



— B E L M A T T —  
HEALTHCARE TRAINING

# Introduction to asthma

## Agenda



**Some asthma statistics**  
**Asthma – What is it**  
**Diagnosis**  
**Long-established treatment**

# Statistics

- In the UK 8 million people diagnosed
  - 12% of the total population
- 5.4 million receive treatment
  - ?Considerable over-diagnosis
- Plateauing diagnosis in recent years
  - 3% increase
- Asthma is still the most common lung condition

# Statistics

- Approximately 160,000 people a year receive the diagnosis
- Incidence has reduced – Reasons?
  - Asthma becoming less common?
  - Reduction in misdiagnosis?
  - Previous backlog cleared – so only new cases?
- Throughout diagnosis more common in females
- Lifetime prevalence:
  - ↓ in children
  - ↑ in adults
- Incidence rates 36% higher in deprived communities

# Statistics

- Around 60,000 hospital admissions
  - 200,000 bed days a year
  - Many more attend A&E
- 
- Around 1200 deaths due to asthma
    - 1.1% of total deaths due to lung disease

## Asthma



- Asthma is a very manageable condition
- Admissions, bed days and deaths should be closer to 0

- Asthma is an inflammatory disease of the airways.
- Asthma causes symptoms of shortness of breath, chest tightness, wheezing, cough or mucus production
- Symptoms vary in intensity and frequency
- Symptoms are associated with variable airflow expiratory airflow obstruction due to bronchoconstriction and airway wall thickening
- Asthma can be acute or chronic

## What is asthma?

## Acute vs Chronic Asthma

- Acute asthma is the progressive worsening of asthma symptoms, including breathlessness, wheeze, cough, and chest tightness.
- The chronic inflammation leads to recurrent episodes of wheezing, breathlessness, chest tightness, and cough especially at night and early morning.
- These episodes are associated with widespread but variable airflow obstruction that is usually reversible **spontaneously or with treatment**

# Asthma

- The clinical course of asthma is unpredictable, ranging from periods of adequate control, to exacerbations with poor control

# Pathophysiology

- The primary pathophysiologic process in asthma is persistent but variable airway inflammation.
- The airway is limited because the inflammation results in:
  - Bronchoconstriction
  - airway hyper responsiveness (hyperactivity)
  - airway oedema.

# Pathophysiology

Normal bronchiole

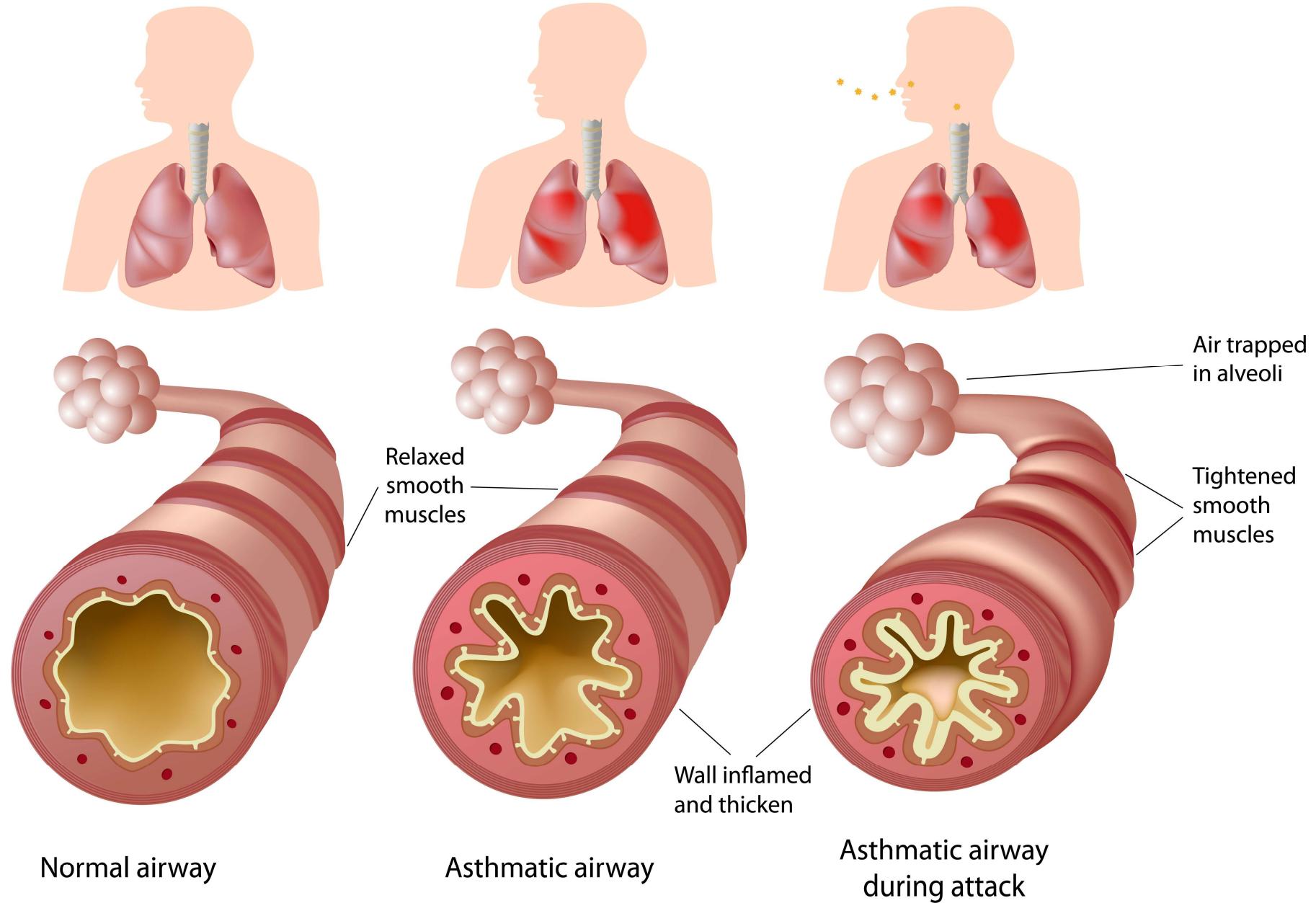


Asthmatic bronchiole



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# Pathology of Asthma



Normal airway

Asthmatic airway

Asthmatic airway  
during attack

# Diagnosis

## **Under diagnosis of asthma is common**

In general, health care personnel should consider the diagnosis of asthma if there are various indications (i.e. clinical manifestation, health history, peak flow variability or spirometry) are positive.

- detailed history helps to identify asthma triggers
- pulmonary function tests determine the reversibility of bronchoconstriction and thus establishing diagnosis.

**(spirometry is the preferred test to diagnose asthma, where there is no access, peak flow can be used to demonstrate reversibility)**

- serum IgE levels and eosinophil count when elevated is highly suggestive of allergic tendency.
- Allergy skin testing can be used to determine sensitivity to specific allergens

# Diagnosis

- Peak flow variability
- Spirometry FeV1/FVC ratio of <70% positive for obstructed airways disease
- Bronchodilator reversibility (BDR) FeV1 improvement of 12% and 200mls as a positive test
- Fractional Exhaled Nitric Oxide (FeNo) 40ppb or more is a positive test
- Methacholine challenge test 8mg/ml or less as a positive test

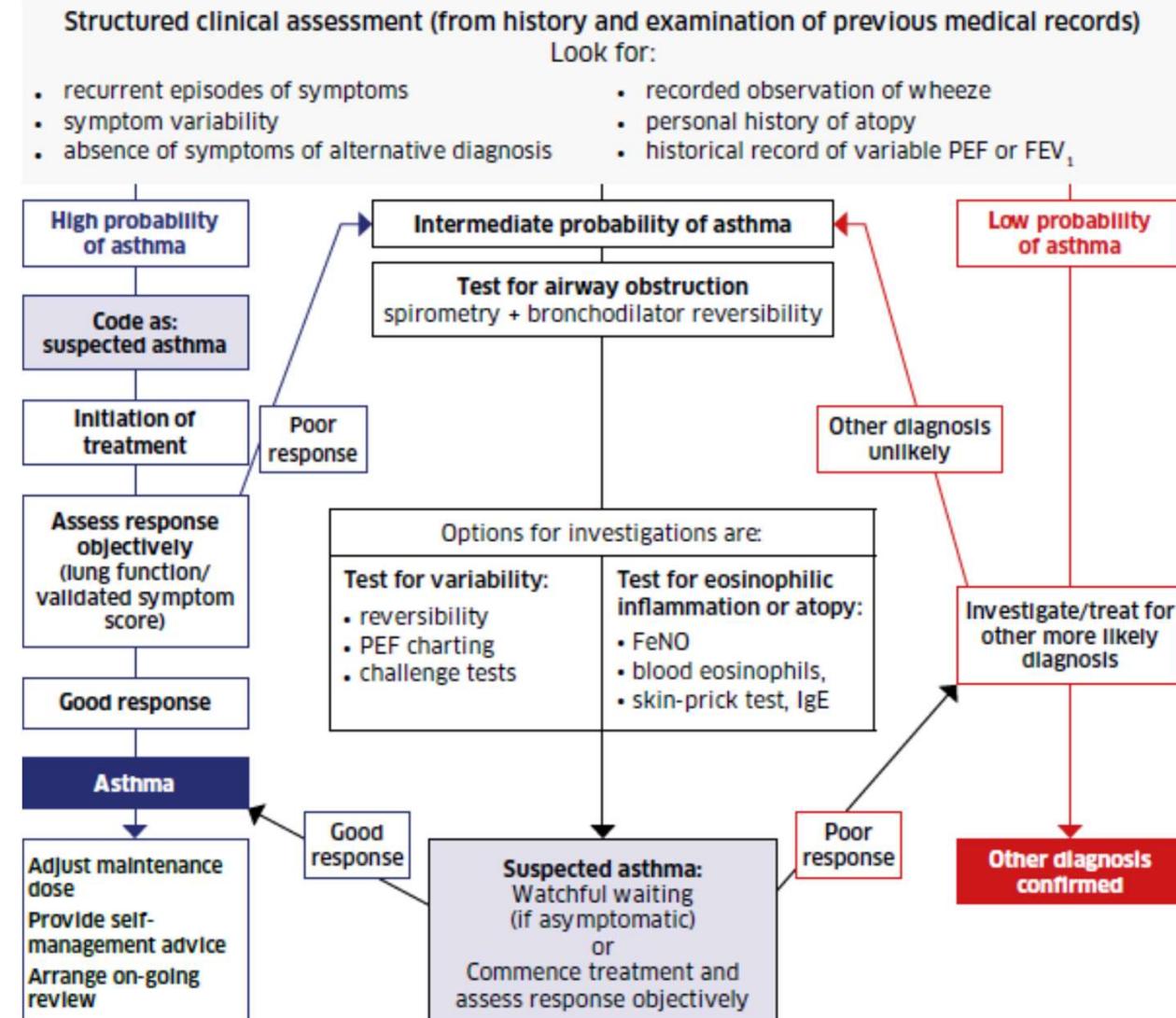
# Diagnosis

Features that increase high probability of asthma in adults -

More than one of the following:

- Wheeze
- Cough
- Breathlessness
- Chest tightness (particularly if it occurs in or worse at night or early morning)
- Symptoms occur in response to exercise, allergen exposure or cold air
- After taking aspirin, betablockers NSAID
- History of atopy
- Family history of asthma or atopy,
- Wide spread of wheeze, heard on auscultation
- Unexplained low fev1 or serial peak flow
- Move straight to treatment

# Diagnostic algorithm BTS SIGN Guideline



<sup>1</sup> In children under 5 years and others unable to undertake spirometry In whom there is a high or intermediate probability of asthma, the options are monitored initiation of treatment or watchful waiting according to the assessed probability of asthma.

# Diagnostic indication for referral BTS-SIGN

Adults	Children
<b>Referral for tests not available in primary care</b>	
Diagnosis unclear	Diagnosis unclear
Suspected occupational asthma (symptoms that improve when patient is not at work, adult-onset asthma and workers in high-risk occupations) <sup>84</sup>	
Poor response to asthma treatment	Poor response to monitored initiation of asthma treatment
Severe/life-threatening asthma attack	Severe/life-threatening asthma attack
<b>'Red flags' and indicators of other diagnoses</b>	
Prominent systemic features (myalgia, fever, weight loss)	Failure to thrive
Unexpected clinical findings (eg crackles, clubbing, cyanosis, cardiac disease, monophonic wheeze or stridor)	Unexplained clinical findings (eg focal signs, abnormal voice or cry, dysphagia, inspiratory stridor)
Persistent non-variable breathlessness	Symptoms present from birth or perinatal lung problem
Chronic sputum production	Excessive vomiting or posseting
Unexplained restrictive spirometry	Severe upper respiratory tract infection
Chest X-ray shadowing	Persistent wet or productive cough
Marked blood eosinophilia	Family history of unusual chest disease
	Nasal polyps
<b>Patient or parental anxiety or need for reassurance</b>	

# Diagnosis GINA 2023

- 1. History of variable respiratory symptoms
- 2. Confirmed variable expiratory airflow limitation
  - Documented excessive variability in lung function
  - AND
  - Documented expiratory airflow limitation

# Diagnosis GINA 2023 Variable respiratory symptoms

- Symptoms:
  - Wheeze
  - shortness of breath
  - chest tightness
  - Cough
- The descriptions may vary between cultures and by age
- More than 1 symptom present
- Symptom variability over time and intensity
- Symptoms worse at night or on waking
- Symptoms triggered by exercise, laughter, allergens, cold air
- Symptoms often appear or worsen with viral infections

# Diagnosis GINA 2023 Variability in lung function (one or more)

- Positive bronchodilator reversibility
- Excessive diurnal PEF variability over 2 weeks
  - Adults: >10%
  - Children > 13%
- Increase in lung function after 4 weeks treatment in adults
  - Increase in FEV1 by 12% and >200ml
  - Increase in PEF by >20%
- Excessive variation in lung function between visits
  - Adults: FEV1 >12% and >200ml
  - Children: PEF >15%
- Positive bronchial test
- Positive exercise challenge test

# Diagnosis GINA 2023 Expiratory airflow limitation

- Confirmation with spirometry at a time when FEV1 is reduced
- FEV1/FVC should be reduced compared to lower limit of normal:
  - Adults: <75%
  - Children: <90%

- SABA = Short Acting  $\beta$  Agonist = Salbutamol
- ICS = Inhaled CorticoSteroid = Beclomethasone, fluticasone
- LABA = Long Acting  $\beta$  Agonist = Salmeterol/ Formoterol
- LTRA = Leukotriene Receptor Antagonist = Montelukast, Zafirlukast
- SAMA = Short-Acting Muscarinic Antagonist
- LAMA = Long-Acting Muscarinic Antagonist
- OCS = Oral CorticoSteroid
- MART/SMART = Maintenance And Reliever Therapy – Single inhaler

## Abbreviations

# Established (Long in the tooth) NICE 2017

## Newly diagnosed asthma:

- Age 5 – 16 or 17 and over First option: SABA only treatment
- If worsening: Low dose ICS
- If worsening: Add LTRA
- If worsening: Low dose ICS+LABA +/- LTRA
- If worsening: Low dose ICS+LABA as MART +/- LTRA
- If worsening: As above but with Moderate dose ICS or Fixed dose ICS+LABA + SABA
- If worsening: Fixed High dose ICS+LABA
- If worsening: Moderate dose ICS+LABA+LAMA
- If worsening: Refer to a specialist
  
- each step to be tried out for 4 – 8 weeks

# My problem with NICE 2017

Newly diagnosed asthma:

- Age 5 – 16 or 17 and over First option: SABA only treatment

# My problem with NICE 2017 Use and Overuse of SABA

- 3 things we know:
- 1. SABA overuse leads to worsening symptoms and ↑risk of death
- 2. Controller medication underuse leads to worsening symptoms and ↑risk of exacerbations and death
- 3. There is significant non-adherence with controller medication

X SABA  
ONLY as  
1<sup>st</sup> line  
treatment  
for asthma

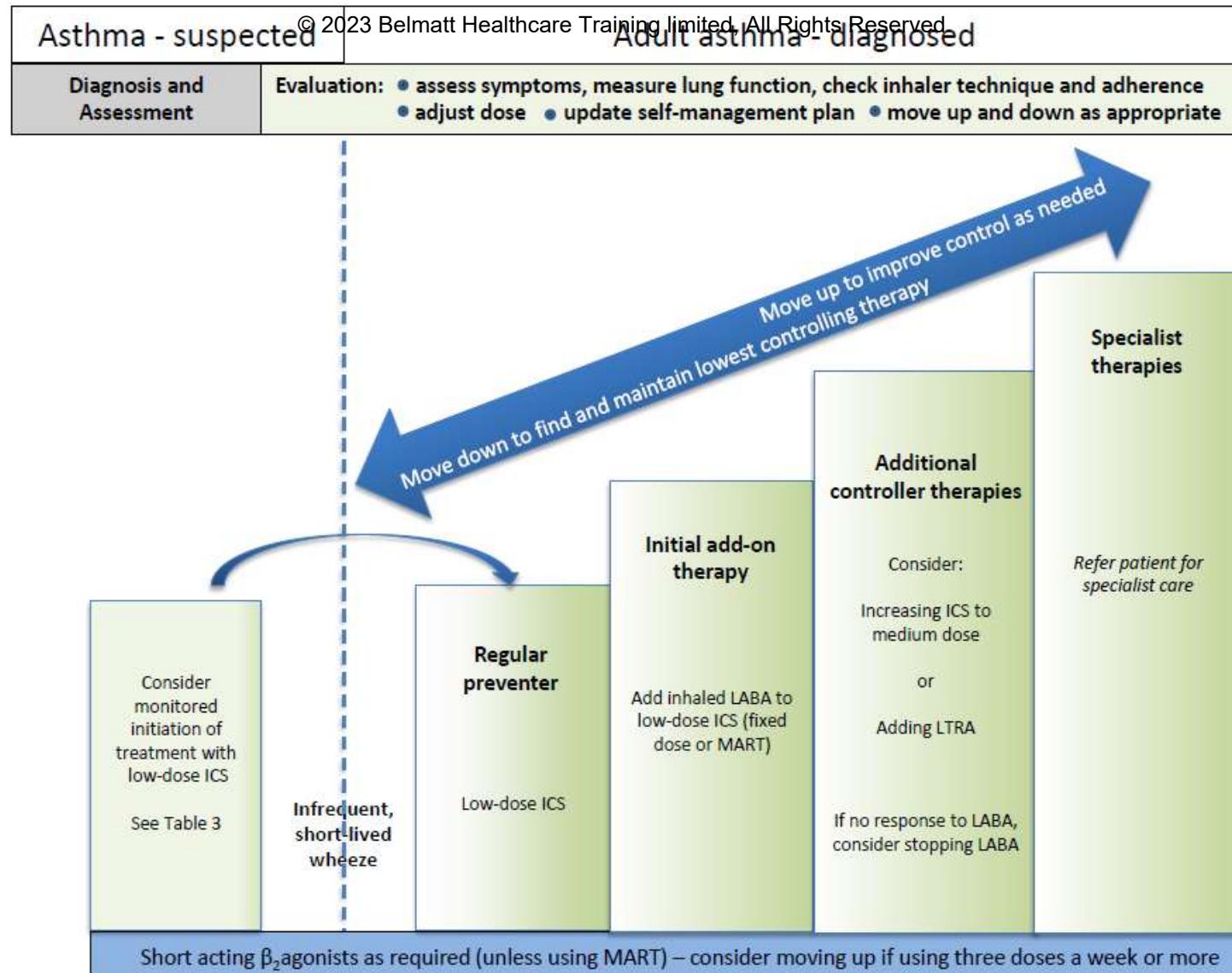
- This dates from an era when asthma was thought to be a disease of bronchoconstriction
- Patient satisfaction with, and reliance on, SABA treatment is reinforced by:
  - its rapid relief of symptoms
  - its prominence in A&E and hospital management of exacerbations
  - low cost
- *“My reliever gives me control over my breathing!”*
- When the reliever is SABA, poor adherence with maintenance controller exposes the patient to risks of SABA-only treatment

# Risks of regular SABA use and Overuse

- Regular or frequent use of SABA is associated with tachyphylaxis
  - $\beta$ -receptor downregulation
  - decreased broncho-protection
  - rebound hyperresponsiveness
  - decreased bronchodilator response (*Hancox, Respir Med 2000*)
- Increased allergic response
- increased eosinophilic airway inflammation (*Aldridge, AJRCCM 2000*)

# Risks of regular SABA use and Overuse

- In Asthma higher use of SABA is associated with adverse clinical outcomes
  - Dispensing of  $\geq 3$  canisters per year (average 1.7 puffs/day) is associated with higher risk of emergency department presentations (*Stanford, AAAI 2012*)
  - Dispensing of  $\geq 12$  canisters per year is associated with higher risk of death (*Suissa, AJRCCM 1994*)



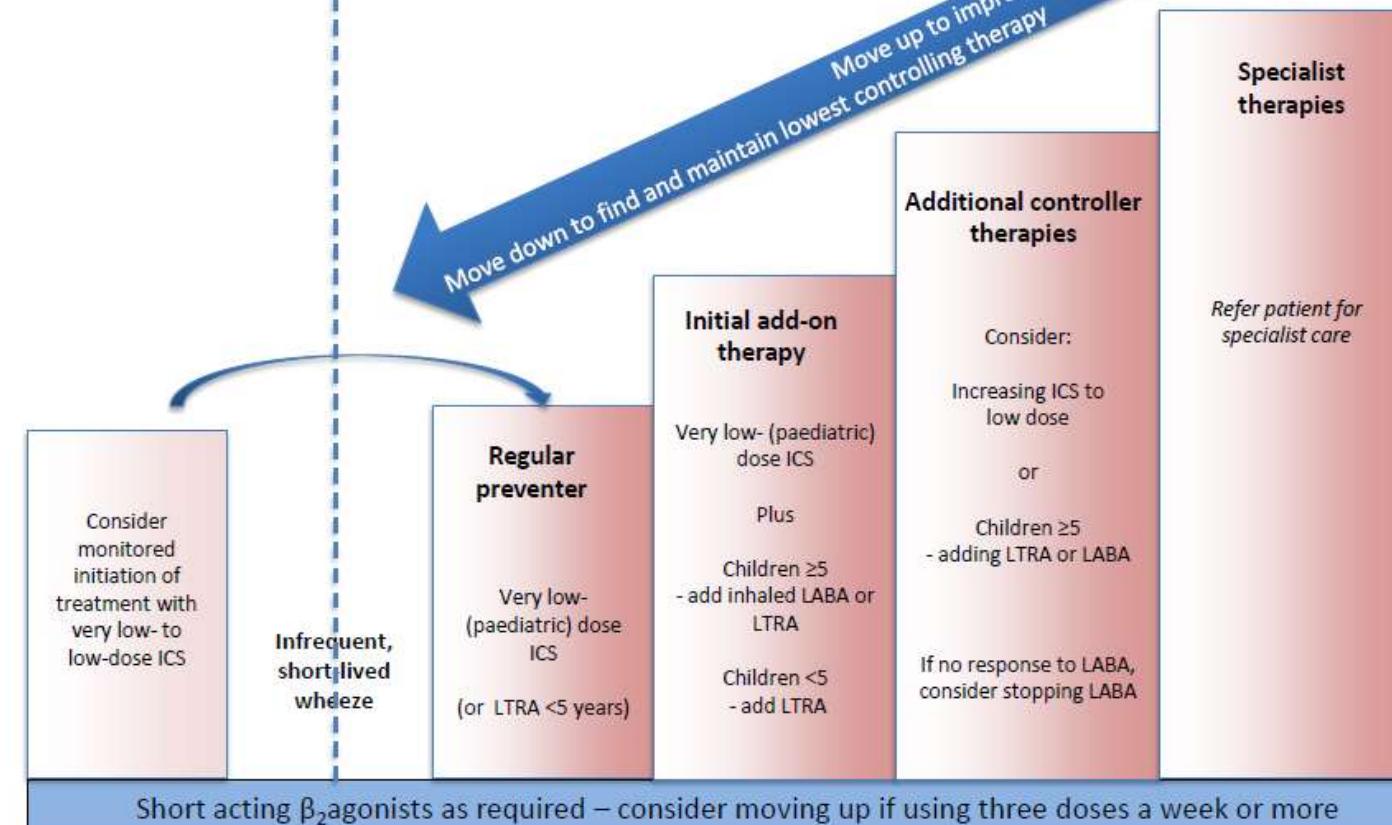
# Established BTS-SIGN Asthma guidelines 2019

## Asthma - suspected

## Paediatric asthma - diagnosed

## Diagnosis and Assessment

- Evaluation:**
- assess symptoms, measure lung function, check inhaler technique and adherence
  - adjust dose    • update self-management plan    • move up and down as appropriate







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# Asthma review

What should one consist of?



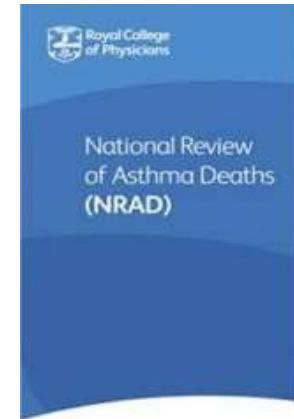
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# NRAD Report

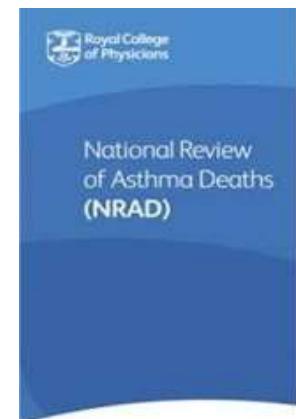
NRAD found widespread issues with the quality of asthma care amongst those who died, with several areas of key findings:

- Only 16% were judged to have good care
- 20% had A+E attendance in previous year
- 39% were prescribed more than 12 reliever inhalers
- 5% patients were prescribed LABAs without an ICS
- 19% people had not been referred to specialist
- 69% patients had their last review in Primary Care
- 27% had their asthma control assessed
- 42% had their medication use checked
- 71% had their inhaler technique checked
- Only 23% had written personal asthma action plan



# NRAD Report

- NRAD identified a number of avoidable factors in relation to both the care people received, the recognition of risk and avoidable factors relating to patients and their families and environments. The 19 recommendations put forward include:
  - hospitals and general practices having a named clinical asthma lead
  - patients attending follow-up appointments after emergency admissions or using the out-of-hours service
  - annual structured asthma reviews, which record known triggers and current treatment
  - appropriate prescribing, and monitoring of inhaler technique. Find out more about inhalers, treatments and medicines.
  - encouraging patient self-management, and education about the exposure to allergens, when and how to use their asthma medication
  - referring smokers with asthma to smoking cessation clinics



# 2023-2024 QOF asthma review indicators

- Validated asthma questionnaire
- Recording of the number of exacerbations
- Written personalised asthma action plans
- Inhaler technique assessment – this should be face to face
- Exposure to smoking or second-hand smoke

# Asthma review

- What should one consist of?

# Confirmation of diagnosis

When was asthma diagnosed?

How (and where) was the diagnosis made?

Are there any objective measures recorded?

- Peak flow variability
- Spirometry
- Bronchial Challenge Testing
- Blood / sputum eosinophils

# Exposure to smoking or second-hand smoke

Impaired response to inhaled corticosteroids

Accelerated decline in lung function

Parental smoking is associated with more severe disease in CYP

Delayed recovery from acute attack

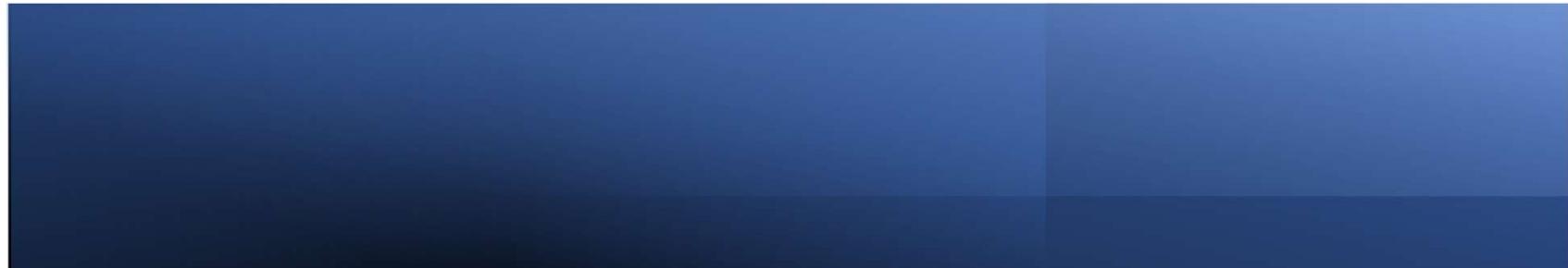
Offer smoking cessation

# Triggers

- Dust Mite
- Emotions
- Exercise
- Fur/feathers
- Moulds/Fungus
- Pollen
- Pollution
  - Exhaust fumes
  - Perfumes
  - Oxidants
  - Cigarette Smoke
  - Aerosol Sprays
- Weather
- Inflammation and infection
  - Viral Upper Respiratory Infection
  - Sinusitis
  - Allergic Rhinitis
- Foods
  - Beer
  - Wine
  - Dry Fruits
  - Shrimp

### **Exposure to allergens or irritants initiates the inflammatory cascade:**

- As the inflammatory process begins, mast cells in the bronchial wall degranulate and releases multiple inflammatory mediators including leukotrienes, histamine, cytokines, prostaglandines.
- This process causes vascular congestion, edema, production of thick tenacious mucus, bronchial spasms, thickening of airway walls and increase bronchial hyper responsiveness
- This process can occur within 30 to 60 minutes after exposure to triggers
- Avoiding a trigger = avoiding an asthma attack



# Symptoms

## Episodic symptoms:

- Cough
- Shortness of Breath
- Wheeze
- Chest tightness

## How often?

- More than twice a week in the day
- Once or more at night

# Assessment of asthma control

<b>Q1</b>	During the <b>past 4 weeks</b> , how often did your asthma prevent you from getting as much done at work, school or home?					Score:
	All of the time 1	Most of the time 2	Some of the time 3	A little of the time 4	None of the time 5	
<b>Q2</b>	During the <b>past 4 weeks</b> , how often have you had shortness of breath?					Score:
	More than once a day 1	Once a day 2	3-6 times a week 3	1-2 times a week 4	Not at all 5	
<b>Q3</b>	During the <b>past 4 weeks</b> , how often did your asthma symptoms (wheezing, coughing, chest tightness, shortness of breath) wake you up at night or earlier than usual in the morning?					Score:
	4 or more times a week 1	2-3 nights a week 2	Once a week 3	Once or twice 4	Not at all 5	
<b>Q4</b>	During the <b>past 4 weeks</b> , how often have you used your reliever inhaler (usually blue)?					Score:
	3 or more times a day 1	1-2 times a day 2	2-3 times a week 3	Once a week or less 4	Not at all 5	
<b>Q5</b>	How would you rate your <b>asthma control</b> during the <b>past 4 weeks</b> ?					Score:
	Not controlled 1	Poorly controlled 2	Somewhat controlled 3	Well controlled 4	Completely controlled 5	
						<b>Total Score</b>

## What does your score mean?

### Score: 25 – WELL DONE

- Your asthma appears to have been **UNDER CONTROL** over the last 4 weeks.
- However, if you are experiencing any problems with your asthma, you should see your doctor or nurse.

### Score: 20 to 24 – ON TARGET

- Your asthma appears to have been **REASONABLY WELL CONTROLLED** during the past 4 weeks.
- However, if you are experiencing symptoms your doctor or nurse may be able to help you.

### Score: less than 20 – OFF TARGET

- Your asthma may **NOT HAVE BEEN CONTROLLED** during the past 4 weeks.
- Your doctor or nurse can recommend an asthma action plan to help improve your asthma control.

# Assessment of risk of poor outcomes

- Previous asthma attacks
- Pregnancy
- Rhinitis and sinusitis
- Obesity
- GERD
- Anxiety and depression
- Food allergy and anaphylaxis
- Elderly
- Concurrent COPD
- Over-use of SABA
- Under-use of ICS

# Concordance with medication



# Inhaler technique

# Personalised Asthma Action Plan

- What they are on
- What to do if asthma is worsening
- What to do in an asthma attack
  
- A question to all: what should an asthma action plan look like?

# What should a review consist of?

- Confirmation of diagnosis
- Exposure to smoking or second-hand smoke
- Triggers
- Symptoms
- Assessment of asthma control
- Assessment of risk of poor outcomes
- Concordance with medication
- Inhaler technique
- Personalised Asthma Action Plan

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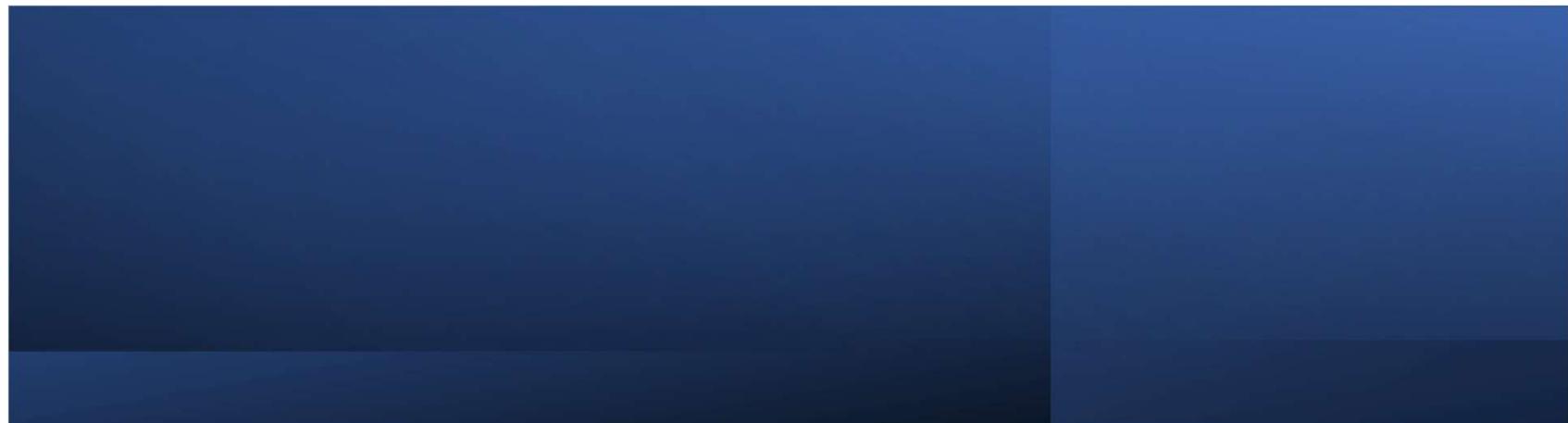


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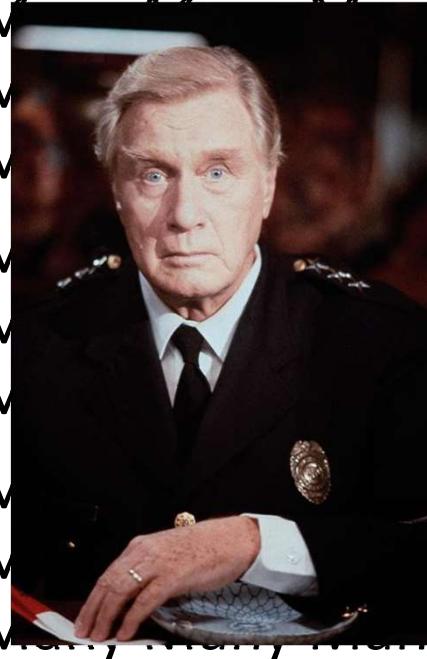


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# Asthma Update Inhalers and inhaler technique



# How many inhalers are there?









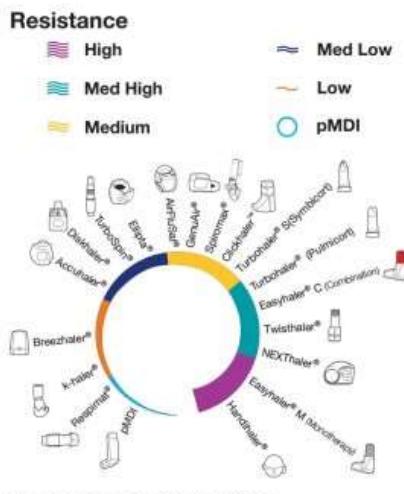
Gentle and  
Deep



# Spacers



# InCheck device



**International alternatives**

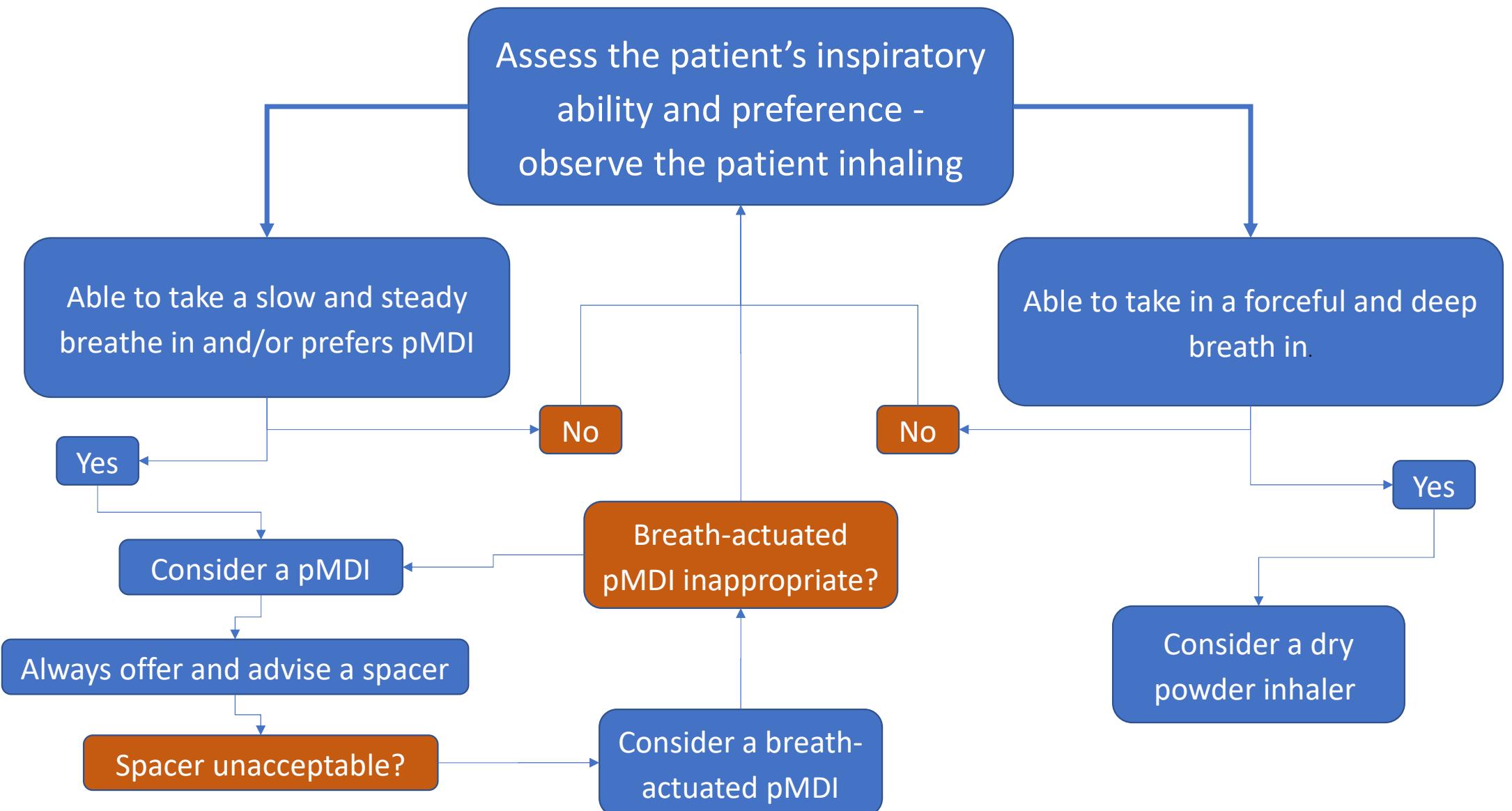
Handihaler®	AirFluSal®
Easyhaler®	Ellipta®
NEXThaler®	TurboSpin®
Twisthaler®	Diskhaler®
Turbuhaler®	Diskus®
Turbuhaler®, Flexhaler®	Breezhaler®, Aerolizer®, Neohaler®
Clickhaler™	k-haler®
RespClick®, Spiromax®	Respimat®
Novolizer®, Genuair®, Pressair®	



## Inspiratory effort requirement

	Inspiratory DPI resistance (kPa <sup>0.5</sup> L/min)	Inspiratory flow rate (L/min)
Breezhaler®	0.017	111
Aerolizer®	0.019	102
Ellipta®	0.027	74
Novolizer®	0.027	72
Accuhaler/Diskus®	0.027	72
Genuair®	0.031	64
Nexthaler®	0.036	54
Turbohaler®	0.039	54
Handihaler®	0.058	37





# Inhaler technique resources

- RightBreathe
- <https://www.rightbreathe.com/>
- Asthma UK
- <https://www.asthma.org.uk/advice/inhaler-videos/>

# What about the environment



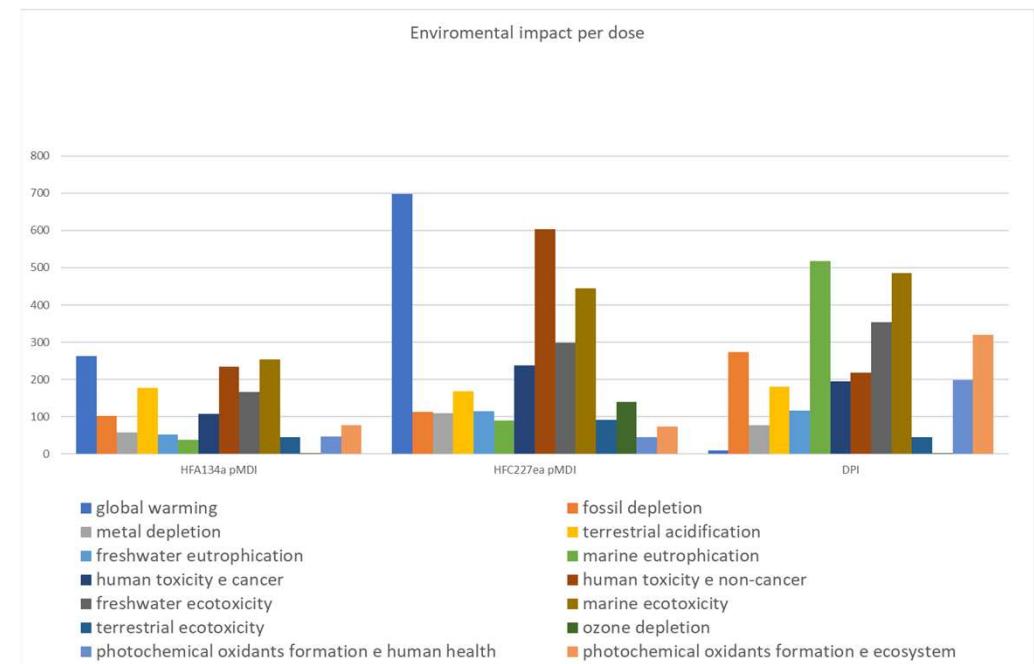
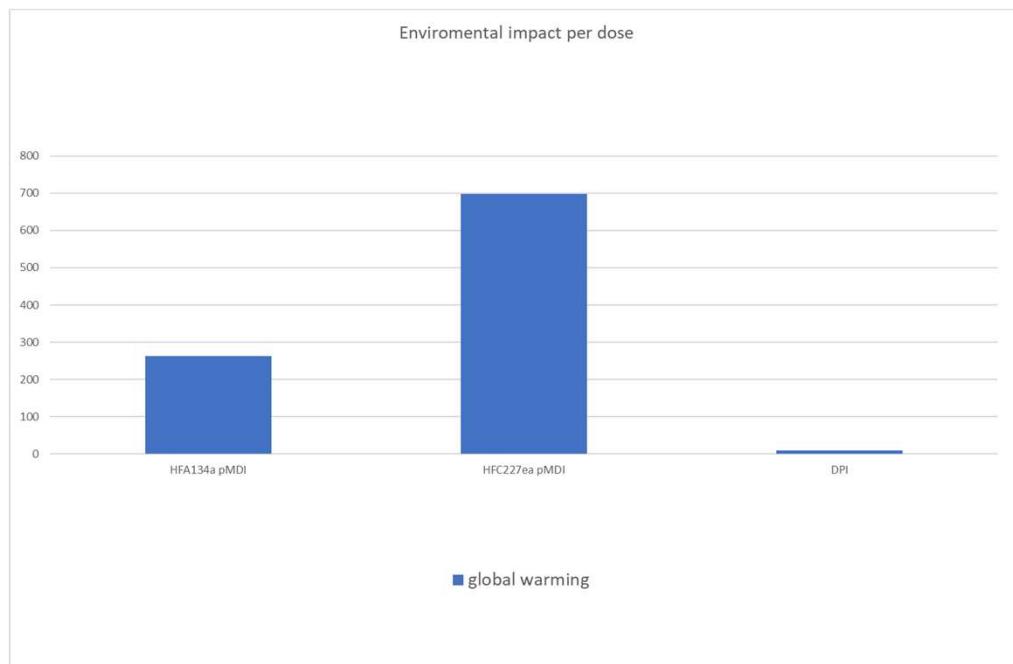
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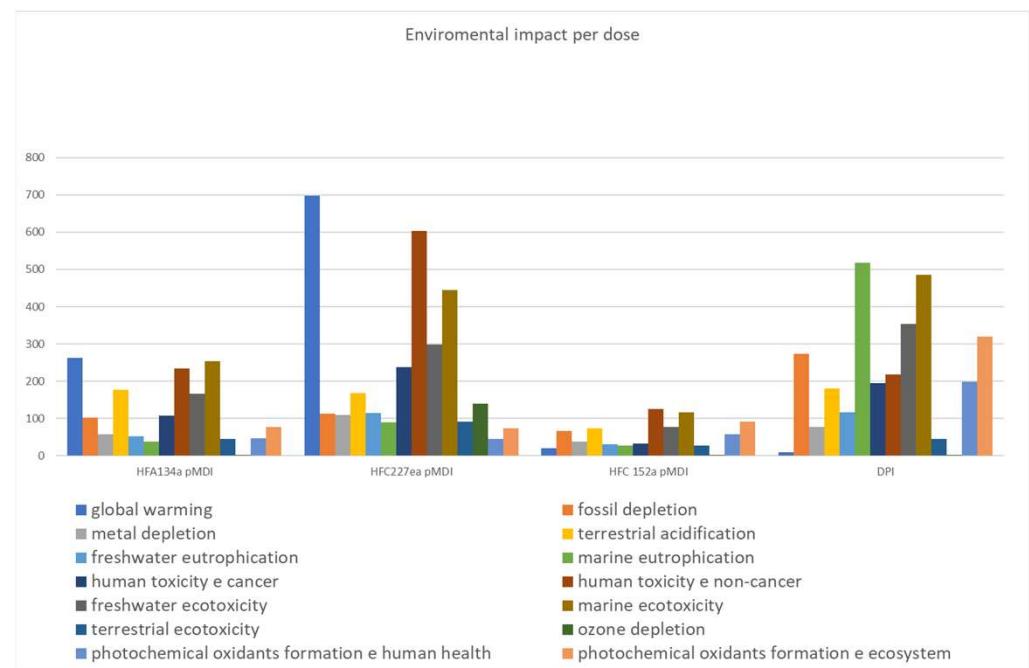
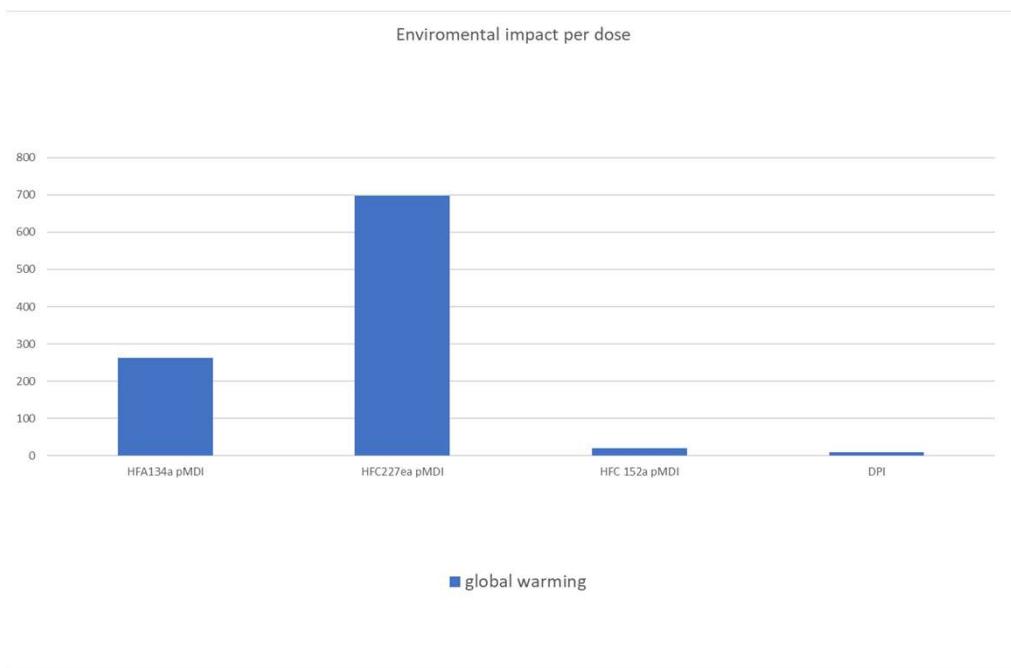
# Greenness of inhalers – a lateral view

(HK Jeswani et al 2019)



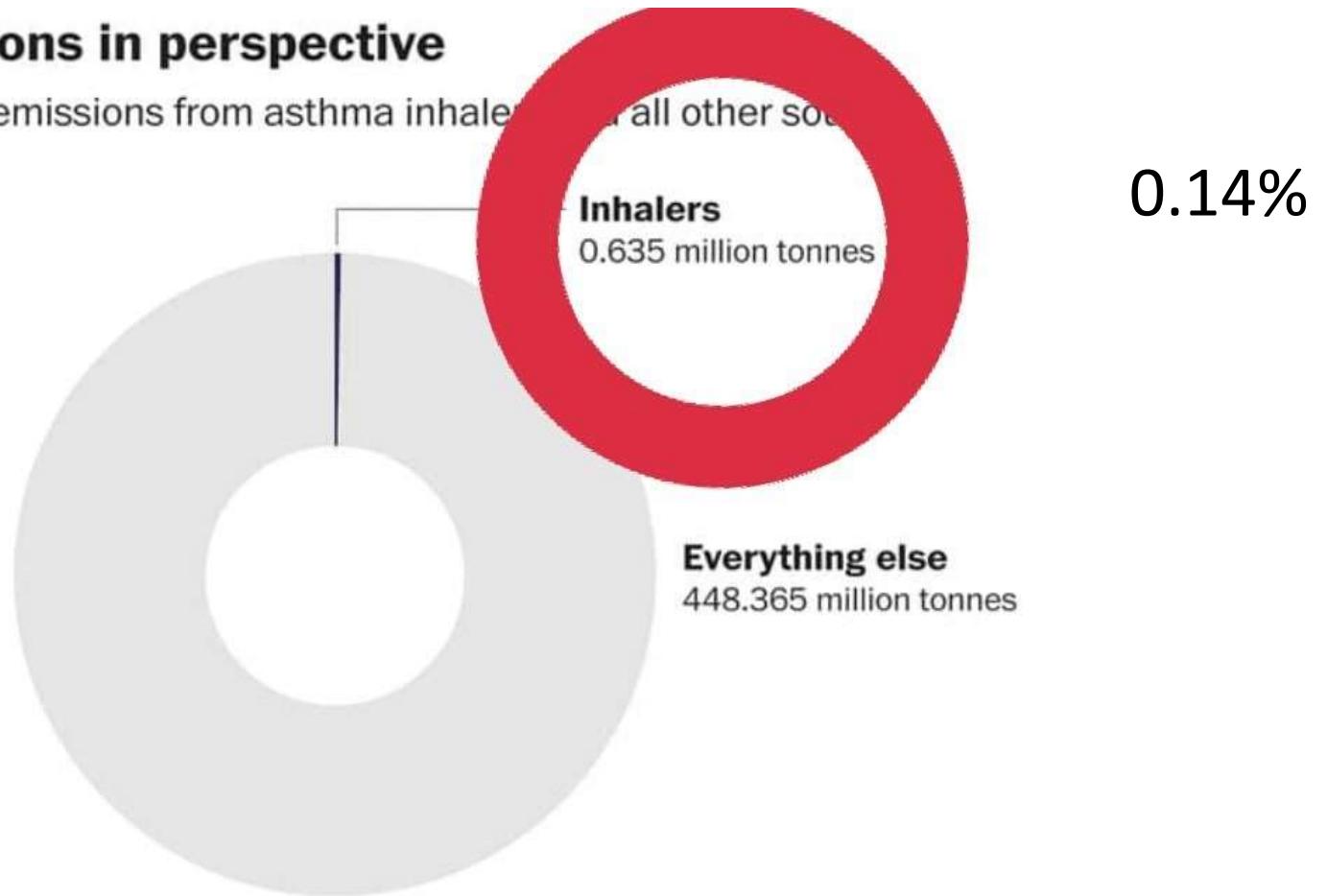
# Greenness of inhalers – a lateral view

(HK Jeswani et al 2019)



## Inhaler emissions in perspective

Annual U.K. carbon emissions from asthma inhalers are tiny compared to all other sources.



Sources: Wilkinson et al., U.K. Dept.for Business, Energy & Industrial Strategy THE WASHINGTON POST

# Greenness of inhalers - Carbon footprint



Ventolin Eohaler  
CO<sub>2</sub> equivalent = 25kg



175 miles – London to Sheffield



Ventolin Accuhaler  
CO<sub>2</sub> equivalent = 625g



4 miles – London to another bit of London



Salamol

Salamol pMDI  
CO<sub>2</sub> equivalent = 10.6kg



74 miles – London to Milton Keynes



A&E overnight admission  
CO<sub>2</sub> equivalent = 125kg



875 miles – London to Hamburg, Germany and back

# A quiz

- Which is the most appropriate inhaler for:
- 1. A child under 12 years of age
- 2. A young adult
- 3. An older adult
- Which inhalers should be on formulary?
- Which is the ‘greenest’ inhaler?
- Which is the most expensive inhaler?



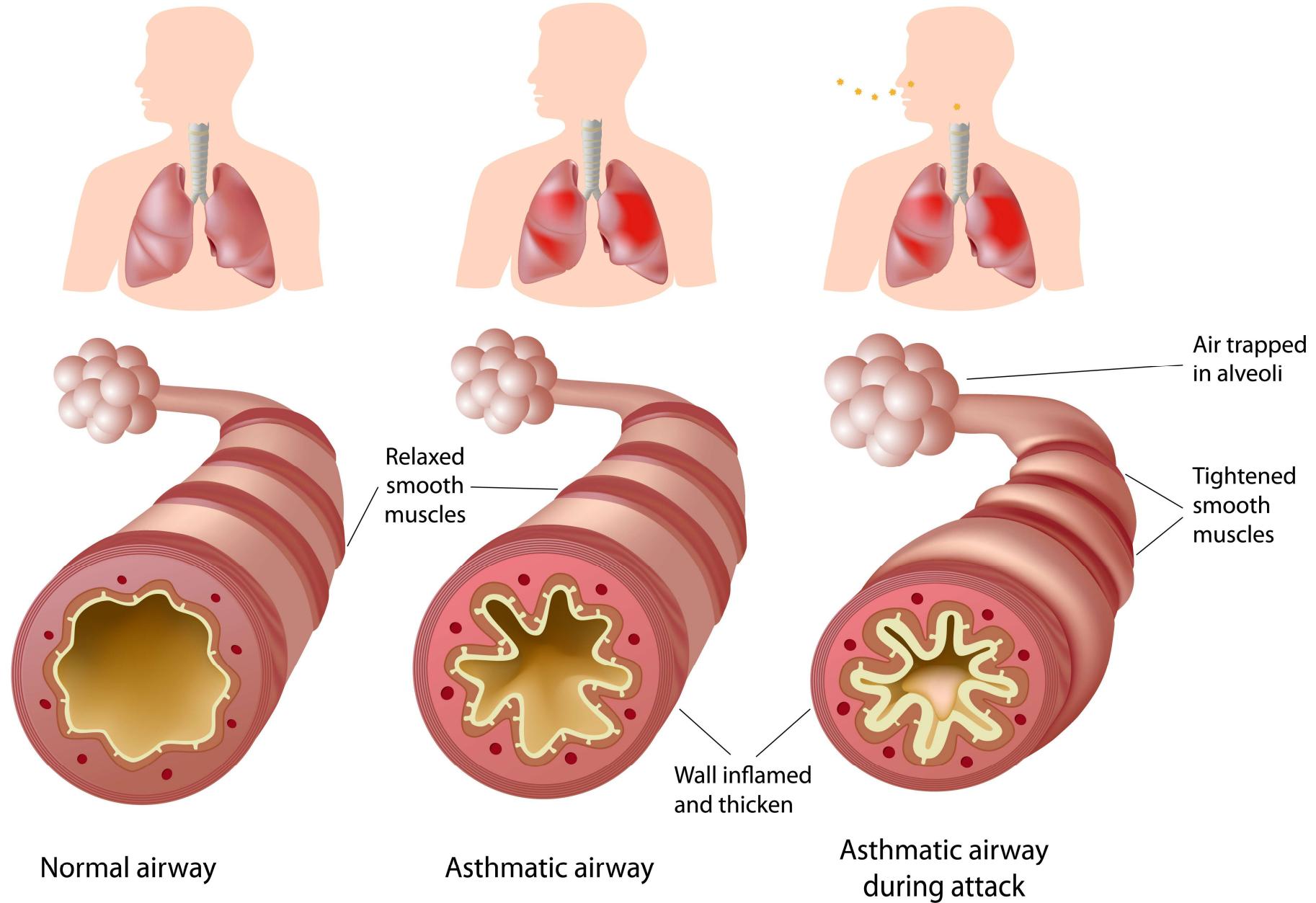
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# Asthma Exacerbation

# Aim of management

- **No daytime symptoms**
- **No night-time waking due to asthma**
- **No need for rescue medication**
- **No asthma attacks**
- **No limitations on activity including exercise.**
- **Normal-near normal lung function (FEV1 and/or PEF > 80% predicted or best).**
- **No or minimal side-effects from medication**
- **Adequate knowledge to manage their disease**

# Pathology of Asthma



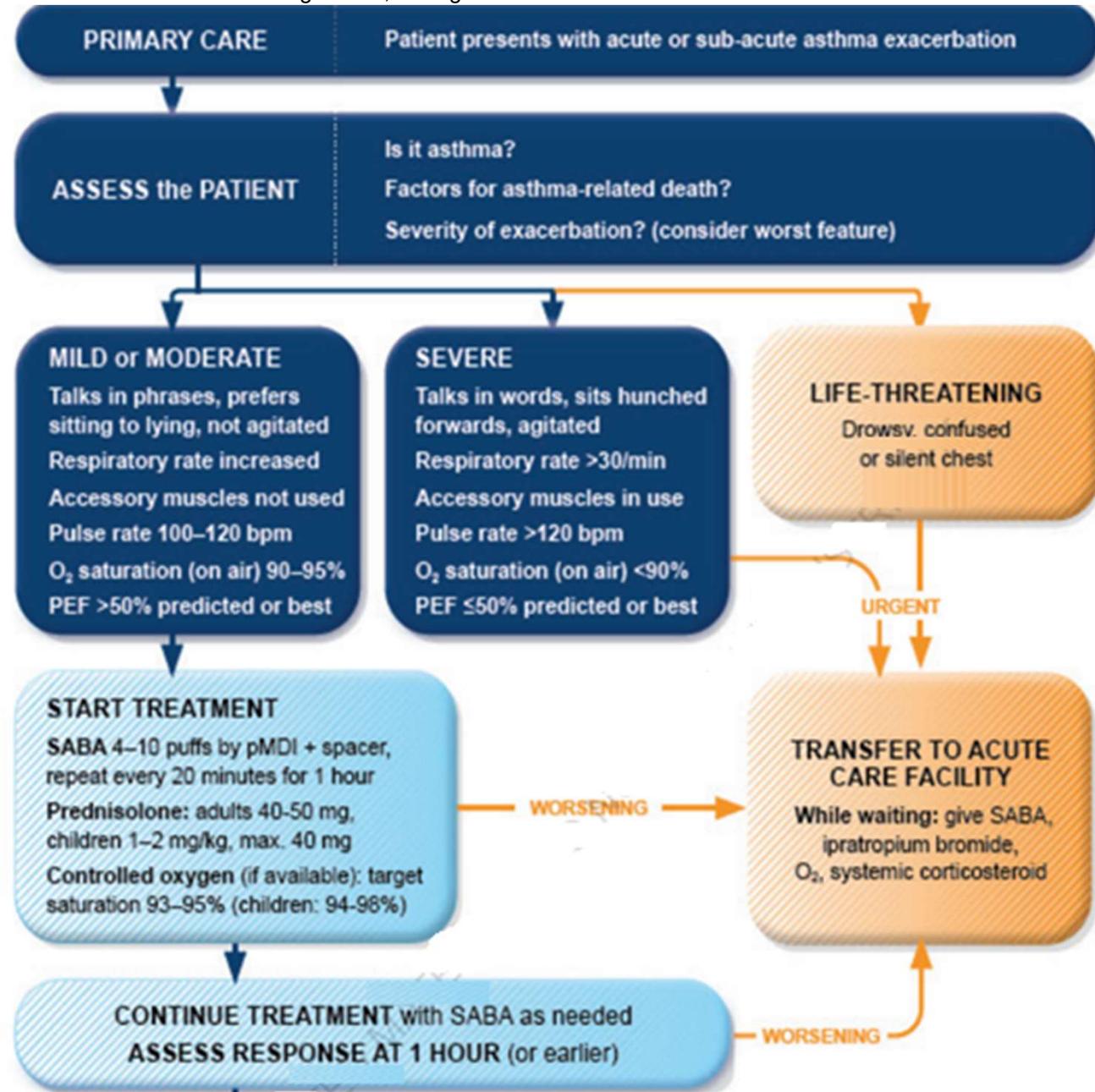
# Exacerbation of Asthma

- Inflammation of airways
- Broncho-constriction
- Excess mucus production

An exacerbation can pass quickly with or without medication. It can also last for many hours. The longer it goes on, the more likely it is to affect the ability to breathe. The signs and symptoms of an acute attack of asthma include:

- agitation
- hyperventilation
- increased heart rate
- decreased lung function
- difficulty speaking or breathing

# Exacerbation of Asthma



## Exacerbation of Asthma

- An exacerbation is a failure of treatment
- **Post exacerbation review in 48 hours – What went wrong**
- ?Concordance
- ?Inhaler Technique
- ?Inadequate treatment
- ?Triggers

## Exacerbation of Asthma

- *Patient with 'mild' asthma are at risk of severe adverse event (Dusser, Allergy 2007)*
  - 30 – 37% of adults with acute asthma
  - 16% of patients with near-fatal asthma
  - 15-20% of adults who died of asthma
- **All had symptoms less than weekly in the previous 3 months**
- **Exacerbation triggers are NOT predictable**





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# Asthma Maintenance And Reliever Therapy

Ameet Gordhan  
Clinical Pharmacist



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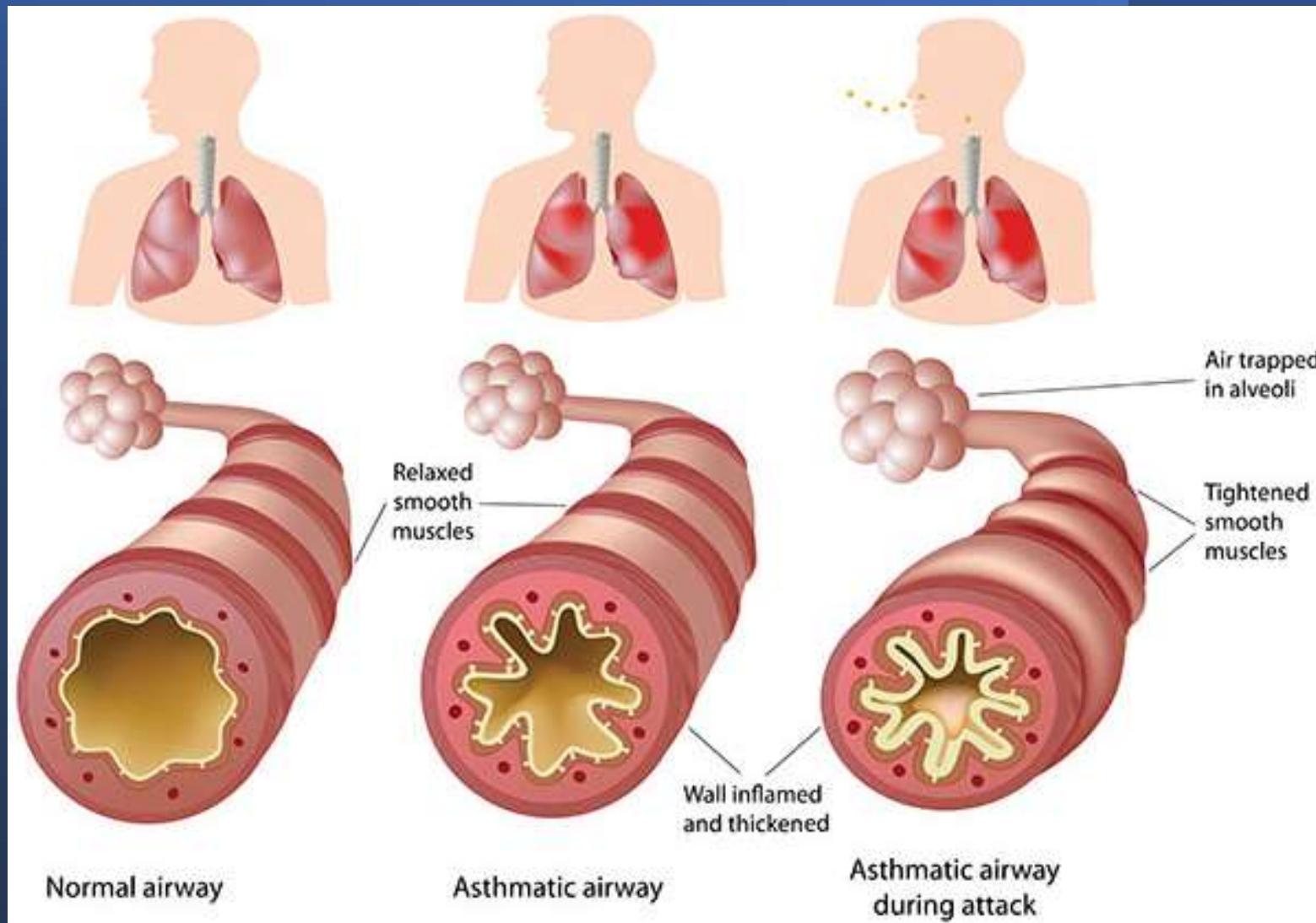
# Asthma



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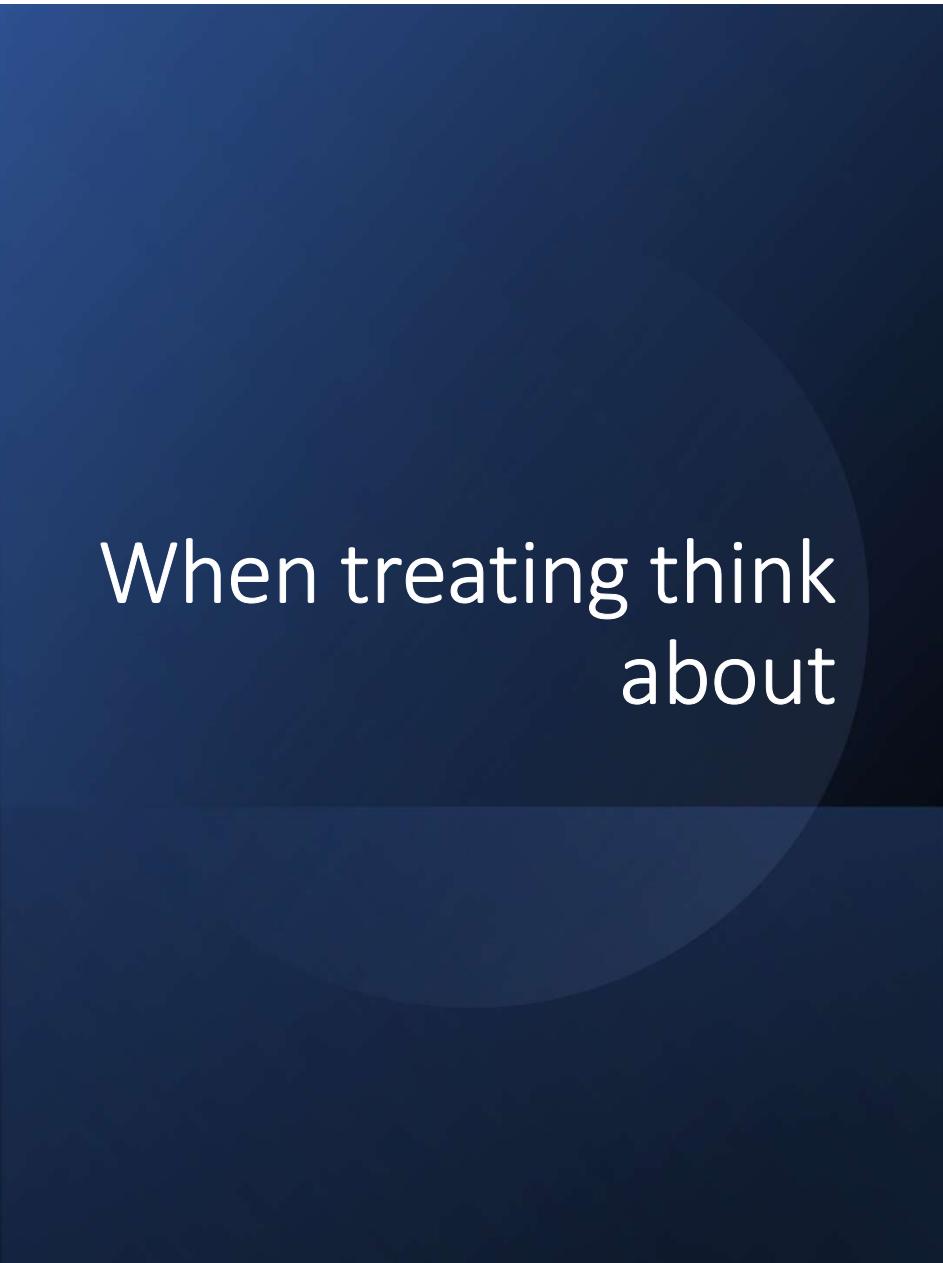
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- Variable and reversible obstruction of the airways
- Inflammatory condition combined with bronchial hyper-responsiveness
- Not preventable



# Aim of management

- No daytime symptoms
- No night-time waking due to asthma
- No need for rescue medication
- No asthma attacks
- No limitations on activity including exercise
- Normal-near normal lung function (FEV<sub>1</sub> and/or PEF > 80% predicted or best)
- No or minimal side-effects from medication
- Adequate knowledge to manage disease



When treating think  
about

- Take into account:
  - ✓ Smoking
  - ✓ **Lack of adherence**
  - ✓ Suboptimal inhaler technique
  - ✓ Alternative diagnosis
  - ✓ Occupational exposures
  - ✓ Seasonal factors

- This dates from an era when asthma was thought to be a disease of broncho-constriction
- Patient satisfaction with, and reliance on, SABA treatment is reinforced by:
  - its rapid relief of symptoms
  - its prominence in A&E and hospital management of exacerbations
  - low cost
- “*My reliever gives me control over my asthma!*”
- When the reliever is SABA, poor adherence with maintenance controller exposes the patient to risks of SABA-only treatment

## SABA as 1<sup>st</sup> line treatment for asthma

- *Patient with 'mild' asthma are at risk of severe adverse event (Dusser, Allergy 2007)*
  - *30 – 37% of adults with acute asthma*
  - *16% of patients with near-fatal asthma*
  - *15-20% of adults who died of asthma*
- *All had symptoms less than weekly in the previous 3 months*
- *Exacerbation triggers are NOT predictable*

## SABA as 1<sup>st</sup> line treatment for asthma

# Risks of regular SABA use

- Regular or frequent use of SABA is associated with adverse effects
  - $\beta$ -receptor downregulation
  - decreased broncho-protection
  - rebound hyperresponsiveness
  - decreased bronchodilator response(*Hancox, Respir Med 2000*)
  - Increased allergic response
  - increased eosinophilic airway inflammation(*Aldridge, AJRCCM 2000*)
- Higher use of SABA is associated with adverse clinical outcomes
  - Dispensing of  $\geq 3$  canisters per year (average 1.7 puffs/day) is associated with higher risk of emergency department presentations (*Stanford, AAAI 2012*)
  - Dispensing of  $\geq 12$  canisters per year is associated with higher risk of death (*Suissa, AJRCCM 1994*)

# Maintenance And Reliever Therapy

- Single inhaler
- Daily dosing, even when feeling well
- If symptoms get worse take an extra dose
- BTS/SIGN: Option at 'Initial add on therapy' step
- NICE: If asthma is uncontrolled in adults (aged 17 and over) on a low dose of ICS and a LABA, with or without an LTRA, as maintenance therapy, offer to change the person's ICS and LABA maintenance therapy to a MART regimen with a low maintenance ICS dose
- GINA:

# Which inhalers?

Contain budesonide and formoterol



Fobumix Easyhaler 80/4.5 & 160/4.5

Symbicort 100/6 & 200/6

Contain beclomethasone

Fostair 100/6pMDI & 100/6 NEXTHALER

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# Special ingredient?

- Formoterol
  - potent selective beta<sub>2</sub>-adrenergic stimulant
  - rapid effect within 1-3 minutes (Salbutamol < 5minutes)
  - effect significant 12 hours after inhalation (Salbutamol = 4-6 hours)
  - effective daily dose range 12mcg – 48mcg per day (9mcg – 40mcg)
  - Maximum dose = 72mcg per day (54mcg)

# Care: special but not magical

- As with all beta<sub>2</sub>-adrenergic stimulants
  - Headache
  - Tremor
  - Palpitations
- Aggression, psychomotor hyperactivity, anxiety, sleep disorders
- Dizziness
- Blurred vision
- Tachycardia
- Muscle cramps
- Nausea
- Bruising
- Paradoxical bronchospasm
- Cardiac arrhythmias, e.g. atrial fibrillation, supraventricular tachycardia, extrasystoles

# Benefits of MART

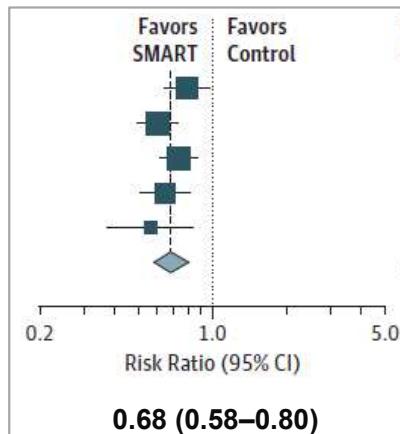
- Better for concordance (easier to only have to use one inhaler)
- Reduced intake of inhaled steroids to control asthma symptoms and prevent asthma attacks
- Evidence of reduction in risk even if non-concordant and using only PRN
- Increase availability of ICS when needed is effective in aborting exacerbations
- Cheaper prescription costs
- Reduced carbon footprint~
  - Fostair pMDI\* – benefit is in needing 1 inhaler instead of 2
  - Rest of the available MART inhalers are DPIs

**\*Always use with a spacer device**

**~ carbon footprint is not the only environmental impact an inhaler has**

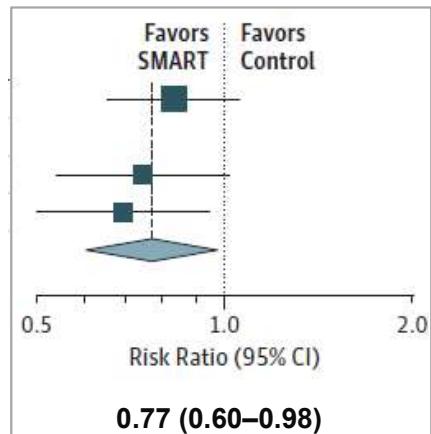
# Maintenance and reliever therapy (MART)

- MART with ICS-formoterol reduces severe exacerbations compared with ICS or ICS-LABA plus SABA reliever, with similar symptom control
  - Confirmed by regulatory studies and pragmatic open-label studies, n~30,000
- Both budesonide and formoterol contribute to the reduction in severe exacerbations

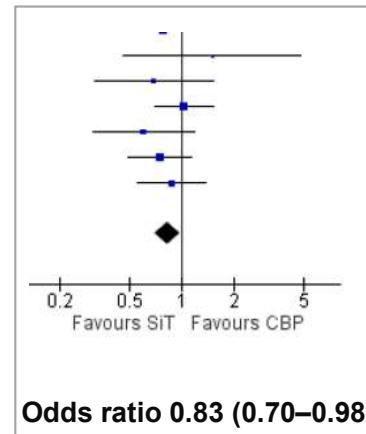


Compared with same dose ICS-LABA +SABA

*Sobieraj et al,*  
*JAMA 2018*  
*(n=22,748)*

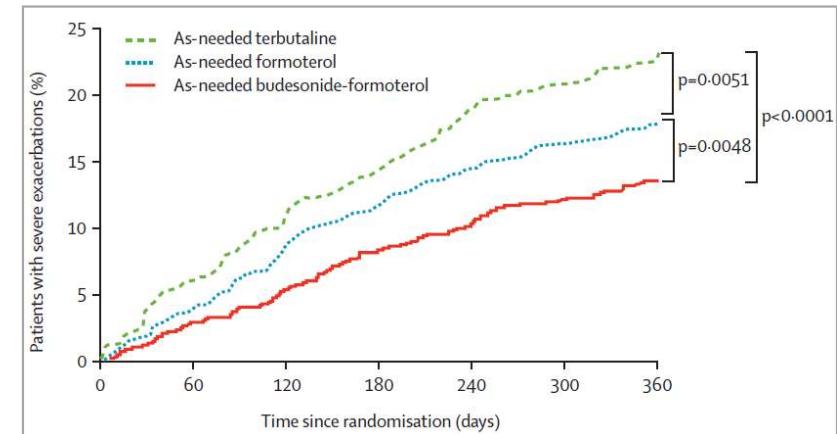


Compared with higher dose ICS-LABA + SABA



Compared with conventional best practice

*Cates et al,*  
*Cochrane 2013*  
*(n=4,433)*



Compared with formoterol or SABA reliever

*Rabe, Lancet 2006*  
*N=3,395, all taking maintenance budesonide-formoterol*

## Care needed

- Most not for children under 18
- Duoresp Spiromax and Symbicort licensed in >12 years of age
- Ensure patient is able to effectively use one of the inhalers licensed for MART
- Not appropriate when another ICS is needed
- Not appropriate with any other type of ICS/LABA combination
- Don't change those who are stable and concordant on current treatment.
- Careful education of patients about the specific issues around this management strategy is required

# AIR regimen

- Anti-inflammatory reliever therapy
- **Symbicort Turbohaler is now indicated as reliever therapy for adults and adolescents (12 years and older) with mild asthma.**



# The SYGMA studies

1 year and >3000 patients

## SYGMA 1

- 3 groups:
  - Placebo BD + Terbutaline PRN
  - Placebo BD + Symbicort PRN
  - Budesonide BD + Terbutaline PRN

## SYGMA 2

- 2 groups:
  - Placebo BD + Symbicort PRN
  - Budesonide BD + Terbutaline PRN

# Results

## SYGMA 1

- PRN Symbicort > PRN terbutaline for asthma control and reduced exacerbations
- PRN Symbicort < Budesonide maintenance in asthma control achievement (study adherence = 79%)
- PRN Symbicort = Budesonide maintenance for reduction in asthma exacerbation

## SYGMA 2

- PRN Symbicort < Budesonide maintenance for symptom control
- PRN Symbicort = Budesonide maintenance for reduction in exacerbations with less ICS
- Budesonide maintenance was better for asthma control achievement (study adherence = 63%)

# PRN low dose Symbicort in mild asthma

12-month studies, open-label, no twice-daily placebo, i.e. the way it would be used in real life

- Novel START (*Beasley et al, NEJM 2019, n=668*)
- PRACTICAL (*Hardy et al, Lancet 2019, independent study, n=885*)
- ↓severe exacerbations vs SABA alone, and vs maintenance ICS, with small or no difference in symptom control, and lower average ICS dose

## As-needed-only low-dose ICS-formoterol

- Risk of severe exacerbations (*Crossingham et al, Cochrane 2021*)
  - Compared with as-needed SABA alone: **55% reduction** (OR 0.45 [0.34–0.60])
  - Compared with daily ICS plus as-needed SABA: (OR 0.79 [0.59–1.07])
- Risk of emergency department visits or hospitalizations (*Crossingham et al, Cochrane 2021*)
  - Compared with as-needed SABA alone: **65% reduction** (OR 0.35 [0.20–0.60])
  - Compared with daily ICS plus as-needed SABA: **37% reduction** (OR 0.63 [0.44–0.91])
  - Large population-level reduction in healthcare utilization

## As-needed-only ICS-SABA

### Combination as-needed ICS-SABA

- BEST study, combination BDP-albuterol (*Papi et al, NEJM 2007, n=445, 6 months*)
  - Mean number of exacerbations per patient per year lower with as-needed combination (0.74) and regular BDP (0.71) compared with as-needed albuterol (1.63,  $P<0.001$ ) and regular combination BDP-albuterol (1.76,  $P<0.001$ )

### Taking ICS whenever SABA taken with separate inhalers

- TREXA study, BDP and albuterol, children and adolescents (*Martinez et al, Lancet 2011, n=288, 9 months*)
  - Frequency of exacerbations highest with albuterol alone (49%); lower with daily BDP (28%,  $p=0.03$ ), daily plus as-needed BDP and SABA (31%,  $p=0.07$ ) and as-needed BDP+SABA (35%,  $p=0.07$ )
  - Growth 1.1cm less in daily and combined groups but not as-needed-only group
- BASALT study, BDP and albuterol, adults (*Calhoun et al, JAMA 2012, n=342, 9 months*)
  - Similar exacerbations with as-needed BDP+SABA as with 6-weekly physician-adjusted or FeNO-adjusted ICS
- ASIST study, BDP and albuterol, African-American children and adolescents (*Sumino et al, Annals ATS 2020, n=206, 12 months*)
  - Similar symptoms control and exacerbations compared with physician-adjusted ICS

BDP: beclometasone dipropionate; ICS: inhaled corticosteroids; SABA: short-acting beta2-agonists

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# Effects of these studies on guidelines and recommendations

## GINA 2019 – landmark changes in asthma management



- For safety, GINA no longer recommends SABA-only treatment for Step 1 in adults and adolescents
  - This decision was based on evidence that SABA-only treatment increases the risk of severe exacerbations, and that adding any ICS significantly reduces the risk
- GINA now recommends that all adults and adolescents with asthma should receive ICS-containing controller treatment, to reduce the risk of serious exacerbations
  - The ICS can be delivered by regular daily treatment or, in mild asthma, by as-needed low dose ICS-formoterol
- This is a population-level risk reduction strategy
  - Other examples: statins, anti-hypertensives
  - The aim is to reduce the probability of serious adverse outcomes at a population level
  - Individual patients may not necessarily experience (or be aware of) short-term clinical benefit

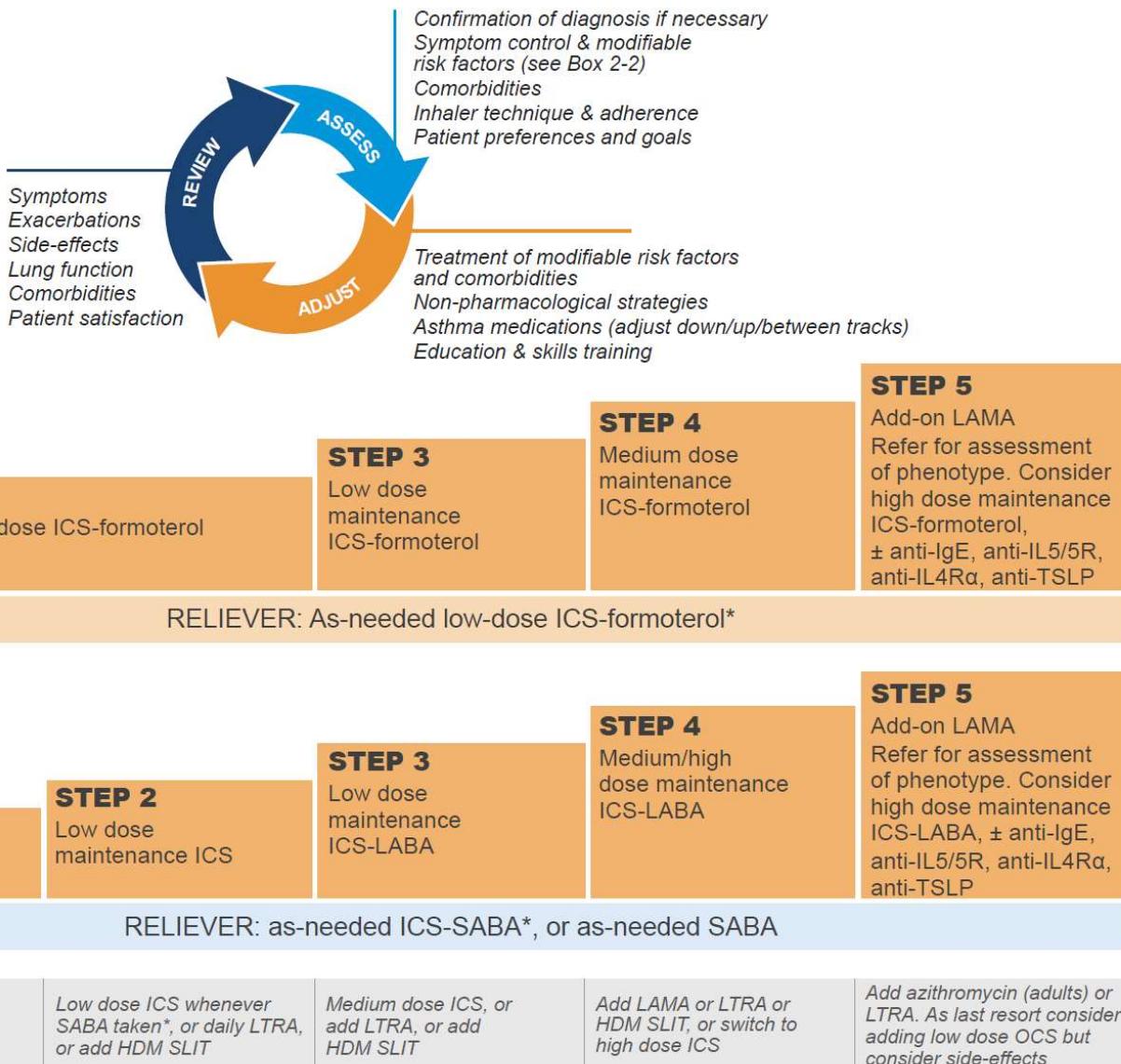
ICS: inhaled corticosteroids; SABA: short-acting beta<sub>2</sub>-agonist

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# GINA 2023 – Adults & adolescents 12+ years

## Personalized asthma management

Assess, Adjust, Review  
for individual patient needs

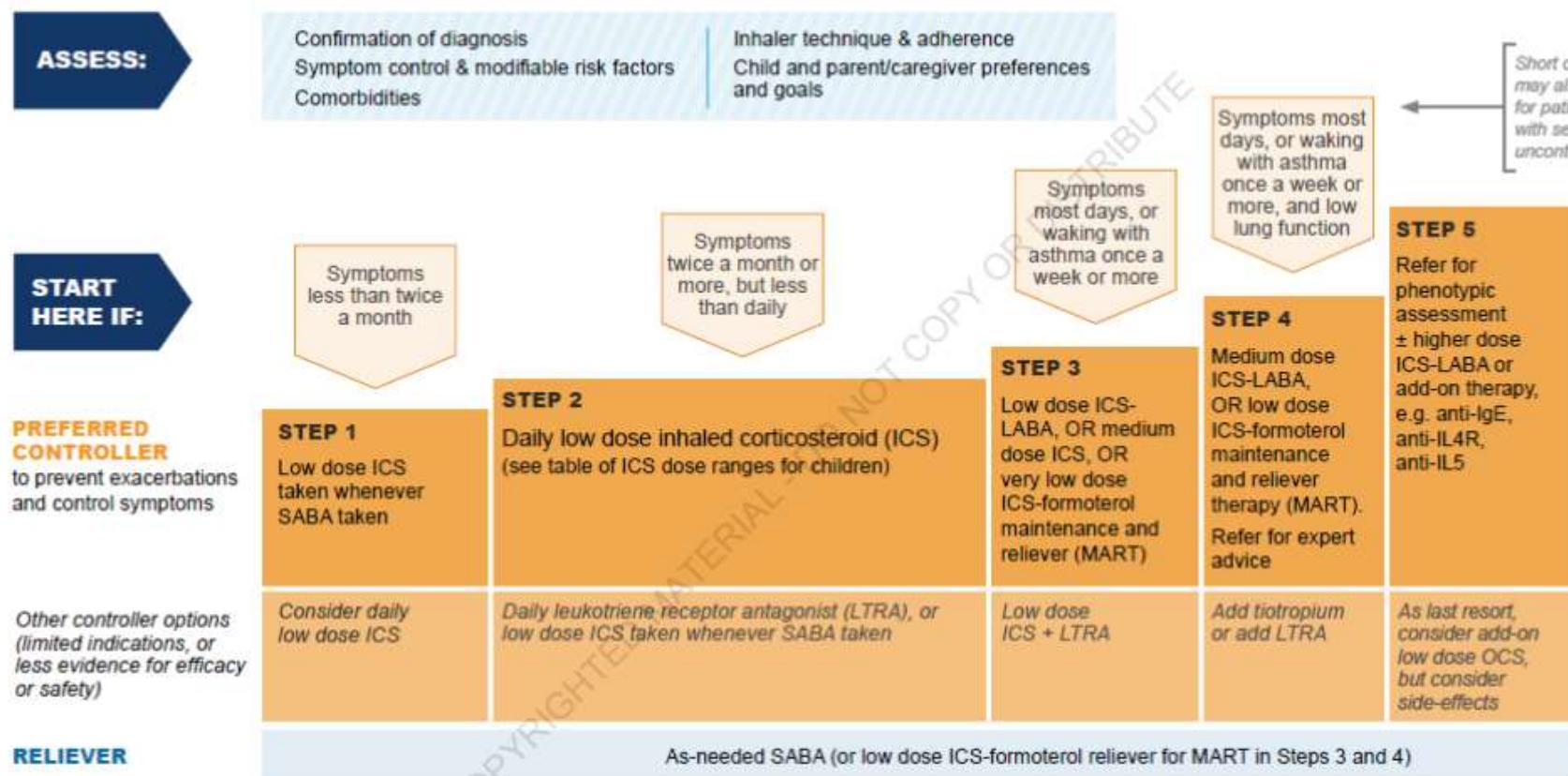


\*Anti-inflammatory reliever (AIR)

**Box 3-10. Selecting initial treatment in children aged 6–11 years with a diagnosis of asthma**

**GINA 2023 – STARTING TREATMENT**

Children 6–11 years with a diagnosis of asthma



See list of abbreviations (p.21). See Box 3-14, p.67 for low, medium and high ICS doses in children. See Box 3-15, p.80 for medications and doses for MART in children.



## PCRS guide to the management of asthma aged 12 and over in primary care

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**Before treating asthma, check that the criteria for diagnosis are present and correct\*.**

Ensure that you, as the prescriber, can describe to the person with asthma:

The criteria by which they have been given the diagnosis

What they can do to help manage it

What can happen if it's left unmanaged

Any asthma treatment will be more effective if it is created and agreed by both the patient and the clinician, reflects the patient's wishes, encourages self-management and clearly states when to seek further clinician support. **These wishes and choices should:**



Be written down or recorded in another way e.g. voice or video note that is understood



Include inhaler choice with respect to design, usability, cost and environmental impact



Describe communication options when help is needed or the plan isn't working anymore

Confirm that the person with asthma understands that the foundation of asthma medical therapy is ensuring that any airway inflammation arising due to triggers such as allergens, pollutants and infections is controlled by an inhaled corticosteroid.



Short-acting beta-agonists are used to dilate airways and do not treat underlying asthma inflammation. Over-reliance on SABA in asthma is associated with an increased risk of asthma attacks and asthma deaths.

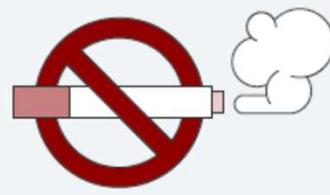
Patients may be successfully managed on a lower dose of inhaled corticosteroids and require fewer doses if they can be supported to:



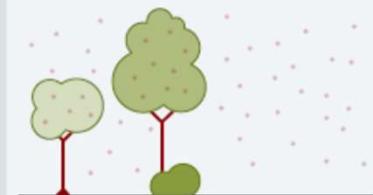
Maintain a healthy weight and be active



Understand the impact of indoor and outdoor air pollution and, where possible, how to avoid it



Avoid smoking/smoky environments and/or seek support to quit smoking



Understand asthma triggers (pollen, animal fur, perfumes etc.) and how to avoid or modify their effect

\*Where asthma is suspected but there is a delay in diagnostic testing, treatment should be initiated based on clinical judgement while awaiting objective diagnostic testing results

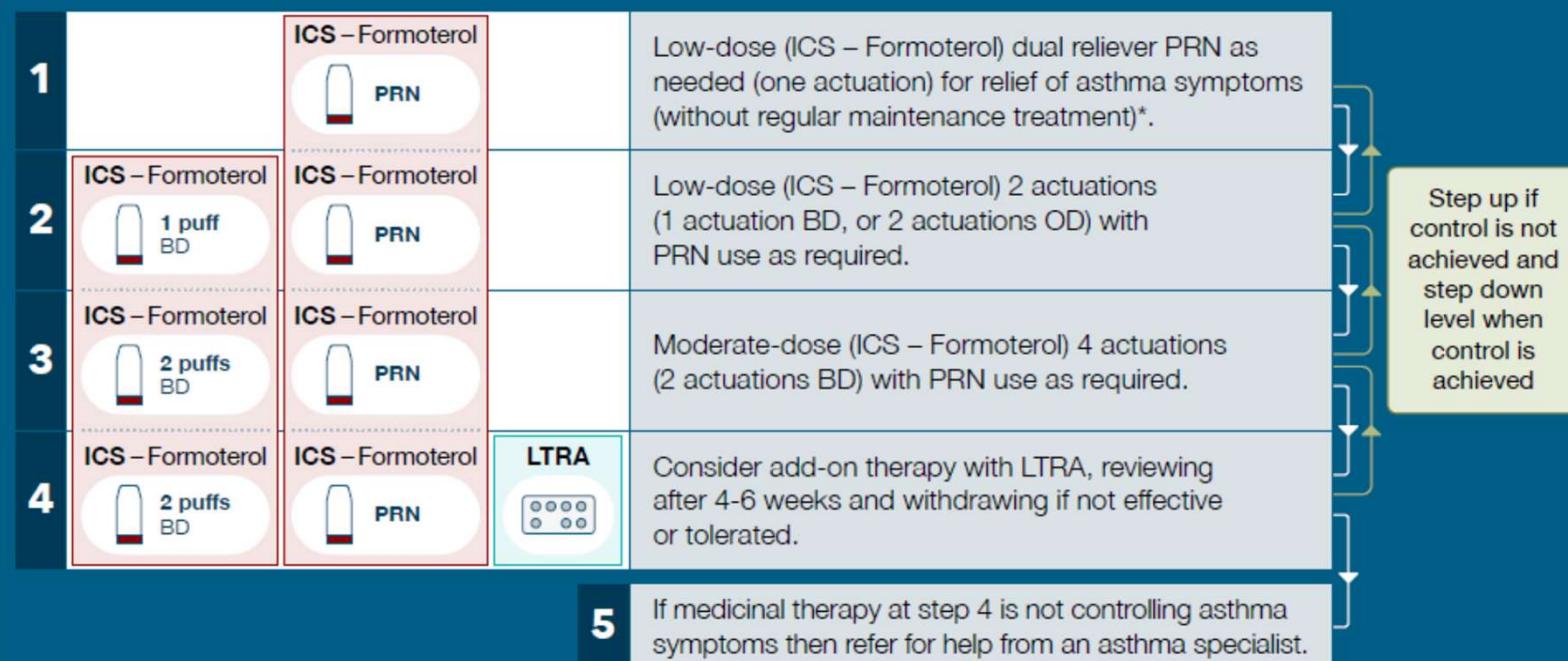
## Path 1: Dual anti-inflammatory reliever pathway

### Low-dose (ICS-Formoterol)

200mcg budesonide and 6mcg formoterol, 2 actuations per day

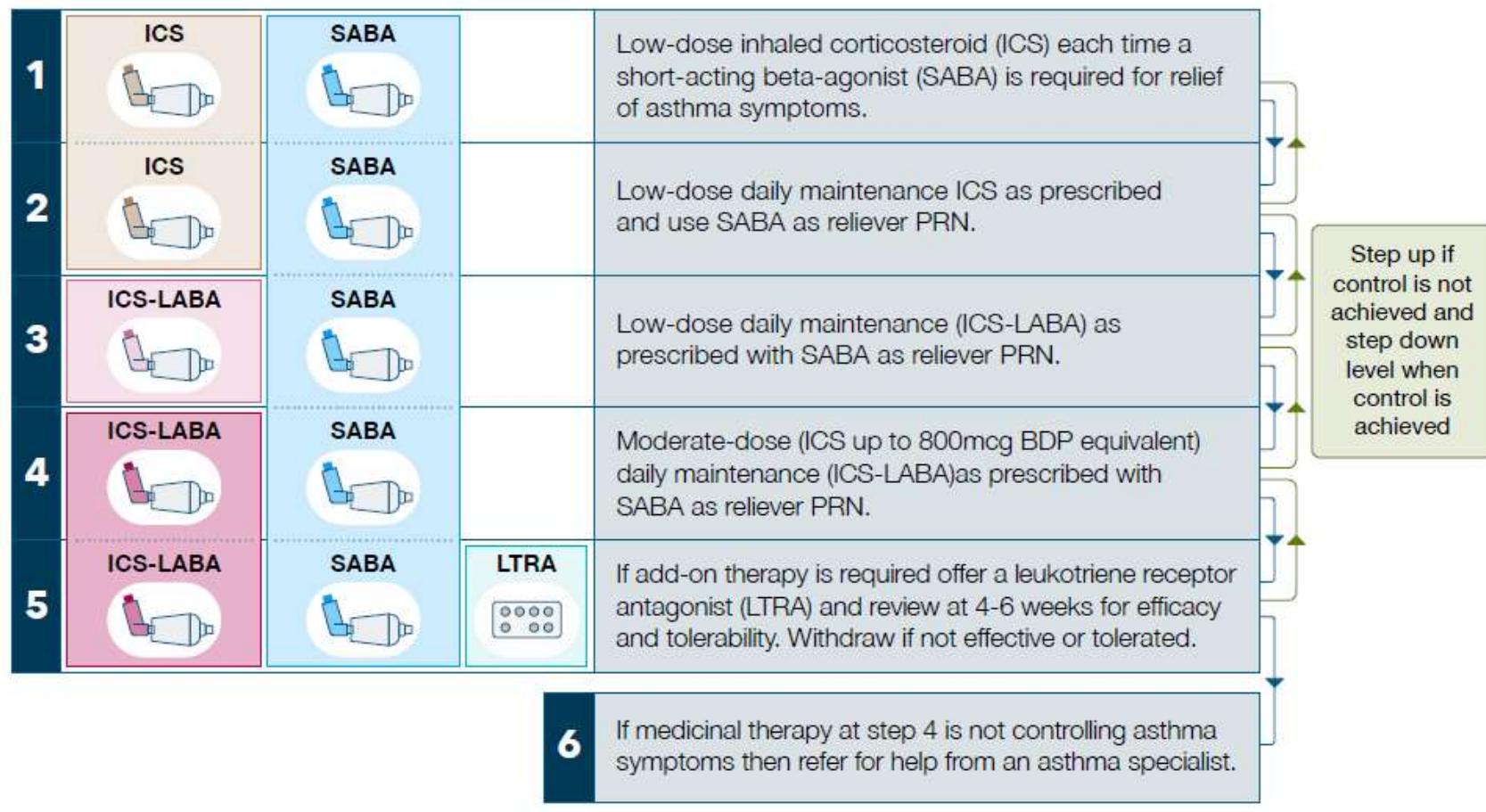
### Moderate-dose (ICS-Formoterol)

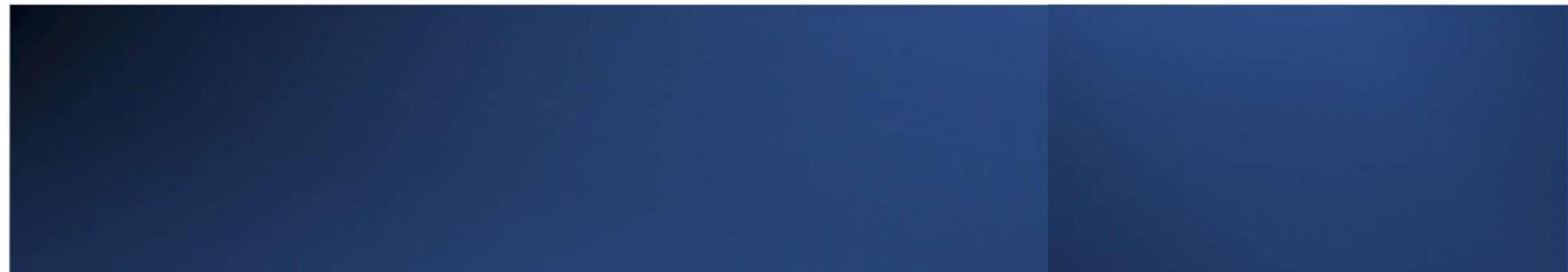
200mcg budesonide and 6mcg formoterol, 4 actuations per day



\* Budesonide 200mcg and Formoterol 6mcg is licensed for use as a reliever, as needed in response to asthma symptoms in Step 1 without regular maintenance treatment

## Path 2: Alternative path – Traditional approach







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# Focus on asthma: The GINA Approach to Managing Asthma



**Darush Attar Zadeh,<sup>1</sup> Katherine Hickman,<sup>2</sup> Ren Lawlor,<sup>3</sup> Alicia Piwko,<sup>4</sup> Lizzie Williams<sup>5</sup>**

<sup>1</sup> PCRS Conference Organising Committee Lead and Pharmacist (Medicines Optimisation); <sup>2</sup> Chair PCRS Executive, GP Partner, Bradford and Respiratory Lead for West Yorkshire Health and Care Partnership; <sup>3</sup> PCRS Vice Chair and Education Lead; <sup>4</sup> Specialist Respiratory Pharmacist, Guy's and St Thomas' NHS Foundation Trust & Quay Health Solutions; <sup>5</sup> Specialist Respiratory Nurse, PCRS Service Development Committee



**Asthma is a long-term condition characterised for the vast majority by eosinophilic airway inflammation. In the UK, anti-inflammatory therapy options are easily accessed, affordable and are highly effective with minimal side effects. However, many people with asthma do not use enough or timely amounts of this therapy in order to control their symptoms and prevent attacks. This is seen when people attend in crisis at emergency departments, make urgent appointments with their GPs, miss work or school; and sadly, poor management still causes death.**



In 2022, using the available Quality and Outcomes Framework (QOF) data from UK general practice registers, 6.5% or 3,745,077 people over the age of six were diagnosed with asthma.<sup>1</sup> The vast majority of asthma care occurs in general practice. Planned and routine asthma care can allow the vast majority to live well with asthma and avoid emergency care.



This spring, the Primary Care Respiratory Society brings you a new focus on asthma and outlines a new approach to ensure timely use of anti-inflammatory medicine for people that have not benefited as well from historic treatment pathways.



The Medicines and Healthcare Products Regulatory Agency (MHRA) has for the first time approved the use of a dual (ICS/Formoterol) combination treatment to be used as a reliever therapy for people aged 12 and over with the therapy choice situated early in the asthma treatment pathway as an alternative to its current use as a preventer or MART therapy sitting later in traditional treatment pathways.<sup>2</sup>

The MHRA approval is for Budesonide 200mcg/Formoterol 6mcg combination that is delivered as dry powder via a turbohaler. In recent trials, the use of this dual therapy, utilising the fast-acting property of formoterol for quick relief resulted in reductions in asthma attacks compared to the use of short acting beta agonists alone.<sup>3</sup>

In the UK, this new therapy option does not yet sit within an approved national guideline as NICE last updated its treatment pathway in 2020.<sup>4</sup> We await a new national asthma guideline but do not anticipate this new joint approach between NICE, BTS and SIGN to publish until 2024.

In the meantime, PCRS has looked to the latest Global Initiative for Asthma (GINA) approach to asthma treatment to see how this new approach fits and we have developed a simple algorithm for healthcare practitioners to see where this new treatment option sits.<sup>5</sup>

# Primary Care Respiratory Update

At PCRS, we know how busy primary care is and realise that introducing a new treatment choice means change and that changes takes time, can use up scarce resources, and can feel burdensome. In this Spring's issue of *Primary Care Respiratory Update* we will also show you how to take small steps to try out this new treatment pathway on a limited patient group, using a real-world test of change in a GP practice and show the key steps to help make implementation a success.

## Acknowledgements

PCRS would like to acknowledge the work undertaken in New Zealand by Richard Beasley et al in developing a pragmatic approach to the implementation of GINA recommendations.

We would also like to acknowledge the following clinicians for their support in the preparation of this work for providing literature and advice on the preparation of the following infographic:-

- Professor Eric Bateman, GINA Committee
- Helena Cummings, Severe Asthma Service Lead, Hull University Teaching Hospitals NHS Trust
- Dr Mike Crooks, Hull University Teaching Hospitals NHS Trust
- Dr Andrew Whittamore, Asthma and Lung UK
- Dr Alex Wilkinson, East and North Herts NHS Trust

## References

1. NHS UK GP QOF Contract Database. 2022 <http://www.gpcontract.co.uk>.
2. Medicines regulator approves UK's first dual combination inhaler for mild asthma. The Pharmaceutical Journal <https://pharmaceutical-journal.com/article/news/medicines-regulator-approves-uks-first-dual-combination-inhaler-for-mild-asthma> (2023).
3. O'Byrne, PM et al. Inhaled Combined Budenoside–Formoterol as Needed in Mild Asthma N Engl J Med 378, 1865–1876 (2018).
4. NICE. NICE guideline [NG80] Asthma: diagnosis, monitoring and chronic asthma management. Published date: 29 November 2017 Last updated: 12 February 2020 <https://www.nice.org.uk/guidance/ng80>.
5. GINA. GINA-2022-Pocket-Guide-WMS. Global Initiative for Asthma 1–50 <https://ginasthma.org/wp-content/uploads/2022/07/GINA-2022-Pocket-Guide-WMS.pdf> (2022).

## For more information see

Richard Beasley, Irene Braithwaite, Alex Semprini, Ciléin Kearns, Mark Weatherall, Tim W. Harrison, Alberto Papi, Ian D. Pavord. ICS-formoterol reliever therapy stepwise treatment algorithm for adult asthma European Respiratory Journal 2020 55: 1901407; DOI: 10.1183/13993003.01407-2019  
Also see <https://www.asthmafoundation.org.nz/assets/images/NZ-Asthma-Guidelines-Quick-Reference-Guide-2020-Online-09-21.pdf>

We'll also be bringing you a series of resources in this Spring's Primary Care Respiratory Update which includes more information on how to assess asthma control as well as a series of other resources including:



- The presenting features of asthma and the importance of correct diagnosis using objective airflow measurement and Fractional Exhaled NO (FENO) to support any clinical suspicion.
- The non-pharmacological elements of asthma care that ensure the use of anti-inflammatory therapy is clinically effective and safe.
- How to deliver an effective asthma review in ten minutes
- The importance of choice of therapy and device, and that the greenest asthma care is a well-managed asthma patient using an inhaler device they can and will use
- How to recognise when asthma is difficult to manage and severe and know when to ask for help.



You can view all our asthma resources including online learning modules, asthma myths videos and other tools directly from the PCRS website



# PCRS guide to the management of asthma aged 12 and over in primary care

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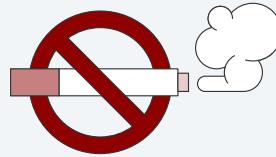
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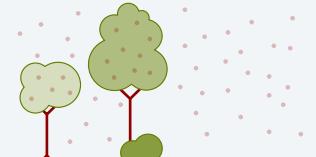
Maintain a healthy weight and be active



Understand the impact of indoor and outdoor air pollution and, where possible, how to avoid it

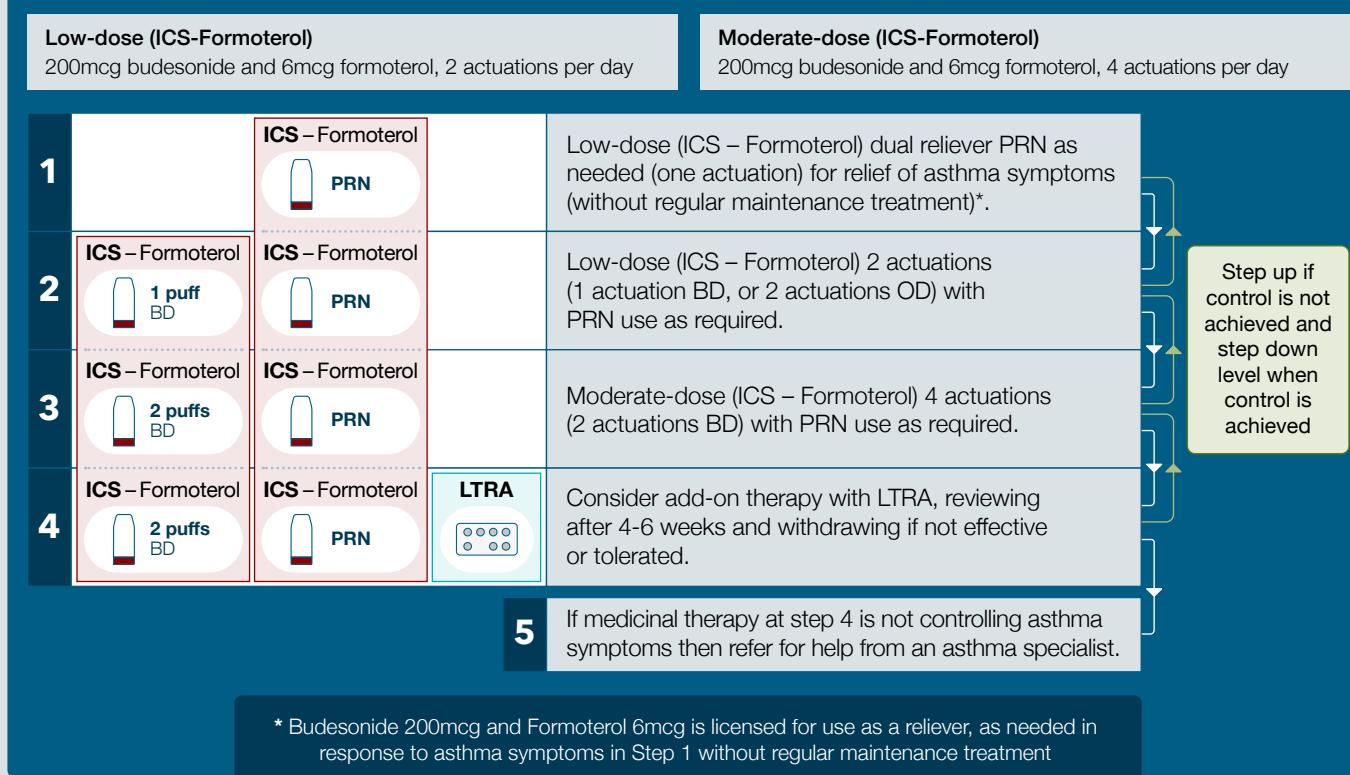


Avoid smoking/smoky environments and/or seek support to quit smoking

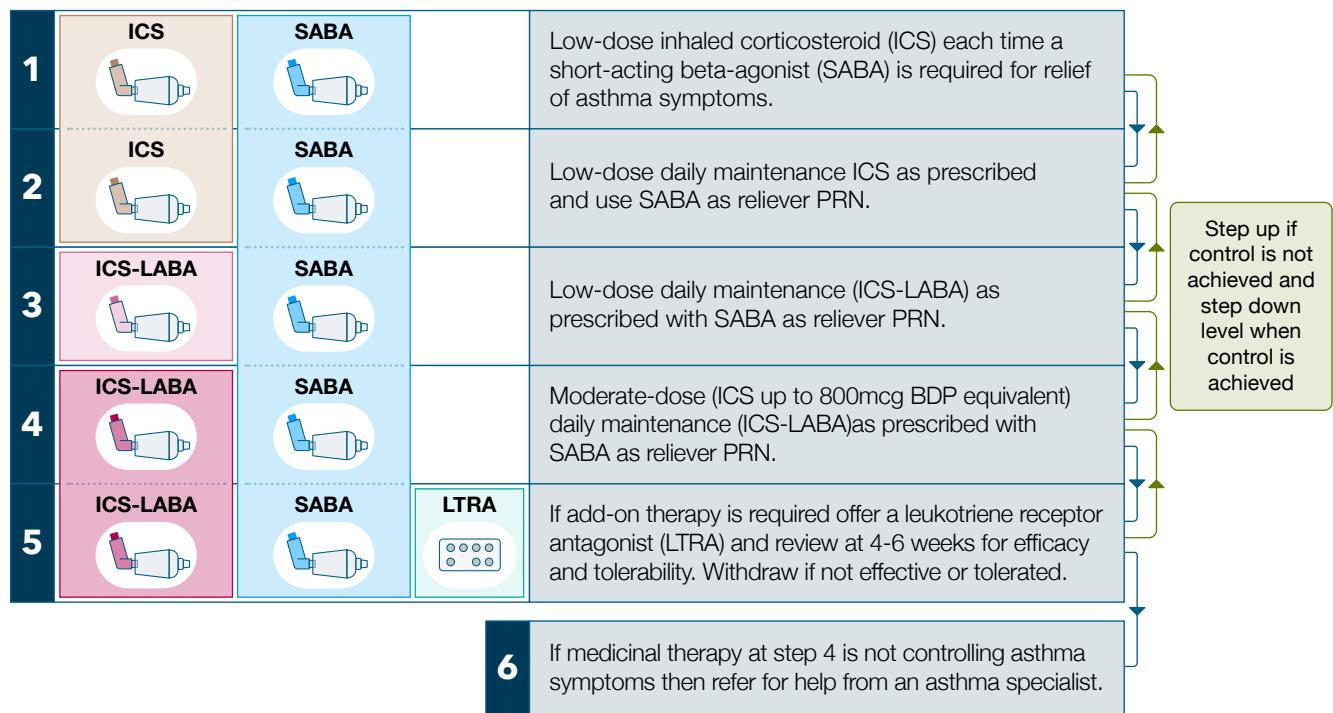


Understand asthma triggers (pollen, animal fur, perfumes etc.) and how to avoid or modify their effect

## Path 1: Dual anti-inflammatory reliever pathway



## Path 2: Alternative path – Traditional approach



### Notes

- Inhalers shown in this document are for illustrative purposes only. Please see prior page regarding inhaler selection
- Some medicines in this document are only licensed in people aged 18 years and above
- Please see [link](#) for advice regarding asthma control [or use QR code]



Scan the QR code for more on asthma control