DEVICE MATTERS: LOOKING BEYOND THE DRUG

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MEETING SUMMARY

Prof Helen Reddel opened the symposium by discussing the need to examine the modifiable non-pharmacological factors in the treatment of asthma and chronic obstructive pulmonary disease (COPD) that can be addressed to improve clinical outcomes. Dr Kai-Michael Beeh set the scene and discussed the need to review patient behaviour and drug delivery mechanisms to improve outcomes for patients with asthma and COPD. Dr John Haughney then discussed how patient preferences for inhalers can impact real-world outcomes. Prof Sinthia Bosnic-Anticevich outlined the challenges in learning and maintaining correct inhaler technique, while Prof Henry Chrystyn highlighted how inhaler design can help minimise the impact of inhaler errors on clinical outcomes. Prof Helen Reddel closed the session by bridging the gap between guidelines and clinical care, describing ways to incorporate regular checking and training of inhaler skills into a range of settings.

The meeting objectives were to look beyond drugs to the role of devices in optimising asthma and COPD management, to understand the impact of inhaler technique on treatment efficacy, to review how patient perspectives about their inhaler can impact on clinical outcomes, and to discuss how to implement current clinical guidelines on inhaler technique in day-to-day clinical care.

Introduction

Professor Helen Reddel

Much of the discussion surrounding improving treatment outcomes for patients with asthma and COPD focusses on developing new pharmacotherapies. However, there are a number of modifiable non-pharmacological factors that can also be targeted. Patient lifestyle changes such as quitting smoking may offer significant gains, but from a therapeutic perspective there is also the opportunity to improve not just the efficacy, but the delivery of pharmacotherapy for asthma and COPD using new devices and improved inhaler technique.

Looking Beyond the Drug in Asthma and Chronic Obstructive Pulmonary Disease

Doctor Kai-Michael Beeh

Global healthcare spending has increased steadily over the past decade.[1] However, while increasing investment in healthcare initially corresponded to fewer hospitalisations for patients with asthma, increasing expenditure has not translated into further benefits in recent years.[2] Therefore, the focus for improving outcomes for patients with asthma or COPD has turned to allocating healthcare resources to strategies beyond drug therapy, such as increasing therapeutic adherence and personalising patient care.

Outcomes for patients with asthma may also be stagnating because physicians are misdiagnosing asthma severity. A 2014 National Review of Asthma Deaths report following an audit of asthma deaths in the UK found that of the 155 people who died from asthma, 58% were labelled by their physician as having mild or mild-to-moderate asthma.[3] These concerns have been validated in a Canadian study where physicians were asked to rate disease severity in patients with confirmed uncontrolled asthma.[4] Despite having confirmed uncontrolled asthma, 43% of these patients were labelled by the physician as having adequate, good, or very good asthma control, indicating that physicians are misunderstanding or underestimating the importance of the concept of asthma control.[4] However, inaccurate physician assessment of asthma control may be due to patients' inability to accurately recall their symptoms or a poor perception of some symptoms.[5]

As they are chronic conditions, therapeutic adherence is the cornerstone of both asthma and COPD management. Treatment adherence (>80% use of medication) in patients with COPD, in particular, is associated with a significantly lower risk of severe exacerbations and a reduced risk of mortality.[6] Despite this, adherence is relatively poor, with approximately 25–46% of patients remaining adherent to maintenance therapy.[7]

While it could be argued that a large proportion of these patients have mild disease and therefore do not require frequent medication, it has been demonstrated that adherence is independent of disease severity.[8] For this reason, it is now recognised that there are multiple behavioural features which underpin medication non-adherence including:[9]

- At-risk behaviours
- Patients not applying their preventive strategies, such as smoking cessation
- Use of non-observed medications
- Missed appointments
- Erratic/intermittent adherence
- Auto-adjustment of doses

Inhaler satisfaction is also strongly associated with increased therapeutic adherence, with one study demonstrating that greater patient-rated inhaler satisfaction is associated with better physician-assessed treatment compliance.[10] Despite clinical outcomes being reliant on adherence and patient satisfaction, these features are rarely taken into consideration in health technology assessments evaluating pharmaceuticals.

The emergence of phenotype-based drugs for asthma has also made the personalisation of therapy possible. For example, the anti-interleukin-5 therapy reslizumab has shown significant benefit in reducing the annual exacerbation rate for patients with elevated blood eosinophils (≥400 cells/μL).[11]

By tailoring treatment according to this phenotype, potential non-responders can be identified and avoid unnecessary exposure to a drug that is likely to be ineffective.

In conclusion, increased healthcare expenditure does not necessarily translate to better clinical outcomes for patients with COPD or asthma, highlighting the need to prioritise resource allocation to increase the value of patient care.[1,2] Existing options for resource allocation include disease assessment and monitoring and management of the disease. Additionally, the emergence of phenotype-based drugs for asthma makes treatment personalisation a reality[11] and further resources should be allocated towards tailoring treatment towards the likelihood of a clinical response.

Do Inhalers and Their Correct Use Contribute to Good Patient Management?

Doctor John Haughney

Achieving good asthma control is complex, with many contributing factors, such as diagnosis, concomitant conditions, inhaler technique, compliance, and drug therapy selection.[5] While good asthma control is an elusive goal for many patients, it may be achieved by addressing each of the following factors.[5] Key determinants of the effectiveness of inhaled treatments include:[12]

- Efficacy through pharmacological properties
- Optimal drug delivery
- The way treatments are used (e.g. correct inhaler technique and treatment adherence)

Advances over the last 20–30 years in inhaler drug delivery technology have improved inhaler efficiency.[5,13] However, the study of inhalers in randomised controlled trials (RCTs) was slowed by the publication of findings from a systematic review in 2001, in which it was demonstrated that alternative inhaler devices were no more effective than pressurised metered dose inhalers (MDI).[14] This led to pressurised MDIs becoming the recommended first-line delivery device.

However, the question arises as to whether the findings of these RCTs can be generalised to real life. Compared with the real world, selection bias in RCTs can exclude patients with poor device technique, and clinical studies are conducted with an increased focus on educating subjects on inhaler technique and promoting treatment adherence. A further systematic review of inhaler efficiency showed that when each device is used with the correct inhalation technique, each device offers equivalent efficacy.[13] However, many patients do not know how to use their device correctly and incorrect inhaler use is associated with poor asthma control.[5,15] Therefore, poor inhaler technique and adherence are key contributors to treatment failure in real life.

A real-world study examining the relationship between inhaler satisfaction, treatment adherence, and outcomes has reported that drug delivery attributes of the inhaler and higher adherence are related to better treatment outcomes.[16] While the relationship was not statistically significant, it was noted that being able to use the device properly was related to optimal medication delivery, and therefore likely to contribute to device satisfaction and improved asthma control.[16] The FINHALER study examined patient preferences across three different devices and found that whilst an intuitive device can play a role in achieving correct device technique and improved compliance, face-to-face education is essential for achieving a high prevalence of correct inhaler technique and improving patient outcomes.[17]

Individual perceptions and preferences should be considered during inhaler treatment selection, where factors such as adherence and inhalation technique are associated with patient preference.[12] A structured approach to individual patient treatment is important, as is an understanding that good control will not be achieved by a 'magic bullet' but rather by an attempt to better manage all elements, including device selection and correct inhaler technique.

Inhaler Device Mastery: Results from Handling Studies

Professor Sinthia Bosnic-Anticevich

Considering the plethora of information available to inhaler users, the fact that inhalers are still routinely used incorrectly is a multifaceted problem. Recent data show that 73% of patients consider their inhaler technique to be good or excellent, 86% of patients consider their inhaler easy to use, and as many as 96% of patients have not had their inhaler technique checked in the last

12 months.[18,19] Therefore, while there is a need to actively train inhaler users on proper technique, it has previously been shown that written package inserts alone may be ineffective.[20,21]

Furthermore, considering that a high proportion of patients inaccurately believe that their technique is adequate,[18] there appears to be a disconnect between inhaler technique theory and practice, as mastery at the time of teaching does not translate into maintenance of correct inhaler technique over time.[20,21] In particular, many common inhaler errors that can translate into poorer clinical outcomes are related to both the incorrect operation of the device itself as well as poor inhalation technique.[5,15]

In a recent proof-of-concept study, methods of instructing subjects on optimal inhaler technique have been investigated in non-asthma sufferers who were naïve to correct inhaler technique.[22] Subjects were provided with one of two dry powder inhalers (DPIs), a Turbuhaler® (AstraZeneca) or a Spiromax® (Teva Pharma), without any formal training.[23,24] If correctly using the inhaler was not immediately intuitive, participants were given written instructions to assist them. If this was not effective subjects were instructed using a video, and if they were still unable to demonstrate correct inhaler technique individual feedback was provided on the particular errors they were making.[23,24] One month after receiving training, patients were required to demonstrate their inhaler technique and it was found that there was a significant difference between the two inhalers.[23,24] A significantly greater proportion of subjects who failed to intuitively demonstrate correct inhaler technique with both inhalers, but who had received written and video instruction, maintained correct inhaler technique.[23,24] Moreover, subjects who had received written or video instruction were also more likely to maintain correct inhaler technique when using a Spiromax compared with a Turbuhaler.[23,24] Subjects also reported a preference for Spiromax.[23,24] Interestingly, a learning effect was found in that after subjects were taught the proper technique for the first inhaler, they were faster at demonstrating correct inhaler technique with the subsequent inhaler.[23,24]

Overall, correct inhaler technique is an important skill to master but it appears to be subject to skill fade. The correct technique for using some inhalers, such as the Spiromax, does however appear to be easier to maintain than others, such as the Turbuhaler, and appropriate instructional techniques need to be investigated.[21,23,24,26] Identifying patient-related factors and predictors of poor inhaler usage when patients begin to use inhalers could help to alleviate long-term problems with inhaler technique before they manifest.

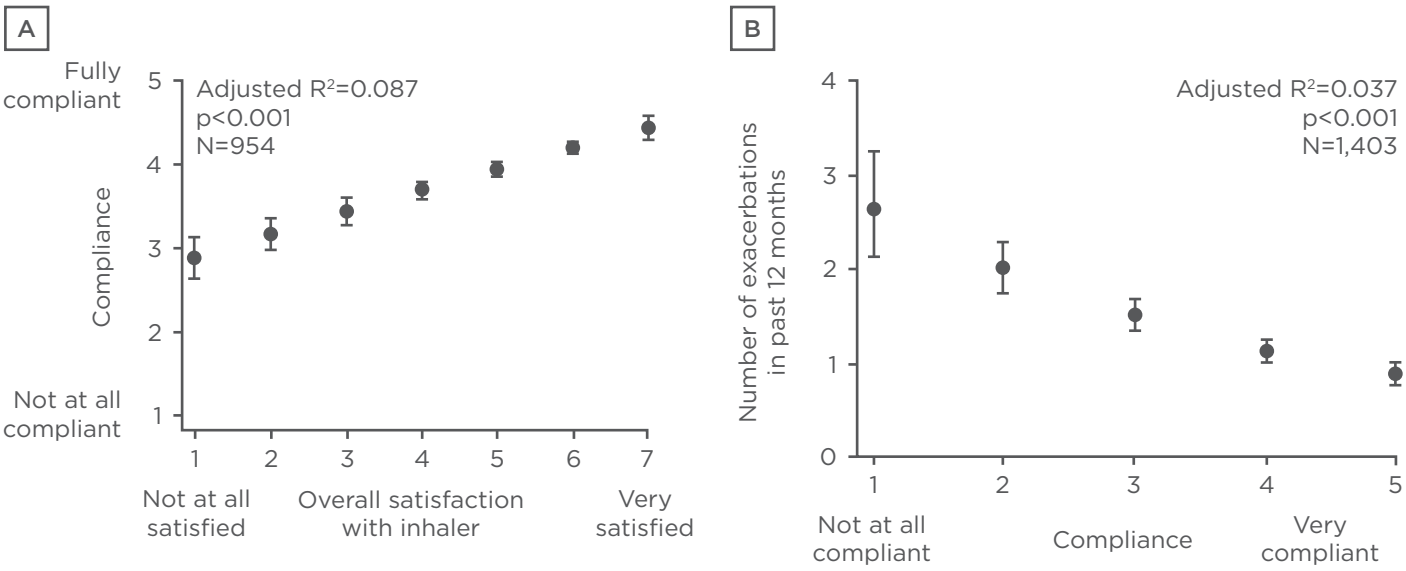

Figure 1: Relationship between A) patient compliance and overall satisfaction with inhaler, and B) patient compliance and exacerbations for patients with chronic obstructive pulmonary disease expressed as mean ±95% confidence intervals.

Coefficients of determination (R^2) are derived from a generalised additive model.

Adapted from Chrystyn 2010.[10]

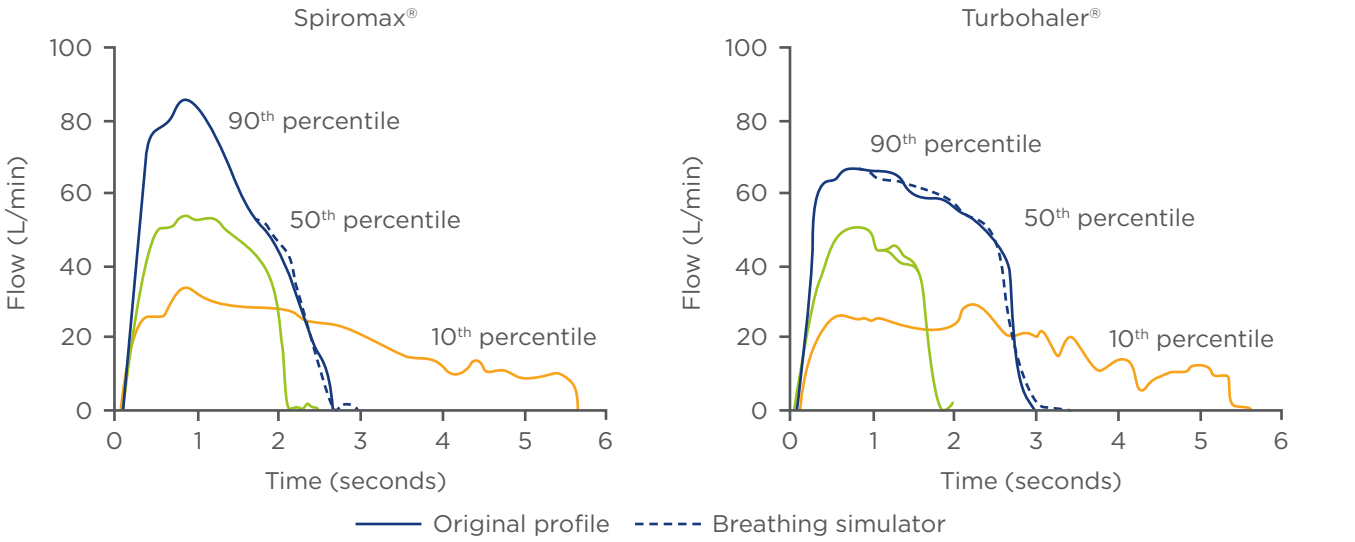

Figure 2: Selected (source) and replayed (simulated) flow profiles for patients using the Spiromax® and Turbuhaler® inhalers using weak (10th percentile), medium (50th percentile), and strong (90th percentile) inhalation profiles.
Adapted from Chrystyn 2015.[36]

The Patient's Perspective: What is Happening Outside the Clinic?

Professor Henry Chrystyn

Real-world patients rarely have perfect inhalation technique and inhaler errors contribute to the more than €400 million in annual healthcare costs in the UK alone (>€500/person with asthma or COPD annually).[26] Therefore, to achieve optimal outcomes for patients with asthma or COPD it is necessary to provide an inhaler that is simple and intuitive to use, while also being minimally affected by a patient's technique to ensure maximum efficacy.[27,28] Patients who are satisfied with the ease of use and efficacy of their inhaler are more likely to have good treatment adherence and to comply with any treatment instructions leading to a positive feedback loop as they achieve improved disease control and greater satisfaction with their inhaler (Figure 1).[10]

Inhaler errors can be classified into three categories:

- Dose emission errors
- Dose preparation errors
- Inhalation manoeuvre errors

Dose emission and preparation errors are often a function of the inhaler device itself. MDIs offer consistent dose emission, whereas the dose emission for DPIs ranges from consistent to erratic. Dose preparation errors are also device-specific, and can be a result of the operation and loading of the device, orientation when used, or whether or not the device is shaken prior to use.

Preparing the dose in the wrong orientation is one of the most common inhaler errors, but the orientation of a Spiromax inhaler does not affect dose emission.[29-31] The removal of dose orientation as an inhaler error accounts for a large proportion of the 39% lower odds of inhaler errors after 12 weeks of using a Spiromax versus a Turbuhaler inhaler (95% confidence interval: 16–56%, p=0.003), highlighting the ability of inhaler design to minimise errors.[32]

Inhalation errors are common for all inhalers and relate to the generic instruction to inhale as fast as you can and to continue for as long as possible. This instruction is necessary to ensure appropriate flow-dependent dose emission, particularly for DPIs,[33,34] but given that inhalation errors are patient as opposed to device-dependent, no significant difference in inhalation errors was observed between the Spiromax and Turbuhaler.

As peak inspiratory flow is also highly variable between patients,[35,36] device design is often the most effective method for minimising the impact of flow rate on dose emission. For example, Spiromax offers consistent fine particle dose delivery, regardless of inhalation profile (Figure 2), whereas the fine particle dose delivery with a Turbuhaler is flow-dependent.[36]

Table 1: Opportunities to demonstrate proper inhaler technique in healthcare and community settings.

Setting	Opportunity
Specialist clinics or a clinic where respiratory function laboratory testing is performed	• Patients can be asked to demonstrate their current inhaler technique when given a bronchodilator during spirometry • Patients can be educated about proper inhaler technique alongside other routine clinical education, such as self-management education
Hospital ward	• Inhaler technique can be demonstrated either while the patient is on the ward or upon hospital discharge
Emergency department	• Time may be severely limited, so proper processes need to be implemented to ensure that a consistent technique is taught to staff and subsequently passed onto patients • Inhaler technique can be demonstrated either while the patient is in the department or upon discharge
Primary care	• During scheduled review visits • After discharge from hospital • On tablets or a television, while patients are in the waiting room
Pharmacy	• When a new prescription is dispensed, because the pharmacist is the last healthcare professional to see a patient prior to using their inhaler • Patients presenting with a flare-up
In the community	• Patient organisations and clubs, or lay educators, can teach and/or correct inhaler technique

Therefore, patients with asthma or COPD should use inhalers that minimise the risk of errors through effective and intuitive inhaler design as this can improve clinical outcomes and treatment adherence, which is likely to translate to these patients and place a reduced economic burden on healthcare systems.

Inhaler Skills Training: Bridging the Gaps Between Guidelines and Clinical Care

Professor Helen Reddel

The Global Initiative for Asthma (GINA) strategy report together with multiple national guidelines emphasise the importance of correct inhaler technique and adherence for patients with asthma. While these resources recommend that inhaler skills training should be provided frequently, e.g. before initiating therapy, during self-management education, after hospital discharge, and before stepping up therapy, healthcare professionals (HCPs) have a limited timeframe within which they can check and communicate the correct technique with their patients.

Despite this, practical steps can be taken to ensure that correct inhaler technique skills are taught and maintained. At every opportunity, inhaler technique should be checked and re-checked. As a guide, HCPs should aim to follow the three 'E's:

- Equipment: HCPs should have appropriate equipment available to demonstrate correct inhaler technique. Placebo inhalers and inhaler technique checklists are suitable tools for demonstrating proper inhaler usage and instructing a patient
- Expertise: HCPs should practice the technique required for different inhalers until they are familiar; videos are available, e.g. www.nationalasthma.org.au/health-professionals/how-to-videos
- Expectation: HCPs should encourage all staff to routinely check their patients' inhaler technique, reinforce proper technique, and correct errors

An effective way to start a conversation with patients about their inhaler technique is to ask "Can you show me how you use your inhaler at present?" There are several scenarios where demonstrating proper inhaler technique can be incorporated into clinical practice (Table 1). Media platforms such as World Asthma Day are also effective in reminding both practitioners and patients to check that inhaler technique is being taught and used correctly.

Perhaps the key message is to help HCPs understand that not all inhaler devices are the same and that inhaler skills training is needed.[37,38]

Although both HCPs and patients can be taught the correct use of inhalers, errors often re-emerge over time. For HCPs, using inhaler technique checklists to check and correct their patients' inhaler technique may help to maintain their own skills.[38] For patients, the simple solution of placing a label with a checklist of steps on their inhaler with their initial inhaler technique errors was highlighted; this was recently found to improve maintenance of correct technique compared with no label when patients were assessed 3 months later (Basheti et al., unpublished data). More technological tools have been developed, including educational apps for patients, however the relative success of these interventions is still unclear.[39]

In conclusion, it is important to reinforce that teaching correct inhaler technique is the responsibility of every member of a healthcare team, and although HCP roles are demanding there is a need to be creative about how proper inhaler technique can be taught in clinical practice.

Question and Answer Session

Q: In regards to children learning inhaler technique, who do they learn it from and are they learning it correctly?

Prof Bosnic-Anticevich replied that most patients with asthma start using an inhaler as a child and it is important to look at the scenario and environment in which they are learning to use their inhalers. The aim should be for the child to be autonomous in their use of inhaler and transition to managing their medications themselves. Data show that parents have concerns about medications and may not know how to properly use the inhalers, and would like to receive more education.

Q: What can we do in current research to increase awareness of the importance of patient perspective and variability between patients?

Dr Beeh replied that the best way to persuade regulators is to generate good evidence that accounting for patient perspective and variability is linked to meaningful outcomes, and that this can be demonstrated with clinical studies on inhaler technique and adherence.

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