

# Physicians' attitudes towards combination therapy with inhaled corticosteroids and long-acting $\beta_2$ -agonists: an observational study in UK specialist care

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**Purpose:** Recent real-world studies have demonstrated that asthma control remains suboptimal in many patients. The aim of this study was to evaluate physicians' perceptions of the effectiveness of combination therapy with an inhaled corticosteroid (ICS) and a long-acting  $\beta_2$ -agonist (LABA) in routine clinical practice.

**Methods:** In November 2009, UK respiratory specialists were invited by medeConnect Healthcare Insight to complete a survey on the effectiveness of different single- or dual-inhaler combinations of an ICS and a LABA in the context of asthma management. Respondents were permitted to specify combinations of available ICSs and LABAs, based on their knowledge and experience of the individual components. Questions elicited both unprompted free-text responses and prompted responses selected from a list of options.

**Results:** A total of 98 physicians completed the survey, of whom 82 (84%) gave permission to publish their data. The majority of respondents (63%) were consultants and 57% reported a caseload of more than 40 patients with asthma or chronic obstructive pulmonary disease per month. Fluticasone and formoterol were considered to be the most effective combination for the treatment of asthma (37% unprompted, 41% prompted), followed by budesonide and formoterol (22% unprompted, 24% prompted). The most common reasons for choosing specific combinations were: rapid onset of action (60%), high potency of the ICS (39%), efficacy (15%), experience of prescribing (13%), clinical evidence (12%), and long-lasting effect (10%). Key properties of the preferred fluticasone and formoterol combination were rapid onset of action and high potency of the ICS (79% for both).

**Conclusion:** The results of this survey suggest that the ICS and LABA combination considered most effective by UK physicians in the management of asthma is fluticasone and formoterol, which is not currently available as a single-inhaler combination. The development of new single-inhaler combinations of ICSs and LABAs may improve real-world asthma management.

**Keywords:** asthma, LABA, ICS, combination, effectiveness, real-world

## Introduction

Inhaled corticosteroids (ICSs) are the cornerstone of asthma management. National and international guidelines recommend combination therapy with an ICS and a long-acting  $\beta_2$ -agonist (LABA) as the first step-up option for adults and children aged 5 years and over whose asthma is not controlled by low-dose ICS monotherapy.<sup>1-3</sup> Data from robust clinical trials have shown that currently available ICS and LABA combinations are effective in the management of asthma;<sup>4-9</sup> however, recent real-world studies have

demonstrated that asthma control often remains suboptimal in terms of both acute symptom relief and reduction in the risk of future exacerbations<sup>10,11</sup> even in those receiving treatment,<sup>12,13</sup> and this may not be immediately apparent to physicians and patients.

It is unclear whether or not the ICS and LABA combinations that show similar efficacy in clinical trials have equivalent effectiveness in real-world practice. This study set out to evaluate physician perceptions of the effectiveness of combinations of currently available ICSs and LABAs for the management of asthma in routine clinical practice.

## Methods

In November 2009, UK respiratory specialists (defined as hospital specialists with a minimum of 5 years' experience who were seeing at least 20 patients with asthma or chronic obstructive pulmonary disease [COPD] per month) were invited to complete an online survey on the effectiveness of different combinations of an ICS and a LABA. Physicians were recruited by medeConnect Healthcare Insight via Doctors.net.uk, the largest online network of medical professionals in the UK.

In the context of a questionnaire about the management of asthma, respondents were asked a series of questions to establish which single-inhaler (fixed) or dual-inhaler (free) combination of an ICS and a LABA they considered to be the most effective treatment (see Supplementary information). Each question was asked twice: the first time (unprompted), the respondent provided free-text responses to open-ended questions, and the second time (prompted), the respondent selected their response to a closed question from a list of options. Unprompted (recall) questions avoid priming of responses through free-text answers, but may have limitations of under-reporting because of respondents' memory; surveys using prompted (recognition) questions tend to find higher levels of knowledge than those using an unprompted format but risk seeding answers in respondents' minds.<sup>14,15</sup> For the unprompted response, any text could be entered. For the prompted responses, participants could choose between the following single-inhaler or dual-inhaler combinations of an ICS and a LABA: fluticasone and formoterol, fluticasone and salmeterol, budesonide and formoterol, budesonide and salmeterol, beclometasone and formoterol, and beclometasone and salmeterol. There was also the option of "Other", to allow participants to specify any unlisted combination that they believed was likely to be the most effective. Respondents were permitted to state

available and hypothetical single-inhaler or dual-inhaler combinations, based on their knowledge and experience of the individual components.

Before analysis, unprompted responses were grouped either by generic drug name (for answers about the most effective ICS and LABA combination) or by theme (for answers regarding the reasons for a particular choice). Representativeness was assessed in relation to National Health Service Workforce data on medical and dental staff by specialty and grade in 2009 in England<sup>16</sup> and Wales.<sup>17</sup> Detailed information on workforce characteristics was only available for England.

## Results

### Demographic and clinical characteristics

Of the 98 respondents, 82 (84%) gave permission for their data to be included in the analysis, all of whom answered both the unprompted and prompted questions. Almost three-quarters of the participants (73%) were aged 31–40 years. Most (63%) were consultants and the majority (57%) reported having a caseload of more than 40 patients with asthma or COPD per month (see Table 1).

Overall, 83% of respondents were from England, 9% from Scotland, 6% from Northern Ireland, and 2% from Wales. Job grade, sex, and geographical distribution of English respondents were similar to those of all consultants, associate specialists, staff grades, and registrars in respiratory medicine in England, although specialist registrars, and staff in the Yorkshire and Humber region, were slightly over-represented (Table 1). Of all consultants, associate specialists, staff grades and registrars in respiratory medicine, we surveyed approximately 5% (68/1358) in England and 3% (2/59) in Wales.

### Most effective ICS and LABA combinations

Respondents considered that the most effective combinations (irrespective of their current availability as single-inhaler or dual-inhaler combinations) would be fluticasone and formoterol (37% unprompted, 41% prompted), followed by budesonide and formoterol (22% unprompted, 24% prompted) (Figure 1).

When analyzing the components individually, the ICS considered to be most effective was fluticasone (44% unprompted, 49% prompted), followed by budesonide (22% unprompted, 26% prompted), and beclometasone (17% unprompted, 22% prompted) (Figure 2A). The most effective LABA was thought to be formoterol

**Table 1** Demographic and clinical characteristics of respondents

| Characteristic                                     | Study population (UK) <sup>a</sup><br>(n = 82) |      | Study population (England) <sup>a</sup><br>(n = 68) |      | Source population (England) <sup>b</sup><br>(n = 1241) |      |
|--|--|------|---|------|--|------|
|  | n  | (%)  | n   | (%)  | n  | (%)  |
| Sex  |  |      |   |      |  |      |
| Male   | 59   | (72) | 46  | (68) | 879  | (65) |
| Female   | 23   | (28) | 22  | (32) | 479  | (35) |
| Age  |  |      |   |      |  |      |
| 31–40 years  | 60   | (73) | 49  | (72) | NR   | NR   |
| 41–50 years  | 17   | (21) | 15  | (22) |  |      |
| >51 years  | 5  | (6)  | 4   | (5)  |  |      |
| Job grade  |  |      |   |      |  |      |
| Consultant   | 52   | (63) | 42  | (62) | 645  | (47) |
| Associate specialist                               | 1  | (1)  | 1   | (1)  | 11   | (1)  |
| Staff grade  | 1  | (1)  | 1   | (1)  | 10   | (1)  |
| Specialist registrar                               | 28   | (34) | 24  | (35) | 692  | (51) |
| Year of qualification                              |  |      |   |      |  |      |
| 1965–1989  | 11   | (13) | 9   | (7)  | NR   | NR   |
| 1990–1994  | 21   | (26) | 19  | (28) |  |      |
| 1995–1999  | 34   | (41) | 28  | (41) |  |      |
| 2000–2005  | 16   | (20) | 12  | (18) |  |      |
| Number of patients with asthma/COPD seen per month |  |      |   |      |  |      |
| 20–40  | 35   | (43) | 21  | (31) | NR   | NR   |
| 41–60  | 16   | (20) | 5   | (7)  |  |      |
| 61–80  | 7  | (9)  | 4   | (6)  |  |      |
| 81–100   | 17   | (21) | 8   | (12) |  |      |
| >100   | 7  | (9)  | 4   | (6)  |  |      |
| Location of current practice                       |  |      |   |      |  |      |
| North-West   | 11   | (13) | 11  | (16) | 218  | (16) |
| North-East   | 5  | (6)  | 5   | (7)  | 92   | (7)  |
| Yorkshire and Humber                               | 4  | (5)  | 4   | (6)  | 186  | (14) |
| East Midlands                                      | 5  | (6)  | 5   | (7)  | 93   | (7)  |
| West Midlands                                      | 6  | (7)  | 6   | (9)  | 160  | (12) |
| East of England                                    | 6  | (7)  | 6   | (9)  | 113  | (8)  |
| London   | 15   | (18) | 15  | (22) | 267  | (20) |
| South-East coast                                   | 2  | (2)  | 2   | (3)  | 42   | (3)  |
| South Central                                      | 6  | (7)  | 6   | (9)  | 75   | (6)  |
| South-West   | 8  | (10) | 8   | (12) | 112  | (8)  |
| Scotland   | 7  | (9)  |   |      | NR   | NR   |
| Wales  | 2  | (2)  |   |      | NR   | NR   |
| Northern Ireland                                   | 5  | (6)  |   |      | NR   | NR   |

**Notes:** <sup>a</sup>Hospital specialists with at least 5 years' experience; <sup>b</sup>NHS Workforce data (2009) on all consultants, associate specialists, staff grade, or registrars in respiratory medicine in England.<sup>16</sup>

**Abbreviations:** COPD, chronic obstructive pulmonary disease; NHS, National Health Service; NR, not reported.

(84% unprompted, 87% prompted), followed by salmeterol (11% unprompted, 12% prompted) (Figure 2B).

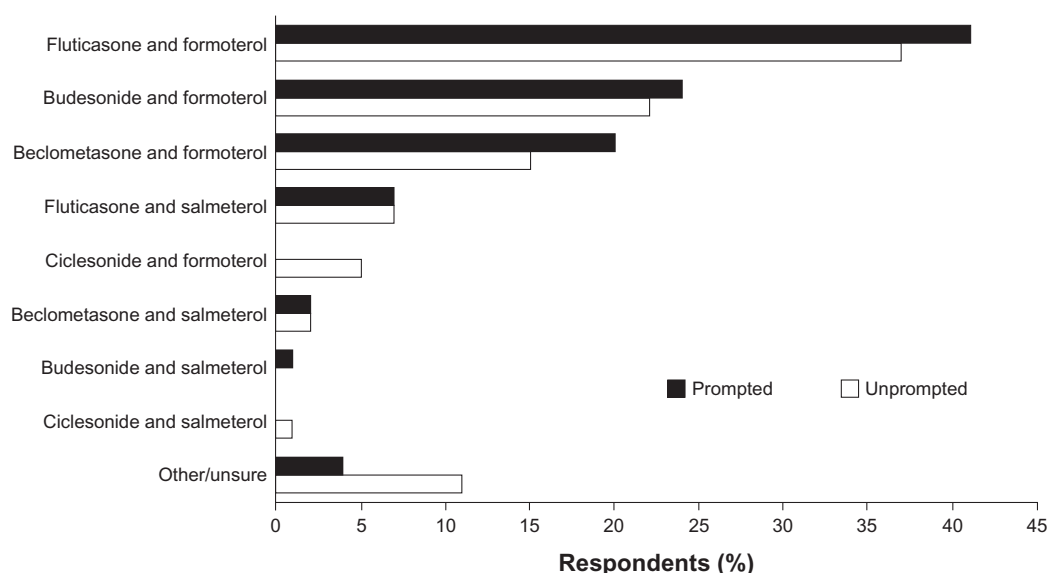
## Reasons for ICS and LABA choice

The most common reasons that respondents gave for choosing the ICS and LABA combination they considered to be most effective were: rapid onset of action (60%), high potency of the ICS (39%), efficacy (15%), experience of prescribing (13%), clinical evidence (12%), and long-lasting effect (10%) (Figure 3A). The most common reasons given for selecting

fluticasone and formoterol (the combination most often rated as being most effective) were rapid onset of action (79%) and high potency of the ICS (79%) (Figure 3B).

## Discussion

This study aimed to gain an insight into the opinions of UK physicians regarding the effectiveness of different single-inhaler or dual-inhaler combinations of an ICS and a LABA for the treatment of asthma. Using both unprompted and prompted questions,<sup>14,15</sup> this survey revealed that the



**Figure 1** Choice of most effective ICS and LABA combination (n = 82).  
**Abbreviations:** ICS, inhaled corticosteroid; LABA, long-acting  $\beta_2$ -agonist.

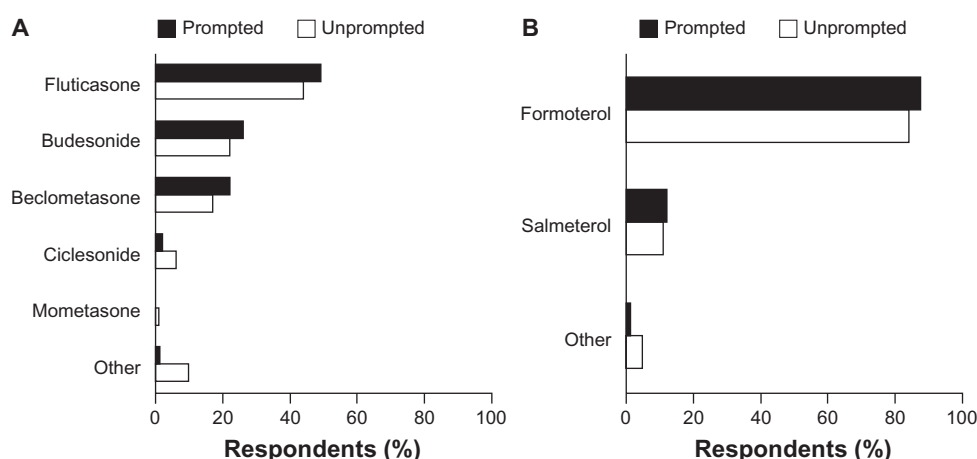
preferred choice of UK-based respiratory specialists to optimize combination therapy (ICS and a LABA) was fluticasone and formoterol, which is currently not available as a single-inhaler combination. This choice was followed by budesonide and formoterol, then beclometasone and formoterol. Our study also suggested that the most important properties of a single- or dual-inhaler combination of an ICS and a LABA are high potency of the ICS and rapid onset of action.

The rating of fluticasone as the most effective ICS in combination therapies for asthma appears to be related to its well-established pharmacological potency. Clinical data show that treatment with fluticasone results in improvements in symptoms and lung function, and reduces the frequency

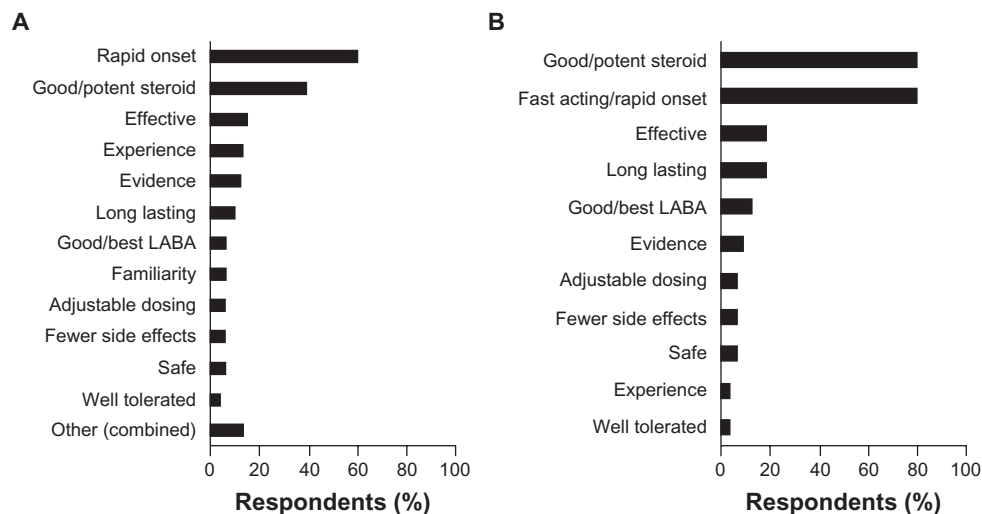
of rescue medication use in adults and children with mild to severe asthma when administered at half the equivalent daily dose of budesonide or beclometasone.<sup>18–20</sup>

The rating of formoterol as the most effective LABA probably reflects its rapid onset of action compared with salmeterol.<sup>21,22</sup> Furthermore, a recent systematic review identified a greater improvement in symptoms (reduced frequency of rescue medication use and more symptom-free days) and in lung function in patients treated with formoterol compared with those treated with salmeterol.<sup>19</sup>

This study has several strengths and limitations. Although the use of an online survey may have led to response bias, survey participants were broadly representative of the target population of respiratory consultants



**Figure 2** Choice of most effective (A) ICS and (B) LABA components (n = 82).  
**Abbreviations:** ICS, inhaled corticosteroid; LABA, long-acting  $\beta_2$ -agonist.



**Figure 3** Reasons for choice of most effective ICS and LABA components **(A)** overall (n = 82) and **(B)** for fluticasone and formoterol (n = 34).

**Abbreviations:** ICS, inhaled corticosteroid; LABA, long-acting  $\beta_2$ -agonist.

and specialist registrars, in terms of sex and geographical distribution. Participants were asked to give unprompted responses first, and these were consistent with the prompted responses that followed. The fact that some available ICSs and LABAs (eg, ciclesonide and indacaterol [not available in the UK at the time of the survey]) were not included in the list of prompted responses is unlikely to have influenced our results, because they were not mentioned unprompted or (with the exception of two mentions of ciclesonide) in the prompted “Other” category. Specific limitations include data collection from respiratory specialists, rather than from primary care where the majority of asthma management takes place, and by focusing on efficacy, this study did not specifically address the question of safety for ICSs and LABAs. Also, this observational survey was a study of “theoretical preference”, and was not designed to capture current prescribing patterns, medication usage, or dosage modifications of current formulations. To do this, a prescribing database would be required.

Finally, data from this study are UK specific and may not be representative of the attitudes of respiratory specialists within the wider community in Europe. However, the results are consistent with a recent pan-European study of ICS-prescribing trends, in which fluticasone was shown to be the most widely prescribed ICS (included in 38% of inhalers prescribed), followed by budesonide and beclometasone.<sup>23</sup> Further similar research would be useful to evaluate physician perceptions of the effectiveness of combinations of currently available ICSs and LABAs for the management of other respiratory diseases, especially COPD, both in the specialist setting and in primary care.

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Mundipharma, Novartis, and Teva. He or his research team has received grants and support for research into respiratory disease from the following organizations in the past 5 years: Aerocrine, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Merck Sharp & Dohme, Mundipharma, Novartis, Nycomed, Pfizer, Teva, and the UK National Health Service. He has given presentations for AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Merck Sharp & Dohme, Mundipharma, Pfizer, and Teva. In addition, D Price has shares in AKL Ltd, which produces phytopharmaceuticals. He is the sole owner of Research in Real Life Ltd.

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## Supplementary information

### Respiratory questionnaire

#### Eligibility criteria

##### Position

Which of the following best describes the position that you hold?

- Internal medicine
- Surgeon
- Gastrointestinal/colorectal medicine
- Obstetrics
- Gynecology
- Respiratory
- Other

##### Date of qualification

Please write in the year you qualified ...

[MUST BE NUMERICAL BETWEEN 1965 AND 2005]

##### Seniority

Which of the following best describes your role?

- Consultant
- Associate specialist
- Staff grade
- Specialist registrar (year 5+)
- Specialist registrar (year 3–4)
- Specialist registrar (year 1–2)
- Other

##### Location

Where are you currently practicing?

- North-West SHA
- North-East SHA
- Yorkshire and Humber SHA
- East Midlands SHA
- West Midlands SHA
- East of England SHA
- London SHA
- South-East Coast SHA
- South Central SHA
- South-West SHA

- Scotland
- Wales
- Northern Ireland
- Retired
- Not working in the UK

##### Patient caseload

How many patients do you see regarding asthma or COPD in a typical month?

Please write in the number below:

### Asthma management

#### Most effective LABA and ICS combination (current products)

Based upon your knowledge of the **individual LABA and ICS components**, what would you consider to be the **most effective** combination (irrespective of whether it is currently available or not)?

Please explain clearly.

| LABA | ICS |
|------|-----|
|      |     |

#### Most effective LABA and ICS combination (hypothetically speaking)

Again based upon your knowledge of the **individual components** (rather than current availability), which of the following would you say is likely to be the most effective LABA and ICS combination?

Please select one:

- Beclometasone/formoterol
- Beclometasone/salmeterol
- Budesonide/formoterol
- Budesonide/salmeterol
- Fluticasone/formoterol
- Fluticasone/salmeterol
- Other (please specify)

#### Reasons for most effective combination

Why do you say that <answer at Q2> is likely to be the most effective LABA and ICS combination?

Please explain fully.

#### Pragmatic and Observational Research

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Pragmatic and Observational Research is an international, peer-reviewed, open access journal that publishes data from studies designed to reflect more closely medical interventions in real-world clinical practice compared with classical randomized controlled trials (RCTs). The manuscript management system is completely online and includes a very quick and fair peer-review

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