Inhaler technique mastery and maintenance in healthcare professionals trained on different devices

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Financial support: This investigator initiated study (IIS) was conducted and part-funded by Observational and Pragmatic Research Institute Pte Ltd, with institutional support from Teva Pharmaceuticals Europe B.V. Teva Pharmaceuticals Europe B.V. played no role in the design, conduct and reporting of the study.

Running title [no more than 50 characters]: Inhaler technique mastery and maintenance in HCPs.

Keywords [5-7]: clinical trial, dry powder inhaler, device mastery, device mastery maintenance, handling errors, asthma.

Word Count: 3924.

Abstract

Objective: Healthcare professionals (HCPs) are required to assess and train patients in the correct use of inhalers but are often unable to demonstrate correct technique themselves. We sought to assess the level of training required for HCPs to master and maintain device mastery when using two different dry powder inhalers (DPIs). *Methods*: We conducted a randomised, un-blinded, cross-over study in undergraduate HCPs who undertook a stepwise training (from step 1, intuitive use, to step 6, expert tuition) in the use of Turbuhaler® (an established device) and Spiromax® (a newer, reportedly easier to use device). Device mastery (absence of errors) was evaluated by expert assessors at each step. Maintenance of device mastery was assessed 4 ± 1 week (visit 2) and 8 ± 2 weeks (visit 3) after initial training (visit 1). *Results*: Of 516 eligible participants, 113 (22%) demonstrated device mastery prior to training on Spiromax® compared with 20 (4%) on Turbuhaler® ($p<0.001$). The median number of steps required to achieve mastery was 2 (patient information leaflet; interquartile range [IQR] 2–4) for Spiromax® and 3 (instructional video; IQR 2–4) for Turbuhaler® ($p<0.001$). A higher number of participants maintained mastery with Spiromax® compared with Turbuhaler® both at visits 2 and 3 (64% vs 41% and 79% vs 65%, respectively; $p<0.001$). *Conclusions*: There are significant differences in the nature and extent of training required to achieve and maintain mastery for different DPIs. The implications of this on clinical practice, device education delivery and patient outcomes require further evaluation.

Introduction

Inhalers are the most commonly used devices to deliver pharmacological treatments for asthma and chronic obstructive pulmonary disease (COPD). Because correct use of inhalers is central to effective therapy, poor inhaler technique not only compromises disease control [1] but also consequently increases the economic burden of asthma management [2]. Unfortunately, incorrect inhaler use remains common in clinical practice [3] and this aspect has not improved over the past 40 years [4]. This has prompted international organisations of clinicians and health care providers to recognise the importance of patient education by healthcare professionals (HCPs) [5]. The Global Initiative for Asthma (GINA) Guidelines recommend training patients in the use of inhalers as a fundamental and essential component of good clinical practice and consequently advise that HCPs assess and train patients in inhaler use at every clinical encounter [6]. Research has shown that face-to-face training substantially improves patients' ability to use their inhalers correctly [7, 8]. However, as shown by previous studies, many HCPs lack the basic knowledge and technical skill to teach different inhaler techniques [9-11] and they seldom receive formal training in the use of inhalers [12]. Finding solutions to this major problem is of utmost importance to improve the control of asthma and COPD in the population [13]. While it is important to explore the way in which HCPs are currently trained in the use of inhalers, at present it is unfortunately unrealistic to believe that (as is the requirement for patients) each HCP will have the opportunity to receive hands-on individualised training. This puts the onus on each individual HCP and this is where more intuitive devices might be of help. Many of the newer devices are reported to be easier to use [14-16]; however, it is still unknown what this actually means for HCPs. While HCPs have been shown to retain device mastery more efficiently when they have the opportunity to educate their patients [17], it appears important to assess the impact of newer and allegedly more intuitive devices on their ability to retain mastery over time.

The aim of this study was to assess the nature and extent of training required for HCPs to master and maintain correct inhaler technique when using two different dry powder inhalers (DPIs), in

particular comparing the role of newer, reportedly simpler to use DPIs with that of more established DPIs. To address these research questions, we conducted a randomised, un-blinded, cross-over study in pharmacist, physician and nursing undergraduates and compared Spiromax® (an example of a newer device) with Turbuhaler® (an example of an established device). These two particular inhalers were chosen as relevant comparators on the basis that they are both DPIs licensed in Europe for the delivery of budesonide/formoterol combination therapy for asthma but differ in terms of design and dose preparation steps.

Methods

Study design and subjects

This was a multi-centre, randomised, un-blinded, cross-over study conducted between July 2014 and June 2015 (ClinicalTrials.gov Identifier: NCT02570425). The study was approved by the Human Research Ethics Committees of the University of Sydney (Project No.: 2014/344) and was performed in accordance with the National Health and Medical Research Council's (NHMRC) National Statement on Ethical Conduct in Human Research (2007) Australia and with the principles of the Declaration of Helsinki. The sampling frame was all undergraduate Bachelor of Pharmacy students (Year 1) from the University of Sydney (Australia), Bachelor of Nursing Students (Year 1) from the University of Sydney, Doctor of Medicine Students (Year 2) from the University of Sydney, and Doctor of Medicine Students (Year 2) from UNSW Australia. Participants were recruited via relevant e-learning websites, promotion of the study at lectures, and provision of participant information at tutorials. Students who chose to participate in the study were screened for eligibility and enrolled if they met the following inclusion criteria: provided written and informed consent; were willing to comply with study restrictions and attend study visits as specified; were enrolled in one of the specified University departments; had not used or received training in the use of either Turbuhaler® or Spiromax® in the last 6 months.

Potential participants were excluded from the study if they had a current diagnosis of asthma, a past diagnosis of asthma, or both.

Study devices

Turbuhaler® and Spiromax® empty devices were used for this study. Turbuhaler® (AstraZeneca, Sweden) is a multidose DPI consisting of a protective cover, mouthpiece, drug reservoir with dose indicator, and a rotating grip at the base; dose preparation requires holding the device in the upright position and a full rotation of the grip [18]. Spiromax® (Teva Pharmaceutical Industries, Petach Tikva, Israel) is a multidose DPI with design similar to a pressurised metered-dose inhaler (pMDI) but uses an X-ACT® technology for drug delivery [19]. Dose preparation consists in opening the cap until one click is heard while holding the device with the mouthpiece cover at the bottom [20]. For both devices, we compiled a checklist of errors potentially impairing drug delivery to the lungs. These errors were identified *a priori* based on the manufacturer's instructions included in the patient information leaflet [18, 20] and on expert steering committee advice [21]. The checklists include errors associated with dose preparation, position of the inhaler, inhalation manoeuvre, and general knowledge of device use (Table S1).

Study procedures

The study consisted of three visits over a period of 8 ± 2 weeks. At each visit, and before starting any procedure, baseline data (demographic characteristics and history of inhaler device use prior to study) were collected.

At visit 1, participants were randomly assigned to either Turbuhaler® training followed by Spiromax® training or Spiromax® training followed by Turbuhaler® training (cross-over design) (Figure 1). The training procedure was designed to represent best clinical practice, current available mode of education, and to address the educational needs of HCPs. It consisted in a step-wise process in which participants were assessed on their ability to use the device through 6 consecutive steps: (1) intuitive use; (2) use of patient information leaflet; (3) use of instructional

video; (4) expert tuition; (5-6) repeats of expert tuition (see Table S2 for details of instructions provided at each step). At each step, participants were monitored by expert assessors specifically trained to provide education and feedback to device users; errors in device use were recorded according to the device checklist (Table S1). Participants progressed from one step to the next until they achieved device mastery (defined as the ability to demonstrate inhaler use without assessor-observed errors) or until completion of all 6 training steps (Figure 2). They then proceeded to complete the same training and assessment process with the second empty device. At the end of the visit, participants were asked to rate their satisfaction for each device by completing Part II question 15 of the Patient Satisfaction and Preference Questionnaire (PASAPQ). PASAPQ is a multi-item measure of satisfaction and preference for respiratory inhalation devices [22].

Visits 2 and 3 commenced 4 weeks (± 1 week) and 8 weeks (± 2 weeks) after visit 1, respectively. Participants were once again randomly assigned to receive step-by-step device training on Turbuhaler® followed by Spiromax® or Spiromax® followed by Turbuhaler® to determine whether device mastery had been maintained over the 4- and 8-week time period. If they did not maintain device mastery at step 1, participants were trained as in visit 1 until device mastery was re-established. Device preference was again assessed using the PASAPQ Part II question 15 at the end of the visit.

Study definitions and outcomes

Device mastery (yes/no) was defined as the ability to demonstrate inhaler use without assessor-observed errors. Maintenance of device mastery, assessed at visits 2 and 3, was defined as the ability to demonstrate correct inhaler use without the need to undertake any further training (i.e., no errors at step 1).

The primary outcome was maintenance of device mastery at visit 2. Secondary outcomes included maintenance of device mastery at visit 3 and, for each visit, the following: achievement of device

mastery by steps 1, 2, and 3; number of steps required to achieve mastery; number and type of errors made; and participants' preference for the inhaler.

Statistical analyses

Data were analysed using Statistical Analysis Software version 9.3 (SAS Institute Inc). The study was powered on the primary outcome, maintenance of device mastery at visit 2. Based on results from a similar study [7], a sample size of 137 pairs (137 subjects evaluated on both inhalers) was required to have 90% power to detect a difference in proportion of subjects maintaining device mastery of 0.177 (= 0.789-0.612), when the proportion of discordant pairs is expected to be 0.431 and the method of analysis is the McNemar's test of equality of paired proportions (with a 0.05 two-sided significance level). Taking into account a drop-out rate of 10% between visits, a minimum of 144 pairs was therefore required for visit 1.

The McNemar's test was used to compare the proportion of subjects achieving mastery of inhaler technique between the two devices. Conditional logistic regression was used to quantify the difference between the two devices by calculating the odds ratio (OR) for achieving mastery for Spiromax® (with Turbuhaler® as the reference device) with a 95% confidence interval (CI). When CI does not contain 1.00, results are statistically significant at the 5% level. The Chi-squared and Wilcoxon signed rank tests were used to compare the proportion of participants achieving device mastery stratified by the order of randomisation and the mean/median number of levels required to achieve device mastery between the two devices, respectively. For all analyses where P-value is provided, statistical significance was set at 0.05.

Summary statistics collected at each visit included: number of levels required to achieve device mastery, number and type of assessor-observed errors (total of errors made at all steps) and device preference. Continuous variables (including age and number of levels taken to achieve device mastery) were summarised by reporting their mean/median along with their standard deviations/interquartile range (IQR). Categorical variables were reported as frequencies and percentage proportions. In particular, device mastery (yes/no) was expressed as cumulative

number and percentage of participants achieving device mastery by each training step, unless otherwise stated. Participant demographic and baseline characteristics were summarised using descriptive statistics.

Results

Participant disposition and characteristics

A total of 542 participants were enrolled in the study; of these, 516 (39% male, mean age 23 ± 5 years) met the eligibility criteria and were randomised into visit 1. Four hundred ninety-eight and 460 participants were eligible for visits 2 and 3, respectively. Figure S1 and Table S3 show the disposition and the demographic characteristics of participants at each visit of the study, respectively.

Achieving device mastery

At visit 1, the odds of making a device error prior to training was significantly lower for Spiromax® compared with Turbuhaler® (OR 0.16 [95% CI 0.10–0.27]). A total of 113 (22%) participants demonstrated device mastery at step 1 on Spiromax® compared with 20 (4%) participants achieving mastery on Turbuhaler® ($p<0.001$; McNemar's test of paired data) (Table 1). Likewise, a significantly higher number of participants achieved mastery in the use of Spiromax® by steps 2 and 3 ($p<0.001$). This effect was independent of device randomisation order (steps 1 and 2, $p<0.001$ for both randomisation orders; step 3, $p<0.05$ for both randomisation orders; Chi-squared test) (Table 1). By step 4 (expert tuition), about 90% of participants achieved device mastery, with no statistical difference between the devices (data not shown).

At visit 1, the median number of steps required to achieve device mastery was 2 (patient information leaflet; [IQR] 2–4) for Spiromax® and 3 (instructional video; IQR 2–4) for Turbuhaler® ($p<0.001$; Wilcoxon Signed-Rank test).

Maintaining device mastery

Visit 2

At visit 2, a total of 317 (64%) participants had maintained device mastery with Spiromax® compared with 202 (41%) participants who had maintained device mastery with Turbuhaler® ($p<0.001$; McNemar's test of paired data) (Table 2). This effect was independent of device randomisation order (Table 2). The odds of making a device error was significantly lower for Spiromax® compared with Turbuhaler® (OR 0.37 [95% CI 0.28–0.48]).

By steps 2 and 3, a significantly higher number of participants achieved mastery in the use of Spiromax® as compared with Turbuhaler® ($p<0.001$ and $p=0.022$ for steps 2 and 3, respectively; McNemar's test of paired data). This effect was associated with device randomisation order: at both steps, significantly more participants using Spiromax® as first device achieved device mastery compared with participants using Turbuhaler® as first device ($p<0.001$ and $p=0.007$ for steps 2 and 3, respectively; Chi-squared test); however, there was no significant difference in device mastery when Spiromax® and Turbuhaler® were used as second device (step 2, $p=0.347$; step 3, $p=1.00$) (Table 2). The median number of steps required to achieve device mastery was 1 (intuitive use; IQR 1–2) for Spiromax® and 2 (patient information leaflet; IQR 1–2) for Turbuhaler® ($p<0.001$; Wilcoxon Signed-Rank test).

Visit 3

At visit 3, a total of 362 (79%) participants maintained device mastery on Spiromax® prior to training compared with 299 (65%) participants who maintained device mastery on Turbuhaler® ($p<0.001$; McNemar's test of paired data); this effect was independent of device randomisation order (Table 3). The odds of making a device error was significantly lower for Spiromax® compared with Turbuhaler® (OR 0.50 [95% CI 0.37–0.68]).

Already by step 2, over 90% of participants demonstrated device mastery on both inhalers with no significant difference between the two devices (Table 3). Likewise, there was no significant difference in the median number of steps required to achieve device mastery between the two

devices (median number of steps 1, IQR 1–1 for Spiromax® and 1–2 for Turbuhaler®; p=0.111; Wilcoxon Signed-Rank test).

Figure 3 summaries the proportion of participants achieving and maintaining device mastery over the study period.

Number and types of errors made

At each visit, a significantly higher number of errors were made on Turbuhaler® than on Spiromax® (total number of errors made at all steps: 2540 vs 1447 at visit 1; 780 vs 367 at visit 2; 296 vs 175 at visit 3). The most common device errors made at each visit are reported in Table 4. The error 'not twisting the base as far as possible' related to dose preparation was the most common for Turbuhaler® at visits 1 and 2 (made by 389 [75%] and 155 [31%] participants, respectively) and the second most common at visit 3 (Table 4). The error 'inhalation not as fast as possible from the start' in inhalation manoeuvre was the most common for Spiromax® at all visits (337 [65%], 96 [19%] and 50 [11%] at visits 1, 2, and 3, respectively). This error was one of the most frequent also for Turbuhaler® (reported for 323 [63%] and 107 [22%] participants at visits 1 and 2, respectively). Finally, errors related to inhaler position were common for both inhalers (Table 4).

Participants' preference for the inhaler

At visit 1, 487 (94%) participants completed question 15 of the PASAPQ PART II. Of these, 74% rated Spiromax® as their preferred device compared with 16% who rated Turbuhaler® as their preferred device (10% of participants reported no preference). Also at visits 2 and 3, Spiromax® was the preferred device over Turbuhaler® (75% vs 16% at visit 2 [9% no preference], 79% vs 14% at visit 3 [7% no preference]).

Discussion

We conducted a randomised, un-blinded, cross-over study assessing the nature and extent of training required for undergraduate HCPs to master inhaler technique and maintain it over time when using different DPI devices. In particular, we compared the role of newer, reportedly easier to use devices (Spiromax® in this study) with that of more established devices (Turbuhaler® in this study). We found that undergraduate HCPs demonstrated fewer device errors and required fewer training steps to master inhaler technique when using Spiromax® compared with Turbuhaler®. Once established, a higher number of HCPs maintained mastery with Spiromax® than with Turbuhaler® over a period of 2 months. Given that not all HCPs are regular inhaler users, and that there has been an upsurge of new inhalers on the market over the last few years, this study was crucial to understanding how and when undergraduate HCPs need to have their inhaler technique skills developed and refreshed. We believe that this knowledge will help to develop strategies to better support HCPs in the management of patients with respiratory diseases.

Sandler et al [14] have recently shown that Spiromax® is easier to learn to use compared with Turbuhaler® and Easyhaler® when tested in healthy volunteers naïve to all three devices. Our data on device mastery shows that this is the case also for undergraduate HCPs. This may be due to Spiromax® having fewer preparation steps for dose delivery. In our study, a large number of participants failed to correctly demonstrate dose preparation steps for Turbuhaler® (twisting the base as far as possible and holding the device upright); Spiromax® does not require all of these steps for preparing the dose. In terms of the level of training required to achieve mastery, we made the following observations: 1) at visit 1, 60% of participants using Spiromax® achieved mastery with written information, whereas for Turbuhaler® a video instruction was required for a comparable proportion of participants to achieve mastery; 2) although many participants were able to achieve device mastery after the first three steps of training, some participants did require additional training through individualised feedback to achieve mastery. These findings have

practical implications as they suggest that for Spiromax® the written instructions provided in package inserts are sufficient to train a substantial percentage of individuals whereas, for Turbuhaler®, many individuals will need video instructions or demonstration by trained HCPs to learn how to use the device correctly. Further, while video instructions are often provided on both manufacturers' and patients' websites, providing expert tuition would require allocating specific resources for the training of HCPs. From this perspective, it may be important to determine the cost-effectiveness of delivering personalised training to HCPs for different inhalers.

Inhalers that are more intuitive/easier to use may paradoxically increase the risk of errors in subsequent usage, i.e. subjects who demonstrate correct technique or achieve device mastery with little training in the first place may do so by chance and therefore may not perform as well at subsequent visits; by contrast subjects who need more inputs/training may achieve a better understanding of the device and thus perform better in the future. However, when reassessing device mastery 1 month and 2 months after initial training, we found that a higher number of participants maintained correct technique on Spiromax® than on Turbuhaler®. This suggests that, once the technique is established for easier to use inhalers, HCPs may be able to maintain mastery over time with no or little additional training. Nonetheless, it should be noted that 1 and 2 months after the initial training, a high percentage of participants demonstrated correct technique with both devices after refreshing their skills via written instructions. This indicates that, if proper training is provided initially, educating HCPs to refresh their skills periodically via minimal instructions may have a big impact on their ability to use inhalers correctly, and subsequently train patients appropriately, in the long term.

The superior ease of use may explain why the majority of participants rated Spiromax® as their preferred device compared with Turbuhaler®. Similar results were reported by studies that compared device preference between Spiromax® and Turbuhaler® among healthy volunteers [14] and patients with asthma [23]. This may have implications for clinical practice, as patients'

preference may affect adherence and thus is an important factor that HCPs are encouraged to consider when prescribing/switching inhalers [24].

When taking randomisation order into account, we observed a learning effect. During initial training (visit 1), for both Spiromax® and Turbuhaler® the percentage of participants demonstrating device mastery when the inhaler was used as the second device was higher than the percentage of participants demonstrating mastery when the inhaler was used as the first device. This was true for steps 1, 2 and 3 though at step 1 the percentage increased by three and six times for Spiromax® and Turbuhaler®, respectively. This suggests that there may be 'carry-over' effects in terms of generic skills of inhaler use. The presence of any 'carry-over' effect needs to be explored in future research and the implications for practice considered.

When considering the errors, participants made fewer errors when using Spiromax® than when using Turbuhaler®. Throughout the study the errors remained generally consistent for both devices though, as expected, less frequent. The most common error for Turbuhaler® was 'not twisting the base as far as possible until it clicks and not turning it back to the original position', which relates to dose preparation and thus is crucial to ensure correct drug delivery. 'Inhalation not as fast as possible from the start' was the third most common error for Turbuhaler® and the most common error for Spiromax®, and was displayed by a similar proportion of participants for the two devices. Failure to inhale as fast as possible is a common error for DPIs [21, 24, 25], thus the similar number of users demonstrating this error with either device is as expected. Because correct inhalation technique is critical to appropriate medication intake, HCPs should be particularly mindful of this error when training patients in the use of any DPI. It should be noted that although 'holding the inhaler in the upright position (±90°) during dose preparation' was included in the manufacturer's instructions for Spiromax® at the time in which this research was performed, a recent study [19] has shown that dose consistency is maintained with Spiromax® regardless of device orientation (±45° tested in addition to ±90°). In light of this, this position error may not represent a critical error for Spiromax®.

Basheti et al [26] have recently addressed the issue of heterogeneity of error checklists in the field and provided recommendations about standardised checklists for two DPIs, Diskus® and Turbuhaler®. The list used for Turbuhaler® in the present study followed their recommendations and although such recommendations are not currently available for the more recent device Spiromax®, our checklists were generated by expert opinion and included errors that have been used in previous studies [14]. The errors considered here are those commonly seen in clinical practice, which have potential implications on device effectiveness; however, they are not a validated measure. Although some studies have investigated the impact of inhaler misuse or the number of inhaler errors on asthma control [3, 25] and management [1], knowledge of the relationship between individual inhaler errors and asthma outcomes is still limited. This knowledge would be crucial to better identify critical errors and develop educational interventions for HCPs and patients tailored to address such errors specifically.

There are some limitations in the study design. This was primarily an 'evaluation-of-concept' study that analysed a cohort of undergraduate HCPs with a mean age of 23. This is a very specific cohort and thus our findings may not be generalisable to patients with chronic airways disease or to practicing HCPs.

Conclusions

This study shows that there are significant differences in the nature and extent of training required for HCPs to achieve and maintain mastery with different DPI devices. Inhalers that are easier to use may facilitate achievement of device mastery and its maintenance over time. Expert tuition during initial training may help to optimise HCP knowledge of inhaler use to the extent that refreshing HCP skills with minimal instructions (such as written instructions) may be sufficient to maintain correct technique over time. Future research should explore the impact of tailored education for HCPs on the health care system in terms of clinical and economic outcomes.

Acknowledgements

The authors wish to thank Daina Lim and Jo Steele for assistance with study and data management, and Vicky Thomas for reviewing data analyses. They would also like to thank Smita Shah, Lorraine Smith, and Lisa Pont for their assistance with participant recruitment. Alessandra Cifra provided writing support, funded by Observational and Pragmatic Research Institute Pte Ltd.

Declaration of interest

SBA sits on an advisory board for TEVA and has consulted for TEVA, GSK, Mundipharma.

CC & VN were employees of Observational and Pragmatic Research Institute Pte Ltd at the time of the study. Observational and Pragmatic Research Institute Pte Ltd conducted this study and has conducted paid research in respiratory disease on behalf of the following other organizations in the past 5 years: UK National Health Service, British Lung Foundation, Aerocrine, AKL Ltd, AstraZeneca, Boehringer Ingelheim, Chiesi, Meda, Mundipharma, Napp, Novartis, Pfizer, Respiratory Effectiveness Group, Takeda, Teva Pharmaceuticals, Theravance, and Zentiva.

HC has no shares in any pharmaceutical companies. He has received sponsorship to carry out studies, together with Board Membership, consultant agreements and honoraria for presentation, from several pharmaceutical companies that market inhaled products. These include Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Innovata Biomed, Meda, Napp Pharmaceuticals, Mundipharma, NorPharma, Norvartis, Orion, Sanofi, Teva, Truddell Medical International, UCB and Zentiva. Research sponsorship has also been received from grant awarding bodies (EPSRC and MRC). He is the owner of Inhalation Consultancy Ltd. He is also an employee of Observational and Pragmatic Research Institute Pte Ltd, which conducted this study and has conducted paid research in respiratory disease on behalf of the following other organizations in the past 5 years: UK National Health Service, British Lung Foundation,

Aerocrine, AKL Ltd, AstraZeneca, Boehringer Ingelheim, Chiesi, Meda, Mundipharma, Napp, Novartis, Pfizer, Respiratory Effectiveness Group, Takeda, Teva Pharmaceuticals, Theravance, and Zentiva.

FL received in the last 5 years fees for speaking or honoraria for attending advisory boards from the following pharmaceutical companies: Boehringer Ingelheim, Chiesi, CIPLA, TEVA, AstraZeneca, Menarini International.

VK received over the past 3 years fees for speaking for AstraZeneca, GlaxoSmithKline, and Pfizer**.**

PNRD and/or his department have received unrestricted educational grants from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Mundipharma, Takeda and Teva; consulting and advisory fees from AstraZeneca, Boehringer Ingelheim, Takeda, Chiesi, Zambon, Novartis and Teva.

NR has received over the past 3 years (i) fees for speaking, organising education, participation in advisory boards or consulting from 3M, Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, GlaxoSmithKline, MSD-Chibret, Mundipharma, Novartis, Pfizer, Sandoz, Sanofi, Takeda, Teva, Zambon; (ii) research grants from Novartis, Boehringer Ingelheim and Pfizer.

LB has received over the past 3 years fees for speaking, or participation in advisory boards for Aerocrine, Arsonette, Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Mundipharma, Novartis, Sandoz, Sanofi, Takeda and Teva.

CR reports membership on a TEVA scientific advisory board and consulting for TEVA.

NZ declares no shares in any pharma companies. However, he is a chief investigator on a grant from GSK Australia for a project on self-management support for patients with COPD.

DBP has board membership with Aerocrine, Amgen, AstraZeneca, Boehringer Ingelheim, Chiesi, Meda, Mundipharma, Napp, Novartis, and Teva Pharmaceuticals; consultancy with Almirall, Amgen, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Meda, Mundipharma, Napp, Novartis, Pfizer, Teva Pharmaceuticals, and Theravance; grants and unrestricted funding for investigator-initiated studies (conducted through Observational and Pragmatic Research Institute Pte Ltd) from UK National Health Service, British Lung Foundation, Aerocrine, AKL Ltd, AstraZeneca, Boehringer Ingelheim, Chiesi, Meda, Mundipharma, Napp, Novartis, Pfizer, Respiratory Effectiveness Group, Takeda, Teva Pharmaceuticals, Zentiva, and Theravance; payment for lectures/speaking engagements from Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, GlaxoSmithKline, Kyorin, Meda, Merck, Mundipharma, Novartis, Pfizer, Skyepharma, Takeda, and Teva Pharmaceuticals; payment for manuscript preparation from Mundipharma and Teva Pharmaceuticals; payment for the development of educational materials from Novartis and Mundipharma; payment for travel/accommodation/meeting expenses from Aerocrine, Boehringer Ingelheim, Mundipharma, Napp, Novartis, Teva Pharmaceuticals, and AstraZeneca; funding for patient enrolment or completion of research from Chiesi, Teva Pharmaceuticals, Zentiva, and Novartis; stock/stock options from AKL Ltd which produces phytopharmaceuticals; owns 74% of the social enterprise Optimum Patient Care Ltd, UK and 74% of Observational and Pragmatic Research Institute Pte Ltd, Singapore; and is peer reviewer for grant committees of the Medical Research Council, Efficacy and Mechanism Evaluation programme, and HTA.

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Figure legends

Figure 1: Overall study design

At visit 1, participants were randomly assigned to either Spiromax® training followed by Turbohaler® training or Turbohaler® training followed by Spiromax® training, in a cross-over stage design. Training consisted of 6 consecutive steps until device mastery was achieved, as shown in Figure 2. At visits 2 and 3, which commenced 4±1 week and 8±2 weeks after visit 1, respectively, participants undertook the same training procedure.

Figure 2: Inhaler technique assessment and training

At each study visit, participants were assessed on their ability to use the empty study devices without training followed by training in a step-wise approach. Training consisted of 6 consecutive steps: step 1, intuitive use; step 2, use of patient information leaflet; step 3, use of instructional video; steps 4-6, expert tuition. Participants progressed from one step to the next until device mastery was achieved (defined as absence of assessor-observed serious errors) or until all 6 steps were completed. Upon attainment of device mastery, participants proceeded to complete the same training and assessment procedure with the second empty device.
Abbreviations: HCPs = healthcare professionals.

Figure 3: Proportion of participants achieving and maintaining device mastery over the study period

The chart shows the cumulative proportion (%) of participants demonstrating correct inhaler technique with the two study devices at each step during the study visits. Total number of participants: visit 1, n=516; visit 2, n=498; visit 3, n=460.

Table 1. Participants achieving device mastery at visit 1

	Irrespective of randomisation order			First randomised device			Second randomised device		
Training step	Turbuhaler® (n=516)	Spiromax® (n=516)	p-value[a]	Turbuhaler® (n=242)	Spiromax® (n=274)	p-value[b]	Turbuhaler® (n=274)	Spiromax® (n=242)	p-value[b]
1: Intuitive use (no training)	20 (4)	113 (22)	<0.001	3 (1)	30 (11)	<0.001	17 (6)	83 (34)	<0.001
2: Patient information leaflet	162 (31)	299 (58)	<0.001	41 (17)	121 (44)	<0.001	121 (44)	178 (74)	<0.001
3: Instructional video	338 (66)	386 (75)	<0.001	130 (54)	182 (66)	0.004	208 (76)	204 (84)	0.024

Data are expressed as cumulative n (%) of participants achieving device mastery by each step. Device mastery (yes/no) was defined as the ability to demonstrate inhaler use without assessor-observed errors. Steps 4-6 are not displayed, as no significant difference was detected between the devices at these steps.
[a]McNemar's test of paired data. [b]Chi-squared test.

Table 2. Participants maintaining and achieving device mastery at visit 2

	Maintenance of device mastery								
	Irrespective of randomisation order			First randomised device			Second randomised device		
Training step	Turbuhaler® (n=498)	Spiromax® (n=498)	p-value[a]	Turbuhaler® (n=247)	Spiromax® (n=251)	p-value[b]	Turbuhaler® (n=251)	Spiromax® (n=247)	p-value[b]
1: Intuitive use (no training)	202 (41)	317 (64)	<0.001	78 (32)	156 (62)	<0.001	124 (49)	161 (65)	<0.001
Achievement of device mastery									
2: Patient information leaflet	384 (77)	430 (86)	<0.001	174 (70)	215 (86)	<0.001	210 (84)	215 (87)	0.347
3: Instructional video	444 (89)	464 (93)	0.022	211 (85)	234 (93)	0.007	233 (93)	230 (93)	1.00

Data are expressed as cumulative n (%) of participants maintaining/achieving device mastery by each step. Device mastery (yes/no) was defined as the ability to demonstrate inhaler use without assessor-observed errors. Steps 4-6 are not displayed, as no significant difference was detected between the devices at these steps.
[a]McNemar's test of paired data. [b]Chi-squared test.

Table 3. Participants maintaining and achieving device mastery at Visit 3

	Maintenance of device mastery								
	Irrespective of randomisation order			First randomised device			Second randomised device		
Training step	Turbuhaler® (n=460)	Spiromax® (n=460)	p-value[a]	Turbuhaler® (n=231)	Spiromax® (n=229)	p-value[b]	Turbuhaler® (n=229)	Spiromax® (n=231)	p-value[b]
1: Intuitive use (no training)	299 (65)	362 (79)	<0.001	143 (62)	168 (73)	0.012	156 (68)	194 (84)	<0.001
Achievement of device mastery									
2: Patient information leaflet	426 (93)	425 (92)	0.893	211 (91)	206 (90)	0.726	215 (94)	219 (95)	0.822
3: Instructional video	446 (97)	441 (96)	0.353	220 (95)	216 (94)	0.817	226 (99)	225 (97)	0.519

Data are expressed as cumulative n (%) of participants maintaining/achieving device mastery by each step. Device mastery (yes/no) was defined as the ability to demonstrate inhaler use without assessor-observed errors. As at steps 2-3, also at steps 4-6 (not shown) no significant difference was detected between the devices. [a]McNemar's test of paired data. [b]Chi-squared test.

Table 4. Most common device errors at each visit

Visit 1 (participants=516)					
Turbuhaler®			**Spiromax®**		
Type of error	**Description**	**n (%)[a]**	**Type of error**	**Description**	**n (%)[a]**
Dose preparation	Not twisting the base as far as possible until it clicks and not turning it back to the original position	389 (75)	Inhalation manoeuvre	Inhalation not as fast as possible from the start	337 (65)
Position	Inhaler not held upright (mouthpiece pointed skywards ±45°) when a dose is prepared	374 (72)	Position	Inhaler not held upright (±90° is correct) when a dose is prepared	225 (44)
Inhalation manoeuvre	Inhalation not as fast as possible from the start	323 (63)	General knowledge	Fails to put in mouth and seal lips around mouthpiece	111 (22)
Visit 2 (participants=498)					
Dose preparation	Not twisting the base as far as possible until it clicks and not turning it back to the original position	155 (31)	Inhalation manoeuvre	Inhalation not as fast as possible from the start	96 (19)
Position	Inhaler not held upright (mouthpiece pointed skywards ±45°) when a dose is prepared	132 (27)	Position	Inhaler not held upright (±90° is correct) when a dose is prepared	75 (15)
Inhalation manoeuvre	Inhalation not as fast as possible from the start	107 (22)	General knowledge	Puts finger (or face) over the air inlet during an inhalation (at front above the mouthpiece)	30 (6)
Visit 3 (participants=460)					
Position	Inhaler not held upright (mouthpiece pointed skywards ±45°) when a dose is prepared	57 (12)	Inhalation manoeuvre	Inhalation not as fast as possible from the start	50 (11)
Dose preparation	Not twisting the base as far as possible until it clicks and not turning it back to the original position	35 (8)	General knowledge	Puts finger (or face) over the air inlet during an inhalation (at front above the mouthpiece)	24 (5)
Position	Inhaler not held upright (mouthpiece pointed skywards ±45°) after the base is twisted until	21(5)	Position	Inhaler not held upright (±90° is correct) when a dose is prepared	21 (5)

	inhalation

The table shows the distribution of most common types of errors made at each visit, at all steps. [a]Number and % of participants who made the error.