model of care poses limitations in providing continuous and refined medication management and psychological support. This creates a clear space and necessity for pharmaceutical interventions. In 2020, the National Health Commission of the People's Republic of China issued the "Notice on the issuance of five norms, including the norms for pharmacy outpatient services in medical institutions" (NHCotPsRo., 2021), which proposed a series of standardized requirements for expanding pharmaceutical services. Aligning with national and provincial policy directives, measures to improve the quality of medical services provided by clinical pharmacists were actively promoted at the study hospital. To address this unmet need, this study therefore aims to investigate the impact of a structured clinical pharmacist intervention—integrating psychological symptom assessment, inhaler technique optimization and mental health support—on both anxiety/depression scores and objective measures of inhaler response, with the goal of

providing a novel, feasible strategy to improve management.

## MATERIALS AND METHODS

### Study design

This single-center, prospective, randomized cohort study enrolled 100 patients from July 2023 to December 2023, with a 6-month follow-up period, at a public tertiary hospital. The study received approval from the Medical Research and Ethics Committee of the First Hospital of Putian City. This trial was prospectively registered in the Chinese Clinical Trials Registry (ChiCTR2400090585, registered 10 January 2024; URL: <https://www.chictr.org.cn/showproj.aspx?proj=2400090585>). This study was approved by the First Hospital of Putian City Research and Ethics Office (2023--088). The procedures adhered to the ethical standards of the Program for the Protection of Human Subjects and the 1975 Declaration of Helsinki. All the participating clinicians and patients provided written informed consent.

### Sample size calculation

A priori sample size estimation was performed during the study design phase. Using the sample size calculation method for comparing two independent means ( $\alpha = 0.05$ , two-tailed test, target power = 80%) and based on previous studies reporting (Cohen's  $d \approx 0.5$ ), the required sample size was estimated to be approximately 42 patients per group to achieve sufficient statistical power. Considering potential loss to follow-up, the final sample size was determined based on the actual data collection period. A minimum of 45 patients per group was required; 100 patients were enrolled to account for a 10% dropout rate.

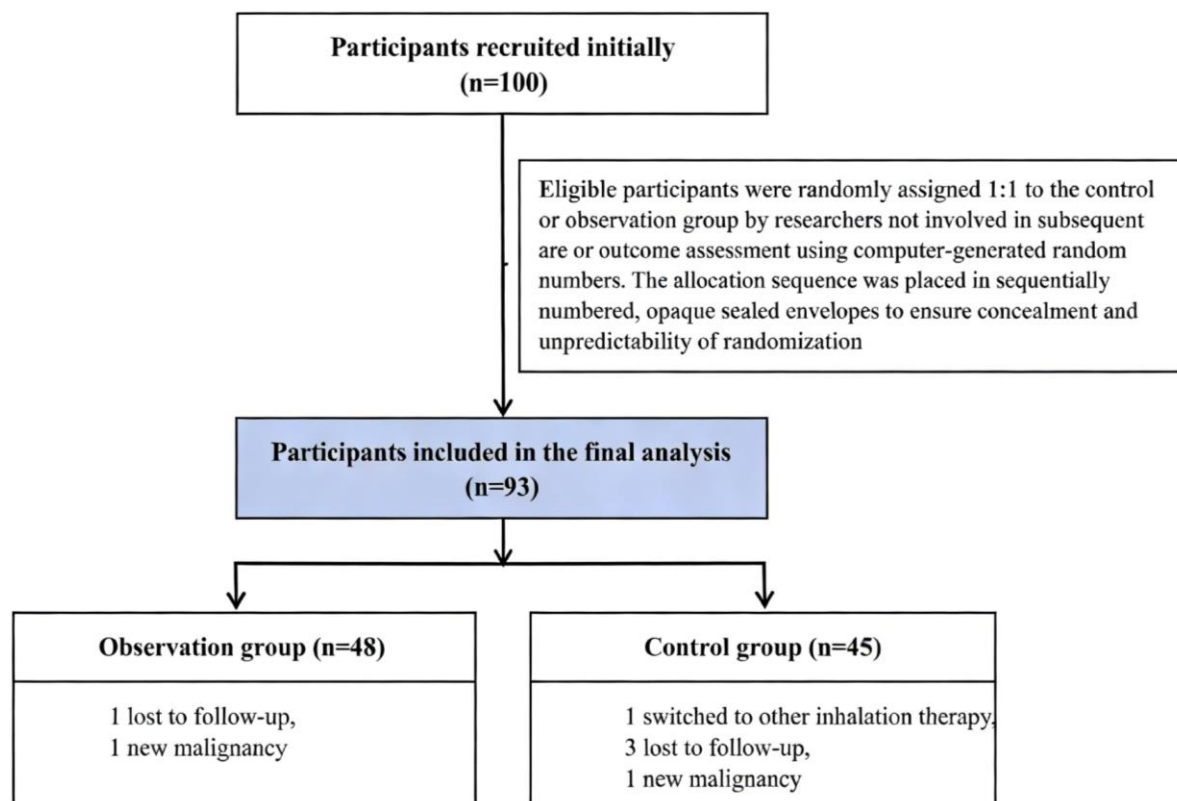
### Study population

**Inclusion criteria:** (1) inhaled BGF; (2) in the stable disease stage; (3) aged between 40 and 80 years; (4) clear consciousness, no communication barriers and the ability to express their intentions correctly. (5) COPD; the diagnosis and disease severity classification were meeting the "Guidelines for the diagnosis and management of chronic obstructive pulmonary disease ("[Guidelines for the diagnosis and management of chronic obstructive pulmonary disease (revised version 2021)]," 2021)".

**Exclusion criteria:** (1) refusal to cooperate with the follow-up plan; (2) comorbidity with mental disorders, severe organic diseases, or hepatic/renal dysfunction; (3) current use of antidepressant or antipsychotic medication.

**Withdrawal criteria for patients:** (1) lost to follow-up; (2) newly diagnosed with malignant tumors.

After enrolment, an investigator with no role in subsequent care or outcome assessment used computer-generated random numbers to allocate eligible participants 1:1 to the control or observation group (Fig. 1).



**Fig. 1:** CONSORT flow diagram of patient enrollment and analysis in the study.

The allocation sequence was placed in sequentially numbered, opaque, sealed envelopes, ensuring concealment and the unpredictability of randomness. This study initially enrolled 100 patients, of whom 93 patients eventually completed the follow-up study, with 48 patients in the experimental group (1 patient lost to follow-up and 1 patient with a newly developed malignant tumor) and 45 patients in the control group (1 patient switched to another inhalation, 3 patients lost to follow-up and 1 patient with a newly developed malignant tumor). The full selection flow is depicted in Fig. 1.

**Randomization process**

Patients were randomized by a researcher who was not involved in study implementation, using a random-number table method. Patients were assigned to either the control group or the observation group in a 1:1 ratio. Outcome assessors (who evaluated SAS/SDS scores and inhaler technique) were blinded to group allocation; patients and treating clinicians were not blinded.

**Clinical pharmacist-led intervention**

The control group patients received routine medical services jointly by physicians and nurses, comprising disease assessment, pharmacological prescribing, basic medication education and routine nursing follow-up. No intervention by clinical pharmacists was provided.

medical services, based on the “Structure of Clinical Pharmacist Intervention Guidelines” (developed by the study hospital and comprising:

*Medication guidance:* Individual medication evaluation and one-to-one coaching were provided, focusing on BGF, particularly the correct use of inhalers. An incorrect operation was identified using medication training devices and video demonstrations. The operation was repeatedly practiced and corrected at the scene until the patient became proficient, thereby enhancing medication compliance. Educational materials for inhaler use were distributed, addressing the issue of lengthy instructions that fail to highlight key medication points. Using the study hospital's specialized BGF inhaler technique scoring checklist, the pharmacists quantitatively assessed patients’ inhaler technique.

*Psychological support:* During ward rounds, medication guidance and routine contacts, the clinical pharmacist actively listened to the patient’s BGF use and offered basic emotional support and health counseling. When the anxiety/depression scores indicated significant distress, the pharmacist immediately alerted the attending physician and facilitated referral under the physician’s or a psychological counselor’s supervision, ensuring professional psychological intervention.

*Establishment of health records and follow-up:* A comprehensive profile documenting medication use,

The experimental group patients adopted clinical pharmacist-led interventions in addition to the routine

comorbidities and baseline anxiety/depression scores was established at admission. All patients were scheduled for uniform follow-ups after discharge via outpatient visit or, if non-attending, telephone. The continuity of medication use was ensured. Follow-up timing and modality were identical for both the control and experimental groups.

**Enhancing disease awareness:** Regarding lifestyle or medication habit changes, such as quitting smoking and adhering to regular medication regimens, clinical pharmacists provide monthly explanations of their importance to patients, as well as careful and attentive "three-heart service."

**Intervention modality and frequency:** When in-hospital, patients received at least 3 face-to-face sessions (early admission and pre-discharge). After discharge, patients had 6 months of follow-up (outpatient or by telephone). For individuals with poor adherence or marked anxiety/depression, extra follow-ups were provided and referrals were assisted when indicated.

#### **Observational indicators and evaluation criteria**

The following indicators were recorded for both groups of patients at baseline, 1 month, 3 months and 6 months of follow-up.

**Anxiety** was assessed using the Self-Rating Anxiety Scale (SAS). According to the scale criteria, a score of <50 indicated no anxiety, 50–59 indicated mild anxiety, 60–69 indicated moderate anxiety and  $\geq 70$  indicated severe anxiety. The rate of moderate-to-severe anxiety was calculated as (Moderate + Severe) / Total cases \* 100%.

**Depression** was assessed via the Self-Rating Depression Scale (SDS). Per the established scoring criteria of the scale, scores < 53 denoted no depression, 53–62 denoted mild depression, 63–72 denoted moderate depression and > 72 denoted severe depression. The rate of moderate-to-severe depression was calculated as (Moderate + Severe) / Total cases \* 100%.

**ADR:** All adverse reactions were ascertained by dual sources; patient self-report and medical record review. In-hospitals, clinical pharmacists and attending physicians documented suspected drug-related adverse reactions during daily ward rounds. Post-discharge (1-, 3- and 6-month follow-up) adverse reactions were inquired about and recorded at outpatient visits or via telephone.

**Causality assessment:** Causality was assessed against the China Annual ADR Monitoring Guidelines and the WHO User Manual for Causality Assessment.

**Inhaler technique scores:** Based on the drug instructions, our hospital has developed a scoring system for inhalation preparations to assess inhalation technique. The total score for BGF inhalation preparations is 100 points; a higher score indicates a better technique.

Body mass index (BMI):  $BMI = \text{weight (kg)} / [\text{height (m)}]^2$

#### **Statistical analysis**

The data were analyzed using SPSS 26.0. For categorical variables presented as counts (n) and percentages (%), the  $\chi^2$  test was used for intergroup comparisons. Continuous variables were first examined for normality. Normally distributed data were expressed as  $(\bar{x} \pm s)$  and the comparisons between groups were performed using the t-test, while the comparisons within groups were conducted using repeated-measures ANOVA. All tests were two-tailed and  $p < 0.05$  was considered statistically significant. All analyses were performed on the complete-case population, which included participants who completed the 6-month follow-up (48 in the experimental group, 45 in the control group). Participants who withdrew, were lost to follow-up, or discontinued the intervention were excluded from the analysis. Missing outcome data due to loss to follow-up or discontinuation were not imputed; only participants with complete data at each time point were included in the analysis (complete-case analysis).

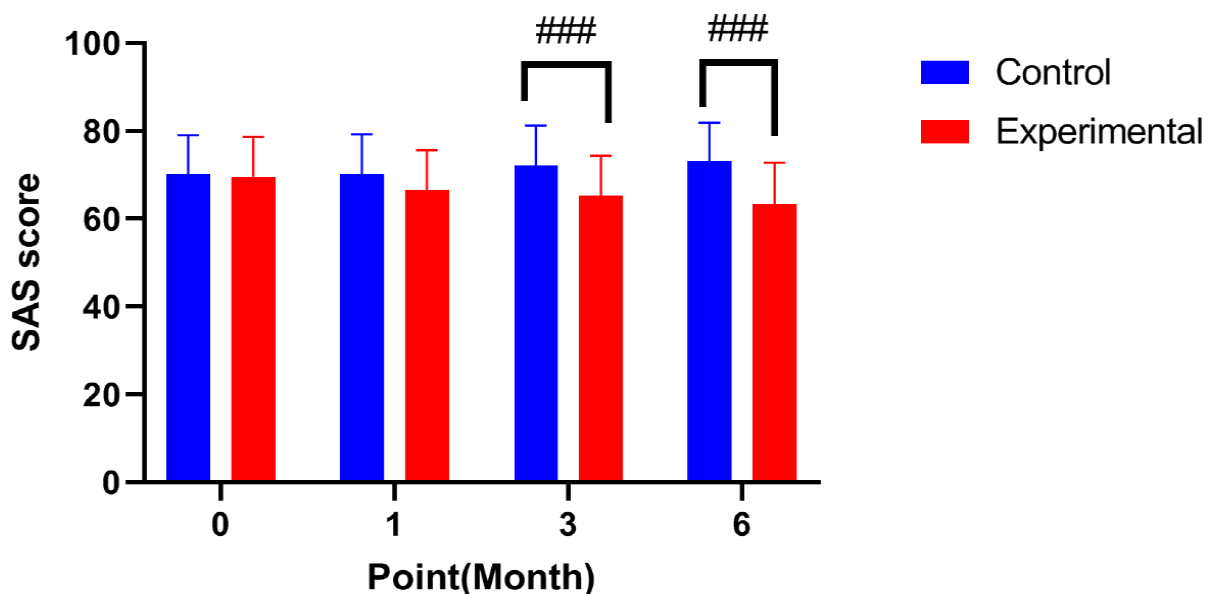
## **RESULTS**

There were no statistically significant differences between the two groups in terms of age, sex, educational level or other baseline characteristics ( $p > 0.05$ ), confirming their comparability. The baseline characteristics of the study participants are presented in Table S1.

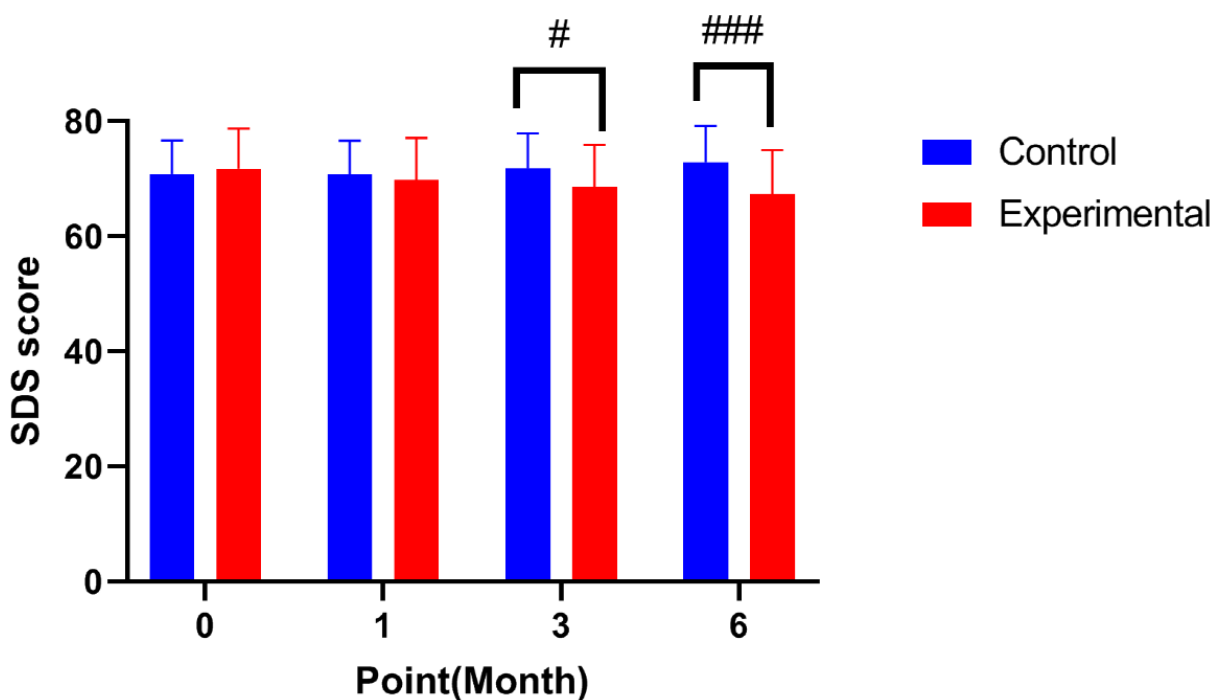
#### **Comparison of anxiety between the two groups**

SAS scores at 1-, 3- and 6- month follow-up of the control and experimental groups are shown in Fig. 2. At 3- and 6-month follow-up, the experimental group had significantly lower SAS scores than the control group ( $p < 0.05$ ), whereas baseline scores were not significantly different ( $p > 0.05$ ). At 6 months, the mean SAS score was 63.5 (SD 9.5) in the experimental group versus 73.2 (SD 8.7) in the control group (mean difference -9.7, 95% CI: -13.4 to -5.9,  $p < 0.001$ ). Repeated-measures ANOVA revealed statistically significant main effects of time ( $F = 62.700$ ,  $p < 0.05$ ), group ( $F = 7.685$ ,  $p < 0.05$ ) and a significant time-by-group interaction effect ( $F = 452.28$ ,  $p < 0.05$ ) for SAS scores.

The distribution of SAS severity levels and the proportion of moderate-to-severe anxiety at 1-, 3- and 6- month follow-up are presented in Table S2. The rate of moderate-to-severe anxiety in the experimental group was lower than that in the control group only at 6 months follow-up ( $p < 0.05$ ) and the overall severity distribution differed significantly between groups at 6- month follow-up ( $p < 0.05$ ). The absolute risk difference for moderate-to-severe anxiety at 6 months was -24.6% (95% CI: -39.2% to -10.0%); relative risk = 0.74 (95% CI: 0.59 to 0.92),  $p = 0.003$ .



**Fig. 2:** Self-Rating Anxiety Scale (SAS) scores of patients using BGF in two groups at different time points (mean ± SD). Note: ###  $p < 0.01$ .



**Fig. 3:** Self-Rating Depression Scale (SDS) scores of patients using BGF in two groups at different time points (mean ± SD). Note: #  $p < 0.05$ , ###  $p < 0.01$ .

#### Comparison of depression between the two groups

SDS scores at 1-, 3- and 6- month follow-up of the control and experimental groups are summarized in Fig. 3. The experimental group exhibited lower SDS scores than the control group at 3- and 6-month follow-up ( $p < 0.05$ ). At 6 months, the mean SDS score was 67.5 (SD 7.7) in the experimental group versus 73.0 (SD 6.4) in the control group (mean difference -5.5, 95% CI: -8.4 to -2.6,  $p <$

0.001), whereas no between-group differences were detected at baseline or 1 month ( $p > 0.05$ ). For SDS scores, repeated-measures ANOVA demonstrated a statistically significant main effect of time ( $F = 44.807$ ,  $p < 0.05$ ) and a significant time-by-group interaction effect ( $F = 277.662$ ,  $p < 0.05$ ), while the main effect of group was not statistically significant ( $F = 2.479$ ,  $p = 0.119$ ).

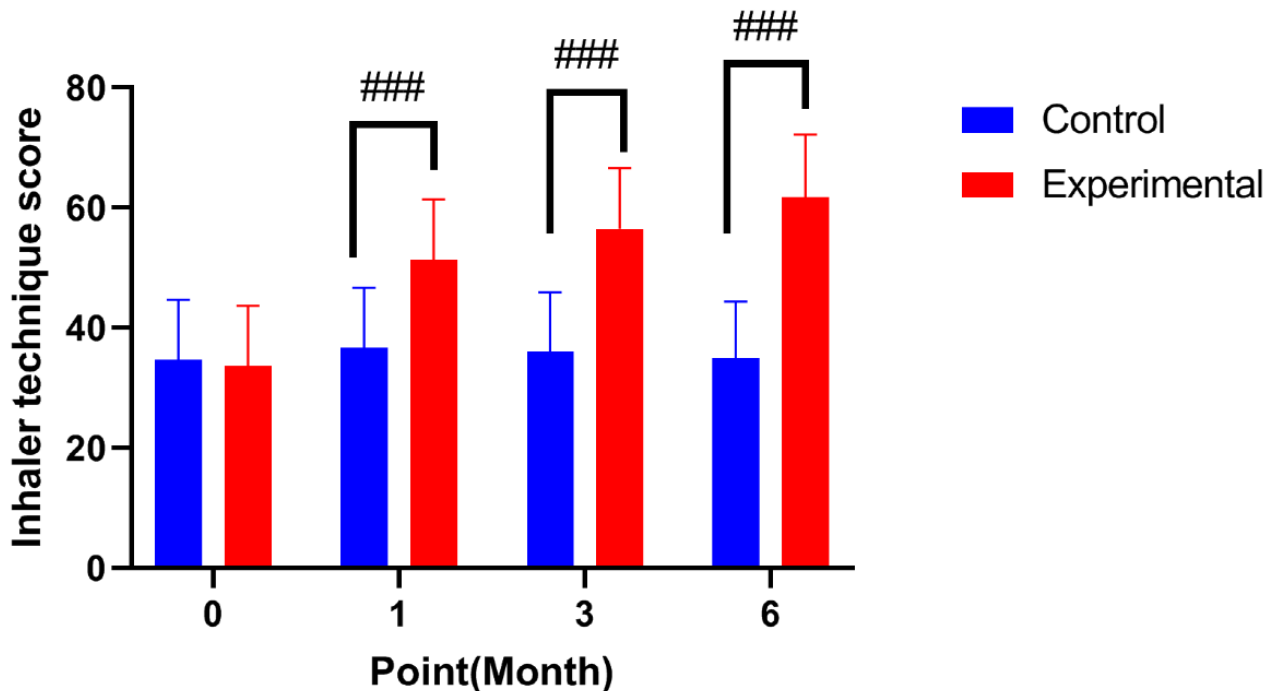


Fig. 4: Inhaler technique scores of patients using BGF in the two groups at different time points (mean  $\pm$  SD).

The distribution of SDS severity levels and the proportion of moderate-to-severe depression at 1-,3- and 6- month follow-up are presented in Table S3. At 6 months, the overall severity distribution of depression in the experimental group was lower than that in the control group ( $p=0.001$ ). The absolute risk difference for moderate-to-severe depression at 6 months was -10.0% (95% CI: -22.1% to 2.1%); relative risk = 0.89 (95% CI: 0.77 to 1.03),  $p = 0.136$ .

#### Comparison of BGF inhaler technique score between the two groups

BGF inhaler technique score at 1-,3- and 6- month follow-up of the control and experimental groups are shown in Fig. 4. Across all follow-up points, the experimental group had significantly higher BGF inhaler technique score than the control group ( $p < 0.05$ ), whereas baseline scores were not significantly different ( $p > 0.05$ ). At 6 months, the mean inhaler technique score was 56.4 (SD 9.8) in the experimental group versus 37.2 (SD 9.8) in the control group (mean difference 19.2, 95% CI: 15.2 to 23.3,  $p < 0.001$ ). BGF inhaler technique score showed statistically significant main effects of time and group, as well as a significant time-by-group interaction effect ( $F = 577.843$  for time,  $F = 56.721$  for group,  $F = 520.294$  for time-by-group interaction; all  $p < 0.05$ ).

#### Comparison of ADR between the two groups

After the 6-month follow-up, the number of ADR was 2 in the experimental group (1 patient with vocal problems and 1 patient with oral candidiasis) and 5 in the control group (2 patients with vocal problems, 1 patient with oral

candidiasis and 1 patient with insomnia). The absolute risk difference for any ADR was -6.0% (95% CI: -16.4% to 4.4%); relative risk = 0.40 (95% CI: 0.08 to 1.97),  $p = 0.205$ .

#### Comparison of BMI between two groups

Before the intervention, the BMI of the experimental group was  $20.43 \pm 2.90$ , whereas that of the control group was  $20.61 \pm 3.34$  ( $\chi^2=0.287$ ,  $p=0.775$ ). The BMI of the experimental group was  $20.56 \pm 3.02$ , whereas that of the control group was  $19.87 \pm 3.52$  after a 6-month follow-up. The mean difference was 0.69 (95% CI: -0.66 to 2.04),  $p = 0.312$ . The BMI of the experimental group increased slightly, whereas the BMI of the control group decreased gradually; however, these changes were not statistically significant.

## DISCUSSION

This prospective randomized cohort study showed that, after pharmacist intervention, anxiety and depression scores, as well as the incidence of moderate-to-severe rates, decreased markedly. The incidence of ADR was also lower than in the control group. These findings align with prior evidence that pharmacist-led promotion both improves clinical outcomes and patient empowerment in the long term.

#### Clinical pharmacists alleviate anxiety and depressive states in patients using BGF

Due to illness, patients experience a decline in sleep quality and appetite, which can lead to anxiety and depression

(Saguban *et al.*, 2025). Moreover, depression and inflammation are bidirectionally related: depression causes an increase in inflammation (Cao, Jiang, Chen, & Dai, 2025), while increased inflammation also heightens susceptibility to depression, creating a vicious cycle that exacerbates the patient's condition. Researchers identified a statistically significant correlation between anxiety and non-adherence to medication, where greater levels of anxiety were associated with lower rates of adherence (Alkadi *et al.*, 2025).

Relevant prior research has substantiated the applicability of SAS and SDS in populations with chronic airway diseases (Chen *et al.*, 2025) and SAS and SDS have garnered recognition and application in clinical research (Chen *et al.*, 2023). In this study, the experimental group presented a reduction in anxiety and depression ( $p < 0.05$ ), with the benefit becoming even more pronounced in the medium-and long-term. Furthermore, following the clinical pharmacist intervention, the experimental group presented a downward trend in anxiety and depression at follow-up compared with pre-follow-up ( $p < 0.05$ ). These findings underscore the importance of providing continuous, effective pharmaceutical services to patients with BGF. Although few studies have directly examined the impact of pharmacist intervention on psychological status in patients, our results echoed reports from other chronic diseases showing that patient-centered, "companion-style" monitoring and continuous health education enhance patients' sense of control and therapeutic confidence.

Physicians, constrained by time, often cannot address psychosocial needs in depth, while pharmacists are ideally positioned to close this gap. Medication, disease and health education are provided to patients, safe medication information leaflets are distributed and a healthy and harmonious living environment is actively fostered to reduce fluctuations in patient anxiety and depression. Frequent communication and interaction with patients and their families enhances a sense of belonging and personal value, thereby increasing confidence in treatment. This project will continue to strengthen follow-up efforts, particularly by providing more intensive medication education and psychological counseling to patients with lower educational backgrounds, to obtain more clinical data. The potential effect of mental health concerns on adherence to treatment needs to be considered by medical practitioners (Volpato *et al.*, 2021).

#### **Clinical pharmacists improved the inhaler technique scores of patients using the BGF**

Delivery technology, such as BGF formulation, allows for more consistent dose administration than dry powder inhalers (DPI) (Maes, *et al.*, 2019). However, the optimal therapeutic effects of this medication can be achieved only when patients have a certain level of hand-mouth

coordination and use the inhaler correctly. In the traditional treatment model, medical institutions lack dedicated consultation areas for inhaled formulations (Ali, *et al.*, 2022), leading to poor mastery of inhaled BGF formulations. The involvement of clinical pharmacist-led in the management of inhaled BGF formulations is a strong supplement to the treatment process:

(1) Compared with doctors, clinical pharmacists are prior inhaler technique trainers (Klijn *et al.*, 2017) of BGF characteristics, operation procedures and adverse reactions, thereby providing professional recommendations for clinical medication; (2) Clinical pharmacists have more sufficient time to provide medication guidance to patients and their family members; and (3) Through BGF promotional materials, clinical pharmacists repeatedly reinforce and demonstrate the technical points where patients tend to make operational errors, which improves the correctness of patients' inhaler device use.

The BGF inhaler technique scores were relatively low in this study, which was attributed to the fact that most patients in the region have low educational levels, resulting in a poor ability to understand and master correct BGF inhaler use. The inhaler technique scores of BGF were consistently greater in the experimental group across all follow-up points and compared with those in the prefollow-up period, the inhaler technique scores also increased. These results indicated that pharmaceutical care intervention is a positive and effective model of drug management. In the future, it is necessary to increase the frequency of professional guidance on inhaler techniques provided by clinical pharmacists to improve the inhaler technique of BGF patients.

#### **Clinical pharmacists reduce ADR in patients using BGF**

In addition to alleviating anxiety and depressive states, the experimental group demonstrated lower ADR compared with the control group. This finding is particularly impactful, as this improvement was likely driven by the intervention of clinical pharmacists, which accords with reports (Ruan *et al.*, 2024). In the future, it will be ensured that patients receive guidance before medication, reference during medication and solutions when ADR occur, guaranteeing the safety of medication use throughout the entire process.

#### **Clinical pharmacists increase BMI in patients using BGF**

Efficient pulmonary function is an important determinant of BGF. Recent research has approximated that 25–40% of patients with COPD are underweight, whereas 35% of these patients have severely low fat-free mass indices (Keogh and Mark Williams, 2021). BMI is positively correlated with muscle mass, whereas muscle mass is positively correlated with the inhalation force required for inhaled formulations. Therefore, nutritional education for BGF patients should be increased and their muscle strength

should be improved, thereby indirectly enhancing inhalation efficacy.

In this study, although the lower incidence of ADR in the experimental group did not reach statistical significance, the downward trend is clinically meaningful and corroborates the safety-enhancing role of pharmaceutical care in long-term therapy. Clinical pharmacists not only improved the BMI of patients in the experimental group but also indirectly elevated their inhaler technique scores. Meanwhile, improved BMI can strengthen patients' immune function, thereby further delaying disease progression.

#### **Limitation and future recommendations**

Several limitations should be acknowledged. First, the study was conducted at a single center with inpatients. Although the sample size was estimated and shown to meet statistical requirements, selection bias may still exist, limiting the generalizability of the findings. Second, primary endpoints were anxiety and depression scores. Readmission rates and acute exacerbation frequency were not systematically captured, precluding a full assessment of the long-term clinical impact. Third, this study is constrained by the limited range of psychological assessment tools used, which may limit the comprehensiveness of the psychological outcome measures. Lastly, the predominance of elderly participants with low educational attainment may have impaired recognition and reporting of adverse drug reactions, leading to underestimation of true incidence. Future multicenter, larger-scale studies with longer follow-up and a broader set of hard clinical end-points are warranted to confirm the value of pharmacist-led intervention in BGF management.

#### **CONCLUSION**

Pharmacist-led intervention significantly reduces anxiety and depression scores in BGF users, improves inhaler technique proficiency and lowers adverse drug reaction incidence. The model confirms that clinical pharmacists, as members of the multidisciplinary team, can make a tangible contribution to the long-term management of BGF. Integrating clinical pharmacist-led intervention is recommended as an essential component of comprehensive BGF management programs. This research team plans to conduct comprehensive training in professional knowledge in the future to enhance the capabilities of clinical pharmacists and anticipates conducting medication studies with larger sample sizes and involving different drugs.

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#### **Authors' contributions**

Meiying Lin: Conceptualized the study, conducted formal analysis, drafted the original manuscript and prepared

visualizations; Zhiyong Wang: Developed methodology, validated the study and supervised the work; Zhibin Chen: Conducted investigation and provided resources; Youwei Chen: Conducted investigation, curated data and supervised the work; Qifeng Zou: Provided software support, conducted investigation and curated data. All authors contributed to manuscript writing and approved the final version of the paper.

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#### **Data availability statement**

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

#### **Ethical approval**

The approval for conduct and publication was obtained from the First Hospital of Putian City Research and Ethics Office (Approval No. 2023--088). This study was also approved and registered in the Chinese Clinical Trials Registry (ChiCTR2400090585). This study was performed in adherence with the CONSORT guidelines. See supplementary file for the CONSORT checklist.

#### **Conflict of interest**

The authors declare no conflicts of interest.

#### **Supplementary data**

#### **REFERENCES**

- Abbas Q, Latif S, Ayaz Habib H, Shahzad S, Sarwar U, Shahzadi M, Ramzan Z and Washdev W (2023). Cognitive behavior therapy for diabetes distress, depression, health anxiety, quality of life and treatment adherence among patients with type-II diabetes mellitus: A randomized control trial. *BMC Psychiatry*, **23**(1): 86.
- Ali MAS, Amirhalingam P, Alatawi Y and Aljabri A (2022). Patient satisfaction of ambulatory care pharmacy services. *J Patient Exp*, **9**: 23743735221112631.
- Alkadi AN, Alajlani AH, Alnawah AK, Alturkie FM, Almutawah AN and Elsheikh E (2025). Anxiety and depression among hypertensive patients and its effect on medication adherence. *Clin Ter*, **176**(4): 418-426.
- Cabasag P, Beyene K, Sundram F, Chan AHY, Wilson H and Harrison J (2025). A qualitative exploration of community pharmacist views on providing a mental health and well-being intervention for long-term condition patients. *Explor Res Clin Soc Pharm*, **19**: 100629.
- Cao R, Jiang H, Chen P and Dai C (2025). Role of depression-mediated alterations in pro-inflammatory

- cytokines in carcinogenesis. *Front Immunol*, **16**: 1659153.
- Chen C, Zhou Y, Wang D, Li G, Yin K, Tao H, Wang C Y, Li ZS, Wei C and Hu LH (2023). Anxiety, depression and coping styles among patients with chronic pancreatitis in East China. *BMC Psychiatry*, **23**(1): 212.
- Chen M, Gong Z, Wang J, Hu Y, Zhang Q, Huang S, Liang J, Wu J, Zhao X, Chen Y, Zhao W, Cai S and Zhao H (2026). High anxiety in COPD: A barrier to effective inhaler medication adherence and disease management. *J Clin Nurs*, **35**(1): 208-218.
- Chen ZZ, Yang CY, He Y, Yang K and Wang ZP (2025). Psychological nursing effect on chronic obstructive pulmonary disease patients with respiratory failure. *Medicine (Baltimore)*, **104**(30): e43515.
- Cui J, Li M, Wei Y, Li H, He X, Yang Q, Li Z, Duan J, Wu Z, Chen Q, Chen B, Li G, Ming X, Xiong L and Qin D (2022). Inhalation aromatherapy via brain-targeted nasal delivery: Natural volatiles or essential oils on mood disorders. *Front Pharmacol*, **13**: 860043.
- Dorinsky P, DePetrillo P, DeAngelis K, Trivedi R, Darken P and Gillen M (2020). Relative bioavailability of budesonide/glycopyrrolate/formoterol fumarate metered dose inhaler administered with and without a spacer: Results of a phase I, randomized, crossover trial in healthy adults. *Clin Ther*, **42**(4): 634-648.
- Grana-Castro O, Izquierdo E, Pinas-Mesa A, Menasalvas E and Chivato-Perez T (2024). Assessing the impact of new technologies on managing chronic respiratory diseases. *J Clin Med*, **13**(22): 6913.
- Guidelines for the diagnosis and management of chronic obstructive pulmonary disease (revised version 2021). (2021). *Zhonghua Jie He He Hu Xi Za Zhi*, **44**(3): 170-205.
- Heo YA (2021). Budesonide/glycopyrronium/formoterol: A review in COPD. *Drugs*, **81**(12): 1411-1422.
- Keogh E and Mark Williams E (2021). Managing malnutrition in COPD: A review. *Respir Med*, **176**: 106248.
- Klijn SL, Hilgsmann M, Evers S, Roman-Rodriguez M, van der Molen T and van Boven JFM (2017). Effectiveness and success factors of educational inhaler technique interventions in asthma & COPD patients: A systematic review. *NPJ Prim Care Respir Med*, **27**(1): 24.
- Li W, Guo W, Chen H, Lu W, Yu S, Wang M, Zheng F, Wu H and Yang Q (2025). Access to single-inhaler triple medicines for chronic obstructive pulmonary disease in China: A national survey on accessibility and utilisation. *J Pharm Policy Pract*, **18**(1): 2466215.
- Maes A, DePetrillo P, Siddiqui S, Reisner C and Dorinsky P (2019). Pharmacokinetics of co-suspension delivery technology budesonide/glycopyrronium/formoterol fumarate dihydrate (BGF MDI) and budesonide/formoterol fumarate dihydrate (BFF MDI) fixed-dose combinations compared with an active control: A phase 1, randomized, single-dose, crossover study in healthy adults. *Clin Pharmacol Drug Dev*, **8**(2): 223-233.
- Mannino D, Weng S, Germain G, Boudreau J, Tardif-Samson A, Forero-Schwanhaeuser S, Laliberte F, Gravelle P, Compton CH, Noorduyn SG and Paczkowski R (2025). Comparative effectiveness of fluticasone furoate/umeclidinium/vilanterol and budesonide/glycopyrrolate/formoterol fumarate among US patients with chronic obstructive pulmonary disease. *Adv Ther*, **42**(2): 1131-1146.
- Martinez-Gestoso S, Garcia-Sanz MT, Carreira JM, Salgado FJ, Calvo-Alvarez U, Doval-Oubina L, Camba-Matos S, Peleteiro-Pedraza L, Gonzalez-Perez MA, Penela-Penela P, Vilas-Iglesias A and Gonzalez-Barcala FJ (2022). Impact of anxiety and depression on the prognosis of COPD exacerbations. *BMC Pulm Med*, **22**(1): 169.
- NHCotPsRo C (2021). Notice of the general office of the national health commission of the people's republic of China on issuing the standards for pharmacy outpatient services in medical institutions and four other standards. Retrieved from <https://www.nhc.gov.cn/wjw/c100175/202110/62f649973090453da0ad7a39123df41c.shtml>.
- Perumal R, Leite M and van Zyl-Smit RN (2020). The relationship between clinical trial participation and inhaler technique errors in asthma and COPD patients. *Int J Chron Obstruct Pulmon Dis*, **15**: 1217-1224.
- Ruan Z, Wang C, Yuan S, Fan Y, Xu B, Cong X, Li D and Miao Q. (2024). High-risk adverse events in two types of single inhaler triple-therapy: A pharmacovigilance study based on the FAERS database. *Front Pharmacol*, **15**: 1460407.
- Saguban R, AlAbd AMA, Rondilla E, Buta J, Marzouk S A, Maestrado R, Sankarapandian C, Alkubati SA, Mostoles R, Jr, Alshammari SA, Alrashidi MS, Gonzales A, Lagura GA and Gonzales F (2025). Investigating the interplay between sleep, anxiety and depression in chronic kidney disease patients: Implications for mental health. *Healthcare (Basel)*, **13**(3): 294.
- Sarwar MR, McDonald VM, Abramson MJ, Wilson S, Holland AE, Bonevski B, Mahal A, Paul E, Meier B and George J (2025). Credentialed pharmacist-led home medicine reviews targeting treatable traits and their impact on health outcomes in people with chronic obstructive pulmonary disease: A pre- and post-intervention study. *Int J Clin Pharm*, **47**(1): 157-165.
- Singh D, Roche N, Wu L, Sadafi H, De Backer J, Monshi Tousi N and Marshall J (2025). *In-silico* lung deposition profiles of three single-inhaler triple therapies in patients with COPD using functional respiratory imaging. *Int J Chron Obstruct Pulmon Dis*, **20**: 2103-2116.
- Takahashi K, Makita N, Castaneda-Sanabria J, Argoubi R, Nowacki G, Issa S, Matsumoto I, Yoshida Y and Müllerova H (2024). Characteristics of patients with COPD initiating budesonide/glycopyrronium/

- formoterol or other triple therapies in Japan: A real-world healthcare claims database study (MITOS-AURA). *Adv Ther*, **41**(12): 4518-4536.
- Taylor DA, Taylor ADJ, Jones M and Family HE (2024). Community pharmacist involvement in social prescribing for mental health: A qualitative study. *Prim Health Care Res Dev*, **25**: e69.
- Van Geffen WH, Tan DJ, Walters JA and Walters EH (2023). Inhaled corticosteroids in combination with inhaled long-acting beta2-agonists and long-acting muscarinic antagonists for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*, **12**(12): Cd011600.
- Volpato E, Toniolo S, Pagnini F and Banfi P (2021). The relationship between anxiety, depression and treatment adherence in chronic obstructive pulmonary disease: A systematic review. *Int J Chron Obstruct Pulmon Dis*, **16**: 2001-2021.
- Xiong T, Bai X, Wei X, Wang L, Li F, Shi H and Shi Y (2023). Exercise rehabilitation and chronic respiratory diseases: Effects, mechanisms and therapeutic benefits. *Int. J. Chron Obstruct Pulmon Dis.*, **18**: 1251-1266.
- Zhai Y, Zhu C, Zhu T, Song W, Tang Y, Jiang L, Ruan F, Xu Z, Li L, Fu X, Liu D, Chen A and Wu Q (2025). Global, regional and national burden of chronic respiratory diseases, 1990-2021 and predictions to 2035: Analysis of data from the global burden of disease study 2021. *Ann Med*, **57**(1): 2530225.