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Impact of pharmacist-led intervention in medication adherence and inhaler usage on asthma and chronic obstructive pulmonary disease control: a quasi-experimental study

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Abstract

Background Despite recent advances in the management of asthma and chronic obstructive pulmonary disease (COPD), patients still experience suboptimal disease control largely due to medication non-adherence and inappropriate use of inhaler. This study evaluates the impact of pharmacist-led intervention in medication adherence and inhaler usage on asthma and COPD control among out-patients attending the premier tertiary hospital in Nigeria.

Method A quasi-experimental study carried-out among eligible out-patients attending pulmonology clinic of University College Hospital, Ibadan. Baseline questionnaire explored medication adherence using a comprehensive-medication-adherence-assessment-scale (CMAAS-12) developed by the study co-investigators, use of pressurized-metered-dose (pMDI) and Diskus inhalers, as well as asthma/COPD control using validated asthma control test (ACT) and COPD assessment test (CAT). Subsequently, patients were allocated into control ($n=65$) or intervention group ($n=65$) using odd or even number. Intervention group received 2-month follow-up educational and/or cognitive-behavioural interventions to resolve identified adherence barriers, while control group continued with traditional care. Descriptive statistics, Chi-square and Wilcoxon-signed-ranked tests were used for analysis at $p<0.05$.

Results Overall, patients with optimal adherence were 11(18.6%) and 16(27.1%), $p=0.132$ (control), but 20(33.3%) and 38(63.3%), $p<0.001$ (intervention) at baseline and post-baseline, respectively. Specifically, in the intervention group, the identified adherence barriers at baseline were summarized into knowledge (120;40.4%), practical (115;38.7%) and attitudinal (62;20.9%). Patients with correct use of pMDI were 11(21.6%) baseline and 19(36.5%) post-baseline, $p=0.011$ (control), but 13(22.8%) and 46(80.7%) respectively, $p<0.001$ (intervention). Correct use of Diskus inhaler were 5(50.0%) and 4(40.0%), $p=0.157$ (control), but 7(35.0%) and 14(70.0%), $p=0.025$ (intervention) at baseline and post-baseline, respectively. Patients with 'well-controlled asthma' were 25(44.6%) and 26 (47.3%), $p=0.025$ (control), but 18(35.3%) and 32(60.4%), $p<0.001$ (intervention) at baseline and post-baseline, respectively. The COPD-specific health status indicated that 0(0.0%) and 1(14.3%), $p=0.059$ (control), but 0(0.0%) and 7(50.0%), $p<0.001$ (intervention) at baseline and post-baseline, respectively, belonged to 'low COPD impact'.

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Conclusion Pharmacist-led intervention significantly enhanced medication adherence and appropriate use of inhaler among the intervention cohort, with subsequent significant improvement in asthma control and reduced COPD impact compared with the control group. This underscores the need for active involvement of pharmacists in collaborative management of patients with chronic respiratory diseases in clinical practice.

Trial registration ClinicalTrials.gov identifier: NCT06417931. Retrospectively-registered.

Keywords Asthma, COPD, Medication adherence, Inhaler techniques, Pharmacist-intervention, Nigeria

Background

Asthma and chronic obstructive pulmonary disease (COPD) are the two most common chronic pulmonary diseases recognized as the leading cause of disability adjusted life years, morbidity and mortality, particularly in low- and middle-income countries [1–5]. Asthma currently affects about 300 million persons globally, and every ten years, the prevalence has been shown to rise by 50% [3, 4, 6]. In Nigeria, the number of persons with clinical asthma has been estimated to be about 13 million, which is the highest in Africa [7, 8]. On the other hand, COPD is the third largest cause of death and the seventh most common cause of poor health globally [9]. The burden of COPD in Nigeria is high, with a prevalence of 9.2% [10, 11], and it is usually associated with other serious medical conditions such as lung cancer, respiratory failure, and increased risk of cardiovascular disease [10, 11].

Due to the burden of chronic pulmonary diseases, there have been recent developments in the knowledge of the pathogenesis of asthma and COPD, which has led to the creation of novel treatments to manage the disease [12]. However, despite these advances, asthma and COPD patients still experience poor disease control, with a resultant effect in high exacerbation, more deaths and disabilities, as well as lower quality of life [12, 13]. It is increasingly recognized that out of the most important causes of suboptimal disease control among patients with asthma and COPD, medication non-adherence and incorrect use of inhaler devices are of significant concern [14, 15]. Studies have estimated that approximately 50% of medications prescribed for patients with chronic diseases are not taken as prescribed [16] with the adherence rates tending to be much lower (22–78%) among patients with asthma and COPD [17]. A variety of factors are associated with suboptimal adherence among these patients which include complex dosage regimens, presence of comorbidities, forgetfulness, poor understanding of inhaler use, side effects, patients' beliefs, and the cost of medication [16–19]. In addition, research has revealed that up to 85% of patients do not correctly use their inhaler devices [20]. Incorrect handling and inaccurate inhalation technique are linked to decreased medication delivery resulting in poor disease control, which may subsequently lead to increased risk of exacerbations and hospitalization [21–24].

In general, higher adherence to therapy as well as proper inhaler technique are associated with positive health outcomes such as improved disease control, reduced emergency room visits and length of hospital stays, as well as lower healthcare costs [12, 18, 25]. Pharmacists by virtue of their strategic position in healthcare delivery system, especially with regards to comprehensive management of patients' therapy, have the opportunity of providing a value-added service in medication use and adherence enhancement among people living with asthma and COPD [26–28]. This can be largely achieved by educating and counseling patients on the disease condition, purpose of each prescribed medication, the appropriate use of their inhaler medication device, as well as measure(s) for prevention of allergens and triggers, with the overall goal of improving patients' health outcomes [26–28].

Although, studies have shown the beneficial effects of pharmacists' involvement in medication adherence and inhaler use among patients with asthma and COPD in some developed countries [27, 29–32] as well as a few low- and medium-income countries [33–35]. There still exist gaps in literature on evidence-based study that employed an adherence assessment tool which takes into consideration the multifaceted domains of medication adherence as a basis for providing targeted intervention(s), while relating it to the overall disease control and therapy outcome.

Aims and objectives

Our study therefore employed a newly developed and validated comprehensive medication adherence assessment scale tagged CMAAS-12 to evaluate medication adherence among ambulatory patients with asthma and COPD assigned into control and intervention groups. The new CMAAS-12 was purposely designed and developed by the study co-investigators to largely address some of the gaps in the pre-existing adherence assessment scales or methods, especially in terms of not only assessing the medication adherence status of patients, but also to simultaneously explore and capture the specific adherence determinants, adherence barrier(s) and the associated reason(s) for non-adherence. The CMAAS-12 attributes are clearly deficient in many of the commonly used pre-existing medication adherence assessment

scales including the 4 - and 8-point Morisky adherence scales [36, 37] as well as the electronic monitor of medication adherence among others [38, 39]. In addition, we assessed the appropriate use of inhaler medication device(s) in accordance with the American Lung Association standard sequential steps of inhaler technique [40] among the cohorts., while patients' disease control status using the asthma control test (ACT) [41, 42] and COPD assessment (CAT) questionnaire [43, 44] were also evaluated. Subsequently, after the baseline interaction, a pharmacist-led individualized educational and/or cognitive-behavioural interventions were provided to the intervention cohort, while the control group continued with the traditional/usual care. The primary outcomes were the changes in CMAAS-12 score and appropriate use of inhaler device, from baseline to the 2-month post-baseline among patients in the control and the intervention groups. Secondary outcomes were the difference in the asthma control status or COPD clinical health status among patients in both groups at baseline and post-baseline contacts.

Methods

Study site

The pulmonology outpatient clinic of University College Hospital (UCH), a tertiary healthcare institution located in Ibadan North Local Government Area, Ibadan, Oyo state in southwest Nigeria. The UCH is a 900-bed foremost teaching hospital in Nigeria and is affiliated with University of Ibadan, the premier university in the country.

Study design

A two-arm, prospective, single-blind, quasi-experimental study carried-out among patients with asthma and/or COPD attending the pulmonology outpatient clinic of the hospital. Eligible and consented patients were chronologically assigned number during the baseline contact, while odd or even number was used to allocate patients into control or intervention group respectively. The intervention group received 2-month follow-up educational and/ cognitive-behavioural interventions, while the control group continued with the traditional/usual care.

Study population/inclusion and exclusion criteria

Adult ambulatory patients aged 18 years and above with a primary diagnosis of asthma and/or COPD were included. Eligible patients must also voluntarily consent to fully participate in the study till completion, as well as had an active telephone access. Excluded were asthma and/or COPD patients booked for inpatient admission, and those discovered not be taken any of the asthma/COPD-related medications at any point during the study period, as well as the non-consenting patients.

Sample size

The representative sample size (M) was determined using the Woodward sample size formular [45].

$$M = 2\,[Z_{(1-\alpha/2)} + Z_{(1-\beta)}]^{\,2} \over \delta^2$$

The standard assumptions considered in the sample size calculation based on the study primary outcomes include 95% confidence level and 5% margin of error, standard values for power of study ($Z_{(1-\beta)}$) at 80% = 0.842, significance level ($Z_{(1-\alpha/2)}$) at 5% = 1.96, and the effect size (δ) of 0.5 representing a conservative estimate that may be needed to detect the difference in the two study groups [45]. Also, equal allocation of participants to each of the study groups was considered. This gave a target sample size of approximately 63 patients per group, which was rounded off to 65 patients recruited in each group. Provision for non-response or attrition rate was not strictly considered in the Woodward sample size calculation because all the relevant parameters to achieve the targeted power of study and treatment effect have been appropriately defined and incorporated into the formular.

Data collection instrument

Questionnaire as the main instrument for data collection was constructed and developed following the previous research experience and expertise of the study co-investigators in the subject area, as well as extensive review of relevant literature [18, 46–49]. The questionnaire comprised four sections. Section A captured the demographic data and patient-specific characteristics. Section B comprised the comprehensive medication adherence assessment scale (CMAAS-12) to assess the pattern and extent of medication adherence, as well as possible barriers to adherence among the patients. Questions 1 to 5. in the CMAAS-12 tool predominantly explored the knowledge-related barrier(s) to medication adherence and the associated intentional and/or unintentional reason(s) for engaging in a particular medication-taking behaviour. Questions 6 and 7 explored the primary non-adherence as a possible trigger for secondary non-adherence behaviour, while questions 8 to 11 were included to evaluate the attitudinal-related barrier(s) to medication adherence and the accompanied reason(s). Question 12 explored the self-rated medication-taking commitment by each patient. Out of the 12 questions, nine items were scored, specifically questions 1 to 3 and 6 to 11, with one option out of the listed response options for each question being the correct option suggestive of adherence to medication as expected. The maximum obtainable score for each patient was nine [See additional file 1], while the overall CMAAS-12 score was subsequently converted into binary categories of 'optimal' (score ≥ 8) and 'suboptimal' (score < 8) medication adherence. The cut-off for

medication adherence score was adapted from related relevant studies [50, 51].

Section C explored the patients' knowledge on appropriate use of either pressurized metered-dose inhaler (pMDI) or Diskus inhaler, following individual patient demonstration of how they specifically used their inhaler device. A purposely designed checklist was used by the principal investigator to assess the patient's accuracy of inhaler usage in line with the American Lung Association seven standard sequential steps of correct inhaler technique [40]. In this study, each step got correctly by the patient was assigned a score of one, while a correct/appropriate use of inhaler was defined as the patient who got all the seven sequential steps correctly [See additional file 1]. Section D comprised the validated 5-item survey on Asthma Control Test (ACT) [41, 42] and the 8-item questionnaire for the COPD Assessment Test (CAT) [43, 44]. Each item in the ACT has five options with assigned number ranging from 1 to 5, with higher number indicating better asthma control. The maximum obtainable score ranged from 5 (poor control of asthma) to 25 (full control of asthma). A total ACT score of 5 to 15 indicates 'very poorly-controlled' asthma, scores of 16 to 19 indicates 'not well-controlled' asthma, and 20 to 25 was classified as 'well-controlled' asthma [41, 42]. The COPD Assessment Test (CAT) is specially developed to measure clinical control in patients with COPD. Each item in CAT has five options with assigned number ranging from 0 (e.g. I never cough) to 5 (e.g. I cough all the time). The maximum obtainable score ranged from 0 to 40. Summarily, a total CAT score of 0 to 9 was classified as 'low COPD impact', 10 to 20 as 'medium', 21 to 30 as 'high' and 31 to 40 was classified as 'very high/severe' impact of COPD on patient's health status [43, 44].

Pre-test and validation of data collection instrument

The questionnaire was assessed for content validity by a consultant pulmonologist from the University College Hospital, as well as six clinical pharmacy lecturers in the department of Clinical Pharmacy and Pharmacy Administration, University of Ibadan, with a vast knowledge of teaching and research in chronic diseases including asthma. A pre-test of the questionnaire was later done among twelve purposely selected asthma/COPD patients attending the University of Ibadan Health Service clinic. Corrections and adjustments were made on the questionnaire based on the feedbacks from pre-test and content validation. Specifically, the inclusion of follow-up prompts to stimulate patient's thoughts on the precise medication-taking habit, and appropriate reconstruction of some sentences for ease of comprehension. Participants for the pre-test were excluded from the main study and final analysis. Aside from the general pre-test and content validation of the instrument, the CMAAS-12 component was distinctly subjected to rigorous intra-scale items validation checks including the determination of content validity index (I-CVI) and content validity ratio (CVR) which gave a value of 1.0 each, indicating that all the 12 items are relevant and essential according to the Lawshe's Table [52]. Reliability assessment of the scale was also done, with Kuder-Richardson-20 to test for interrelatedness among CMAAS-12 items and the intraclass correlation gave a coefficient of 0.5 each, indicating a moderately reliable and internal consistent scale. Kuder-Richardson-20 coefficient is preferred for instrument that has most of its items with a dichotomous response option instead of Likert or polytomous options. Also, assessment of the sampling adequacy of the scale with Kaiser-Meyer-Olkin (KMO) gave a coefficient of 0.6 indicating the CMAAS-12 as a suitable scale, while the Bartlett's test for sphericity was statistically significant ($\chi^2 = 358.9$, $p < 0.001$) suggesting adequate correlation between items. These were some of the essential psychometric assessments carried out on CMAAS-12 to ascertain its suitability and reliability as a new scale.

Sampling, recruitment and data collection procedure

Eligible patients were approached for participation while waiting to see the attending physicians. Objectives of the study and detailed procedures were explained verbally to each participant, after which the consent was obtained. Only the consented patients on each clinic day were recruited and administered the study instrument. The baseline questionnaire was interviewer-administered to individual participants in both the intervention and control groups. Only the principal investigator was aware of the participant's study group, while the patients themselves were unaware of the group they belonged. The discrepancies identified from the patients in each group were carefully documented in participant's questionnaire, especially in respect of the sections on CMAAS-12, ACT/CAT assessment, and the demonstration of inhaler usage. An average of 8 to 12 patients were usually recruited per weekly clinic day, while the chronologic numbering of participants was consistently followed till the target sample size for each study group was achieved. The baseline recruitment of participants took about three months, with each participant having different start and end dates. After the baseline interaction, the intervention cohort was individually followed up for a period of 2 months with follow-up modalities comprising combination of approaches including face-to-face interaction for those who came for further physician clinic appointment within the study period, and test message as short message service (SMS) sent once in a week to every patient in the intervention group, while a 2–3 min phone call was also made a day after the message was sent to buttress the message and clarify any unclear information.

Participants in the intervention were also informed that they could initiate phone call at any time, if needed. Once the 2-month period of involvement in the study by a patient is completed, then, the baseline questionnaire was re-administered to the patient via direct face-to-face interaction for re-evaluation of the sections of the questionnaire on CMAAS-12, ACT/CAT assessment as well as appropriateness of inhaler usage. The re-assessment was done for every patient who completed the study in both the control and intervention groups, and this signify the termination of individual's involvement in the study.

Intervention provided for the intervention cohort

The interventions were largely patient-specific depending on the gaps and barriers identified at baseline interaction through the response to CMAAS-12, ACT and CAT, as well as use of inhalers, pMDI and Diskus. Specifically, educational intervention was used to resolve knowledge-related barriers by providing insights into the disease and making appropriate clarifications on various misconceptions about asthma/COPD and the inhaler medications, while recommendations on practicable and functional alternative approach were made to resolve adherence barriers related to practical impediments such as side effects and medicine unaffordability. Also, attitudinal-related barriers to medication adherence as well as intentional reason(s) for non-adherence were largely addressed using combination of motivational appeals [53, 54] and consistent reinforcement at every follow-up contact, the importance of optimal therapy adherence for better disease control and outcome. The content of the short message service was primarily a summary of corrective measure(s), as well as shared and agreed decision on resolution approach for the barriers to medication adherence and inhaler usage identified in each patient during the baseline interaction. The intervention was provided by the principal investigator based on previous professional practice experience as well as vast knowledge on management of respiratory diseases. The co-investigators were duly involved in monitoring the progress of the study, while ensuring adequate compliance with data collection procedure as outlined in the approved study protocol, as well as maintaining a careful audit of data obtained from the field at weekly interval. The intervention was carried out following the Template for Intervention Description and Replication Checklist (TiDieR) [55].

Data analysis

The statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 27.0. Descriptive statistics including mean±standard deviation, frequency, and percentage were used to summarize the data. Specifically, Wilcoxon-signed ranked test was used to compare the association and extent of change in study outcomes within the control and the intervention groups when the baseline and post-baseline data were paired. Pearson's Chi-square or Fishers exact test as may be appropriate was used to evaluate the association of medication adherence and appropriateness of inhaler usage with the ACT and CAT status at baseline and post-baseline for the control and intervention groups. Independent t-test was used to evaluate the mean value of the continuous variables including ACT and CAT scores at baseline and 2-month post-baseline between the control and the intervention groups. The priori level of statistical significance was considered at $p<0.05$.

Results

Overall, 11 (8.5%) participants from both study groups were lost to follow-up at the end of the study period, comprising six (6/65=9.2%) patients in the control and five (5/65=7.7%) in the intervention group. The characteristic trend observed with the lost to follow-up participants included mean age (67.7±21.2 years), 7 (63.7%) were female, 6 (54.5%) were COPD patients, 6 (54.5%) were retirees, and 6 (54.5%) had duration of diagnosis between 0 and 5 years. Details on participants' enrollment and the specific reason(s) for those who were lost to follow-up are shown in the CONSORT flow diagram (Fig. 1).

Demographic characteristics of participants

A total of 59 (90.8%) and 60 (92.3%) in the control and intervention groups, respectively completed the study. The mean age was 43.4±20.5 years in the control and 48.4±20.6 years in the intervention group. Patients with asthma alone, COPD alone and asthma/COPD overlap syndrome (ACOS) were 52 (88.1%), 4 (6.8%) and 3 (5.1%) respectively, in the control group, while in the intervention group were 46 (76.7%), 9 (15%), and 5 (8.3%), respectively (Table 1). A total of 51 (86.4%) in the control and 57 (95.0%) in the intervention were using inhaler device(s). Out of which, pMDI was the most commonly used, 40 (78.4%) in the control and 37 (64.9%) in the intervention group. Ten (19.6%) patients in the control and 20 (35.1%) in the intervention were using both pMDI and Diskus inhalers, while only one (2.0%) in the control and none in the intervention group used both pMDI and Turbohaler.

Participants' responses to comprehensive medication adherence assessment scale (CMAAS-12) at baseline and post-baseline contacts

Overall, at baseline, 11 (18.6%) patients in the control and 20 (33.3%) in the intervention group had optimal medication adherence ($p=0.068$). However, at the end of 2-month post-baseline, 16 (27.1%) in the control and 38 (63.3%) in the intervention had optimal medication

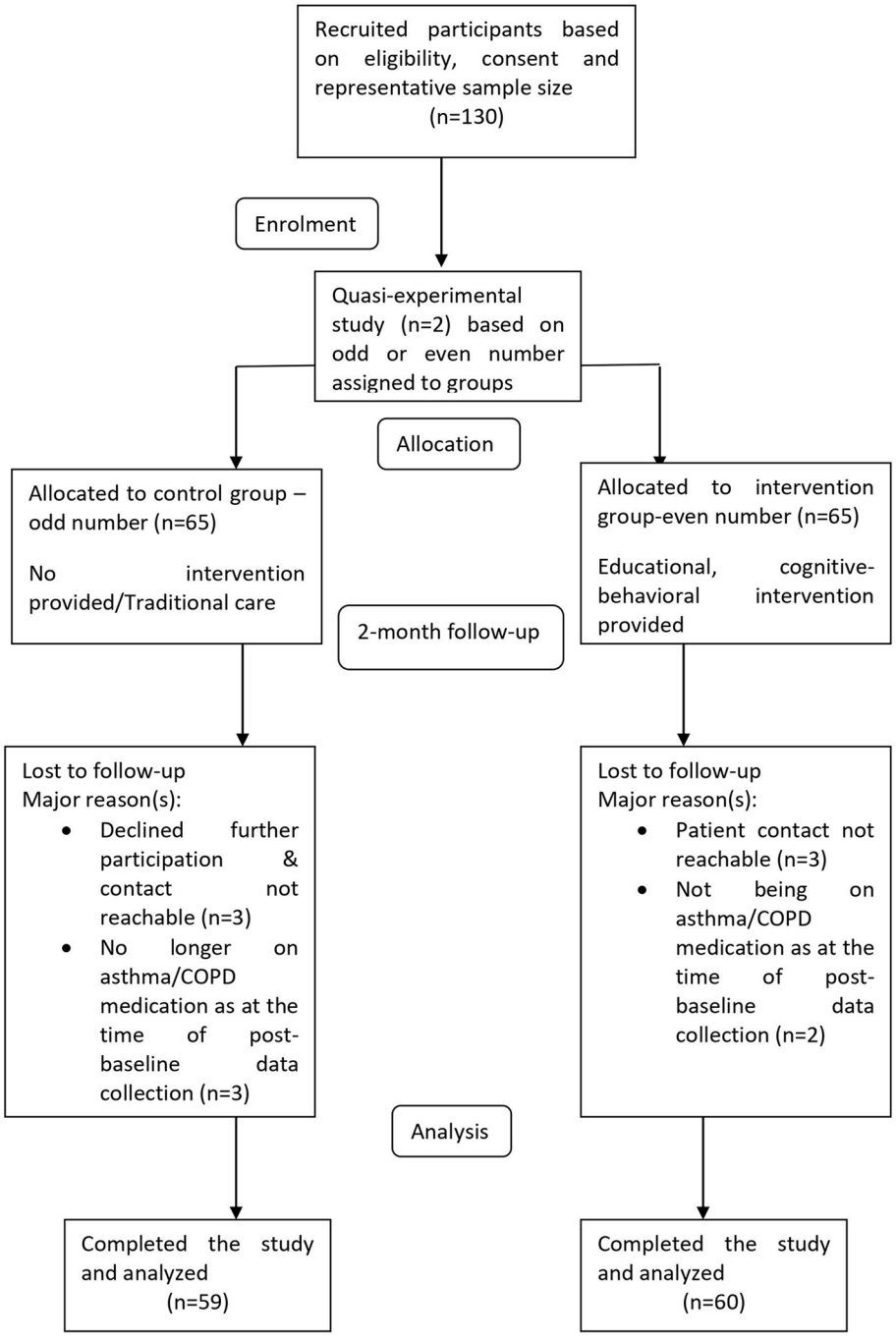

Fig. 1 CONSORT flow diagram for participants' enrolment

adherence ($p<0.001$) Table 2. Evaluation of participants' baseline response to CMAAS-12 question items which were suggestive of medication non-adherence behaviour revealed the barriers to medication adherence to include knowledge-related barrier such as poor insight of their disease, unsure of measure to take when a dose of the prescribed medication is missed and seldom/premature discontinuation of medication(s) on account of perceived disappearance of symptoms among others [Control: 55 (27.8%); Intervention: 58 (30.7%)]; practical-related barrier including nonavailability of prescribed medicine(s) in the pharmacy, financial constraints at the point of purchase, tight work schedule, medication side effects warranting stoppage of medicine(s), confusion of dosage regimens due to polypharmacy among others [Control: 76 (38.4%), Intervention: 69 (36.5%)]; duo of knowledge and attitudinal-related barriers such as boredom/not feeling like taking the medicine(s), wrong

Table 1 Demographic and relevant patient-specific characteristics of participants

Variable	Control (*n* = 59) *n* (%)	Intervention (*n* = 60) *n* (%)	*p*-value
Age (years)			
18–30	20 (33.9)	17 (28.3)	
31–45	12 (20.3)	9 (15.0)	
46–59	11 (18.6)	10 (16.7)	0.520
> 60	16 (27.1)	24 (40.0)	
Gender			
Male	24 (40.7)	21 (35.0)	
Female	35 (59.3)	39 (65.0)	0.523
Highest Education received			
Primary	2 (3.4)	2 (3.3)	
Secondary	16 (37.1)	21 (35.0)	
Vocational	5 (8.5)	5 (8.3)	0.848
Tertiary	36 (61.0)	32 (53.3)	
Working status			
Student	15 (25.4)	12 (20.0)	
Unemployed	3 (5.1)	0 (0.0)	
Paid employment	11 (18.6)	12 (20.0)	
Self employed	19 (32.2)	17 (28.3)	0.254
Retired	11 (18.6)	19 (31.7)	
Clinical condition			
Asthma	52 (88.1)	46 (76.7)	
COPD	4 (6.8)	9 (15.0)	
ACOS	3 (5.1)	5 (8.3)	0.229
Duration of diagnosis (years)			
0–5	14 (23.7)	23 (38.3)	
6–10	8 (13.6)	10 (16.7)	
> 10	37 (62.7)	27 (45.0)	0.138
Duration of treatment (years)			
0–5	14 (23.7)	25 (41.7)	
6–10	11 (18.6)	9 (15.0)	
> 10	34 (57.6)	26 (43.3)	0.113
Family History			
Yes	20 (33.9)	19 (31.7)	
No	39 (66.1)	41 (68.3)	0.715
Clinic attendance[a]	*n* = 63	*n* = 63	
Only on my clinic appointment date	31 (49.2)	37 (58.7)	
Whenever my asthma/COPD symptoms recur	16 (25.4)	17 (27.0)	
I dislike coming to the clinic	16 (25.4)	9 (14.3)	0.355
Smoking Status			
Ex-smoker	1 (1.7)	2 (3.3)	
Current smoker	0 (0.0)	1 (1.7)	
Secondary Smoker	1 (1.7)	1 (1.7)	1.000
None	57 (96.6)	56 (93.3)	

COPD Chronic obstructive pulmonary disease, *ACOS* Asthma-COPD overlap syndrome

[a]Multiple response; Fishers exact test was used for contingency table value < 5 while Pearsons Chi-square test for contingency table values ≥ 5

*Level of statistical significance $p < 0.05$

beliefs/misconception about the disease and orthodox asthma/COPD medicine(s), stigma/ashamed of using inhaler in the public, and strong belief in herbal medicine over the orthodox medicine [Control: 28 (14.1%), Intervention: 16 (8.5%)]; while trio of knowledge, practical and attitudinal-related barriers constituted [Control: 39 (19.7), Intervention: 46 (24.3%)], Table 2. Also, at baseline, the identified reasons for suboptimal medication adherence among patients in both groups were generally classified into unintentional (258; 66.7%) and overlaps or mix of intentional and unintentional, 129 (33.3%), while none was identified as a stand-alone intentional reason. Details of non-adherence components with the associated reason(s) among participants and the specific intervention approach employed for resolving the identified barriers in the intervention cohort are shown in Table 3.

Participants' knowledge of appropriate inhaler technique

At baseline and post-baseline, step 1 (shake the inhaler for 10 s) and step 2 (remove the inhaler's cap and ensure the inhaler is clean) of pMDI technique were got correctly by most patients (> 90% each) in both groups. However, step 3 which has to do with 'breathe out away from the device' was largely missed at baseline in both groups. At post-baseline, the proportion of patients who got the step 3 correctly increased to approximately 40% (control) versus 83% (intervention), $p < 0.001$. Figure 2. Overall, the baseline assessment of appropriateness of pMDI use among the patients showed that 11 (21.6%) in the control and 13 (22.8%) in the intervention group, respectively were accurate with the seven standard sequential steps of pMDI technique. At post-baseline, the proportion of patients who correctly got the seven sequential steps were 19 (37.3%) in the control and 46 (80.7%) in the intervention ($X^2 = 22.032$, $p < 0.001$) (Fig. 2). Among the patients using Diskus inhaler, overall, at baseline, 5 out of 10 (50.0%) in the control and 7 out of 20 (35.0%) in the intervention groups were accurate with the seven standard sequential steps. At post-baseline, 4 (40.0%) in the control, and 14 (70.0%) in the intervention got the 7-step correctly.

Comparison of changes in the study primary outcomes from baseline to post-baseline within the control and intervention groups

For the medication adherence, the proportion of patients with optimal medication adherence increased from 11 (18.6%) at baseline to 16 (27.1%) at post-baseline ($p = 0.132$) in the control, whereas, in the intervention group, the proportion with optimal adherence increased from 20 (33.3%) at baseline to 38 (63.3%) post-baseline ($p < 0.001$). For appropriate use of pMDI, there was an increase from 11 (21.6%) at baseline to 19 (37.3%) at post-baseline ($p = 0.011$) in the control, while in the intervention, an increase from 13 (22.8%) at baseline to

Table 2 Participants' response to Comprehensive Medication Adherence Assessment Scale (CMAAS-12)

Statement	Response category	Baseline, *n* (%)		*p*-value	Post-baseline, *n* (%)		*p*-value
		Control	Intervention		Control	Intervention	
Q1. Do you know why you are taking your prescribed medications? *	Yes**	58 (98.3)	57 (95.0)	0.619	58 (98.3)	60 (100.0)	**0.496**
	No	1 (1.7)	3 (5.0)		1 (1.7)	0 (0.0)	
		n = 77	*n* = 76		*n* = 82	*n* = 91	
If yes, where do you obtain the information on purpose of the medicine(s) prescribed for you?[a]	Physician/Doctor	50 (64.9)	58 (76.3)	0.742	46 (56.1)	45 (49.5)	**0.032***
	Pharmacist	18 (23.4)	16 (21.1)		24 (29.3)	31 (34.1)	
	Nurses	3 (3.9)	5 (6.6)		0 (0.0)	0 (0.0)	
	All of the above	4 (5.2)	4 (5.3)		10 (12.2)	15 (16.5)	
	Google	2 (2.6)	1 (1.3)		2 (12.4)	0 (0.0)	
Q2. Did you fill or refill your prescribed medications in the clinic during your last visit? *	Yes, I filled/refilled some of them but not all	17 (28.8)	23 (38.3)	0.660	15 (25.4)	28 (46.7)	0.08
	Yes, I refilled all my prescribed medications in the clinic during my last visit**	6 (10.2)	8 (13.3)		10 (16.9)	14 (23.3)	
	No I have all the prescribed medications at home	1 (1.7)	0 (0.0)		0 (0.0)	0 (0.0)	
	No, I have some of the prescribed medications at home	2 (3.4)	1 (1.7)		0 (0.0)	1 (1.7)	
	No I fill/refill my medications in a nearby pharmacy	31 (52.5)	25 (41.7)		33 (55.9)	16 (26.7)	
	No, my family/children send the medicines to me	2 (3.4)	3 (5.0)		1 (1.7)	1 (1.7)	
Q3. Taking daily medications may be challenging for individuals, do you occasionally miss/skip taking the dose of your prescribed medicines for reasons other than forgetting? *	Yes	29 (49.2)	31 (51.7)	0.748	21 (35.6)	15 (25.0)	0.208
	No**	30 (50.8)	29 (48.3)		38 (64.4)	45 (75.0)	
		n = 29	*n* = 33		*n* = 33	*n* = 21	
Q4. **If yes, what are those other reason(s)?**[+]	Travel	2 (6.9)	1 (3.0)	0.145	0 (0.0)	1 (4.8)	0.366
	Tight work schedule	0 (0.0)	4 (12.1)		2 (6.1)	1 (4.8)	
	Not feeling like taking the medication(s)	12 (41.4)	13 (39.4)		5 (15.2)	2 (9.5)	
	Financial constraints	5 (17.2)	5 (15.2)		10 (30.3)	7 (33.3)	
	Unavailability of medications	2 (6.9)	6 (18.2)		7 (21.2)	3 (14.3)	
	Unwanted side effects	1 (3.4)	2 (6.1)		0 (0.0)	0 (0.0)	
	Symptoms seemed controlled	7 (24.1)	2 (6.1)		9 (27.3)	7 (33.3)	
Q5. When you miss/forget to take your prescribed medicines, what measures do you usually take?	Take the next dose at the appropriate time	25 (42.4)	31 (51.7)		17 (28.8)	9 (15.0)	
	Take double the dose the next time	1 (1.7)	0 (0.0)		0 (0.0)	0 (0.0)	
	Take the next dose as soon as remembered	29 (49.2)	28 (46.7)		40 (67.8)	50 (83.3)	
	Call my healthcare provider for advice or counsel	1 (1.7)	0 (0.0)	0.45	1 (1.7)	1 (1.7)	0.09

Table 2 (continued)

Statement	Response category	Baseline, *n* (%)		*p*-value	Post-baseline, *n* (%)		*p*-value
		Control	Intervention		Control	Intervention	
	Not missed (others)	3 (5.1)	1 (1.7)		1 (1.7)	0 (0.0)	
Q6. Do you need/ seek assistance of someone before taking your prescribed medicines? *	Yes, my children/neighbor/relative	7 (11.9)	2 (3.3)	0.09	5 (8.5)	3 (5.0)	0.49
	No, I do not need/seek anyone assistance before I take my medications**	52 (88.1)	58 (96.7)		54 (91.5)	57 (95.0)	
Q7. Can you recognize/identify each of your prescribed medicines? *	Yes**	54 (91.5)	55 (91.7)	1.00	56 (94.9**)**	60 (100.0)	0.12
	No	5 (8.5)	5 (8.3)		3 (5.1)	0 (0.0)	
		n = 63	***n* = 61**		***n* = 56**	***n* = 59**	
If yes, how do you usually recognize the medicine(s)?+	By the name written on the dispensing label or carton	44 (69.8)	53 (86.8)		46 (82.1)	57 (96.6)	
	By a sign/symbol/logo on the medicines	11 (17.4)	4 (6.6)		4 (7.1)	0 (0.0)	
	Others (color, shape)	5 (7.9)	4 (6.6)		4 (7.1)	1 (1.7)	
	All of the above	3 (4.8)	0 (0.0)		2 (3.6)	1 (1.7)	
Q8. Do you at times/ occasionally discontinue any of your prescribed medicines because of the side effects? *	Yes	11 (18.6)	10 (16.7)	0.78	9 (15.3)	4 (6.7)	0.13
	No**	48 (81.4)	50 (83.3)		50 (84.7)	56 (93.3)	
Q9. When you feel the disease symptoms is under control, do you seldom discontinue taking your prescribed medicines without your doctor's counsel or advice? *	Yes, because I do not think I should continue using the medicines	25 (42.4)	18 (30.0)	0.32	18 (30.5)	4 (6.7)	**0.03***
	Yes, because I feel bored taking the medicines on a continuous or daily basis	3 (5.1)	6 (10.0)		2 (3.4)	2 (3.3)	
	No, I know I have to continue despite control of symptoms **	31 (52.5)	36 (60.0)		39 (66.1)	54 (90.0)	
Q10. When you feel any discomfort with your prescribed medicines, do you at times discontinue taking your medicines? *	Yes	28 (47.4)	16 (26.7)	**0.02***	24 (40.7)	13 (21.7)	**0.03***
	No**	31 (52.5)	44 (73.3)		35 (59.3)	47 (78.3)	
Q11. Do you have any other medicine(s) you are taking either as a supplement or otherwise aside from your prescribed medicine(s)? *	Yes	10 (16.9)	15 (25.0)	0.281	5 (8.5)	5 (8.3)	1.000
	No**	49 (83.1)	45 (75.0)		54 (91.5)	55 (91.7)	
		***n* = 13**	***n* = 20**		***n* = 3**	***n* = 5**	
If yes, could you kindly itemize those medicines or supplements+	Tab Vitamin C	3 (23.0)	5 (25.0)		0 (0.0)	0 (40.0)	
	NSAIDs	1 (7.7)	1 (5.0)		0 (0.0)	0 (0.0)	
	Multivitamins/immune boosters	6 (46.1)	3 (15.0)		2 (66.7)	1 (20.0)	
	Herbal concoctions	1 (7.7)	5 (25.0)		0 (0.0)	1 (20.0)	

Table 2 (continued)

Statement	Response category	Baseline, *n* (%)		*p*-value	Post-baseline, *n* (%)		*p*-value
		Control	Intervention		Control	Intervention	
	OTC sleep tabs	1 (7.7)	0 (0.0)		0 (0.0)		
	Herbal supplements	1 (7.7)	3 (15.0)		0 (0.0)	1 (20.0)	
	Oral prednisolone and salbutamol	0 (0.0)	0 (0.0)		1 (33.3)	0 (0.0)	
	Others (blood tonics, Codliver oil, Ricinus communis oil)	0 (0.0)	3 (15.0)		0 (0.0)	0 (0.0)	
Q12. Rate your level of commitment to medication-taking as prescribed by the doctor on a scale of 1 to 10, where 'one' is no commitment and 'ten' is full commitment to medication-taking							
Score ≥ 8	High commitment	31 (52.5)	33 (55.0)	0.788	38 (64.4)	50 (83.3)	**0.019***
Score < 8	Low commitment	28 (47.5)	27 (45.0)		21 (55.6)	10 (16.7)	
CMAAS overall adherence score							
Score ≥ 8	Optimal adherence	11 (18.6	20 (33.3)	0.068	16 (27.1)	38 (63.3)	
Score < 8	Suboptimal adherence	48 (81.4)	40 (66.7)		43 (72.9	22 (36.7)	**< 0.001***
Pattern and magnitude of medication adherence barriers among the participants							
		n = 198	*n* = 189		*n* = 154	*n* = 101	
Adherence barrier+		**Control**	**Intervention**		**Control**	**Intervention**	
Knowledge-related		55 (27.8)	58 (30.7)		38 (24.7)	15 (14.9)	
Practical impediment		76 (38.4)	69 (36.5)		66 (42.9)	53 (52.5)	
Knowledge + Attitudinal		28 (14.1)	16 (8.5)		24 (15.6)	13 (12.9)	
Knowledge + Attitudinal + Practical		39 (19.7)	46 (24.3)		26 (16.9)	20 (19.8)	

+ Multiple response; *= Scorable items in CMAAS-12; ** = Correct answers to suggest medication adherence; Maximum obtainable score = 9. Fishers exact test was used for contingency table value < 5, while Pearson Chi-square for contingency table values ≥ 5; *= Significant level at $p < 0.05$

Maximum obtainable score = 9; + = Multiple response; Fishers exact test was used for contingency table value < 5 while Pearson's Chi-square for contingency table values ≥ 5; * = significant level at $p < 0.05$; * = Scorable items in CMAAS-12 scale; ** = Correct answer to suggest medication adherence; CMAAS = Comprehensive medication adherence assessment scale; NSAID – Non-steroidal anti-inflammatory drugs; OTC = Over-the-counter drug

46 (80.7%) at post-baseline ($p < 0.001$) was observed. For the Diskus inhaler, the proportion of patients with correct use decreased by 20% from 5 (50.0%) at baseline to 4 (40.0%) at post-baseline ($p = 0.157$) in the control, while in the intervention group, the number increased by 100% from 7 (35.0%) at baseline to 14 (70.0%) at post-baseline ($p = 0.025$) Table 4.

Participants' response to asthma control test (ACT) and COPD assessment test (CAT) at baseline and post-baseline

The details of ACT and CAT assessment score categories for the participants at baseline and post-baseline contacts were shown in additional files 2 and 3, respectively. The ACT score assessment indicated that there was a minimal increase in the proportion of patients with 'well-controlled asthma' from 25 (45.4%) at baseline to 26 (47.3%) at post-baseline ($p = 0.025$) in the control group, while in the intervention, a greater increase from 18 (35.3%) at baseline to 32 (62.7%) at post-baseline was observed ($p = 0.001$). For the CAT score assessment, the proportion of patients with CAT score within the 'low COPD impact' (score 0–9) increased from 0 (0.0%) at baseline to 1 (14.3%) at post-baseline ($p = 0.059$) in the control, whereas, there was an increase from 0 (0.0%) at baseline to 7 (50.0%) at post-baseline ($p = 0.001$) in the intervention group (Table 4).

Association between medication adherence and inhaler usage versus asthma and COPD control among the patients at baseline and post-baseline

There was no significant difference in asthma control among patients with optimal or suboptimal medication adherence in the control group at baseline and post-baseline [$X^2 = 0.150$, $p = 1.000$; and $X^2 = 3.834$, $p = 0.145$], respectively. However, in the intervention group at post-baseline, patients who had optimal medication adherence (24; 75.0%) constituting the highest proportion with a 'well-controlled asthma' compared to those with suboptimal adherence (8; 25.0%), $X^2 = 9.703$, $p = 0.005$. Also, at post-baseline, the highest proportion of patients in the intervention group who correctly got the sequential steps of pMDI technique had 'well-controlled asthma' (28; 93.3%) versus 2 (6.7%) for those who were incorrect. Details of association between medication adherence and other parameters are shown in Table 5. For the COPD assessment test, generally there was no significance difference in baseline COPD control status of patients with respect to optimal or suboptimal medication adherence in the control and intervention groups.

Table 6 shows details of the association between relevant demographic characteristics and medication adherence at baseline and post-baseline in the control and intervention groups. At baseline, there was no significant difference in medication adherence status of patients in the control ($p = 0.388$) and the intervention

Table 3 Non-adherence components among participants at baseline contact and the specific intervention approach for resolving the identified barriers in the intervention group

CMAAS-12 Question	Response suggestive of non-adherence *n* (%)	Specific cause/ reason for the non-adherence behaviour	Specific intervention provided to resolve the barriers/deficits in the intervention group only
Do you know why you are taking the prescribed medicine(s)?	No 4 (3.5%)	Patient not informed/told of the name of the disease, especially among the COPD patients ***(Knowledge barrier - unintentional reason)***	Patients were provided insights on the disease condition, the chronic nature of asthma/COPD, and how the medications can help improve their health. Also, the purpose of each prescribed medication, as well as when and how to take the medication was emphasized, using the teach-back method.
Did you fill or refill your prescribed medication(s) in the clinic during your last appointment?	No 105 (88.2%)	Non-availability of prescribed medicines at the hospital pharmacy Financial constraints at the point of purchase Medicines were being purchased by relatives (***Practical barrier - unintentional reason)***	Concerned patients were educated on the importance of prompt refill of prescribed medicines on their disease control. Generic substitute with cheaper and comparative efficacy were suggested as necessary but with input from the patient and the attending physician. Non-refill of medicines on time as prescribed may constitutes a primary non-adherence behaviour that could trigger secondary non-adherence habit. Also, medication reconciliation was done for the patients who were in the clinic with some or all of their prescribed medications, so as to ensure resolution of discrepancies in medicine use.
Taking daily medication(s) may be challenging for individuals, do you occasionally miss/skip taking the dose of your prescribed medicine(s) for reason(s) other than forgetting?	Yes 60 (50.4%)	Travel Tight work schedule (***Practical barrier - may be intentional or unintentional reason***) Boredom/not feeling like taking the medicine (***Attitudinal barriers – intentional reason***) Financial constraints and unavailability of prescribed medications **(*Practical barrier – unintentional reason***) Wrong beliefs about the disease and conventional medications e.g. believing inhaler use can make their symptoms worse on the long run Not using preventer medicines once symptoms subside (***Knowledge and attitudinal barriers – Intentional reason***) Confusion of dosage regimen due to polypharmacy and other disease conditions (***Practical barrier – unintentional reason***)	The use of medication reminder system such as short message service remainders and alarms, was advised. Other approach encouraged include linking medication-taking to daily activity, and involvement of family members when necessary. Combined approach in motivational interviewing skills was utilized to guide counseling of patients who were bored/tired of their medication(s). Also, focus on individual patient concerns, and emphasis on the significance of taking the medication(s) and link it to expected benefits in respect of clinical outcomes and quality of life were/ reinforced. To reduce the financial burden of medication purchase and in cases of unavailability of specific brands Efforts were concentrated on providing a trusted cost-effective generic product with comparable efficacy to the specific brand, while such alternative generic products were written out for the patient to give his or her primary care physician More insights were provided on the chronic nature of the management modalities for asthma/COPD, before a consistent improvement in symptoms and quality of life can occur, while other misconceptions were appropriately corrected among the concerned patients. A medication list was prepared for the concerned individuals to indicate the time at which each drug should be taken
When you miss/forget to take your prescribed medicine(s), what measure(s) do you usually take?	Take double the dose or wait till the time for the next dose 57 (47.9%)	Not sure of what to do when a dose is missed (***Knowledge barrier – unintentional reason*)**	Patients were adequately enlightened on the need to take any missed medication dose as soon as remembered, as the most appropriate measures/step whenever a prescribed dose is forgotten/missed.

Table 3 (continued)

CMAAS-12 Question	Response suggestive of non-adherence *n* (%)	Specific cause/ reason for the non-adherence behaviour	Specific intervention provided to resolve the barriers/deficits in the intervention group only
Do you need/seek assistance of someone before taking your prescribed medicine(s)?	Yes 9 (7.6%)	Presence of comorbidities including ocular diseases, cognitive problems, motor disturbances, as well as issues with mobility (***Practical barrier – unintentional reason*****)**	All the oral medications being used by the concerned patients were legibly labeled. Also, use of colour of inhaler device to differentiate between reliever and controller. Patients were advised to ensure that the same relatives who accompanied them to the hospital on clinic visits should preferably be the one to guide/assist for medication-taking so as to ensure consistency of first-hand information as directed by the attending healthcare providers in the hospital.
Can you recognize or identify each of your prescribed medicine(s)?	No 10 (8.4%)	Inability to recognize each prescribed medicine ***(Practical barrier – unintentional reason*****)**	Patients were shown the simple and easy way(s) that can be used to recognize their medication (e.g. using the name or colour of inhaler, as well as sign/symbol/color of tablet)
Do you at times/occasionally discontinue any of your prescribed medicine(s) because of side effect(s)?	Yes 21 (17.6%)	Side effects such as severe fatigue, drowsiness, and tremors (with oral and inhaled salbutamol), as well as weight gain (with oral prednisolone) were experienced that warrant stoppage of the medicine, because it affected daily activities ***(Practical barrier – unintentional reason)***	Patients were pre-knowledge and educated about the expected side effects of each medicine, and tips to manage them. Patients were also encouraged to promptly inform or report to their physician any adverse effects experienced with their medication(s), while reiterating the importance of keeping the physician informed before stopping any medications.
When you feel the disease symptom(s) is under control, do you seldom discontinue taking your prescribed medicine(s) without your doctor's counsel or advice?	Yes 52 (43.7%)	Seldom discontinuation of medication on account of perceived disappearance of symptom(s) ***(Knowledge barrier – unintentional/intentional reason)***	Patients were educated and enlightened on the need for continuing intake of prescribed medication(s) even if the experienced symptoms have subsided except when the attending physician advised otherwise. Also, the importance of consistent intake of prescribed medication(s) to achieve the target clinical outcomes was highlighted. However, patients were advised to contact their attending physician if feeling worse
When you feel any discomfort with your prescribed medicine(s), do you at times discontinue taking your medicine(s)?	Yes 44 (37.0%)	Wrong perception about using inhaler medication. For instance, some patients are ashamed to use their inhalers in public, on account of the believe that it will reveal their ill-health to others. Others believed that use of inhaled medication will make their disease worse, and thereby resort to oral medication alternatives that are not prescribed by their physicians ***(Attitudinal/knowledge barrier – may be intentional or unintentional reason***)	Generally, Motivational Interviewing (MI) skills following the: Roll with patient resistance-R, Empathy–E, Avoid argument-A, Develop discrepancy-D, Support self-efficacy or motivation –S (READS) and universal statement approach guided the resolution of attitudinal barriers to adherence., including the perceived social stigma from inhaler use. Also, reinforcement of the importance of taking medication as prescribed was done

Table 3 (continued)

CMAAS-12 Question	Response suggestive of non-adherence *n* (%)	Specific cause/ reason for the non-adherence behaviour	Specific intervention provided to resolve the barriers/deficits in the intervention group only
Do you have any other medicine(s) you are taking either as a supplement or otherwise aside from your prescribed medicine(s)?	Yes 25 (21.0%)	Patients have a strong belief in traditional medicines over orthodox medications ***(Knowledge/Attitudinal barrier – intentional reason)*.** Also, patients using unprescribed oral short acting beta agonists (SABA) and oral prednisolone, sometimes due to the cost of inhaled medications ***(Practical/Knowledge barrier -unintentional reason)***	Patients were educated on the concerns with herbal medicine usage, especially in relation to the safety profile. Also, reiterated were the possible dangers of using unprescribed medicines, herbal concoction and supplements, particularly with respect to the risk of drug interactions and adverse effects, Clarifications were appropriately provided on the detrimental effects of oral intake of SABA and prednisolone compared to the beneficial effects of inhaled medication in the management of asthma or COPD.

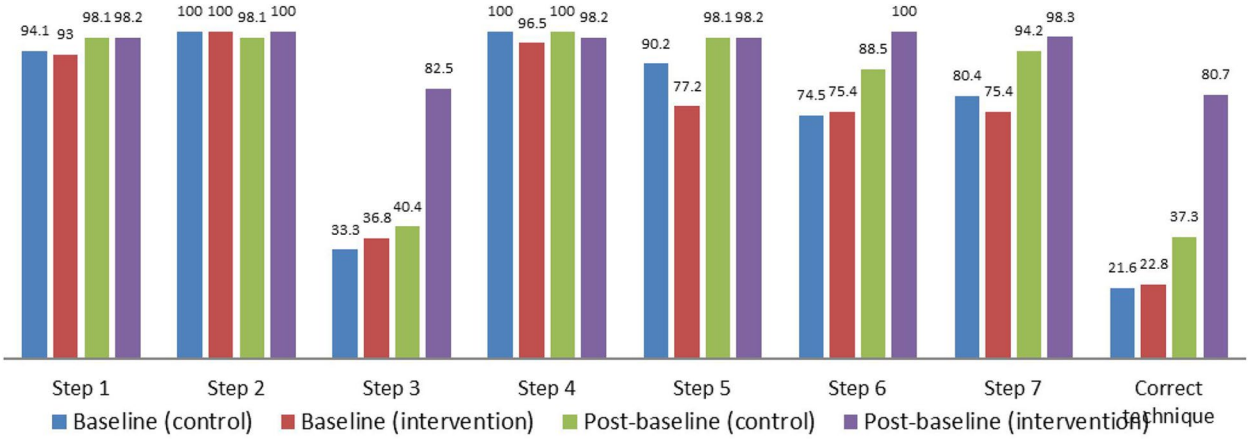

Fig. 2 Participants' appropriateness with the seven standard steps for pressurized metered-dose inhaler techniques among control and intervention groups at baseline and post-baseline

group ($p=0.133$) who reported experience of medication side effect or not, but at post-baseline, in the intervention group, the highest proportion of patients with optimal medication adherence (27; 71.1%) were those who did not report any experience of medication side effect ($p=0.049$) Table 6.

Discussion

In this study, we evaluated medication adherence, patient-specific barriers to adherence and the associated reason(s) for non-adherence, appropriate use of inhaler device(s), as well as the resultant effect of medication adherence and inhaler use on asthma and COPD control among patients who were assigned into control and intervention groups. In our study, it is noteworthy to mention that the educational and/or cognitive-behavioural interventions provided for patients in the intervention group were dependent on the identified knowledge-related, practical and attitudinal barriers to adherence during the baseline interaction. At the end of the 2-month follow-up intervention period, our study showed that the pharmacist-led intervention succinctly improved medication adherence and appropriate use of inhaler device (pMDI and Diskus), with a corresponding increase in the proportion of patients with well-controlled asthma, and a reduced COPD impact on health of the patients in the intervention compared to the control group. Studies have shown that optimal adherence to prescribed therapies and appropriate use of inhaler are important determinants for asthma and COPD control, as well as achievement of positive health outcomes [18, 25, 56, 57].

Specifically, in our study, the baseline evaluation of medication adherence among patients revealed that less than one-fifth in the control and about one-third in the intervention had optimal medication adherence. This is consistent with reports from previous studies where estimates of adherence among asthma or COPD patients range widely from 22 to 78% [17, 58–61]. Interestingly, nearly all participants in both groups knew the purpose for which they were taking the prescribed medication(s),

Table 4 Comparison of changes in study outcomes from baseline to post-baseline contacts within the control and intervention groups

Variable	Control, *n* (%)		*p*-value	Intervention, *n* (%)		*p*-value
	Baseline	Post-baseline		Baseline	Post-baseline	
Use of pMDI						
Correct	11 (21.6)	19 (37.3)		13 (22.8)	46 (80.7)	
Incorrect	40 (78.4)	32 (62.7)	**0.011***	44 (77.2)	11 (19.3)	**< 0.001***
Use of Diskus inhaler						
Correct	5 (50.0)	4 (80.0)		7 (35.0)	14 (87.5)	
Incorrect	5 (50.0)	1 (20.0)	0.157	13 (65.0)	2 (12.5)	**0.025***
CMAAS-12 score in category						
Optimal adherence	11 (18.6)	16 (27.1)		20 (33.3)	38 (63.3)	
Suboptimal adherence	48 (81.4)	43 (72.9)	0.132	40 (66.7)	22 (36.7)	**0.000***
ACT score in category						
Poorly-controlled	20 (36.4)	7 (12.7)	**0.025***	16 (31.4)	7 (13.7)	**0.001***
Not well-controlled	10 (18.2)	22 (40.0)		17 (33.3)	12 (23.5)	
Well-controlled	25 (45.4)	26 (47.3)		18 (35.3)	32 (62.7)	
CAT score in category						
Low	0 (0.0)	1 (14.3)	0.059	0 (0.0)	7 (50.0)	**0.001***
Medium	3 (42.9)	5 (71.4)		6 (42.9)	7 (50.0)	
High	3 (42.9)	1 (14.3)		8 (57.1)	0 (0.0)	
Very high	1 (14.3)	0 (0.0)		0 (0.0)	0 (0.0)	

COPD Chronic Obstructive Pulmonary Disease, *pMDI* Pressurized metered-dose inhaler, *ACT* Asthma control test, *CAT* COPD assessment test, *CMAAS-12* Comprehensive Medication Adherence Assessment Scale – 12 item; Wilcoxon signed rank test was used for the comparison

*Significant level at $p < 0.05$

however, more than two-third of those participants obtained the information from their physician, with only about one-fifth who mentioned the pharmacist. Although this finding may be expected, since physicians are typically the primary custodian of patients receiving care, However, it may also reveal the likelihood of non-proactive involvement of pharmacists in asthma/COPD care, which is of concern, especially when pharmacists are supposed to play a value-added active role in medication therapy management for patients on long-term medication regimen including asthma/COPD. Also, a larger percentage of patients reported to fill/refill some or all of their medications at pharmacies outside the hospital due to nonavailability of the prescribed inhaler medications in the hospital pharmacy at the time of this study. Patronizing different outlets, especially outside of the hospital pharmacy environment where the prescription was issued may constitutes a primary non-adherence behaviour that may consequently triggered secondary non-adherence habit among the patients. In addition, nonavailability and unaffordability of asthma and COPD medicines in public hospitals has been previously reported in Nigeria [62], where asthma and COPD medicines were more available in private hospitals compared to the public hospitals' pharmacies, while inhaled corticosteroids, which are the mainstay for asthma and COPD treatment were available in only 23% of public hospitals' pharmacies compared to 75% of private pharmacies nationwide [62]. It is therefore expedient to recommend that hospital pharmacists in low-and middle-income countries (LMICs) like Nigeria should take proactive role in the care of asthma/COPD patients by continually acquiring the necessary soft skills and communication tips for ensuring purposeful counselling, while maintaining adequate stocks of essential medications commonly prescribed for these categories of patients in order to guarantee improved care.

In different proportional order, the medication adherence barriers identified in our study include knowledge barrier which is largely related to poor insight and knowledge about the disease and medications; practical barrier mostly financial constraints and nonavailability of prescribed medicine(s) in the hospital, and attitudinal barrier including boredom or not feeling like continuing taking the medicine, as well as misconception about conventional asthma/COPD medications and treatment among others. Medication-related knowledge barriers constitute the highest of the identified barriers. In our study, consideration was giving to all the identified barriers at the baseline interaction with patients in both control and the intervention groups, while an individual-specific and patient-centred intervention in different combination was provided to the intervention cohort. At the end of 2-month post-baseline follow-up, there was two times increase in the proportion of patients with optimal medication adherence in the intervention compared to the control cohort. The improvement in medication adherence status of patients in the intervention

Table 5 Association between medication adherence and inhaler usage versus asthma control among patients at baseline and post-baseline

	Asthma Control Test (ACT)					
	Baseline, n(%)					
	Control			**Intervention**		
Variable	**Poorly-controlled**	**Not-well Controlled**	**Well-Controlled**	**Poorly-controlled**	**Not well-controlled**	**Well-controlled**
CMAAS-12						
Optimal adherence	4 (20.0)	2 (20.0)	5 (20.0)	2 (12.5)	4 (23.5)	8 (44.4)
Suboptimal adherence	16 (80.0)	8 (80.0)	20 (80.0)	14 (87.5)	13 (76.5)	10 (55.6)
	$X^2 = 0.150, p = 1.000$			**$X^2 = 4.265, p = 0.115$**		
Use of pMDI						
Correct	3 (15.0)	1 (14.3)	7 (31.8)	4 (25.0)	1 (6.3)	6 (35.3)
Incorrect	17 (85.0)	6 (85.7)	15 (68.2)	12 (75.0)	15 (93.7)	11 (64.7)
	$X^2 = 1.807, p = 0.512$			**$X^2 = 4.119, p = 0.149$**		
Use of Diskus inhaler						
Correct	1 (25.0)	1 (100.0)	2 (50.0)	1 (14.3)	1 (25.0)	3 (60.0)
Incorrect	3 (75.0)	0 (0.0)	2 (50.0)	6 (85.7)	3 (75.0)	2 (40.0)
	$X^2 = 1.863, p = 0.714$			**$X^2 = 2.725, p = 0.327$**		
	Post-baseline, n (%)					
	Control			**Intervention**		
	Poorly-controlled	**Not-well Controlled**	**Well-Controlled**	**Poorly-controlled**	**Not well-controlled**	**Well-controlled**
CMAAS-12						
Optimal adherence	1 (14.3)	4 (18.2)	11 (42.3)	3 (42.9)	3 (25.0)	24 (75.0)
Suboptimal adherence	6 (85.7)	18 (81.8)	15 (57.7)	4 (57.1)	9 (75.0)	8 (25.0)
	$X^2 = 3.834, p = 0.145$			**$X^2 = 9.703, p = 0.005$***		
Use of pMDI						
Correct	2 (28.6)	5 (25.0)	11 (50.0)	5 (71.4)	6 (50.0)	28 (93.3)
Incorrect	5 (71.4)	15 (75.0)	11 (50.0)	2 (28.6)	6 (50.0)	2 (6.7)
	$X^2 = 2.938, p = 0.237$			**$X^2 = 9.781, p = 0.005$***		
Use of Diskus inhaler						
Correct	1 (100.0)	1 (50.0)	2 (100.0)	1 (100.0)	2 (66.7)	9 (100.0)
Incorrect	0 (0.0)	1 (50.0)	0 (0.0)	0 (0.0)	1 (33.3)	0 (0.0)
	$X^2 = 2.045, p = 1.000$			**$X^2 = 3.816, p = 0.308$**		

X^2=Fishers exact test value for variables with contingency table value<5 while $X^{2=}$ Pearson's Chi-square value for contingency table values≥5; CMAAS-12=Comprehensive medication adherence assessment scale-12 items; Optimal adherence=CMAAS-12 score≥8 out of 10, while suboptimal adherence=CMAAS-12 score<8; Correct use of pressurized metered dose inhaler (pMDI)=those who were accurate with the seven standard sequential steps of pMDI techniques, while incorrect use of pMDI=those who missed any of the seven standard sequential step s, Correct use of Diskus inhaler=those who were accurate with the seven standard sequential steps of Diskus inhaler techniques, while incorrect use=those who missed any of the seven standard sequential steps

*Significance at $p<0.05$)

group may be linked to the propensity of CMAAS-12 question items in revealing the specific type of medication adherence barrier(s) in individual patient, thereby paving way for the provision of targeted intervention(s) to resolve the individual-specific barrier(s).

Although, there is really no 'one size fit all' approach for adherence enhancement in clinical setting [15, 63–67], but where knowledge barrier to medication adherence exists in a patient, educational intervention seems to be the most appropriate measure and strategy to clarify or fill the gap(s) in knowledge Providing tailored educational counseling raises the level of patient confidence, self-efficacy and improves their understanding on how to take their medications [33, 68, 69]. However, for practical impediment or barrier to adherence, a pragmatic intervention approach with efforts geared towards ensuring a shared decision making with the patient may be essential for improved medication adherence, and subsequently the treatment outcome. In our study, patients with practical barrier related to financial constraints or unavailability of prescribed brand of medicine in the hospital were handled by suggestion of a relatively cheaper and comparatively effective generic substitute, but with necessary input from the attending physician and the patient. Implementing a shared decision-making process regarding medication and dose regimen choices between healthcare provider and patient can improve adherence with better symptom control in patients with asthma and/COPD [70, 71]. In addition, attitudinal-related barriers were largely addressed using the combination of skills in motivational interviewing [53, 54], as well as reinforcement at every follow-up contact, the importance of

Table 6 Association between socio-demographic of participants and adherence for control and intervention groups at baseline and post-baseline

	Baseline, *n* (%)				Post-baseline, *n* (%)			
	Control		Intervention		Control		Intervention	
	Sub-optimal adherence	Optimal adherence	Sub-optimal adherence	Optimal adherence	Sub-optimal adherence	Optimal adherence	Sub-optimal adherence	Optimal adherence
Age (years)								
18–30	18 (37.5)	2 (18.2)	15 (37.5)	2 (10.0)	15 (34.9)	5 (31.3)	11 (50.0)	6 (15.8)
31–44	10 (20.8)	2 (18.2)	6 (15.0)	3 (15.0)	9 (20.9)	3 (18.8)	4 (18.2)	5 (13.2)
46–59	8 (16.7)	3 (27.3)	6 (15.0)	4 (20.0)	7 (16.3)	4 (25.0)	3 (13.6)	7 (18.4)
≥60	12 (25.0)	4 (36.4)	13 (32.5)	11 (55.0)	12 (27.9)	4 (25.0)	4 (18.6)	20 (52.6)
	$p=0.589$		$p=0.124$		$p=0.933$		$\mathbf{p=0.014}$*	
Gender								
Male	22 (45.8)	2 (18.7)	11 (27.5)	10 (50.0)	18 (41.9)	6 (37.5)	5 (22.7)	16 (42.1)
Female	26 (54.2)	9 (81.8)	29 (72.5)	10 (50.0)	25 (58.1)	10 (62.5)	17 (77.3)	22 (57.9)
	$p=0.172$		$p=0.085$		$p=0.762$		$p=0.129$	
Education level								
Primary	1 (2.1)	1 (9.1)	1 (2.5)	1 (5.0)	1 (2.3)	1 (6.3)	0 (0.0)	2 (5.3)
Secondary	16 (33.3)	0 (0.0)	15 (37.5)	6 (15.0)	13 (30.2)	3 (18.8)	11 (50.0)	10 (26.3)
Vocational	4 (8.3)	1 (9.1)	2 (5.0)	3 (15.0)	4 (9.3)	1(6.3)	2 (9.1)	3 (7.9)
Tertiary	27 (56.3)	9 (81.8)	22 (55.0)	10 (50.0)	25(58.1)	11(68.8)	9 (40.9)	23 (60.5)
	$p=0.057$		$p=0.490$		$p=0.643$		$p=0.258$	
Working status								
Student	13 (27.1)	2 (18.2)	10 (15.0)	2 (10.0)	11 (25.6)	4 (25.0)	7 (31.8)	5 (13.2)
Unemployed	2 (4.2)	1 (9.1)	0 (0.0)-	0 (0.0)-	2 (4.7)	1 (6.3)	0 (0.0)-	0 (0.0)-
Paid employment	10 (20.8)	1 (9.1)	9 (22.5)	3 (15.5)	7 (16.3)	4 (25.0)	6 (27.3)	6 (15.8)
Self-employed	16(33.3)	13(27.3)	10(25.0)	7 (35.5)	16 (37.2)	3 (18.8)	6 (27.3)	11 (28.9)
Retired	7(14.6)	4(34.6)	11(27.5)	8 (40.0)	7 (16.3)	4 (25.0)	3 (13.6)	16 (42.1)
	$p=0.442$		$p=0.409$		$p=0.654$		$p=0.063$	
Duration of treatment (years)								
0–5	13 (27.1)	1 (9.1)	17 (42.5)	8 (40.0)	11 (25.6)	3 (18.8)	8 (36.4)	17 (44.7)
6–10	10 (20.8)	1 (9.1)	8 (20.0)	1 (5.0)	9 (20.9)	2 (12.5)	6 (27.3)	3 (7.9)
>10	25 (52.1)	9 (81.8)	15 (37.5)	11(55.0)	23 (53.5)	11 (68.8)	8 (36.4)	18 (47.4)
	$p=0.302$		$p=0.734$		$p=0.564$		$p=0.141$	
Family History								
Yes	17 (35.4)	3 (27.3)	16 (40.0)	3 (15.0)	13 (30.2)	7 (43.8)	8 (36.4)	11 (28.9)
No	31 (64.6)	8 (72.7)	24 (60.0)	17 (85.0)	30 (69.8)	9 (56.3)	14 (63.6)	27 (71.1)
	$p=0.734$		$p=0.077$		$p = 0.329$		$p=0.552$	
Peak flow meter								
Yes	5 (10.4)	5 (45.5)	5 (12.5)	5 (25.0)	6 (14.0)	4 (25.0)	4 (18.2)	6 (15.8)
No	43 (89.6)	6 (54.5)	35 (87.5)	15 (75.0)	37 (86.0)	12 (75.0)	18 (81.8)	32 (84.2)
	$\mathbf{p=0.005}$*			$p = 0.278$		$p=0.456$		$p=1.000$
Other disease condition								
Yes	14 (29.2)	4 (36.4)	18 (45.0)	11 (55.0)	14 (32.6)	4 (25.0)	9 (40.9)	20 (52.6)
No	34 (70.8)	7 (63.6)	22 (55.0)	9 (45.0)	29 (67.4)	12 (75.0)	13 (59.1)	18 (47.4)
	$p=0.721$		$p=0.586$		$p=0.381$		$p=0.353$	
Experienced side effect								
Yes	15 (31.2)	2 (18.2)	18 (45.0)	5 (25.0)	14 (32.6)	3 (18.8)	12 (54.5)	11 (28.9)
No	33 (68.8)	9 (81.8)	22 (55.0)	15 (75.0)	29 (67.4)	13 (81.3)	10 (45.5)	27 (71.1)
	$p=0.388$		$p=0.133$		$p=0.353$		$\mathbf{p=0.049}$*	

*Significance ($p<0.05$) Fishers exact test was used for variables with contingency value < 5, while Pearson's chi-square test was used for contingency values ≥ 5

optimal medication adherence and correct inhaler usage. Regular reinforcement of correct medication information has been found useful to achieve better disease control and outcome [71, 72]. Overall, our study has shown that, the use of an instrument with multidimensional outlook as seen in CMAAS-12 may be necessary to comprehensively explore the medication adherence commitment of patients on long-term medication regimen including asthma/COPD, while also revealing the barriers to adherence as well as the associated reason(s).

In addition, following the baseline assessment of inhaler usage among the patients in accordance with the American Lung Association guideline for pMDI and Diskus inhaler techniques, approximately one-fifth each in the control and intervention groups correctly got all the seven standard sequential steps for pMDI, while a relatively higher number (>one-third in each group) accurately got all the seven standard steps of Diskus inhaler. The most frequently committed error in the handling of both the pMDI and Diskus inhaler was failure to breathe out away from the device, that is, step 3, which was missed by a large number of patients in both groups. A systematic review and meta-analysis of 10 studies also reported that 86.7% of patients made at least one inhalation technique error [20–22, 24, 73]. Incorrect inhaler technique is a manifestation of unintentional non-adherence behaviour, which may be considered as a practical barrier to adherence that should be critically explored and appropriately corrected at every encounter with asthma/COPD patients. This approach was largely employed among the intervention cohort in our study. At post-baseline, the proportional increase in the number of patients who correctly got the seven standard sequential steps of pMDI in the intervention group is three times greater than the increment observed among the control cohort. The improvement in the appropriate pMDI usage among the intervention cohort might have contributed to better asthma and COPD control in the group. To buttress this, our study recorded approximately 78% significant increase in the proportion of patients with well-controlled asthma in the intervention cohort at post-baseline compared to the marginal increase of 4% among patients in the control group. This is consistent with the results of a cluster randomized trial carried out in Australian community pharmacies, where patients with poorly-controlled asthma had better asthma control after intervention from pharmacists [31]. Also, other previous studies have showed significant improvement in asthma control following pharmacists' intervention [29, 30, 32-35], although, the study settings and methodological approach differs.

Precisely, in the intervention group, the percentage of patients with 'low COPD impact' on patients' status increased from 0% at baseline to 50% at post-baseline contact. The improvement seems consistent with reports from other previous studies on pharmacists' conducted intervention among patients with COPD [29, 74–76]. The improvement in asthma and COPD control among the intervention cohort may perhaps be linked with the effectiveness of the combined intervention approach adopted in our study, which is hinged on the robust and comprehensive medication- and inhaler-related knowledge, practical and attitudinal gaps unfolded by the CMAAS-12 instrument. Although, the CMAAS-12 tool may still not be regarded as a foolproof instrument, and may perhaps look like a time-consuming tool, however, the inherent benefits of its effective use as clearly seen in our study far outweigh the supposed time-consuming outlook. Thus, its use in routine clinical practice is recommended for healthcare providers in general and pharmacists in particular, when trying to have holistic interrogation on medication adherence-related issues or problems. The international guidelines for both asthma and COPD reiterates the importance of primary care provider, particularly physician and pharmacist, to have emphatic and holistic exploration and discussion with patients to assess adherence along with symptom control and inhaler technique at every office visit [12, 60, 67, 77, 78].

Strengths and limitations of the study

Our study used CMAAS-12, an exploratory and multidimensional adherence assessment tool that revealed overlap of barriers to medication adherence, as well as the associated intentional and unintentional reason(s) for non-adherence among the patients. Generally, the robust findings from our study will be a useful information to relevant stakeholders in asthma and COPD care, Specifically, the wide-ranging information from the CMAAS-12 dictates the appropriate individual-specific intervention(s) to resolve the identified barrier(s) that led to improved medication adherence and correct use of inhaler device, with better asthma and COPD control among patients in the intervention compared to their control group counterparts. Nevertheless, there is a need for further study to consider replicating the use of CMAAS-12 for treatment adherence evaluation among patients with other chronic diseases, while also involving other hospital pharmacists who might have been purposely trained on the necessary soft skills and compassionate care approach needed to drive the question-items in CMAAS-12 to elicit sincere and honest response from the patients. The measure will also ensure reproducibility of use of CMAAS-12 across different patients' population. In addition, our future study will consider the inter-scale validation of CMAAS-12 against other commonly use pre-existing adherence assessment scales, as this will complement the extensive intra-scale items validation currently done on CMAAS-12. Ensuring these

measures in our future study will guarantee CMAAS-12 standardization and the likelihood of making a far-reaching conclusion on its suitability and reliability as an adherence assessment scale that can be used across different healthcare setting.

Other limitation worthy to mention include self-reported nature of the CMAAS-12 instrument with its associated inherent limitation such as recall or memory bias in which the patients may either overestimate or underestimate the information they offered [49, 63, 66]. Generally, there is no gold-standard scale or method for measuring adherence in clinical practice, each has its own limitation(s) and advantage(s) [15, 63–67]. Nonetheless, the various sections in our study instrument including the CMAAS-12 component, were subjected to rigorous intra-scale item validation checks before its deployment for use. Also, the styles of question in the study instrument which were largely presented in a non-threatening and nonjudgmental approach might encourage the patients to provide a frank and truthful response. Another limitation of our study is the use of quasi-experimental design, where participants were assigned into control or intervention groups using odd or even number, respectively. Thus, the possibility of selection/allocation bias may not be totally ruled out. In addition, the perceived short duration of follow-up might have allowed for higher retention of the corrective measures and adherence information provided to the intervention cohort, which perhaps accounted for the significant improvement observed in their study outcomes. However, future study may want to consider a 3 to 6-month of follow-up intervention, possibly to ensure sustained retention of counselling information that may help in achieving continuous improvement in disease control among the patients. Nonetheless, literature has indicated that the predictors of success of intervention include low baseline performance, outpatient setting and short follow-up duration [57, 58, 60], which were all clearly expressed and reflected in our study.

Furthermore, the total sample size in our study appears relatively small, especially with respect to the COPD patients, however, it is a representative sample. Generally, a large number of attendees at the pulmonology outpatient clinic of our study site are typically asthma patients, with only a few COPD patents, possibly because of less vulnerability of individual to COPD in our environment compared to asthma, even though the COPD patients may typically experience a more severe consequence(s) if not properly managed [10.11]. Overall, our study findings should be carefully considered in line with the identified study limitations before making generalization of the results.

Conclusion

Our study shows that the pharmacist-led intervention significantly enhanced medication adherence and appropriate use of inhaler medication device among the intervention cohort, with subsequent significant increase in the proportion of patients with well-controlled asthma, as well as reduced COPD impact, when compared with their control counterparts. This further underscores the need for active involvement of pharmacists in low-and medium-countries (LMICs) like Nigeria, in collaborative management of patients with chronic respiratory diseases. However, this will entail the pharmacists' continuous acquisition of the necessary soft skills and communication tips, as well as imbibing compassionate counselling approach during patient-healthcare provider's encounters. The focus should largely be on shared-decision with the patients in order to unravel medication adherence barriers, while ensuring routine review of patients correct inhaler usage to ensure better disease control and optimal care. Overall, pharmacists in LMICs should consistently accept responsibility for the therapeutic intervention provided to patients which is vital and integral to the practice of pharmaceutical care.

Supplementary Information

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Supplementary Material 1. Questionnaire for the study.

Supplementary Material 2. Participants' responses to asthma control test (ACT) at baseline and post-baseline.

Supplementary Material 3. Participants' responses to COPD assessment test (CAT) at baseline and post-baseline.

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Authors' contributions

RA was involved in the design of the study, statistical analysis, monitored the study progress and intervention process, as well as development of the manuscript and subsequent corrections of the final write-up. UFU involved in the design of the study, collected the data, conducted the statistical analysis and developed the manuscript draft, as well as involved in the final write-up. OMI was involved in the design of the study, monitored the study progress and intervention process, and correction of the manuscript. All the authors read and approved the final submission.

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Availability of data and materials
The data sets used and/or analyzed during the study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
Ethics approval for the study was obtained from the University of Ibadan/University College Hospital Ethics Review Committee with registration/approval number NHREC/05/01/2008a/UI/EC/23/0404. Subsequently, permission for access to the medical out-patients unit of the hospital for patients' recruitment was obtained from the Chairman Medical Advisory Committee of the hospital before the commencement of the study. Verbal informed consent in accordance with the approved study protocol by the Ethics committee was obtained from each participant after explaining the objectives and procedure of the study to the participants individually. The information in the informed consent form was explicitly read and explained to individual participant on every clinic day before the commencement of the interview. Only the consented participants within the study period were enrolled.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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