Asthma Update 2023

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Goals/Objectives

1. Briefly review the diagnosis of asthma including information about asthma phenotypes
2. Review information about the current Global Initiative for Asthma (GINA) for short including July 2023 update
3. Discuss current treatment options related to biologic medications

Asthma Defined

- Heterogenous
- Most often characterized as chronic inflammatory process of the airways
- Usually assess by wheeze, shortness of breath, chest tightness and cough
- Often variable within the same patient in symptoms and intensity at different times
- Often with variability in airflow (expiratory, limited airflow and can have persistent limitations later in the disease)

Assessment of Symptoms

- Cough
- Chest tightness
- Wheeze – caution here as patients will sometimes use the term "wheeze" to describe things other than wheeze or conditions other than asthma that wheeze (laryngeal obstruction, COPD, respiratory infections, tracheomalacia, inhaled foreign body)

- Crackles and inspiratory wheeze are NOT typical features of asthma

Asthma Phenotypes

- Allergic asthma
- Non-allergic asthma
- Adult onset
- Asthma with persistent airflow limitation
- Asthma with obesity

  - Often does not correlate to specific pathologic patterns or response to treatment

Asthma in the Primary Care Setting

- Many patients get “diagnosed” as asthmatic in the primary care setting
- **Estimates of 25% to 35% cannot be confirmed as asthmatic (23, 38-41)**

Documentation of Airflow Limitation

- Typically, an FEV1 that increases post-bronchodilator challenge by 12% and/or 200mL
- Use of bronchial provocation test (methacholine, histamine, exercise, inhaled mannitol)
  - Moderately sensitive for asthma, but not as specific
  - Hyperresponsiveness has been described in COPD, CF and bronchopulmonary dysplasia patients
- Allergy testing is recommended if history is c/w atopy
  - Skin testing is expensive, but most often less expensive than serum testing
  - Use of exhaled nitric oxide measurement helpful to identify eosinophilic asthma

Goals of asthma treatment

- Few asthma symptoms
- No sleep disturbance
- No exercise limitation

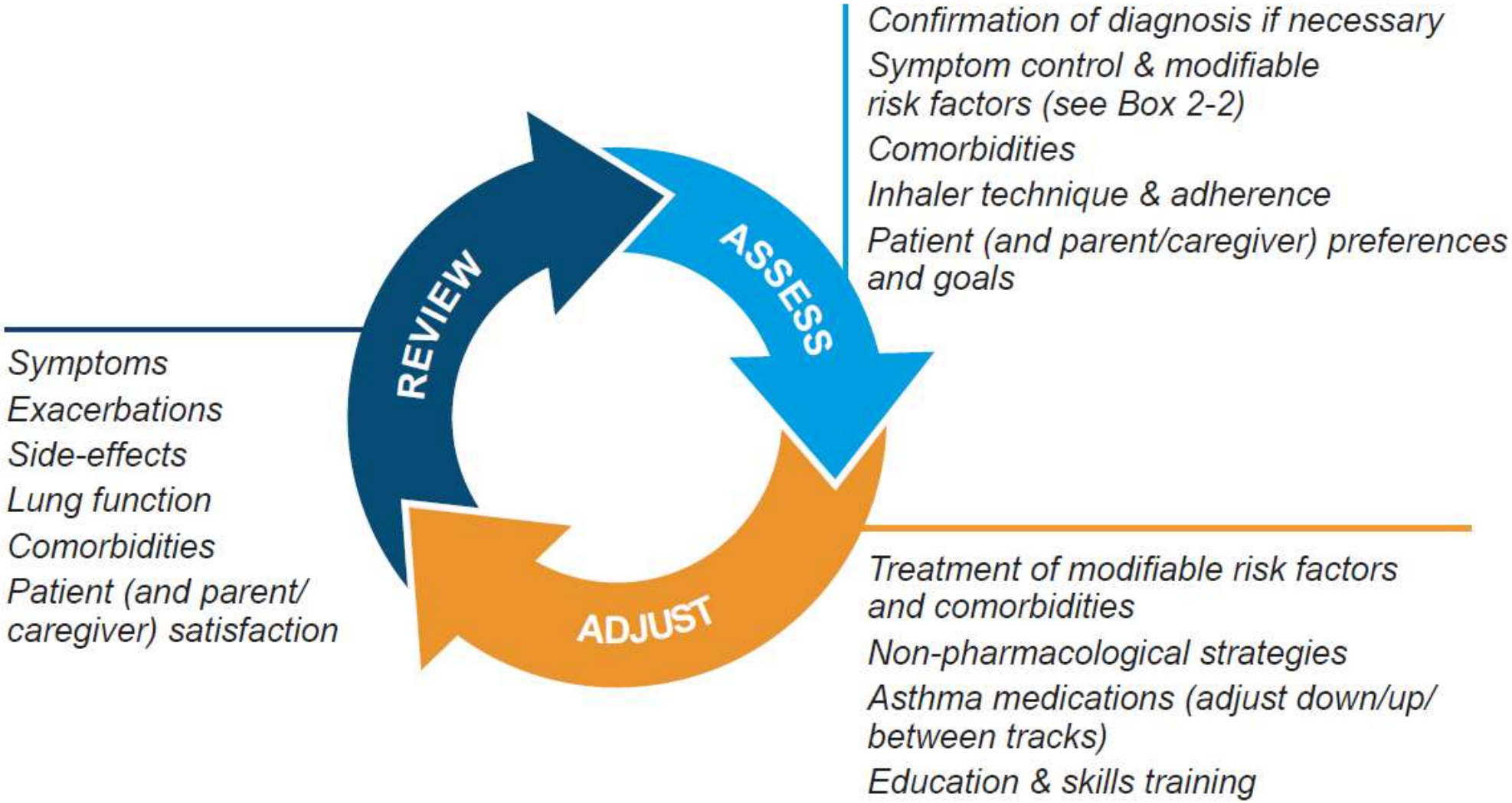
} Symptom control (e.g. ACT, ACQ)

- Maintain normal lung function
- Prevent flare-ups (exacerbations)
- Prevent asthma deaths
- Minimize medication side-effects (including OCS)

} Risk reduction

- The patient's goals may be different
- Symptom control and risk may be discordant
  - Patients with few symptoms can still have severe exacerbations

ACQ: Asthma Control Questionnaire; ACT: Asthma Control Test; OCS: oral corticosteroids



What's new in GINA 2023?

Global Strategy for Asthma Management and Prevention

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Terminology

- Reliever
  - For symptom relief, or before exercise or allergen exposure
- Controller
  - Function: targets both domains of asthma control (symptom control and future risk)
  - Mostly used for ICS-containing treatment
- Maintenance treatment
  - Frequency: regularly scheduled, e.g. twice daily

ICS: inhaled corticosteroid; SABA: short-acting beta$_2$-agonist

Terminology

- **A**nti-**I**nflammatory **R**eliever = **AIR**
  - e.g. ICS-formoterol, ICS-SABA
  - Provides rapid symptom relief, plus a small dose of ICS
  - Reduces the risk of exacerbations, compared with using a SABA reliever

Regimens with ICS-formoterol anti-inflammatory reliever

- As-needed-only ICS-formoterol = **AIR-only**
  - The patient takes low-dose ICS-formoterol whenever needed for symptom relief
- **M**aintenance **A**nd **R**eliever **T**herapy with ICS-formoterol = **MART**
  - A low dose of ICS-formoterol is used as the patient's maintenance treatment, plus whenever needed for symptom relief
- ICS-formoterol can also be used before exercise or allergen exposure

ICS: inhaled corticosteroid: SABA: short-acting beta$_2$-agonist; MART is sometimes also called SMART

GINA 2023 – Adults & adolescents 12+ years

Personalized asthma management
Assess, Adjust, Review
for individual patient needs

Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (see Box 2-2)
Comorbidities
Inhaler technique & adherence
Patient preferences and goals

Symptoms
Exacerbations
Side-effects
Lung function
Comorbidities
Patient satisfaction

Treatment of modifiable risk factors and comorbidities
Non-pharmacological strategies
Asthma medications (adjust down/up/between tracks)
Education & skills training

TRACK 1: PREFERRED CONTROLLER and RELIEVER
Using ICS-formoterol as the reliever* reduces the risk of exacerbations compared with using a SABA reliever, and is a simpler regimen

STEPS 1 – 2	STEP 3	STEP 4	STEP 5
As-needed-only low dose ICS-formoterol	Low dose maintenance ICS-formoterol	Medium dose maintenance ICS-formoterol	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-formoterol, ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP

RELIEVER: As-needed low-dose ICS-formoterol*

See GINA severe asthma guide

TRACK 2: Alternative CONTROLLER and RELIEVER
Before considering a regimen with SABA reliever, check if the patient is likely to adhere to daily controller treatment

STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
Take ICS whenever SABA taken*	Low dose maintenance ICS	Low dose maintenance ICS-LABA	Medium/high dose maintenance ICS-LABA	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP

RELIEVER: as-needed ICS-SABA*, or as-needed SABA

Other controller options (limited indications, or less evidence for efficacy or safety – see text)	*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*

*Anti-inflammatory reliever (AIR)

Track 1, Steps 1–2: As-needed-only low-dose ICS-formoterol

COMPARED WITH AS-NEEDED SABA

- Two studies *(SYGMA 1, O'Byrne et al, NEJM 2018, n=3836; Novel START, Beasley et al, NEJM 2019, n=668)*
- Risk of severe exacerbations was reduced by 60–64% *(SYGMA 1, Novel START)*

COMPARED WITH MAINTENANCE LOW DOSE ICS plus as-needed SABA

- Four studies *(SYGMA 1; SYGMA 2, Bateman et al, NEJM 2018, n=4176; Novel START; PRACTICAL, Hardy et al, Lancet 2019, n=885)*
- Risk of severe exacerbations similar *(SYGMA 1 & 2)*, or lower *(Novel START, PRACTICAL)*
- Symptoms very slightly more, e.g. ACQ-5 0.15 (vs 0.5 MCID), not worsening over 12 months
- Pre-BD FEV_1 slightly lower (~54 mL), not worsening over 12 months
- FeNO slightly higher (10ppb), not increasing over 12 months *(Novel START, PRACTICAL)*
- As-needed ICS-formoterol used on ~ 30% of days → average ICS dose ~50–100mcg budesonide/day
- Benefit independent of T2 status, lung function, exacerbation history *(Novel START, PRACTICAL)*
- Qualitative research: most patients preferred as-needed ICS-formoterol *(Baggott Thorax 2020, ERJ 2020; Foster Respir Med 2020, BMJ Open 2022)*

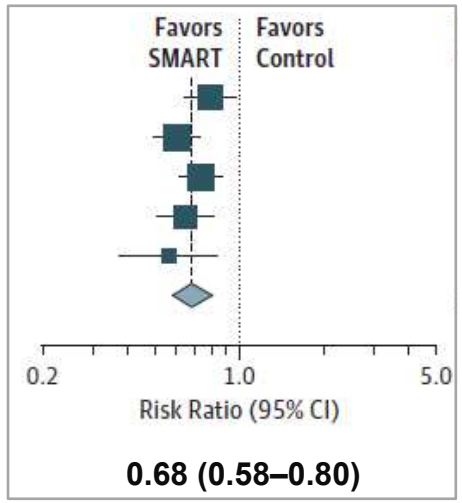
*Budesonide-formoterol 200/6 [160/4.5] mcg by Turbuhaler, 1 inhalation as needed for symptom relief

Track 1, Steps 1–2: As-needed-only low-dose ICS-formoterol

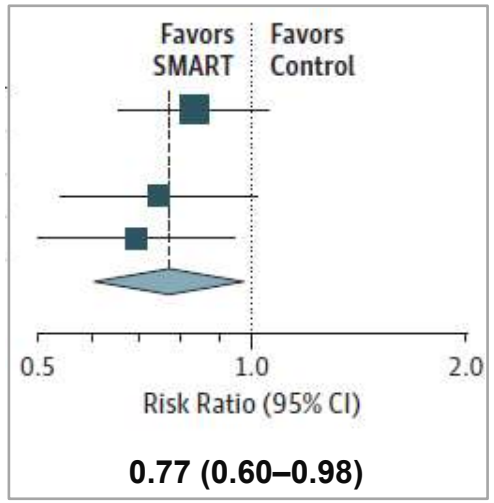
- Risk of severe exacerbations *(Crossingham et al, Cochrane 2021)*
  - Compared with as-needed SABA alone: **55% reduction** (OR 0.45 [0.34–0.60])
  - Compared with daily ICS plus as-needed SABA: (OR 0.79 [0.59–1.07])
- Risk of emergency department visits or hospitalizations *(Crossingham et al, Cochrane 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

Track 1, Steps 3–5: 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

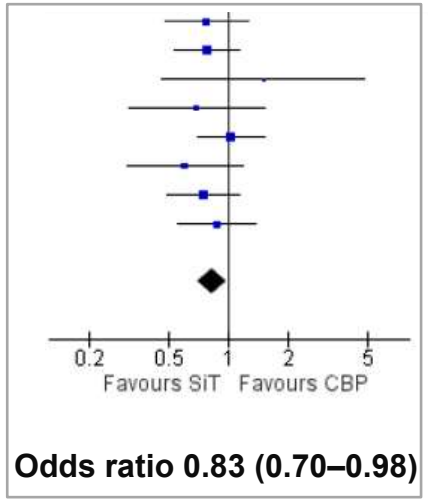


Compared with same dose ICS-LABA +SABA



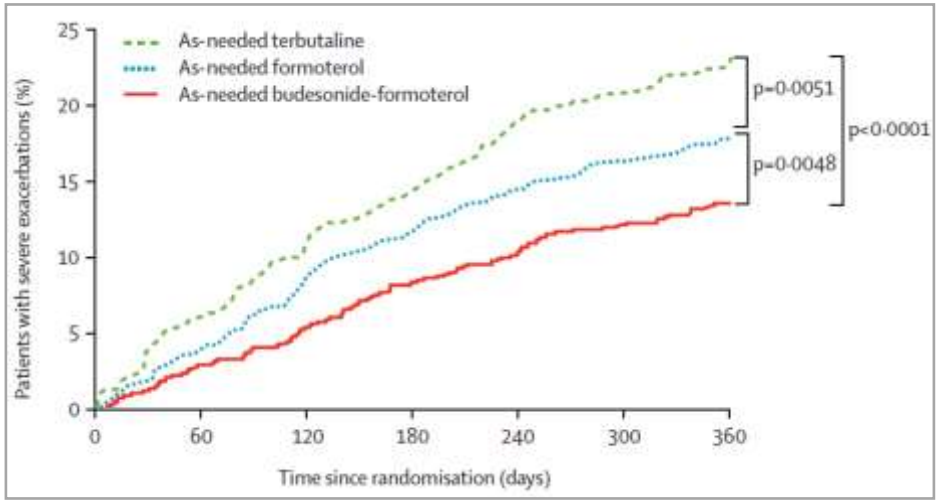
Compared with higher dose ICS-LABA + SABA

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



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

GINA 2023 – Adults and adolescents
Track 1

Maintenance and reliever therapy (MART) with ICS-formoterol

As-needed-only ICS-formoterol ('AIR-only')

TRACK 1: PREFERRED CONTROLLER and RELIEVER
Using ICS-formoterol as the reliever* reduces the risk of exacerbations compared with using a SABA reliever, and is a simpler regimen

STEPS 1 – 2
As-needed-only low dose ICS-formoterol*

STEP 3
Low dose maintenance ICS-formoterol*

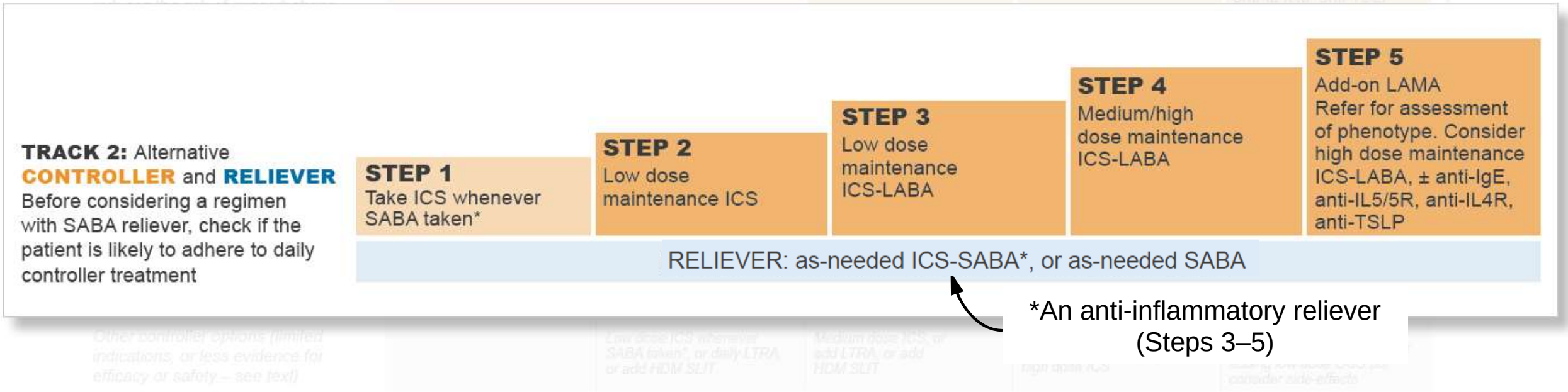
STEP 4
Medium dose maintenance ICS-formoterol

STEP 5
Add-on LAMA
Refer for assessment of phenotype. Consider high dose maintenance ICS-formoterol, ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP

RELIEVER: As-needed low-dose ICS-formoterol*

*An anti-inflammatory reliever (AIR)

GINA 2023 – Adults and adolescents
Track 2



Track 2, Steps 1–2: As-needed-only ICS-SABA

Combination as-needed ICS-SABA

- BEST study, combination BDP-albuterol *(Papi et al, NEJMed 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

GINA 2023 – Adults and adolescents

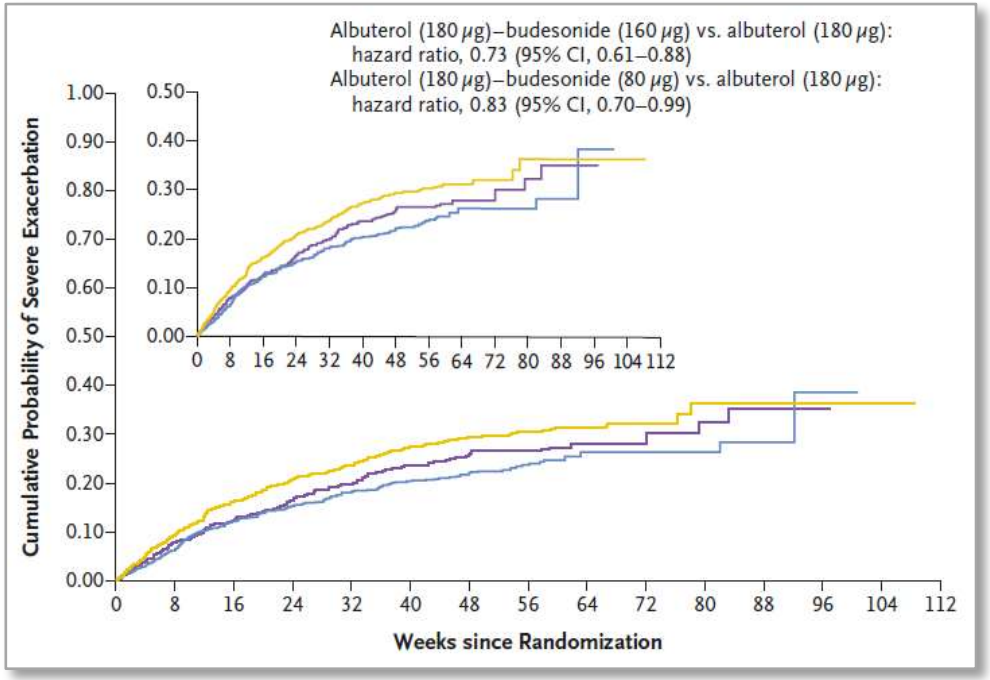
Other controller options (limited indications, or less evidence for efficacy or safety – see text)		*Low dose ICS whenever SABA taken*, or daily LTRA, or add HDM SLIT*	*Medium dose ICS, or add LTRA, or add HDM SLIT*	*Add LAMA or LTRA or HDM SLIT, or switch to high dose ICS*	*Add azithromycin (adults) or LTRA. As last resort consider adding low dose OCS but consider side-effects*

Track 2, Steps 3–5: as-needed ICS-SABA added to maintenance treatment

Papi et al, NEJMed 2022 (n=3,132)

In patients taking Step 3–5 maintenance treatment:

- Hazard ratio for probability of severe exacerbations was 0.73 (95% CI 0.61–0.88) with higher dose of as-needed albuterol-budesonide compared with as-needed albuterol
- Most benefit seen in Step 3



Why is GINA Track 1 with ICS-formoterol preferred?

- **Steps 1–2**: weight of evidence for effectiveness and safety compared with SABA alone, or low-dose ICS plus as-needed SABA (4x12 month studies, n~10,000) *(Crossingham et al, Cochrane 2021)*
  - As-needed ICS-SABA: only one 6-month RCT (n=455) *(Papi et al, NEJMed 2007)*
- **Steps 3–5**: weight of evidence for effectiveness and safety of MART versus regimens with as-needed SABA (n~30,000) *(Sobieraj et al, JAMA 2018; Cates et al, Cochrane 2013)*
  - As-needed ICS-SABA: only one RCT (n=3,132) vs as-needed SABA *(Papi et al, NEJMed 2022);* cannot be used for maintenance and reliever therapy
- Both the ICS and the formoterol contribute to reduction in severe exacerbations *(Tattersfield et al, Lancet 2001; Pauwels et al, ERJ 2003; Rabe et al, Lancet 2006)*
  - Safety established up to total 12 inhalations in any day, in large studies
- **Simplicity of approach** for patients and clinicians
  - A single medication for both symptom relief and maintenance treatment (if needed) from diagnosis
  - Avoids confusion about inhaler technique with different devices
  - Short-term increase in symptoms → patient increases the number of **as-needed** doses
  - Step treatment down or up by changing the number of maintenance doses

GINA 2023 – Adults & adolescents 12+ years

Personalized asthma management
Assess, Adjust, Review
for individual patient needs

Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (see Box 2-2)
Comorbidities
Inhaler technique & adherence
Patient preferences and goals

Symptoms
Exacerbations
Side-effects
Lung function
Comorbidities
Patient satisfaction

Treatment of modifiable risk factors and comorbidities
Non-pharmacological strategies
Asthma medications (adjust down/up/between tracks)
Education & skills training

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RELIEVER: As-needed low-dose ICS-formoterol*

See GINA severe asthma guide

TRACK 2: Alternative CONTROLLER and RELIEVER
Before considering a regimen with SABA reliever, check if the patient is likely to adhere to daily controller treatment

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Take ICS whenever SABA taken*	Low dose maintenance ICS	Low dose maintenance ICS-LABA	Medium/high dose maintenance ICS-LABA	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP

RELIEVER: as-needed ICS-SABA*, or as-needed SABA

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*Anti-inflammatory reliever (AIR)

How to prescribe low-dose ICS-formoterol in GINA Track 1

Example: budesonide-formoterol 200/6 mcg [160/4.5 delivered dose]

- **Steps 1–2**: take 1 inhalation whenever needed for symptoms
- **Step 3**: take 1 inhalation twice a day (or once a day) PLUS 1 inhalation whenever needed for symptoms
- **Steps 4–5**: take 2 inhalations twice a day PLUS 1 inhalation whenever needed for symptoms
- As-needed doses of ICS-formoterol can also be taken before exercise *(Lazarinis et al, Thorax 2014)* or before allergen exposure *(Duong et al, JACI 2007)*

See following slides for medications, doses, and maximum number of inhalations in any day for GINA Track 1

Step	Age (years)	Medication and device (check patient can use inhaler)	Metered dose (mcg/inhalation)	Delivered dose (mcg/inhalation)	Dosage
Steps 1–2 (AIR-only)	6–11	(No evidence)	-	-	-
	12–17 ≥18	Budesonide-formoterol DPI	200/6	160/4.5	**1 inhalation whenever needed**
Step 3 MART	6–11	Budesonide-formoterol DPI	100/6	80/4.5	**1 inhalation once daily**, PLUS 1 inhalation whenever needed
	12–17 ≥18	Budesonide-formoterol DPI	200/6	160/4.5	**1 inhalation once or twice daily,** PLUS 1 inhalation whenever needed
	≥18	BDP-formoterol pMDI	100/6	84.6/5.0	
Step 4 MART	6–11	Budesonide-formoterol DPI	100/6	80/4.5	**1 inhalation twice daily**, PLUS 1 inhalation whenever needed
	12–17 ≥18	Budesonide-formoterol DPI	200/6	160/4.5	**2 inhalations twice daily**, PLUS 1 inhalation whenever needed
	≥18	BDP-formoterol pMDI	100/6	84.6/5.0	
Step 5 MART	6–11	(No evidence)	-	-	-
	12–17 ≥18	Budesonide-formoterol DPI	200/6	160/4.5	**2 inhalations twice daily**, PLUS 1 inhalation whenever needed
	≥18	BDP-formoterol pMDI	100/6	84.6/5.0	

DPI: dry powder inhaler; pMDI: pressurized metered dose inhaler. For budesonide-formoterol pMDI with 3 mcg [2.25 mcg] formoterol, use double number of puffs

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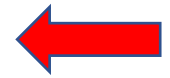

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	12–17 ≥18	Budesonide-formoterol DPI	200/6	160/4.5	**2 inhalations twice daily**, PLUS 1 inhalation whenever needed
	≥18	BDP-formoterol pMDI	100/6	84.6/5.0	

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Reliever doses of ICS-formoterol - how much can be taken?

- For ICS-formoterol with 6 mcg (4.5 mcg delivered dose) of formoterol, take **1 inhalation** whenever needed for symptom relief
- Another inhalation can be taken after a few minutes if needed
- Maximum total number of inhalations in any single day (as-needed + maintenance)
  - **Budesonide-formoterol**: maximum 12 inhalations* for adults, 8 inhalations for children, based on extensive safety data *(Tattersfield et al, Lancet 2001; Pauwels et al, ERJ 2003)*
  - **Beclometasone-formoterol**: maximum total 8 inhalations in any day *(Papi et al, Lancet Respir Med 2013)*
- Emphasize that most patients need far fewer doses than this!

- For pMDIs containing 3 mcg formoterol (2.25 mcg delivered dose), take 2 inhalations each time

**For budesonide-formoterol 200/6 [delivered dose 160/4.5 mcg], 12 inhalations gives 72 mcg formoterol (54 mcg delivered dose)*

Practical advice for GINA Track 1

- At first, patients may be unsure whether ICS-formoterol will work as well as their previous SABA reliever
  - In the PRACTICAL study, 69% patients said ICS-formoterol worked as fast as, or faster than, their previous SABA *(Baggott et al, ERJ 2020)*
  - Suggest to the patient that they try out the new reliever at a convenient time
  - Emphasise that they should use the ICS-formoterol **instead of** their previous SABA, and that they should take an additional inhalation when they have more symptoms
- Advise patients to have two inhalers (if possible), 1 at home, 1 in bag/pocket
- Advise patients to rinse and spit out after maintenance doses, but this is not needed with reliever doses
  - No increased incidence of candidiasis in RCTs with this recommendation (n~40,000)
- Use an action plan customised to MART
  - The patient continues their usual maintenance ICS-formoterol inhalations, but takes more **as-needed** ICS-formoterol inhalations
  - Taking extra as-needed inhalations reduces the risk of progressing to a severe exacerbation needing oral corticosteroids *(Bousquet et al, Respir Med 2007; Buhl et al, Respir Res 2012; O'Byrne et al, Lancet Respir Med 2021)*
- Additional practical advice for MART *(Reddel et al, JACI in Practice 2022)*

Action plan for MART with ICS-formoterol

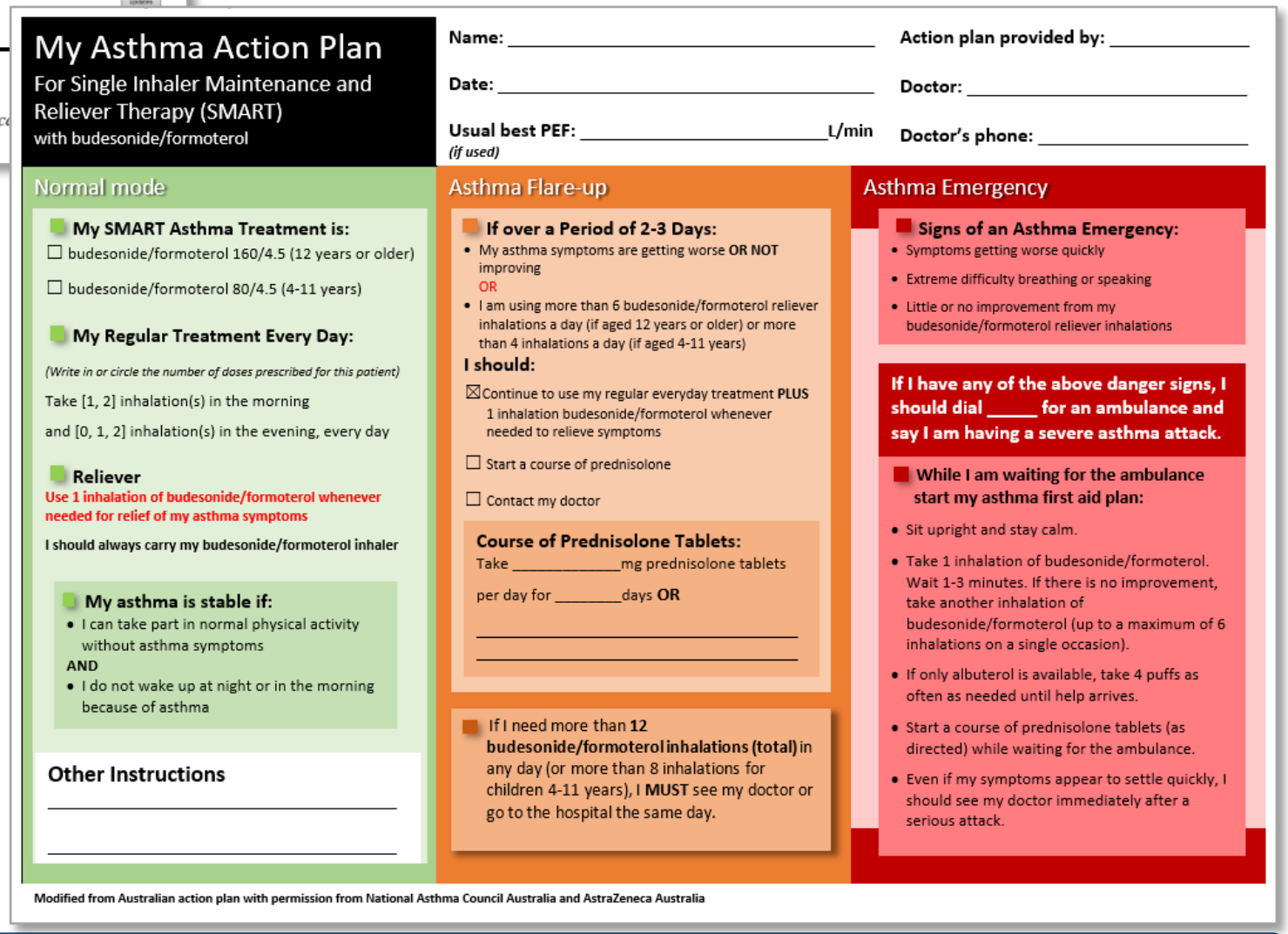
A Practical Guide to Implementing SMART in Asthma Management

Helen K. Reddel, MB, BS, PhD[a,*], Eric D. Bateman, MB, ChB, MD[b,*], Michael Schatz, MD, MS[c], Jerry A. Krishnan, MD, PhD[d], and Michelle M. Cloutier, MD[e] *Sydney, Australia; Cape Town, South Africa; Chicago, Ill; and Farmington, Conn*

Reddel et al, JACI in Practice 2022; 10: S31-s38

This article includes a writable action plan template
That can be modified for other combination ICS-formoterol inhalers, and for as-needed-only ICS-formoterol

For additional action plans with ICS-formoterol reliever, see National Asthma Council Australia Action plan library
www.nationalasthma.org.au/health-professionals/asthma-action-plans



My Asthma Action Plan

For Single Inhaler Maintenance and Reliever Therapy (SMART)
with budesonide/formoterol

Name: _____ Action plan provided by: _____

Date: _____ Doctor: _____

Usual best PEF: _____ L/min *(if used)* Doctor's phone: _____

Normal mode

My SMART Asthma Treatment is:

☐ budesonide/formoterol 160/4.5 (12 years or older)

☐ budesonide/formoterol 80/4.5 (4-11 years)

My Regular Treatment Every Day:

(Write in or circle the number of doses prescribed for this patient)

Take [1, 2] inhalation(s) in the morning

and [0, 1, 2] inhalation(s) in the evening, every day

Reliever

Use 1 inhalation of budesonide/formoterol whenever needed for relief of my asthma symptoms

I should always carry my budesonide/formoterol inhaler

My asthma is stable if:

- I can take part in normal physical activity without asthma symptoms

AND

- I do not wake up at night or in the morning because of asthma

Other Instructions

_____

_____

Asthma Flare-up

If over a Period of 2-3 Days:

- My asthma symptoms are getting worse **OR NOT** improving

OR

- I am using more than 6 budesonide/formoterol reliever inhalations a day (if aged 12 years or older) or more than 4 inhalations a day (if aged 4-11 years)

I should:

☒ Continue to use my regular everyday treatment **PLUS** 1 inhalation budesonide/formoterol whenever needed to relieve symptoms

☐ Start a course of prednisolone

☐ Contact my doctor

Course of Prednisolone Tablets:

Take _____mg prednisolone tablets

per day for _____days **OR**

_____

_____

If I need more than **12 budesonide/formoterol inhalations (total)** in any day (or more than 8 inhalations for children 4-11 years), I **MUST** see my doctor or go to the hospital the same day.

Asthma Emergency

Signs of an Asthma Emergency:

- Symptoms getting worse quickly
- Extreme difficulty breathing or speaking
- Little or no improvement from my budesonide/formoterol reliever inhalations

If I have any of the above danger signs, I should dial _____ for an ambulance and say I am having a severe asthma attack.

While I am waiting for the ambulance start my asthma first aid plan:

- Sit upright and stay calm.
- Take 1 inhalation of budesonide/formoterol. Wait 1-3 minutes. If there is no improvement, take another inhalation of budesonide/formoterol (up to a maximum of 6 inhalations on a single occasion).
- If only albuterol is available, take 4 puffs as often as needed until help arrives.
- Start a course of prednisolone tablets (as directed) while waiting for the ambulance.
- Even if my symptoms appear to settle quickly, I should see my doctor immediately after a serious attack.

Modified from Australian action plan with permission from National Asthma Council Australia and AstraZeneca Australia

Supplement to Reddel et al, JACI in Practice 2022; 10: S31-s38

This template can be modified for other ICS-formoterol combinations or for as-needed-only ICS-formoterol.
The action plan on which it is based has been widely used in Australia and other countries since 2007.

My Asthma Action Plan

For Single Inhaler Maintenance and Reliever Therapy (SMART)
with budesonide/formoterol

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Date: _____ **Doctor:** _____

Usual best PEF: _____ L/min *(if used)* **Doctor's phone:** _____

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_____

_____

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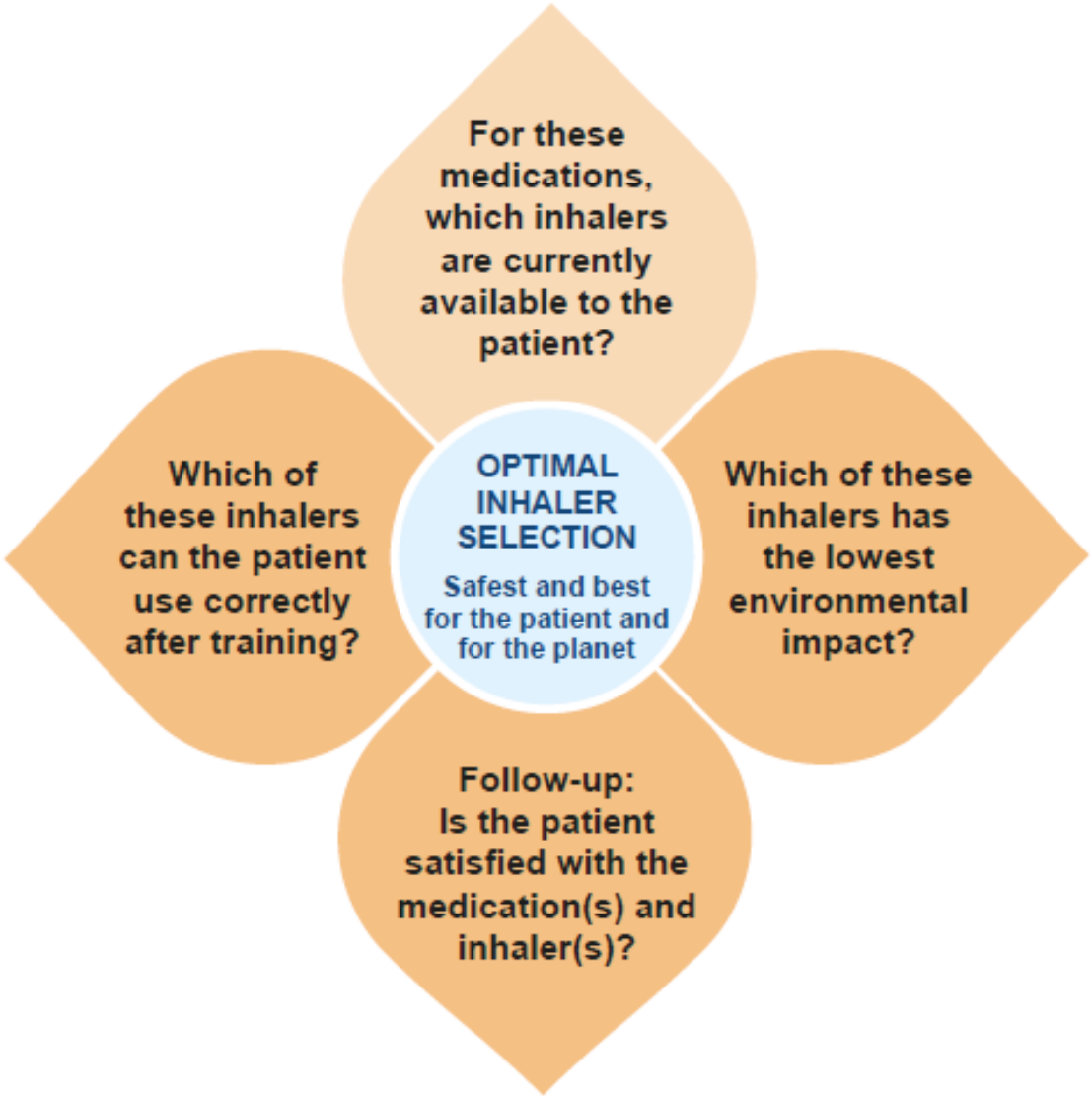
- If only albuterol is available, take 4 puffs as often as needed until help arrives.
- Start a course of prednisolone tablets (as directed) while waiting for the ambulance.
- Even if my symptoms appear to settle quickly, I should see my doctor immediately after a serious attack.

Inhaler choice and environmental considerations

- Inhaled corticosteroids markedly reduce the risk of asthma exacerbations and death
  - But limited availability and access in low and middle income countries
- Many inhaler types available, with different techniques
- Some inhalers are not suitable for some patients. For example:
  - DPIs are not suitable for children ≤5 years and some elderly
  - pMDIs difficult for patients with arthritis or weak muscles
  - Capsule devices are difficult for patients with tremor
- Most patients don't use their inhaler correctly
  - More than one inhaler → more errors
- Incorrect technique → more symptoms → worse adherence → more exacerbations → higher environmental impact
- Propellants in current pMDIs have 25x global warming potential compared with dry powder inhalers
  - New propellants are being developed but not yet approved
- Choice of inhaler is important!

For this patient, which is the right class of medication?



Inhaler choice and environmental considerations

- First, what is the right medication for this patient?
  - Control symptoms and reduce exacerbations
  - Urgent healthcare and hospitalization have a heavy environmental burden
- Which inhaler(s) can the patient access for this medication?
  - Low/middle income countries often have limited choice and access
  - Cost of inhalers is a major burden
- Which of these inhalers can the patient use correctly?
  - Incorrect technique → more exacerbations
- What are the environmental implications of these inhaler(s)?
  - Manufacture
  - Propellant (for pMDIs)
  - Recycling potential
- Is the patient satisfied with the treatment and the inhaler?
  - Consider the patient's environmental priorities
  - Avoid 'green guilt', which may contribute to poor adherence
  - Check inhaler technique frequently

Difficult-to-treat and severe asthma

- Changes in GINA 2023
  - Double-blind study of withdrawal of mepolizumab in adults with severe eosinophilic asthma found more exacerbations in those who ceased mepolizumab than those who continued treatment *(Moore et al, ERJ 2022)*
  - Mepolizumab (anti-IL5) added as a Step 5 option for children 6–11 years with severe eosinophilic asthma *(Jackson et al, Lancet 2022)*
- Regardless of regulatory approvals, GINA recommends biologic therapy for asthma **only** if asthma is severe, and **only** if treatment has been optimized
- Head-to-head studies are needed
- Non-asthma indications for biologic therapy are mentioned only if the condition is relevant to asthma management, or if it is commonly associated with asthma
- Severe asthma guide published mid-2023 in large format

Other changes

- Pulse oximetry: FDA safety communication
  - Potential overestimation of oxygen saturation in people with dark skin color
- Risk of drug interactions between salmeterol or vilanterol and ritonavir-boosted nirmatrelvir (NMV/r)
  - Risk of cardiovascular adverse effects *(Carr et al, JACI 2023; 151: 809-817)*
  - Drug interaction websites recommend cessation of the LABA for duration of treatment, without warning about risks
  - Options (if available): prescribe alternative antiviral therapy, or switch to ICS or ICS-formoterol for duration of therapy plus 5 days. Remember to teach correct technique if prescribing a new inhaler
  - (ICS effects unlikely given short duration of treatment)
- FeNO-guided treatment: well-conducted multinational study in children found no reduction in exacerbations *(Turner et al, Lancet Respir Med 2022)*. Update of Cochrane reviews awaited
- Updated advice about describing asthma severity
  - Consider using the term ‘apparently mild asthma’ in health professional education: patients with apparently mild asthma can still have severe or fatal asthma exacerbations
- See GINA report for full list of changes

Global priorities for asthma management

Improving lung health in low-income and middle-income countries: from challenges to solutions

Jamilah Meghji*, Kevin Mortimer*, Alvar Agusti, Brian W Allwood, Innes Asher, Eric D Bateman, Karen Bissell, Charlotte E Bolton, Andrew Bush, Bartolome Celli, Chen-Yuan Chiang, Alvaro A Cruz, Anh-Tuan Dinh-Xuan, Asma El Sony, Kwun M Fong, Paula I Fujiwara, Mina Gaga, Luis Garcia-Marcos, David M G Halpin, John R Hurst, Shamanthi Jayasooriya, Ajay Kumar, Maria V Lopez-Varela, Refiloe Masekela, Bertrand H Mbatchou Ngahane, Maria Montes de Oca, Neil Pearce, Helen K Reddel, Sundeep Salvi, Sally J Singh, Cherian Varghese, Claus F Vogelmeier, Paul Walker, Heather J Zar, Guy B Marks

Lancet 2021

J Pan Afr Thorac Soc 2022

The reality of managing asthma in sub-Saharan Africa – Priorities and strategies for improving care

Kevin Mortimer[1], Refiloe Masekela[2], Obianuju B Ozoh[3], Eric Donn Bateman[4], Rebecca Nantanda[5], Arzu A. Yorgancıoğlu[6], Jeremiah Chakaya[7], Helen K. Reddel[8]

Asthma management in low and middle income countries: case for change

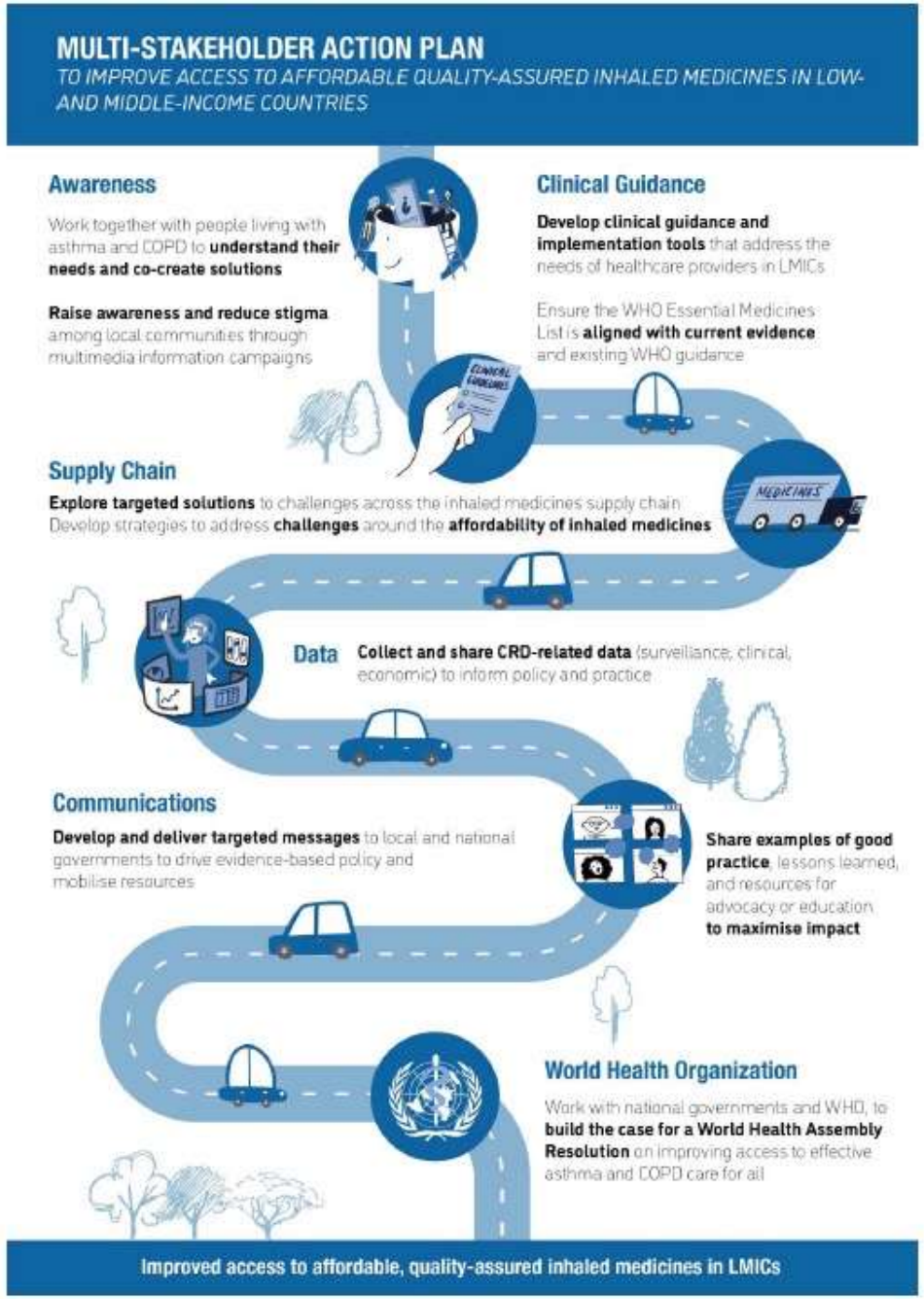
Kevin Mortimer[1,2], Helen K. Reddel[3], Paulo M. Pitrez[4] and Eric D. Bateman[5]

ERJ 2022

Int J Tuberc Lung Dis 2022

Improving access to affordable quality-assured inhaled medicines in low- and middle-income countries

M. Stolbrink,[1,2] M. J. Chinouya,[3] S. Jayasooriya,[4] R. Nightingale,[1,5] L. Evans-Hill,[6] K. Allan,[7] H. Allen,[8] J. Balen,[9] T. Beacon,[10] K. Bissell,[11] J. Chakaya,[1,12] C-Y. Chiang,[13,14,15] M. Cohen,[16] G. Devereux,[1] A. El Sony,[17] D. M. G. Halpin,[18] J. R. Hurst,[19] C. Kiprop,[5] A. Lawson,[20] C. Macé,[13] A. Makhanu,[5] P. Makokha,[5] R. Masekela,[21] H. Meme,[22] E. M. Khoo,[23,24] R. Nantanda,[25] S. Pasternak,[26] C. Perrin,[13] H. Reddel,[27,28] S. Rylance,[29] P. Schweikert,[20] C. Were,[26] S. Williams,[24] T. Winders,[30] A. Yorgancioglu,[31,32] G. B. Marks,[13,33] K. Mortimer[13,34]



Biologics - Omaluzimab

- Injectable
- Inhibits the binding of IgE to mast cells and basophils which reduces the release of mediators for these cells which create the allergic response
- Now labeled for chronic urticaria as well as nasal polyposis
- Has box warning for late anaphylaxis
- Requires star tin office with recommended wait period of 2 hours
- Has some association with cardiac events and cancer

Biologics - Omaluzimab

Now can be prescribed for self-injection (thank you COVID)

Biologics - Dupilumab

- Injectable
- Inhibits IL-4 and IL-13 (proinflammatory cytokines)
- Limited immunosuppression
- Labeled initially for atopic dermatitis, now has indications for nasal polyposis and asthma
- It is associated with keratitis and conjunctivitis as a known side effect
- Recommend avoidance of live vaccines
- Also can be self-injected

Biologics - Benralizumab

- Injectable
- Binds to IL-5 of basophils and eosinophils resulting in destruction of those cells
- Initially dosed with every 4 weeks x 3, then dosed every 8 weeks
- Can also be self-administered
- NOT labeled for nasal polyposis

Biologics - Mepolizumab

- Injectable
- Inhibits IL-5 and decreases eosinophilic inflammation however complete mechanism of action not understood
- Also labeled for nasal polyposis
- Fixed dosing (independent of weight)
- Dosed every 4 weeks with no loading dose

Questions for CME…..

Question #1

- Which one of the following biologic medications has a box warning for late anaphylaxis?

1. Mepolizumab
2. Benralizumab
3. Omalizumab
4. Dupilimab

Question #1

- Which one of the following biologic medications has a box warning for late anaphylaxis?

1. Mepolizumab
2. Benralizumab
3. **Omalizumab**
4. Dupilumab

Question #2

- Which one of the following biologic medications is associated with conjunctivitis and keratitis as known side effects?

1. Dupilumab
2. Mepolizumab
3. Benralizumab
4. Omalizumab

Question #2

- Which one of the following biologic medications is associated with conjunctivitis and keratitis as known side effects?

1. Dupilumab
2. Mepolizumab
3. Benralizumab
4. Omalizumab

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- Which one of the following biologic medications is associated with conjunctivitis and keratitis as known side effects?

1. **Dupilumab**
2. Mepolizumab
3. Benralizumab
4. Omalizumab

Question # 3

- All of the following biologic medications have approved indications for nasal polyposis EXCEPT:

1. Dupilumab
2. Mepolizumab
3. Benralizumab
4. Omalizumab

Question # 3

- All of the following biologic medications have approved indications for nasal polyposis EXCEPT:

1. Dupilumab
2. Mepolizumab
3. **Benralizumab**
4. Omalizumab

Question # 4

- True or False

- The updated GINA 2023 Guidelines now allow for ICS-SABA as both a maintenance as well as a reliever medication?

Question # 4

- True or False

- The updated GINA 2023 Guidelines now allow for ICS-SABA as both a maintenance as well as a reliever medication?

- **TRUE!**

Question # 5

- True or False

- According to GINA guidance and recommendations, patient should be instructed to rinse their mouths after use of an ICS-SABA inhaler?

Question # 5

- True or False

- According to GINA guidance and recommendations, patient should be instructed to rinse their mouths after use of an ICS-SABA inhaler?

- **True, when used as a daily medication, False when used as a reliever medication**

References

- Selected references are included on the individual slides in today's presentation, however, a complete list of references (over 800) for the updated GINA 2023 guidelines is available for download at www.ginasthma.org


QUESTIONS


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Thank you!