What's new in GINA 2024?

GINA 2024 update published 22 May 2024

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GINA Global Strategy for Asthma Management and Prevention

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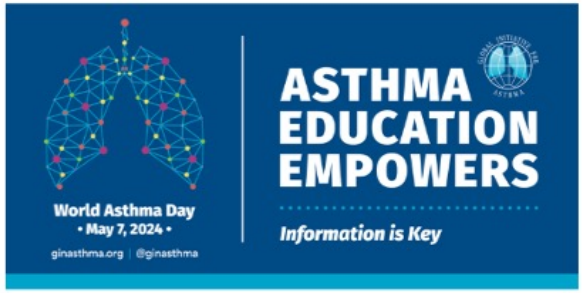
The Global Initiative for Asthma (GINA)

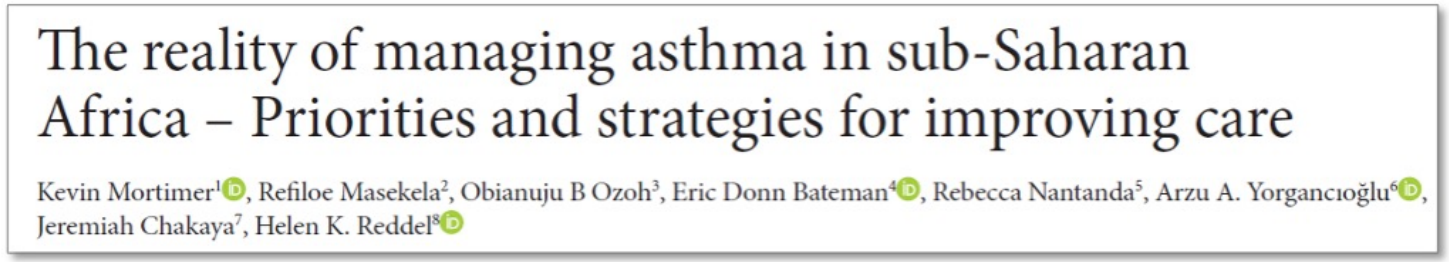
- The GINA Strategy Report is a global evidence-based strategy that can be adapted for local health systems and medicine availability
  - GINA 2024 report is available from www.ginasthma.org/reports
- The GINA Report is updated every year
  - Twice-yearly cumulative review and systematic evaluation of new evidence about asthma
  - Evidence integrated across the whole asthma strategy, not isolated PICOT questions
  - Careful attention to study design, populations, and clinical relevance
  - Extensive external review
  - Practical focus: not just 'what', but 'why' and 'how'
- Widely used
  - Downloaded from >200 countries
  - 2023 report downloaded >500,000 times
- GINA 2024 report was launched on World Asthma Day, May 7, 2024
  - See section on "What's new in GINA 2024?" for more details
  - Update published on 22 May, as we became aware that some medication doses in Box 4-8 were being misread



Diagnosis of asthma

- Over-diagnosis and under-diagnosis of asthma are common
- Respiratory symptoms are often non-specific
  - Multiple differential diagnoses for dyspnea and cough
- Globally, most clinicians do not have (timely) access to (quality) spirometry
  - Including in high-income countries
- Peak expiratory flow (PEF) is less reliable than spirometry, but better than nothing
  - PEF meters included in WHO-PEN Package of Essential Noncommunicable disease interventions

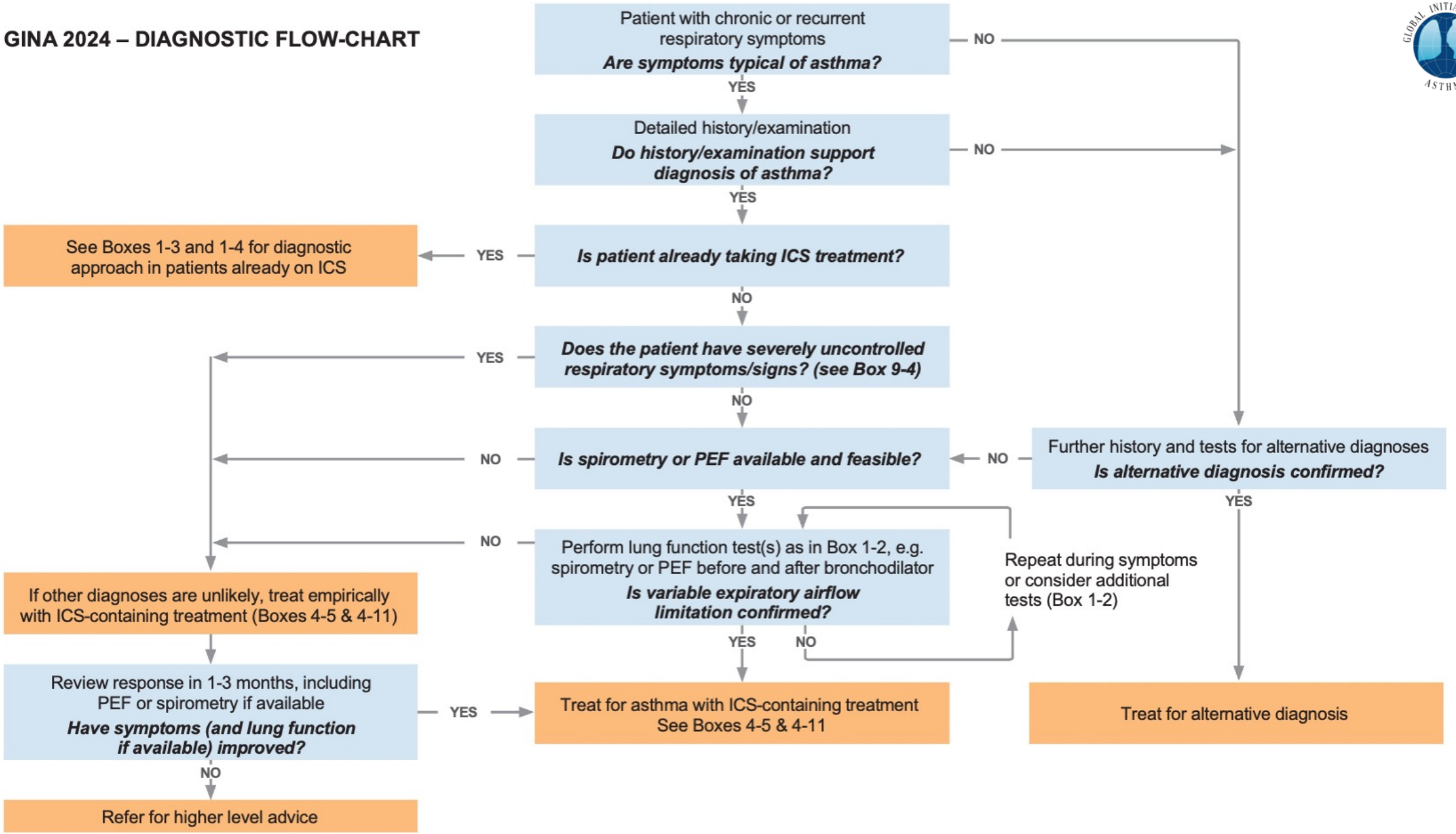
→ Use PEF if spirometry not available, while we continue to advocate for better diagnostic tools


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]

Mortimer et al, JPATS 2022

GINA 2024 – DIAGNOSTIC FLOW-CHART



Bronchodilator (BD) responsiveness

- **Untreated asthma:** patients obtain quick symptomatic relief with rapid-onset BD
  - Reflected in an increase in FEV_1 and PEF (and sometimes FVC) within 10-15 minutes
- **Random BD testing** has very limited utility, especially if long after disease onset *(Beasley et al, AJRCCM 2024)*
  - Asthma is variable: symptoms (and bronchoconstriction) not present all the time
  - ICS-containing treatment → increased pre-bronchodilator FEV_1 → decreased BD responsiveness
  - Longer asthma duration → some patients develop persistent airflow limitation → decreased BD responsiveness
  - Some patients with a diagnosis of COPD (with/without asthma) have significant BD responsiveness
- **Current ERS/ATS criterion for BD responsiveness in clinical practice** is an increase in FEV_1 or FVC from baseline by ≥12% and ≥200 mL of the **baseline** value
  - Used as one of gold standards in 2022 ERS Guidelines on Diagnosis of Asthma *(Louis et al, ERJ 2022)*
- **ERS/ATS Technical Standards Committee** proposed changing this criterion to an increase in FEV_1 or FVC from baseline by >10% of the **predicted** value *(Stanojevic et al, ERJ 2021)*
  - Based on data for mortality; not compared with other diagnostic tests for asthma
  - The Technical Committee did not advocate adoption of this change for clinical practice
- GINA will review this again when more data are available; no change recommended in the meantime

Asthma is often inappropriately treated as a recurrent acute disease, with no treatment in between

- Burden to patients, family, health system, economy
- Risk of asthma mortality
- Cumulative risk of adverse effects of oral corticosteroids, with even 4–5 lifetime courses *(Price, 2018)*
- Asthma morbidity and mortality are largely preventable

GINA goal of asthma management

The goal is to achieve the **best possible long-term asthma outcomes** for each patient:

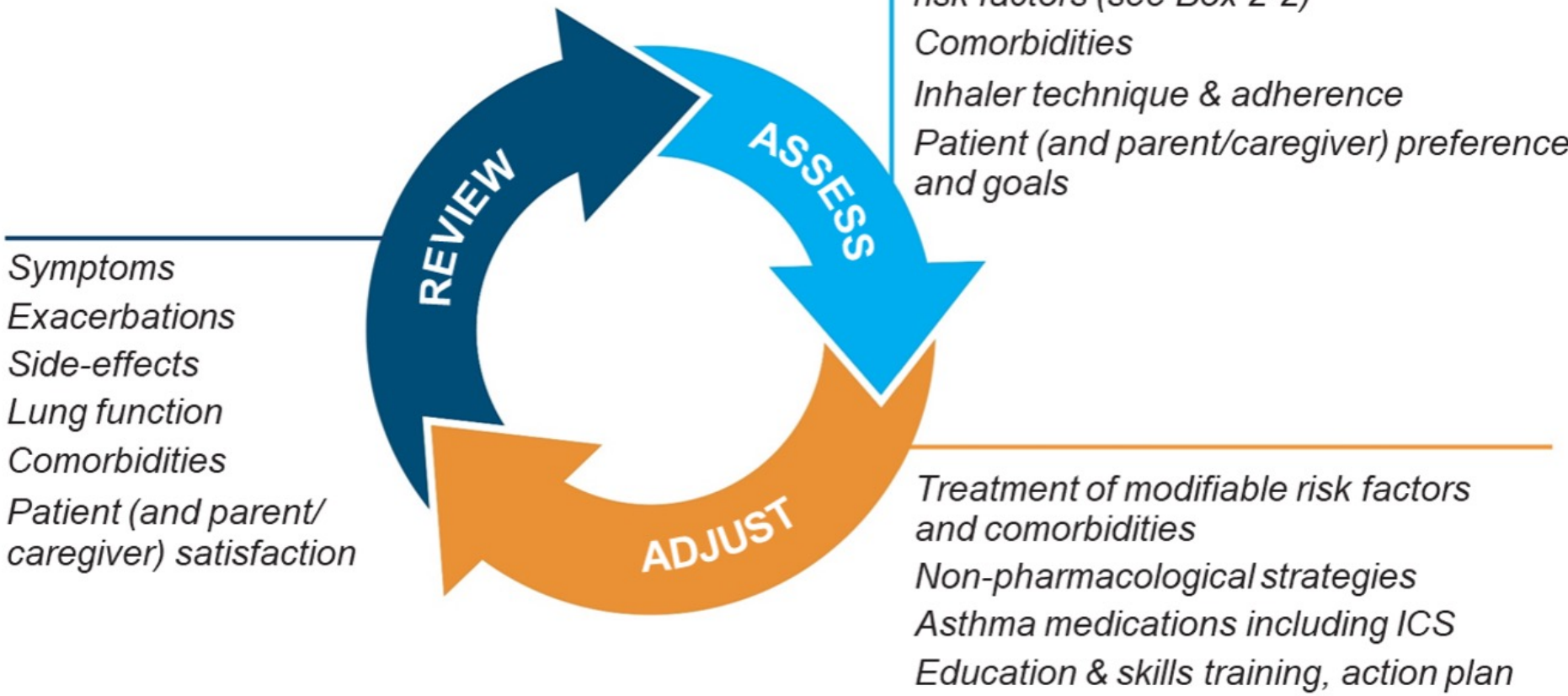
- Long-term symptom control, which may include:
  - Few/no asthma symptoms, quickly relieved
  - No sleep disturbance
  - Unimpaired physical activity
- Long-term asthma risk minimization, which may include:
  - No exacerbations
  - Improved or stable personal best lung function
  - No requirement for maintenance oral corticosteroids
  - No medication side-effects

When discussing best possible long-term outcomes with a patient, consider:

- Their asthma phenotype
- Clinical features
- Multimorbidity
- Risk factors (e.g. poor adherence, smoking, persistent airflow limitation)
- Availability, cost and adverse effects of medications
- The patient's goals (these may be different from medical goals)

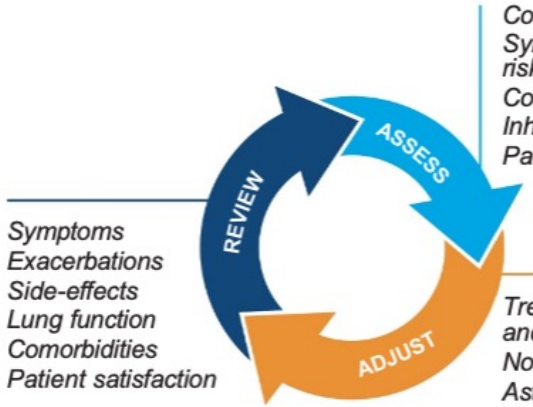
- Assessing symptom control is not enough! Patients with few asthma symptoms can still have severe or fatal exacerbations related to individual risk factors or external triggers (viruses, allergen, pollution)
- Encourage referral for expert advice for patients with difficult-to-treat or severe asthma

Asthma treatment is not ‘set and forget’, and not just medications



GINA 2024 – 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 including ICS (as below)
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

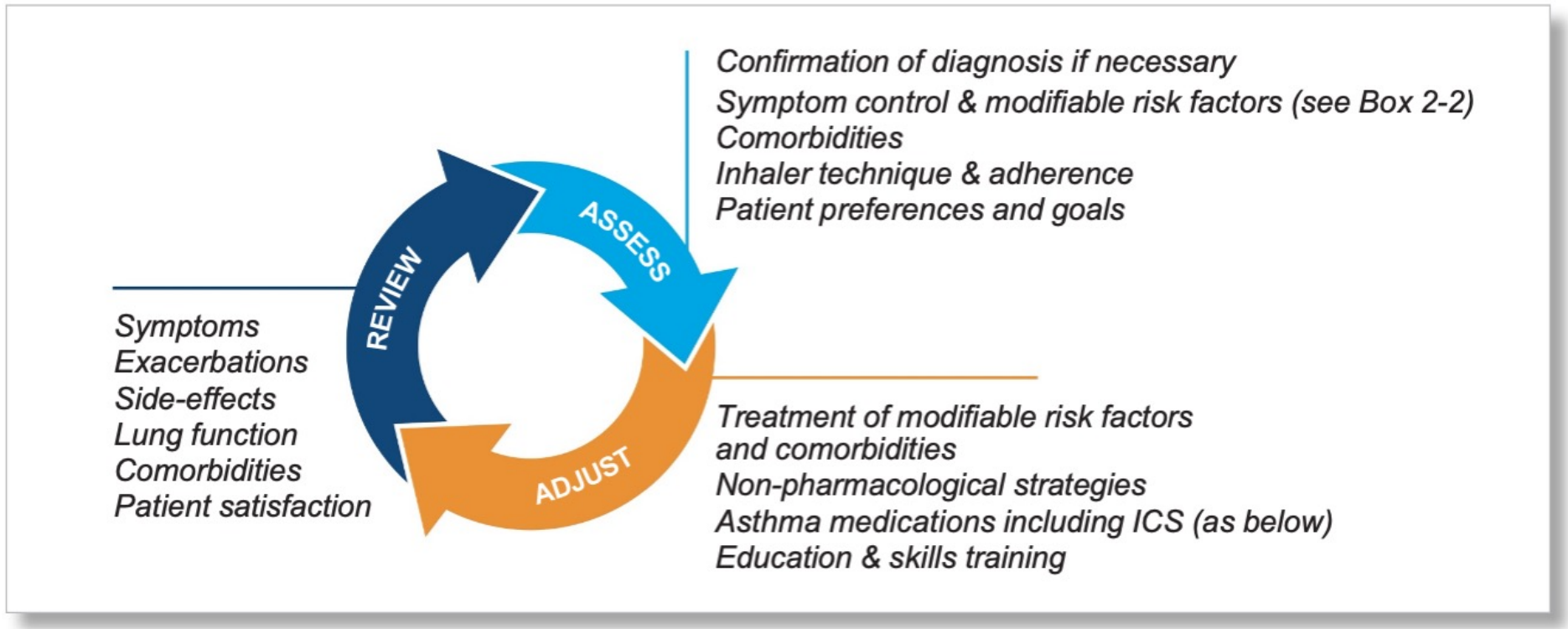
RELIEVER: As-needed ICS-SABA*, or as-needed SABA

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

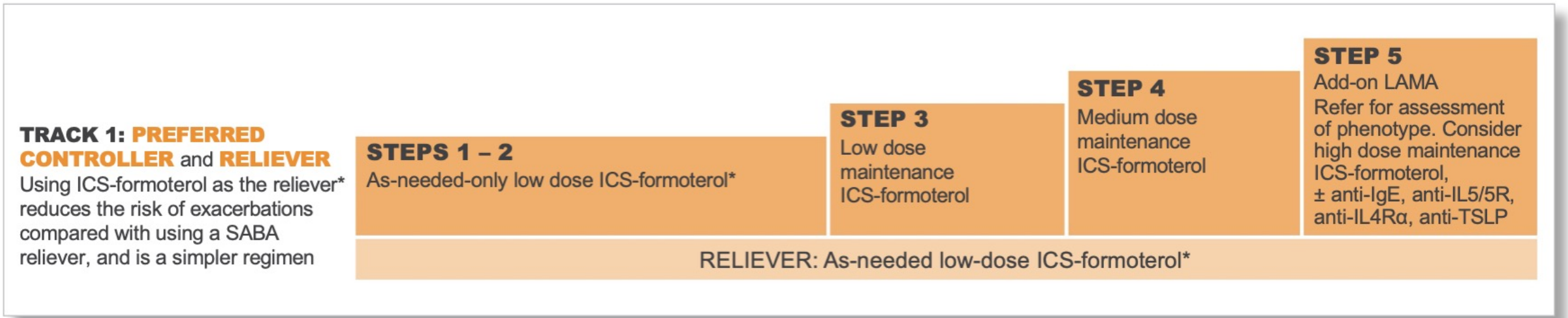
Low dose ICS whenever SABA taken, or daily LTRA†, or add HDM SLIT*	*Medium dose ICS, or add LTRA†, or add HDM SLIT*	*Add LAMA or add LTRA† or add HDM SLIT, or switch to high dose ICS-only*	*Add azithromycin (adults) or add LTRA†. As last resort consider adding low dose OCS but consider side-effects*

*Anti-inflammatory reliever; †advise about risk of neuropsychiatric adverse effects

GINA 2024 Box 4-6

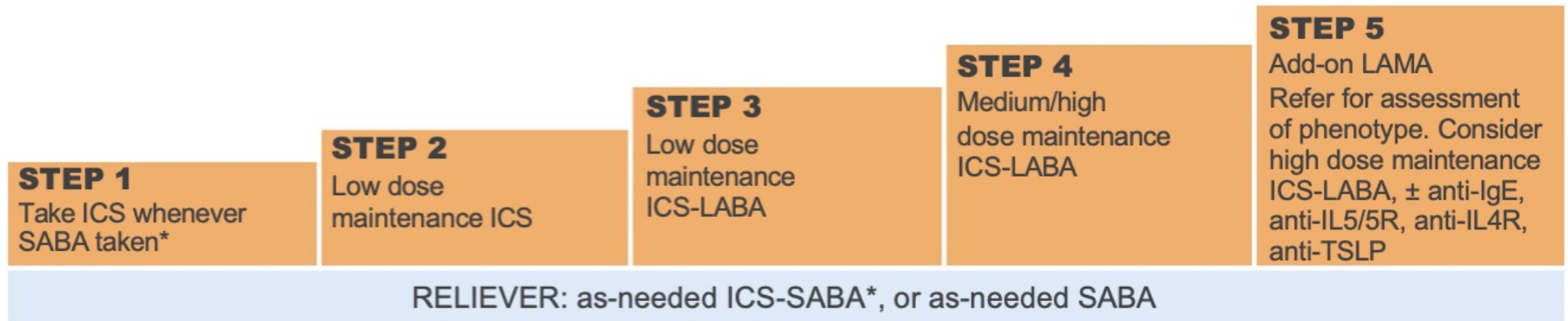


TRACK 1: PREFERRED CONTROLLER and RELIEVER
Using ICS-formoterol as the reliever* reduces the risk of exacerbations compared with using a SABA reliever, and is a simpler regimen



*Anti-inflammatory reliever

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



*Anti-inflammatory reliever

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-only, or add LTRA†, or add HDM SLIT*	*Add LAMA or add LTRA† or add HDM SLIT, or switch to high dose ICS-only*	*Add azithromycin (adults) or add LTRA†. As last resort consider adding low dose OCS but consider side-effects*

*Anti-inflammatory reliever; †advise about risk of neuropsychiatric adverse effects

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 FitzGerald[2], Eric D. Bateman[3], Leonard B. Bacharier[4], Allan Becker[5], Guy Brusselle[6], Roland Buhl[7], Alvaro A. Cruz[8], Louise Fleming[9], Hiromasa Inoue[10], Fanny Wai-san Ko[11], Jerry A. Krishnan[12], Mark L. Levy[13], Jiangtao Lin[14], Søren E. Pedersen[15], Aziz Sheikh[16], Arzu Yorgancioglu[17] and Louis-Philippe Boulet[18]

Why not treat with inhaled short-acting beta$_2$-agonists (SABA) alone?

- SABA treats the symptoms, but not the disease
- People with apparently mild asthma can have severe or fatal exacerbations *(Dusser, 2007)*
  - Up to 27% asthma deaths are in patients with occasional symptoms *(Bergstrom, 2008)*
  - Exacerbation triggers are unpredictable (viral, allergen, pollution, stress)
  - Even 4–5 **lifetime** OCS courses increase the cumulative risk of adverse events including osteoporosis, diabetes, cataract, heart failure, pneumonia *(Price et al, J Asthma Allerg 2018)*
- **Regular** use of SABA, even for 1–2 weeks, is associated with increased AHR, reduced bronchodilator effect, increased allergic response, increased eosinophils *(e.g. Cockcroft 2006)*
  - Can lead to a vicious cycle encouraging overuse
  - Over-use of SABA is associated with ↑ exacerbations and ↑ mortality *(e.g. Suissa 1994, Nwaru 2020)*
- Starting treatment with SABA **trains** the patient to regard it as their primary asthma treatment
  - Poor adherence with ICS is almost inevitable
- There is strong evidence for a more effective and safer alternative than SABA alone, or ICS plus as-needed SABA: **as-needed ICS-formoterol**

The blue one's good because you can just have a couple of squirts and get back to what you were doing

Cole et al, BMJ Open 2013

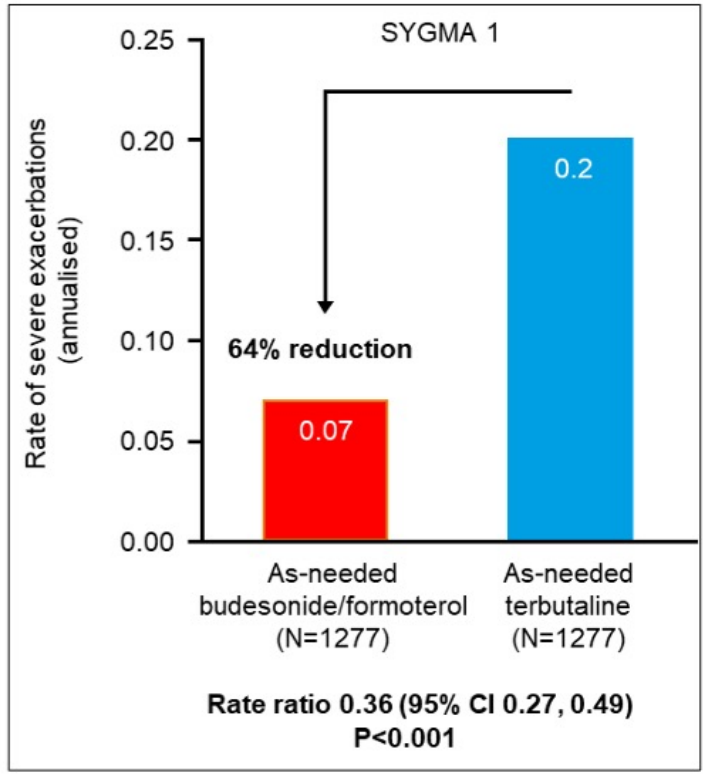
As-needed low-dose ICS-formoterol* in mild asthma (n=9,565)

COMPARED WITH AS-NEEDED SABA

- Risk of severe exacerbations reduced by 60–64% (SYGMA 1, Novel START)

COMPARED WITH MAINTENANCE LOW DOSE ICS plus as-needed SABA

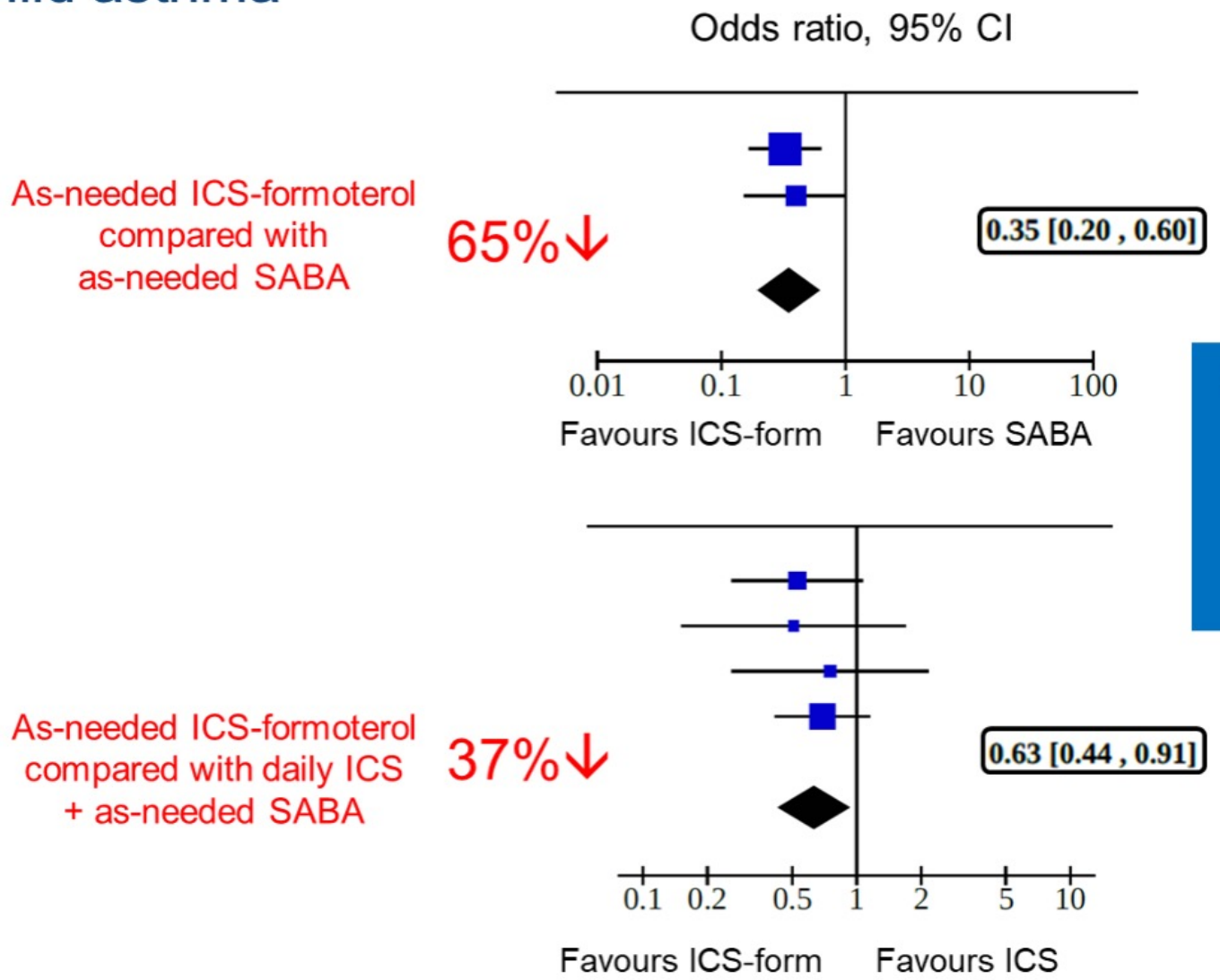
- Risk of severe exacerbations similar (SYGMA 1 & 2), or lower (Novel START, PRACTICAL)
- No clinically important differences in symptom control or FEV_1 (all 4 studies) or in FeNO (Novel START, PRACTICAL), and no worsening in these outcomes over 12 months
- Patients used the as-needed inhaler on ~30% of days: very low ICS dose
- Outcomes for severe exacerbations and ACQ-5 were independent of baseline characteristics including blood eosinophils, FeNO, lung function, history of exacerbations (Novel START, PRACTICAL)
- Embedded qualitative research demonstrated most patients preferred as-needed combination treatment over regular daily treatment *(Baggott 2020 & 2022; Foster 2020 & 2022)*



O'Byrne et al, NEJM 2018

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

As-needed-only ICS-formoterol reduces emergency visits and hospitalisations in patients with mild asthma



Approved by regulators in ~50 countries
Recommended in asthma guidelines of ~32 countries

From Crossingham et al, Cochrane Database Syst Rev 2021 (n=9565)

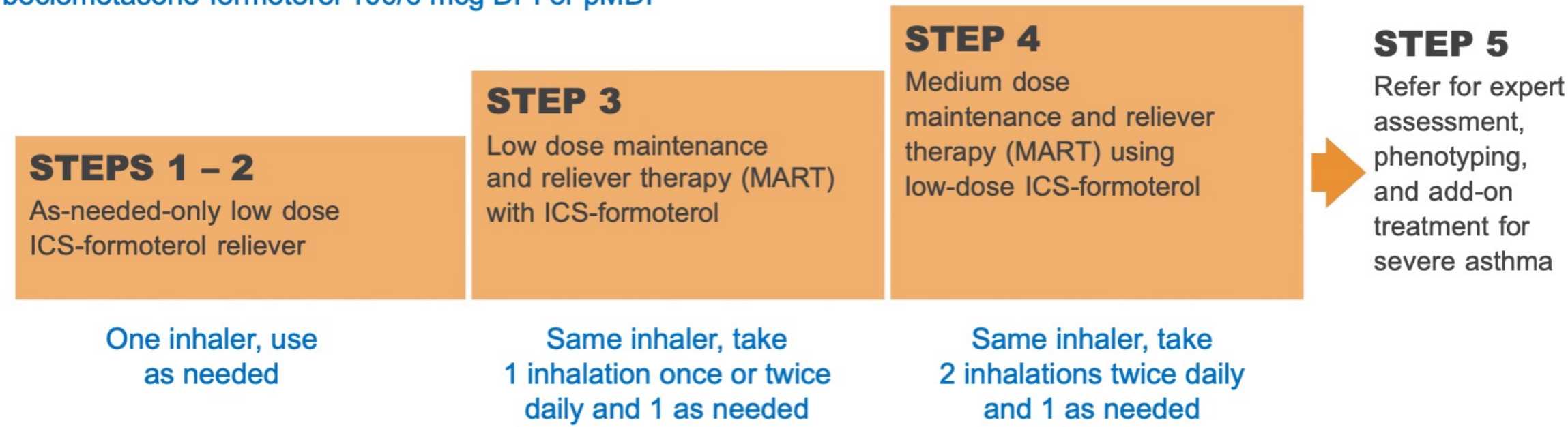
GINA Track 1, Steps 3–5: Maintenance and reliever therapy (MART) with low-dose ICS-formoterol

- MART with ICS-formoterol reduces the risk of severe exacerbations requiring oral corticosteroids, compared with other regimens plus SABA reliever, with similar symptom control
  - 32% reduction compared with same dose ICS-LABA *(Sobieraj, JAMA 2018)*
  - 23% reduction compared with higher dose ICS-LABA *(Sobieraj, JAMA 2018)*
  - 17% reduction compared with conventional best practice *(Cates et al, Cochrane 2013)*
- Not just an anti-inflammatory effect
  - Formoterol as reliever reduces risk of severe exacerbations compared with SABA reliever, but greater reduction if the reliever is ICS-formoterol *(Rabe, Lancet 2006)*
- MART is more effective than ICS-LABA plus SABA reliever in both eosinophilic and non-eosinophilic asthma
  - Benefit of MART further increased with higher blood eosinophils *(Brusselle et al, ERJ 2021)*
- MART is approved in ~120 countries

TRACK 1, Steps 1–4: PREFERRED CONTROLLER and RELIEVER for adults and adolescents.

Using ICS-formoterol as an anti-inflammatory reliever (AIR), with or without maintenance ICS-formoterol, reduces the risk of exacerbations compared with using a SABA reliever, and is a simpler regimen, with a single medication across treatment steps.

For budesonide-formoterol 200/6 mcg [160/4.5] DPI or pMDI*, or beclometasone-formoterol 100/6 mcg DPI or pMDI



*In some countries, a budesonide-formoterol pMDI with 100/3 [80/2.25] mcg per actuation is available for AIR-only or MART. For this pMDI, the recommended number of inhalations is double those shown above above.

Which formulations and doses of ICS-formoterol can be used as anti-inflammatory relievers in AIR-only or MART?

- **Budesonide-formoterol**
  - Adults and adolescents: 200/6 mcg metered dose [160/4.5 delivered dose] by DPI or pMDI, 1 inhalation per dose*
  - Children 6–11 years: 100/6 mcg metered dose [80/4.5 delivered dose] by DPI or pMDI, 1 inhalation per dose*
- **Beclometasone-formoterol**
  - Adults: 100/6 mcg metered dose by DPI or pMDI, 1 inhalation per dose; no data in adolescents or children to date
- Use of higher or lower dose formulations than these is **not** recommended*
- The maximum total dose of formoterol **in any one day** (reliever plus maintenance doses, if used) with any formulation is 72 mcg [54 mcg delivered dose] for adults/adolescents, and 48 mcg [36 mcg delivered dose] for children 6–11 years
- ICS-formoterol is the only ICS-LABA that can be used as an anti-inflammatory reliever

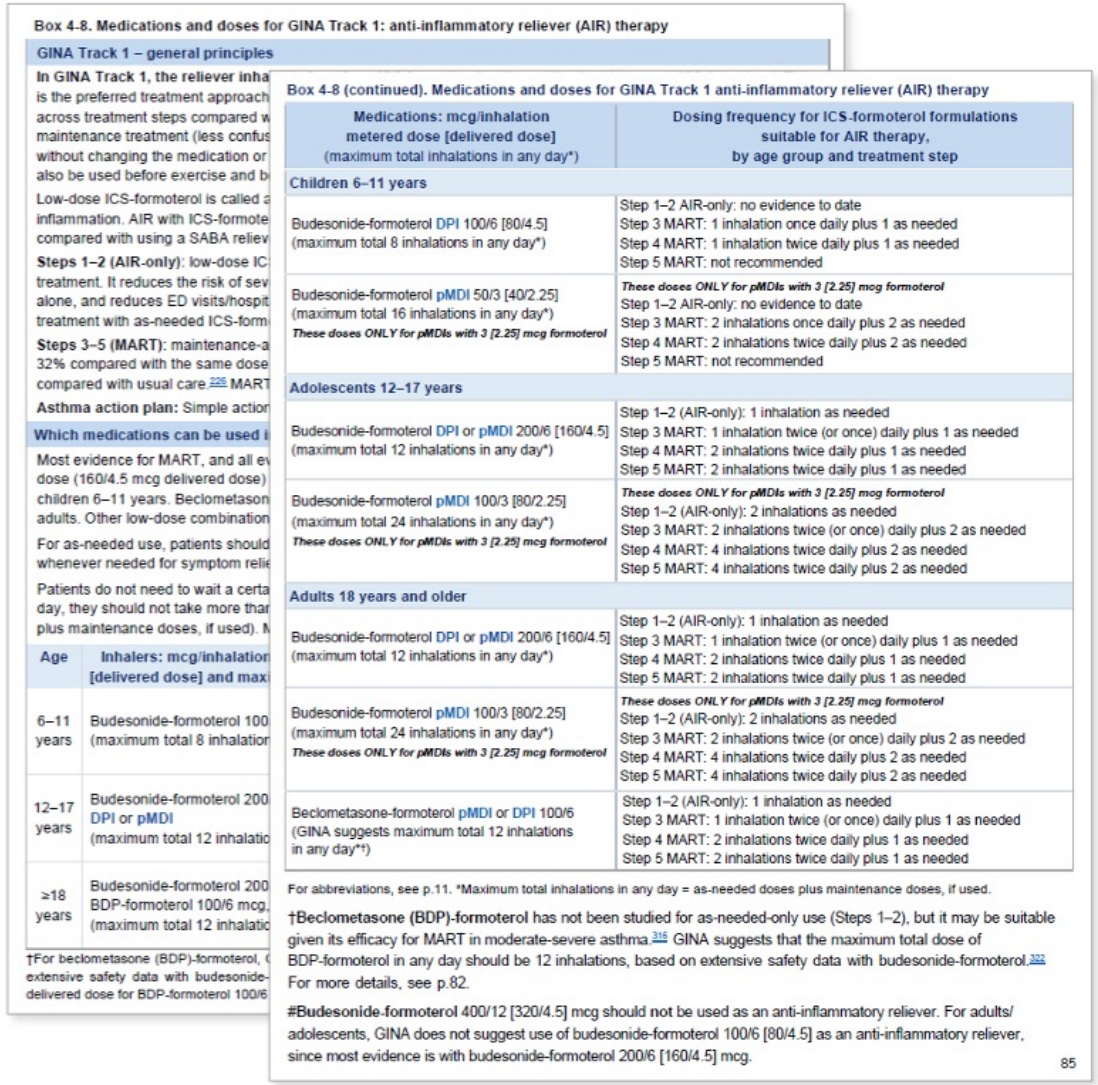
*In some countries, a budesonide-formoterol pMDI with 100/3 [80/2.25] mcg per actuation is available for adults and adolescents, and a pMDI with 50/3 mcg [40/2.25] per actuation is available for children. For these pMDIs, the recommended number of inhalations is double that for the formulations above.

AIR: anti-inflammatory reliever; BDP: beclometasone dipropionate; DPI: dry powder inhaler; MART: maintenance and reliever therapy with ICS-formoterol; pMDI: pressurized metered dose inhaler

GINA Track 1: medications & doses for anti-inflammatory reliever therapy

- Evidence to date is with budesonide-formoterol and beclometasone (BDP)-formoterol
- For patients ≥12 yrs: maximum total in any one day is 12 inhalations of budesonide-formoterol 200/6 [160/4.5] mcg
  - Extensive safety data to maximum total of 72 mcg formoterol metered dose [54 mcg delivered dose]
  - GINA suggests the same maximum total dose can be used with BDP-formoterol
- **Very few patients ever need this much!**

- See **GINA 2024 Box 4-8** for more details about recommended formulations and doses
- Do not use ICS-formoterol as the reliever with other maintenance ICS-LABAs *(Reddel et al, JACI IP 2023)*



Box 4-8. Medications and doses for GINA Track 1: anti-inflammatory reliever (AIR) therapy

GINA Track 1 – general principles

In GINA Track 1, the reliever inha
is the preferred treatment approach
across treatment steps compared w
maintenance treatment (less confus
without changing the medication or
also be used before exercise and b

Low-dose ICS-formoterol is called a
inflammation. AIR with ICS-formote
compared with using a SABA reliev

Steps 1–2 (AIR-only): low-dose IC
treatment. It reduces the risk of sev
alone, and reduces ED visits/hospit
treatment with as-needed ICS-form

Steps 3–5 (MART): maintenance-a
32% compared with the same dose
compared with usual care.[226] MART

Asthma action plan: Simple actior

Which medications can be used i

Most evidence for MART, and all ev
dose (160/4.5 mcg delivered dose)
children 6–11 years. Beclometason
adults. Other low-dose combination

For as-needed use, patients should
whenever needed for symptom relie

Patients do not need to wait a certa
day, they should not take more thar
plus maintenance doses, if used). N

Age	Inhalers: mcg/inhalation [delivered dose] and maxi
6–11 years	Budesonide-formoterol 100 (maximum total 8 inhalation
12–17 years	Budesonide-formoterol 200 DPI or pMDI (maximum total 12 inhalatio
≥18 years	Budesonide-formoterol 200 BDP-formoterol 100/6 mcg, (maximum total 12 inhalatio

†For beclometasone (BDP)-formoterol, (extensive safety data with budesonide- delivered dose for BDP-formoterol 100/6

Box 4-8 (continued). Medications and doses for GINA Track 1 anti-inflammatory reliever (AIR) therapy

Medications: mcg/inhalation metered dose [delivered dose] (maximum total inhalations in any day*)	Dosing frequency for ICS-formoterol formulations suitable for AIR therapy, by age group and treatment step
Children 6–11 years	
Budesonide-formoterol DPI 100/6 [80/4.5] (maximum total 8 inhalations in any day*)	Step 1–2 AIR-only: no evidence to date Step 3 MART: 1 inhalation once daily plus 1 as needed Step 4 MART: 1 inhalation twice daily plus 1 as needed Step 5 MART: not recommended
Budesonide-formoterol pMDI 50/3 [40/2.25] (maximum total 16 inhalations in any day*) ***These doses ONLY for pMDIs with 3 [2.25] mcg formoterol***	***These doses ONLY for pMDIs with 3 [2.25] mcg formoterol*** Step 1–2 AIR-only: no evidence to date Step 3 MART: 2 inhalations once daily plus 2 as needed Step 4 MART: 2 inhalations twice daily plus 2 as needed Step 5 MART: not recommended
Adolescents 12–17 years	
Budesonide-formoterol DPI or pMDI 200/6 [160/4.5] (maximum total 12 inhalations in any day*)	Step 1–2 (AIR-only): 1 inhalation as needed Step 3 MART: 1 inhalation twice (or once) daily plus 1 as needed Step 4 MART: 2 inhalations twice daily plus 1 as needed Step 5 MART: 2 inhalations twice daily plus 1 as needed
Budesonide-formoterol pMDI 100/3 [80/2.25] (maximum total 24 inhalations in any day*) ***These doses ONLY for pMDIs with 3 [2.25] mcg formoterol***	***These doses ONLY for pMDIs with 3 [2.25] mcg formoterol*** Step 1–2 (AIR-only): 2 inhalations as needed Step 3 MART: 2 inhalations twice (or once) daily plus 2 as needed Step 4 MART: 4 inhalations twice daily plus 2 as needed Step 5 MART: 4 inhalations twice daily plus 2 as needed
Adults 18 years and older	
Budesonide-formoterol DPI or pMDI 200/6 [160/4.5] (maximum total 12 inhalations in any day*)	Step 1–2 (AIR-only): 1 inhalation as needed Step 3 MART: 1 inhalation twice (or once) daily plus 1 as needed Step 4 MART: 2 inhalations twice daily plus 1 as needed Step 5 MART: 2 inhalations twice daily plus 1 as needed
Budesonide-formoterol pMDI 100/3 [80/2.25] (maximum total 24 inhalations in any day*) ***These doses ONLY for pMDIs with 3 [2.25] mcg formoterol***	***These doses ONLY for pMDIs with 3 [2.25] mcg formoterol*** Step 1–2 (AIR-only): 2 inhalations as needed Step 3 MART: 2 inhalations twice (or once) daily plus 2 as needed Step 4 MART: 4 inhalations twice daily plus 2 as needed Step 5 MART: 4 inhalations twice daily plus 2 as needed
Beclometasone-formoterol pMDI or DPI 100/6 (GINA suggests maximum total 12 inhalations in any day*†)	Step 1–2 (AIR-only): 1 inhalation as needed Step 3 MART: 1 inhalation twice (or once) daily plus 1 as needed Step 4 MART: 2 inhalations twice daily plus 1 as needed Step 5 MART: 2 inhalations twice daily plus 1 as needed

For abbreviations, see p.11. *Maximum total inhalations in any day = as-needed doses plus maintenance doses, if used.

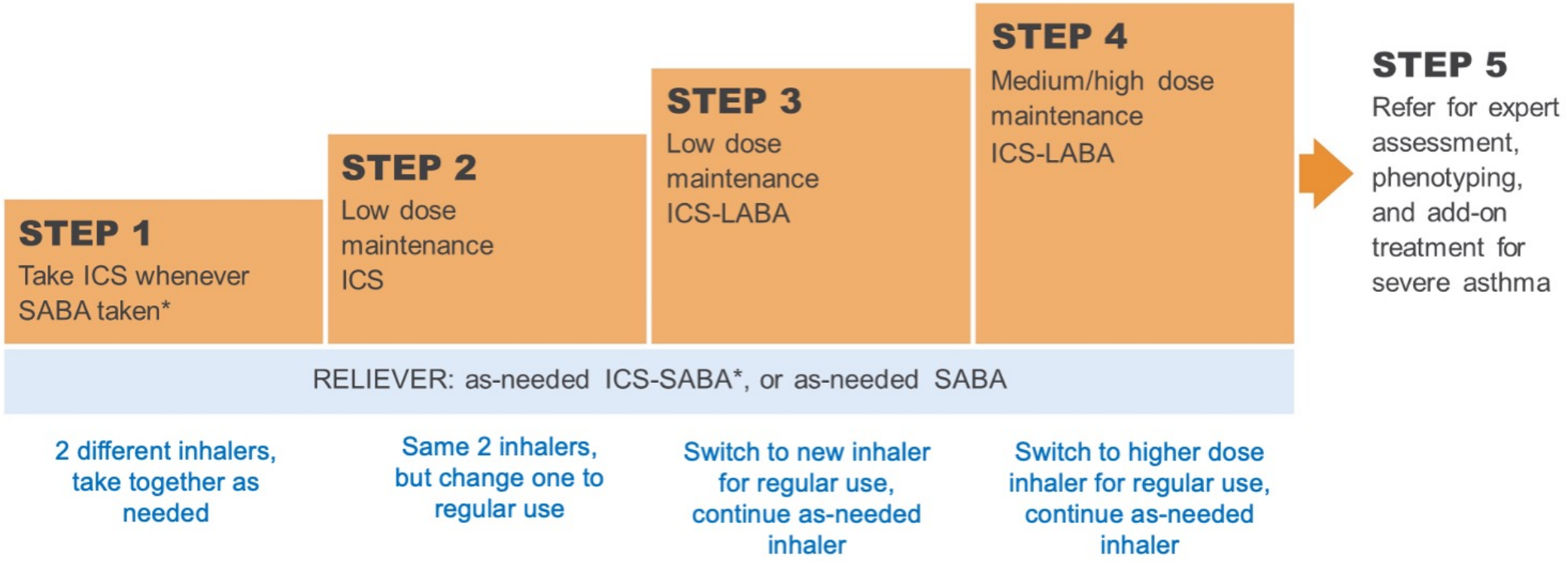
†**Beclometasone (BDP)-formoterol** has not been studied for as-needed-only use (Steps 1–2), but it may be suitable given its efficacy for MART in moderate-severe asthma.[316] GINA suggests that the maximum total dose of BDP-formoterol in any day should be 12 inhalations, based on extensive safety data with budesonide-formoterol.[322] For more details, see p.82.

#**Budesonide-formoterol** 400/12 [320/4.5] mcg should not be used as an anti-inflammatory reliever. For adults/adolescents, GINA does not suggest use of budesonide-formoterol 100/6 [80/4.5] as an anti-inflammatory reliever, since most evidence is with budesonide-formoterol 200/6 [160/4.5] mcg.

85

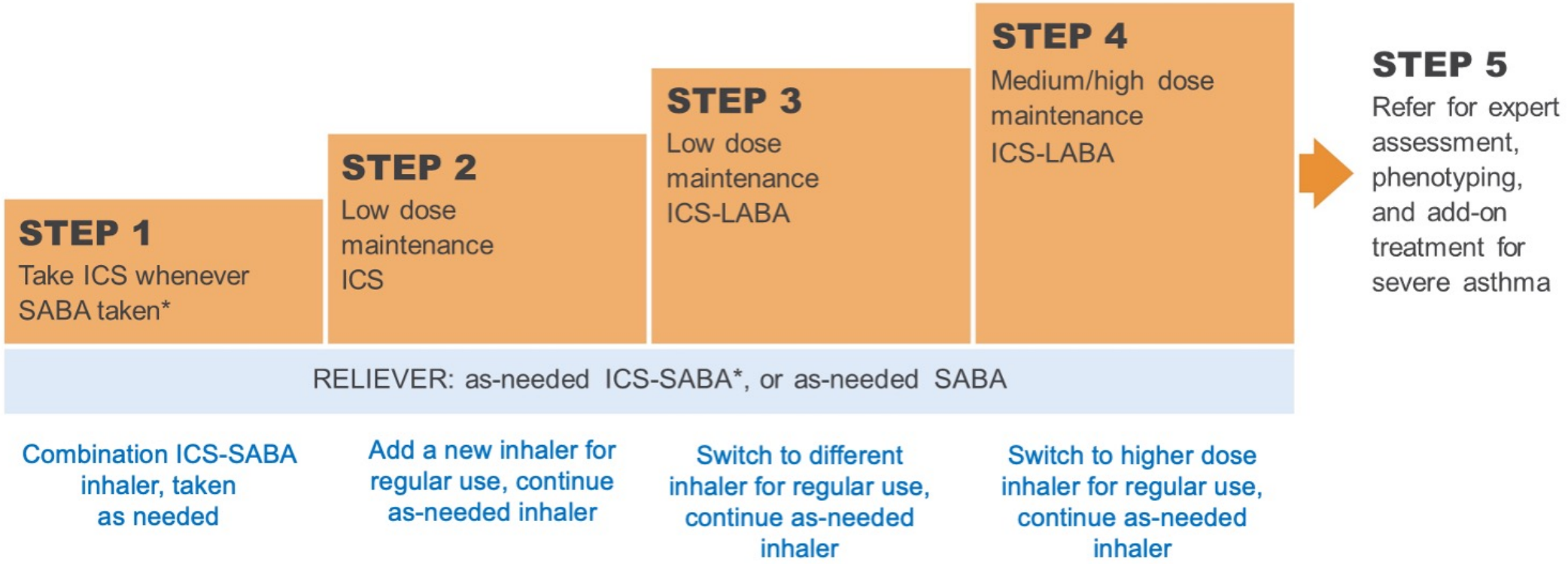
TRACK 2, Steps 1–4: Alternative CONTROLLER and RELIEVER for adults and adolescents, with SABA reliever

Before considering a regimen with SABA reliever, check if the patient is likely to adhere to daily ICS treatment. If controller and reliever are in different types of inhaler device, or if changing steps requires a change in device, train patient in correct inhaler technique.



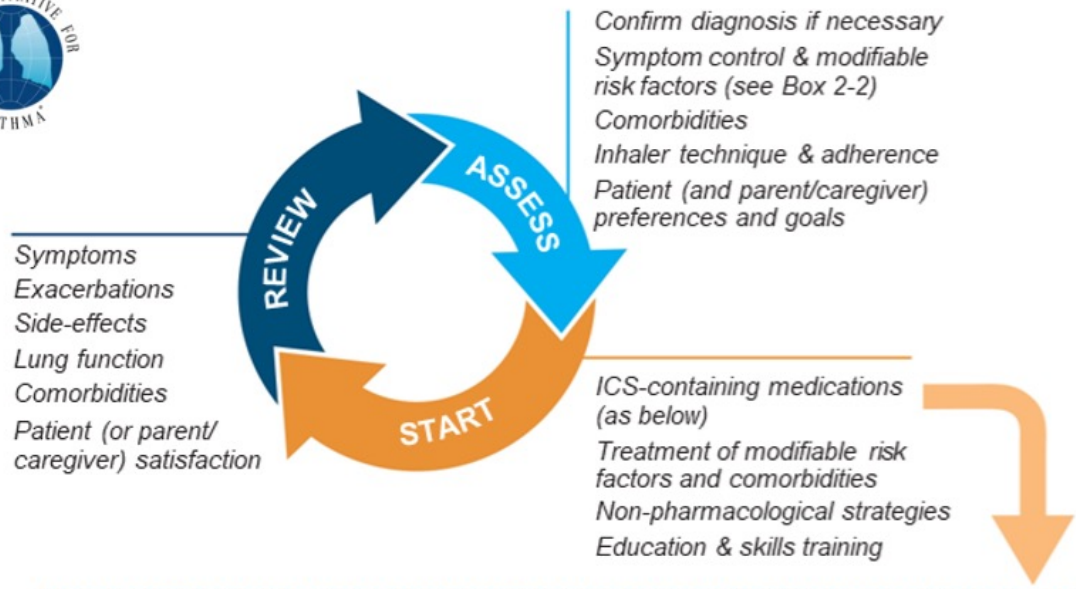
TRACK 2, Steps 1–4: Alternative CONTROLLER and RELIEVER for adults and adolescents, with ICS-SABA reliever

If maintenance and reliever medications are in different types of inhaler device, or if changing steps requires a change in device, train patient in correct inhaler technique. Make sure the patient knows which inhaler should be taken regularly, and which one as needed.



GINA 2024 – STARTING TREATMENT

in adults and adolescents 12+ years with a diagnosis of asthma



These recommendations are based on the (little) available evidence and consensus

IF the patient has:	START WITH:	TRACK 1 (preferred)	OR	TRACK 2	
Daily symptoms, waking at night once a week or more and low lung function, or recent exacerbation	YES →	Medium dose ICS-formoterol maintenance and reliever (MART)		Medium/high dose ICS-LABA + as-needed SABA (or ICS-SABA)	**STEP 4** …. *Short course of OCS may also be needed for patients presenting during an exacerbation*
NO ↓					
Symptoms most days, or waking at night once a week or more, or low lung function	YES →	Low dose ICS-formoterol maintenance and reliever (MART)		Low dose ICS-LABA + as-needed SABA (or ICS-SABA)	**STEP 3**
NO ↓					
Symptoms less than 3–5 days a week, with normal (or mildly reduced) lung function	YES →	As-needed-only low dose ICS-formoterol		Low dose ICS + as-needed SABA (or ICS-SABA)	**STEP 2** …. *In patients with symptoms 1–2 days a week or less, adherence with daily ICS would be very poor, so taking low-dose ICS whenever SABA is taken could reduce the risk of exacerbations*
				Take low dose ICS whenever SABA is taken	**STEP 1**

Difficult-to-treat and severe asthma

- Resources
  - Section 8 of the GINA 2024 report
  - GINA 2024 Short Guide on difficult-to-treat and severe asthma
  - Both resources include the GINA decision tree

GP OR SPECIALIST CARE

Investigate and manage difficult-to-treat asthma in adults and adolescents

Consider referring to specialist or severe asthma clinic at any stage

DIAGNOSIS: ***"Difficult-to-treat asthma"***

For adolescents and adults with symptoms and/or exacerbations despite medium or high dose ICS-LABA, or taking maintenance OCS

1 Confirm the diagnosis (asthma/differential diagnoses)

2 Look for factors contributing to symptoms, exacerbations and poor quality of life:

- Incorrect inhaler technique
- Suboptimal adherence
- Comorbidities including obesity, GERD, chronic rhinosinusitis, OSA
- Modifiable risk factors and triggers at home or work, including smoking, environmental exposures, allergen exposure (if sensitized); medications such as beta-blockers and NSAIDs
- Overuse of SABA relievers
- Medication side effects
- Anxiety, depression and social difficulties

3 Optimize management, including:

- Asthma education
- Optimize treatment (e.g. check and correct inhaler technique and adherence; switch to ICS-formoterol maintenance and reliever therapy, if available)
- Consider non-pharmacological interventions (e.g. smoking cessation, exercise, weight loss, mucus clearance, influenza and COVID-19 vaccination)
- Treat comorbidities and modifiable risk factors
- Consider non-biologic add-on therapy (e.g. LABA, LAMA, LM/LTRA, if not used)
- Consider trial of high dose ICS-LABA, if not used

4 Review response after ~3-6 months

Is asthma still uncontrolled?

yes

DIAGNOSIS: ***"Severe asthma"***

If not done by now, refer to a specialist, if possible

no

Consider stepping down treatment, OCS first (if used)

Does asthma become uncontrolled when treatment is stepped down?

yes

Restore previous dose

no

Continue optimizing management

Key

decision, filters

intervention, treatment

diagnosis, confirmation

SPECIALIST CARE; SEVERE ASTHMA CLINIC IF AVAILABLE

Assess and treat severe asthma phenotypes

Continue to optimize management as in section **3** (including inhaler technique, adherence, comorbidities, non-pharmacologic strategies)

5 ***Investigate*** further and provide ***patient support*** → **6** Assess the ***severe asthma phenotype*** → **7** Consider ***other*** treatments

- Investigate for comorbidities/differential diagnoses and treat/refer as appropriate
  - Consider: CBC, CRP, IgG, IgA, IgM, IgE, fungal precipitins; CXR and/or HRCT chest; DLCO; DEXA scan
  - Skin prick testing or specific IgE for relevant allergens, if not already done
  - Consider screening for adrenal insufficiency in patients taking maintenance OCS or high dose ICS
  - If blood eosinophils ≥300/µl, look for and treat non-asthma causes, including parasites (e.g. Strongyloides serology, or stool examination)
  - If hypereosinophilia e.g. ≥1500/µl, consider causes such as EGPA
  - Other directed testing (e.g. ANCA, CT sinuses, BNP, echocardiogram) based on clinical suspicion
- Consider need for social/psychological support
- Involve multidisciplinary team care (if available)
- Invite patient to enroll in registry (if available) or clinical trial (if appropriate)

Could patient have Type 2 airway inflammation?

yes

Type 2 airway inflammation

- Consider adherence tests
- Consider increasing the ICS dose for 3-6 months
- Consider add-on non-biologic treatment for specific Type 2 clinical phenotypes, e.g. AERD, ABPA, chronic rhinosinusitis, nasal polyposis, atopic dermatitis

Is add-on Type 2 biologic therapy available/ affordable?

yes

no

If add-on Type 2-targeted biologic therapy is NOT available/affordable

- Consider higher dose ICS, if not used
- Consider other add-on therapy (e.g. LAMA, LM/LTRA, low dose azithromycin)
- As last resort, consider add-on low dose OCS, but implement strategies to minimize side-effects
- Stop ineffective add-on therapies

Go to section **10**

no

Type 2 inflammation

- Blood eosinophils ≥150/µl and/or
- FeNO ≥20 ppb and/or
- Sputum eosinophils ≥2%, and/or
- Asthma is clinically allergen-driven

(Repeat blood eosinophils and FeNO up to 3x, at least 1-2 weeks after OCS or on lowest possible OCS dose)

*Note: these are **not** the criteria for add-on biologic therapy (see **8**)*

No evidence of Type 2 airway inflammation

- Review the basics: differential diagnosis, inhaler technique, adherence, comorbidities, side-effects
- Avoid exposures (tobacco smoke, allergens, irritants)
- Consider investigations (if available and not done)
  - Sputum induction
  - High resolution chest CT
  - Bronchoscopy for alternative/additional diagnoses
- Consider trial of add-on treatments (if available and not already tried)
  - LAMA
  - Low dose azithromycin
  - Anti-IL4Rα* if taking maintenance OCS
  - Anti-TSLP* (but insufficient evidence in patients on maintenance OCS)
  - As last resort, consider add-on low dose OCS, but implement strategies to minimize side-effects
- Consider bronchial thermoplasty (+ registry)
- Stop ineffective add-on therapies

Not currently eligible for T2-targeted biologic therapy

Go to section **10**

* *Check local eligibility criteria for specific biologic therapies as these may vary from those listed*

Assess and treat severe asthma phenotypes *cont'd*

Continue to optimize management as in section **3** (including inhaler technique, adherence, comorbidities, non-pharmacologic strategies)

8 Consider *add-on biologic Type 2-targeted* treatments

- Consider add-on Type 2-targeted biologic therapy for patients with exacerbations or poor symptom control on high dose ICS-LABA, who have evidence of Type 2 inflammation*
- Consider **local payer eligibility criteria***, **comorbidities** and **predictors of response** when choosing between available therapies
- Also consider cost, dosing frequency, route (SC or IV), patient preference

Which biologic is appropriate to start first?

Eligibility | *Predictors of asthma response*

Anti-IgE *(omalizumab)*

*Is the patient eligible for **anti-IgE** for severe allergic asthma?**

- Sensitization on skin prick testing or specific IgE
- Total serum IgE and weight within dosage range
- Exacerbations in last year

What factors may predict good asthma response to anti-IgE?

- Blood eosinophils ≥260/µl ++
- FeNO ≥20 ppb +
- Allergen-driven symptoms +
- Childhood-onset asthma +

no / *no*

Anti-IL5 / Anti-IL5R *(benralizumab, mepolizumab, reslizumab)*

*Is the patient eligible for **anti-IL5 / anti-IL5R** for severe eosinophilic asthma?**

- Exacerbations in last year
- Blood eosinophils, e.g. ≥150/µl or ≥300/µl

What factors may predict good asthma response to anti-IL5/5R?

- Higher blood eosinophils +++
- More exacerbations in previous year +++
- Adult-onset of asthma ++
- Nasal polyposis ++

no / *no*

Anti-IL4Rα *(dupilumab)*

*Is the patient eligible for **anti-IL4Rα** for severe eosinophilic/Type 2 asthma?**

- Exacerbations in last year
- Blood eosinophils ≥150 and ≤1500/µl, or FeNO ≥25 ppb, or taking maintenance OCS

What factors may predict good asthma response to anti-IL4Rα?

- Higher blood eosinophils +++
- Higher FeNO +++

no / *no*

Anti-TSLP *(tezepelumab)*

*Is the patient eligible for **anti-TSLP** for severe asthma?**

- Exacerbations in last year

What factors may predict good asthma response to anti-TSLP?

- Higher blood eosinophils +++
- Higher FeNO +++

Eligible for none? Return to section **7**

Choose one if eligible*; trial for at least 4 months and assess response

*Good asthma response?**

yes → **Good response to T2-targeted therapy**

unclear → Extend trial to 6-12 months*

no → **STOP add-on**

Consider switching to a different Type 2-targeted therapy, if eligible*

no → **Little/no response to T2-targeted therapy**

No evidence of Type 2 airway inflammation

No evidence of Type 2 airway inflammation. Go to section **10**

* *Check local eligibility criteria for specific biologic therapies as these may vary from those listed*

Monitor / Manage severe asthma treatment

Continue to optimize management

9 Review response

- Asthma: symptom control, exacerbations, lung function
- Type 2 comorbidities e.g. nasal polyposis, atopic dermatitis
- Medications: treatment intensity, side-effects, affordability
- Patient satisfaction

yes

If good response to Type 2-targeted therapy

- Re-evaluate the patient every 3-6 months*
- First, consider decreasing/stopping OCS (and check for adrenal insufficiency), then consider stopping other add-on asthma medications
- Then, if asthma well-controlled for 3-6 months, consider reducing maintenance ICS-LABA dose, but do not stop maintenance ICS-LABA. See text for details.
- Re-evaluate need for ongoing biologic therapy
- Order of reduction of treatments based on observed benefit, potential side-effects, cost and patient preference

no

If no good response to Type 2-targeted therapy

- Stop the biologic therapy
- Review the basics: differential diagnosis, inhaler technique, adherence, comorbidities, side-effects, emotional support
- Consider high resolution chest CT (if not done)
- Reassess phenotype and treatment options
  - Induced sputum (if available)
  - Consider add-on low dose azithromycin
  - Consider bronchoscopy for alternative/additional diagnoses
  - As last resort, consider add-on low dose OCS, but implement strategies to minimize side-effects
  - Consider bronchial thermoplasty (+ registry)
- Stop ineffective add-on therapies
- Do not stop ICS

No evidence of Type 2 airway inflammation. Go to section 10

10 Continue to **optimize management** as in section **3**, including:

- Inhaler technique
- Adherence
- Comorbidity management
- Non-pharmacologic strategies
- Patients' social/emotional needs
- Two-way communication with GP for ongoing care

Notes:

* *Check local eligibility criteria for specific biologic therapies as these may vary from those listed*

Monitor / Manage severe asthma treatment

9 Review response

- Asthma: symptom control, exacerbations, lung function
- Type 2 comorbidities e.g. nasal polyposis, atopic dermatitis
- Medications: treatment intensity, side-effects, affordability
- Patient satisfaction

If good response to Type 2-targeted therapy

- Re-evaluate the patient every 3-6 months*
- First, consider decreasing/stopping OCS (and check for adrenal insufficiency), then consider stopping other add-on asthma medications
- Then, if asthma well-controlled for 3-6 months, consider reducing maintenance ICS-LABA dose, but do not stop maintenance ICS-LABA. See text for details.
- Re-evaluate need for ongoing biologic therapy
- Order of reduction of treatments based on observed benefit, potential side-effects, cost and patient preference

yes

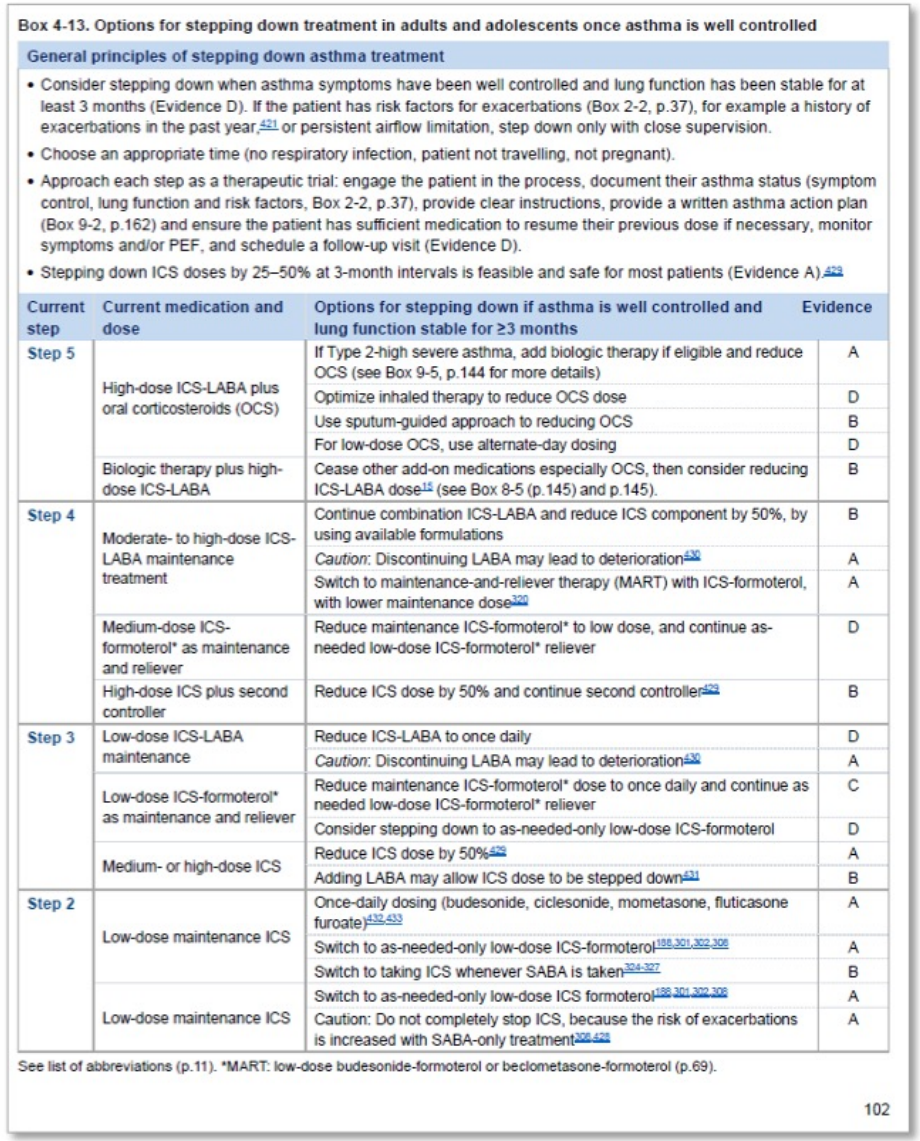
- Stop ineffective add-on therapies
- Do not stop ICS

No evidence of Type 2 airway inflammation. Go to section 10

* *Check local eligibility criteria for specific biologic therapies as these may vary from those listed*

Stepping down asthma treatment

- Consider stepping down when symptoms are well-controlled and lung function stable for ≥3 months
  - If patient has exacerbation risk factors, e.g. severe exacerbation in past year, step down only with close supervision
- Choose an appropriate time
- Treat each step as a therapeutic trial
  - Engage the patient in the process
  - Document asthma status
  - Provide clear instructions and an action plan
  - Sufficient medication to resume previous dose
  - Monitor symptoms and/or PEF
  - Schedule a follow-up visit
- Do not stop ICS-containing treatment
  - In severe asthma, do not stop maintenance ICS-LABA



Box 4-13. Options for stepping down treatment in adults and adolescents once asthma is well controlled

General principles of stepping down asthma treatment

- Consider stepping down when asthma symptoms have been well controlled and lung function has been stable for at least 3 months (Evidence D). If the patient has risk factors for exacerbations (Box 2-2, p.37), for example a history of exacerbations in the past year,[421] or persistent airflow limitation, step down only with close supervision.
- Choose an appropriate time (no respiratory infection, patient not travelling, not pregnant).
- Approach each step as a therapeutic trial: engage the patient in the process, document their asthma status (symptom control, lung function and risk factors, Box 2-2, p.37), provide clear instructions, provide a written asthma action plan (Box 9-2, p.162) and ensure the patient has sufficient medication to resume their previous dose if necessary, monitor symptoms and/or PEF, and schedule a follow-up visit (Evidence D).
- Stepping down ICS doses by 25–50% at 3-month intervals is feasible and safe for most patients (Evidence A).[429]

Current step	Current medication and dose	Options for stepping down if asthma is well controlled and lung function stable for ≥3 months	Evidence
Step 5	High-dose ICS-LABA plus oral corticosteroids (OCS)	If Type 2-high severe asthma, add biologic therapy if eligible and reduce OCS (see Box 9-5, p.144 for more details)	A
		Optimize inhaled therapy to reduce OCS dose	D
		Use sputum-guided approach to reducing OCS	B
		For low-dose OCS, use alternate-day dosing	D
	Biologic therapy plus high-dose ICS-LABA	Cease other add-on medications especially OCS, then consider reducing ICS-LABA dose[15] (see Box 8-5 (p.145) and p.145).	B
Step 4	Moderate- to high-dose ICS-LABA maintenance treatment	Continue combination ICS-LABA and reduce ICS component by 50%, by using available formulations	B
		Caution: Discontinuing LABA may lead to deterioration[430]	A
		Switch to maintenance-and-reliever therapy (MART) with ICS-formoterol, with lower maintenance dose[320]	A
	Medium-dose ICS-formoterol* as maintenance and reliever	Reduce maintenance ICS-formoterol* to low dose, and continue as-needed low-dose ICS-formoterol* reliever	D
	High-dose ICS plus second controller	Reduce ICS dose by 50% and continue second controller[429]	B
Step 3	Low-dose ICS-LABA maintenance	Reduce ICS-LABA to once daily	D
		Caution: Discontinuing LABA may lead to deterioration[430]	A
	Low-dose ICS-formoterol* as maintenance and reliever	Reduce maintenance ICS-formoterol* dose to once daily and continue as needed low-dose ICS-formoterol* reliever	C
		Consider stepping down to as-needed-only low-dose ICS-formoterol	D
	Medium- or high-dose ICS	Reduce ICS dose by 50%[429]	A
		Adding LABA may allow ICS dose to be stepped down[431]	B
Step 2	Low-dose maintenance ICS	Once-daily dosing (budesonide, ciclesonide, mometasone, fluticasone furoate)[432,433]	A
		Switch to as-needed-only low-dose ICS-formoterol[188,301,302,308]	A
		Switch to taking ICS whenever SABA is taken[324-327]	B
	Low-dose maintenance ICS	Switch to as-needed-only low-dose ICS formoterol[188,301,302,308]	A
		Caution: Do not completely stop ICS, because the risk of exacerbations is increased with SABA-only treatment[328,428]	A

See list of abbreviations (p.11). *MART: low-dose budesonide-formoterol or beclometasone-formoterol (p.69).

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GINA 2024 – Children 6–11 years

Personalized asthma management:
Assess, Adjust, Review

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

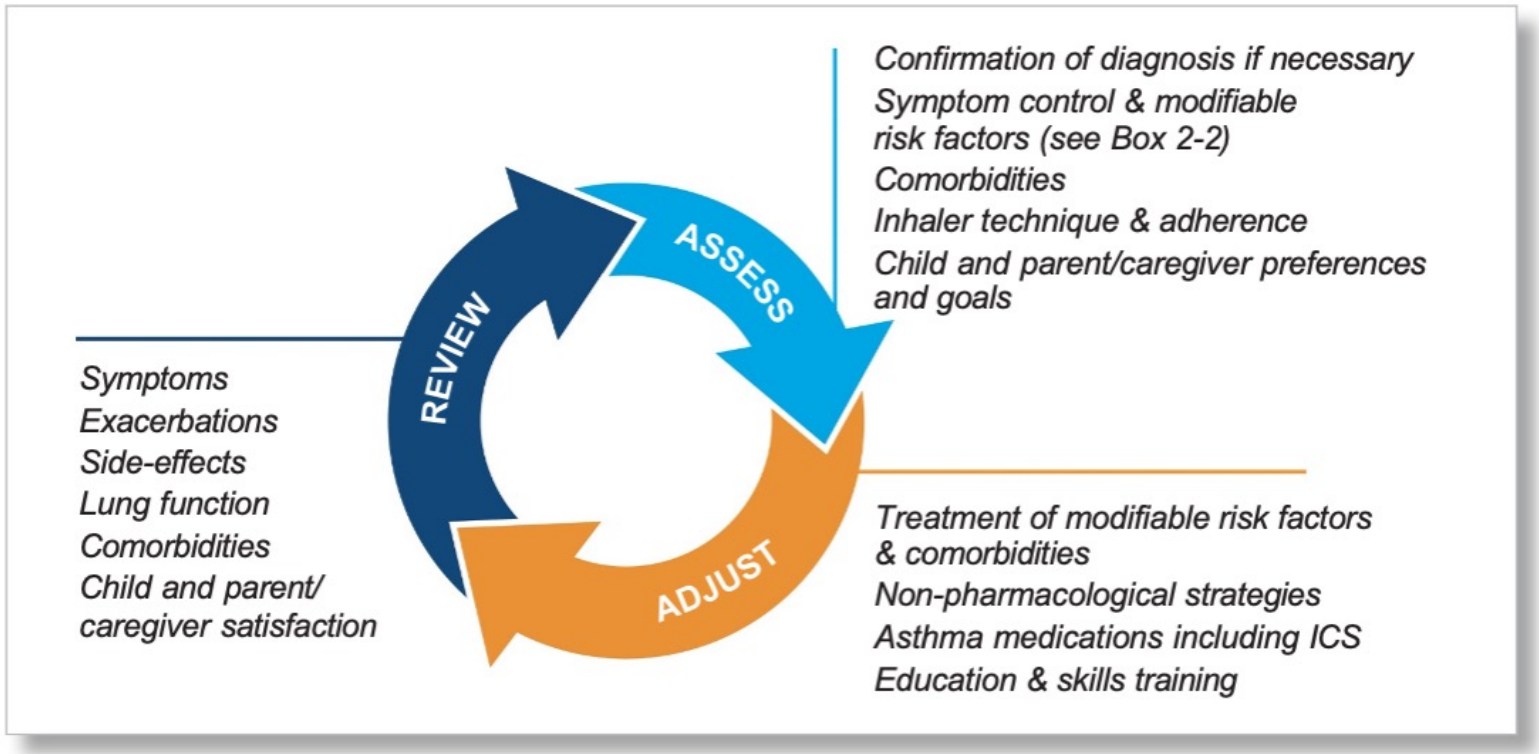
Symptoms
Exacerbations
Side-effects
Lung function
Comorbidities
Child and parent/ caregiver satisfaction

Treatment of modifiable risk factors & comorbidities
Non-pharmacological strategies
Asthma medications including ICS
Education & skills training

Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms	Low dose ICS taken whenever SABA taken*	Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for children)	Low dose ICS-LABA, OR medium dose ICS, OR very low dose ICS-formoterol maintenance and reliever therapy (MART)	Refer for expert advice, OR medium dose ICS-LABA, OR low dose ICS-formoterol maintenance and reliever therapy (MART)	Refer for phenotypic assessment ± higher dose ICS-LABA or add-on therapy, e.g. anti-IgE, anti-IL4Rα, anti-IL5
Other controller options (limited indications, or less evidence for efficacy or safety)		*Daily leukotriene receptor antagonist (LTRA†), or low dose ICS taken whenever SABA taken**	*Low dose ICS + LTRA†*	*Add tiotropium or add LTRA†*	*As last resort, consider add-on low dose OCS, but consider side-effects*
RELIEVER	As-needed SABA (or ICS-formoterol reliever* in MART in Steps 3 and 4)				

*Anti-inflammatory reliever; †advise about risk of neuropsychiatric adverse effects



Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms	Low dose ICS taken whenever SABA taken*				
Other controller options (limited indications, or less evidence for efficacy or safety)					
RELIEVER	As-needed SABA (or ICS-formoterol reliever* in MART in Steps 3 and 4)				

*Anti-inflammatory reliever

Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms		**Daily low dose inhaled corticosteroid (ICS)** (see table of ICS dose ranges for children)			
Other controller options (limited indications, or less evidence for efficacy or safety)		*Daily leukotriene receptor antagonist (LTRA†), or low dose ICS taken whenever SABA taken**			
RELIEVER	As-needed SABA (or ICS-formoterol reliever* in MART in Steps 3 and 4)				

*Anti-inflammatory reliever; †advise about risk of neuropsychiatric adverse effects

Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms			Low dose ICS-LABA, OR medium dose ICS, OR very low dose ICS-formoterol maintenance and reliever (MART)		
Other controller options (limited indications, or less evidence for efficacy or safety)			*Low dose ICS + LTRA†*		
RELIEVER	As-needed SABA (or ICS-formoterol reliever* in MART in Steps 3 and 4)				

*Anti-inflammatory reliever; †advise about risk of neuropsychiatric adverse effects

*Anti-inflammatory reliever; †advise about risk of neuropsychiatric adverse effects

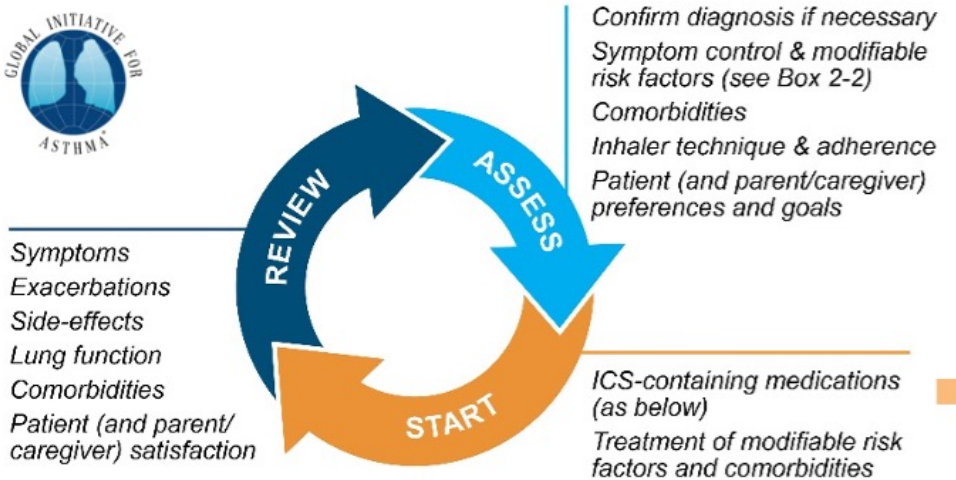
Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms					Refer for phenotypic assessment ± higher dose ICS-LABA or add-on therapy, e.g. anti-IgE, anti-IL4Rα, anti-IL5
Other controller options (limited indications, or less evidence for efficacy or safety)					*As last resort, consider add-on low dose OCS, but consider side-effects*
RELIEVER	As-needed SABA (or ICS-formoterol reliever* in MART in Steps 3 and 4)				

*Anti-inflammatory reliever

GINA 2024 – STARTING TREATMENT

in children aged 6–11 years with a diagnosis of asthma



These recommendations are based on the (little) available evidence and consensus

IF the patient has:		START WITH:	
Symptoms most days, waking at night once or more a week, and low lung function	YES	Refer for expert advice, or medium dose ICS-LABA plus as-needed SABA, or low-dose MART	**STEP 4**
NO			
Symptoms most days, or waking at night once or more a week	YES	Low-dose ICS-LABA or medium-dose ICS plus as-needed SABA; or very-low-dose MART	**STEP 3**
NO			
Symptoms 2–5 days a week	YES	Daily low-dose ICS plus as-needed SABA	**STEP 2**
NO			
Symptoms less than two days a week	YES	Take low dose ICS whenever SABA is taken	**STEP 1**

Short course of OCS may also be needed for children presenting with an exacerbation

For children with symptoms 1–2 days a week or less, adherence with daily ICS is likely to be very poor, so taking low-dose ICS whenever SABA is taken may be a better option for reducing exacerbation risk

MART for children 6–11 years: medications and doses

- MART is an option for this agegroup in Steps 3 and 4
- Recommended doses: budesonide-formoterol 100/6 mcg [80/4.5 mcg delivered dose] DPI or pMDI
  - Step 3: 1 inhalation **once** daily plus 1 inhalation as needed*
  - Step 4: 1 inhalation **twice** daily plus 1 inhalation as needed*
- Evidence for MART to date in children is with budesonide-formoterol 100/6 [80/4.5] DPI
  - In children 4–11 years with a history of at least one exacerbation, MART 100/6 [80/4.5] mcg 1 inhalation once daily plus 1 inhalation as needed reduced severe exacerbations compared with the same dose of budesonide-formoterol or with 4 times the dose of ICS alone, plus SABA reliever *(O'Byrne 2005; Bisgaard 2006)*
- Maximum total dose in any one day (maintenance and reliever doses)
  - 8 inhalations* of budesonide-formoterol 100/6 mcg [80/4.5 mcg delivered dose]
- **Very few patients ever need this much!**
- Several RCTs are underway with AIR-only and MART in children
- Do not use ICS-formoterol as the reliever with other maintenance ICS-LABAs

*In some countries, a budesonide-formoterol pMDI with 50/3 [40/2.25] mcg per actuation is available. For this pMDI, the recommended number of inhalations is double that for the 100/6 [80/4.5] mcg formulation above.

Low, medium and high doses of ICS

Inhaled corticosteroid (alone or in combination with LABA)	Total daily ICS dose (mcg) – see notes above		
	Low	Medium	High
Adults and adolescents (12 years and older)			
Beclometasone dipropionate (pMDI, standard particle, HFA)	200–500	>500–1000	>1000
Beclometasone dipropionate (DPI or pMDI, extrafine particle, HFA)	100–200	>200–400	>400
Budesonide (DPI, or pMDI, standard particle, HFA)	200–400	>400–800	>800
Ciclesonide (pMDI, extrafine particle, HFA)	80–160	>160–320	>320
Fluticasone furoate (DPI)	100		200
Fluticasone propionate (DPI)	100–250	>250–500	>500
Fluticasone propionate (pMDI, standard particle, HFA)	100–250	>250–500	>500
Mometasone furoate (DPI)	Depends on DPI device – see product information		
Mometasone furoate (pMDI, standard particle, HFA)	200–400		>400
Children 6–11 years – see notes above (for children 5 years and younger, see Box 11-3, p.191			
Beclometasone dipropionate (pMDI, standard particle, HFA)	100–200	>200–400	>400
Beclometasone dipropionate (pMDI, extrafine particle, HFA)	50–100	>100–200	>200
Budesonide (DPI, or pMDI, standard particle, HFA)	100–200	>200–400	>400
Budesonide (nebules)	250–500	>500–1000	>1000
Ciclesonide (pMDI, extrafine particle*, HFA)	80	>80–160	>160
Fluticasone furoate (DPI)	50		n.a.
Fluticasone propionate (DPI)	50–100	>100–200	>200
Fluticasone propionate (pMDI, standard particle, HFA)	50–100	>100–200	>200
Mometasone furoate (pMDI, standard particle, HFA)	100		200

- This is a table of low, medium and high doses of various ICS
- **It does NOT imply equivalent potency**
- For example, if you switch a patient from a 'medium' dose of one ICS to a 'medium' dose of another ICS, this may represent a *decrease* in potency, so their asthma may worsen, or it might represent an *increase* in potency and the patient may experience more adverse effects
- Always monitor patients after any change in medication, dose or device, to ensure they are stable

Remission of asthma

- Children vs adults
- Clinical vs complete remission
- “Off treatment” vs “on treatment”
- Multiple definitions, operationalized in many ways
  - Often assessed over only 12 months
  - “No exacerbations” and “no maintenance OCS” assessed from electronic medical record or patient interview
  - “No symptoms over 12 months” often assessed from Asthma Control Questionnaire (i.e. the last 7 days!)
- No validated tools for assessment of symptoms over periods longer than 4 weeks

Remission of asthma

- Remission from childhood wheezing or asthma, off treatment
  - Parents/caregivers often ask if their child will 'grow out of their asthma'
  - Rates vary depending on population and age, e.g. 59% at age 6, 15% at age 26
  - Asthma often recurs: remission is not cure, and patients may develop persistent airflow limitation
  - Say to parent/caregiver 'Their asthma has gone quiet for a while'
- Remission in adults, on treatment
  - Current reports are mostly for patients with severe asthma treated with biologic therapy
  - Remission also seen in non-severe asthma with ICS-containing treatment, and sometimes spontaneously
  - Research needed to identify pathways in patients who have ongoing respiratory symptoms, e.g. multimorbidity, anxiety and/or depression, moderate or severe persistent airflow limitation
- Evidence about goal-setting tells us that treatment goals for patients should be personalized and achievable
- Avoid encouraging automatic step-up of therapy
  - Treat comorbidities and modifiable risk factors first (including poor inhaler technique and poor adherence); use non-pharmacologic strategies; if high-dose ICS or ICS-LABA is used, limit to 3–6 months whenever possible
  - Use GINA Track 1 regimen to reduce exacerbations using *lower* ICS doses

GINA goal of asthma management

The goal is to achieve the **best possible long-term asthma outcomes** for each patient:

- Long-term symptom control, which may include:
  - Few/no asthma symptoms, quickly relieved
  - No sleep disturbance
  - Unimpaired physical activity
- Long-term asthma risk minimization, which may include:
  - No exacerbations
  - Improved or stable personal best lung function
  - No requirement for maintenance oral corticosteroids
  - No medication side-effects

When discussing best possible long-term outcomes with a patient, consider:

- Their asthma phenotype
- Clinical features
- Multimorbidity
- Risk factors (e.g. poor adherence, smoking, persistent airflow limitation)
- Availability, cost and adverse effects of medications
- The patient's goals (these may be different from medical goals)

- Assessing symptom control is not enough! Patients with few asthma symptoms can still have severe or fatal exacerbations related to individual risk factors or external triggers (viruses, allergen, pollution)
- Encourage referral for expert advice for patients with difficult-to-treat or severe asthma

Role of FeNO in asthma management

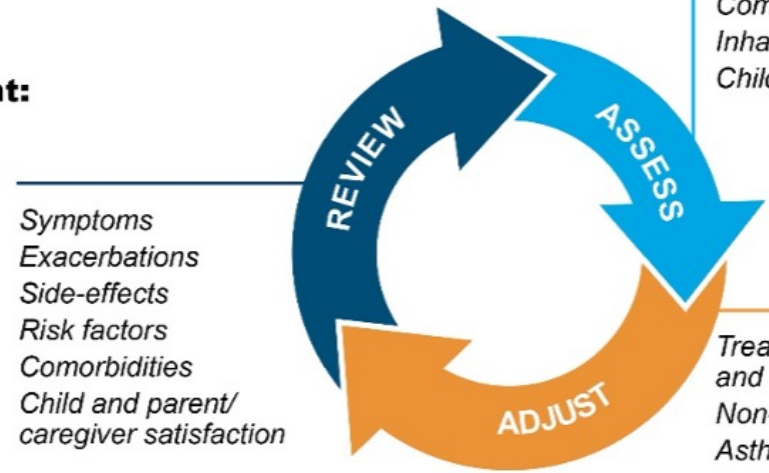
- Diagnosis
  - FeNO is higher in many patients with T2-high asthma (IL-13 pathways), but it is also elevated in non-asthma conditions with T2 inflammation (e.g., eosinophilic bronchitis, atopy, allergic rhinitis, eczema)
  - Not elevated in T2-low asthma
  - Can support a diagnosis of T2-high asthma, but cannot rule in or rule out asthma
- Factors affecting FeNO
  - Lower during bronchoconstriction; lower in early allergic response; lower in smokers
  - Relationship with other T2 markers is lost in obesity
  - In most patients with asthma, FeNO decreases when ICS-containing treatment is started or adherence increases
- Risk assessment
  - High FeNO in patients taking inhaled corticosteroids is associated with increased risk of exacerbations
- Main role remains in helping to guide treatment decisions in moderate or severe asthma
  - FeNO suppression test – distinguish between poor adherence and corticosteroid refractory asthma
  - Choice of biologic therapy: higher FeNO associated with greater response to dupilumab or omalizumab
  - Monitoring of ICS-LABA reduction in patients on biologic therapy: In patients with well-controlled asthma on benralizumab who were randomized to maintenance and reliever therapy (MART), FEV_1 decreased and FeNO increased in those who ceased maintenance ICS-formoterol *(Jackson et al, Lancet Respir Med 2024)*

Allergen immunotherapy

- Allergen immunotherapy may be considered as add-on therapy for adults and children with asthma who have clinically significant sensitization to aeroallergens
  - The only intervention with both an immune modifying effect and long-term efficacy on the allergic response
  - Most evidence is for house dust mite (HDM) and grass pollens, in patients with allergic rhinitis
- Few studies in asthma comparing immunotherapy with pharmacologic therapy, or reporting standardized asthma outcomes, e.g. exacerbations
- Subcutaneous immunotherapy (SCIT)
  - May reduce ICS requirement (moderate strength evidence), may improve QOL/lung function (low strength evidence)
  - Consider potential benefits vs risk of adverse effects, inconvenience, cost, minimum 30 min wait after injections
  - Asthma or food allergy are risk factors for severe anaphylactic reactions
  - Limit to practitioners with specific training + resources for anaphylaxis + safety protocols + standardized extracts
- Sublingual immunotherapy (SLIT)
  - Adults sensitized to HDM: consider adding if persistent symptoms despite ICS, but only if FEV_1 >70% predicted
  - Children sensitized to ragweed: consider adding before and during ragweed season, but only if FEV_1 ≥80% predicted
  - Shared decision-making to consider benefits against costs and risks

GINA 2024 – Children 5 years and younger

Personalized asthma management:
Assess, Adjust, Review response



Exclude alternative diagnoses
Symptom control & modifiable risk factors
Comorbidities
Inhaler technique & adherence
Child and parent/caregiver preferences and goals

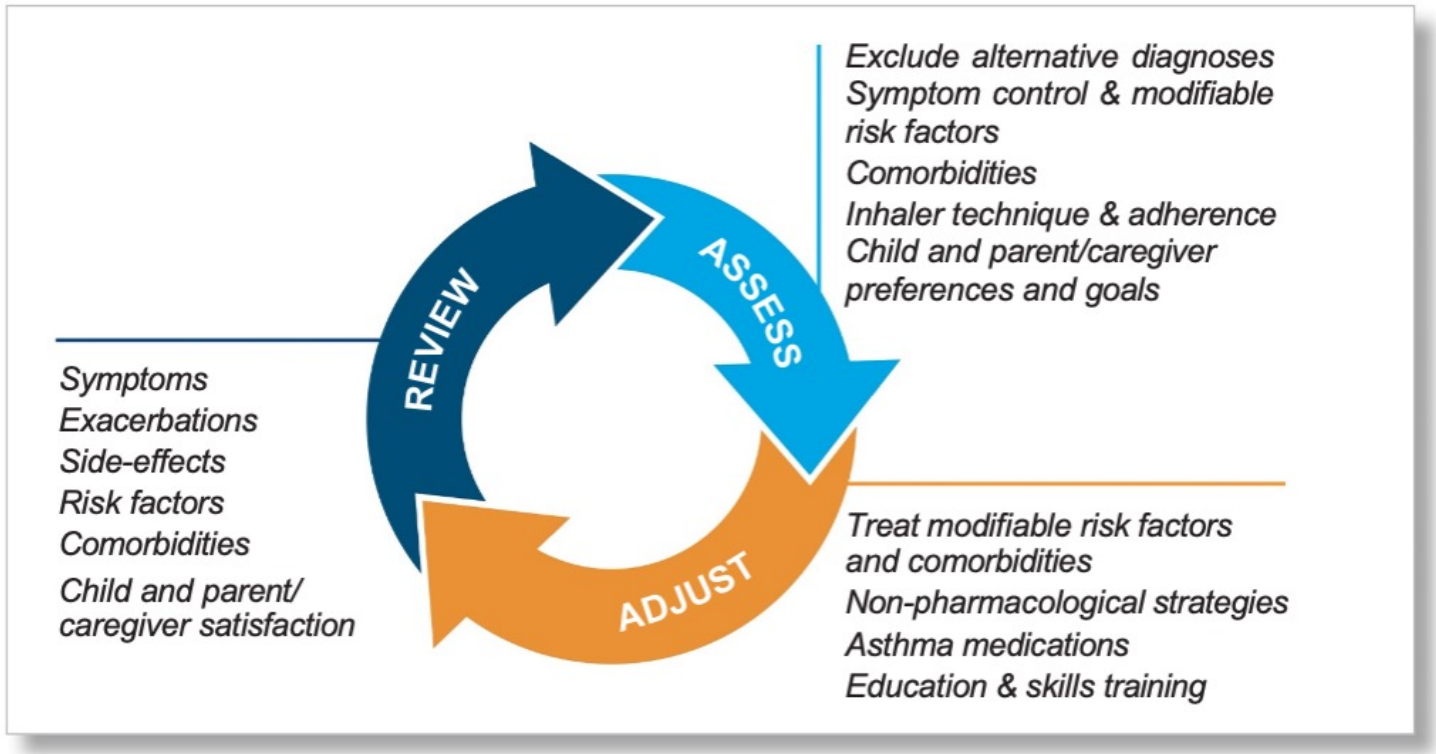
Symptoms
Exacerbations
Side-effects
Risk factors
Comorbidities
Child and parent/ caregiver satisfaction

Treat modifiable risk factors and comorbidities
Non-pharmacological strategies
Asthma medications
Education & skills training

Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4
PREFERRED CONTROLLER CHOICE	*(Insufficient evidence for daily controller)*	Daily low dose inhaled corticosteroid (ICS) (see Box 11-3 for ICS dose ranges for pre-school children)	Double 'low dose' ICS *(See Box 11-3)*	Continue controller & refer for specialist assessment
Other controller options (limited indications, or less evidence for efficacy or safety)	*Consider intermittent short course ICS at onset of viral illness*	*Daily leukotriene receptor antagonist (LTRA†), or intermittent short course of ICS at onset of respiratory illness*	*Low dose ICS + LTRA† Consider specialist referral*	*Add LTRA†, or increase ICS frequency, or add intermittent ICS*
RELIEVER	As-needed short-acting beta$_2$-agonist			
CONSIDER THIS STEP FOR CHILDREN WITH:	Infrequent viral wheezing and no or few interval symptoms	Symptom pattern not consistent with asthma but wheezing episodes requiring SABA occur frequently, e.g. ≥3 per year. Give diagnostic trial for 3 months. Consider specialist referral.	Asthma diagnosis, and asthma not well-controlled on low dose ICS	Asthma not well-controlled on double ICS
		Symptom pattern consistent with asthma, and asthma symptoms not well-controlled or ≥3 exacerbations per year.	Before stepping up, check for alternative diagnosis, check inhaler skills, review adherence and exposures	

*†Advise about risk of neuropsychiatric adverse effects



Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4
PREFERRED CONTROLLER CHOICE	*(Insufficient evidence for daily controller)*			
Other controller options (limited indications, or less evidence for efficacy or safety)	*Consider intermittent short course ICS at onset of viral illness*			
RELIEVER	As-needed short-acting beta$_2$-agonist			
CONSIDER THIS STEP FOR CHILDREN WITH:	Infrequent viral wheezing and no or few interval symptoms			

Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4
PREFERRED CONTROLLER CHOICE		Daily low dose inhaled corticosteroid (ICS) (see Box 11-3 of ICS dose ranges for pre-school children)		
Other controller options (limited indications, or less evidence for efficacy or safety)		*Daily leukotriene receptor antagonist (LTRA†), or intermittent short course of ICS at onset of respiratory illness*		
RELIEVER	As-needed short-acting beta$_2$-agonist			
CONSIDER THIS STEP FOR CHILDREN WITH:		Symptom pattern not consistent with asthma but wheezing episodes requiring SABA occur frequently, e.g. ≥3 per year. Give diagnostic trial for 3 months. Consider specialist referral.		
		Symptom pattern consistent with asthma, and asthma symptoms not well-controlled or ≥3 exacerbations per year.		

*†Advise about risk of neuropsychiatric adverse effects

Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4
PREFERRED CONTROLLER CHOICE			Double 'low dose' ICS *(See Box 11-3)*	
Other controller options (limited indications, or less evidence for efficacy or safety)			*Low dose ICS + LTRA†* *Consider specialist referral*	
RELIEVER	As-needed short-acting beta$_2$-agonist			
CONSIDER THIS STEP FOR CHILDREN WITH:			Asthma diagnosis, and asthma not well-controlled on low dose ICS	
			Before stepping up, check for alternative diagnosis, check inhaler skills, review adherence and exposures	

*†Advise about risk of neuropsychiatric adverse effects

Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4
PREFERRED CONTROLLER CHOICE				Continue controller & refer for specialist assessment
Other controller options (limited indications, or less evidence for efficacy or safety)				*Add LTRA†, or increase ICS frequency, or add intermittent ICS*
RELIEVER	As-needed short-acting beta$_2$-agonist			
CONSIDER THIS STEP FOR CHILDREN WITH:			Asthma not well-controlled on double ICS	
			Before stepping up, check for alternative diagnosis, check inhaler skills, review adherence and exposures	

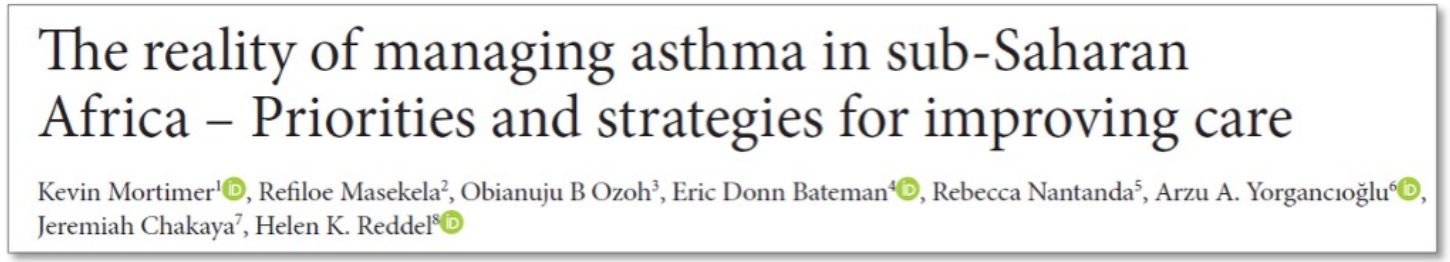
*†Advise about risk of neuropsychiatric adverse effects

Other changes in GINA 2024 include…

- Cough variant asthma
  - Common in some countries
  - Spirometry may be normal, diagnosed with bronchial provocation test
  - Treatment as for asthma, with inhaled corticosteroids
- Bronchodilator responsiveness
  - Proposal by ERS/ATS Technical Committee to change criterion from an increase from baseline in FEV_1 or FVC by ≥12% and ≥200 mL, to an increase from baseline in FEV_1 or FVC by >10% predicted
  - Based on long-term analyses of mortality
  - Not yet compared with other diagnostic tests for asthma, so not recommended for clinical use
- Montelukast (leukotriene receptor antagonist)
  - Consistent advice throughout GINA 2024 to advise patients/caregivers about potential neuropsychiatric effects
  - Increased attention in social media
- Pulmonary rehabilitation for asthma
  - Systematic review demonstrated benefit for functional exercise capacity and quality of life in people with asthma *(Osadnik et al, Cochrane Database 2022)*

Oral bronchodilators are NOT recommended

- Salbutamol tablets/syrup, and oral theophylline are **not recommended**
  - Slow onset of action
  - Less effective for symptom relief than inhaled bronchodilators
  - More adverse effects
  - They do not treat the airway inflammation that is characteristic of asthma
- Advocate for global access to essential inhaled medicines for all
- In the meantime, if only oral agents are available, see article below about which/how to use


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

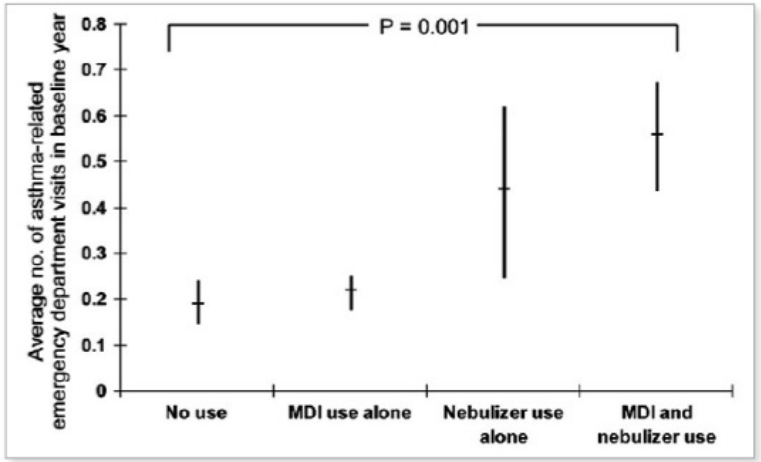
Kevin Mortimer[1], Refiloe Masekela[2], Obianuju B Ozoh[3], Eric Donn Bateman[4], Rebecca Nantanda[5], Arzu A. Yorgancıoğlu[6], Jeremiah Chakaya[7], Helen K. Reddel[8]

Mortimer et al, JPATS 2022

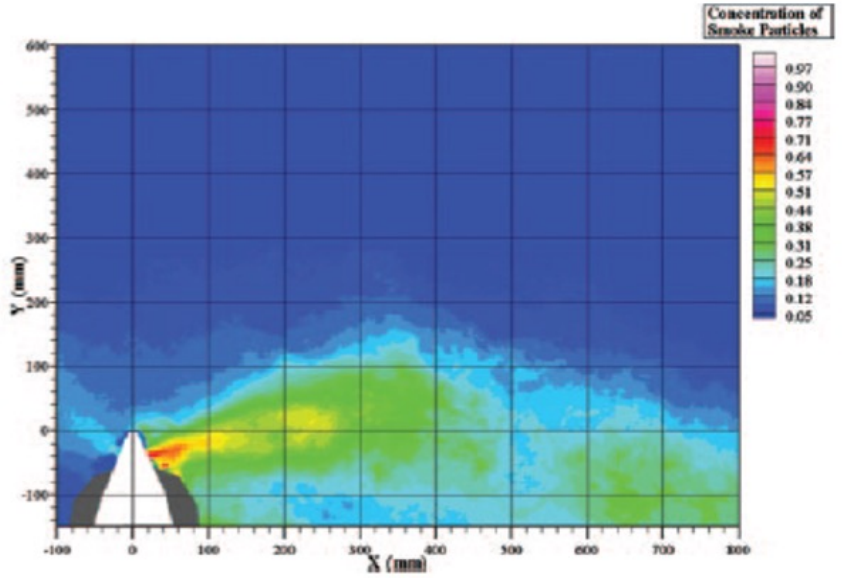
Home nebulization of SABA is not recommended

Home nebulization of SABA is associated with increased risk

- Increased risk of severe exacerbations
  - ED visits for asthma (aHR 6.3) *(Paris, 2008)*
  - Relapse after ED visit for asthma (OR 2.2) *(Emerman, 1999)*
  - Asthma hospitalisations (aHR 21.6) *(Paris, 2008)*
- Increased risk of asthma mortality
  - aOR 4.6 *(Abramson, 2000)*
- Increased risk of transmission of infection
  - SARS Co-V-1: 138 hospital workers infected from index case
  - Potential infection of family members
- SABA by pMDI and spacer provides quicker relief and less risk



Paris et al, Ann Allergy Asthma Immunol 2008



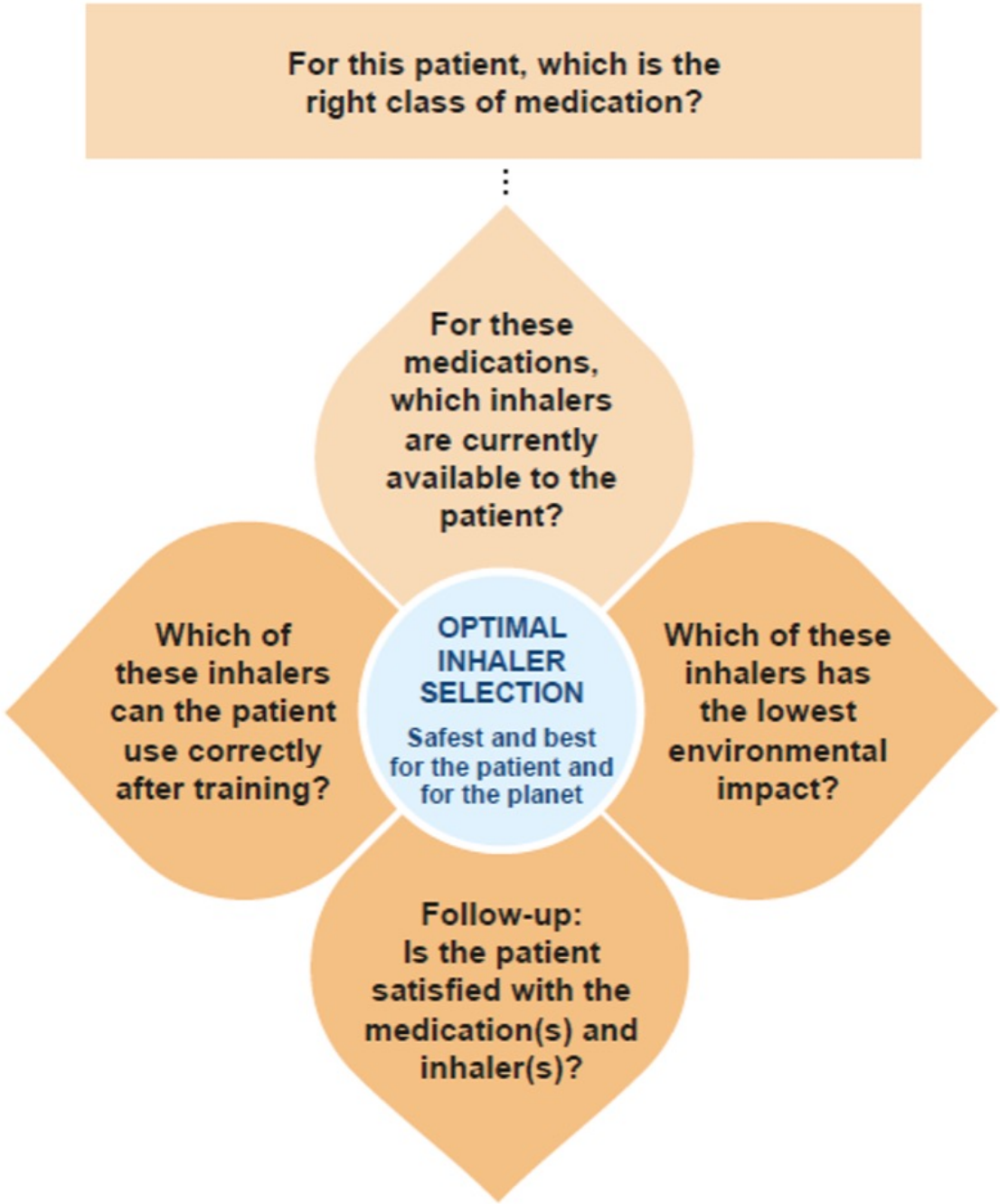
Hui et al, Chest 2009

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!

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



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GINA Global Strategy for Asthma Management and Prevention