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## SHORT COMMUNICATION

# Retail sales of inhalation devices in European countries: So much for a global policy

F. Lavorini <sup>a,\*</sup>, C.J. Corrigan <sup>b</sup>, P.J. Barnes <sup>c</sup>, P.R.N. Dekhuijzen <sup>d</sup>,  
M.L. Levy <sup>e</sup>, S. Pedersen <sup>f</sup>, N. Roche <sup>g</sup>, W. Vincken <sup>h</sup>, G.K. Crompton <sup>i</sup>,  
on behalf of The Aerosol Drug Management Improvement Team (ADMIT)<sup>j</sup>

<sup>a</sup> Department of Internal Medicine, Section of Immunoallergology, Respiratory Diseases and Cell Therapy, University of Florence, Italy

<sup>b</sup> Department of Asthma, Allergy & Respiratory Science, King's College London School of Medicine, London, UK

<sup>c</sup> National Heart and Lung Institute, Imperial College London, UK

<sup>d</sup> Radboud University Nijmegen Medical Centre, The Netherlands

<sup>e</sup> Senior Clinical Research Fellow, Allergy & Respiratory Research Group, Division of Community Health Sciences: GP Section, University of Edinburgh, UK

<sup>f</sup> Research Unit, Department of Paediatrics, Kolding Hospital, Kolding, Denmark

<sup>g</sup> Service de Pneumologie et Réanimation, Hôpital Hôtel Dieu, Paris, France

<sup>h</sup> Respiratory Division, University Hospital UZ Brussel, Belgium

<sup>i</sup> Western General Hospital, Edinburgh, UK

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## Summary

**Objective:** To evaluate the retail sales of pressurised metered-dose inhalers (pMDIs), dry-powder inhalers (DPIs) and liquids for nebulisation in 16 European countries.

**Methods:** Retail sales data relating to pMDIs, DPIs and liquids for nebulisation delivering short- and long-acting bronchodilators, corticosteroids and combinations between 2002 and 2008 were obtained from the IMS sales database. The IMS database ensured that wholesalers' stock sales accurately matched that of retail pharmacies and included purchases by panel

\* Corresponding author. Department of Internal Medicine, Section of Immunoallergology, Respiratory Diseases and Cell Therapy, University of Florence, Viale Morgagni 85, 50134, Florence, Italy. Tel.: +39 055 413183; fax: +39 055 4223202.

E-mail address: [federico.lavorini@unifi.it](mailto:federico.lavorini@unifi.it) (F. Lavorini).

<sup>j</sup> Members of the Aerosol Drug Management Improvement Team (ADMIT): Graham K Crompton, Edinburgh, UK, (Chair); Peter J Barnes, London, UK; Marielle Broeders, Nijmegen, The Netherlands; Lorenzo Corbetta, University of Florence, Italy; Chris Corrigan, London, UK; Richard Dekhuijzen, Nijmegen, The Netherlands; Jean Christophe Dubus, Marseille, France; Thomas Hausen, Essen, Germany; Meinhard Kneussl, Vienna, Austria; Federico Lavorini, University of Florence, Italy; Mark L Levy, Edinburgh, UK; Søren Pedersen, Kolding, Denmark; Antonio Ramalho de Almeida, Portugal; Nicholas Roche, Service de Pneumologie et Réanimation, Hôtel-Dieu, Paris, France; Joaquin Sanchez, Barcelona, Spain; José L Viejo, Hospital General Yagüe de Burgos, Spain; Walter Vincken, Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel, Brussels, Belgium; Thomas Voshaar, Moers, Germany.

pharmacies directly from pharmaceutical manufacturers, specialist wholesalers and distribution cooperatives.

**Results:** Mean inhaler retail sales (expressed as percentages of total sales) were 47.5% for pMDIs, 39.5% for DPIs and 13% for nebulisers. The distribution of inhaler sales differed significantly between the countries with pMDI sales greatest in the United Kingdom and Hungary compared to other countries, where DPI sales prevailed. Sales of nebulisation liquids were high in Italy. The pMDI was the most frequently prescribed inhaler for bronchodilators. In contrast, retail sales of DPIs were similar to those of pMDIs for inhaled corticosteroids, and higher in the case of inhalers with combined long-acting  $\beta_2$ -agonist and corticosteroid.

**Conclusion:** We found a high degree of variability in inhaler prescription between European countries. Differing health policies, costs, health insurance issues, pharmaceutical/commercial aspects and prescribers' and patients' preferences may explain this variation. We suggest a need for more uniform, outcome-led inhaler prescribing practice across Europe to improve the efficacy and cost effectiveness of the treatment of obstructive airways diseases.

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## Introduction

There are more than 230 different device–drug combinations available in Europe<sup>1</sup> for inhaled therapy of respiratory conditions, particularly asthma and chronic obstructive pulmonary disease (COPD). Although variety helps with finding an inhaler to suit every patient, for prescribers it complicates choosing a device and keeping abreast of what is available and how to use it. Incorrect inhaler usage may partly explain why many treated patients continue to report symptoms. Inhaler misuse is extremely common<sup>2–4</sup> and may partly explain why many patients treated with potentially effective inhaled therapy continue to report symptoms.<sup>5,6</sup> Marketed inhalation devices can be broadly classified as pressurised metered-dose inhalers (pMDIs), dry-powder inhalers (DPIs) and liquids for nebulisation. The efficiency with which these devices deliver inhaled medications to the lower respiratory tract is influenced by a multitude of factors, including their design and characteristics, the formulation (i.e. solution, suspension) of the contained medication, the particle size and velocity of the aerosol produced and the ease with which patients can perform the required critical steps to use them properly.<sup>7</sup> In addition, even with correct inhalation technique, lung deposition for different inhaler devices varies greatly from 4% for beclometasone delivered by chlorofluorocarbon-propellant MDIs to 53% for extra-fine beclometasone delivered by CFC-free hydroflouroalkane-propellant pMDIs.<sup>8</sup> Patient preference is important because it may influence adherence to treatment.<sup>7</sup> It is clearly pointless to prescribe an inhaler device which the patient will not, or cannot use correctly. Thus, choosing the correct inhaler for each patient is just as important as choosing the most appropriate medication.

Prescribing is a major element of the delivery of primary healthcare and prescribing practice varies considerably across Europe<sup>9</sup> at many levels, from the organisation of national health services to the environment and expertise of individual prescribers.<sup>10</sup> Many other influences such as demography, morbidity and practice policies have been shown to influence prescribing habits.<sup>10</sup> In some countries, primary care prescribing is led primarily by cost.<sup>11</sup> Pharmaco-epidemiological analysis is difficult when single drugs

are used for a wide variety of indications; however, inhaled medications are mainly used for a limited and relatively well defined set of indications, (asthma and COPD) according to management guidelines which are broadly uniform across Europe, making comparison feasible.

To investigate how far national prescribing practice for inhaled drugs varies across Europe, we assessed European retail sales data for inhaled medications delivered by pMDIs, DPIs, and liquids for nebulisation commonly used for the treatment of asthma and COPD.

## Methods

### Data source

We retrospectively evaluated in 16 European countries retail sales of short-acting  $\beta$ -adrenergic (SABA) and anti-muscarinic (SAMA) bronchodilators, long-acting  $\beta$ -adrenergic (LABA) and anti-muscarinic (LAMA) bronchodilators, inhaled corticosteroids (ICS) alone and fixed combinations of LABA with ICS using the IMS Health databases.<sup>12</sup> Retail sales of inhalers delivering sodium cromoglycate and nedocromil sodium were not evaluated. IMS is an international healthcare information company specialising in the collection and interpretation of anonymised health information, and often the only source of information on aspects of medicine utilisation across the world.<sup>12</sup> Its databases represent an invaluable source for pharmaco-epidemiological studies. For the present study, we used the IMS DPM audit (database) covering inhaler sales data for 7 years (2002–2008) in Austria, Belgium, Denmark, Finland, France, Germany, Hungary, Italy, Netherlands, Norway, Poland, Portugal, Spain, Sweden, Switzerland and United Kingdom. For each country, the data included supplies by all wholesalers as well as those directly supplied by manufactures to a representative panel of approximately 4000 pharmacies.<sup>12</sup>

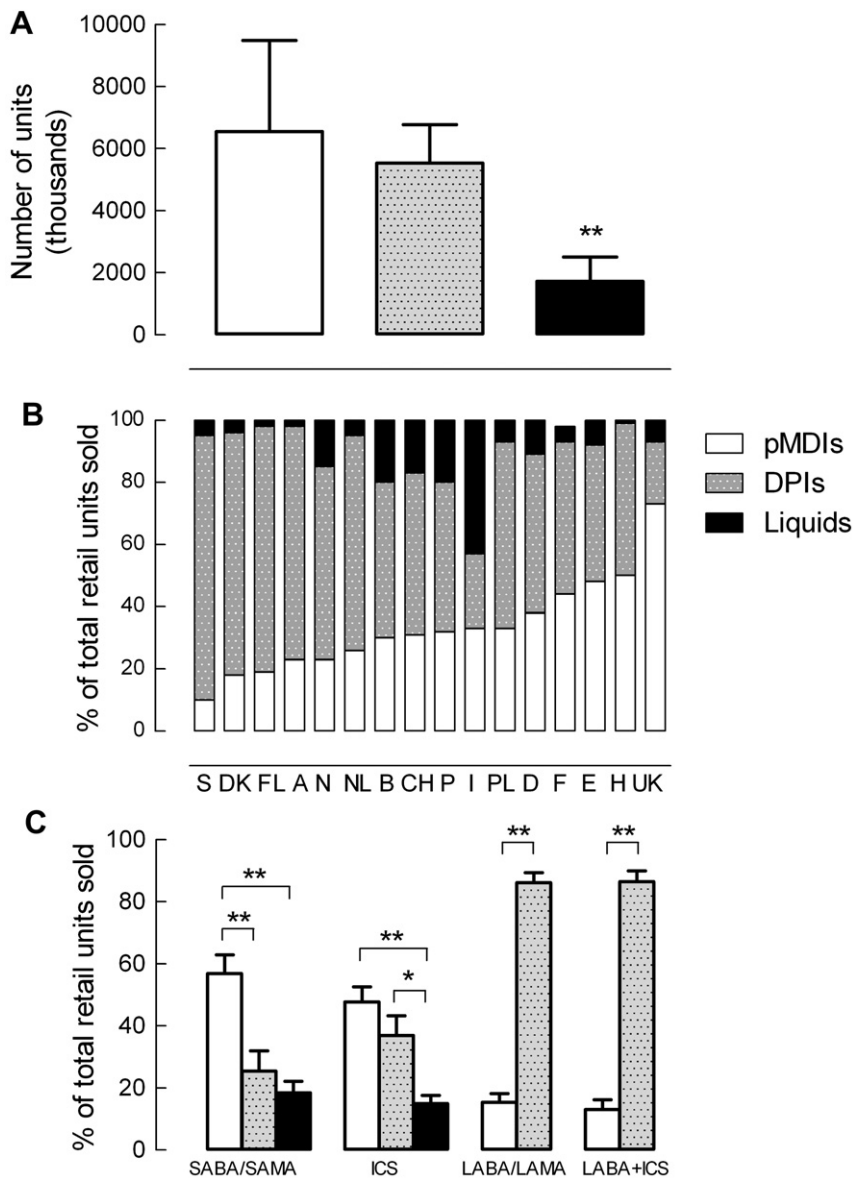
### Data analysis

Annual inhaler retail sales of inhaler units by country over the 7 years were averaged and expressed as percentages of

the total numbers sold. For pMDIs and DPIs, a unit was defined as a single inhaler; for liquids, a unit was defined as a single package of nebuliser solution. Differences in total retail sales between countries were assessed using the chi-squared test and analysis of standardised residuals. Differences between pMDIs, DPIs, and liquids sales were assessed using analysis of variance followed by Dunn's multiple comparison test. Since LABA and LABA + ICS are not available as liquids, sales of pMDIs delivering these drugs were compared using Student's *t*-test. In all cases,  $P < 0.05$  was considered as significant.

## Results

During this 7-year period, the total number of pMDI and DPI units sold were significantly ( $P < 0.01$ ) higher than those of liquids for nebulisers (47.5%, 39.5% and 13% of the total units sold, respectively, Fig. 1A). The distribution of units sold significantly ( $P < 0.01$ ) differed between the countries, with pMDI retail sales greatest in the United Kingdom and Hungary compared to the other countries in which retail sales of DPIs prevailed (Fig. 1B). The sale of liquids for nebulisation was significantly ( $P < 0.01$ ) higher in Italy (Fig. 1B) than in the



**Figure 1** Panel A: Total units sold over the time period 2002–2008. Panel B: Retail sales of inhalation devices, expressed as percentages of the total sales, in 16 European countries over the time period 2002–2008. A, Austria; B, Belgium; CH, Switzerland; DK, Denmark; E, Spain; F, France; FL, Finland; H, Hungary; I, Italy; D, Germany; N, Norway; NL, The Netherlands; P, Portugal; PL, Poland; S, Sweden; UK, United Kingdom. Panel C: Mean ( $\pm$ SD) retail sales of inhalation devices delivering short-acting  $\beta$ -adrenergic (SABA) and anti-muscarinic (SAMA) bronchodilators, long-acting  $\beta$ -adrenergic (LABA) and anti-muscarinic (LAMA) bronchodilators, inhaled corticosteroids (ICS) and combination of LABA + ICS expressed as percentages of the total retail sales, during the time period 2002–2008. pMDIs, pressurised metered-dose inhalers; DPIs dry-powder inhalers. \*,  $P < 0.05$ ; \*\*,  $P < 0.01$ .

other countries. Dividing sales by type of medication, pMDIs were most frequently ( $P < 0.01$ ) prescribed for bronchodilators, pMDIs and DPIs were prescribed with an approximately equal frequency for ICS alone while fixed combinations of LABA + ICS were much more frequently ( $P < 0.01$ ) prescribed as DPIs than pMDIs (Fig. 1C). Repartition of devices delivering specific inhaled medications (i.e. SABA, SAMA, LABA, LAMA, ICS and fixed combination of LABA plus ICS) across European countries is reported in Fig. 2.

## Discussion

With rare exceptions (for example in cases of emergency) inhaler sales in Europe result from doctors prescriptions. Assuming that inhaled therapy is prescribed for asthma and COPD according to roughly concordant national guidelines across Europe, with inhaler prescriptions matched to individual patient needs and ability, it follows that these should be roughly equivalent across Europe. Our findings, however, demonstrate this is not the case. The pMDI is widely prescribed in Europe, most likely because of its low cost and widespread availability of medications delivered by such inhaler. This is paradoxical when one considers that this device is often used incorrectly by patients.<sup>2</sup> A series of studies performed by Crompton et al.<sup>13–15</sup> and others,<sup>2,16</sup> suggested that only about 20% of patients use a pMDI correctly after simply reading the package insert, while only just over 50% are able to do so even after specific instruction. These data raise concern that local prescribing may not be influenced primarily by the ability of the patient to use the prescribed device, but by other factors such as cost, marketing strategies and prescribers' and patients' biases. The choice of the device is also influenced by the knowledge and ability of the prescriber to use the device. It has been shown about 50% of respiratory nurses, medical doctors and

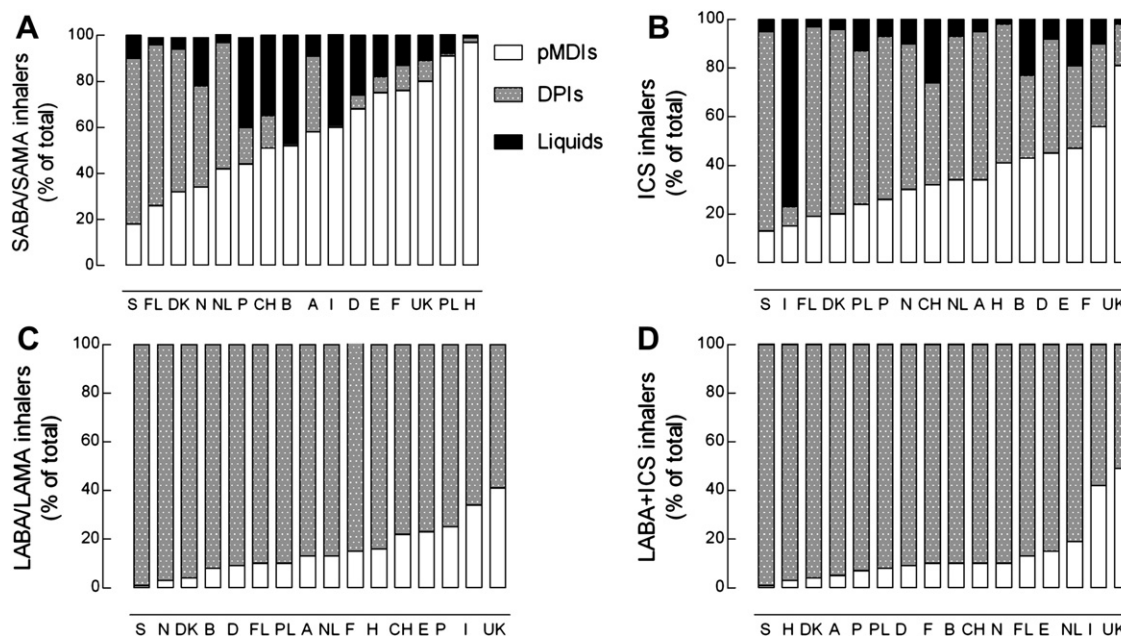
respiratory therapists were unable to use inhalation devices correctly.<sup>17–19</sup> Various explanations may account for this such as lack of familiarity with specific devices, inadequate time to teach, poor training techniques, poor training materials, all influencing prescribers choice.

The reasons underlying the relatively high sales of devices delivering SABA/SAMA in some countries are unknown. These may reflect poor disease control in those populations; however, this may also reflect prescribing patterns in keeping with locally used asthma/COPD self management plans.

Despite the overall predominance of pMDI sales, DPIs sales are high in many European countries and sales of inhaled liquids for nebulisation particularly in Italy (approximately 45% of the total Italian sales). The latter finding might reflect high prescriptions of nebulised corticosteroids (see Fig. 2, panel B), likely for acute respiratory illnesses other than asthma or COPD, particularly in children.<sup>20</sup>

There are some obvious limitations when interpreting the data in the present study. The figures take no account of possible differences in the prevalence of asthma and COPD and the characteristics (i.e. age, severity of the disease) of affected patients in European countries, or the possibility that some of the prescribing was for diseases other than asthma or COPD. In addition, retail sales do not necessarily equate to individual patient prescriptions; however, due to the nature of the database used in the present study, it was not possible to accurately estimate daily defined dosages for the different device/drug combinations. This is clearly a subject for future research if we are to learn from the different approaches throughout Europe.

The nature of the IMS database analysed for this study did not allow us to differentiate between sales of breath-actuated and simple pMDIs. This may be a topic for further study, particularly, if these differences could be related to asthma outcomes. Despite these limitations, we believe this study is of interest in highlighting the variability in



**Figure 2** Repartition across European countries of inhalation devices delivering SABA/SAMA, LABA/LAMA, ICS and combination of LABA + ICS expressed as percentages of the total retail sales over the time period 2002–2008. See Fig. 1 for abbreviations.

inhaler prescribing practice across Europe and the dichotomy between the relative proportions of devices prescribed and those most likely to be used properly. The data suggest a need for more uniform, outcome-led inhaler prescribing practice across Europe, and for better education about the advantages and limitations of specific devices for prescribers and patients in order to improve the efficacy and cost effectiveness of the treatment of obstructive airways diseases. Perhaps, this improvement could be achieved through more attention by guideline developers to implementation of guidelines.

### Conflict of interest statement

**Peter J. Barnes** has been reimbursed for attending conferences and/or giving talks by, and acted as consultant for Altana/Nycomed, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Novartis, Pfizer, Meda AB. **Chris Corrigan** has been reimbursed for attending conferences and/or giving talks by, acted as consultant for Schering-Plough, Allergy Therapeutics, Meda AB, UCB Pharma, GlaxoSmithKline Novartis, ALK-Abello, Allergy Therapeutics Merck Sharpe Dohme, Allergopharma Joachim Ganzer AB. **Graham K. Crompton** has been reimbursed by Meda AB for attending conferences and/or giving talks, and he serves as consultant for Meda AB. **Richard Dekhuijzen** has been reimbursed for attending conferences and/or giving talks by, and acted as consultant for GlaxoSmithKline, AstraZeneca, Boehringer Ingelheim, Zambon, Actelion, Altana, Teva. **Federico Lavorini** has been reimbursed for attending conferences and/or giving talks by, and acted as consultant for Menarini Industrie Farmaceutiche, AstraZeneca, Chiesi Framaceutici Mundipharma, Teva and Meda AB. **Mark Levy** has been reimbursed for attending conferences and/or giving talks by, and acted as consultant for AstraZeneca, GlaxoSmithKline, Ivax, 3M, Novartis, MSD, Altana Meda AB, Trinity Chiesi, Boehringer Ingelheim, Ranbaxy, Innovata Biomedica, Schering Plough. **Søren Pedersen** has given talks for Nycomed, GlaxoSmithKline (GSK) and Meda AB and acted as a consultant for Nycomed and AstraZeneca. **Nicholas Roche** has been reimbursed by Meda AB for attending conferences and/or giving talks, and he serves as consultant for Meda AB. **Walter Vinken** has been reimbursed by Meda AB for attending conferences and/or giving talks, and he serves as consultant for Meda AB.

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