

Is Inhaler Technique Adequately Assessed and Reported in Clinical Trials of Asthma and Chronic Obstructive Pulmonary Disease Therapy? A Systematic Review and Suggested Best Practice Checklist



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What is already known about this topic? Correct use of inhaler devices is fundamental for optimal control of obstructive airways disease, yet critical inhaler technique errors are made by approximately 90% of patients. In the randomized controlled trial setting, this may introduce misleading bias.

What does this article add to our knowledge? We found that 88% of all RCTs in the past 10 years that addressed the efficacy of baseline and escalated inhaled therapy for asthma and COPD did not document in any published data either whether the technique was checked or the quality or frequency of inhaler technique assessment. This raises the possibility that such an assessment was afforded low priority or inadequate, or omitted.

How does this study impact current management guidelines? We propose a structure for a best practice inhaler technique assessment and reporting checklist, which, after appropriate validation, could be used as a framework to ensure that an assessment of inhaler technique is practiced and documented as an essential element of RCT protocols and publications.

BACKGROUND: Inhaled medications are central to treating asthma and chronic obstructive pulmonary disease (COPD), yet critical inhaler technique errors are made by up to 90% of patients. In the clinical research setting, recruitment of subjects with poor inhaler technique may give a false impression of both the benefits and the necessity of add-on treatments such as biologic therapies. **OBJECTIVE:** To assess the frequency with which inhaler technique is assessed and reliably optimized before and during

patient enrollment into randomized controlled trials (RCTs) addressing the efficacy of topical therapy, and the escalation of therapy for asthma and COPD.

METHODS: Systematic searches were conducted of PubMed and Embase for RCTs published in the past 10 years involving patients with a diagnosis of asthma or COPD undergoing escalation of baseline inhaled therapy (stepping up, changing, adding, switching, increasing, etc) or the introduction of biologic agents.

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Abbreviations used

ADMIT- Aerosol Drug Management Improvement Team
 COPD- Chronic obstructive pulmonary disease
 pMDI- Pressurized metered-dose inhaler
 RCT- Randomized controlled trial

RESULTS: Searches highlighted 1,014 studies, 118 of which were eligible after the removal of duplicates as well as screening and full text review. Of these, only 14 (11.9%) included accessible information in the methods section or referred to such information in online supplements or protocols concerning assessment of participants' inhaler technique. We therefore developed the proposed Best Practice Inhaler Technique Assessment and Reporting Checklist.

CONCLUSIONS: Our study identifies a concerning lack of checking and correcting inhaler technique, or at least reporting that this was undertaken, before enrollment in asthma and COPD RCTs, which may affect the conclusions drawn. Mandating the use of a standardized checklist in RCT protocols and ensuring all published RCTs report checking and correcting inhaler technique before enrollment are important next steps. © 2022 The Authors. Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>). (J Allergy Clin Immunol Pract 2022;10:1813-24)

Key words: Asthma; COPD; Obstructive airway diseases; Inhaler technique; Inhaled medication; Inhaler error; Critical error; Inhaler device; pMDI; Checklist

INTRODUCTION

Efficient delivery of inhaled medications to the airways using pressurized metered-dose (pMDI), dry-powder, and soft-mist inhalers is fundamental for the optimal control of obstructive airway diseases (asthma and chronic obstructive pulmonary disease [COPD]) in both adults and children. Correct inhaler technique is essential to ensure optimal outcomes, yet studies show that critical inhaler technique errors are made by up to

90% of patients,^{1,2} a situation that has not improved over the past 4 decades.³

Critical inhaler technique errors are those that have a direct impact on the effectiveness of drug delivery, resulting in the potential for poor disease control.² A meta-analysis of 72 studies performed in 2017 revealed that across all device types, 14% to 92% of asthma and COPD patients made at least one critical error; in the case of pMDIs, 87% of patients made technique errors and 46% made critical errors (95% confidence interval, 26% to 67%).² Another meta-analysis, performed in 2019, investigating inhaler technique errors with pMDIs, reported that 87% of adult patients with obstructive lung diseases used pMDIs incorrectly.⁴ The study showed that common inhaler technique errors included failure to exhale fully before inhalation (66%); hold the breath for a sufficient time after inhalation (42%); inhale slowly and deeply (39%); exhale after inhalation (36%); and shake the inhaler, when appropriate, before use (34%).⁴ Many patients, particularly children and elderly people, may also have difficulty with the dexterity and coordination required.⁵ Sufficient dexterity is needed to handle, load, shake, and prime the inhaler, whereas ample coordination is required to synchronize inhalation with the operation of the device (if not breath-actuated and particularly if a spacer device is not used with a pMDI), ensuring fluidity of the inhalation maneuver.

Correct inhaler technique is central to successfully managing obstructive airways disease, and evidence supports the need for training in correct inhalation technique for patients receiving inhaled medications.⁶ The training must be tailored to the specific device and repeated sufficiently often to ensure that the correct technique is maintained.⁷ The Aerosol Drug Management Improvement Team (ADMIT) (<https://www.inhalers4u.org/>)^{6,8} was established to foster the correct use of inhaled therapy for obstructive pulmonary diseases by providing free information, resources, and instructions for all available inhaler types. Studies suggested that although even a single education session can significantly improve inhalation technique,⁹ at least three rounds of education are likely required to eliminate all errors for a sustained period,¹⁰ and that repeated training has a greater clinical impact on disease control than the precise type of inhaler used.⁵

Given these facts, it is unsurprising that poor inhaler technique has health economic and societal implications.^{1,11} Inhaler

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errors may reduce (or even annul) the quantity of medication reaching the airways, resulting in poor symptom control and increasing the risk for exacerbations. In turn, these outcomes result in unnecessary additional health care costs and use.^{4,12} Importantly, in the clinical research setting, recruitment of patients with poor inhaler technique may exaggerate the severity of the disease as well as provide a false impression of both the benefits and necessity of add-on therapies that are not delivered by inhalation, such as biologic therapies. There are currently no universal guidelines or standards to guarantee appropriate scrutiny, correction, and maintenance of inhaler technique where necessary in this setting.

In this study, we set out to determine whether and how often inhaler technique is assessed in randomized controlled trials (RCTs), in which it seemed clear that this should have been checked and optimized before, during, or after patient enrollment. We carried out a systematic literature review to determine the frequency of inhaler technique assessment, optimization, and reporting in RCTs of therapy of asthma and COPD involving patients with a diagnosis of asthma or COPD who received some form of inhaled therapy at baseline. We examined an all-inclusive list of interventions including stepping up or increasing the dosage; changing, adding, or switching the treatment and/or inhaler device; and adding therapy with biologic agents.

METHODS

Literature review

We conducted systematic literature searches in PubMed and Embase for the 10-year period beginning September 2010. Inclusion criteria were RCTs or RCT protocols that enrolled patients of any age who received a diagnosis of asthma or COPD, and who received some form of inhaled therapy at baseline. Interventions were identified using the search terms “step-up,” “changing,” “switching,” “increased dose,” “changing inhaler device,” and “adding or changing treatment.” Randomized controlled trials of approved biologic agents (monoclonal antibodies such as mepolizumab, reslizumab, benralizumab, omalizumab, or dupilumab or novel anticytokines for asthma) were included as a separate group. Search strings used are listed as Supplemental Material (in this article’s Online Repository at www.jaci-inpractice.org). Exclusion criteria were trials with no comparator group (ie, uncontrolled studies) and RCTs that specifically investigated inhaler technique and interventions in a hospital or emergency setting involving nebulized therapy. Conference proceedings, meeting abstracts, and publications with no abstract were ineligible. After duplicates were removed, two independent reviewers randomly allocated titles and abstracts and screened them for eligibility. Any discrepancies were resolved by a third reviewer. The full-text manuscripts of eligible studies were then reviewed to identify whether there was evidence that examination and/or optimization of inhaler technique had been undertaken and reported, and details were recorded onto a customized data extraction form in Excel software (Microsoft, Redmond, WA). The online supplementary material or study protocols referred to in the methodology were also checked. Items of interest for data extraction included the questions: Was inhaler technique checked? Was inhaler technique rechecked? How were patients instructed? What training methods were used? Were standardized protocols used? Who conducted the assessment? How was the assessor trained? Data that were extracted were cross-checked by the second reviewer.

Checklist development

A proposed inhaler technique checklist was developed based on an appraisal of the published literature. Elements considered for the checklist were checking inhaler technique at enrollment, repeated checking of inhaler technique, checking patient characteristics, inclusion of the inhaler technique in the study protocol, use of standardized training protocols, checking inhaler technique by trained personnel, and documenting patient education in inhaler technique. Discussion and development were conducted among the ADMIT group until full consensus was reached. The list of items and their exact formulation were built, discussed within the entire ADMIT group, and amended under the supervision of three authors (P.N.R.D., M.L.L., and C.J.C.) until full consensus was reached.

RESULTS

Literature searches yielded 1,014 relevant publications. [Figure 1](#) shows a flowchart of studies excluded at each step of the review process. After screening and a full text review, 118 unique RCTs were identified that involved recruiting patients with asthma or COPD using inhaled medication at baseline with an intervention that altered the dosage of existing therapy or changed the inhaler device or added to it. Of these RCTs, 14 (11.9%; 12 asthma and two COPD) included accessible information in the methods section or referred to this information in online supplements or protocols about checking participants’ inhaler technique. [Table I](#) lists inhaler techniques checked from the methods section of each publication. For RCTs investigating the effects of biologic agents, after screening and full-text review, only one in 54 studies (1.9%) stated that inhaler technique was examined at baseline.²⁶

Of the 14 RCTs in which inhaler technique was assessed, only six included key checklist elements (ie, confirming that inhaler technique was checked and rechecked, how patients were instructed, and who conducted the assessment).^{13,14,16,18,20,24} For example, Akamatsu et al¹³ stated that “The inhaler technique of each patient was checked by the involved doctors, nurses, or pharmacists not only during the run-in period but when switching the regimens and during the treatment period. We used the training whistles for Diskus and Turbuhaler supplied by each pharmaceutical company to assess adequate peak inspiratory flow.” Similarly, Huang et al¹⁶ stated that “Patients were instructed by study personnel on inhaler technique/how to take medication at the time they were given study medication. Patients were required to practice inhalation technique as many times as necessary until they could demonstrate proper inhaler technique to the supervising investigator/study nurse. In addition, patients received written information (in local language) on how to use the inhalers, as well as the importance of complying with the study regimen.” No studies reported objective verification of patients’ ability to achieve sufficient inspiratory flow or manifest sufficient dexterity to prime their devices and coordinate inhalation successfully. Another element missing from all but one study was documentation of the training and qualifications of the staff assessing inhaler technique.¹⁷

DISCUSSION

In this analysis of published RCTs involving patients with asthma or COPD using inhalers at baseline and receiving some form of escalation of treatment, we found that only 11.9% reported checking inhaler technique. Although documentation

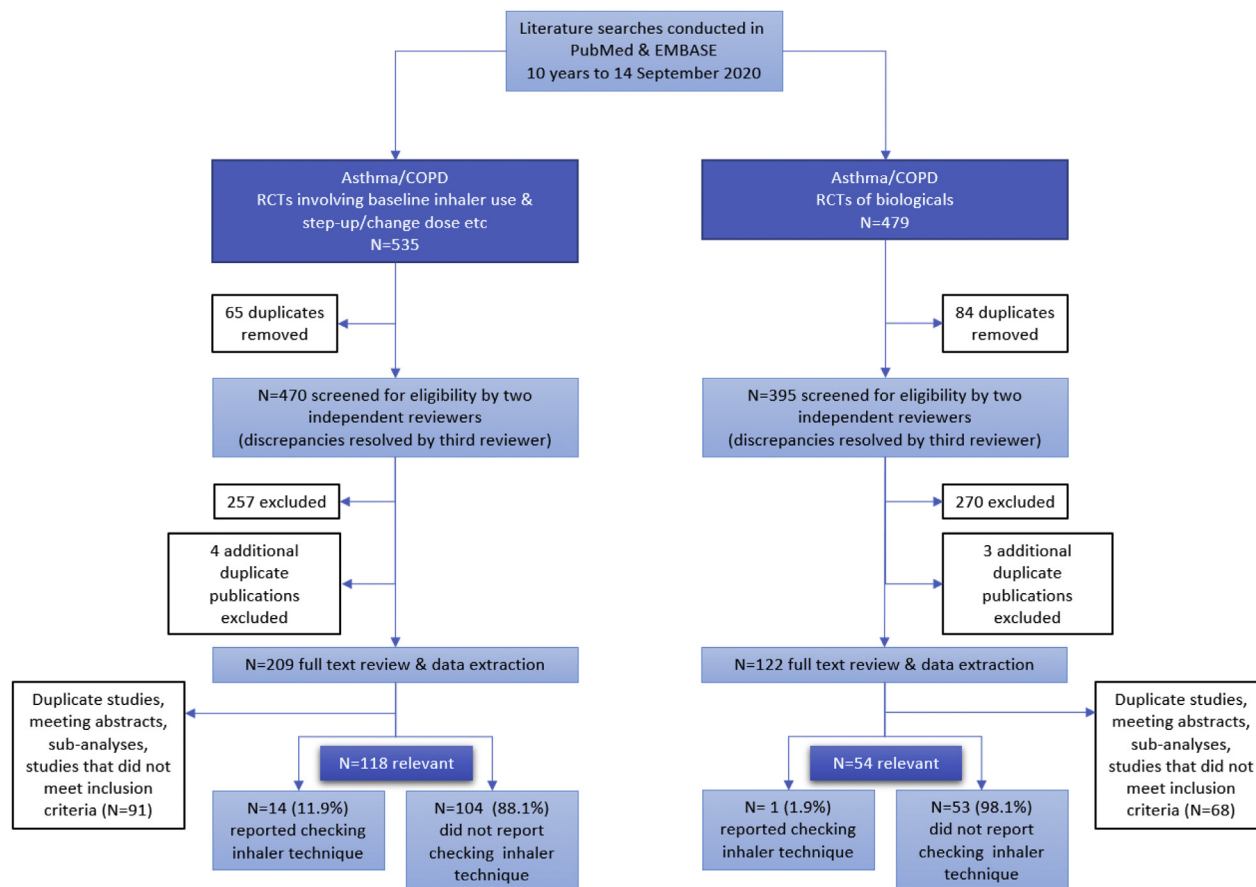


FIGURE 1. Flowchart of review process. *COPD*, chronic obstructive pulmonary disease; *RCTs*, randomized controlled trials.

mandating, directing, and recording checking of inhaler technique may have been confined to manuals of operation related to some of these studies that were not published in the final study reports or were not otherwise uncovered by our search strategies, the lack of this information in most identified studies may reflect the failure either to check inhaler technique altogether or to report that it was checked (and if so, adequately). In either case, this is considerably concerning.

In support of the possibility that inhaler technique was assessed and optimized in many of these RCTs but not reported, there is evidence that patients who participated in multiple RCTs involving inhaler therapy were less likely to demonstrate inhaler error.²⁷ On the other hand, if an assessment and optimization of inhaler technique were not carried out as part of the study protocol in most relevant RCTs of asthma and COPD therapy, this detracts from the credibility of the data and the robustness of the conclusions. For instance, in a 2018 RCT of 111 patients with “severe, uncontrolled” asthma, asthma control was either achieved or improved in 54 of patients (49%) after a program of inhaler technique and adherence assessment, and add-on therapy was consequently rendered redundant.²⁸ Similarly, a meta-analysis of pooled data from four RCTs documenting exacerbation rates in patients with COPD showed a nearly 30% mean reduction in exacerbation rates after inhaler technique review compared with controls (relative ratio = 0.71; 95% confidence interval, 0.59-0.86).²⁹ Finally, in the Management of Asthma in

School Age Children on Therapy study of poorly controlled asthma in children, it was estimated that an improvement in inhaler technique, education, and attention to adherence would result in 50% of participants being ineligible for randomization.¹⁸ This study also emphasized the interaction between ineffective inhaler technique and adherence: Patients were less likely to comply with a treatment they did not perceive to be beneficial.

Therefore, our findings have implications for conclusions drawn from studies in which subjects’ inhaler technique was not assessed, corrected, and rechecked before inclusion and at further intervals when appropriate. Inattention to this key aspect of disease management has the potential to inflate the perceived additional clinical benefits and cost-effectiveness of add-on therapeutic agents such as biologic agents. Indeed, a number of RCTs of biologic agents in uncontrolled severe asthma reported significant improvements in asthma control for patients in the placebo arm, highlighting the positive effect of improved adherence and/or inhaler technique. That the misuse of inhaler devices is rife is further underlined by a meta-analysis that concluded that despite constant remonstrations to health professionals to examine and perfect it in guidelines, the frequency with which patients’ suboptimal inhaler technique occurs has not significantly altered in the past 4 decades.³ One might conclude from this finding that the quality of the assessment, in addition to whether it is carried out, is also critical. This further underlines

TABLE I. Randomized controlled trials (RCTs) that included information in the methods section regarding checking participants' inhaler technique before randomization

Study	Trial name and National Clinical Trial number	Asthma or COPD?	Baseline treatment/ inclusion criteria	Intervention	Was checking of inhaler technique mentioned in methods?	Inhaler technique text	Additional notes or comments
Akamatsu et al ¹³	Not specified	Asthma	Receiving SFC 50/250 mg twice a day for >8 wk	Randomized into FBC 9/320 mg twice a day or the same dose of SFC continued for 12 wk	Yes	"The inhaler technique of each patient was checked by the involved doctors, nurses, or pharmacists not only during the run-in period but when switching the regimens and during the treatment period. We used the training whistles for Diskus and Turbuhaler supplied by each pharmaceutical company to assess adequate peak inspiratory flow."	
Cardet et al ¹⁴	PREPARE (pilot study for PARTICS), NCT02995733	Asthma	33 Black and Hispanic patients with persistent asthma, aged 18-75 y, who were currently prescribed ICS controller therapy (with or without other controller therapies such as LABA)	Participants were randomized 3:1 to PARTICS intervention QVAR (beclomethasone dipropionate HFA, 80 mg/puff) inhalers or enhanced usual care	Yes	<p>"Clinicians managing these participants' care in the community were asked to complete the American Academy of Allergy, Asthma, and Immunology Asthma IQ education program for Continued Medical Education credit to standardize and enhance 'usual care' to guideline-recommended care before enrolling participants."</p> <p>"All participants received guideline-based educational videos on recognizing and treating asthma symptoms (all materials were available in English and Spanish). An introductory video before randomization explained the study question, design, interventions, and recognizing and treating asthma symptoms. One segment of this video is based on an American Lung Association video that describes features of asthma as a disease, and also delves into the definition of 'rescue' and 'controller' therapy for asthma, emphasizing the need for controller therapy to be used daily as prescribed by clinicians. Additional prandomization videos show patients demonstrating how to use metered-dose inhalers and Diskus inhalers (these introductory videos can be found at https://www.youtube.com/channel/UC1A_Gak_r5XZ6tx_olc1gsQ). After randomization to either the PARTICS or enhanced usual care groups, all participants also received an inhaler storage pouch to increase adherence to asthma medications in both trial arms. Both groups viewed videos instructing them to carry their study pouch with their inhalers with them at all times. Each group was shown a video either on how to implement PARTICS in addition to usual controller medications or how to continue using their controller therapy as prescribed. A patient advisory committee reviewed all materials administered to participants and the study design itself to ensure patient-centeredness.</p>	"Additional prandomization videos show patients demonstrating how to use metered-dose inhalers and Diskus inhalers (these introductory videos can be found at https://www.youtube.com/channel/UC1A_Gak_r5XZ6tx_olc1gsQ)."

(continued)

TABLE I. (Continued)

Study	Trial name and National Clinical Trial number	Asthma or COPD?	Baseline treatment/ inclusion criteria	Intervention	Was checking of inhaler technique mentioned in methods?	Inhaler technique text	Additional notes or comments
Hodgson et al ¹⁵	SPIRA, NCT01171365	Asthma	Refractory asthma. Receiving high-dose ICS and persistent sputum eosinophils (>3%) and clinical improvement after oral prednisolone (30 mg for 2 wk)	Ciclesonide 320 µg twice daily for 8 wk via pMDI with small particles	Yes	"Subjects underwent instruction and assessment of inhaler technique with the trial drug MDI, and those that were unable to achieve an adequate technique with additional instruction (n = 4) were issued an AeroChamber Plus (GSK, Middlesex, UK)."	No details of how inhaler technique was assessed
Huang et al ¹⁶	NCT01415518	COPD	Severe COPD with ipratropium and oral theophylline	Addition of BUD/Form DPI b.d.	Yes	"Patients were instructed by study personnel on inhaler technique/how to take medication at the time they were given study medication. Patients were required to practice inhalation technique as many times as necessary until they could demonstrate proper inhaler technique to the supervising Investigator/study nurse. In addition, patients received written information (in local language) on how to correctly use the inhalers, as well as the importance of complying with the study regimen."	
Kuna et al ¹⁷	EudraCT no. 2007-005620-32	Asthma	Adolescent and adult patients with moderate to severe persistent asthma	Patients received treatment with FP-Sal novel mDPI 100 to 50 µg or 500 to 50 µg, or originator device 100 to 50 µg or 500 to 50 µg in a double-blind, double-dummy, parallel group, multicenter study	Yes	"Patients were given training on the correct use and handling of the inhaler device and an asthma monitor used for peak expiratory flow (PEF) assessment. Assessment of PEF by Patients at Home. Each patient was provided with a numbered identifiable asthma monitor (Vitalograph asma-1) (Vitalograph Inc, Lenexa, KS) at the screening visit, and the participant or guardian was instructed on the correct use of the monitor. Triplicate readings of PEF were taken twice daily, before the study medication was taken, in the morning on waking and in the evening before going to bed. All readings were recorded on diary cards."	

Lenney et al ¹⁸	MASCOT, ISRCTN03556343	Asthma	Children aged 6-14 y with asthma requiring frequent short-acting β_2 -agonist relief, with symptoms of asthma resulting in nocturnal wakening and/or asthma that interfered with usual activities	Three groups were compared: (1) inhaled fluticasone propionate 100 μ g twice daily plus placebo tablet once daily; (2) inhaled fluticasone propionate 100 μ g and salmeterol 50 μ g twice daily (combination inhaler) plus placebo tablet once daily; and (3) inhaled fluticasone propionate 100 μ g twice daily plus montelukast 5-mg tablet once daily	Yes	<p>Inhaler technique correction - mentioned in abstract</p> <p>Mentioned in main text of publication:</p> <ul style="list-style-type: none"> - Eligible children who were able to give informed consent entered a 4-week run-in period in which expert inhaler technique training was given by the research nurse along with a prescription for fluticasone propionate inhaler (100 μg twice daily). - Following full informed written (proxy) consent, those eligible were registered into the study, had their inhaler technique checked (with additional training if necessary) and were provided with information about asthma and its management. All research centres taking part were centrally trained and instructed in appropriate strategies of approaching patients and their families in an attempt to obtain uniformity. - The purpose of the run-in period was to ensure that recruitment was limited to patients for whom control of their asthma presented a problem, rather than patients for whom only inhaler technique and management advice was sufficient to provide good control. Most run-ins lose approximately 25% of patients; it was anticipated that improved inhaler technique, education and attention to compliance as well as patients all using the same ICS may well make up to 50% ineligible for entry into the randomized part of the study. 	A number of children achieved control in 4 wk run-in after they and parents received inhaler technique instruction.
Lipworth et al ¹⁹	BREATHE database NCT00655616	Asthma	Children with persistent asthma	Salmeterol (50 μ g, twice daily) or montelukast (5 or 10 mg, once daily) as add-on to inhaled fluticasone for 1 y	Yes	"Baseline visit - check inhaler technique with Accuhaler device; view inhalers and check inhaler technique at all other visits."	

(continued)

TABLE I. (Continued)

Study	Trial name and National Clinical Trial number	Asthma or COPD?	Baseline treatment/ inclusion criteria	Intervention	Was checking of inhaler technique mentioned in methods?	Inhaler technique text	Additional notes or comments
Maltais et al ²⁰	NCT03162055	COPD	Moderate to very severe COPD	Assessed efficacy and safety of GFF MDI relative to umeclidinium/vilanterol dry-powder inhaler (UV DPI)	Yes	“As the technique for inhalation differs between MDIs and DPIs, it was important to ensure that patients applied the correct inhalation technique for both types of inhalers. Training devices were available at each study site for instructional purposes, as well as for patients to practice correct inhalation technique. Instruction on device handling (including priming and shaking of the MDI) and inhalation practice occurred before study medication was dispensed, and the patients’ inhalation technique was reviewed at clinic visits throughout the study. Use of a spacer device with the MDI was not permitted. An electronic patient-reported outcome (ePRO) device was used to record symptom assessments as well as the administration of study medication. Compliance with study drug treatment was assessed by site personnel by checking patients’ self-reported records in their ePRO devices at each visit. Overall compliance was assessed as the proportion of the total number of inhalations used relative to the expected number of inhalations.”	
Nabil et al ²¹	Not specified	Asthma	Severe persistent asthma, uncontrolled with beclomethasone or budesonide DPI 400 µg/d	Parallel group study: patients randomized to formoterol/budesonide 12/400 Aerolizer or budesonide 800 Aerolizer twice daily	Yes	“At these (weekly) visits, the patient’s questions were discussed, and any problems with asthma and its treatment are reviewed. Checking of the inhaler device technique with correction and re-checking if it is inadequate were done until the period of treatment ended.”	
Usmani et al ²²	NCT02388373	Asthma	Well-controlled asthma	Maintain high-dose fluticasone propionate/salmeterol xinafoate (FP/SAL, 1,000/100 mg) or switch to FP/FOR (1,000/40 mg)	Yes	“Patients demonstrated a satisfactory inhaler technique without serious inhaler technique errors, after device training if required, at screening.”	
Papi et al ²³	NCT00497237	Asthma	Treated with 1,000 µg fluticasone propionate plus 100 µg salmeterol daily for ≥4 wk before screening visit	250/50 µg fluticasone/salmeterol (FP/S) Diskus DPI or 100/6 µg beclomethasone/formoterol (BDP/F) pMDI	Yes	The morning dose of the study drugs was taken after the PFTs were performed at the clinic sites, under the investigator’s supervision, to assess proper inhaler technique.	

Lemanske et al ²⁴	NCT00395304	Asthma	Children with uncontrolled asthma while receiving 100 µg of fluticasone twice daily	250 µg of fluticasone twice daily (ICS step-up), 100 µg fluticasone plus 50 µg of long-acting β-agonist twice daily (LABA step-up), or 100 µg fluticasone twice daily plus 5 or 10 mg of leukotriene receptor antagonist daily (step-up)	Yes (in supplementary material)	Patients received an open-label metered-dose inhaler of albuterol, prednisone, and a customized written action plan to guide use.	The study protocol was available in an online Supplementary Appendix. Page 22: Visit 0 - inhaler technique reviewed Page 29: E. Inhalation techniques. To minimize the variability in the dose of both the ICS and LABA delivered to the lungs, the patient's medication technique will be reviewed at each study visit. Objective feedback will be given to each participant to improve performance. The precise technique utilized will be dependent on the ICS/LABA, ICS, and matching placebo that are successfully obtained from the pharmaceutical companies currently manufacturing these products.
Brand et al ²⁵	NCT00163449	Asthma	Uncontrolled wheeze: preschool	RCT add-on ciclesonide, three doses	Yes, At onset of study - not during the study	"All children had to demonstrate the use of inhaler and spacer to the study staff until these were satisfied that drug administration and inhalation technique were correct; children aged 2-3 y were equipped with a facemask (medium size Comfort Seal facemask fitted to the AeroChamber Plus by the manufacturer) if unable to use the inhaler with a spacer and mouthpiece."	
Bernstein et al ¹¹	NCT01576718	Asthma	Severe asthma	RCT, dose ranging	Yes, At recruitment; however not checked during the study	"The study enrolled male and female patients aged 12 years as of screening or patients aged 18 years in countries where local regulations or drug regulatory status permitted adult enrollment only, with a diagnosis of asthma (as defined by the National Institutes of Health) and a best predose, prebronchodilator AM FEV ₁ of 40% to 85% of predicted normal value and a demonstrated 12% reversibility of FEV ₁ within 30 minutes following 2 to 4 inhalations of albuterol/salbutamol inhalation aerosol."	

BUD/Form DPI, budesonide-formoterol dry powder inhaler; *b.d.*, twice daily; *COPD*, chronic obstructive pulmonary disease; *DPI*, dry-powder inhaler; *FBC*, formoterol-budesonide combination; *GFF MDI*, glycopyrrolate/formoterol fumarate metered dose inhaler; *ICS*, inhaled corticosteroid; *LABA*, long-acting β-agonist; *pMDI*, pressurized metered-dose inhaler; *SFC*, salmeterol-fluticasone combination.

ADMIT - The Aerosol Drug Management Improvement Team

2021 ADMIT Best-Practice Inhaler Technique Assessment & Reporting Checklist

This checklist aims to facilitate uniform assessment and maintenance of correct inhaler technique.

Regular assessment of inhaler technique is essential as correct inhalation is central to successful asthma and COPD management. All asthma and COPD guidelines recommend regular assessment of inhaler technique but evidence shows this is rarely carried out and/or reported.

This checklist should be used prior to patient enrollment into any randomized controlled trial (RCT) or clinical study that involves the use of inhaled medication at baseline or as an intervention (except where examination and/or improvement of technique is an outcome measure). Correcting inhaler technique may lead to better symptom control, improved lung function, and reduced exacerbation rate, and therefore alter eligibility for entry into a study. Where technique is unsatisfactory, this should be re-verified following appropriate training, along with the patient's eligibility for participation in the trial/study.

The checklist can guide development of study protocols, best-practice reporting and facilitate a standardized approach across studies. It can also be used for patients who are insufficiently controlled on their current inhaled medication **before** switching devices and/or increasing dosages.

Patient instruction videos and downloadable written instructions for adults and children, and all inhaler types, are available from the ADMIT website: inhalers4u.org

Item no.	ADMIT INHALER TECHNIQUE ASSESSMENT CHECKLIST ITEM	Checked at enrolment	Checked again	Not applicable/Unknown*	Reported on page no.
1	Check patient characteristics:				
	a) Able to achieve sufficient inspiratory flow (e.g., observe duration of inhalation or assess PIF or hear a 'click' with inhalers that make a clicking noise)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	b) Dexterity				
	i. Priming (ability to handle/load/shake device)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	ii. Coordination	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	iii. Fluidity of inhalation maneuver	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
2	FOR EXISTING DEVICES USED PRIOR TO ENROLLMENT/AT BASELINE				
2A	Does the study protocol include assessment of inhaler technique?	Yes / No			
2B	Was inhaler technique assessed by a trained individual?				
	a) Checked with the patient's current device(s)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	b) Checked using a placebo device, or tool such as the In-Check Dial, ClioTone, Vitalograph AIM device, or similar	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
2C	If inhaler technique was suboptimal, how was the patient educated?				
	a) Face-to-face contact	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	b) Remotely	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	c) Video	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	d) Teach-back method	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	e) Supporting materials provided	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
2D	Who educated the patient?				
	a) Doctor	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	b) Nurse	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	c) Pharmacist	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	d) Physiotherapist	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	e) Other	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
2E	Were uniform, standardized, device-specific, training protocols used?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
2F	Was inhaler technique re-checked at next visit to ensure good				

FIGURE 2. Proposed Best Practice Inhaler Technique Assessment and Reporting Checklist for use before patient enrolment into a randomized controlled trial or clinical study involving the use of inhaled medication at baseline or as an intervention. *COPD*, chronic obstructive pulmonary disease.

our findings suggesting the urgent need for international guidelines and standards for a formal assessment of inhaler technique in all study participants as in clinical practice, with retraining of participants when necessary to comply with a

uniform minimum objective standard of proficiency that could be reassessed periodically.

Surprisingly, whereas there is an implicit duty of care to ensure correct inhaler technique in any clinical setting, there are no

	technique was maintained? If not, specify at what intervals inhaler technique was re-verified.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3	FOR NEW DEVICES USED AS INTERVENTION			
3A	Was the patient educated in the use of any new device(s) by a trained individual?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3B	If the device was entirely new, was a uniform, standardized training protocol available and used?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3C	How was the patient educated?			
	a) Face-to-face contact	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	b) Remotely	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	c) Video	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	d) Teach-back method	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	e) Supporting materials provided	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3D	Who educated the patient to use the device correctly?			
	a) Doctor	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	b) Nurse	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	c) Pharmacist	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	d) Physiotherapist	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	e) Other	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3E	Were uniform, standardized, device-specific, training protocols used?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3F	Was inhaler technique re-checked at next visit to ensure good technique was maintained? If not, specify at what intervals inhaler technique was re-verified.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

*Please provide an explanation about why this step was not applicable

FIGURE 2. Continued.

existing standards governing their frequency and quality. In 2017, Chrystyn et al² highlighted the lack of standardized checklists for checking inhaler technique. Thus, we produced a framework structure for the development of a best practice inhaler technique assessment and reporting checklist (Figure 2), which, when it is operational, perhaps validated by further revision and adaptation to assess technique with particular inhaler devices or groups of devices, and eventually widely employed, will facilitate uniform reporting and verifiable assessment and maintenance of correct inhaler technique in the RCT setting. It is anticipated that this checklist will be a useful tool to guide the development of study protocols as well as best practice reporting and facilitate a standardized approach across studies. The checklist will also be suitable for the routine assessment of patients who are insufficiently controlled on current inhaled medication before switching devices or increasing dosages. The next step in developing this resource is to verify its use in the clinical trial setting. Once validated, we encourage journal editors and reviewers to make its use mandatory when reporting results of asthma and COPD RCTs.

Furthermore, a large RCT of therapy for asthmatic patients who are deemed uncontrolled or unresponsive to inhaled therapy is an attractive arena in which to verify and quantify the existence and clinical implications of poor inhaler technique through the inclusion of two separate control groups assigned to usual treatment. These groups are further randomized to receive or not receive systematic instruction in optimizing inhaler technique, because among these patients there will be some who are truly unresponsive to therapy owing to the nature of airways inflammation and remodeling, and some who are potentially fully responsive if the therapy is delivered consistently and reliably to the airways. These are also patients who would be expected to have been shown how to use the inhaler devices, and whose inhaler technique was assessed on multiple occasions in the past. In our opinion, it

would be considered ethical to underline and define any possible scope for improvement in the effectiveness of a patient's usual therapy by including such a control group with the patient's informed consent. On the other hand, this would obviously add to the recruitment burden of such trials, and there is undoubtedly also a role for stand-alone studies dedicated to examining the clinical impact of appropriate training in inhaler technique in patients with poorly controlled asthma. Such studies would also aid in refining the appropriate content and frequency of training regimens and enable power calculations.

A corollary issue regards the person who may be considered suitably qualified to assess and correct inhaler technique in such studies. Appropriately trained personnel should conduct the assessment. Interestingly, we identified only one study that reported study staff had been trained specifically to deliver inhaler training.¹⁴ There is currently no universal definition of appropriate training, but although schemes exist, such as the American Academy of Allergy Asthma and Immunology Asthma IQ: Patient Management and Outcomes training,³⁰ an international training and revalidation program would be ideal.

The recent development of smart digital inhaler devices with the capacity to provide and transmit data may also have a role in assessing and maintaining correct inhaler technique as well as medication use, provided they record at least some aspects of the inhaler technique that are critical for optimal drug delivery.

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ONLINE REPOSITORY

Literature searches

Embase

Randomized controlled trial. ((asthma or copd) and inhal* and (step-up or step-down or switch* or add-on or adding or "increasing dose" or "increased dose" or "changing treatment" or "changing inhaler device")).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]

LIMIT TO (randomized controlled trial and last 10 years)

Biologics search. ((asthma or copd) and (anti-IL1 or anti-IL4 or anti-IL5 or anti-IL5R or anti-IL13 or anti-TNF or anti-TSLP or mepolizumab or reslizumab or benralizumab or anti-cytokines or anti-IgE or omalizumab or dupilumab)).mp. [mp=title, abstract, heading word, drug trade name, original

title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
LIMIT TO (randomized controlled trial and last 10 years)

PubMed

Randomized controlled trial search. Search: ((asthma or copd) and inhal* and (step-up or step-down or switch* or add-on or adding or "increasing dose" or "increased dose" or "changing treatment" or "changing inhaler device")) AND (random*[Title])
Filters: In the last 10 years Sort by: Publication Date

Biologics search. Search: (asthma or copd) and (anti-IL1 or anti-IL4 or anti-IL5 or anti-IL5R or anti-IL13 or anti-TNF or anti-TSLP or mepolizumab or reslizumab or benralizumab or anti-cytokines or anti-IgE or omalizumab or dupilumab)
Filters: Randomized Controlled Trial, in the last 10 years Sort by: Publication Date