Clinical Commentary Review

The Impact of Inhaler Device Regimen in Patients with Asthma or COPD

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Many inhaler devices with varying handling requirements for optimal use are available for the treatment of asthma and chronic obstructive pulmonary disease (COPD). Patients may be prescribed different device types for reliever and maintenance medications, which may lead to confusion and suboptimal device use. We aimed to understand whether simplifying inhaler regimens by employing a single device type in patients who use multiple devices or prescribing a device with which a patient was already experienced could improve clinical and economic outcomes in asthma and COPD management. A targeted literature search was performed and additional articles were identified through hand searching citations within screened publications. A total of 114 articles were included in the final review. Findings suggest that simplifying inhaler regimens by applying the same type of inhaler for concomitant inhaled medications over time minimizes device misuse, leading to improved clinical outcomes and reduced health care use in patients with asthma or COPD. Physicians should consider a patient’s suitability for a device and training needs when prescribing an inhaled medication and before changing the medication type or dose, especially when suboptimal treatment outcomes are observed. Further research is required to determine whether consistent use of the same device type is associated with better treatment adherence and persistence in patients with asthma or COPD. Nevertheless, this literature review identified clinical benefits and reduced health care use with simplified inhaler regimens. © 2021 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 2021;9:3033-40)

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INTRODUCTION

Inhaled bronchodilators and corticosteroids are the mainstay of clinical management for asthma and chronic obstructive pulmonary disease (COPD).1,2 Pressurized metered dose inhalers (pMDIs), dry powder inhalers (DPIs), nebulizers, and soft mist inhalers (SMIs) are available.3 Each device requires different preparation, handling, and inhalation techniques, and each has specific requirements to optimize drug delivery to the lungs.3,6 Patients using multiple concomitant inhaled medications may not necessarily be prescribed the same device.7,9 To understand the value of simplifying the inhaler regimen in terms of the number and different types of devices used, we conducted a targeted literature review to determine whether a change or addition of a treatment, or using the same type of inhaler device, was associated with clinical or health-economic benefits in asthma and COPD management.

SEARCH STRATEGY AND SELECTION CRITERIA

We performed targeted literature searches to identify English-language publications investigating asthma and COPD in MEDLINE® and conference abstracts in Embase® (Asthma: January 1, 2007 to December 12, 2020; COPD: January 1, 2007 to December 31, 2017, and January 1, 2017 to December 12, 2020) (see Table E1 in this article’s Online Repository at www.jaci-inpractice.org). Articles were also identified by hand searching for references cited within screened publications. Findings reported in the selected studies were synthesized qualitatively.10 Additional articles were identified during the writing of the report and manuscript after the formal targeted literature search.
Abbreviations used
COPD- Chronic obstructive pulmonary disease
DPI- Dry powder inhaler
N/A- Not applicable
OR- Odds ratio
pMDI- Pressurized metered dose inhaler
R²- Coefficient of determination
SMI- Soft mist inhaler

search and data extractions were performed. To focus the review on a manageable number of references, abstracts from conferences were excluded, because there were no data of major interest that had not been included elsewhere.

OBJECTIVES

Objectives of the targeted literature search included the impact of the inhaler regimen in patients with asthma or COPD on (1) clinical efficacy and exacerbations; (2) ease of use, device preference, and patient satisfaction; (3) patient adherence, device technique, and handling errors; and (4) health care resource utilization.

STUDIES SELECTED

Figure 1 shows an article selection flow diagram. Of the 114 extracted articles, 47 covered both COPD and asthma, 39 focused on COPD only, and 28 focused on asthma only. After further review, 26 articles are cited here because this review focuses on only certain topics from the targeted literature search. Table I lists study selection criteria. Twenty-one additional relevant articles identified during the development and writing of this article are included.

IMPACT OF INHALER REGIMEN ON CLINICAL EFFICACY AND EXACERBATIONS

A meta-analysis of two randomized controlled trials in 1421 patients with COPD found no difference in the risk for exacerbations in patients treated with the same medication delivered through an SMI or a chlorofluorocarbon pMDI (now phased out of clinical practice). In studies investigating tiotropium delivered through a DPI versus an SMI, no differences were observed in measures of lung function or risk for exacerbations. 

A randomized, open-label study evaluated ipratropium bromide/albuterol delivered by an SMI compared with a chlorofluorocarbon pMDI, and to the simultaneous administration of two separate hydrofluoroalkane pMDIs in patients with COPD. In that study, patient satisfaction was significantly higher with an SMI compared with chlorofluorocarbon or hydrofluoroalkane pMDIs. However, differences in lung function results were not clinically significant, and no significant differences between treatments were observed for time to first exacerbation, time to first exacerbation leading to hospitalization, or the number of hospitalizations of rescue medication used at week 48.

In contrast to controlled clinical trials, real-world studies reported differences in disease control between devices, which may be explained by their contrasting environments. A United Kingdom database study of patients with COPD treated with fluticasone propionate/salmeterol xinafoate reported differences in clinical outcomes based on whether treatment was delivered by a DPI or pMDI. In that observational study, patients treated with a pMDI versus a DPI had significantly fewer moderate or severe COPD exacerbations and significantly lower odds of receiving a long-acting muscarinic antagonist prescription (indicating a reduced need to escalate maintenance treatment). However, no differences were reported between pMDIs and DPIs in a randomized, controlled 12-week trial of the same inhaled medication in patients with COPD. These discrepancies may have resulted from the clinical trials being structured, ideal situations in which patients normally have exceptional adherence and receive training on the device technique, which does not reflect routine clinical practice.

Using different inhaler devices in asthma and COPD can confuse patients and lead to errors in device use, which may be reduced by employing the same inhaler device for multiple inhaler regimens, because the inhaler technique required for optimal device use will be consistent. For example, in a prospective, cross-sectional observational study, patients with asthma or COPD who used more than one device had higher odds of demonstrating an incorrect inhalation technique compared with those who used only one device (Table II).

In a retrospective analysis of 2 years’ continuous data, COPD outcomes were compared between groups of patients who used multiple devices requiring different inhalation techniques (eg, pMDI plus a DPI), and those who used multiple devices requiring a similar inhalation technique (eg, pMDIs, pMDIs with spacers, SMIs, and breath-actuated inhalers, or all DPIs). Patients who used similar devices had a lower rate of moderate or severe exacerbations and were less likely to be in a higher short-acting β₂-agonist dose group (suggesting better symptom control) than those who used mixed devices (Table II). The authors proposed that in patients using mixed devices, variations in inhalation technique may have led to inhalation errors, resulting in reduced effectiveness.

Switching specific devices, even to a similar type of inhaler, may also affect clinical outcomes. An observational matched cohort analysis of 926 patients with mild asthma found that switching budesonide DPI resulted in increased exacerbation rates in the year after the switch (0.40 and 0.32 per year for switched and non-switched patients, respectively; P = .047). In addition, among patients who switched, those who had a primary health care visit at switch had significantly fewer outpatient hospital visits in the year after switching than those with no primary health care visit at switch (0.81 and 2.01 visits per year, respectively; P < .001).

IMPACT OF INHALER REGIMEN ON EASE OF USE, DEVICE PREFERENCE, AND PATIENT SATISFACTION

Device selection should be individually tailored to a specific patient and consider patient-centric factors, such as using the same inhaler for multiple medications to reduce complexity for the patient, patient training requirements and device preference, lifestyle (active versus sedentary), peak inspiratory flow, and a patient’s ability to use the device correctly. Experts suggested that a patient’s inspiratory ability could guide selection of the most appropriate device for delivery.

In an observational study in which most patients had COPD or asthma, most patients (76%) made at least one device error when using a pMDI, and approximately half of patients (49% to 55%) still made at least one device error when using a breath-actuated inhaler. Furthermore, in an observational study in
New Zealand, almost half of patients with COPD or asthma (47%) who used a pMDI (with or without a spacer) or a DPI had poor device technique. In addition, in a cross-sectional study in Italy, in which most patients had COPD or asthma, critical errors in pMDI or DPI device technique occurred in 12% to 44% of patients.

**TABLE I. Criteria for study selection**

| Criteria | Inclusion criteria | Exclusion criteria |
|----------|--------------------|--------------------|
| Population(s) | Adults with COPD or asthma | Children, other respiratory diseases |
| Devices of interest | Inhaled medication for COPD or asthma delivered by pressurized metered dose inhaler, dry powder inhaler, small volume nebulizer, soft mist inhaler, or nebulizer | N/A |
| Outcomes | Efficacy, safety, health outcomes, cost, resource utilization, training time, value of continuity, and cost of switching Patient preference, adherence, ease of use, errors or misuse, patient satisfaction, and identifying patient characteristics best suited to different devices | Studies not reporting outcomes of interest for study population |
| Time | Indexed databases in MEDLINE® and conference abstracts in Embase® (Asthma: January 1, 2007 to December 12, 2020; COPD: January 1, 2007 to December 31, 2017, and January 1, 2017 to December 12, 2020) | Studies published outside these time limits (except a few articles identified by hand searching) |
| Study design | Randomized trials (phases II and III); observational and cohort studies; interventional (nonrandomized) studies; studies conducting surveys and questionnaires; systematic reviews and review articles | Animal studies, case reports, editorials, ongoing studies, and interim analyses |
| Other | English language only; no limits on geographic location of study | Articles not published in English |

COPD, chronic obstructive pulmonary disease; N/A, not applicable.
| Study design                                    | Patients   | Population | Medication type                     | Outcome                                                                 |
|------------------------------------------------|------------|------------|-------------------------------------|-------------------------------------------------------------------------|
| Inhalation errors                              | COPD or asthma | n = 139 (single device) n = 161 (multiple devices) | Not reported                                                   | ↓ Single device users had incorrect device handling versus multiple device users (53% versus 76%) |
| Treatment outcomes                             | COPD       | n = 8225 matched pairs (similar devices versus mixed devices) | Inhaled corticosteroid, maintenance, reliever               | ↓ Exacerbations (rate ratio = 0.82) and ↓ short-acting β₂-agonist dose (OR = 0.54) in similar versus mixed device cohort |
| Patient preference                             | COPD or asthma | n = 301 participants using 464 devices (overall) | Not reported                                                   | ↑ Easiest to use device: 56% chose current inhaler; 10% had previously used inhaler; 34% inhaler had not used before* |
| Cross-sectional real-world survey              | COPD       | n = 1443 patients | Maintenance                         | ↑ Patient satisfaction with inhaler associated with ↑ treatment adherence (R² = 0.09), ↓ exacerbations (R² 0.03) and ↑ health-related quality of life (EuroQol-5D R² = 0.04) |
| Adherence                                      | COPD       | n = 11,747 matched pairs (single device versus multiple devices) | Inhaled corticosteroid, maintenance                           | ↑ Discontinuation rate (hazard ratio = 1.40) and ↓ adherence† (proportion of days covered OR = 0.66) in multiple versus single device users |
|                                              | COPD or asthma | n = 428 (single device) n = 658 (multiple devices) | reliever                                                      | ↑ adherence (OR = 1.77), ↓ risk for emergency department visit or hospitalization (relative risk = 0.58), ↓ health care charges (mean difference $46 per person/mo), ↓ hospital stay length (2.05 versus 4.61 d) with single versus multiple device use |

*↑, increased; ↓, decreased; COPD, chronic obstructive pulmonary disease; OR, odds ratio; R², coefficient of determination.

A representative sample of studies investigating the benefits of simplifying the inhaler regimen on clinical outcomes was selected for inclusion in the table, particularly those with a large sample size.

*This review assessed patient device preference but did not highlight the specific benefits of simplifying the device regimen.

†Adherence was defined as 80% of days or greater covered over 1 year.
In an observational study focusing on different types of DPIs, in which most patients had asthma or COPD, 32% of examinations identified at least one operating error that had a substantial impact on lung deposition or caused insufficient inspiratory flow; the frequency of operating errors varies among devices. The error rates in inhaler technique increased significantly with age and the severity of airway obstruction. A cross-sectional observational study found that only one in five patients with COPD or asthma used the DPI correctly and at the correct time; errors included inadequate inspiratory flow generation, drug priming without inhalation, exhalation into the inhaler, and multiple inhalations observed in 24% of attempted inhalations. Furthermore, a systematic literature review reported huge variability in the proportion of patients with COPD or asthma who used the DPI devices correctly, which depended on the type of inhaler assessed and the method of assessment.

Increased satisfaction with and preference for a prescribed device may lead to improved adherence and consequently better health outcomes. For example, in a multinational, cross-sectional, real-world survey in which patients with COPD rated inhaler satisfaction and physicians assessed their treatment adherence, patient satisfaction with the inhaler was significantly associated with treatment adherence. Furthermore, patient satisfaction and treatment adherence were associated with fewer exacerbations and increased health-related quality of life; treatment adherence was also associated with fewer hospitalizations owing to exacerbations (Table II). Inhaler attributes influencing satisfaction were related to device durability, ergonomics (easy to hold and carry), and ease of use. Similarly, in an observational study of 778 patients with moderate or severe asthma treated with maintenance inhalers, a high level of patient satisfaction with an inhaler was significantly associated with asthma control.

Interestingly, in a Portuguese cross-sectional study in which patients with COPD or asthma tested 10 different DPI, SMI, and pMDI devices to determine patient preferences, there was no consensus on the inhaler device considered easiest to use or preferred for daily use. However, preference for the easiest device to use was influenced by the prescription experience of patients, because 66% chose a device they were currently using or had previously used. This wide distribution of device preference and the diverging reasons for the choice of device show that inhaler treatment for each patient must be considered individually.

**IMPACT OF INHALER REGIMEN ON PATIENT ADHERENCE, DEVICE TECHNIQUE, AND HANDLING ERRORS**

Problems with adherence are common in patients with asthma or COPD, because the patients require long-term pharmacotherapy, use multiple medications, and may have comorbidities. Poor adherence leads to negative clinical consequences, which may have an economic impact, as shown in a retrospective study of patients aged 65 years and older with moderate-to-severe asthma, COPD, chronic bronchitis, chronic airway obstruction, or emphysema, who were treated with inhaled corticosteroids. Poorer medication adherence was associated with a significant increase in total annual physician visits, and better adherence was associated with a significant decrease in the number of annual hospitalizations.

Studies suggest that inhaler device and preference can influence adherence, persistence, or both. For example, a multicenter, retrospective analysis of medical and pharmacy claims in patients with COPD prescribed an inhaled corticosteroid/long-acting β2-agonist fixed-dose combination identified that the inhaler device, together with a patient’s clinical and socioeconomic characteristics, influenced adherence to long-term COPD medication. A multicenter crossover study reported that 90% of patients with COPD or asthma stated that they would comply with treatment when their most preferred form of inhaler was prescribed.

In a retrospective analysis of health care claims data, patients with COPD who were prescribed multiple maintenance inhalers were significantly less likely to adhere to treatment and discontinue therapy at a significantly higher rate than did single inhaler users, which may be related to the need for patients to learn the technique for using a second type of inhaler to use each device properly (Table II). In addition, a retrospective cohort study in patients with COPD found that using a single inhaler containing both ipratropium and albuterol was associated with a significantly lower risk for a visit to an emergency department or hospitalization, lower mean monthly health care charges, shorter hospital stay, and a greater likelihood of adherence compared with the use of separate inhalers (Table II).

Poor inhaler technique can also affect medication adherence and clinical outcomes. In an observational study of 727 patients with asthma, poor asthma control was independently associated with both poor inhaler technique and poor self-reported adherence. Separately, a cross-sectional analysis of 165 patients with asthma or COPD enrolled in the Adherence-Trial found a wide variance in incorrect inhaler technique (range, 0% to 53%) across seven types of inhaler. Patients with incorrect inhaler handling had experienced 30% more exacerbations in the 12 months before the start of the study compared with participants with correct inhaler handling. In addition, in patients with COPD, incorrect device application was associated with a significant negative impact on mean COPD Assessment Test scores. In a further real-world observational study of 254 patients with asthma receiving controller therapy, asynchrony between inhalation and actuation resulted in increased odds of an asthma exacerbation compared with absence of asynchrony. Similarly, among 623 adult patients with asthma using a Diskus® inhaler (GSK, Brentford, Middlesex, United Kingdom) in a cross-sectional observational study, 341 patients (55%) made one or more serious handling errors. Furthermore, both poor asthma control and asthma-related hospitalizations in the previous year were significantly associated with patients making one or more serious handling errors.

Data from multiple clinical studies of patient errors with inhaler devices were appraised in a systematic review of studies in asthma or COPD. A higher frequency of patient device error was associated with poor disease outcomes, primarily in asthma (nine studies) and in one study of asthma and COPD.

**IMPACT OF INHALER REGIMEN ON HEALTH CARE RESOURCE USE**

Alongside clinical outcomes, there are also economic consequences of poor inhaler technique. A cross-sectional, observational study reported that the risk for hospitalization, emergency department visits, antimicrobial use, and corticosteroid use was significantly higher in patients with COPD or asthma who committed one or more critical device errors, compared with...
those who did not. A systematic review of asthma or COPD studies that reported patient errors with inhaler devices identified that health care resource use and costs increased as a consequence of poor inhaler technique and/or patient errors in inhaler use.

Evidence from an observational study suggested that simpler treatment regimens, such as using the same or similar devices in multiple-inhaler regimens, are more effective in improving COPD outcomes. In addition, in patients with COPD, it was shown that users of single inhalers versus multiple inhalers, and similar devices versus mixed devices, experienced fewer exacerbations and reduced health care resource utilization, leading to lower health care costs.

An observational, real-world study estimated the economic impact on the Italian National Health Service caused by handling errors if patients were to have medication switched without adequate training. The investigators observed that patients with asthma or COPD who made one or more critical device handling errors had more hospitalizations, emergency department visits, antimicrobial courses, and corticosteroid courses compared with patients who made no device errors. These differences in resource use resulted in an annual cost increase resulting from patient device handling errors of €23,444 for 100 patients with COPD and €44,104 for 100 patients with asthma. The biggest contributor to cost was hospitalization, which accounted for more than 75% of the total cost difference between patients who made critical device handling errors and those who did not.

**STRENGTHS AND LIMITATIONS**

This targeted literature review was limited by less rigorous methods and controls compared with a systematic review. However, this flexible approach was also a strength, because there are no specific National Library of Medicine Medical Subject Headings for the impact of the use of the same device, and authors may describe their work differently; therefore, these studies may be challenging to index and identify using restricted search terms. Also, this approach permitted the inclusion of key guidelines and opinion pieces from experts. Our search strategy used multiple free-text terms to capture the concept, which we believe were appropriate to identify this research, although this strategy may have excluded some publications not using these terms. A variety of study designs were included in this review, which was both a strength and a limitation, because this allowed all types of studies to be included, but direct comparisons could not be made. Few studies had evaluated the effects of using the same device or device experience on clinical efficacy, correct use, patient preference, and ease of use; therefore, most resulting conclusions were indirect. We did not assess the quality of the included articles.

| Topic | Conclusion | Ideas for further research |
|-------|------------|---------------------------|
| **Device continuity/familiarity** | Several observational studies support the benefit of device continuity. Evidence suggests better clinical outcomes and inhaler technique when patients use a similar device type than when patients use mixed device types | Additional research is needed to identify the economic impact of device continuity as well as the impact on adherence, device misuse, and preference. Research could take the form of database analyses or prospective observational studies |
| **Individual patient needs for a device** | Appropriate device selection requires matching the needs of patients with the attributes offered by the specific delivery device. Inappropriate device selection may lead to clinical or economic consequences; however, studies evaluating these implications are limited | Working group with subject area experts, clinicians, payers, and patient representatives to generate a consolidated and validated list of patient archetypes matched to the different devices |
| **Training requirements** | Physicians need to consider a patient's suitability for a device and training needs when prescribing an inhaled medication, and when suboptimal treatment outcomes are reported (before changing the type or dose of medication). Systems are required to promote correct inhaler use and monitor adherence | An observational study could be conducted in patients with asthma or COPD to evaluate the frequency of changing device type/medication, and the factors that lead to these changes, including assessing the impact of patient training. Initiatives are required to make teaching of inhaler techniques to trainee healthcare providers mandatory |
| **Payer concepts** | Understanding whether, and to what degree, evidence that supports the clinical and/or economic impact of device continuity is important to payers for reimbursement decisions is poor | Survey payers on concepts supported by existing data (or future work) to understand the issues identified in this gap analysis that need further investigation |

**FIGURE 2.** Ideas for future research. COPD, chronic obstructive pulmonary disease.
The time frame for the search was limited to 10 years for publications and 3 years for conference abstracts, to allow for retrieval of a manageable number of citations; however, a strength of this approach was that it allowed for the selection of the most recent and relevant information on the topics. Although previous relevant publications were excluded, relevant data may have been captured in the review articles included in the targeted literature review.

DISCUSSION AND CONCLUSIONS

The findings of our review suggest that using the same inhaler device for multiple-inhaler regimens, and simplifying inhaler regimens by promoting the use of the same device, can lead to improved clinical outcomes and reduced health care use in patients with asthma or COPD. The review also highlighted the high frequency of inhaler handling errors and poor inhaler technique in patients treated for asthma or COPD, and the adverse impact on adherence, disease control, and associated health care costs. In addition, the absence of health care support with device training was linked to reduced disease control. If a patient’s condition deteriorates owing to suboptimal treatment, this may not be solely the result of the medication the patient is receiving; it may also be due to suboptimal use of the inhalation device. Hence, we suggest that physicians consider a patient’s suitability for a device and the training needs initially (before changing the type or dose of medication). This is in line with the recommendations of the Global Initiative for Asthma and Global Initiative for Chronic Obstructive Lung Disease reports. Furthermore, proactive consideration of a patient’s inhaler regimen when physicians prescribe inhalated medications could potentially prevent the occurrence of suboptimal treatment outcomes.

Inhaled devices have attracted criticism because of their impact on the environment. As such, the UK House of Commons Environmental Audit Committee has recommended that by 2022 at least 50% of UK National Health Service-prescribed inhalers should be of low global warming potential. However, the evidence discussed in this review highlighting the importance of the choice of device on patient outcomes supports expert opinion that switching a device solely on the basis of environmental impact could be detrimental to patients. Alternatively, consideration of inhaler choice and training as well as education for physicians and patients regarding proper inhaler use would prevent the wasteful use of inhalers while improving disease control.

Despite evidence that training improves inhaler technique at least in the short term, a survey reported that more than half of patients with COPD could not recall receiving training on how to use the device after a COPD diagnosis; this highlights the need for improvements in patient education by health care providers. Patient device education may be delivered by multiple providers. Therefore, it needs to be consistent across health care professionals. Training of health care professionals needs to be improved, because most health care professionals have shown inadequate knowledge of correct inhaler technique. Patient training should reinforce critical educational messages and identify communications that have the highest impact on patient outcomes. Also, it should be ascertained how this education can be integrated into routine clinical practice. Patients using multiple inhalers will require additional training time from health care providers. Physicians should also be aware that patient expectations may influence willingness to comply with the prescribed therapy. Therapy adherence is lower for medications that do not have an immediate effect on symptoms; therefore, setting appropriate expectations for medication effects could improve adherence. Different devices should be accessible within each drug class, allowing physicians and patients to select the most appropriate device. Many fixed-dose combination therapies that deliver multiple medications in the same inhaler are available for treating patients with asthma or COPD.

Employing a single inhaler device improves clinical outcomes and reduces health care use compared with multiple-inhaler regimens for patients with asthma or COPD. Further research in the form of database analyses or prospective observational studies to determine the effects of consistent use of the same type of device on treatment adherence and persistence could strengthen existing evidence for simplifying inhaler regimens for patients with asthma or COPD.

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TABLE E1. Search strategy

| Number | Description |
|--------|-------------|
| 1.     | exp "pulmonary disease, chronic obstructive" |
| 2.     | (copp or (chronic obstructive adj (lung or pulmonary))).ti. |
| 3.     | (device$ or inhaler$ or mdi or dpi or pmdi).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |
| 4.     | exp "nebulizers and vaporizers" |
| 5.     | ((device$ or inhaler$) adj3 (familiar$ or ((previous or prior) adj3 ("use" or user or users))) or (switch$ or conversion or convert$ or substitut$ or chang$ or continu$) or (multiple or concomitant$ or concurrent$)).mp. |
| 6.     | ((device$ or inhaler$ or (technique$ or handling)) adj3 (differ$ or same or similar or mixed or interchangeable)).mp. |
| 7.     | ((disease or copd or symptom or treatment or drug$ or medication$ or inhaler$ or device$ or clinical$) adj4 (effective$ or benefit or outcome$ or control$)).mp. |
| 8.     | (exacerbation$ or hospitalization or hospitalisation or complication$ or mortality or morbidity or efficacy or (resource adj2 (utilization or utilisation or consumption)) or ((office or care or health$) adj2 visit$) or econom$ or cost$ or pharmacoeconomic$).mp. |
| 9.     | treatment outcome/or exp pulmonary disease, chronic obstructive/co or exp health status indicators/(2140732). |
| 10.    | (SABA or short acting beta-agonists or short-acting bronchodilator or short acting muscarinic receptor antagonists or SAMA) or (ICS or OCS or inhaled corticosteroid or oral corticosteroid or systemic corticosteroid) or (antibiotics).mp (566212). |
| 11.    | cost of illness/or exp health care costs/or exp health expenditures/or exp utilization review/(490356). |
| 12.    | patient education as topic/or equipment failure/or equipment failure analysis/or medication errors/(281505). |
| 13.    | (train$ or educat$ or instruct$ or mistake$ or error$ or misuse$ or (incorrect or wrong) adj3 ("use" or usage or utilization or utilisation or (technique$ or handling))).mp. (4558652). |
| 14.    | ((device$ or inhaler$) adj4 (train$ or educat$ or instruct$ or mistake$ or error$ or misuse$ or ((incorrect or wrong) adj3 ("use" or usage or utilization or utilisation or (technique$ or handling))).mp. (10862). |
| 15.    | patient compliance/or medication adherence/(229518). |
| 16.    | (compliance or adher$ or persist$).mp. (2063377). |
| 17.    | ((satisf$ or complain$ or discontent$ or nonconsensual or unhappy or uncomfortable or discomfort or (prefer$ or willing$ or select$ or pick or choice or chose or choos$ or acceptable or unacceptable or report$ or question$ or interview$ or determin$) adj3 (patient$ or subject$ or individual$)).mp. (2050160). |
| 18.    | exp patient satisfaction/(232731). |
| 19.    | ((prefer$ or willing$ or select$ or pick or choice or chose or choos$ or acceptable or unacceptable or suitab$ or appropriate$ or inappropriate$ or ideal or report$ or question$ or interview$ or determin$) adj3 (physician$ or provider$ or health$ adj1 professional$)).mp. (107248). |
| 20.    | (suitab$ or appropriate$ or inappropriate$ or ideal or proper) adj3 (patient$ or subject$ or individual$).mp. (137400). |
| 21.    | ((Environ$ or sustain$ or green or carbon$ or recycl$) or (plastic$) or (CO2 or carbon dioxide or CO2 equivalent or CO2e)).mp. (5791534). |
| 22.    | ((SABA or short acting beta-agonists or short-acting bronchodilator or short acting muscarinic receptor antagonists or SAMA) or (ICS or OCS or inhaled corticosteroid or oral corticosteroid or systemic corticosteroid) or (antibiotics).mp (566212). |
| 23.    | (1 or 2) and (3 or 4) and (5 or 6) and (7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16) (609). |
| 24.    | (1 or 2) and (3 or 4) and (17 or 18 or 19 or 20 or 21) (2172). |
| 25.    | (22 or 23 (2554). |
| 26.    | limit 24 to (english language and yr="2017-current") (948). |
| 27.    | limit 25 to (article or article in press) (577). |
| 28.    | limit 25 to (conference abstract or conference paper) (565). |
| 29.    | 26 or 27 (859). |
| 30.    | exp *asthma/(270817). |
| 31.    | asthma.ti (194173). |
| 32.    | (exp *pulmonary disease, chronic obstructive/(117006) and (January 01, 2007 to December 12, 2020>). |
| 33.    | (January 01, 2007 to December 31, 2017> and (January 01, 2017 to December 12, 2020>). |
| 34.    | limit 34 to (english language and yr="2007 -Current") (3953). |
| 35.    | limit 35 to (article or article in press) (2388). |
| 36.    | limit 35 to (conference abstract or conference paper) and yr="2017-current") (804). |
| 37.    | 36 or 37 (2785). |
| 38.    | 26 or 27 (859). |
| 39.    | Remove duplicates from 38 (2037). |
| 40.    | 28 or 39 (2804). |
| 41.    | Remove duplicates from 40 (2616). |