Inhalers: to switch or not to switch? That is the question

Anna Claire Murphy

We know that there is an increasing prevalence of asthma and COPD worldwide, leading to increased inhaler use. Chapter 3 of the British National Formulary[1] has grown significantly over the years in terms of the number of inhaler options. There are currently, in the UK, more than 20 different inhaler devices available, with over 118 possible combinations of drug and device to prescribe. The inhaler market has become very crowded, with patents expiring for some of the most widely used inhaled drugs. Several analogues of branded inhaled corticosteroids/long-acting β2-adrenoceptor agonists (ICS/LABA) fixed-dose combinations have entered the market with different inhaler devices, and longer-acting 'me-too' formulations have appeared. Incorrect or suboptimal patient technique in using inhalers has led to yet further inhaler devices being developed, and combination/triple inhalers have been launched to support patients.

Current clinical evidence suggests that, although existing inhaled therapy has the potential to control disease in most patients with asthma, control is often not achieved in practice.[2] Suboptimal inhaler technique is the prominent reason for the lack of efficacy; no matter how good a drug or device is, it cannot be effective if the drug does not reach the targeted airways. Inhaler errors are associated with worsening in disease control, increased rate of exacerbations, increased healthcare resource consumption, and consequently increased healthcare expenditure.[3–5] A recent systematic literature review and meta-analysis found that incorrect inhaler technique is common across devices, with up to 100% of patients demonstrating at least one error. Moreover, up to 92% of patients experience critical errors, that is, one that may impact the effectiveness of the delivered drug.[6] While Chrystyn *et al*'s[3] team found high critical error rates reported across all devices, their meta-analysis and systematic review highlighted significant gaps in knowledge regarding different inhalers and associated error rates, and how these affect clinical outcomes. The researchers call for indepth studies into device use, alongside standardised checklists and definitions for such studies to use to ensure consistency.

Patients making errors with their inhalers were recognised soon after the launch of the pressurised metered-dose inhalers (MDIs). The findings of a large, systematic review demonstrated a high frequency of poor and/or suboptimal inhaler use for all types of devices, and there was no indication that the problem of incorrect or suboptimal use had diminished over a 40-year period, despite considerable effort and investment in education, training and device development over this time.[7] Most healthcare professionals would agree that the strategies to improve patients' inhaler technique include careful instruction, observation of the patient's inhalation technique, followed by individualised pairing up of a patient with an inhaler device based on the patient's needs and abilities. Training can then be supported by a variety of means: device demonstration, repeated tuition, video instructions as well as written materials. Unfortunately, the plethora of evidence showing the extent of suboptimal inhaler technique in the UK suggests that either these measures are insufficient or training recommendations generally are not implemented. Patients may have used their inhaler for long periods since they last received instruction, they may have received little or no instruction, or they may have been instructed in busy clinics and/or by untrained healthcare professionals.[8]

The National Health Service (NHS) spends over £1 billion on inhalers each year.[9] Inhalers are among the highest drug expenditure items in the UK. As in the management of other diseases, the cost of prescription treatments for respiratory diseases is an easily identified direct cost, and given current pressures on NHS healthcare budgets it is understandable that extending the use of generics and branded generics is considered an important element in most prescribing strategies to achieve substantial savings. Are these savings theoretical? Do we know the effects on patients by undertaking this approach to switching inhalers? In theory, the transition from branded to generic drugs should have no deleterious effects on patient care; the products should be equally effective. However, if not implemented carefully, there is considerable potential for patient harm from confusion, anxiety and mishandling of a different inhaler device. Some patients may be uncomfortable with accepting a substitute for a medication that their doctor has prescribed and they have become familiar with using, particularly if the reasons for the switch are not discussed. In the UK, regulations allow patients to be switched from one inhaler device to a cheaper bioequivalent product, generic or branded, at the discretion of the dispensing pharmacist, as long as the prescription is written generically (international nonproprietary name (INN)). This can lead to potential patient confusion if the patient is not part of this decision. UK prescriptions have to be specific to the brand name to prevent switching but despite national guidance are often still written generically. Brand name prescribing is the way to guarantee the continuity of a certain device.

As discussed, it is clear that a patient-centred approach to inhaler prescribing is recommended. It is therefore important to consider what the possible outcomes of switching inhaler devices from one to another is for our patients in practice. A recent study by Roggeri and colleagues[10] highlights that the misuse of inhaler devices following switching is associated with not only a decrease in disease control but also an increase in healthcare resource consumption and costs. A further study highlighted the possible issues related to non-consented inhaler switches without adequate training in patients with COPD.[10] So while it may appear to be a benign decision, changing or switching inhaler device may have a large effect on disease control. It is therefore crucial to consider all relevant costs—not just the cost of the inhaler itself, but including those related to training sessions, additional consultations, repeated prescriptions and management of acute events; these costs may contribute to reducing the potential benefit coming from switching inhalers. Addressing the need for correct structured diagnosis, addressing smoking, medicine adherence and patient self-management, including pulmonary rehabilitation, are paramount and a cost-effective approach to respiratory care.[11] It therefore seems inevitable that many healthcare professionals are concerned about switching between inhaler types without patients' consent, knowledge or training because it may negatively affect subsequent patient care and do not support this practice.

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Other studies have however shown only marginal concerns with switching inhaler devices. A recent study aimed to assess the persistence and effectiveness of switching from a dry powder inhaler (DPI) to a pressurised metered dose inhaler (pMDI) for ICS/LABA.[12] The authors concluded that switching to and persisting with pMDI were associated with decreased asthma exacerbations and improved asthma control. The majority of patients persisted with the switch to pMDI for ICS/LABA treatment. In this study, inhaler device switch occurred during consultations, highlighting the importance of proper physician–patient communication during the switch of inhaler devices, which could be the confounding factor in the results. Conversely studies have investigated the results of switching from any other inhaler, including pMDIs, to a DPI device. One such study by Price *et al*[13] focused on patients with stable asthma and investigated the switch to the Easyhaler device in a real-life setting. Their hypothesis—that such a switch would result in a significant reduction in clinical effectiveness and thus a significant increase in the costs of asthma therapy—was disproven. Interestingly, approximately one in three of the Easyhaler device patients in this study were switched without a face-to-face consultation, and possibly even without the patient's knowledge and consent in some cases. Thus, patient training with the new device was not always ideal but still demonstrated positive outcomes.

In a recent issue of *Thorax*, Bloom *et al*[14] aimed to describe the prevalence and health impact of financially motivated inhaler switching, for non-clinical motivation, in the UK and the subsequent health impact. This real-life independently financed study demonstrated a significant reduction in exacerbations after switching from a brand to generic inhalers, with no significant association between the rate of consultations and switching. Remarkably, inhaler adherence, measured by prescription refill data, significantly improved after the inhaler switch. However, these results need to be interpreted with care as the follow-up period following the inhaler switch, known as the risk period, was only 3 months. It could be argued that 3 months is an insufficient time to determine whether the outcomes associated with the inhaler changes persisted. Furthermore, in the 3-month risk period, the only control outcome documented was an exacerbation event requiring oral corticosteroids. Inherent to retrospective studies, this study is unable to account for confounding factors not recorded in the database. It is not known if the patient's asthma control changed during this period but not sufficiently to require rescue treatment. Also how much input the patient received in terms of inhaler education or instruction by the general practitioner, nurse or pharmacist at the time of the switch is unknown. Would the outcomes be the same in both scenarios? It could be argued that because of the poor quality of inhaler technique teaching in the UK the absence of a face-to-face review with a change of inhaler was not important and that the improvements observed were incurred as a result of an intervention, which in this case was simply changing the device.

It is interesting that this study showed that adherence to the switched inhaler was significantly higher than adherence to the preswitch equivalent inhaler. Adherence was calculated using the medication possession ratio (MPR), the sum of the day's medication prescribed in primary care, divided by the total number of days between the first and the last prescription, plus the duration of the last prescription. MPR is a practical tool but is only one marker to assess medicine adherence, and care should be taken in interpreting adherence behaviour. Most probably, undersupply signifies gaps in patients' medicine supply, that is, periods when the patients do not have medicine available and therefore have no possibility to be adherent. For patients with oversupplies, it is possible that they use too much of the prescribed medicines and in a sense they are non-adherent. However, patients may also be stockpiling medicines, particularly if they are exempt from payment. Furthermore, complete analysis of a patient's utilisation of repeat prescriptions would necessitate comparison of prescriber records with the actual dispensations to the patients. Studies indicate that 10%–20% of repeat prescriptions never reach a pharmacy.[15] In the total cohort of 665 105 regular inhaler users in the Bloom *et al*[14] study, there was an alternative cheaper equivalent generic inhaler available for 28% of prescriptions (LABA-ICS or long-acting muscarinic antagonist (LAMA)) in 2016; switching to these could have saved approximately £1.97 million, assuming all patients were suitable for switching to the alternative. This could be a substantial worthwhile saving for the NHS.

The impact on switching inhaler devices is important not just in terms of saving costs but now being highlighted as a way to reduce the impact on climate change. A less commonly advocated, but arguably as important, reason to switch an inhaler is to reduce the large environmental impact that MDI inhalers produce. Hydrofluorocarbon inhalers are estimated to contribute 4% of the NHS's entire carbon footprint, with MDIs identified as a 'carbon hotspot' in the NHS.[16] Switching from a pMDI to a DPI, which uses significantly less greenhouse gases than traditional pMDIs, is thought to decrease the carbon footprint by a factor of 18. Observational data suggest only around a third of inhalers prescribed for patients with asthma, and half of those prescribed for patients with COPD, are DPIs. The NHS long-term plan aims to deliver the Climate Change Act target of a reduction in the health service's carbon footprint of 34% by 2020 and 51% by 2025, and states that a shift to lower carbon inhalers will deliver a reduction of 4%.[17] Alongside the switch to DPIs, better education of healthcare professionals and patients in inhaler use would ultimately lead to more effective and less wasteful use of inhalers overall. It is possible that newer DPI branded generic inhalers may offer cost savings while reducing carbon footprint, contingent on patients receiving a change to their prescription.

Surely, the direction of care should not be the switching of patients to cheaper climate-saving inhaled medication but rather switching to inhalers which can provide improved cost-effectiveness while individualising the choice to the needs of the patient. Regular review of inhaled treatment adjusting to the patient's disease control and optimisation of adherence and inhaler technique are essential to ensure waste is reduced. Consideration to the class of all the patient's prescribed inhaler devices is important. The study by Bosnic-Anticevich and colleagues[18] demonstrated that patients with COPD who were prescribed one or more additional inhaler devices requiring similar inhalation techniques to their previous device(s) showed better outcomes than those who were prescribed devices requiring different techniques. Patients in the similar-devices cohort had a lower rate of exacerbations compared with those in the mixed-devices cohort and were less likely to be in a higher-dose short-acting β2-adrenoceptor agonists group. Ensuring more careful consideration to the choice of prescribed inhaler devices not only improves respiratory disease control but also reduces the impact of the number of inhalers prescribed on the environment.

To switch or not to switch? That is the question.

The insights afforded by the study by Bloom *et al* offer reassurance that switching inhalers may not be detrimental

to our patients and in fact could have a positive effect on medicine adherence and disease control. However, a further replicated study is required to validate these findings. The importance of direct healthcare professional contact with the patient when switching inhalers cannot be overemphasised. The role of healthcare professionals in ensuring correct inhaler use has been described as critical, both in achieving correct inhaler technique initially and in maintaining correct inhaler use over time. Should substitution of a generic for a branded inhaler be permitted, safeguards are required to ensure that patients receive adequate training and are willing to use the new device. Monitoring is also required to ensure that disease control is not compromised.

Further research is required not only to address the issues of clinical effectiveness of switching inhalers but also to identify new and/or better approaches to optimising inhaled delivery of drugs.

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