Shared decision-making facilitates inhaler choice in patients with newly-diagnosed chronic obstructive pulmonary disease:
a multicenter prospective study

Supplementary Data

Yi-Han Hsiao [1,2,3], Ching-Min Tseng [2,4], Chau-Chyun Sheu [5,6], Hsin-Yi Wang [7,8],
Hsin-Kuo Ko [2,9], Kang-Cheng Su [2,10], Chi-Wei Tao [4], Ming-Ju Tsai [5,6,*], Yen-Fu Chen [7,8,*]

1   Division of General Chest Medicine, Department of Chest Medicine, Taipei Veterans General Hospital, Taipei, Taiwan; yihanhsiao@gmail.com (Y.H.H.)

2   School of Medicine, College of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan

3   Department and Institute of Physiology, College of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan

4   Division of Chest Medicine, Department of Internal Medicine, Cheng-Hsin General Hospital, Taipei, Taiwan; ponda0294@gmail.com (C.M.T.); davidtao_2001@yahoo.com (C.W.T.)

5   Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Taiwan; sheucc@gmail.com (C.C.S.); SiegfriedTsai@gmail.com (M.J.T.)

6   Department of Internal Medicine, School of Medicine, Kaohsiung Medical University, Taiwan

7   Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, National Taiwan University Hospital Yunlin Branch, Yunlin, Taiwan; mimihsinyi0817@gmail.com (H.Y.W.); yenfu1228@gmail.com (Y.F.C.)

8   Graduate Institute of Clinical Medicine, College of Medicine, National Taiwan University, Taipei, Taiwan

9   Division of Respiratory Therapy, Department of Chest Medicine, Taipei Veterans General Hospital, Taipei, Taiwan; kuohsink@ms67.hinet.net (H.K.K.)

10 Division of Clinical Respiratory Physiology, Department of Chest Medicine, Taipei Veterans General Hospital, Taipei, Taiwan; kcsu@vghtpe.gov.tw (K.C.S.)

* Corresponding authors (M.J.T. and Y.F.C. contributed equally to this article.)

Correspondence:

Ming-Ju Tsai, M.D., Ph.D.   (ORCID: 0000-0003-3621-3334)

Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine,
Kaohsiung Medical University Hospital, No.100, Tz-You 1st Road, 807 Kaohsiung, Taiwan
Tel.: +886 7 3121101, ext., 5651   Fax: +886 7 3161210
E-mail: SiegfriedTsai@gmail.com

Yen-Fu Chen, M.D.

Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine,
National Taiwan University Hospital Yunlin Branch, Yunlin, Taiwan
Tel.: +886 5 5323911, ext. 2501
E-mail: yenfu1228@gmail.com

Shared decision-making (SDM) for choosing inhaler
in patients with newly-diagnosed COPD

Who will need this information?

- Patients who are diagnosed as chronic obstructive pulmonary disease (COPD) by physician and in need of inhaled dual bronchodilator treatment.

Why and what should I know about the disease?

- COPD is a disease mostly resulted from smoking. The disease will make you have chronic respiratory symptoms such as cough, sputum production, and/or shortness of breath.

- An inhaled dual bronchodilator treatment is a combination of drugs with two different mechanisms in a single inhaler. This treatment dilates your obstructed bronchi, relieves your respiratory symptoms, and prevent you from acute exacerbation of COPD.

- An inhaler is a container for your dual bronchodilator treatment, and a device that make the drugs be easily delivered into your lungs. There are currently two common choices for your dual bronchodilator treatment in Taiwan:

  - **Soft mist inhaler (SMI):** This inhaler allows the drugs been released as slowly moving aerosol that looks like soft mist.

  - **Dry powder inhaler (DPI):** This inhaler contains and delivers the drug as a dry powder.

- Wrong operation or irregular use of inhaler will lead to less effectiveness and/or increased adverse effects of your dual bronchodilator treatment.

- After reading this leaflet, discussing with your physician, and seeing demonstration by the educators, you will get better understanding with your inhaler choices. This "shared decision making (SDM)" process will help you explore your preferences and support your involvement in deciding the optimal inhaler.

Which inhaler can I choose for my inhaled dual bronchodilator?

There are three choices as the following:

	Spiolto® Respimat® soft mist inhaler (SMI)	Anoro® Ellipta® dry powder inhaler (DPI)	Ultibro® Breezhaler® dry powder inhaler (DPI)
Frequency	Once daily	Once daily	Once daily
Dose	2 puffs	1 puff	1 puff (capsule)
How to use the inhaler	Turn – Open – Press – Inhale – Close	Slide cover down until a "click" – Inhale – Slide the cover upwards to cover the mouthpiece	Open inhaler – Insert the capsule – Close inhaler – Pierce capsule – Inhale – Remove empty capsule
Minimal inspiratory flow rate	Not required	Required	Required
Dose counter	Yes	Yes	By blister card
Adverse effects*			
Dry mouth	Common	Common	Uncommon
Upper respiratory tract infection	Rare	Common	Very common
Nasopharyngitis	Rare	Common	Common
Cough	Uncommon	Common	Common
Allergy	Rare	Uncommon	Common

* The frequency of adverse effects:
 very common (10%), common (1-10%), uncommon (0.1-1%), rare (0.01%-0.1%) (CIOMS III).

What should I do next?

- The educator will demonstrate these three inhalers in randomized order and answer your questions. You will be asked to choose **one** inhaler and answer the **reasons** why you choose the inhaler.

- You will be asked to demonstrate how to use your inhaler and the educator will record the errors during your demonstration.

- The educator will make sure you can use the inhaler completely correctly before you go home.

- An outpatient clinic appointment will be made **a month later**. You will be asked to demonstrate how to use your inhaler and the educator will record the errors during your demonstration.

- You will be asked to answer a questionnaire regarding your adherence, satisfaction score and willingness to keep the initial inhaler.

Shared decision-making (SDM) for choosing inhaler
in patients with newly diagnosed COPD

- **Patient No.:** _____

- **Order of demonstration:** (check random number table)
  (1: Respimat®, 2: Ellipta®, 3: Breezhaler®): _____

- **The patient's choice** (1: Respimat®, 2: Ellipta®, 3: Breezhaler®): _____

- **Reasons of choosing the inhaler**
  _____ Easy to carry, _____ Appears more effective, _____ Visible inhaled medication
  _____ Delicate and textured, _____ Prefer the way of use this device, _____ Simple using
  Others: _____

- **Adherence (according to the patient's answer)**:
  _____ Good (Use as the prescription daily); _____ Fair (Use in 5-6 days per week)
  _____ Poor (Use ≤4 days per week)

- **Satisfaction score (according to the patient's answer)**:
  ___ 1 (Very unsatisfied); ___ 2 (unsatisfied); ___ 3 (fair); ___ 4 (satisfied); ___ 5 (very satisfied)

- **Willingness to keep the initial inhaler (according to the patient's answer)**:
  _____ YES; _____ NO

● **Checklist of errors**:

Steps (use the corresponding steps of the patient's inhaler)	Visit 1		Visit 2	
	Totally correct (O) or Any error (X)	How many times of re-education needed until the patient can correctly use?	Totally correct (O) or Any error (X)	How many times of re-education needed until the patient can correctly use?
Steps of Respimat®				
Step 1: Press the safety catch button while firmly pulling the clear base straight off with your other hand. Be careful not to touch the piercing element.				
Step 2: Insert the narrow end of your medication cartridge into the inhaler.				
Step 3: Place the inhaler on a flat surface, and push down firmly until it clicks into place.				
Step 4: With the cap closed, turn the clear base in the direction of the arrows on the label until it clicks (half a turn). Push up on the small, circular opening tab until the cap snaps fully open. With the inhaler pointed toward the ground, press the dose release button. Look for a mist. Repeat 3 times until visible mists have been dispensed.				
Step 5: With the cap closed, turn the clear base in the direction of the arrows on the label until it clicks (half a turn).				
Step 6: Open the hinged cap by pushing up on the small, circular tab until the cap snaps fully open.				
Step 7: Breathe out slowly and fully. Close your lips around the mouthpiece without covering the air vents. Point the inhaler to the back of your throat. While taking a slow, deep breath through your mouth, press the dark gray dose release button and continue to breathe in. Hold your breath for 10 seconds or for as long as comfortable.				
Step 8: Close the cap until you use your inhaler again. Repeat Turn, Open, Press (TOP) for your prescribed dosage.				
Steps of Ellipta®				
Step 1: Open the cover of the inhaler. Slide the cover down to expose the mouthpiece. You should hear a "click." The counter will count down by 1 number. You do not need to shake this kind of inhaler. Your inhaler is now ready to use.				
Step 2: While holding the inhaler away from your mouth, breathe out (exhale) fully. Do not breathe out into the mouthpiece. Put the mouthpiece between your lips and close your lips firmly around it. Your lips should fit over the curved shape of the mouthpiece. Take one long, steady, deep breath in through your mouth. Do not breathe in through your nose. Do not block the air vent with your fingers.				

Steps (use the corresponding steps of the patient's inhaler)	Visit 1		Visit 2	
	Totally correct (O) or Any error (X)	How many times of re-education needed until the patient can correctly use?	Totally correct (O) or Any error (X)	How many times of re-education needed until the patient can correctly use?
Step 3: Remove the inhaler from your mouth and hold your breath for about 3 to 4 seconds (or as long as is comfortable for you).				
Step 4: Breathe out slowly and gently. You may not taste or feel the medicine, even when you are using the inhaler correctly. Do not take another dose from the inhaler even if you do not feel or taste the medicine.				
Step 5: Slide the cover up and over the mouthpiece as far as it will go.				
Steps of Breezhaler®				
Step 1: Take the blister card from the box.				
Step 2: Separate one of the blisters from the blister card.				
Step 3: Peel open the blister.				
Step 4: remove a capsule from the blister.				
Step 5: Pull off cap and open inhaler				
Step 6: Insert the capsule in the compartment.				
Step 7: Close inhaler and hear a "click".				
Step 8: Hold the inhaler upright. Pierce capsule by firmly pressing both side buttons at the same time. You should hear a noise as the capsule is pierced. Then release side buttons.				
Step 9: Breathe out fully. Do not blow into the inhaler. Place the mouthpiece in your mouth and close your lips firmly around it. Do not press the side buttons. Breathe in quickly and as deeply as you can. During inhalation you will hear a whirring noise. You may taste the medicine as you inhale. Hold your breath for up to 5 seconds.				
Step 10: Check capsule is empty. Open the inhaler to see if any powder is left in the capsule. If there is powder left in the capsule: Close the inhaler and repeat step 9.				
Step 11: Remove empty capsule. Put the empty capsule in your household waste. Close the inhaler and replace the cap.				

Supplementary Figures

Visit 1 (Baseline)

Patients of **newly-diagnosed COPD**
in need of **dual bronchodilator** treatment
in outpatient setting and meet the study criteria

↓

Pulmonologists and educators evaluated the patients
who were **eligible for all three inhalers**
(Respimat®, Ellipta®, and Breezhaler®)

↓

First-time demonstration by educators
(all three inhalers in randomized order)

↓

Patients were asked to **choose one inhaler**
and answered the reasons of the choice

↓

The pulmonologists **prescribed the inhaler** accordingly

↓

Second-time demonstration by educators
(only the inhaler of patient's choice)

↓

Patients were asked to use the inhaler independently,
and the educators **evaluated the correctness**

Totally correct / Any error → **Re-education**

End of Visit 1

Visit 2 (One month later)

Patients were asked to use the inhaler independently,
and the educators **evaluated the correctness**

Totally correct / Any error → **Re-education**

↓

Patients completed a questionnaire about
the **adherence**, **satisfaction score**, and
willingness to keep using the inhaler

↓

Meet pulmonologists and **end of Visit 2**

The times of error(s) that
required re-education
in each step of the inhaler were
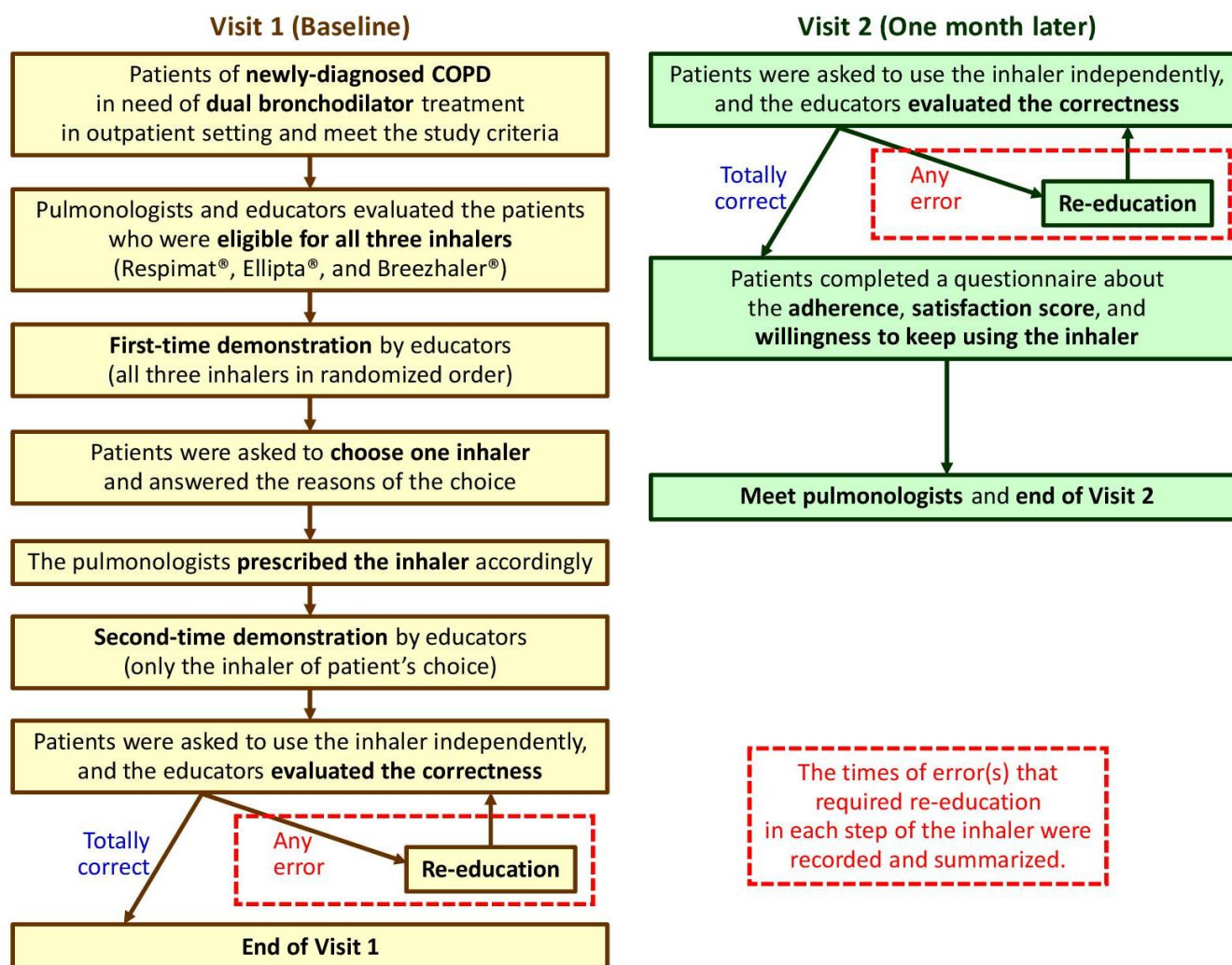recorded and summarized.

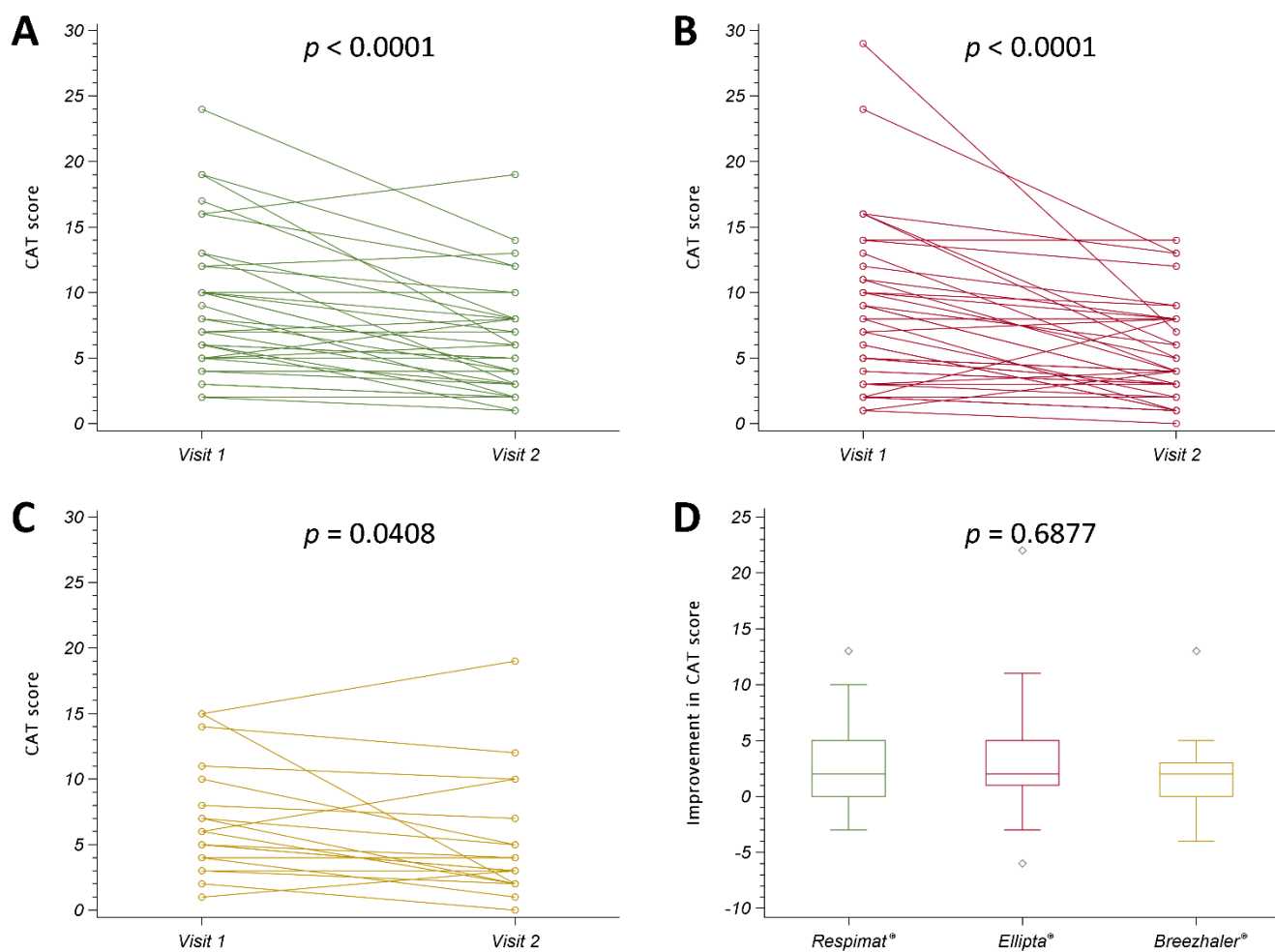**Figure S1.** Flowchart of the study. Abbreviation: CAT = Chronic Obstructive Lung Disease Assessment Test.

Figure S2. Changes in CAT score on visit 1 and visit 2 in the patients initially choosing Respimat® (**A**), Ellipta® (**B**), and Breezhaler® (**C**). (**D**) Comparing the improvement in CAT score in patients initially choosing different inhalers. *P* values were assessed with Wilcoxon signed-rank test (**A,B,C**) or Kruskal-Wallis test (**D**). Abbreviation: CAT = Chronic Obstructive Lung Disease Assessment Test.
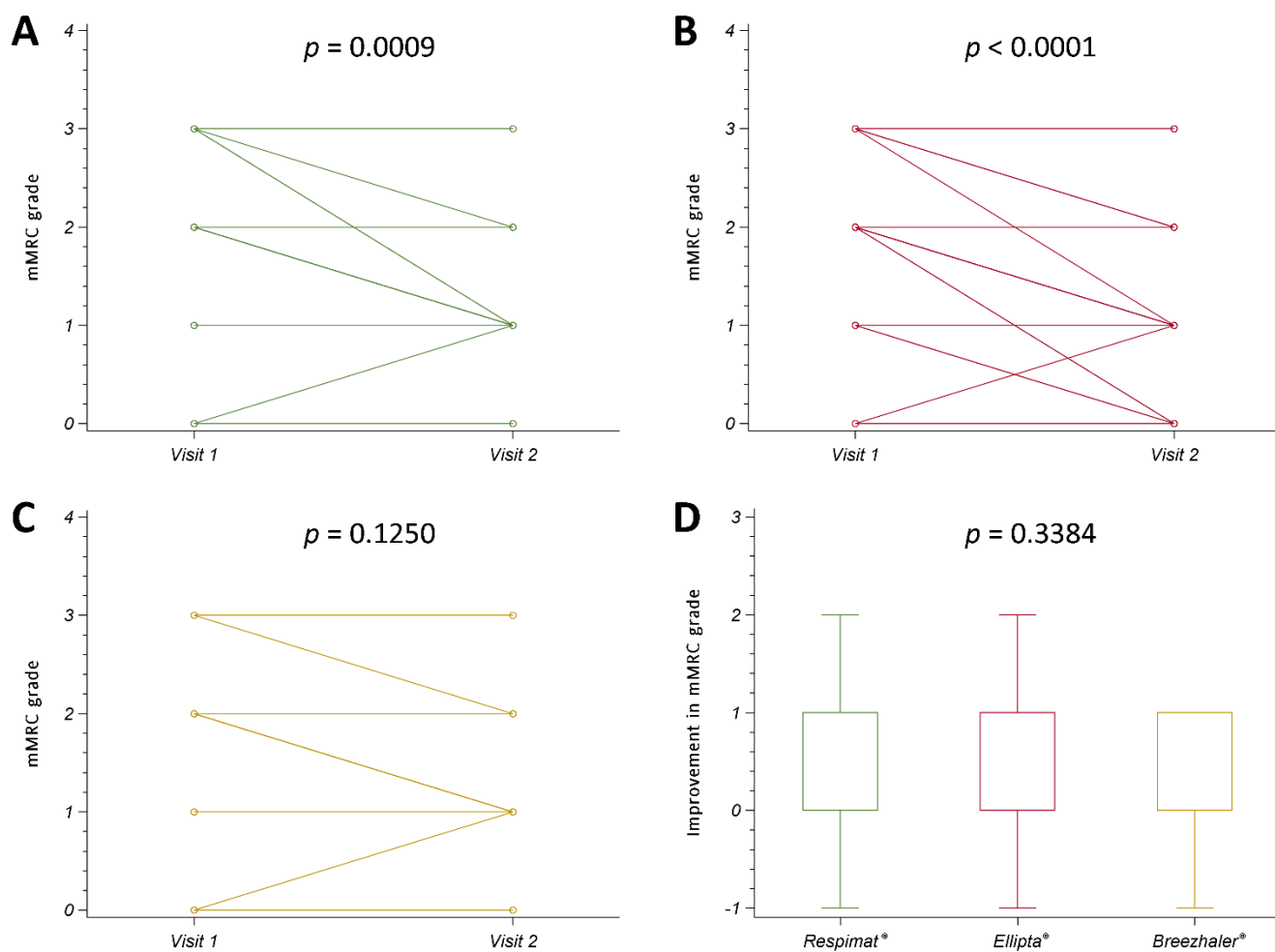
Figure S3. Changes in mMRC grade on visit 1 and visit 2 in the patients initially choosing Respimat® (**A**), Ellipta® (**B**), and Breezhaler® (**C**). (**D**) Comparing the improvement in mMRC grade in patients initially choosing different inhalers. *P* values were assessed with Wilcoxon signed-rank test (**A,B,C**) or Kruskal-Wallis test (**D**). Abbreviation: mMRC = Modified British Medical Research Council.
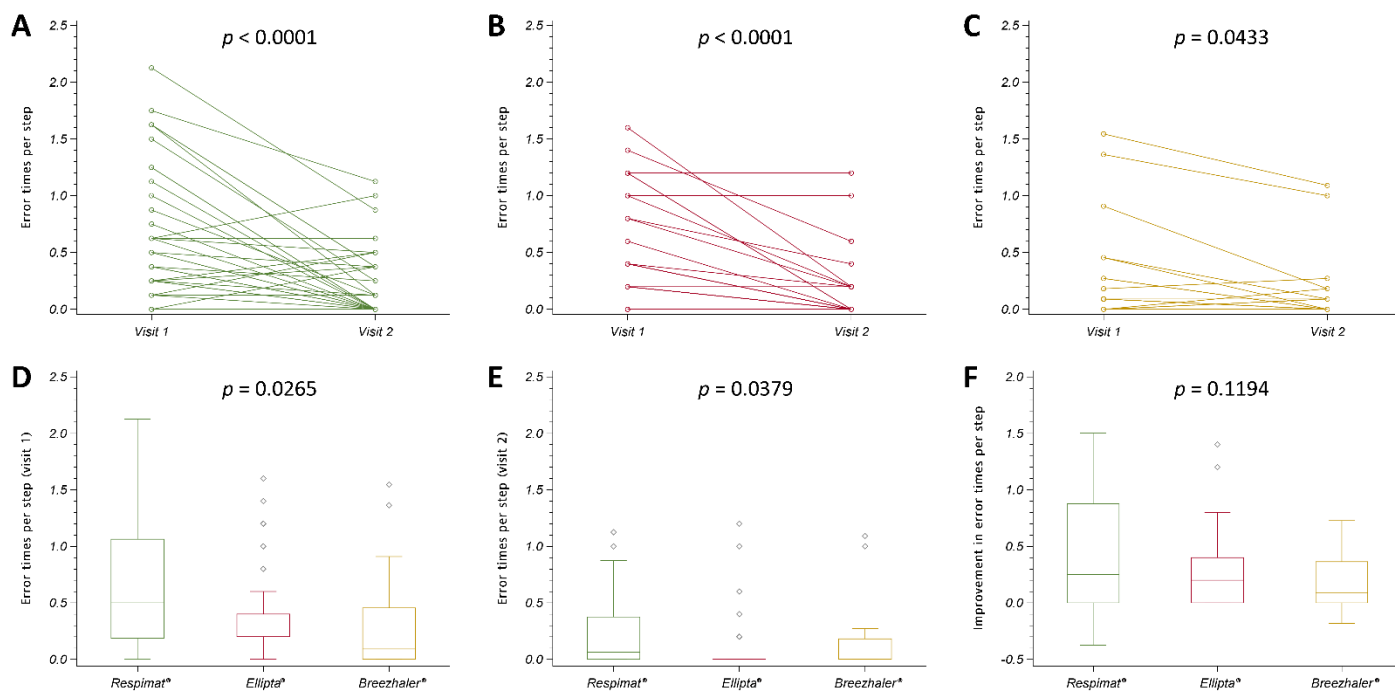
Figure S4. Changes in error times per step on visit 1 and visit 2 in the patients initially choosing Respimat® (**A**), Ellipta® (**B**), and Breezhaler® (**C**). Comparing the error times per step on visit 1 (**D**) and visit 2 (**E**) and the improvement in error times per step in patients initially choosing different inhalers. *P* values were assessed with Wilcoxon signed-rank test (**A,B,C**) or Kruskal-Wallis test (**D,E,F**).

Supplementary Tables

Table S1. Baseline characteristics of all enrolled patients.

Variables	Respimat®	Ellipta®	Breezhaler®	*P* value
Number	43	45	21	
Age (years old)	66 (61-72)	69 (63-72)	66 (64-74)	0.5964
Male	39 (91%)	43 (96%)	20 (95%)	0.6915
Education				
Junior high school or lower	20 (47%)	27 (60%)	11 (52%)	0.2575
Senior high school or higher	23 (53%)	18 (40%)	10 (48%)	
Smoking history				
Current smoker	29 (67%)	21 (47%)	9 (43%)	0.0444
Ex-smoker	10 (23%)	21 (47%)	12 (57%)	
Comorbidity (any)	37 (86%)	42 (93%)	17 (81%)	0.2676
Hand Tremor	0 (0%)	1 (2%)	0 (0%)	>0.999
Old cerebral vascular accident	3 (7%)	3 (7%)	1 (5%)	>0.999
Depression	2 (5%)	1 (2%)	1 (5%)	0.6786
Insomnia	5 (12%)	6 (13%)	4 (19%)	0.7147
Obstructive sleep apnea	1 (2%)	0 (0%)	0 (0%)	0.5872
Cataract	9 (21%)	6 (13%)	3 (14%)	0.6677
Other eye diseases	3 (7%)	1 (2%)	0 (0%)	0.4155
Coronary artery disease / MI	7 (16%)	9 (20%)	5 (24%)	0.7356
Heart failure	0 (0%)	1 (2%)	1 (5%)	0.5031
Hypertension	18 (42%)	26 (58%)	11 (52%)	0.3413
Arrhythmia	6 (14%)	4 (9%)	2 (10%)	0.7898
Diabetes mellitus	8 (19%)	10 (22%)	5 (24%)	0.8651
Dyslipidemia	10 (23%)	7 (16%)	2 (10%)	0.4067
Pulmonary fibrosis	1 (2%)	1 (2%)	0 (0%)	>0.999
Bronchiectasis	1 (2%)	3 (7%)	0 (0%)	0.5252
Chronic kidney disease	0 (0%)	3 (7%)	1 (5%)	0.2427
Cirrhosis	0 (0%)	1 (2%)	0 (0%)	>0.999
Dental problems	7 (16%)	1 (2%)	1 (5%)	0.0369
Malignancy	5 (12%)	5 (11%)	1 (5%)	0.8390
Others	11 (26%)	14 (31%)	5 (24%)	0.8175
Airflow limitation (GOLD grade)				
1 ($FEV_1 \geq 80\%$pred)	10 (23%)	15 (33%)	6 (29%)	0.2471
2 (80%pred > $FEV_1 \geq 50\%$pred)	30 (70%)	24 (53%)	10 (48%)	
3 (50%pred > $FEV_1 \geq 30\%$pred)	3 (7%)	6 (13%)	4 (19%)	
4 ($FEV_1 < 30\%$pred)	0 (0%)	0 (0%)	1 (5%)	

Variables	Respimat®	Ellipta®	Breezhaler®	P value
Baseline CAT score	8 (5-13)	7 (4-11)	6 (4-10)	0.1802
<10	23 (53%)	29 (64%)	15 (71%)	0.3600
≥10	20 (47%)	16 (36%)	6 (29%)	
Baseline mMRC grade	2 (1-2)	2 (1-2)	2 (1-2)	0.7820
<2	17 (40%)	15 (33%)	8 (38%)	0.8406
≥2	26 (60%)	30 (67%)	13 (62%)	
Acute exacerbation (AE) in the past year				
No	37 (86%)	41 (91%)	19 (90%)	0.9302
Mild AE (≥1 time)	2 (5%)	2 (4%)	1 (5%)	
Moderate AE (once)	2 (5%)	0 (0%)	0 (0%)	
≥2 moderate AE or ≥1 severe AE	2 (5%)	2 (4%)	1 (5%)	
GOLD group				
A	11 (26%)	14 (31%)	8 (38%)	0.4215
B	31 (72%)	29 (64%)	12 (57%)	
C	0 (0%)	2 (4%)	0 (0%)	
D	1 (2%)	0 (0%)	1 (5%)	

Data are presented in n (%) or median (interquartile range).

P values were assessed with Fisher's exact test or Kruskal-Wallis test.

Abbreviations: MI = myocardial infarction; pred = predicted; GOLD = Global Initiative for Chronic Obstructive Lung Disease; CAT = COPD Assessment Test; mMRC = Modified British Medical Research Council.

Table S2. Order of demonstration and reasons of choosing the inhaler in patients completed two visits (N = 96).

Variables	Respimat®	Ellipta®	Breezhaler®	*P* value
Order of demonstration				
Respimat® – Ellipta® – Breezhaler®	10 (28%)	8 (20%)	3 (16%)	0.8249
Respimat® – Breezhaler® – Ellipta®	5 (14%)	4 (10%)	3 (16%)	
Ellipta® – Respimat® – Breezhaler®	5 (14%)	8 (20%)	4 (21%)	
Ellipta® – Breezhaler® – Respimat®	5 (14%)	10 (24%)	2 (11%)	
Breezhaler® – Respimat® – Ellipta®	7 (19%)	4 (10%)	4 (21%)	
Breezhaler® – Ellipta® – Respimat®	4 (11%)	7 (17%)	3 (16%)	
Reasons of choosing the inhaler				
Easy to carry	3 (8%)	4 (10%)	5 (26%)	0.1567
Appears more effective	6 (17%)	1 (2%)	2 (11%)	0.0599
Visible inhaled medication	11 (31%)	0 (0%)	12 (63%)	<0.0001
Delicate and textured	1 (3%)	0 (0%)	2 (11%)	0.0499
Prefer the way of use this device	12 (33%)	12 (29%)	9 (47%)	0.3962
Simple using	12 (33%)	37 (90%)	9 (47%)	<0.0001
Others	10 (28%)[*]	0 (0%)	3 (16%)	0.0004

Data are presented in n (%).

P values were assessed with Fisher's exact test.

[*] Six patients preferred soft mist rather than dry powder because of worrying about potential choking sensation or cough induced by dry powder; two patients felt that it was easier to inhale the mist sprayed from Respimat than to forcefully inhale the powder from Ellipta or Breezhaler.

Table S3. Order of demonstration and reasons of choosing the inhaler in all enrolled patients (N = 109).

Variables	Respimat®	Ellipta®	Breezhaler®	*P* value
Order of demonstration				
Respimat® – Ellipta® – Breezhaler®	13 (30%)	9 (20%)	3 (14%)	0.3754
Respimat® – Breezhaler® – Ellipta®	7 (16%)	4 (9%)	5 (24%)	
Ellipta® – Respimat® – Breezhaler®	5 (12%)	8 (18%)	4 (19%)	
Ellipta® – Breezhaler® – Respimat®	6 (14%)	12 (27%)	2 (10%)	
Breezhaler® – Respimat® – Ellipta®	8 (19%)	4 (9%)	4 (19%)	
Breezhaler® – Ellipta® – Respimat®	4 (9%)	8 (18%)	3 (14%)	
Reasons of choosing the inhaler				
Easy to carry	5 (12%)	5 (11%)	6 (29%)	0.1698
Appears more effective	7 (16%)	1 (2%)	3 (14%)	0.0362
Visible	16 (37%)	0 (0%)	12 (57%)	<0.0001
Delicate and textured	1 (2%)	0 (0%)	2 (10%)	0.0493
The way of use	14 (33%)	13 (29%)	10 (48%)	0.3277
Simple using	14 (33%)	40 (89%)	10 (48%)	<0.0001
Others	10 (23%)	0 (0%)	3 (14%)	0.0009

Data are presented in n (%).

P values were assessed with Fisher's exact test.

Table S4. Number of patients with error(s) and times of error(s) that required re-education in all enrolled patients.

Variables	Respimat®	Ellipta®	Breezhaler®	*P* value
Correctness (visit 1)				
Any error	37 (86%)	33 (73%)	13 (62%)	0.0862
Totally correct	6 (14%)	12 (27%)	8 (38%)	
Error times per step (visit 1)	0.5 (0.3-1.3)	0.2 (0-0.4)	0.1 (0-0.3)	0.0039
Critical error (visit 1)	33 (77%)	33 (73%)	13 (62%)	0.4627
Critical preparation error (visit 1)	23 (53%)	13 (29%)	10 (48%)	0.0594
Did not twist the base one half-turn	20 (47%)	N/A	N/A	
Did not open the device correctly	8 (19%)	13 (29%)	4 (19%)	
Did not place capsule in the chamber	N/A	N/A	3 (14%)	
Did not close the mouthpiece	N/A	N/A	3 (14%)	
Did not press button to pierce the capsule	N/A	N/A	7 (33%)	
Critical delivery error (visit 1)	30 (70%)	30 (67%)	9 (43%)	0.1050
Did not seal lips around mouthpiece during inhalation, synchronize actuation and inhalation (Respimat only), inhale slowly (Respimat)/forcefully (Ellipta)/quickly (Breezhaler) and deeply, or hold breath after inhalation	30 (70%)	30 (67%)	9 (43%)	
Did not remove capsule and check for powder residue	N/A	N/A	4 (19%)	

Data are presented in n (%) or median (interquartile range).

P values were assessed with Fisher's exact test or Kruskal-Wallis test.

Table S5. Number of patients with error(s) and times of error(s) that required re-education in patients initially choosing Respimat®.

Steps	Numbers of patients with error(s)			Times of error(s) that required re-education		
	Visit 1	Visit 2	P value[†]	Visit 1	Visit 2	P value[‡]
Step 1: Press the safety catch button while firmly pulling the clear base straight off with your other hand. Be careful not to touch the piercing element.	17 (47%)	9 (25%)	0.0850	34, 0 (0-2)	13, 0 (0-0.5)	0.0017
Step 2: Insert the narrow end of your medication cartridge into the inhaler.	8 (22%)	5 (14%)	0.5414	13, 0 (0-0)	5, 0 (0-0)	0.0859
Step 3: Place the inhaler on a flat surface, and push down firmly until it clicks into place.	9 (25%)	4 (11%)	0.2196	14, 0 (0-0.5)	4, 0 (0-0)	0.0474
Step 4: With the cap closed, turn the clear base in the direction of the arrows on the label until it clicks (half a turn). Push up on the small, circular opening tab until the cap snaps fully open. With the inhaler pointed toward the ground, press the dose release button. Look for a mist. Repeat 3 times until visible mists have been dispensed.	13 (36%)	9 (25%)	0.4432	26, 0 (0-1.5)	11, 0 (0-0.5)	0.0371
Step 5: With the cap closed, turn the clear base in the direction of the arrows on the label until it clicks (half a turn).	16 (44%)	2 (6%)	0.0002	28, 0 (0-1)	3, 0 (0-0)	0.0011
Step 6: Open the hinged cap by pushing up on the small, circular tab until the cap snaps fully open.	7 (19%)	3 (8%)	0.3070	11, 0 (0-0)	4, 0 (0-0)	0.1719
Step 7: Breathe out slowly and fully. Close your lips around the mouthpiece without covering the air vents. Point the inhaler to the back of your throat. While taking a slow, deep breath through your mouth, press the dark gray dose release button and continue to breathe in. Hold your breath for 10 seconds or for as long as comfortable.	24 (67%)	8 (22%)	0.0003	43, 1 (0-2)	16, 0 (0-0)	0.0012
Step 8: Close the cap until you use your inhaler again. Repeat Turn, Open, Press (TOP) for your prescribed dosage.	12 (33%)	6 (17%)	0.1727	17, 0 (0-1)	8, 0 (0-0)	0.0938

Numbers of patients with error(s) are presented in n (%).
Times of error(s) that required re-education are presented in sum, median (interquartile range).
[†] Fisher's exact test.
[‡] Wilcoxon signed-rank test.

Table S6. Number of patients with error(s) and times of error(s) that required re-education in patients initially choosing Ellipta®.

Steps	Numbers of patients with error(s)			Times of error(s) that required re-education		
	Visit 1	Visit 2	*P* value[†]	Visit 1	Visit 2	*P* value[‡]
Step 1: Open the cover of the inhaler. Slide the cover down to expose the mouthpiece. You should hear a "click." The counter will count down by 1 number. You do not need to shake this kind of inhaler. Your inhaler is now ready to use.	11 (27%)	2 (5%)	0.0131	12, 0 (0-1)	2, 0 (0-0)	0.0039
Step 2: While holding the inhaler away from your mouth, breathe out (exhale) fully. Do not breathe out into the mouthpiece. Put the mouthpiece between your lips and close your lips firmly around it. Your lips should fit over the curved shape of the mouthpiece. Take one long, steady, deep breath in through your mouth. Do not breathe in through your nose. Do not block the air vent with your fingers.	26 (63%)	7 (18%)	<0.0001	39, 1 (0-1)	8, 0 (0-0)	<0.0001
Step 3: Remove the inhaler from your mouth and hold your breath for about 3 to 4 seconds (or as long as is comfortable for you).	17 (41%)	5 (13%)	0.0054	21, 0 (0-1)	6, 0 (0-0)	0.0002
Step 4: Breathe out slowly and gently. You may not taste or feel the medicine, even when you are using the inhaler correctly. Do not take another dose from the inhaler even if you do not feel or taste the medicine.	7 (17%)	2 (5%)	0.1549	8, 0 (0-0)	3, 0 (0-0)	0.1875
Step 5: Slide the cover up and over the mouthpiece as far as it will go.	5 (12%)	2 (5%)	0.4321	5, 0 (0-0)	2, 0 (0-0)	0.2500

Numbers of patients with error(s) are presented in n (%).

Times of error(s) that required re-education are presented in sum, median (interquartile range).

[†] Fisher's exact test.

[‡] Wilcoxon signed-rank test.

Table S7. Number of patients with error(s) and times of error(s) that required re-education in patients initially choosing Breezhaler®.

Steps	Numbers of patients with error(s)			Times of error(s) that required re-education		
	Visit 1	Visit 2	*P* value†	Visit 1	Visit 2	*P* value‡
Step 1: Take the blister card from the box.	4 (21%)	2 (11%)	0.6599	4, 0 (0-0)	2, 0 (0-0)	0.5000
Step 2: Separate one of the blisters from the blister card.	4 (21%)	2 (11%)	0.6599	5, 0 (0-0)	2, 0 (0-0)	0.2500
Step 3: Peel open the blister.	5 (26%)	2 (11%)	0.4048	5, 0 (0-1)	2, 0 (0-0)	0.2500
Step 4: remove a capsule from the blister.	3 (16%)	2 (11%)	>0.999	3, 0 (0-0)	2, 0 (0-0)	>0.999
Step 5: Pull off cap and open inhaler	4 (21%)	2 (11%)	0.6599	4, 0 (0-0)	2, 0 (0-0)	0.5000
Step 6: Insert the capsule in the compartment.	3 (16%)	2 (11%)	>0.999	4, 0 (0-0)	2, 0 (0-0)	0.5000
Step 7: Close inhaler and hear a "click".	3 (16%)	2 (11%)	>0.999	4, 0 (0-0)	2, 0 (0-0)	0.5000
Step 8: Hold the inhaler upright. Pierce capsule by firmly pressing both side buttons at the same time. You should hear a noise as the capsule is pierced. Then release side buttons.	6 (32%)	3 (16%)	0.4470	8, 0 (0-1)	3, 0 (0-0)	0.1875
Step 9: Breathe out fully. Do not blow into the inhaler. Place the mouthpiece in your mouth and close your lips firmly around it. Do not press the side buttons. Breathe in quickly and as deeply as you can. During inhalation you will hear a whirring noise. You may taste the medicine as you inhale. Hold your breath for up to 5 seconds.	8 (42%)	8 (42%)	>0.999	18, 0 (0-2)	12, 0 (0-1)	0.4243
Step 10: Check capsule is empty. Open the inhaler to see if any powder is left in the capsule. If there is powder left in the capsule: Close the inhaler and repeat step 9.	4 (21%)	3 (16%)	>0.999	7, 0 (0-0)	3, 0 (0-0)	0.2500
Step 11: Remove empty capsule. Put the empty capsule in your household waste. Close the inhaler and replace the cap.	2 (11%)	2 (11%)	>0.999	2, 0 (0-0)	2, 0 (0-0)	#

Numbers of patients with error(s) are presented in n (%).

Times of error(s) that required re-education are presented in sum, median (interquartile range).

† Fisher's exact test.

‡ Wilcoxon signed-rank test.

The *p* value cannot be assessed due to exactly equal values in both visits.

Table S8. Number of patients with error(s) and times of error(s) that required re-education in two visits.

Variables	Visit 1	Visit 2	*P* value
Correctness			
Any error	73 (76%)	36 (38%)	<0.0001
Totally correct	23 (24%)	60 (63%)	
Error times per step	46.1, 0.3 (0.1-0.7)	15.3, 0.0 (0.0-0.2)	<0.0001‡
Critical error	69 (72%)	28 (29%)	<0.0001
Critical preparation error	38 (40%)	8 (8%)	<0.0001
Did not twist the base one half-turn	16 (44%)	2 (6%)	0.0002
Did not open the device correctly	22 (23%)	7 (7%)	0.0042
Did not place capsule in the chamber	3 (16%)	2 (11%)	>0.999
Did not close the mouthpiece	3 (16%)	2 (11%)	>0.999
Did not press button to pierce the capsule	6 (32%)	3 (16%)	0.4470
Critical delivery error	60 (63%)	25 (26%)	<0.0001
Did not seal lips around mouthpiece during inhalation, synchronize actuation and inhalation (Respimat® only), inhale slowly (Respimat®)/forcefully (Ellipta®)/quickly (Breezhaler®) and deeply, or hold breath after inhalation	60 (63%)	25 (26%)	<0.0001
Did not remove capsule and check for powder residue	4 (21%)	3 (16%)	>0.999

Data are presented in n (%) or sum, median (interquartile range).

P values were assessed with Fisher's exact test except for those labelled with ‡ (using Wilcoxon signed-rank test).

† Fisher's exact test.

‡ Wilcoxon signed-rank test.

Table S9. Factors associated with any critical error in two visits.

Variable	Any critical error (visit 1)		Any critical error (visit 2)	
	Univariate	Multivariable	Univariate	Multivariable
Inhaler chosen initially				
Respimat®	1.5 [0.5-5.0]	1.6 [0.4-5.9]	0.4 [0.1-1.4]	0.4 [0.1-1.6]
Ellipta®	1.8 [0.6-5.8]	2.0 [0.6-7.0]	0.3 [0.1-1.0]	0.3 [0.1-1.1]
Breezhaler®	ref	ref	ref	ref
Age				
<65	ref	ref	ref	ref
≥65	0.9 [0.4-2.4]	0.9 [0.3-2.6]	1.5 [0.6-3.8]	1.3 [0.4-3.7]
Sex				
Female	ref	ref	ref	ref
Male	0.5 [0.1-4.4]	0.3 [0-6.7]	0.8 [0.1-4.7]	0.5 [0.0-7.7]
Education				
Junior high school or lower	ref	ref	ref	ref
Senior high school or higher	0.5 [0.2-1.2]	0.6 [0.2-1.6]	0.6 [0.3-1.6]	0.7 [0.3-2.0]
Smoking history				
Never smoker	ref	ref	ref	ref
Ever smoker	1.3 [0.2-7.5]	2.5 [0.2-33.6]	2.1 [0.2-19.2]	3.0 [0.1-81.1]
Comorbidity				
No	ref	ref	ref	ref
Yes	0.6 [0.1-3.1]	0.4 [0.1-2.6]	1.7 [0.3-8.7]	1.7 [0.3-10.7]
Airflow limitation (GOLD grade)				
1 or 2 ($FEV_1 \geq 50\%$pred)	ref	ref	ref	ref
3 or 4 ($FEV_1 < 50\%$pred)	1.0 [0.3-3.4]	1.1 [0.3-5.2]	2.9 [0.9-9.3]	1.5 [0.4-6.4]
Acute exacerbation within a year				
No	ref	ref	ref	ref
Yes	0.8 [0.2-3.3]	0.6 [0.1-3.4]	3.5 [0.9-14.1]	3.0 [0.5-16.3]
CAT score (visit 1)				
<10	ref	ref	ref	ref
≥10	2.4 [0.9-6.7]	2.3 [0.8-7.0]	1.9 [0.8-4.8]	1.7 [0.6-4.6]

Data are analysed by logistic regression and presented in odds ratio (95% confidence interval).

Abbreviations: pred = predicted; GOLD = Global Initiative for Chronic Obstructive Lung Disease; CAT = COPD Assessment Test.

Table S10. Factors associated with any critical error in visit 1 (all enrolled patients).

Variable	Any critical error (visit 1)	
	Univariate	Multivariable
Inhaler chosen initially		
Respimat®	2.0 [0.7-6.3]	2.0 [0.6-7.0]
Ellipta®	1.7 [0.6-5.1]	1.8 [0.6-5.8]
Breezhaler®	ref	ref
Age		
<65	ref	ref
≥65	1.0 [0.4-2.3]	1.0 [0.4-2.5]
Sex		
Female	ref	ref
Male	0.4 [0.0-3.6]	0.3 [0.0-5.4]
Education		
Junior high school or lower	ref	ref
Senior high school or higher	0.6 [0.2-1.3]	0.6 [0.3-1.6]
Smoking history		
Never smoker	ref	ref
Ever smoker	1.1 [0.2-5.8]	2.6 [0.2-34.6]
Comorbidity		
No	ref	ref
Yes	0.8 [0.2-3.0]	0.6 [0.1-2.7]
Airflow limitation (GOLD grade)		
1 or 2 (FEV_1 ≥ 50%pred)	ref	ref
3 or 4 (FEV_1 < 50%pred)	0.9 [0.3-3.3]	1.0 [0.3-4.4]
Acute exacerbation within a year		
No	ref	ref
Yes	1.2 [0.3-4.6]	1.0 [0.2-4.7]
CAT score (visit 1)		
<10	ref	ref
≥10	2.1 [0.8-5.2]	1.8 [0.7-4.9]

Data are analysed by logistic regression and presented in odds ratio (95% confidence interval).

* *P* value < 0.05.

Abbreviations: pred = predicted; GOLD = Global Initiative for Chronic Obstructive Lung Disease; CAT = COPD Assessment Test.