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# Inhaler mishandling is very common in patients with chronic airflow obstruction and long-term home nebuliser use

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## Summary

Inhalers and nebulisers are devices used for delivering aerosolised drugs in subjects with Chronic Airflow Obstruction (CAO).

This multicentre, cross-sectional observational study was performed in a large population of outpatients with CAO regularly using home aerosol therapy and referring to chest clinics. The aims of the study were to compare the characteristics of the group of subjects with CAO who were using home nebulisers but also experienced with inhalers vs. those only using inhalers and to investigate whether the first group of subjects was particularly prone to inhaler misuse.

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Information was gained evaluating the responses to a standardised questionnaire on home aerosol therapy and the observations of inhaler technique.

We enrolled 1527 patients (58% males; mean  $\pm$  SE; aged  $61.1 \pm 0.4$  years; FEV1%pred  $69.9 \pm 0.6$ ; 51% and 44% respectively suffering from COPD and asthma) who were only inhaler users (OIU group) and 137 (85% males; aged  $67.7 \pm 1.3$  years; FEV1%pred  $62.3 \pm 2.9$ ; 60% and 23% respectively suffering from COPD and asthma) who were using both nebulisers and inhalers (NIU group).

Nebuliser users were older, had more severe obstruction, related symptoms and health care resources utilisation. Nebulisers users performed more critical inhalers errors than those of the OIU group (49% vs. 36%;  $p = 0.009$ ).

We conclude that our patients with CAO and regular nebuliser treatment had advanced age, severe respiratory conditions and common inhaler misuse.

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## Introduction

Aerosolised drugs are the mainstay of asthma and chronic obstructive pulmonary disease (COPD) pharmacological management. The production of therapeutic aerosols requires specific delivery devices, such as hand-held inhalers and nebulisers. The most currently used guidelines for asthma<sup>1,2</sup> and COPD<sup>3,4</sup> management, as well as for nebuliser<sup>5-7</sup> and aerosol therapy<sup>8</sup> do not provide sufficient, specific guidance on the selection of the most appropriate device. Consequently, and accordingly to the local habits, large variability exists among countries about the diffusion of different delivery devices for aerosol therapy.<sup>9,10</sup>

Nebulisers are cumbersome, time-consuming and less convenient than inhalers.<sup>5</sup> However, many adult patients, mainly elderly, use nebulisers at home not only for occasional episodes of acute severe bronchospasm but even for regular long-term utilisation.<sup>11-14</sup> We have previously investigated the device preference in a group of 636 Italian patients with chronic lung diseases who were regularly using nebulisers at home, but were also experienced with inhalers: half of these subjects felt that nebulisers were more effective than inhalers and preferred them.<sup>13</sup> A systematic review does not confirm that nebulisers are more effective than inhalers; when appropriate doses of drugs are compared and devices are optimally used, inhaler and nebulisers are clinically equivalent.<sup>8</sup> So, the perception of greater benefit of nebulisers over inhalers has been previously attributed to undemonstrated adjunctive properties, such as the capability of reducing the thickness of sputum, or a placebo effect of the mist, perhaps associated to the common use of nebulisers in emergency room departments<sup>15</sup> and hospital.<sup>16</sup> We hypothesized that another possibility explaining because some patients consider nebulisers as the most effective delivery device for aerosol therapy is the poor inhaler technique. Critical inhaler mishandlings may be responsible of inconsistent lung drug delivery. To our knowledge, no previous study did investigate this hypothesis, even if it is known that a proper inhaler use is a challenge for many subjects.<sup>17</sup>

The GENEBI Project ([ClinicalTrials.gov](http://ClinicalTrials.gov) identifier: NCT0925-0586) is a study performed in 2008 by the AIPO (Associazione Italiana Pneumologi Ospedalieri) Educational Group for evaluating home aerosol practice in a large sample of experienced patients with chronic airflow

obstruction (CAO) referring to chest clinics. Data obtained from this survey have shown that mishandling remains common in real life even with the newer more user-friendly inhalers.<sup>18</sup> Most of the enrolled patients were Only Inhaler Users (OIU group), but a subset was also using nebulisers (Nebuliser and Inhaler Users = NIU group).

The primary outcomes of the present study were to investigate 1) whether subjects of the NIU group performed more critical inhaler errors than those of the OIU group; 2) the characteristics of subjects of the NIU group in comparison with the OIU population. The secondary outcome was to analyse current nebuliser practice in Italy.

## Materials and methods

The GENEBI Project was a cross-sectional, observational study carried out in 24 chest clinics throughout Italy to evaluate home aerosol practice. These centers were located at different latitudes across Italy and included highly urbanized as well as rural areas, thus encompassing a wide range of geographical and environmental settings. The study was performed from July to September 2008. The study was conducted in accordance with the declaration of Helsinki. The study protocol was approved by the ethics committee of the participating centers.

## Study population

During the study period all adult (age greater than 18 years) outpatients with spirometrically confirmed Chronic Airflow Obstruction (CAO), attending one of the centers for a scheduled visit and practicing aerosol therapy regularly at home were considered eligible for participation. To the aim of the present survey, regular use was defined as prescription of aerosol therapy at least once daily for 4 weeks in the 3 months before the enrollment and self-reports of effective utilisation. To meet the busy clinical practice of chest clinics with limited time, but to minimize selection bias, investigators were required to enroll their first two consecutive eligible patients in each working day. The enrollment always occurred after full explanation of the study and written informed consent; no one refused to participate to the survey.

## Method

We have already described the study method in detail.<sup>18</sup> Briefly, home aerosol practice was evaluated using a standardised questionnaire, which included a self- and an investigator-compiled part, prepared by the AIPO Educational Group members. Each self-filled part had queries about home aerosol practice with source and modalities of education received. It also included 26 items, mostly ( $N = 23$ ) of closed type, about nebuliser equipment, use, maintenance and subject's opinion and preference for different delivery devices. The physician-filled part evaluated primary respiratory diagnosis, the prescribed devices and the drugs used. On enrollment, subjects underwent a spirometry performed according to the accepted guidelines. Then each patient demonstrated the inhalation technique with all used devices to the investigator in a quiet area using a placebo device. Patients were asked to use their aerosol just as if they would be at home. For each center, a single trained investigator evaluated the modalities of inhaler use; to standardize their findings, periodic meetings were held with all the participating observers. Investigators were blinded to the results of the self-administered questionnaire when recording the mode of inhalation. All observations of inhaler use were reported in accordance to a standardised device checklist, previously described, obtained from review of literature and discussed in detail.<sup>18</sup> This checklist included a variable number of steps for each inhaler focusing the analysis on critical errors (see their list in Tables 2 and 3), which are likely to make therapy aerosol useless.

## Statistical analysis

Statistical analysis was performed using generalized linear models (Stata 9, [www.stata.com](http://www.stata.com)) with Gaussian or

binomial/logit family, as appropriate, including the center as a cluster (which corresponds to add it as a random effect variable) to obtain a robust standard error. Data are presented as the mean  $\pm$  SE unless otherwise specified. A  $p$ -value of  $<0.05$  for a two-tailed test was considered as significant.

## Results

The GENEPI Project included 1527 subjects with CAO who were only inhaler users (OIU group) and 196 who were regularly using nebulisers. Of the latter, 22, 18 and 19 subjects, respectively, had used inhalers in the past, were using them occasionally, or never; the remaining 137 subjects (the NIU group) were utilizing one or more inhalers regularly. Our data about nebuliser users only came out from 14 of the 24 centers participating to the present study; data about nebuliser users who were also utilising inhalers came out from 12 of the 24 centers participating to the present study. The demographic and the clinical characteristics among groups of nebuliser users did not differ (data not shown). The subjects of the NIU group were older (mean age  $\pm$  SE of  $67.7 \pm 1.3$  vs.  $61.1 \pm 0.4$ ;  $p < 0.0001$ ) and with more severe obstruction (mean FEV1% pred  $\pm$  SE of  $62.3 \pm 2.9$  vs.  $69.9 \pm 0.6$ ;  $p < 0.0001$ ; mean FEV1/VC  $\pm$  SE of  $61.0 \pm 1.2$  vs.  $66.3 \pm 0.4$ ;  $p < 0.0001$ ) than those of the OIU group. Other demographic and clinical characteristics of the OIU and NIU groups are described in Table 1: the NIU group also had a greater percentage of males, subjects with COPD, related symptoms (breathlessness episodes, sleep disturbances, limitations in everyday life, feeling of inadequate respiratory disease control) in the last month prior to the study and unscheduled health care resources (hospitalisations, emergency room visits and antibiotic courses) utilisation in the last year prior to enrollment ( $p < 0.001$

**Table 1** Some demographic and clinical characteristics of subjects who were only using inhalers (OIU group) and those using both nebulisers and inhalers (NIU group).

Characteristic	NIU group, n = 137	OIU group, n = 1527	Difference
Gender, %			
• Males	85	58	P < 0.0001
• Females	15	42	
Main respiratory diagnosis, %			
• COPD	51	60	P < 0.0001
• Asthma	44	23	
• Others	5	17	
Smoking status, %			
• Smokers	16	15	NS
• Ex-smokers	59	52	
• Never smokers	25	33	
Educational level, %			
• Fifth grade or less	55	42	P < 0.0001
• Sixth to eighth grade	25	23	
• High school	11	27	
• University	8	8	
Subjects with resting oxyhaemoglobin saturation <90% whilst breathing air, %	22	7.5	P < 0.0001

Table 1 (continued)

Characteristic	NIU group, n = 137	OIU group, n = 1527	Difference
Subjects reporting sputum >3 months per year in the 2 last years, %	72	41	P < 0.0001
Diskus users, %	30	28	NS
HandiHaler users, %	36	31	NS
Aerolizer users, %	5	5	NS
MDIs users, %	50	50	NS
Turbohaler users, %	21	22	NS
Hospitalisations in the last year, %			
• Never	38	72	P < 0.0001
• One	33	18	
• More than one	29	10	
Antibiotic courses in the last year, %			
• Never	15	34	P < 0.0001
• One	20	31	
• More than one	65	35	
Emergency room visits in the last year, %			
• Never	40	76	P < 0.0001
• One	32	16	
• More than one	28	8	
Limited doing desired everyday life due to respiratory symptoms in the last month, %			
• Always or most of time	50	25	P < 0.0001
• Sometimes	31	27	
• Seldom or never	19	48	
Breathlessness episodes in the last month, %			
• More times a day	25	17	P < 0.0005
• At least once a day	13	13	
• A few times a week	24	15	
• Seldom or never	38	55	
Sleep disturbances due to respiratory symptoms in the last month, %			
• Always	6	5	P < 0.001
• Often	21	16	
• Sometimes (once a week)	31	22	
• Seldom or never	42	57	
Rate respiratory disease control in the last month, %			
• Not at all	12	4	P < 0.001
• Poorly controlled	17	14	
• Somewhat controlled	27	22	
• Well or fully controlled	44	59	

for all these variables). After adjustment for age, the difference in gender and primary respiratory diagnosis lost significance, but the NIU group continued to show greater airflow obstruction (FEV1/VC%:  $p = 0.036$ ), more symptoms and health care resources utilisation ( $p < 0.05$  for all these variables).

We have a total of 2288 records of inhaler technique (data of 31 subjects were lacking). The subjects of the NIU and OIU group performed, respectively, 154 and 2134 of these observations. The results are shown in Tables 2 and 3. Critical mistakes were distributed among users of all the inhalers for both groups. Overall, the subjects of the NIU group performed at least a critical inhaler error more often than those of the OIU group (49% vs. 36%;  $p = 0.009$ ). The percentage of subjects of the OIU group reporting some instruction by health caregivers at first inhaler prescription

was greater than that of the NIU group (85% vs. 65%;  $p < 0.001$ ); similarly, as compared to the NIU population, a greater percentage of subjects of the OIU group had received a physical demonstration of inhaler use at first prescription (59% vs. 43%;  $p = 0.006$ ) and at least a practical check of inhaler technique at follow-up visits (50% vs. 38%;  $p = 0.01$ ). Even after adjustment for age, device and any type of instruction by health caregivers, the frequency of critical inhaler errors for the NIU group remained significantly greater than for the OIU group ( $p = 0.03$ ). The percentage of subjects of the NIU group with at least a critical inhaler error who, respectively, considered nebulisers more effective than inhalers (56% vs. 20%; OR  $3.8 \pm 1.1$ ;  $p < 0.001$ ) and preferred the first device (48% vs. 24%; OR  $3.4 \pm 1.3$ ;  $p = 0.001$ ) was greater than for those without any critical inhaler error.

**Table 2** Errors of inhaler technique with MDIs for the group of subjects using only inhalers (OIU group) and that using both inhalers and nebulisers (NIU group).

Checklist of inhalation technique errors	NIU group	OIU group	P-value
Failure to remove cap, <sup>a</sup> %	0	0	NS
Not shaking the inhaler, %	45	36	NS
Hold the mouthpiece inhaler between open lips, %	35	18	$P < 0.001$
Not holding the inhaler in the upright position, %	12	9	NS
No full exhalation before actuation, %	56	50	NS
More actuations for a single inhalation, %	22	18	NS
Actuation against teeth, lips, or tongue, <sup>a</sup> %	1	0	NS
Actuation in the second half of inspiration, %	24	21	NS
Activation after end or before start of inhalation, <sup>a</sup> %	9	5	NS
Stopping inhalation immediately after firing, <sup>a</sup> %	14	10	NS
Forceful inhalation, <sup>a</sup> %	68	50	$P = 0.002$
Inhalation through nose whilst and after actuation, <sup>a</sup> %	6	3	NS
No or short (less than 2–3 s) breath-holding after inhalation, <sup>a</sup> %	49	48	NS

Data are presented as the percentage of subjects for the group performing the error compared to the total number of observations. MDI, Metered Dose Inhaler; NS, non-statistical difference.

<sup>a</sup> Critical mistakes.

Some details of nebuliser practice are displayed in Table 4. Many patients reported that they chose the nebuliser equipment themselves. Most patients (94%) chose the interface system themselves, without any medical information. A minority of subjects had received some information about nebuliser use and maintenance by health caregivers. Most patients (78%) also reported that they did never receive any instruction on the optimal fill volume or drug solvent; the mean fill volume was 3.8 ml. Fifty patients reported information useful to gain, at least partially, the used nebuliser brand; eighteen different models were reported at all with prevalence for the Nebula ( $N = 7$ ) and the Bimboneb ( $N = 11$ ) (Markos-Mefar, Bovezzo, BS), the Vent-Stream ( $N = 4$ ) and the SideStream ( $N = 5$ ), mainly ( $N = 7$ ) powered by an Artsana compressor (Artsana, Grandate, CO), the Clenny ( $N = 5$ ) (Medel, S.Polo di Torriale, PR) and the ultrasonic Universal II ( $N = 3$ ) (FLAEM, S.Martino della Battaglia, BS). According to the available information, jet nebulisers largely prevailed (94% of total) over ultrasonic ones. A minority of jet nebuliser users (16% of total) were using a glass reservoir. The most commonly used types of drugs were corticosteroids ( $N = 104$ ), bronchodilators ( $N = 93$ ), mucolytics ( $N = 16$ ) and cromons ( $N = 19$ ). In decreasing order, the most widely used drugs were beclomethasone dipropionate ( $N = 67$ , at a daily dosage ranging from 0.4 to 1.6 mg), salbutamol ( $N = 79$ , up to a daily dosage of 3.75 mg), ipratropium bromide ( $N = 59$ , up to a daily dosage of 1.25 mg), flunisolide ( $N = 21$ , at a daily dosage of 1–3 mg), nedocromil ( $N = 19$ ), fluticasone propionate ( $N = 11$ , at a daily dosage of 1–2 mg), fenoterol ( $N = 7$ ), oxitropium ( $N = 5$ ) and budesonide ( $N = 5$ , at a daily dosage of 0.5–1.5 mg). Most patients (95%) mixed more active drugs for each nebulisation; more than two third of mixtures included bronchodilators with corticosteroids.

## Discussion

We have found that, as compared to the OIU group, the subjects with CAO using nebulisers were older, with more

unscheduled health care resources utilisation, severe obstruction and respiratory symptoms. The finding that the most severely ill population with CAO often uses home nebulisers is not new.<sup>19,20</sup> More interestingly, we have also shown that subjects of the NIU group performed more critical inhaler errors than those of the OIU group. To our knowledge, no previous study did report that subjects using nebulisers were particularly prone to inhaler misuse. Possibly, poor inhaler technique may explain because many nebuliser users perceived nebulisers as more effective than inhalers and prefer them despite they are less convenient. Of course, our study has some limitations. Firstly, our choice of critical inhaler errors for each device is arbitrary, although based on previous literature.<sup>18</sup> Secondly, our observations of inhalation technique rely on investigators' judgments and have subjective basis. However, we think that our findings are consistent and generalizable, as they include a very large sample of subjects, the used method was standardized and, overall, our findings were in accordance with the results of reviews including studies with similar design.<sup>21,22</sup> Unexpectedly, we have also shown that subjects of the NIU group, often older and severely ill, received less instruction on inhaler technique than those of the OIU group. It is difficult to find a logical explanation to this observation. This finding is certainly a bias of the prescribing physicians: they, perhaps, estimating good inhaler use as a difficult challenge for this subset of patients, gave minimal instruction when inhalers were released for saving time and added the prescription of nebulisers. However, even after adjustment for any type of inhaler education, the frequency to inhaler misuse remained very common in nebuliser users. Possibly, this group of subjects would require more and more education for improving inhaler technique. Future studies should investigate if and how proper instruction by health care givers can revert inhaler mishandling in the short and long-term period for any range of age, disease and technical skillful, the amount of education time required for assuring good inhaler technique with different inhalers and the value of alternative education methods, such as video, web and booklets; because a correct inhaler technique may be lost over time,

**Table 3** Errors of inhaler technique with some commonly used DPIs for the group of subjects using only inhalers (OIU group) and that using both inhalers and nebulisers (NIU group).

Checklist of inhalation technique errors	HandiHaler/Aerolizer		Diskus		Turbuhaler		P-value
	NIU group	OIU group	NIU group	OIU group	NIU group	OIU group	
Failure of loading <sup>a</sup>	18	12	17	7	23	14	NS
Keep the inhaler no more than 45° from the vertical axis during loading <sup>a</sup>	N.A.	N.A.	N.A.	N.A.	48	20	P < 0.001
Exhaling into mouthpiece of device after loading <sup>a</sup>	30	18	49	21	28	12	P = 0.015 P = 0.023
Not sealing lips round mouthpiece during inhalation <sup>a</sup>	8	4	15	6	7	4	NS
Inhaling by nose <sup>a</sup>	6	2	4	1	3	0	NS
Slow and not forceful inhalation <sup>a</sup>	34	23	50	27	31	21	P = 0.035 NS
Exhaling into the mouthpiece of the device after inhalation	36	18	NA	NA	28	9	P = 0.008 P = 0.001
Do not control proper inhalation of powder after first inhalation	50	29	NA	N.A.	N.A.	NA	—

Data are presented as the percentage of subjects for the group performing the error compared to the total number of observations. DPI, Dry Powder Inhaler, NS, non-statistical difference. N.A.: not applicable to that device.  
<sup>a</sup> Critical mistakes.

other studies should clear if all or only some inhalers required repeated checks at follow-up visits for maintaining good inhaler use and the type and the amount of this instruction. Alternatively, if a subset of older and severely ill patients requiring aerosol therapy is not able to use available inhalers correctly despite proper education or unavoidably loses this skill over time, future studies should clear the characteristics of subjects predicting the need of nebulisers.

Nevertheless, although nebuliser use requires less cooperation than inhalers, education by health caregivers is also needed for purchasing a proper nebuliser equipment as well as for its good set-up and maintenance. Even if this study was not devised to investigate the nebuliser equipment of our subjects, we think that some results need a short discussion. We were surprised knowing that approximately half of our patients reported a length of more than 30 min for each single nebulisation. The British Thoracic Society<sup>6</sup> guidelines recommend a nebulisation time for single session not greater than 10 min. Although the long nebulisation time is only a rough index of equipment performances and may also be due to the commonly observed practice of mixing more drugs with high fill volume, we are afraid of suboptimal choices for nebuliser equipment. Some other findings about nebuliser equipment are certainly suboptimal: glass reservoirs, which are no more recommended, remained commonly used as well as ultrasonic nebuliser, which are not suitable to nebulise corticosteroids.<sup>7</sup> Deficiencies in nebuliser equipment would be not unexpected, as most of our subjects bought it themselves. Again, 89% of respondents did never receive any information by health caregivers and/or retailers on the correct usage and hygiene of their nebuliser. This percentage is even worse than that observed in another nationwide survey (although different in material and method) on nebuliser practice in Italy carried out on 1999, where the prescribing physicians specified the operating conditions of nebulisers to be used and the maintenance, respectively, in 37% and 24% of cases.<sup>11,13</sup> In Italy the National Health Service usually supplies most nebulised drugs freely or with a little fee, but most adult subjects who had received the prescription of nebuliser therapy buy the device directly. To the authors' knowledge, except for local and limited situations, no formal widespread servicing and monitoring managed by health caregivers is available for Italian adults. Thus, our subjects using nebulisers not only were prone to inhaler misuse, but their habits also seem to be consistent with suboptimal nebuliser practice.

Our data seem to show that the diffusion of home nebulisers varied largely among participating centers. However, large variations of home nebuliser use are known according to the different local habits.<sup>9,10</sup> Some studies from the UK and Scandinavian countries have shown that long-term treatments with home nebulised bronchodilators may be safe and effective.<sup>23–25</sup> Short-acting beta-agonists and anticholinergics are used throughout Europe, but more common in Belgium, Germany, Swiss, Norway, Italy and Portugal.<sup>10</sup> However, the practice of home nebuliser therapy in Italy has some peculiarities, as not only bronchodilators, but even mucolytics and corticosteroids are largely used.<sup>10</sup> The use of nebulised mucolytics, even in the presence of bronchiectasis with thick sputum, is not evidence-based.<sup>26</sup> The large use of nebulised

**Table 4** Some characteristics of nebuliser practice in the studied population.

Item	Response, N
Who was the first source of nebuliser therapy prescription? N = 133	
• General practitioner	59
• Chest physician	71
• Other physician	3
How many times a day do you usually use your nebuliser? N = 134	
• Once a day	22
• Twice a day	22
• Thrice a day or more	45
• Only on a needed basis	11
How long does your nebulisation last? N = 104	
• Less than 15 min	0
• 15–30 min	6
• More than 30 min	50
• After a fixed time	3
• When the liquid drugs finish	42
Did someone give some indication about the type of nebuliser to buy, N = 132	
• Nurse/physiotherapist	2
• Physician	45
• Retailer	35
• Friend/relative	5
• No-one	13
Did someone ever give some instruction about proper nebuliser use, N = 97	
• Nurse/physiotherapist/physician	0
• Retailer	11
• Friend/relative	28
• No-one, I have read the package instruction	61
Did someone ever give some instruction about proper nebuliser hygiene, N = 70	
• Nurse/physiotherapist/physician	0
• Retailer	11
• Friend/relative	32
• No-one, I have read package instruction	57
When did you get the liquid formulation into the reservoir? N = 144	
• When it is possible	4
• Immediately before the use	96
Did you add any solvent to the active drug into the reservoir? N = 122	
• No	44
• Yes, tap water	2
• Yes, distilled water	7
• Yes, physiologic saline	47
Which do interface system use for the nebulisation?, N = 124	
• Facemask	62
• Mouthpiece	38
Do you inhale aerosol, N = 133	
• By mouth	47
• By nose	9
• By both nose and mouth	44

**Table 4 (continued)**

Item	Response, N
Do you clean your reservoir, N = 130	
• Always after each nebulisation	9
• Once a week	25
• Less than once a week	66
If you don't reach dryness, do you throw the residual liquid formulation away? N = 120	
• Yes	84
• I use it again even some hours after the first interruption	16
Before washing, do you dismantle your reservoir? N = 118	
• It is not possible	12
• Never	26
• Sometimes	35
• Always	27
After washing, do you dry your reservoir? N = 134	
• Never	64
• Always, even if I don't wash the reservoir	9
• Always	27
When did you change your reservoir, N = 128	
• Never	44
• When it is broken	32
• According to the manufacturer indications	24
If you are also using inhalers, which device do you offer more benefits, N = 107	
• Nebuliser	61
• Inhaler	29
• No difference	1
If you are also using inhalers, which is the most comfortable device to use?, N = 110	
• Nebuliser	25
• Inhaler	75
• No difference	10
If you are also using inhalers, which device do you prefer to use, N = 109	
• Nebuliser	40
• Inhaler	57
• No difference	12

corticosteroids has been critically discussed,<sup>27</sup> but it was<sup>13</sup> and, as our study confirms, remains widespread in Italy. Likewise, BDP, the most commonly nebulised corticosteroid in our population, is clinically effective when properly nebulised.<sup>28</sup> Another commonly observed finding in our survey which is not evidence-based is the co-admixture of more nebulised drugs including corticosteroids. Some *in vitro* studies did not show unfavorable physico-chemical interactions when corticosteroids were mixed with salbutamol and ipratropium bromide.<sup>29–31</sup> Other *in vitro* studies did not observe negative consequences in terms of both drug output and aerodynamics when BDP and flunisolide were mixed with salbutamol using both Nebula and Bimboneb<sup>32</sup>; or when budesonide or BDP were mixed to salbutamol and ipratropium bromide using both VentstreamPro and Sidestream powered with AirClinic.<sup>33</sup> Finally, although the habit of mixing drugs for nebulisation needs further

confirmation to be suggested, a recent study reviewing the available studies carried out with mixtures of more nebulised drugs including corticosteroids, has shown good clinical results. However, *in vitro* information indicates that some commercially available nebulisers are unsuitable for nebulising corticosteroids and even the best systems offer a rather poor and inconsistent fine particle fraction.<sup>34</sup>

## Conclusion

We conclude that in Italy a subset of patients with chronic airflow obstruction was regularly using home nebulisers. These patients often have advanced age, severe respiratory conditions and common inhaler misuse. Nebuliser practice also seems to be suboptimally performed. If after proper instruction they can obtain good inhaler technique and be effectively switched to the use of these devices, it remains to be demonstrated; alternatively, subjects who did not obtain a good inhaler technique should receive proper tuition for assuring the best nebuliser practice. More education is needed for these patients because they receive effective aerosol therapy at home.

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## Conflict of interest

All the authors declare that the material is not being considered for publication elsewhere, have read the manuscript and approved its submission, have no conflicts of interest.

All the authors have contributed to design of the study and collected the data. Andrea Melani has proposed and written the study and Piersante Sestini has performed the statistical analysis. Mario Del Donno has also corrected the manuscript.

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## Appendix

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