

# Inhalation errors due to device switch in patients with chronic obstructive pulmonary disease and asthma: critical health and economic issues

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**Background:** Different inhalation devices are characterized by different techniques of use. The untrained switching of device in chronic obstructive pulmonary disease (COPD) and asthma patients may be associated with inadequate inhalation technique and, consequently, could lead to a reduction in adherence to treatment and limit control of the disease. The aim of this analysis was to estimate the potential economic impact related to errors in inhalation in patients switching device without adequate training.

**Methods:** An Italian real-practice study conducted in patients affected by COPD and asthma has shown an increase in health care resource consumption associated with misuse of inhalers. Particularly, significantly higher rates of hospitalizations, emergency room visits (ER), and pharmacological treatments (steroids and antimicrobials) were observed. In this analysis, those differences in resource consumption were monetized considering the Italian National Health Service (INHS) perspective.

**Results:** Comparing a hypothetical cohort of 100 COPD patients with at least a critical error in inhalation vs 100 COPD patients without errors in inhalation, a yearly excess of 11.5 hospitalizations, 13 ER visits, 19.5 antimicrobial courses, and 47 corticosteroid courses for the first population were revealed. In the same way, considering 100 asthma patients with at least a critical error in inhalation vs 100 asthma patients without errors in inhalation, the first population is associated with a yearly excess of 19 hospitalizations, 26.5 ER visits, 4.5 antimicrobial courses, and 21.5 corticosteroid courses. These differences in resource consumption could be associated with an increase in health care expenditure for INHS, due to inhalation errors, of €23,444/yr in COPD and €44,104/yr in asthma for the considered cohorts of 100 patients.

**Conclusion:** This evaluation highlights that misuse of inhaler devices, due to inadequate training or nonconsented switch of inhaled medications, is associated with a decrease in disease control and an increase in health care resource consumption and costs.

**Keywords:** inhalers, devices, switch, training, errors, costs, asthma, COPD

## Introduction

Asthma and chronic obstructive pulmonary disease (COPD) have relevant and increasing epidemiological and economic impact worldwide,<sup>1-4</sup> with costs increasing with the worsening of the pathologies.<sup>5,6</sup>

As a relevant proportion of patients affected by asthma and COPD are treated with inhaled drugs,<sup>7</sup> an appropriate inhaler technique is necessary to obtain and maintain an effective management of these pathologies. As stated by the Guide For Asthma Management and Prevention (updated in 2015),<sup>8</sup> up to 80% of asthma patients do not use their inhaler adequately, and this could lead to poorer symptom control and to a

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higher level of exacerbations. The importance of the choice of inhaler in the treatment of COPD patients is also underlined by the 2015 Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines that point out the importance of effective drug delivery and training in inhaler techniques.<sup>9</sup>

The importance of inhaler devices for the effectiveness of inhaled drugs in the treatment of asthma and COPD is also recognized and underlined by the European Medicines Agency (EMA), which only considers approving the generic version of inhaler products if *in vitro* studies lead to a full therapeutic interchangeability; otherwise, lung deposition test and eventually, pharmacodynamics or even clinical studies might be required. EMA clearly stated that orally inhaled products have to be considered not as “generics” but as “hybrids”.<sup>10</sup>

A recent Italian consensus document of the Italian Society of Allergy, Asthma and Clinical Immunology and the Italian Society of Respiratory Medicine recommend that patients who are familiar and stabilized with one inhaler should not be switched to a different one without their involvement and proper training. Inappropriate inhaler use and a low adherence to inhaled treatments could lead to poorer asthma and COPD control, and switching devices without suitable training could worsen these problems.<sup>11</sup>

Because different inhalation devices require very different techniques of use, the switch of device without training in COPD and asthma patients may be associated with a poor inhalation technique with critical errors and, consequently, in a reduction of adherence and worsening in disease control. An Italian study<sup>12</sup> investigated the prevalence of inhalation errors and related health care resource consumption in a large population of patients with COPD and asthma.

The aim of this analysis was to estimate the possible economic impact on the Italian National Health Service (INHS) due to errors in inhalation in patients switching device without adequate training.

## Materials and methods

An Italian observational, multicenter, cross-sectional study (The GENEBI Project [AIPO, Gruppo Educazionale for NEBulizers and Inhalers]) performed in 2008 conducted by Melani et al<sup>12</sup> investigated the prevalence of inhaler misuse and health care resource consumption in a large population of adult patients experienced in the use of inhalers which referred to chest clinics throughout Italy. A total of 1,664 patients (adolescents and adult outpatients) being treated at 24 chest clinics around Italy were enrolled, most of whom were affected by asthma (42%, mean age 51 years) and COPD (52%, mean age 70 years). All patients attended the clinics

and used inhalers regularly. Mean forced expiratory volume in 1 second was  $60 \pm 20$  in COPD patients and  $80 \pm 23$  in asthma patients. Regarding inhaler education in the selected population, one-third of patients had no education, another one-third received verbal instructions, and the latter one-third received practical demonstration of inhaler use. A detailed checklist of the inhalation technique errors is reported in the paper of Melani et al.<sup>12</sup> The results of this study highlight higher health care resource consumption in patients experiencing critical inhaler errors vs patients without critical errors. Particularly, significantly higher rates of hospitalizations ( $P=0.001$ ), emergency room (ER) visits ( $P<0.001$ ), and pharmacological treatments (steroids and antimicrobials,  $P<0.001$ ) were observed for both pathologies (Table 1). The reported differences in resource consumption remain significant even after considering asthma and COPD separately.

For the aim of the present analysis, these differences in resource consumption were monetized from the INHS perspective by multiplying the differences in average resource consumption for their unitary cost in charge to INHS. National diagnosis related groups (DRGs) tariffs were considered for hospitalizations<sup>13</sup> and ER visits,<sup>14</sup> and the public price for drug consumption (average prices of the most widely used drugs were used to estimate the cost per course of treatment). Unitary costs considered for the base case analysis are shown in Table 2.

In order to test the results, a sensitivity analysis was performed considering Italian real-world data for COPD and asthma hospitalizations; particularly, for COPD, a cost of €3,985/hospitalization<sup>5</sup> was considered while, for asthma, a cost of €2,640.75/hospitalization (adapted from Dal Negro et al<sup>15</sup>) was considered. As highlighted by the unitary costs of hospitalizations derived from real-world evidences, particularly for some pathologies (ie, COPD), hospitalization-related costs could be higher than the standard DRGs tariffs and could represent valid data to perform a scenario analysis. This study was an economic evaluation based on another study (Melani et al<sup>12</sup>), therefore ethical approval and patients consent were not requested.

## Results

Comparing a population of 100 COPD patients with at least a critical error in inhalation with 100 COPD patients without errors in inhalation, the first population was associated with an excess of 11.5 hospitalizations, 13 ER visits, 19.5 antimicrobial courses, and 47 corticosteroids courses. In the same way, when 100 asthma patients with at least a critical error in inhalation, were compared with 100 asthma patients without errors in inhalation, the first population was associated with

**Table 1** Resource consumption associated with inhalation errors

	COPD (n=864)				Absolute difference in health care resource use/100 patients	Asthma (n=703)				Absolute difference in health care resource use/100 patients
	At least a critical inhaler error*		% difference in health care resource use due to critical inhaler errors	At least a critical inhaler error*		% difference in health care resource use due to critical inhaler errors				
	Yes	No		Yes			No			
Hospital admissions, %										
Never	55	62				76	86			
I	26	23	3		3	13	9	4		4
2–3 <sup>a</sup>	16	11	5		12.5	9	3	6		15
>3 <sup>b</sup>	3	4	–1		–4	2	2	0		0
Total variation errors vs no errors/100 patients					11.5					19
Emergency department visits, %										
Never	64	71				69	81			
I	24	22	2		2	16	11	5		5
2–3 <sup>a</sup>	10	4	6		15	10	3	7		17.5
>3 <sup>b</sup>	2	3	–1		–4	5	4	1		4
Total variation errors vs no errors/100 patients					13					26.5
Antimicrobial courses, %										
Never	20	30				34	41			
I	31	29	2		2	25	30	–5		–5
2–3 <sup>a</sup>	33	26	7		17.5	17	18	–1		–2.5
>3 <sup>b</sup>	15	15	0		0	14	11	3		12
Total variation errors vs no errors/100 patients					19.5					4.5
Corticosteroid courses, %										
Never	29	37				27	35			
I	19	22	–3		–3	35	30	5		5
2–3 <sup>a</sup>	26	30	–4		–10	19	22	–3		–7.5
>3 <sup>b</sup>	26	11	15		60	19	13	6		24
Total variation errors vs no errors/100 patients					47					21.5

**Notes:** <sup>a</sup>Considered as 2.5 admissions/courses of treatment, <sup>b</sup>considered as 4 admissions/courses of treatment. \*Reprinted from *Respir Med*, 2011;105(6), Melani AS, Bonavia M, Cilenti V, et al, Inhaler mishandling remains common in real life and is associated with reduced disease control, pages 930–938,<sup>12</sup> Copyright © 2011, with permission from Elsevier.

**Abbreviation:** COPD, chronic obstructive pulmonary disease.

**Table 2** Unitary costs of health care resources for base case analysis

	COPD			Asthma	
	Unitary cost (€)	Source		Unitary cost (€)	Source
Hospital admissions	1,600.00	DRG 88: chronic obstructive pulmonary disease <sup>13</sup>	1,832.00	DRG 97: bronchitis and asthma age >17 years without cc <sup>13</sup>	
Emergency department visits	344.26	Ministry of Health: Mattoni SSN Project: Emergency Room and I18 System: <sup>14</sup> acute pulmonary condition	344.26	Ministry of Health: Mattoni SSN Project: Emergency Room and I18 System: <sup>14</sup> IRDRG 235380: acute pulmonary condition	
Antimicrobial courses <sup>a</sup>	13.04	<sup>b</sup> Public price per pack: levofloxacin: 500 mg/day 10 days; pack 5 tabs 500 mg €6.25 or ciprofloxacin: pack 6 tabs 500 mg, 500 mg BID 7 days €6.79	13.04	<sup>b</sup> Public price per pack: levofloxacin: 500 mg/day 10 days; pack 5 tabs 500 mg €6.25 or ciprofloxacin: 6 tabs 500 mg, 500 mg BID 7 days €6.79	
Corticosteroid courses <sup>a</sup>	6.68	<sup>b</sup> Public price per pack: prednisone: pack 25 mg 10 tabs €5.10 followed by pack 5 mg 10 tabs €1.58	5.34	<sup>b</sup> Public price per pack: prednisone: pack 25 mg 10 tabs €5.10 followed by pack 5 mg 10 tabs €1.58 or methylprednisolone pack 40 mg 1 vial/day €4	

**Note:** <sup>a</sup>For drugs, average values of the most widely used drugs were used to estimate the cost per course of treatment. <sup>13</sup>Italian Medicines Agency. Trasparenza List: All public prices for drugs, except for methylprednisolone. Rome: Italian Medicines Agency; 2015. Available from: [http://www.agenziafarmaco.gov.it/sites/default/files/Elenco\\_farmaci\\_equivalenti\\_Principio\\_attivo\\_15.05.2015.pdf](http://www.agenziafarmaco.gov.it/sites/default/files/Elenco_farmaci_equivalenti_Principio_attivo_15.05.2015.pdf). Methylprednisolone public price is available at Farmadati which is a database containing all the information about the medicines for human or veterinary use registered in Italy, equivalent medicines, homeopathic and parapharmaceutical products; available from: <http://www.farmadati.it>.

**Abbreviations:** BID, twice a day; cc, comorbidities and complications; COPD, chronic obstructive pulmonary disease; DRG, Diagnosis Related Group; IRDRG, International-Refined Diagnosis Related Group.

an excess of 19 hospitalizations, 26.5 ER visits, 4.5 anti-microbial courses, and 21.5 corticosteroids courses. These differences in resource consumption were associated with a yearly incremental health care cost for 100 patients, due to inhalation errors, of €23,444 in COPD patients and €44,104 in asthma patients (Table 3).

The most important health care cost differences between patients with and without critical inhaler errors are related to hospitalizations (accounting for about 78% of the total difference in both pathologies) and ER visits (accounting for about 20% of the total difference).

If the Italian real-world cost data for hospitalizations was considered (already reported), as sensitivity analysis, the incremental cost per 100 patients due to critical inhaler errors increased to €50,871 in COPD patients and to €59,471 in asthma patients, with hospitalizations and ER visits being the most significant cost drivers, accounting for almost the total expenditure difference.

## Discussion

Inhaled therapies have always been central to the treatment of asthma and COPD, and the Global Initiative for Asthma guidelines consider the ability to deliver drugs directly to airways a major advantage of inhaled treatment.<sup>8</sup>

Inhaler errors represent a critical issue in the management of COPD and asthma patients, as they are associated with worsening in disease control, increased rate of exacerbation in COPD patients, increased health care resource consumption, and consequently, increased health care expenditure.

The importance of correct inhalation technique and the correlation between the switch of inhaler therapy, and a worsening in the pathology control, a deterioration in the quality of life of patients, and an increase in resource consumption are widely recognized.<sup>16–21</sup>

With patents expiring for some of the most widely used inhaled drugs, several analogs of branded inhaled corticosteroids/long-acting  $\beta$ -adrenoceptor agonists fixed-dose combinations are entering the market with different inhaler devices.

To improve inhaler techniques and reduce critical inhalation errors, adequate training is essential when a patient is switched from one device to another.<sup>18,22–29</sup>

A very recent study<sup>30</sup> highlighted the possible issues related to nonconsented inhaler switches without adequate training in COPD patients and the relevance of the economic implications of inappropriate switching without performing a specific economic analysis.

The present analysis, which applies Italian health care costs to differences in resource consumption between patients with and without critical errors in the use of inhaler devices reported in a real-world study, highlights the relevance of health care cost increases related to errors in inhalation techniques. Costs ranged from approximately €200 to €600/patient/year (which represented, even without taking into consideration the clinical consequences, a relevant part of the yearly cost of the most widely used inhaled drugs).

While it may appear to be a benign decision, changing or switching inhaler device can have a large effect on disease control. Because different devices require very different techniques for use, switching inhaler device (in particular, nonconsensual switches) may be associated with a poor inhalation technique unless patients are carefully counseled.

It is therefore crucial to consider all relevant costs, including those related to training sessions, additional consultations, repeated prescriptions, and management of acute events: these costs may contribute to reduce the potential benefit coming from switching inhalers.<sup>11</sup>

**Table 3** Incremental yearly expenditure per 100 hypothetical patients with vs without critical inhaler errors

	COPD			Asthma		
	Yearly absolute difference in health care resource use for 100 patients with vs without errors	Unitary cost (€)	Yearly difference in health care cost for 100 patients (€)	Yearly absolute difference in health care resource use for 100 patients with vs without errors	Unitary cost (€)	Yearly difference in health care cost for 100 patients (€)
Hospital admissions	11.5	1,600.00	18,400.00	19	1,832.00	34,808.00
Emergency department visits	13	344.26	4,475.38	26.5	344.26	9,122.89
Antimicrobial courses	19.5	13.04	254.28	4.5	13.04	58.68
Corticosteroid courses	47	6.68	313.96	21.5	5.34	114.81
Total health care costs			23,443.62			44,104.38
Difference/patient/year			234.44			441.04

**Abbreviation:** COPD, chronic obstructive pulmonary disease.

These economic considerations, associated with previously reported clinical issues related to the untrained switch of inhaler devices, emphasize the importance of carefully considering switching, with particular regard to those patients who are familiar and stabilized on one type of inhaler.<sup>11</sup>

## Author contributions

All authors contributed toward data analysis, drafting and critically revising the paper and agree to be accountable for all aspects of the work.

## Disclosure

AR and DPR are consultants for AstraZeneca. CM is a consultant for AstraZeneca and GlaxoSmithKline. This study was funded by an unrestricted grant from AstraZeneca, Italy. The authors report no other conflicts of interest in the work.

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