The paradoxes of asthma management: time for a new approach?

O’Byrne et al., ERJ 2017.

Prices and SmPC available upon request via your medical representative.
Context

- Paradoxes of asthma management
- Practical solutions
- Discussion
National and international surveys continue to reveal inadequate asthma control in more than 50% of patients\(^1\)

O’Byrne et al., ERJ 2017

**REALISE study (N=8,000)**\(^2\)

45.1% of patients had GINA-defined uncontrolled asthma (n=3,611)

**INSPIRE study (N = 3,415)**\(^3\)

51% of patients had uncontrolled asthma, based on ACQ scores (n = 1,732)

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1. O’Byrne et al. ERJ 2017; 50: 1701103
During symptom worsening, patients rely on their SABA immediately but delay taking additional preventer medication.

Stages of symptom worsening

ICS, inhaled corticosteroid; LABA, long-acting β₂-agonist; SABA, short-acting β₂-agonist.

Over-reliance on SABA is irrespective of asthma severity

Medicines used to treat asthma by Symptoms Severity Index: Anti-inflammatories versus quick-relief medications

ICS, inhaled corticosteroid; SABA, short-acting β2-agonist.

“We hypothesise that the roots of this behaviour, and the poor outcomes of asthma treatment in many patients with even mild asthma, are attributable to a number of paradoxes in our treatment approach and advice, which are confusing to patients.

The unintended consequence is the establishment of a pattern of early over-reliance on SABA.”

O’Byrne et al., ERJ 2017
Context

Paradoxes of asthma management

Practical solutions

Discussion
Paradox #1

In step 1, a SABA alone is recommended despite the fact that asthma is a disease of chronic airway inflammation with increased inflammation at the times of exacerbations.¹

Patients are taught from the start that treating symptoms alone is acceptable.

1. O’Byrne et al. ERJ 2017; 50: 1701103
Paradox #2

In step 1, patients are asked to recognise when their condition is becoming troublesome and respond appropriately with SABA use.

However, at steps 2 and higher, this approach used at step 1 has to be unlearnt, when physicians attempt to emphasise the key role of a controller that needs to be taken at fixed doses trying to minimize SABA use.¹

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¹ O’Byrne et al. ERJ 2017; 50: 1701103
Paradox #3

In step 2 and higher, the medication that treats the underlying inflammation (ICS) is not the one that the patient perceives is benefitting them (SABA).¹

Proportion of ICS-treated patients who agree with each statement (n = 3 415)²

1. O’Byrne et al. ERJ 2017; 50: 1701103
Paradox #4

There is a different safety message in the advice given for the use of SABA and LABA (SABA alone being safe and LABA alone being unsafe)\(^1\)

**WARNING**

<table>
<thead>
<tr>
<th></th>
<th>SABA alone</th>
<th>LABA alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>OK</td>
<td></td>
<td>not OK</td>
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</table>

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1. O’Byrne et al. ERJ 2017; 50: 1701103
Paradox #5

There is a dislocation between patients’ understanding of “asthma control” and the frequency, impact and severity of their symptoms.¹

**REALISE study (N=8,000)²**

- 83.7% of these patients perceived their asthma as controlled (n=3,023)
- 45.1% of patients had GINA-defined uncontrolled asthma (n=3,611)
- 69.9% of these patients perceived their asthma as not serious (n=2,523)

Reinforce a patient’s false belief that the asthma has been effectively controlled.

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1. O’Byrne et al. ERJ 2017; 50: 1701103
• Context
• Paradoxes of asthma management

**Practical solutions**
• Discussion
The early introduction of ICS at the time of diagnosis is attractive, but there are several factors that could limit the efficacy of this approach…

...patients will always favour the SABA over the ICS or other controller, because of the rapid relief of symptoms.¹

O’Byrne et al., ERJ 2017

¹ O’Byrne et al. ERJ 2017; 50: 1701103
Continuum of care model: patient-adjusted pharmacotherapy of asthma

1. O’Byrne et al. ERJ 2017; 50: 1701103

FIGURE 3 Continuum of care: patient-adjusted plus physician-directed step-wedge approach to pharmacotherapy in asthma. LABA: long-acting β2-agonist; ICS: inhaled corticosteroid.
Replacing SABA alone as needed by ICS/formoterol as-needed in patients with intermittent or infrequent symptoms could be the solution to these paradoxes.\textsuperscript{1}

<table>
<thead>
<tr>
<th>Paradox</th>
<th>Description</th>
<th>Table 1 Paradoxes in current asthma management</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>In step 1 treatment, a SABA bronchodilator alone is recommended despite the fact that asthma is a disease of chronic airway inflammation with increased inflammation at the times of exacerbations.</td>
<td></td>
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<tr>
<td>2</td>
<td>In step 1 treatment, the patient has autonomy and their perception of treatment as needed to control symptoms is accepted, whereas at higher asthma treatment steps it is assumed that patients will adopt a fixed-dose approach.</td>
<td></td>
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<tr>
<td>3</td>
<td>There is a switch in recommendation from using a SABA alone as-needed at step 1 to advising an ICS fixed-dose regimen at step 2 and minimising SABA use. The medication that treats the underlying disease, which patients are encouraged to take (the ICS) is not the one that the patient perceives is benefitting them (the SABA), which they are now discouraged from taking.</td>
<td></td>
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<tr>
<td>4</td>
<td>There is a different safety message in the advice given for the use of SABA and LABA within the guidelines; SABA alone being safe and LABA alone being unsafe.</td>
<td></td>
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<tr>
<td>5</td>
<td>There is a dislocation between patients’ understanding of “asthma control” and the frequency, impact and severity of their symptoms.</td>
<td></td>
</tr>
</tbody>
</table>

1. O’Byrne et al. ERJ 2017; 50: 1701103
Asthma is a heterogeneous disease, so this approach may be considered an oversimplification (ex: how are non-eosinophilic asthma treated in this continuum of care?).

The approach is deliberately simple for all the Doctors (in primary care in particular) without access to the tools to phenotype/endotype asthma while still providing adequate and acceptable treatment for asthma patients

*O’Byrne et al., ERJ 2017*
It will be vital to conduct studies to show this as a superior approach to SABA as needed, and not inferior to regular ICS for mild asthma.

O’Byrne et al., ERJ 2017

For compliance reasons, AstraZeneca cannot communicate on the results of the SYGMA trials considered as off-label until further notice.
• Context
• Paradoxes of asthma management
• Practical solutions

Discussion
A new approach - **Airflow limitation and risk as a result of eosinophilic airway inflammation** as the most important and recognisable treatable traits\(^1\)

**Figure 7:** Ongoing monitoring of the two dominant treatable traits of airways diseases and precision management

*Combination corticosteroid and rapid-onset $\beta_2$ agonist inhaler is the default rescue medication.*

Time to first severe asthma-related event was **prolonged across all 3 budesonide groups**

The average hazard ratios did not differ across symptom groups.

Reddel et al., Lancet 2017
Rate of severe exacerbations **decreased across all 3 budesonide groups**

No interaction was seen by baseline symptom frequency
Asthma control is poor across disease severity

In the MAGIC study of patients with physician-diagnosed asthma (N = 1286), the incidence of uncontrolled asthma increased with increasing GINA* Steps 2–51.

Asthma control was poor, even at GINA Step 11.

*Based on 2006 GINA guidelines2.
GINA, Global Initiative for Asthma; GCS, glucocorticoids; ICS, inhaled corticosteroid; IgE, immunoglobulin E; LABA, long-acting β2-agonist; SABA, short-acting β2-agonist.
In two Australian studies

16% of patients with near-fatal asthma\(^2\)

15–20% of adults dying of asthma\(^2,3\)

had symptoms less than weekly in the previous 3 months

NRAD report reveals excessive prescribing of SABAs and under-prescribing of preventer medication

The NRAD report was an investigation of recent asthma deaths in the UK by the Royal College of Physicians.

**Evidence of excessive prescribing of reliever medication**

39% of patients who were on short-acting relievers at the time of death had been prescribed more than 12 short-acting reliever inhalers in the year before they died.

4% had been prescribed more than 50 reliever inhalers

**Evidence of under-prescribing of preventer medication**

To comply with recommendations, most patients would usually need at least 12 preventer prescriptions per year.

38% of patients on preventer inhalers* received fewer than 4 inhalers in the year leading up to their death…

and 80% received fewer than 12 preventer inhalers

*Of those patients for which the number of prescriptions was known. Among 189 patients who were on short-acting relievers at the time of death, the number of prescriptions was known for 165. Among 168 patients on preventer inhalers at the time of death, either as stand-alone or in combination, the number of prescriptions was known for 128.

NRAD, National Review of Asthma Deaths; SABA, short-acting β2-agonist

Over-reliance on SABA and under-use of ICS are both associated with an increase in mortality

Over-reliance on SABA at the expense of ICS controller therapy is associated with an increased risk of asthma-related death, as a result of under-treatment of inflammation\(^1\)

Episodes of high reliever use (>6 inhalations/day on at least one day) are also predictive of an increased risk of exacerbations\(^3\)

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ICS, inhaled corticosteroid; SABA, short-acting \(\beta_2\)-agonist.
Potential outcomes with different asthma treatment regimens in response to worsening symptoms

- Symbicort® for maintenance and relief
- Symbicort® adjustable maintenance dosing
- Traditional asthma therapy

Early intervention: temporary increase in treatment by adjusting maintenance dose

Immediate intervention: treatment when breakthrough symptoms occur

Late intervention: treatment adjusted during exacerbation

COPD: Symbicort available in Turbohaler or pMDI*

SmPCs: Symbicort Turbohaler (160/4,5), Symbicort Turbohaler (320/9), Symbicort Aerosol(160/4,5) latest versions

* Symbicort aérosol-doseur is to be used in the treatment of COPD and is not approved within the EU for the treatment of asthma. Symbicort aérosol-doseur is not to be used as a reliever medication, thus obviating its use as maintenance and reliever therapy (ie, SMART).

# Maintenance & Reliever therapy only in asthma for Symbicort Turbohaler (160/4,5)

Maintenance & reliever therapy as of 12 years old#

Available in Triple Pack#
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