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### About the Expert



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### Abbreviations used in this review

- ACO = Asthma Control Questionnaire **ACT =** Asthma Control Test **CI** = confidence interval **COPD =** chronic obstructive pulmonary disease FEV, = forced vital capacity in one second **GOLD =** Global Initiative for Chronic Obstructive Lung Disease **ICS** = inhaled corticosteroids **IVR** = interactive voice recognition **LABA =** long-acting beta<sub>2</sub>-agonist **LAMA =** long-acting muscarinic antagonist **MRA =** Medication Refill Adherence **SABA =** short-acting beta<sub>2</sub>-agonist **SAMA =** short-acting muscarinic antagonist **SMART** = single maintenance and reliever therapy SMS = short message service
- WHO = World Health Organization

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# Maximising Medication Adherence in Asthma and COPD

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This publication reviews strategies for improving medication adherence in patients with asthma and COPD. It focuses on studies which have assessed clinical outcomes as well as adherence. The publication pays particular attention to studies of electronic inhaler monitoring, reflecting the amount of research in this area. This adherence strategy is now available to patients and physicians in New Zealand via the Smartinhaler<sup>™</sup> electronic monitor platform.

## Introduction

Asthma and COPD are very common respiratory illnesses in New Zealand and are major causes of disability, hospital admission and premature death. The prevalence of medicated asthma in New Zealand is 10.8% amongst adults and 16.6% amongst children.<sup>1</sup> Using GOLD diagnostic criteria, the prevalence of COPD in New Zealand has been estimated at 14.2% of the population aged at least 40 years, and it is the fifth most common cause of death amongst both men and women in New Zealand.<sup>2</sup> While effective medications are available for asthma and COPD, adherence with these medications is suboptimal. Poor adherence leads to poor symptom and disease control, lost productivity, hospitalisations and avoidable deaths. A number of strategies for improving medication adherence in asthma and COPD have been studied, with varying degrees of success. Technologies such as the Smartinhaler<sup>™</sup> electronic inhaler monitor with reminders and/or feedback, automated SMS and IVR software are being increasingly utilised in studies and clinical practice, both alone and as a complement to patient education strategies.

## Medication for asthma and COPD

Inhaled therapies are the cornerstone of pharmacological treatment for both asthma and COPD. Both the Asthma and Respiratory Foundation NZ adult asthma guidelines<sup>3</sup> and the Australian and New Zealand guidelines for the management of COPD<sup>2</sup> include stepwise management plans based on symptom severity (and lung function in the case of COPD). Asthma treatment starts with SABA reliever therapy, progresses to ICS + SABA reliever therapy, and finally to ICS/LABA + SABA reliever or ICS/LABA maintenance and reliever therapy, with guidance to refer for expert investigation and add-on treatment. COPD pharmacotherapy starts with SABA or SAMA reliever medication, progresses to LAMA and/or LABA for symptom relief, and finally to ICS/LABA therapy for prevention of exacerbations, with guidance to consider low dose theophylline in severe COPD.

## Burden of non-adherence with medication

A 2003 report from WHO asserted that "*increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments.*" The report highlighted the negative impact of non-adherence on patient health outcomes and subsequent burden on the healthcare system.<sup>4</sup>

The US National Pharmaceutical Council's Task Force for Compliance found that poor adherence to medication added US \$100 billion annually to US healthcare costs.<sup>5</sup> In New Zealand, the total cost of respiratory disease per year (including private and public costs) is NZ \$6 billion, with asthma and COPD accounting for most of the disease burden.<sup>6</sup>

A variety of studies have reported that up to 50% of patients are non-adherent with prescribed ICS.<sup>7</sup> In Australia in 2006-2013, less than 50% of patients with asthma or COPD had ICS prescription refills consistent with regular and appropriate use.<sup>8</sup>

A systematic review comprising predominantly retrospective database studies which measured prescription refill adherence in patients with COPD found increased hospitalisations, mortality, poor quality of life and loss of productivity among non-adherent patients.<sup>9</sup> Further, a systematic review assessing the association between adherence to asthma controller medication and risk of severe exacerbations found that good adherence was associated with lower severe exacerbation risk.<sup>10</sup> Suboptimal adherence with ICS has been identified as a contributing factor to 33% of asthma deaths in the UK.<sup>7</sup>



# Adherence recommendations from treatment guidelines

The Asthma and Respiratory Foundation NZ adult asthma guidelines<sup>3</sup> state that adherence to medication should be routinely assessed and encouragement provided, as part of self-management education. Patients could be encouraged to link their inhaler use with some other activity such as cleaning their teeth. The Australian Asthma Handbook<sup>11</sup> provides some recommendations for assessing and maximising adherence with medication, which are also referenced in the Australian and New Zealand guidelines for the management of COPD<sup>2</sup>:

#### Assessing

- Do not assume the patient is taking the medication dose prescribed most recently. Ask which medications the patient is using, in a nonjudgmental, emphatic manner
- If the patient is not using the prescribed preventer, use non-judgmental questions to find out why
- Before considering any increase in dose or addition to treatment regimen, check the patient's adherence to medication most recently prescribed.

#### Maximising

- Ensure every patient has a written action plan appropriate to their age and self-management capability
- Check that patients and carers understand the dose regimen and the written action plan
- If adherence to prevention medication is inadequate, explore barriers and motivating factors
- Explain to young people that medications do not have any effect on sexual activity or fertility
- Advise pregnant women to continue taking prescribed preventer therapy throughout pregnancy, as the risks of poor disease control outweigh any risks associated with medication
- For patients having difficulty with correct use of medication, consider referral to a disease educator or pharmacist.

A US study of patients with poorly controlled asthma found that adherence with preventer medication was significantly improved when patients were given the opportunity to negotiate a treatment regimen based on their goals and preferences.<sup>12</sup>

# Interventions targeting adherence with medication

The 2003 WHO report  $\!\!\!^4$  categorised the underlying reasons for medication non-adherence as follows:

- Erratic non-adherence (forgetfulness)
- Unwitting non-adherence (lack of knowledge)
- Intelligent non-adherence (intentional).

Simple interventions can address erratic non-adherence by way of electronic reminders, with or without physician feedback. Simplifying the treatment regimen can also influence adherence. More complex interventions designed to address unwitting or intelligent non-adherence include patient education and partnership building between healthcare professionals and patients.<sup>7</sup> A selection of studies, using various strategies to address adherence with medication in patients with asthma and COPD, are reviewed below.

### Asthma

In a recently published Cochrane review of interventions to improve adherence to ICS for asthma, adherence education, electronic trackers or reminders and simplified treatment regimens all improved adherence.<sup>7</sup> Looking at studies which used objective measures of adherence only, education improved adherence by 20% versus control (5 studies<sup>13,14,15,16,17</sup>), electronic trackers or reminders by 19% (6 studies<sup>16,18,19,20,21,22</sup>), and simplified treatment regimens by 4% (3 studies<sup>23,24,25</sup>).

### Adherence education

An individualised problem-solving intervention had no impact on ICS adherence assessed by electronic inhaler monitor or clinical outcomes at 6 months, when compared with standard asthma education in a population of patients from low-income, inner-city neighbourhoods in the US.<sup>13</sup>

A small US study found significantly improved ICS adherence, but not improved asthma control, at 10 weeks with automated IVR telephone calls in asthma patients.<sup>14</sup> Adherence was assessed by electronic inhaler monitoring or canister weight. The effectiveness of IVR technology for improving ICS adherence in patients with asthma has been verified in two large, longer-term trials conducted in US health maintenance organisations.<sup>26,27</sup> In both trials, calls were made when ICS prescription refills were due or overdue, and adherence was assessed via prescription refill records. Neither trial found a significant difference in clinical outcomes between intervention and control groups on primary analysis, but when patients who received 2 or more direct IVR contacts were analysed separately in one study, asthma control was significantly improved.<sup>26</sup>

Teamwork intervention, emphasising the importance of parents and youths sharing responsibility for asthma management, significantly improved electronically-monitored ICS adherence compared with both asthma education and standard care, in a small US study of children aged 9-15 years.<sup>15</sup> Functional severity scores were also significantly lower in the intervention vs control group.

In US asthma patients at high risk of poor adherence, direct clinician-topatient feedback discussions on ICS and beta₂-agonist use from electronic printouts significantly improved adherence over a 10-week period, but not clinical outcomes.<sup>17</sup> Adherence was assessed via electronic inhaler monitoring. However, an Australian study found that personalised adherence discussions had no benefit over usual care for improving adherence with ICS/LABA or clinical outcomes at 6 months in a primary care setting.<sup>16</sup> When personalised adherence discussions were added to electronic inhaler reminders (Smartinhaler<sup>™</sup>) with feedback, there was a small but non-significant improvement in adherence compared with electronic inhaler reminders with feedback alone.

### **Electronic trackers or reminders**

Audiovisual inhaler reminders can improve adherence with ICS therapy in patients with asthma, according to two New Zealand studies using Smartinhaler<sup>™</sup> technology.<sup>18,28</sup> One study assessed adherence over the final 12 weeks of a 24-week study involving patients aged 13-65 years,<sup>18</sup> while the other assessed adherence at 2-6 months in patients aged 6-15 years.<sup>28</sup> The study of adults found no difference in clinical outcomes between the intervention and control groups,<sup>18</sup> while the study of children found significantly improved asthma morbidity and childhood ACT scores with the intervention.<sup>28</sup>

A small Australian study showed that measuring adherence via electronic inhaler monitoring (Smartinhaler<sup>™</sup>) and providing feedback on medication usage improves adherence in children with unstable asthma.<sup>19</sup> Clinical measures of disease control were significantly improved at 4 months in the intervention vs control group. The beneficial effects of feedback, when



combined with electronic inhaler monitoring (Smartinhaler<sup>™</sup>) and reminder alarms, were confirmed in the recent UK-based STAAR study of children with poorly controlled asthma.<sup>20</sup> Adherence with ICS was significantly higher over the 12-month study period in the intervention vs control group. While there was no significant difference between groups in ACQ score, patients in the intervention group required fewer courses of oral corticosteroids and had fewer hospital admissions. As mentioned in the adherence education section, another Australian study found that electronic inhaler reminders (Smartinhaler<sup>™</sup>) with adherence feedback were more effective at improving asthma medication adherence, but not day-to-day asthma control, than behavioural intervention or usual care.<sup>16</sup>

Reminders by way of SMS have also been shown to significantly improve adherence with asthma medication. A small study from Denmark used daily SMS reminders from week 4 of a 12-week study period.<sup>21</sup> Adherence, as assessed by inhaler dose count, was significantly improved in the intervention vs control group. There were no differences between groups in clinical outcomes. A larger trial from the Dutch e-MATIC Study Group used electronic inhaler monitoring (E-haler or Adhaler) combined with SMS reminders, sent only when patients were at risk of missing a dose.<sup>22</sup> The 1-year study of children with asthma found significantly higher adherence in the intervention vs control group, but no differences between groups in asthma control or exacerbations.

A large US study investigated the effectiveness of routinely providing electronic information on ICS adherence in patients with asthma to clinicians.<sup>29</sup> Adherence, as assessed by prescription refills over the last 3 months of the 1-year study, was not significantly different between the intervention and control groups overall, but was significantly improved in the subgroup of patients whose clinicians chose to view patient adherence information.

### Simplified treatment regimens

A UK study conducted in the 1990s used electronic inhaler monitoring to investigate the effect of using a combination ICS/SABA inhaler vs separate inhalers on adherence in asthma patients. The study found no difference between groups in adherence rates.<sup>23</sup> A more recent trial, conducted in New Zealand, assessed adherence with a combination ICS/LABA inhaler vs separate inhalers, also using electronic monitoring (Smartinhaler<sup>™</sup>).<sup>24</sup> Again, the study found no benefit with the combination inhaler in terms of adherence, and no effect on asthma control or lung function.

These findings contrast with those of retrospective cohort studies using prescription refill data to assess adherence, which have shown significantly improved adherence when using a combination ICS/LABA inhaler vs separate inhalers.<sup>30,31,32</sup> They are also at odds with studies showing the positive influence of combination inhalers such as the SMART regimen on asthma exacerbations.<sup>33</sup>

Administering ICS once daily vs twice daily significantly improved adherence in a large UK study of asthma patients.<sup>25</sup> The 12-week study used dose counters on inhalers to assess adherence. There were no significant differences between groups in physician's evaluation of therapeutic response or healthcare utilisation.

### COPD

To date, fewer trials assessing interventions to improve medication adherence in patients with COPD have been published than in patients with asthma, and most have not used objective measures for assessing adherence. However, some randomised controlled trials of electronic monitoring and/or feedback in COPD are ongoing or are awaiting publication. Multi-component interventions consisting of self-management and care co-ordination delivered by pharmacists and primary care teams have been shown to improve medication adherence in patients with COPD.<sup>34</sup>

### Electronic monitoring and feedback

The effectiveness of electronic inhaler monitoring and feedback to improve adherence in patients with COPD was first demonstrated in a subpopulation of the US Lung Health Study, conducted in the 1990s, in which adherence with ipratropium bromide was assessed. Patients in the intervention group were given printed feedback at weeks 1 and 7 and had brief sessions with a health educator every 4 months. Adherence was significantly higher in the intervention vs control group at 4 months,<sup>35</sup> and remained higher at 24 months.<sup>36</sup> The study provided no data on clinical outcomes.

Further studies assessing the impact of electronic inhaler monitoring with reminders on medication adherence and clinical outcomes in patients with COPD are ongoing or are awaiting publication, including trials NCT02864342 and NCT02386722. The latter trial also incorporates support calls if the medication is not inhaled as prescribed for >2 days, or if use of rescue medication doubles. Another study assessing the effectiveness of a digital COPD disease management support service with electronic inhaler monitoring is also ongoing (NCT02300090).

#### Primary-care based, multi-component interventions

A European patient education programme had no effect on adherence with ICS or use of oral corticosteroids at 12 months in COPD patients.<sup>37</sup> However, the trial did find a significant reduction in the use of SABA rescue medication amongst COPD patients in the education vs control group. Adherence was assessed via pharmacy data registers. Another European study also found no effect of an education programme on medication adherence or disease symptoms at 1 and 2 years in patients with COPD.<sup>38</sup> However, inhalation technique was significantly better in the intervention vs control group at both timepoints.

An integrated care intervention in patients discharged from hospital in Spain after a COPD exacerbation found significantly improved self-reported adherence to inhaled therapy at 12 months vs usual care.<sup>39</sup> Intervention consisted of an individual care plan at discharge and a home visit, an individual education session, scheduled phone calls and the option to call a nurse at any time. There was no difference between groups in adherence to oral therapy. The intervention significantly reduced hospital admissions. Another multifactorial educational intervention from Spain found significantly improved adherence with inhaled therapy at 12 months, as assessed by dose count, in a primary care setting.<sup>40</sup> Intervention consisted of a group session at study entry and individual sessions during follow-up visits. Adherence was significantly associated with a lower number of COPD exacerbations.

#### Pharmacist-based, multi-component interventions

A US study of a pharmaceutical care intervention involving COPD patients in an ambulatory setting found no significant difference in medication adherence between the intervention and control groups at 6 months.<sup>41</sup> However, hospitalisations and visits to other healthcare providers were lower in the intervention vs control group. The intervention group received faceto-face and telephone support from pharmacists. A larger, well-designed US study of patients with COPD or asthma conducted at community pharmacies also found no effect of pharmaceutical care on self-reported medication adherence at 12 months.<sup>42</sup>

Structured face-to-face motivational interviewing from a pharmacist at an outpatient clinic, provision of a medication table, and education on symptom control and disease management significantly improved adherence with SABA, LABA, ICS, oral corticosteroids and antibiotics at 6 months in COPD patients in Jordan.<sup>43</sup> The intervention also reduced hospital admissions. A more intensive, individually tailored pharmacist-delivered intervention from Northern Ireland involving an education session on COPD and medications, educational booklets, a customised action plan and telephone follow-up



also significantly improved self-reported medication adherence at 6 and 12 months.<sup>44</sup> Emergency department visits and hospitalisations were also significantly decreased in the intervention vs control group.

The PHARMACOP trial allocated COPD patients to 2 individual counselling sessions from trained community pharmacists in Belgium, and found a significant benefit on MRA-assessed medication adherence at 3 months compared with usual pharmacist care.<sup>45</sup> Hospitalisations were also reduced in the intervention vs usual care group.

# Examples of successful adherence interventions

Recently published, randomised controlled trials which have shown a positive effect of various interventions on medication adherence in patients with asthma or COPD are discussed in detail below. All trials assessed both adherence and clinical outcomes.

# Behavioural intervention vs electronic reminders with feedback in asthma<sup>16</sup>

An Australian study found that electronic inhaler reminders with adherence feedback were more effective at improving adherence with asthma medication in a primary care setting than behavioural intervention or usual care. However, no differential effects were found on day-to-day asthma control.

The study used a cluster 2 x 2 factorial design to randomise 43 GPs from practices in Greater Sydney to: usual care; personalised adherence discussions (PAD); electronic inhaler reminders with feedback (IRF); or IRF + PAD. GPs then enrolled 143 patients aged 14-65 years with suboptimal asthma control (ACT score  $\leq$ 19) who had been prescribed twice-daily ICS/LABA for  $\geq$ 1 month. Each patient was given a Smartinhaler<sup>TM</sup> electronic monitoring device that clipped on to their ICS/LABA inhaler. GPs and patients in the usual care and personalised adherence discussion groups were not advised about the Smartinhaler<sup>TM</sup> recording function until study end.

All GPs received brief training on the delivery of active usual care. GPs randomised to the PAD groups were trained to carry out a personalised discussion around barriers to adherence with controller medication, based on the results of a patient questionnaire, as well as helping with goal setting and achievement for a patient-selected asthma issue. GPs randomised to the IRF groups received electronic data of daily ICS/LABA usage each month and were asked to discuss this with patients at study follow-up. Patients in the IRF groups received twice-daily reminders for missed doses, and were able to view electronic ICS/LABA usage data at any time. Clinic visits were required at enrolment and follow-up, but most data were collected by telephone at baseline, 2 months, 4 months and 6 months.

Mean daily ICS/LABA adherence was 76% in the IRF + PAD group, 71% in the IRF group, 46% in the PAD group and 46% in the usual care group. Adherence was significantly higher in the 2 IRF groups than the 2 non-IRF groups (73% vs 46%; p<0.0001), but not between PAD and non-PAD groups. ACT score improved in the total patient population overall, but there was no difference in effect between groups. There were fewer patients with severe exacerbations in IRF vs non-IRF groups, but this difference was not significant after adjustment for clustering and past self-reported prednisone use.

# Electronic monitoring with audiovisual reminders in asthma<sup>28</sup>

Reminders from an electronic monitoring device can improve both adherence and clinical outcomes in children with asthma, according to a randomised controlled trial conducted in Auckland.

Patients in the trial (n=220) were enrolled 4 weeks after an emergency department visit for asthma exacerbation and were either receiving treatment or required treatment with twice-daily ICS. All patients received fluticasone

propionate via inhalation, and those already receiving an ICS + LABA were switched to a combination fluticasone propionate and salmeterol xinafoate inhaler. Salbutamol sulfate was available as reliever treatment. Smartinhaler<sup>™</sup> devices were fitted to preventer inhalers, with audiovisual reminder functions enabled in the intervention group and disabled in the control group. Smartinhaler<sup>™</sup> devices were also fitted to reliever inhalers. Patients were followed up every 2 months, during which electronic and parent-reported data were collected. Lung function and inhaler technique were also assessed.

Median adherence with preventive ICS was 84% in the intervention group and 30% in the control group (p<0.0001). There was no difference between groups in the proportion of days absent from school for any reason (1.9% vs 1.7% for intervention vs control). However, improvement in asthma morbidity score from baseline to 6 months was significantly greater in the intervention vs control group (2.0 vs 1.2 points, p=0.008). Patients in the intervention group also had a significantly higher childhood ACT score at 2, 4 and 6 months compared with those in the control group (p<0.0001). Median proportion of days on which a reliever inhaler was used was significantly greater in the control vs intervention group (17.4% vs 9.5%; p=0.002). There was no significant difference between groups in FEV<sub>1</sub>.

# Electronic monitoring with SMS reminders in asthma<sup>22</sup>

Electronic inhaler monitoring combined with tailored SMS reminders significantly improved adherence in children but not asthma control or exacerbations, in a trial from the e-MATIC study group.

The multicentre, randomised controlled trial involved 219 children aged 4-11 years with clinically stable asthma recruited from 5 outpatient clinics in the Netherlands. Children had doctor-diagnosed asthma of  $\geq$  6 months duration, had been receiving ICS delivered via metered dose inhaler for  $\geq$  3 months, and had visited the outpatient clinic in the past 12 months. All children received an E-haler or Adhaler device which was attached to their regular inhaler. Caregivers of children in the intervention group also received SMS reminder messages, sent only if a dose was at risk of omission.

SMS reminders were sent about 56.8% of ICS doses in the intervention group, and 53.3% of these reminders led to timely administration. Over the 1-year study period, adherence was 69.3% in the intervention group and 57.3% in the control group, with the overall difference between groups being statistically significant (12.0%; 95% Cl 6.7-17.7%). However, adjusted mean childhood ACT scores and the frequency of asthma exacerbations were not significantly different between the intervention and control groups.

# Electronic monitoring with feedback and alarms in asthma<sup>20</sup>

The STAAR study of children with poorly controlled asthma has shown that significant clinical benefit can be derived from using electronic adherence monitoring with feedback and alarms.

STAAR was a multicentre, open-label, parallel-group, randomised controlled trial involving 90 children with doctor-diagnosed asthma aged 6-16 years attending hospital clinics in Sheffield or Rotherham, UK. Participants were at British Thoracic Society level 3 and had been taking regular ICS with no change to their medication in the past month, and had an ACQ score of  $\geq 1.5$ . Prior to randomisation, all participants had their inhaler technique checked by a qualified asthma nurse and received a brief asthma education session.

Participants in the intervention group had a Smartinhaler<sup>™</sup> device attached to their regular inhaler, and were told the device monitored the date and time of all actuations. Devices also played reminder alarms. Data from the devices were reviewed with the patient and parent/caregiver at clinic visits every 3 months. The adherence rate was discussed and strategies for





Average adherence over the 12-month study period was 70% in the intervention group and 49% in the control group ( $p \le 0.001$ ). There was no significant difference between groups in ACQ score, but significantly fewer courses of oral corticosteroids were required in the intervention vs control group (0.411 vs 0.676 per 100 child-days; p=0.008). Hospital admissions were also significantly lower in the intervention vs control group (0.0254 vs 0.129; p<0.001).

### Primary care programme in COPD patients<sup>40</sup>

A multifactorial intervention involving COPD patients in Spain found significantly improved adherence with inhaled therapy in a primary care setting.

The trial involved 146 patients with COPD diagnosed by spirometry and receiving regular inhaled therapy through primary care centres. Patients were receiving beta<sub>2</sub>-agonists (80.1%), muscarinic antagonists (77.4%) and/or ICS (70.5%), with most patients receiving combination therapy with 2 or more agents. The intervention consisted of a group session at study entry and individual sessions during follow-up visits at 3, 6 and 12 months. Both session types included motivational aspects to improve adherence, cognitive aspects related to treatment adherence and skills development involving training in inhalation techniques. Group sessions lasted 2 hours and included provision of audiovisual and written materials. Adherence was assessed via dose count.

Adherence in the intention-to-treat analysis was 48.6% in the intervention group and 32.4% in the control group (p=0.046) at 12 months. Using multivariate logistic regression, there was a significant association between inhaled medication adherence and number of COPD exacerbations (OR 0.66; 95% Cl 0.48-0.91; p=0.011). There were also trends towards a lower number of healthcare visits and lower disease severity in adherent patients, but these were not statistically significant.

### Pharmacist care programme in COPD patients<sup>45</sup>

Pharmacist care programmes can improve medication adherence and may reduce hospitalisation rates in patients with COPD, according to a European randomised controlled trial.

The 3-month trial involved 170 community pharmacies in Belgium and 734 patients aged  $\geq$ 50 years, with a prescription for daily COPD maintenance medication and a smoking history of  $\geq$ 10 pack-years. Pharmacists receiving a training session on COPD pathophysiology, nonpharmacological and pharmacological treatment according to GOLD guidelines, and important referral criteria. They also received COPD information leaflets, demonstration inhaler units and a list of practical solutions to specific nonadherent behaviour. Patients in the intervention group received one-on-one counselling sessions from pharmacists at study entry and after 1 month. Patients in the control group received usual pharmacist care. Primary outcomes were inhalation technique and adherence; the latter was assessed using the MRA method.

At follow-up, mean adherence was significantly greater in the intervention vs control group (mean estimated difference in MRA score 8.51; p<0.0001). Correct inhalation technique was also significantly greater in the intervention vs control group (mean estimated difference in correctly performed inhalations 13.5%; p<0.0001). Severe exacerbations occurred in 24 intervention group patients and 53 control group patients, resulting in an estimated annual severe exacerbations occurred in 9 intervention vs control group (p<0.007). Hospitalisations occurred in 9 intervention group patients and 35 control group patients, resulting in an estimated annual hospitalisation rate 72% lower in the intervention vs control group (p=0.003).

## TAKE-HOME MESSAGES

- Adherence with medication for asthma and COPD remains a significant problem
- Interventions to improve adherence should focus on both the intentional and non-intentional aspects of non-adherence
- Complex educational interventions involving multiple healthcare personnel and ongoing support have shown benefit, but may have practical limitations
- Technologies such as the Smartinhaler<sup>™</sup> electronic inhaler monitor with reminders and/or feedback, automated SMS and IVR software have improved adherence
- Combining feedback with reminders appears to be more effective than reminders alone, both in terms of improving adherence and clinical outcomes
- Impact on clinical outcomes across all intervention strategies has been inconsistent, and requires confirmation in longer-term, larger studies.

## **Potential future directions**

Outcomes of ongoing and recently completed trials using electronic inhaler monitoring are needed to confirm the benefits of this technology for adherence in patients with COPD. Further, while electronic inhaler monitors provide an objective assessment of patient's adherence to the prescribed treatment frequency (temporal adherence), few devices are able to also assess whether patients are using the inhaler in a correct and effective manner (user technique adherence). Research on electronic measures of user technique adherence is ongoing, and audio-based monitoring systems which record the sounds generated during patient inhaler use have shown promise.<sup>46</sup>

## **EXPERT'S CONCLUDING COMMENTS**

Asthma and COPD are difficult diseases to treat. It is difficult to sell the concept of preventive treatment, (ICS in asthma and LAMAs and LABAS in COPD) - difficult to get patients to use their inhaler correctly, and difficult to get patients to understand the severity of their condition. And as outlined in the sometimes confusing results in differing studies in this edition of Research Review, education of patients about adherence (in many cases) bears no relationship to outcome or improvement. Previous studies have shown that compliance may be improved by a number of factors including simplicity of treatment regime, ease and acceptance of inhaler, perceived effect of medication and perceived seriousness of the condition, and positive relationship with the doctor.

The Smartinhaler<sup>™</sup> uses 21<sup>st</sup> century technology to remind and cajole patients by electronic reminder, and is perhaps the way of the future for asthma and COPD – patients usually do not deliberately not comply with recommended treatment – they simply forget, especially if they do not have symptoms. The device is also capable of relaying information to the doctor so s/he can have forewarning of failure to improve.

So if there is no response to treatment in asthma or COPD do two things – check inhaler technique and check treatment compliance. The latter can be easy with Smartinhaler<sup>TM</sup>.



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