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Real-World Use of Inhaled COPD Medications: the Good, the Bad, the Ugly

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Abstract

Patients with chronic obstructive pulmonary disease (COPD) rely primarily on inhaled medications to control and treat symptoms. Although the medications delivered by inhaler devices are often quite efficacious when delivered to the lung, the real-world effectiveness of these inhaler devices often falls short. Barriers to effective inhaler use include inhaler misuse and cost-related nonadherence. Inhaler misuse can be reduced with appropriate education which leads to improved outcomes. Education can be provided in multiple settings by a wide array of clinicians and clinical team members including pharmacists, respiratory therapists, nurses, physicians, advanced practice nurses, physician assistants, and community health workers, among others. However, despite decades of research and existing effective strategies across settings and types of educators, overall not much progess has been made with respect to effective inhaler technique among populations of patients with COPD in nearly half a century. Similarly, cost-related nonadherence is a long-standing and critical barrier to effective control of COPD, with limited improvements, especially until very recently. This perspective reviews the current promising directions for inhaler-based therapies, ongoing challenges, and critical issues requiring urgent attention.

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Abbreviations:

ATS=American Thoracic Society; **COPD**=chronic obstructive pulmonary disease; **FTC**=Federal Trade Commission; **GOLD**=Global initiative for Obstructive Lung Disease; **pMDIs**=pressurized metered-dose inhalers; **TTG**=teach-to-goal; **VHC**=valved holding chamber

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Introduction

Patients with chronic obstructive pulmonary disease (COPD) rely primarily on inhaled medications to control and treat symptoms.[1-3] While some patients use nebulizer devices to deliver these inhaled therapies,[2] the vast majority of patients with COPD use at least one inhaler device.[2-4] Although medications delivered by inhaler devices are often quite efficacious when delivered to the lung (i.e., the site of action),[5,6] the real-world effectiveness of these inhaler devices often falls short.[7-10] This lack of effectiveness is due to often unrecognized intricacies in the technique required to use the devices.[1,6,11-15] Some intricacies include the number and types of device steps, which often differ across inhaler device types.[6,11] Misuse can also occur when confusing rescue versus controller devices,[1,13,16] due to lack of medication knowledge and/or confusion between similar devices (e.g., some rescue and controller pressurized metered-dose inhalers [pMDIs] are the same color despite worldwide efforts to avoid this).[17,18] Misuse can lead to delivering the medication to the gut, and not to the lungs, particularly with pMDIs.[19,20] Regardless of the reason for misuse, this ongoing rampant inhaler misuse leads to *unintentional nonadherence* that only exacerbates the multitude of medication adherence

challenges that patients face.[3,4,15,21,22]

Consequences of inhaler misuse include lack of symptom control, preventable COPD exacerbations, and acute care utilization including emergency department visits and hospitalization.[7-12,21,23-27] There is also a high cost to inhaler misuse of $5–7 billion.[28] Decades of research on the need for and types of inhaler education exist,[8,9,26,29-31] demonstrating that these errors can be reduced with appropriate education.[7,9,23,29,31] Education can be provided in multiple settings by a wide array of clinicians and clinical team members including pharmacists, respiratory therapists, nurses, physicians, advanced practice nurses, physician assistants, and community health workers, among others.[8,23,26,29,31-34] Further, inhaler education leads to improved outcomes.[7,23,29] Despite these decades-long efforts, a systematic review published now almost 10 years ago, found there had not been significant improvements in proportions of individuals with effective inhaler technique in 40 years.[30] Therefore, currently we are facing over half a century of undertreatment of COPD due to lack of implementation of effective educational strategies to mitigate poor inhaler technique.

Inhaler misuse itself has been in existence since inhalers were first described centuries ago. Some of the earliest depictions of inhalers include an illustration by Christopher Bennet in 1654 and a description of an inhaler by John Mudge in 1778,[35] though inhalation therapy traces back over 4000 years ago to India.[36] However, the first modern inhaler is the pMDI introduced in 1956.[37] Since the invention of the pMDI, dozens of different inhaler device types have been developed. Some changes to inhalers have been based on policies, such as the change from the chlorofluorocarbon-based propellent to the hydrofluoroalkane-based propellent in response to reducing environmental harm to the ozone layer.[38,39] While more environmentally friendly, this change led to large increases in out-of-pocket costs and decreases in utilization.[40] Ideally, new device development would be focused on improving ease of use for patients[6,16,41-43]; but instead, adding a new inhaler or inhaler device type to a patient's regimen often led to more inhaler technique errors.[44] However, often the changes have been motivated by financial gain as a method of increasing years under a patent.[45-47] Regardless of the multitude of changes, some have led to improvements in use and adherence,[21,48] though overall the increasing number and type of devices adds complexity to the regimens,[13] complicated by access issues related to insurance formularies,[24,49,50] and certainly decreasing overall access and adherence to effective treatments.[11,14] Adherence is also critical, as poor adherence is associated with worse health outcomes.[51] To understand the landscape of issues facing patients and clinicians with regard to inhaler-based therapies, this perspective provides a review of recent advances, ongoing challenges, and critical issues regarding the real-world effectiveness of respiratory inhalers.

The "Good": Recent Advances

While decades of research and efforts to improve inhaler technique and outcomes have largely failed to move the needle, there are several recent findings and advances to support and improve the real-world effectiveness of inhaler-based therapies. First, there is increasing specificity for choice of inhalation therapy device and on an educational approach in the Global initiative for Obstructive Lung Disease (GOLD) 2023 Report.[1] With respect to choice of inhalation device (i.e., nebulizer versus inhaler; type of inhaler) the guidelines now list several aspects by which to base inhaler type choice, such as potential limitations including cognition and dexterity, along with several other patient-level and device-level considerations.[1,6,52] The GOLD 2023 Report also specified a recommended method for inhaler education, namely "'teach-back," noting it is a "particularly effective" strategy.[1,52] Data exist that supports the use of teach-back–based educational strategies, including the "teach-to-goal" (TTG) strategy that incorporates rounds of education and teach-back–based assessment.[53] The broad teach-back approach was found to be effective in a systematic review referenced by the GOLD 2023 Report.[1,30] The TTG approach has been found to improve inhaler technique skills for children and adults, using both in-person and virtual approaches, in both inpatient and ambulatory settings.[9,29,31-34,54-55] Importantly, TTG has also been found to be effective at reducing 30-day acute care utilization after hospitalization for COPD compared to brief verbal instructions.[23,56,57]

A second advancement is the limiting of the number of required inhaler devices through combination therapies.[11,13,22,58,59] A single device with multiple medications has several potential advantages while the use of multiple inhalers and types of inhaler devices leads to worse technique, adherence, outcomes (e.g., exacerbations, acute care utilization), and costs.[11,13,14,28] Therefore, it is not surprising that ongoing, emerging evidence supports improvements in outcomes when combining inhaled therapies into a single device. For instance, with regard to single device versus multiple devices for triple therapy, data show improved outcomes including adherence,[60-62] lower acute care utilization,[15] and lower costs.[15,62]

Finally, a third and most recent advancement is directed at improving cost-related access and hence, adherence to medications with the introduction of price caps on several inhaler devices. These price caps

are likely in response to the Federal Trade Commission (FTC) exposing improperly listed patents.[63] High costs of inhaler-based therapies lead to worse adherence and health outcomes.[17,25,28,50] In an American Thoracic Society (ATS) Policy Statement, a recommendation was made unanimously for the establishment of a publicly funded, politically independent, impartial entity that could review the evidence to make policy recommendations that are evidenced-based to address the high costs of respiratory therapies.[17] The Senate Health, Education, Labor, and Pensions Committee launched an investigation into the high price of inhalers in January 2024. As of June 1, 2024, several companies are capping their inhaler-based therapies at $35/month, with more companies on the horizon.[64,65] Increasing access to inhaler-based medications has the potential to decrease cost-related nonadherence.[25]

The "Bad": Ongoing Challenges

Despite these newer advancements, there are many ongoing challenges to patients' effective use of and adherence to respiratory inhaler devices. First, with respect to clinical guidelines, additional specification of inhaler device choice and use of spacers is warranted, as is increased specification of the "when, where, how, and what" of educational strategies to improve inhaler technique and adherence. With respect to type of device, sufficient evidence exists acknowledging that some inhalers are easier or harder to use.[41,43,44,66,67] For instance, pMDIs are among the most difficult to use effectively, particularly without the use of a spacer or valved holding chamber (VHC).[16,68,69] Currently, the GOLD guidelines only recommend spacers for patients "if there is any doubt the patient will not be able to use a pMDI correctly."[1] However, given that the vast majority of patients misuse pMDIs, this recommendation will likely apply to most individuals. Further, there are data that show without spacers/VHCs, medication will primarily go to the gut as opposed to the lungs,[19,20] suggesting that all patients should use a spacer/VHC for correct technique.[69,70] Therefore, a stronger recommendation for the use of spacers/VHCs in clinical guidelines would be more responsive to these existing data. Further, given that well-documented patient preferences exist for different types of devices,[41-43] guidelines could encourage shared decision-making with patients when choosing delivery devices for medication regimens.[42,43,71] Patient preference may be particularly important for disease control given that device type can inform medication adherence.[3,21,48] With respect to education, more specification beyond the recommendation of teach-back is needed.[16] As noted above, the TTG approach that incorporates both assessment and education (both recommended by the guidelines) shows not only effectiveness at improving inhaler technique but also improved health outcomes when compared to simple verbal instruction. However, time, cost, and trained personnel restrictions often lead to under-resourced approaches to inhaler education, including the TTG approach.[16,28,72-77] For instance, in one study of pediatric patients in an ambulatory setting, the clinicians were rarely observed demonstrating technique.[74] Further, clinicians often lack the skills and knowledge regarding inhaler technique education.[3,28,78-82] So while guidelines recommend assessment and education at all health care encounters and now even support a specific approach, i.e., teach-back, guidelines do not support how this education will be taught, resourced, and/or monitored.[8,26,28] Therefore, education is often simply not provided effectively or at all.

Second, with respect to number of and types of devices, there are numerous issues affecting technique and adherence.[83] Insurance formulary changes are common, leading to device switching.[49,50] This leads to vulnerabilities in patients receiving the education required to learn the new device. While formulary switches occur regularly in the outpatient setting, another common vulnerable time for patients with respect to types of inhalers is during hospital admission. While the hospital setting could be an ideal opportunity to assess inhaler technique and provide guideline-recommended education,[3,84] patients often are placed on nebulizer treatments.[85] Further, when they are switched to inhalers during their inpatient stay, they are often placed on different inhaler device(s) due to specific inpatient formularies, for which they rarely receive necessary education. Then upon discharge home, they are at risk for ongoing confusion on the numbers and types of inhalers to use at home. Finally, even if sufficient medication reconciliation occurs, patients on more than one inhaler have additional risk factors, as noted above.

A third ongoing challenge is related to multiple types of devices that exist and that are often prescribed to patients.[6,86] As noted above, not all inhalers are equally easy or difficult to use.[41,43,44,66,67] Devices have different numbers and types of steps, often requiring different skill sets and physical demands.[6,11] pMDIs have an advantage in that they do not require inspiratory effort, though they do require sufficient dexterity, and as noted above are among the most difficult for patients to use correctly. With respect to dexterity, grip strength has been associated with increased risk of rehospitalization after admission for acute exacerbations of COPD.[87] Further, as noted above, pMDIs are not optimally effective without the use of spacers/VCHs, which are infrequently co-prescribed. Dry powder inhalers, on the other hand, have less dexterity demands though they do require sufficient inspiratory effort.[88] Further, adherence to inhaler-based regimens also relies on dosing schedule.[83] Once-a-day regimens are easier to adhere to compared to twice-daily routines.[6,83] Use of similar device types can mitigate risk of increased errors with multiple

device types.[6,62] Due to these device-related intricacies, patients' preferences, physical capabilities (e.g., dexterity, grip strength, inspiratory force), and cognition need to be taken into account when prescribing inhaled therapies including via respiratory inhalers and/or nebulizer-based treatments.[1,42,52,60,86,87] Many of these factors are explicitly stated in the GOLD guidelines.[1] However, without further oversight, companies are likely to continue to add to the array of device types, thereby adding complexity to real-world effectiveness of treatments delivered via respiratory inhalers.[86]

The "Ugly": Critical Issues Requiring Urgent Attention

While most of the challenges identified above have existed for decades and are only slowly being addressed through research, guidelines, and policy, there are still critical issues that require urgent attention. A key critical issue is the ongoing rampant inhaler misuse affecting the majority of patients prescribed respiratory inhalers that leads to patients failing to receive optimal treatment(s) and being at risk for adverse health outcomes. Therefore, increasing recognition of the urgency to address this misuse by funders, policy-makers, and guidelines to increase support and resources to ensure implementation of evidence-based and guideline-supported inhaler education is critically needed. Unfortunately, most of the time inhaler education is not provided, and if provided utilizes less-effective strategies without incorporating assessment through teach-back.

Since educational approaches with teach-back overall, and TTG specifically have demonstrated superior effectiveness compared to non-teach-back strategies,[1,23,57] more evaluation of feasible and sustainable approaches to providing teach-back–based inhaler education is warranted. For instance, given that TTG has demonstrated reduced 30-day acute care utilization among patients hospitalized for COPD, i.e., high-risk patients,[23,57] obtaining additional data on the impact of teach-back–based approaches compared to non-teach-back–based approaches is critical for health systems to identify and obtain resources to provide this important intervention to improve patient self-management and health outcomes.

Further, while some might argue that patients could easily locate training videos, many patients do not recognize that they are misusing their inhalers.[89-91] Further, technology-related access, such as through digital redlining,[92,93] and use issues through low health literacy[94,95] and/or low eHealth literacy,[96-98] limits the ability of patients to equitably access these inhaler education videos.[93] In addition, some might argue that patients receive inhaler education during pulmonary rehabilitation.[99] While this is true and an effective approach for patients receiving pulmonary rehabilitation,[100,101] there are significant access issues for pulmonary rehabilitation.[102-104] Therefore, it is incumbent upon the health care system to take ownership of the need to provide assessment and education of inhaler technique to patients across health care settings.

Another urgent issue requiring rapid attention is addressing the ongoing high costs of inhaler-based therapies which continue to drive cost-related medication nonadherence. It is critical that this issue remains in the spotlight. While the FTC's recent focus on pharmaceutical companies' improper listing of patents has led to self-driven pricing changes by some companies, the ongoing lack of available generic and/or low-cost inhalers will continue to adversely affect patients with COPD.[17,25,50] The inhaler caps noted above are not currently in effect for patients with Medicaid or Medicare.[64,65,105] Further, only a handful of inhalers are capped at $35. Increased regulation by the government, such as through similar drug-pricing–related efforts for Medicare drug pricing,[106] are required. The ATS Policy Statement's recommendation for the establishment of a publicly funded, politically independent, impartial entity could also help address the urgent need to improve cost accessibility to respiratory inhalers.[17]

Summary

Patients with COPD and other types of obstructive lung disease rely on respiratory inhalers to control and relieve symptoms related to their disease. Currently, the vast majority of patients misuse their respiratory inhalers.[7,8,12,26,27,30] There are myriad of device types contributing to the complexity of addressing this misuse.[6,11,13,60,62] Guidelines recommend assessing and teaching patients at all health care encounters, and recently updated their recommendations to specify teach-back as a particularly effective strategy.[1] Data exist that educational strategies employing teach-back, such as TTG, demonstrate reduced 1-month acute care utilization after hospitalization compared to approaches without teach-back such as brief verbal instructions.[1,23,57] However, there is a lack of resources and support to train and pay for educators and education programs.[3,28] In addition to unintentional nonadherence that occurs through misuse of respiratory inhalers, many patients cannot afford these medications leading to cost-related nonadherence.[3,25,50] While some progress is being made with respect to guidance on inhaler education through the 2023 GOLD guideline's teach-back recommendation, combination inhalers to reduce misuse and adherence risk, and inhaler caps for some devices, there are numerous ongoing challenges, with an urgent need to address rampant inhaler misuse and cost-related nonadherence.

Declaration of Interest

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