



Reframing Asthma Management

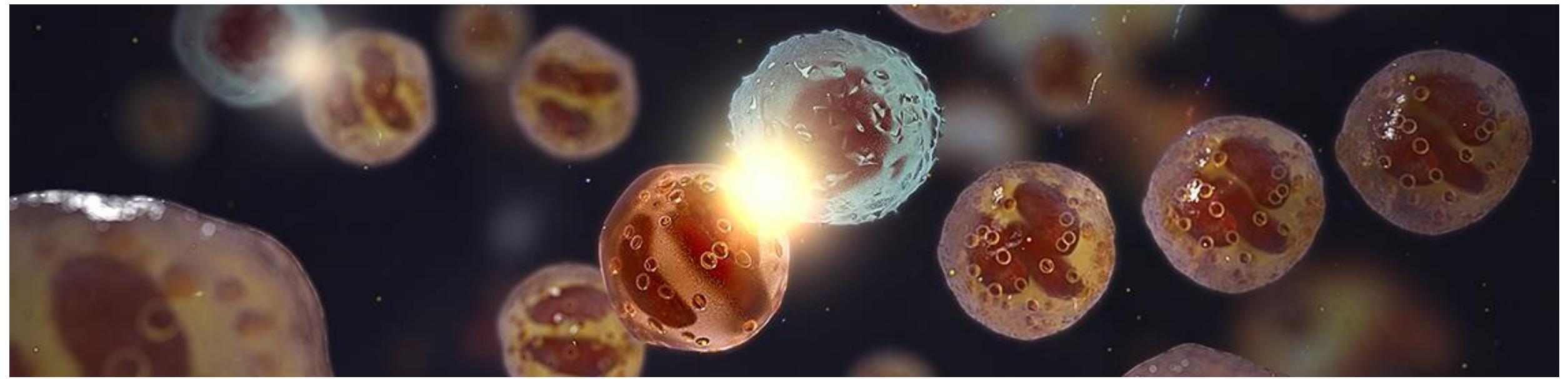
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Head of Pulmonary Critical Care Division, Hotel Dieu de France UMC

LPS annual congress

28th April 2023

SYM-67-SK-0222-0224-NE



Titles

- **Asthma and its Global Burden**
- **Why Symbicort[®] Turbuhaler[®] is different?**
 - **Efficacy**
 - **Efficacy Data: Exacerbations**
 - **Efficacy data: Symptoms and asthma control**
 - **Safety and tolerability profile**
- **The role of Turbuhaler[®]**

Global Asthma Burden



Asthma
300
Million
affected¹

400 M affected
by 2025²

Many Asthmatic patients are struggling to breathe...



Evolution and innovation in Asthma approach: GINA Controlling Asthma

- Asthma, is heterogenous.
- Individual assessment of symptoms and risk factors leading to personalized treatment decisions and NOT « ONE-SIZE-FITS-ALL ».
- Spectrum of treatment: Pharmacological, non pharmacological and treatment of modifiable risk factors.
- It is vital to identify the different patients groups (Phenotypes) to improve therapeutic options.

Problems encountered by Physicians when treating asthmatic patients

- The perception of the patient concerning the control of their asthma : they link their symptoms to the control level.
- The overuse of rescue medication : Why?, the major reason is lack of education of the patients about their conditions, on the correct use of the device.
- the non-control of exacerbating factors and triggers.
- Lack of adherence and compliance to the treatment.
- Positioning of the patient is a crucial step in the management of the asthma:
- Involving the patient in the asthma management plan is important and increase the adherence.

Asthma control in adults in the Middle East and North Africa: Results from the ESMAA study



ELSEVIER

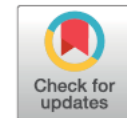
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Asthma control in adults in the Middle East and North Africa: Results from the ESMAA study

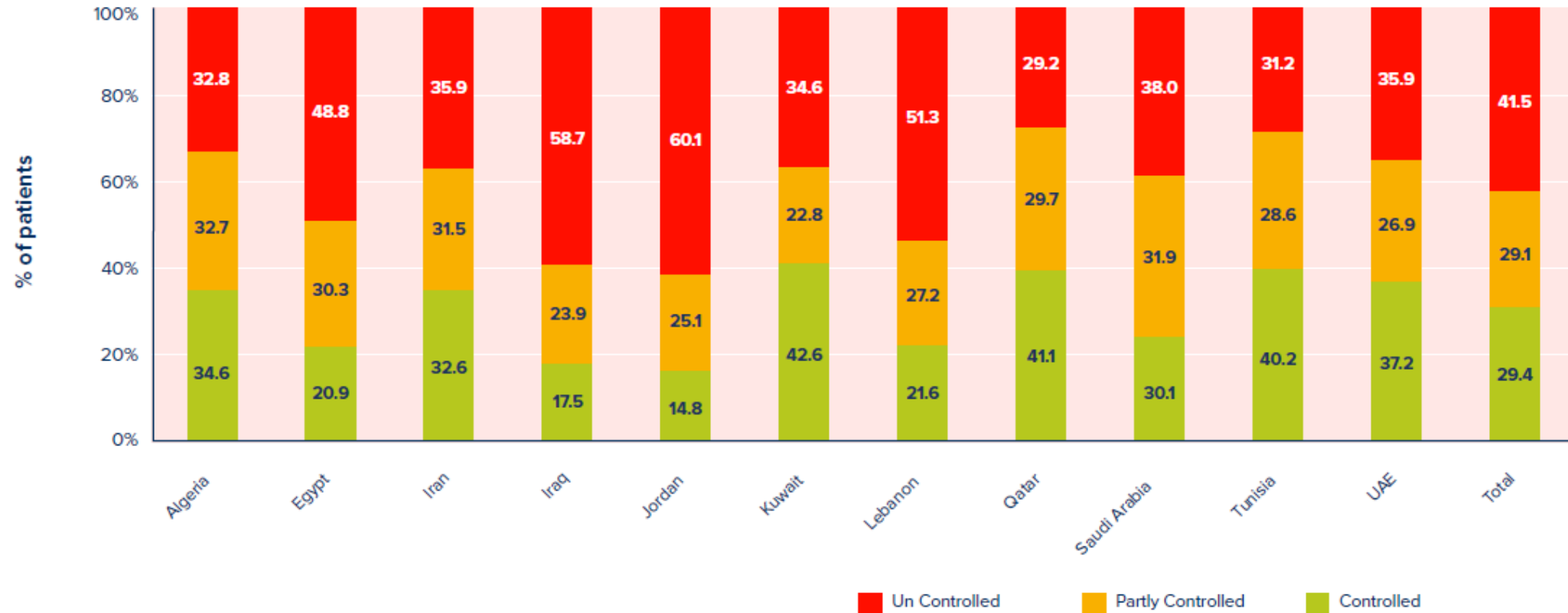


Hesham Tarraf^{a,*}, Hamdan Al-Jahdali^b, Abdul Hameed Al Qaseer^c, Anamarija Gjurovic^d,
Houria Haouichat^e, Basheer Khassawneh^f, Bassam Mahboub^g, Roozbeh Naghshin^h,
François Montestrucⁱ, Naser Behbehani^j

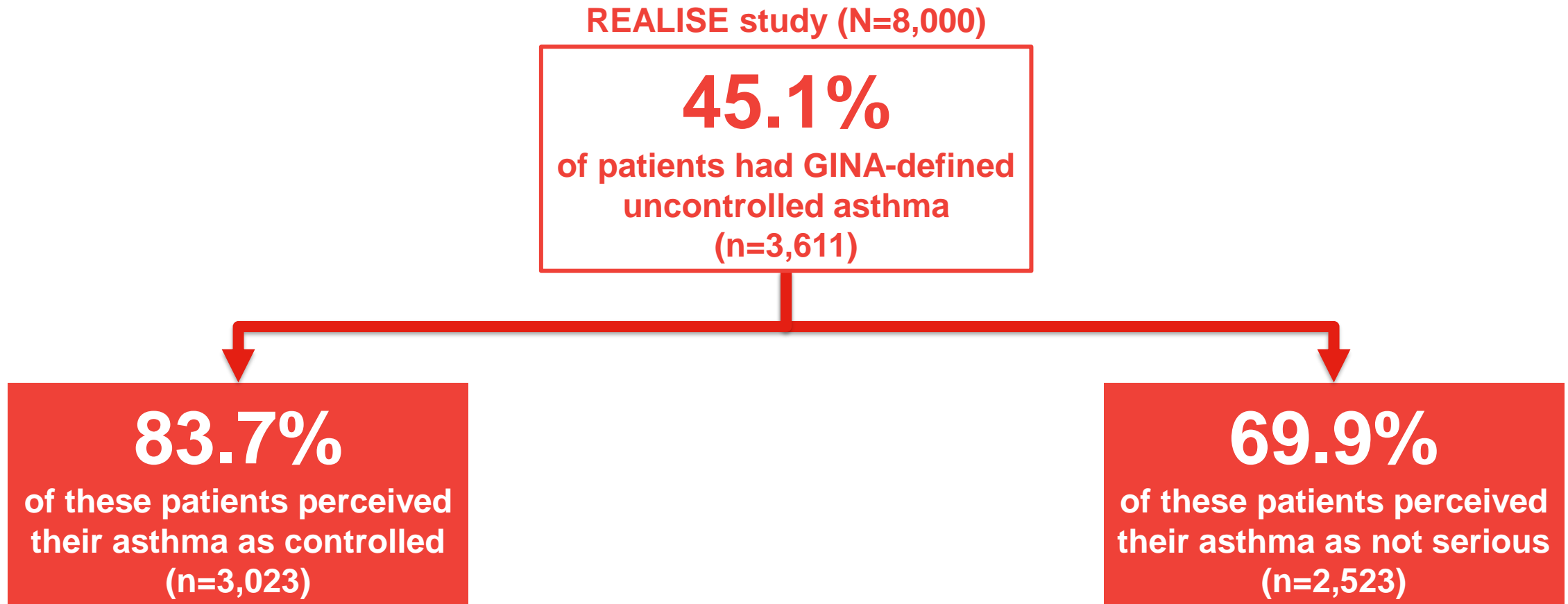
Asthma control in adults in the Middle East and North Africa: Results from the ESMAA study

- Overall **7236** eligible patients were included in **577** sites between June 2014 and December 2015 (median 10 patients/site).

Asthma Control - GINA



There is an unmet need for improved understanding and attainment of asthma control



- The REALISE study demonstrated a large gap between patients' perception of asthma control, and the clinical reality of asthma control

Patients' perception of asthma control does not match the reality

INSPIRE study (N = 3,415)

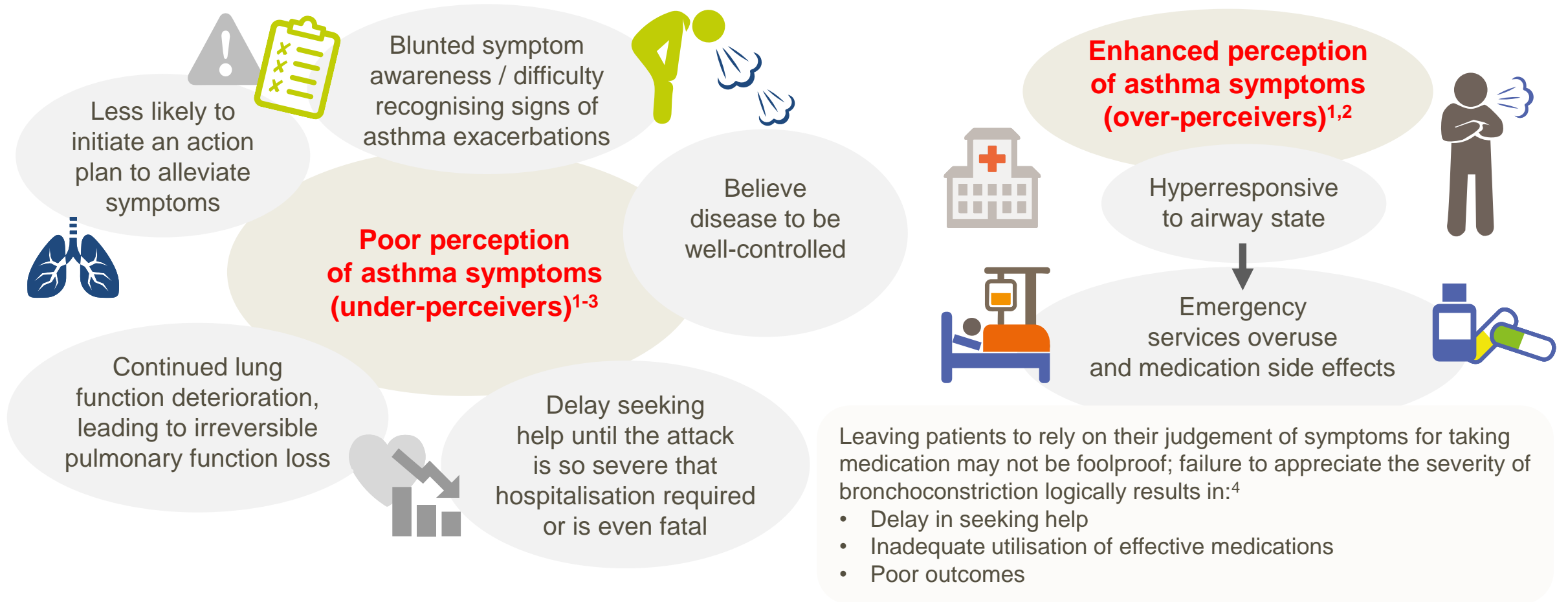
51%
of patients had uncontrolled asthma,
based on ACQ scores (n = 1,732)

55%
of these patients perceived their
asthma control as 'relatively good'

- Levels of asthma control were poor in the INSPIRE study
- However, most patients with poorly controlled asthma were unaware of their asthma control status
- In addition, 74% of patients used ≥ 1 SABA inhalation every day in the previous 7 days

This patient behavior can impact Asthma management

Under- and over-perception of symptoms is common in asthma



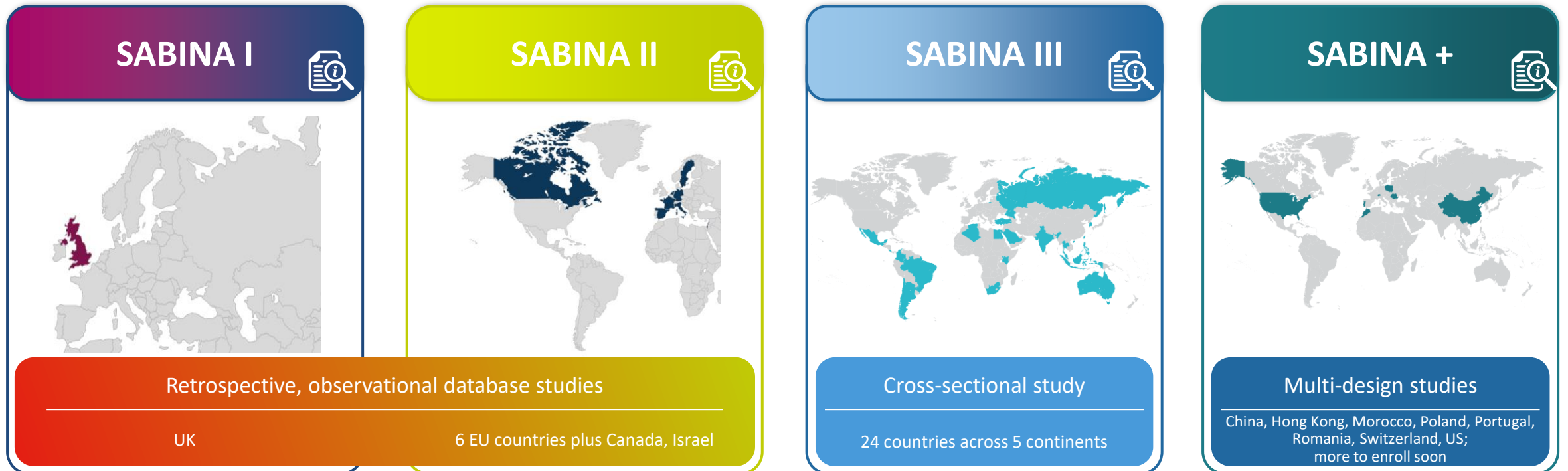
Problems encountered by Physicians when treating asthmatic patients

- The overuse of rescue medication : Why?, the major reason is lack of education of the patients about their conditions, on the correct use of the device.
 - The perception of the patient concerning the control of their asthma : they link their symptoms to the control level.
 - the non-control of exacerbating factors and triggers.
 - Lack of adherence and compliance to the treatment.
 - Positioning of the patient is a crucial step in the management of the asthma:
 - Involving the patient in the asthma management plan is important and increase the adherence.

SABINA Program: To establish global patterns of SABA and maintenance therapy use in asthma, and their relation to asthma outcomes

Largest real-world data analysis on SABA and maintenance therapy globally

Flexible framework with one core protocol and core requirements across pillars to ensure scientific alignment¹



EU, European Union; SABA, short-acting β_2 -agonists; SABINA, SABA use IN Asthma; UK, United Kingdom; US, United States.

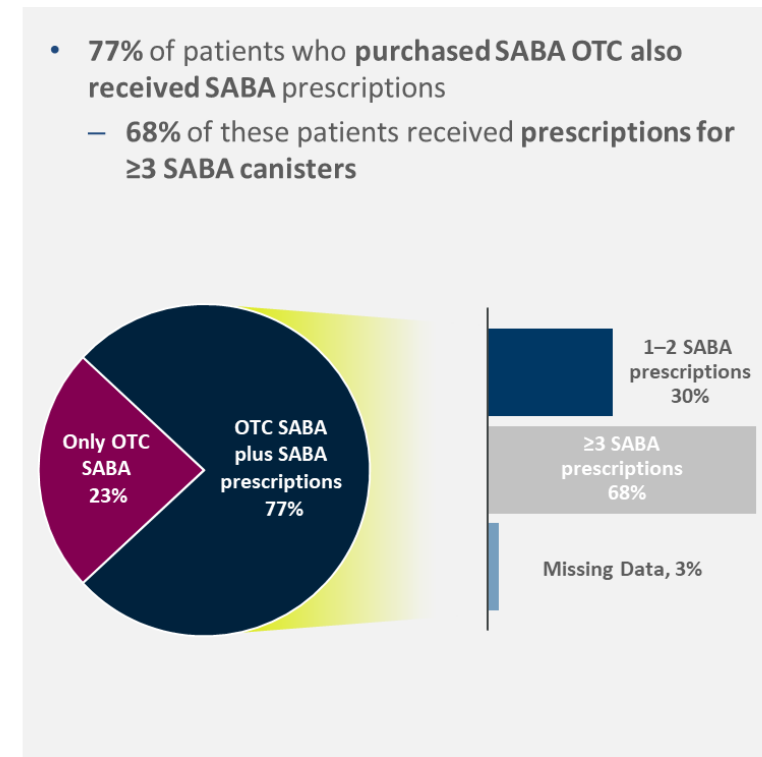
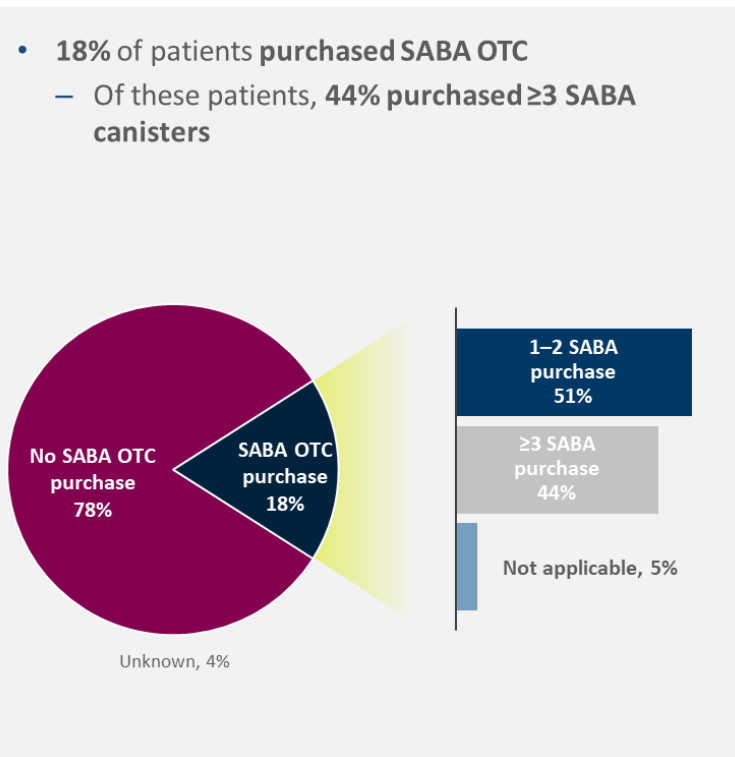
1. Cabrera CS, Nan C, Lindarck N, Beekman MJ, Arnetorp S, van der Valk RJ. SABINA: global programme to evaluate prescriptions and clinical outcomes related to short-acting β_2 -agonist use in asthma. European Respiratory Journal. 2020 Feb 1;55(2).

SABINA III – An observational, cross-sectional study carried out in 24 countries¹

SABA purchase over the counter

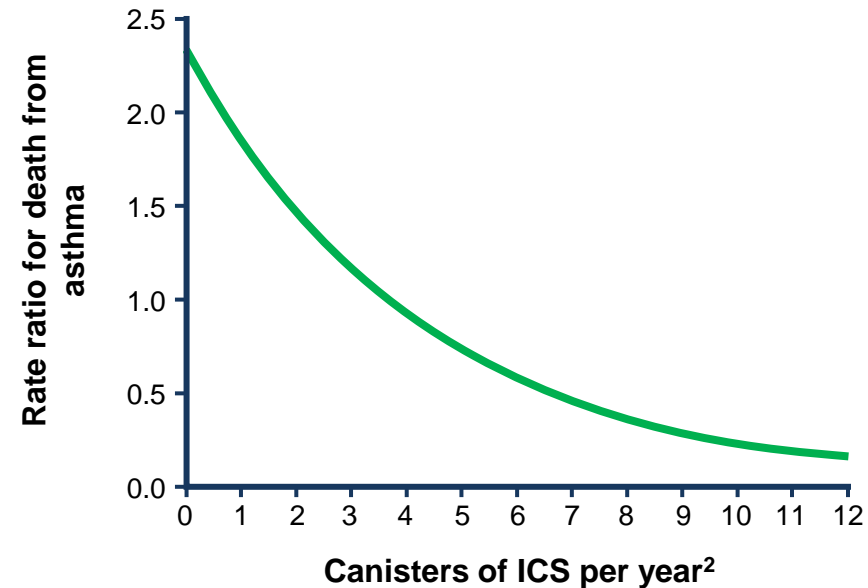
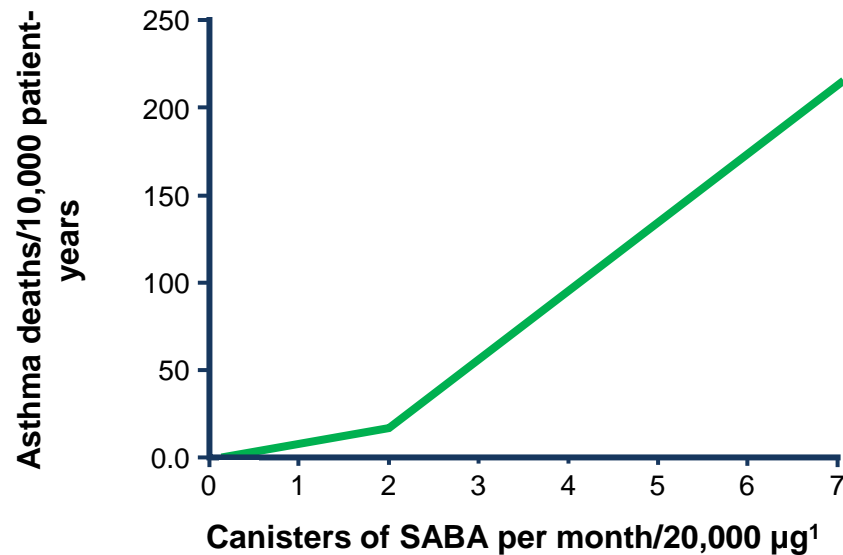
18% of patients purchased SABA OTC, 77% also received SABA prescriptions and of these, 68% had ≥ 3 SABA canister prescriptions

44% of patients who buy SABA as OTC, over use SABA



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

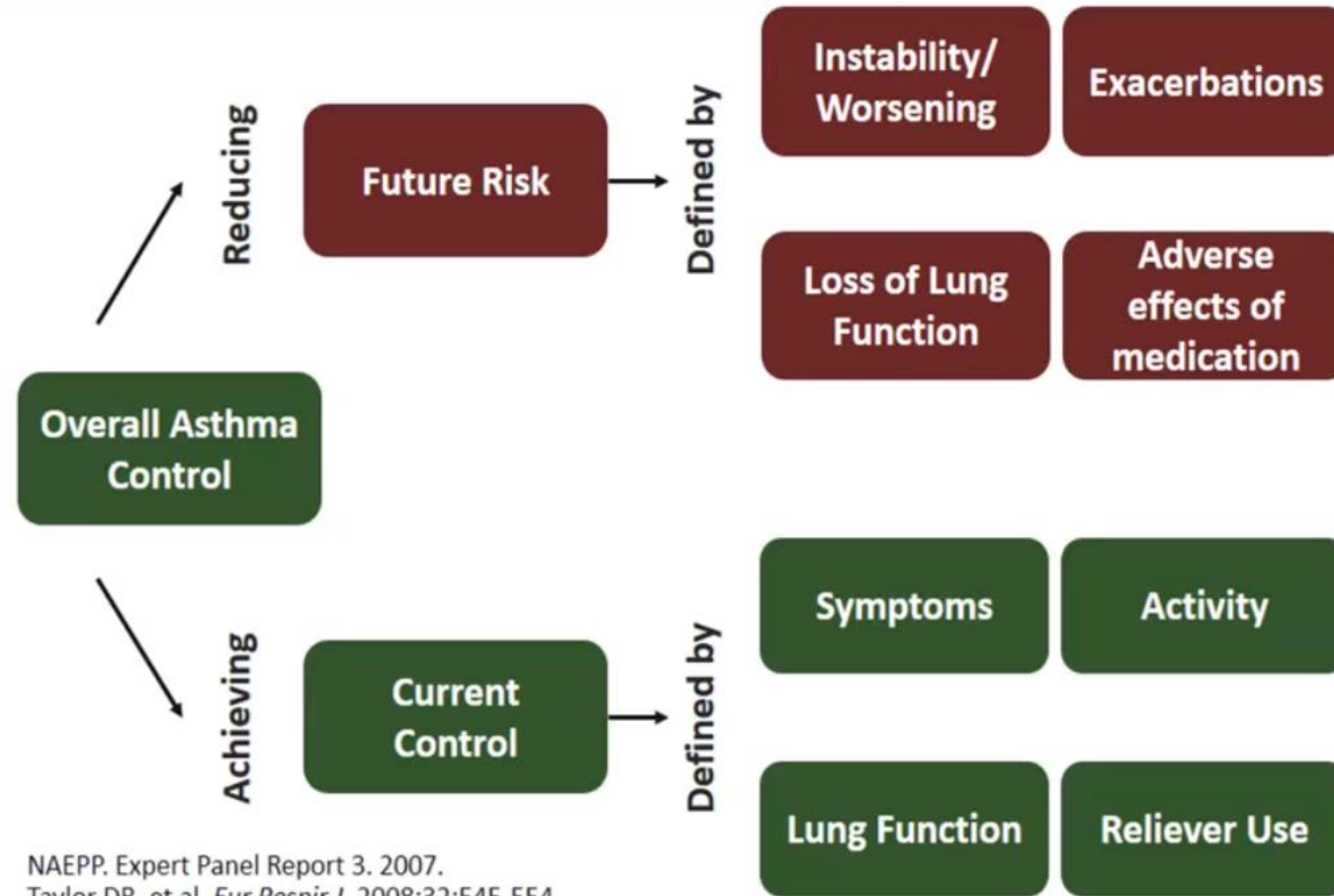
- Over-reliance on SABA at the expense of ICS controller therapy is associated with an increased risk of asthma-related death, as a result of under-treatment of inflammation¹⁻²



- Episodes of high reliever use (>6 inhalations/day on at least one day) are also predictive of an increased risk of exacerbations³

1. Suissa S, Ernst P, Boivin JF, Horwitz RI, Habbick BR, Cockcroft D, Blais L, McNutt M, Buist AS, Spitzer WO. A cohort analysis of excess mortality in asthma and the use of inhaled beta-agonists. *American journal of respiratory and critical care medicine*. 1994 Mar;149(3):604-10. 2. Suissa S, Ernst P, Benayoun S, Baltzan M, Cai B. Low-dose inhaled corticosteroids and the prevention of death from asthma. *New England Journal of Medicine*. 2000 Aug 3;343(5):332-6. 3. Buhl R, Kuna P, Peters MJ, Andersson TL, Naya IP, Peterson S, Rabe KF. The effect of budesonide/formoterol maintenance and reliever therapy on the risk of severe asthma exacerbations following episodes of high reliever use: an exploratory analysis of two randomised, controlled studies with comparisons to standard therapy. *Respiratory research*. 2012 Dec;13(1):59.

Goals of Asthma Management



NAEPP. Expert Panel Report 3. 2007.
Taylor DR, et al. *Eur Respir J*. 2008;32:545-554.





Asthma guidelines have moved towards earlier ICS use



EDITORIAL
GINA 2019

GINA 2019: a fundamental change in asthma management

Treatment of asthma with short-acting bronchodilators alone is no longer recommended for adults and adolescents

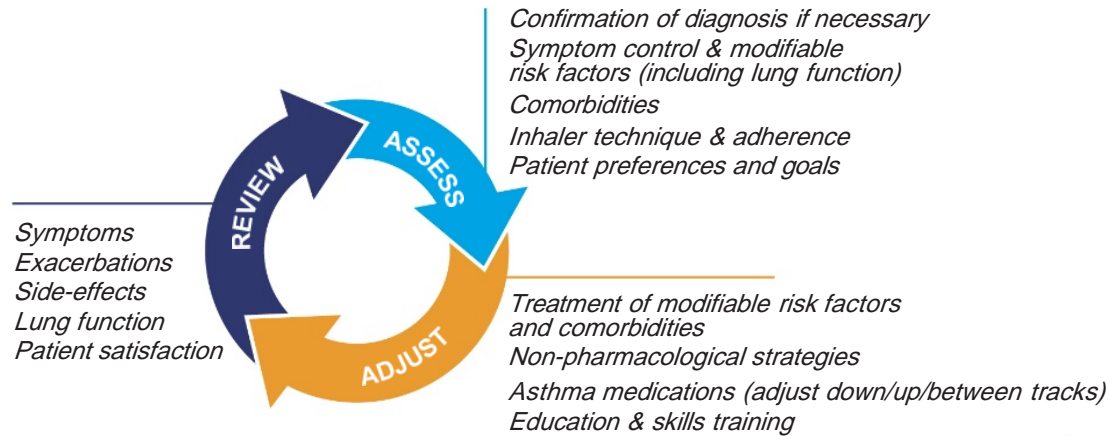
Helen K. Reddel ¹, J. Mark FitzGerald², Eric D. Bateman³,
Leonard B. Bacharier⁴, Allan Becker⁵, Guy Brusselle⁶, Roland Buhl⁷,
Alvaro A. Cruz⁸, Louise Fleming ⁹, Hiromasa Inoue¹⁰, Fanny Wai-san Ko ¹¹,
Jerry A. Krishnan¹², Mark L. Levy ¹³, Jiangtao Lin¹⁴, Søren E. Pedersen¹⁵,
Aziz Sheikh¹⁶, Arzu Yorgancioglu¹⁷ and Louis-Philippe Boulet¹⁸

GINA 2021

Adults & adolescents 12+ years

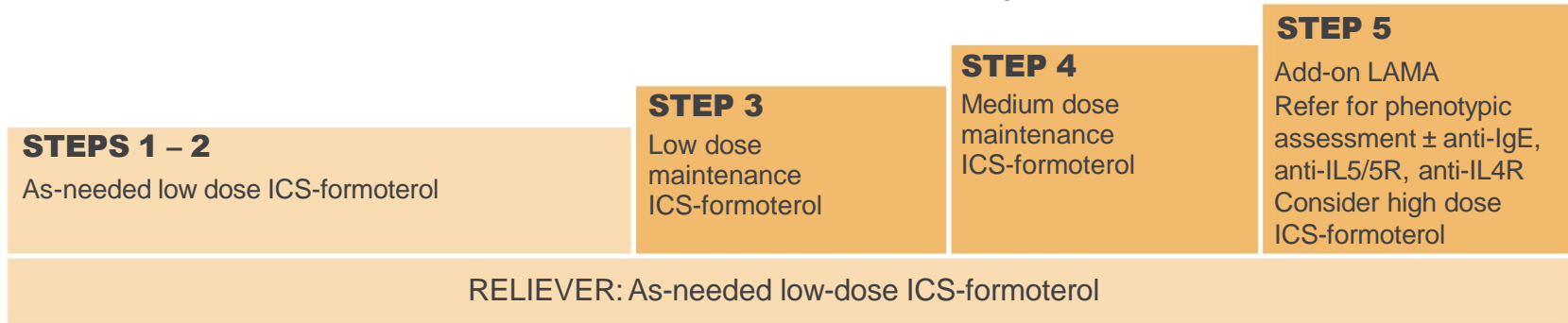
Personalized asthma management

Assess, Adjust, Review
for individual patient needs



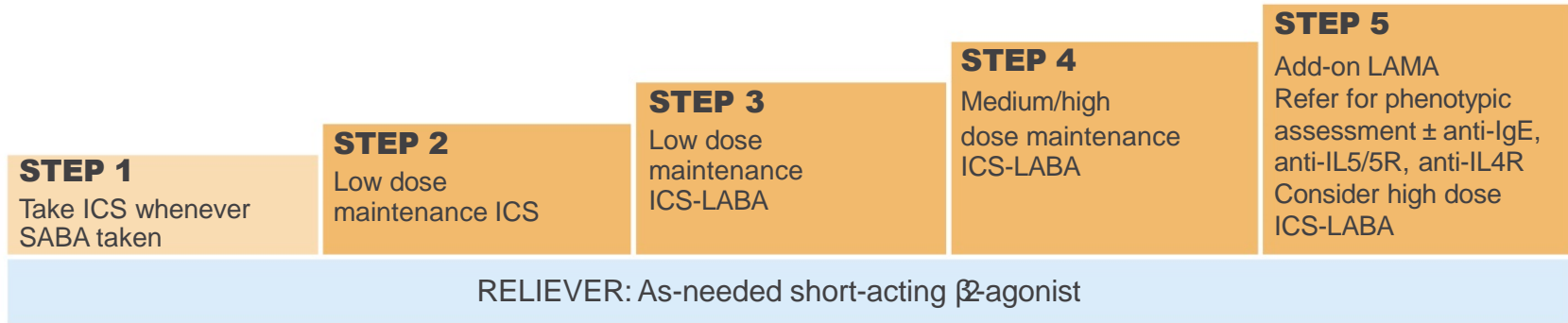
CONTROLLER and PREFERRED RELIEVER

(Track 1). Using ICS-formoterol as reliever reduces the risk of exacerbations compared with using a SABA reliever



CONTROLLER and ALTERNATIVE RELIEVER

(Track 2). Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller



Other controller options for either track

	<i>Low dose ICS whenever SABA taken, or daily LTRA, or add HDM SLIT</i>	<i>Medium dose ICS, or add LTRA, or add HDM SLIT</i>	<i>Add LAMA or LTRA or HDM SLIT, or switch to high dose ICS</i>	<i>Add azithromycin (adults) or LTRA; add low dose OCS but consider side-effects</i>
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Disclaimer : (Budesonide/Formoterol is indicated only in management of Moderate to Severe Asthma (GINA Stage 3 to 5) as per label in Lebanon.



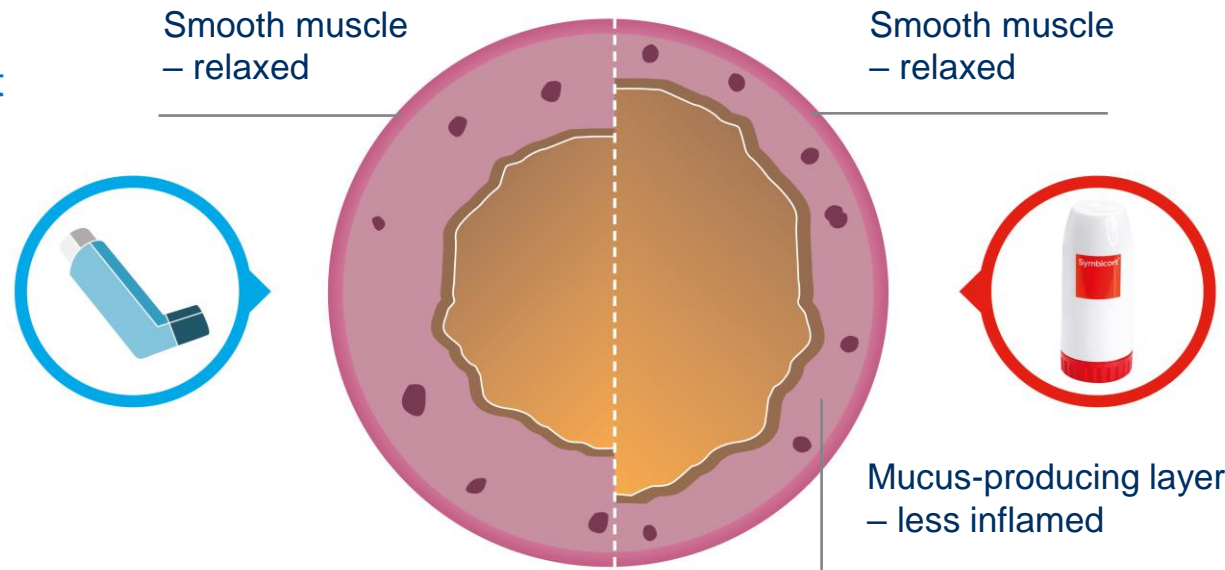
Why Symbicort[®] Turbuhaler[®] is different?

Symbicort[®] – Efficacy Data: Exacerbations

Symbicort®* – anti-inflammatory relief from a single inhaler to reduce exacerbations^{1,2} and provide 24-hour symptom control³

Worsening symptoms are due to bronchoconstriction and inflammation³

SABAs provide only bronchodilation, without inflammatory control³



When Symbicort®* is used as an anti-inflammatory reliever as needed on top of maintenance therapy it provides:

bronchodilation and additional inflammatory control

to reduce exacerbations^{1,2} and provide 24-hour symptom control³

*Symbicort® Maintenance and Reliever

Ref 3: Randomized, double-blind 6-month study of 3335 symptomatic adult and adolescent asthma patients (mean FEV1 73% predicted, mean inhaled corticosteroid dose 745 µg/day). Symbicort® Maintenance and Reliever 160/4.5 µg one inhalation bd + additional inhalations as needed. Symbicort® Maintenance and Reliever prolonged the time to first severe exacerbation requiring hospitalisation, emergency room treatment or oral steroids (primary variable) vs fixed-dose salmeterol/fluticasone and budesonide/formoterol (p=0.0034 and p=0.023 respectively). Symbicort had 7x more asthma control days (defined as no day-time symptoms, no night-time symptoms, no night awakenings caused by asthma, no as-needed medication use) vs baseline: Baseline 5.8% vs Treatment 41.3%. Study results also showed salmeterol/fluticasone 25/125 µg two inhalations bd + terbutaline as needed has similar asthma control days results: Baseline 5.7% vs Treatment 43.7%.

1. Kuna P, Peters MJ, Manjra AI, Jorup C, Naya IP, Martinez-Jimenez NE, Buhl R. Effect of budesonide/formoterol maintenance and reliever therapy on asthma exacerbations. International journal of clinical practice. 2007 May;61(5):725-36. To T, Stanojevic S, Moores G, Gershon AS, Bateman ED, Cruz AA, Boulet LP. Global asthma prevalence in adults: findings from the cross-sectional world health survey. BMC public health. 2012 Dec;12(1):204. 2. Selroos O. A smarter way to manage asthma with a combination of a long-acting β2-agonist and inhaled corticosteroid. Therapeutics and clinical risk management. 2007 Jun;3(2):349. 3. Shahidi N, FitzGerald JM. Current recommendations for the treatment of mild asthma. Journal of asthma and allergy. 2010;3:169.

The formoterol component of Symbicort® produces as rapid bronchodilation as salbutamol

- Improvement in FEV₁ is as rapid and effective with formoterol 4.5 or 9 µg as with salbutamol 100 or 200 µg

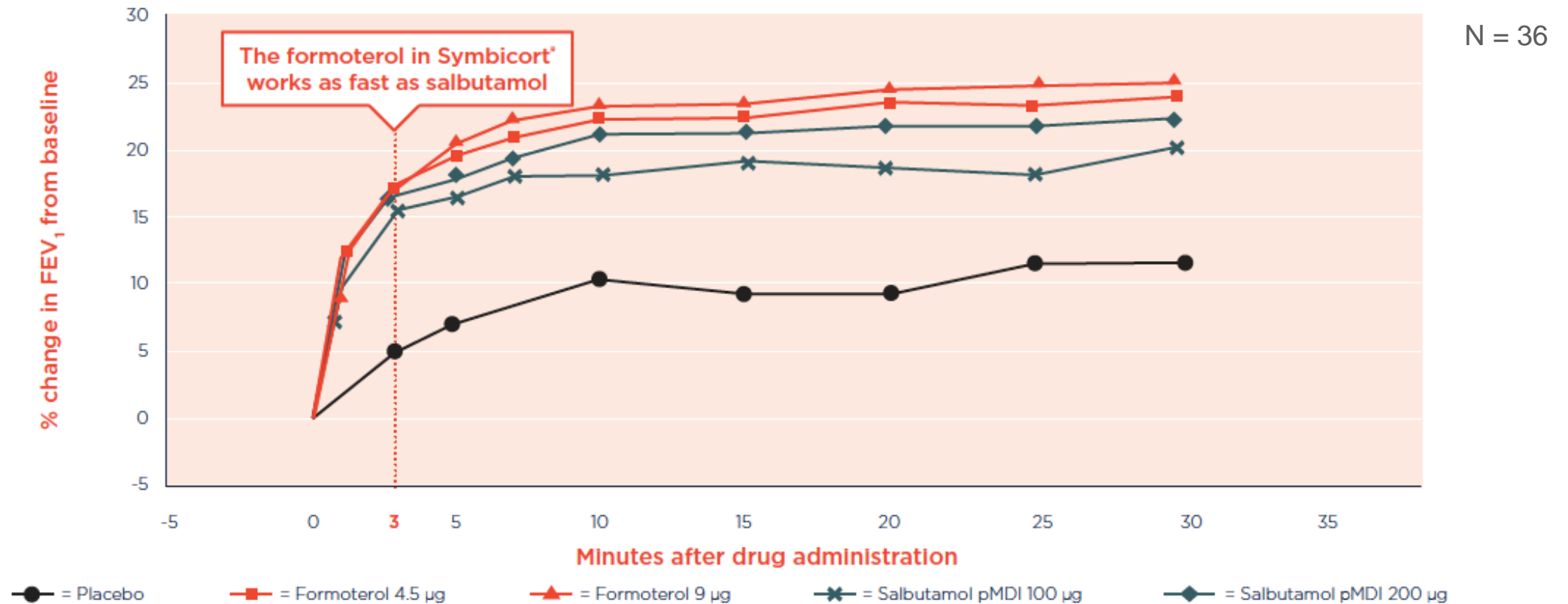


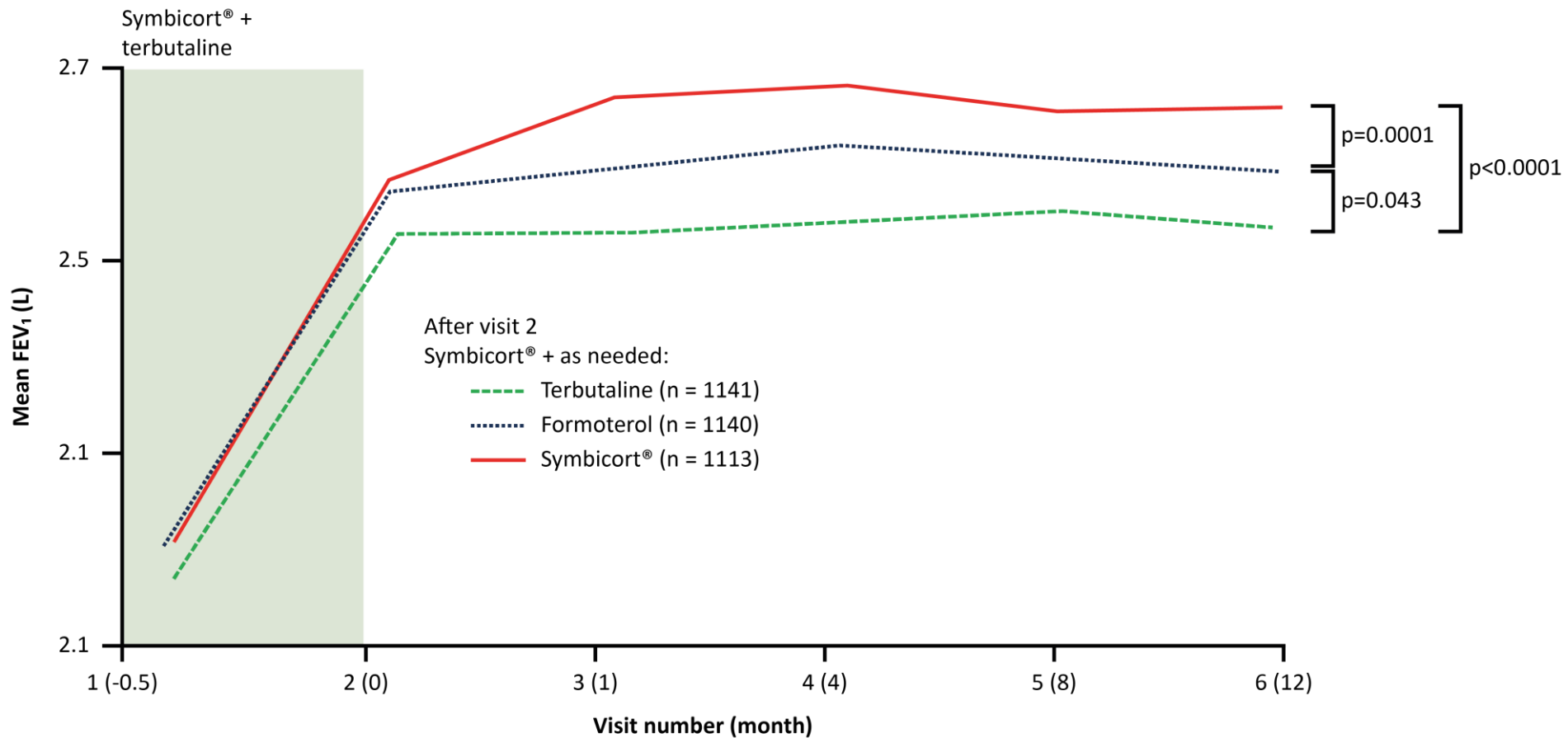
Figure source: Seberová E and Andersson A. 2000

FEV₁, forced expiratory volume in 1 second; pMDI, pressurised metered dose inhaler

Seberová E, Andersson A. Oxis®(formoterol given by Turbuhaler®) showed as rapid an onset of action as salbutamol given by a pMDI. Respiratory medicine. 2000 Jun 1;94(6):607-11..

Symbicort[®] gives additional increase in FEV₁ and sustained bronchodilation over 6 months when used as-needed vs terbutaline or formoterol as-needed

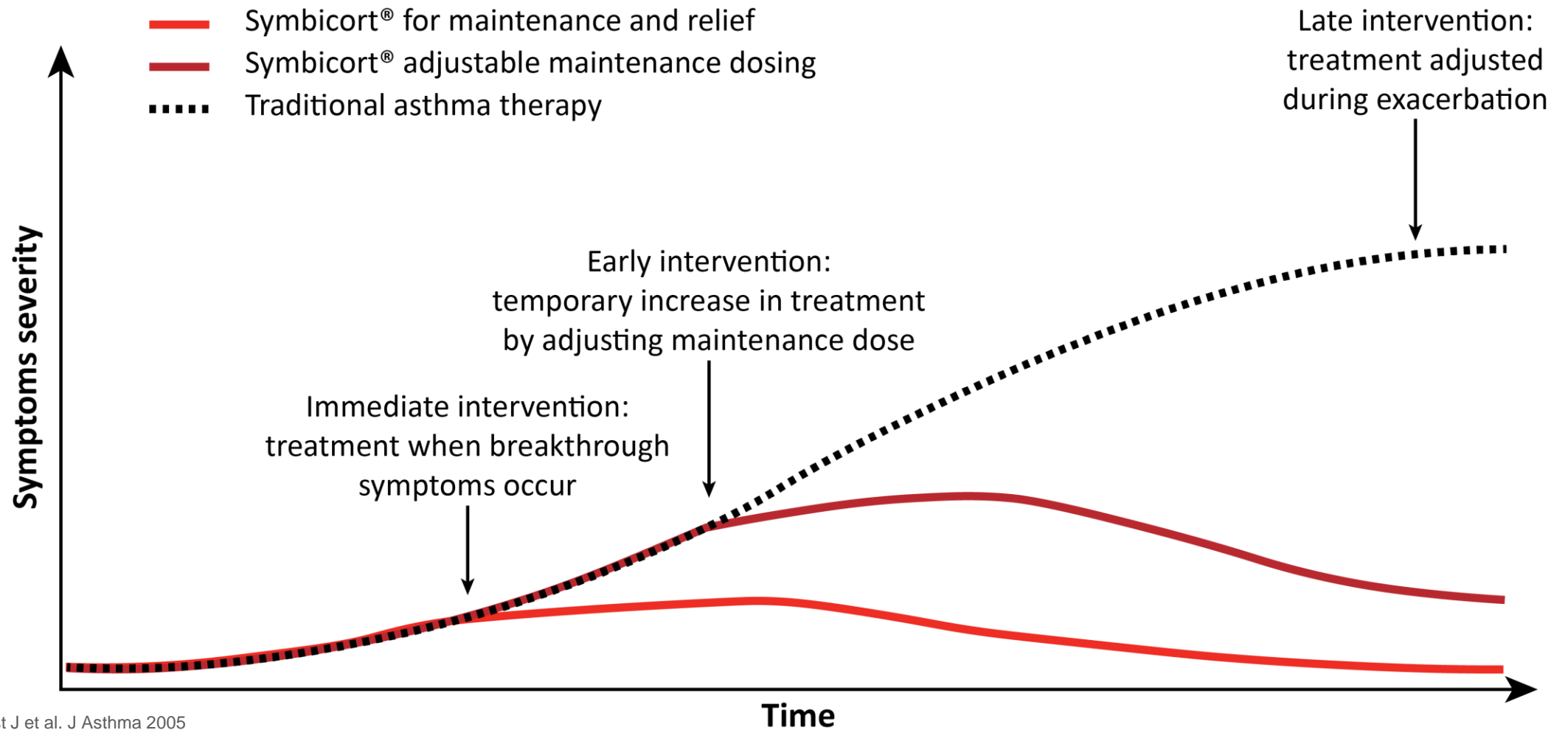
- Increases in FEV₁ occurred in each treatment group during run-in when all patients used budesonide/formoterol maintenance plus SABA, but additional increases in FEV₁ were also seen with as-needed budesonide/formoterol vs formoterol and terbutaline



FEV₁, forced expiratory volume in 1 second; SABA, short-acting β_2 -agonist.

Early intervention with Symbicort® as part of a reliever regimen can prevent exacerbations^{1,2}

Potential outcomes with different asthma treatment regimens in response to worsening symptoms¹



Adapted from Ankerst J et al. J Asthma 2005

1. Ankerst J. Combination inhalers containing inhaled corticosteroids and long-acting β_2 -agonists: improved clinical efficacy and dosing options in patients with asthma. Journal of Asthma. 2005 Jan 1;42(9):715-24. 2. Global Initiative For Asthma (GINA), Global strategy for asthma management and prevention, <http://ginasthma.org>. Last accessed Dec 2019

GINA Recommendation For Maintenance And Reliever Therapy *

1

Track 1: The reliever is as-needed low dose ICS-formoterol.

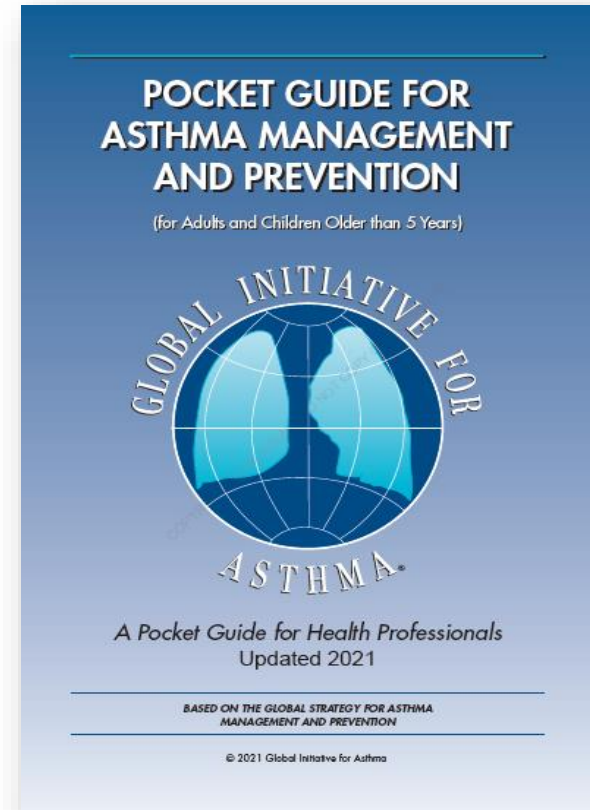
This is the preferred approach recommended by GINA for adults and adolescents. Using low dose ICS-formoterol as reliever reduces the risk of severe exacerbations compared with regimens with SABA as reliever, with similar symptom control. With this approach:

- When a patient at any treatment step has asthma symptoms, they use low dose ICS-formoterol in a single inhaler for symptom relief.
- In Steps 3–5, patients also take ICS-formoterol as their regular daily treatment. This is called ‘maintenance and reliever therapy’ (MART).

ICS-formoterol should not be used as the reliever by patients taking any other ICS-LABA.

Track 2: The reliever is as-needed SABA. This is an alternative approach when Track 1 is not possible or is not preferred by a patient who has no exacerbations on their current therapy.

2



ICS, inhaled corticosteroid; LABA, long-acting β_2 -agonist; SABA, short-acting β_2 -agonist;.

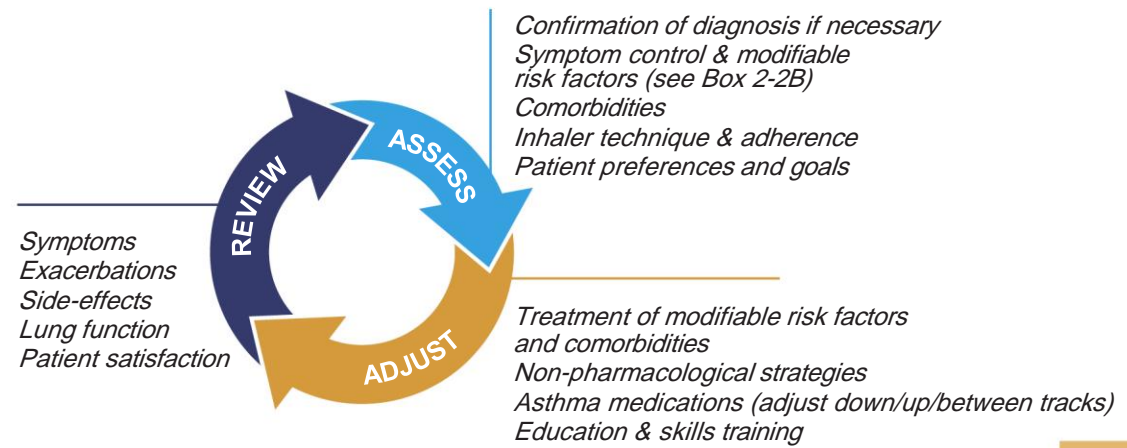
Disclaimer : (Budesonide/Formoterol is indicated only in management of Moderate to Severe Asthma (GINA Stage 3 to 5) as per label in Jordan , Iraq, Syria ,Sudan & Libya

* Global Initiative For Asthma (GINA), Global strategy for asthma management and prevention, <http://ginasthma.org>. Last accessed May 2021.

Adults & adolescents 12+ years

Personalized asthma management

Assess, Adjust, Review
for individual patient needs



CONTROLLER and **PREFERRED RELIEVER** (Track 1). Using ICS-formoterol as reliever reduces the risk of exacerbations compared with using a SABA reliever

STEPS 1 – 2 As-needed low dose ICS-formoterol	STEP 3 Low dose maintenance ICS-formoterol	STEP 4 Medium dose maintenance ICS-formoterol	STEP 5 Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-formoterol, ± anti-IgE, anti-IL5/5R, anti-IL4R, anti-TSLP
RELIEVER: As-needed low-dose ICS-formoterol			

See GINA severe asthma guide

CONTROLLER and **ALTERNATIVE RELIEVER** (Track 2). Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller

STEP 1 Take ICS whenever SABA taken	STEP 2 Low dose maintenance ICS	STEP 3 Low dose maintenance ICS-LABA	STEP 4 Medium/high dose maintenance ICS-LABA	STEP 5 Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE, anti-IL5/5R, anti-IL4R, anti-TSLP
RELIEVER: As-needed short-acting beta ₂ -agonist				

Other controller options for either track (limited indications, or less evidence for efficacy or safety)

	Low dose ICS whenever SABA taken, or daily LTRA, or add HDM SLIT	Medium dose ICS, or add LTRA, or add HDM SLIT	Add LAMA or LTRA or HDM SLIT, or switch to high dose ICS	Add azithromycin (adults) or LTRA. As last resort consider adding low dose OCS but consider side-effects
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Asthma Symptoms Assessment for Asthma control at Each visit

- two or more daytime symptoms per week,
- two or more nighttime symptoms per month,
- interference with activities of daily living,
- use of short-acting beta-agonist > 2 days/week (excluding use for prevention of exercise-induced bronchospasm),
- Peak flow or FEV₁ <80% predicted/personal best .
- Validated self-assessment tools such as the Asthma Control Test (ACT), Asthma Therapy Assessment Questionnaire (ATAQ), or Asthma Control Questionnaire (ACQ) can facilitate consistent measurement and documentation of asthma symptoms during office visits .

Simple screening tools to assess asthma control

Asthma Control Test – a clinically validated measure for asthma control¹⁻³



GINA assessment of symptom control

A. Symptom control

Level of asthma symptom control

In the past 4 weeks, has the patient had:

- Daytime asthma symptoms more than twice a week? Yes No
- Any night waking due to asthma? Yes No
- Reliever needed for symptoms* more than twice a week? Yes No
- Any activity limitation due to asthma? Yes No

Well-controlled	Partly controlled	Uncontrolled
None of these	1-2 of these	3-4 of these

B. Risk factors for poor asthma outcomes

- Assess risk factors at diagnosis and periodically
- Measure FEV₁ at start of treatment, after 3 to 6 months of treatment to record the patient's personal best, then periodically for ongoing risk assessment

ASSESS PATIENT'S RISKS FOR:

- Exacerbations
- Fixed airflow limitation
- Medication side-effects

The Asthma Control Test™ correlates well with treatment decisions made by asthma specialists

- **Evaluation of ACT's** correlation with the treatment decisions and comparison to other conventional parameters
 - One-month diary on symptoms and **PEF** of 383 subjects before assessment
 - Same-day completion of ACT, spirometry and **FeNO** measurement
 - Week before assessment: **BHR** to methacholine of 73 subjects
 - Asthma specialists, blinded to the results of the ACT, FeNO and BHR (but not spirometry and PEF), assessed the patients' level of control according to GINA strategy and made appropriate treatment decisions
- Receiver operating characteristic curve analysis found:
 - **ACT score of < 20** best correlated with **uncontrolled asthma***
 - On ROC analysis, the **ACT score** had the **highest AUC** (0.81, $p < 0.001$) for **changing asthma therapy†**

ACT correlates better with treatment decisions made by asthma specialists than spirometry, PEF and FeNO

*Sensitivity 70.5%, specificity 76.0%, positive predictive value 76.2% and negative predictive value 70.2% for predicting step-up of asthma therapy.

Ko FW, et al. *Respirology*. 2009;14:559-66.

†When compared with FeNO, spirometry, PEF and BHR parameters.

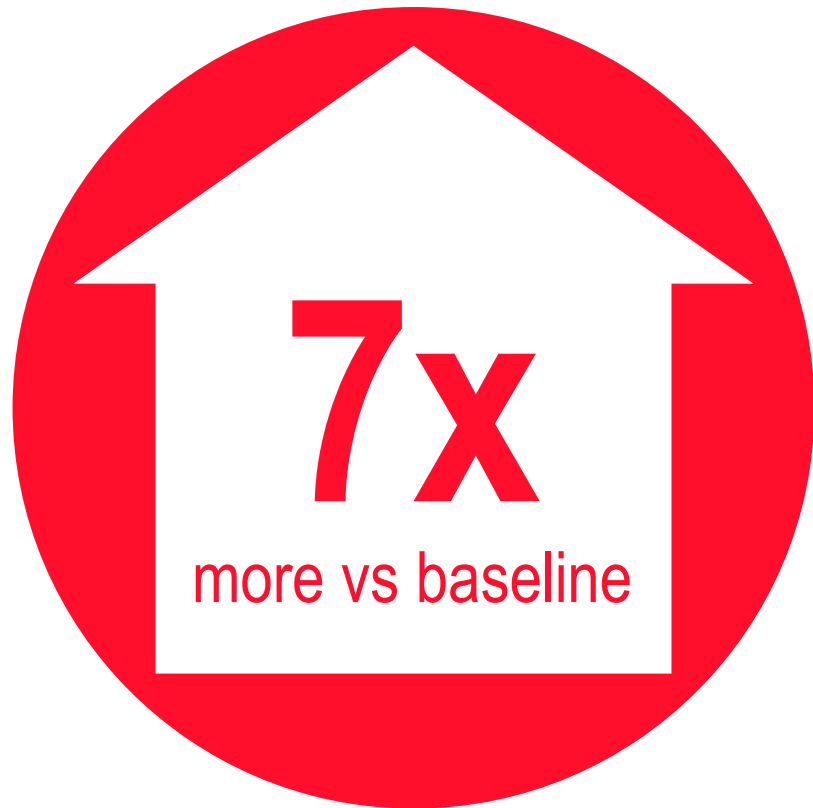
ACT Asthma Control Test; **AUC** area under curve; **BHR** bronchial hyper-responsiveness; **FeNO** fractional exhaled nitric oxide; **GINA** Global Initiative for Asthma; **PEF** peak expiratory flow; **ROC** receiver operating characteristic.



Why Symbicort[®] Turbuhaler[®] is different?

Symbicort[®] – Efficacy data: Symptoms and asthma control

Symbicort®* – standard of care 24-hour symptom control



Asthma control days

Asthma control days defined as:

- no day-time symptoms
- no night-time symptoms
- no night awakenings caused by asthma
- no as-needed medication use

Symbicort®*: Baseline 5.8% vs Treatment 41.3%

*Symbicort® maintenance and reliever therapy

Randomized, double-blind 6-month study of 3335 symptomatic adult and adolescent asthma patients (mean FEV1 73% predicted, mean inhaled corticosteroid dose 745 µg/day). Symbicort® Maintenance and Reliever 160/4.5 µg one inhalation bd + additional inhalations as needed. Symbicort® Maintenance and Reliever prolonged the time to first severe exacerbation requiring hospitalisation, emergency room treatment or oral steroids (primary variable) vs fixed-dose salmeterol/fluticasone (p=0.0034). Study results also showed salmeterol/fluticasone 25/125 µg two inhalations bd + terbutaline as needed has similar asthma control days results: Baseline 5.7% vs Treatment 43.7%.¹



Why Symbicort[®] Turbuhaler[®] is different?

Symbicort[®] – Safety profile

Symbicort®* has comprehensive safety data

- Data from RCTs in >14,000 patients indicate no additional safety findings with Symbicort® as-needed on top of maintenance therapy compared to fixed maintenance dosing¹⁻⁵
- Safety data from the six double-blind RCTs in asthma, where Symbicort®* was used for ≥6 months in adults and adolescents, were assessed⁶
- Data pooling allowed examination of rarer events as well as predictable adverse effects
 - N=14,346
 - Co-primary endpoints: All-cause mortality and asthma-related SAEs
 - Secondary endpoints: Overall and cardiac SAEs, DAEs, asthma-related and cardiac-related DAEs
 - Estimated Mantel-Haenszel relative risks were calculated for Symbicort®* versus comparators

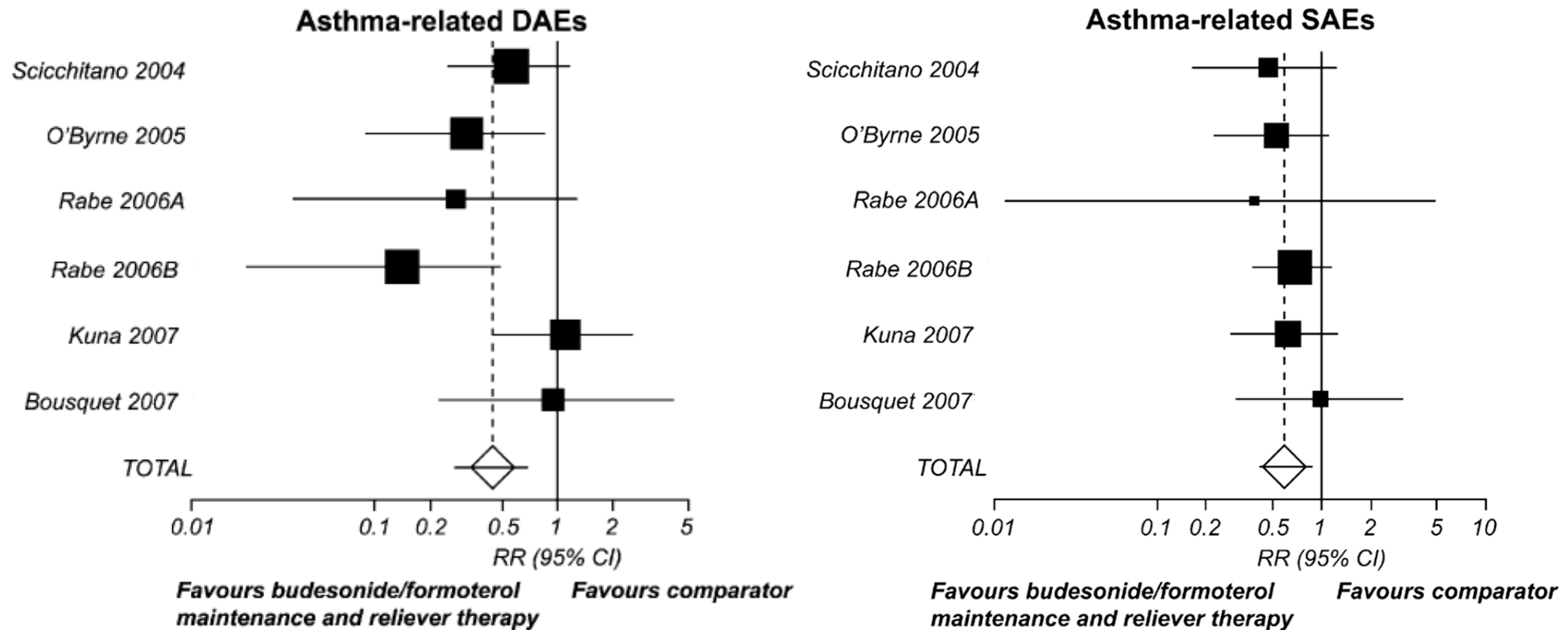
*Symbicort® maintenance and reliever therapy

DAE, discontinuation because of an adverse event; ICS, inhaled corticosteroid; LABA, long-acting β_2 -agonist; RCT, randomised controlled trial; SABA, short-acting β_2 -agonist; SAE, serious adverse event

1. Scicchitano R, Aalbers R, Ukena D, Manjra A, Fouquet L, Centanni S, Boulet LP, Naya IP, Hultquist C. Efficacy and safety of budesonide/formoterol single inhaler therapy versus a higher dose of budesonide in moderate to severe asthma. *Current medical research and opinion*. 2004 Sep 1;20(9):1403-18. 2. Rabe KF, Pizzichini E, Ställberg B, Romero S, Balanzat AM, Atienza T, Lier PA, Jorup C. Budesonide/formoterol in a single inhaler for maintenance and relief in mild-to-moderate asthma: a randomized, double-blind trial. *Chest*. 2006 Feb 1;129(2):246-56. 3. O'Byrne PM, Bisgaard H, Godard PP, Pistolesi M, Palmqvist M, Zhu Y, Ekström T, Bateman ED. Budesonide/formoterol combination therapy as both maintenance and reliever medication in asthma. *American journal of respiratory and critical care medicine*. 2005 Jan 15;171(2):129-36. 4. Kuna P, Peters MJ, Manjra AI, Jorup C, Naya IP, Martinez-Jimenez NE, Buhl R. Effect of budesonide/formoterol maintenance and reliever therapy on asthma exacerbations. *International journal of clinical practice*. 2007 May;61(5):725-36. 5. Bousquet J, Boulet LP, Peters MJ, Magnussen H, Quiralte J, Martinez-Aguilar NE, Carlshamer A. Budesonide/formoterol for maintenance and relief in uncontrolled asthma vs. high-dose salmeterol/fluticasone. *Respiratory medicine*. 2007 Dec 1;101(12):2437-46. 6. Sears MR, Radner F. Safety of budesonide/formoterol maintenance and reliever therapy in asthma trials. *Respiratory medicine*. 2009 Dec 1;103(12):1960-8.

Lower risk of asthma-related DAEs and SAEs with Symbicort[®] anti-inflammatory reliever on top of maintenance compared to FD regimens

- Pooled analysis of safety data from six double RCTs found that asthma-related DAEs and SAEs were significantly reduced with Symbicort^{®*} vs comparator therapy



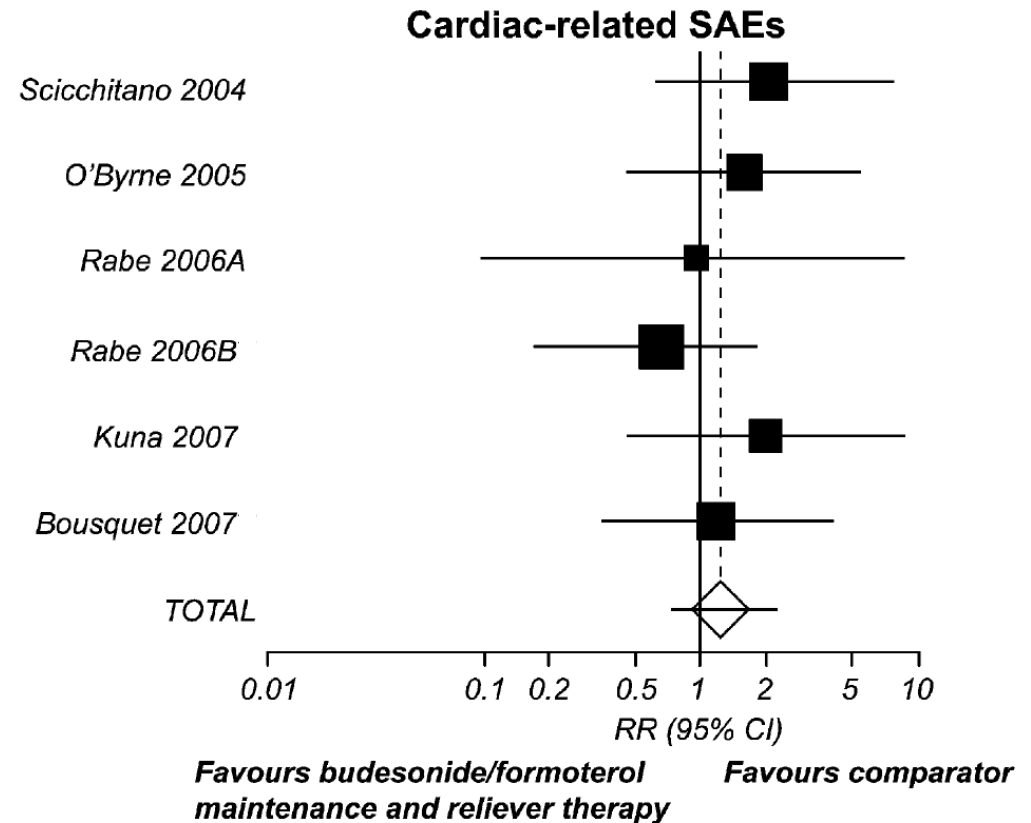
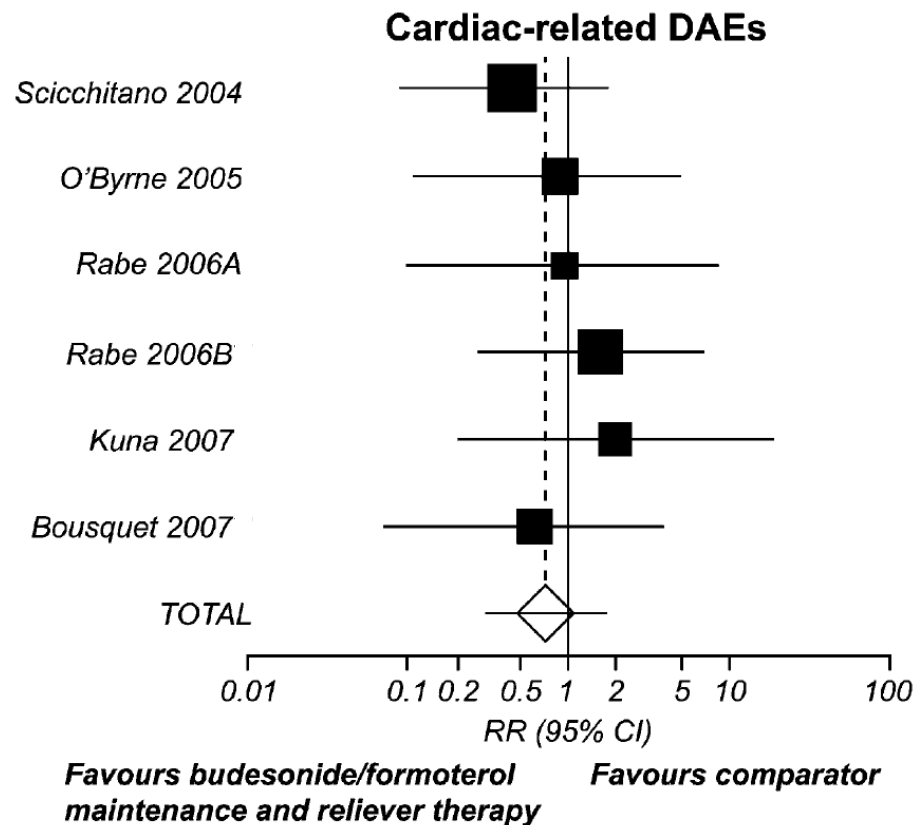
*Symbicort[®] maintenance and reliever therapy

CI, confidence interval; DAE, discontinuation due to adverse events; FD, fixed dose; RCT, randomised clinical trials; RR, relative risk; SAE, serious adverse event..

Sears MR, Radner F. Safety of budesonide/formoterol maintenance and reliever therapy in asthma trials. Respiratory medicine. 2009 Dec 1;103(12):1960-8.

Symbicort[®] anti-inflammatory reliever on top of maintenance is not associated with an increased risk of cardiac-related DAEs or SAEs

- In the pooled analysis of safety data from six RCTs, Symbicort^{®*} was not associated with any increased risk of cardiac-related DAEs or SAEs



*Symbicort[®] maintenance and reliever therapy.

CI, confidence interval; DAE, discontinuation due to adverse events; RCT, randomised clinical trials; RR, relative risk; SAE, serious adverse event.

Sears MR, Radner F. Safety of budesonide/formoterol maintenance and reliever therapy in asthma trials. Respiratory medicine. 2009 Dec 1;103(12):1960-8.

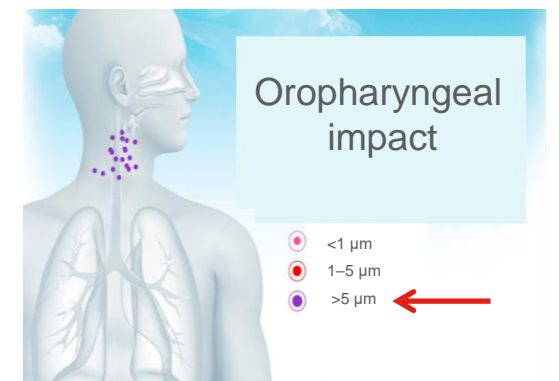
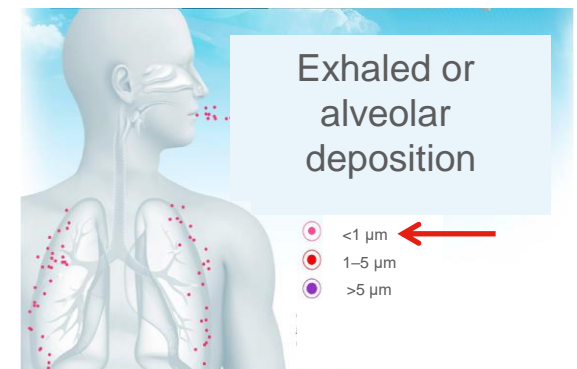
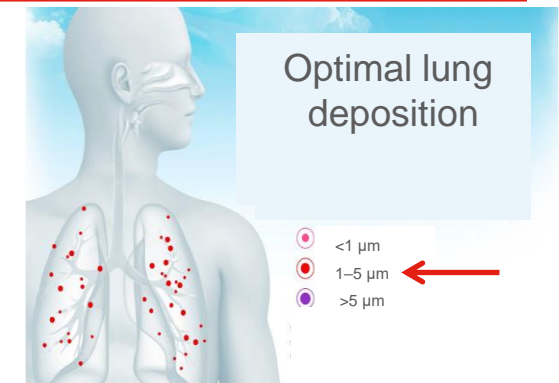


Symbicort® – The role of Turbuhaler®



Particle size range matters for optimal lung deposition

- Particles 1–5 μm are optimal for lung deposition, with those 1–3 μm most likely to be deposited in central and peripheral airways¹
- Particles <1 μm are most likely to be exhaled again but some will reach the alveoli and then enter the systemic circulation^{1,2}
- Particles > 5 μm mainly impact on the oropharynx and are then swallowed^{1,2}
- Oropharyngeal impaction increases at higher inspiratory flow rates^{1,2}
- Turbuhaler was the only DPI of 4 tested* that compensated for higher oropharyngeal losses and the shift in deposition to upper airways at higher flow rates¹
- Turbuhaler delivered the highest fine particle fraction (FPF) 1–3 μm of the 4 DPIs tested* as percent of label claim *in vitro*¹



* Symbicort Turbuhaler, Seretide Diskus, Rolenium Elpenhaler and Foster NEXThaler

Turbuhaler[®] : Design and operation

Mouthpiece is specially designed with spiral channels to deaggregate the dose to respirable particles

Inhalation channel transports dosage of drug aggregates to the mouthpiece

Rotating dosing disc determines the dose of medication for delivery to the inhalation channel



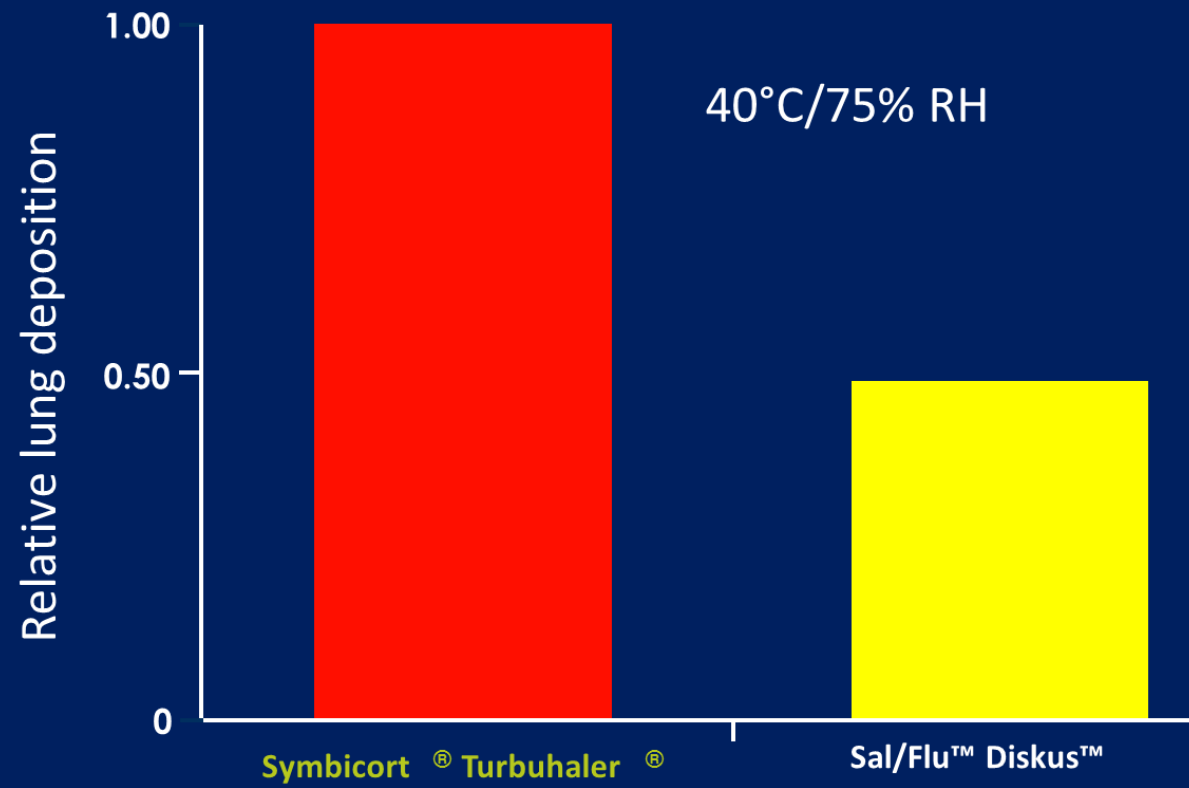
Drug reservoir holds 50,60,100 or 200 doses of medication

Dosing scrapers ensures precise dosing by removing excess amounts of drug

Twist grip loads a single dose when turned completely in one direction and then back again

Effect of storage conditions on lung deposition

Storage under hot and humid conditions significantly reduced lung deposition from salmet/flutica™ Diskus™, but had no effect on drug delivery from Symbicort Turbuhaler.



Summary – asthma disease and management

- Asthma remains a highly prevalent global health concern, with suboptimal levels of control¹
- Asthma control levels are low, regardless of severity, and asthma control is often overestimated by patients³
- Poor adherence to medication and over-reliance on SABAs represent major hurdles to improving asthma control rates^{3–4}
- The over-use of SABA and under-use of ICS both increase the risk of mortality^{5,6}
- The importance of ICS early in disease is now reflected in GINA guidelines⁷

1. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, Shibuya K, Salomon JA, Abdalla S, Aboyans V, Abraham J. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *The Lancet*. 2012 Dec 15;380(9859):2163-96. 2. To T, Stanojevic S, Moores G, Gershon AS, Bateman ED, Cruz AA, Boulet LP. Global asthma prevalence in adults: findings from the cross-sectional world health survey. *BMC public health*. 2012 Dec;12(1):204. 3. Price D, Fletcher M, Van Der Molen T. Asthma control and management in 8,000 European patients: the REcognise Asthma and Link to Symptoms and Experience (REALISE) survey. *NPJ primary care respiratory medicine*. 2014 Jun 12;24:14009. 4. Partridge MR, van der Molen T, Myrseth SE, Busse WW. Attitudes and actions of asthma patients on regular maintenance therapy: the INSPIRE study. *BMC pulmonary medicine*. 2006 Dec;6(1):13. 5. Suissa S, Ernst P, Boivin JF, Horwitz RI, Habbick BR, Cockcroft D, Blais L, McNutt M, Buist AS, Spitzer WO. A cohort analysis of excess mortality in asthma and the use of inhaled beta-agonists. *American journal of respiratory and critical care medicine*. 1994 Mar;149(3):604-10. 6. Suissa S, Ernst P, Benayoun S, Baltzan M, Cai B. Low-dose inhaled corticosteroids and the prevention of death from asthma. *New England Journal of Medicine*. 2000 Aug 3;343(5):332-6. 7. Global Initiative For Asthma (GINA), Global strategy for asthma management and prevention, <http://ginasthma.org>. Last accessed May 2021., available at [www.ginasthma.org](http://ginasthma.org)

Summary – Take Home Messages

- Intervention with Symbicort[®] as-needed at the early stages of symptom-worsening can prevent exacerbations¹
- Across a number of clinical trials, Symbicort^{®*} has demonstrated significant reductions in the risk of severe exacerbations vs comparator therapies in all severities, from mild to severe^{2–10}
- Symbicort^{®*} increases the probability of patients achieving controlled or partially controlled asthma^{1–5}
- Symbicort[®] as-needed on top of maintenance therapy reduces as-needed inhalations, provides good symptom control, and reduces the BDP equivalent ICS dose^{1,4,9}

*Symbicort[®] maintenance and reliever therapy.

SABA, short-acting β_2 -agonist.

1. Ankerst J. Combination inhalers containing inhaled corticosteroids and long-acting β_2 -agonists: improved clinical efficacy and dosing options in patients with asthma. *Journal of Asthma*. 2005 Jan 1;42(9):715-24; 42: 715–24; 2. Kuna P, Peters MJ, Manjra AI, Jorup C, Naya IP, Martinez-Jimenez NE, Buhl R. Effect of budesonide/formoterol maintenance and reliever therapy on asthma exacerbations. *International journal of clinical practice*. 2007 May;61(5):725-36; 3. Bousquet J, Boulet LP, Peters MJ, Magnussen H, Quiralte J, Martinez-Aguilar NE, Carlsheimer A. Budesonide/formoterol for maintenance and relief in uncontrolled asthma vs. high-dose salmeterol/fluticasone. *Respiratory medicine*. 2007 Dec 1;101(12):2437-46.; 4. Rabe KF, Pizzichini E, Ställberg B, Romero S, Balanzat AM, Atienza T, Lier PA, Jorup C. Budesonide/formoterol in a single inhaler for maintenance and relief in mild-to-moderate asthma: a randomized, double-blind trial. *Chest*. 2006 Feb 1;129(2):246-56.; 5. Scicchitano R, Aalbers R, Ukena D, Manjra A, Fouquet L, Centanni S, Boulet LP, Naya IP, Hultquist C. Efficacy and safety of budesonide/formoterol single inhaler therapy versus a higher dose of budesonide in moderate to severe asthma. *Current medical research and opinion*. 2004 Sep 1;20(9):1403-18.; 6. O'Byrne PM, Bisgaard H, Godard PP, Pistolesi M, Palmqvist M, Zhu Y, Ekström T, Bateman ED. Budesonide/formoterol combination therapy as both maintenance and reliever medication in asthma. *American journal of respiratory and critical care medicine*. 2005 Jan 15;171(2):129-36. 7. Rabe KF, Atienza T, Magyar P, Larsson P, Jorup C, Laloo UG. Effect of budesonide in combination with formoterol for reliever therapy in asthma exacerbations: a randomised controlled, double-blind study. *The Lancet*. 2006 Aug 26;368(9537):744-53.;368:744–753; 8. Vogelmeier C, D'Urzo A, Pauwels R, Merino JM, Jaspal M, Boutet S, Naya I, Price D. Budesonide/formoterol maintenance and reliever therapy: an effective asthma treatment option. *European Respiratory Journal*. 2005 Nov 1;26(5):819-28. 9. O'Byrne PM, FitzGerald JM, Bateman ED, Barnes PJ, Zhong N, Keen C, Jorup C, Lamarca R, Ivanov S, Reddel HK. Inhaled combined budesonide-formoterol as needed in mild asthma. *New England Journal of Medicine*. 2018 May 17;378(20):1865-76. 10. Beasley R, Holliday M, Reddel HK, Braithwaite I, Ebmeier S, Hancox RJ, Harrison T, Houghton C, Oldfield K, Papi A, Pavord ID. Controlled trial of budesonide-formoterol as needed for mild asthma. *New England Journal of Medicine*. 2019 May 23;380(21):2020-30.

Ready for discussion

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