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Asthma

Shiraz University Of Medical Science

1401- Spring

Asthma severity, intermittent

- ***Day <= 2 days/ wk,***
- ***Night <= 2/mo***
- ***FEV1>80%***
- ***FEV1/FVC.>85%***

Asthma severity, Mild

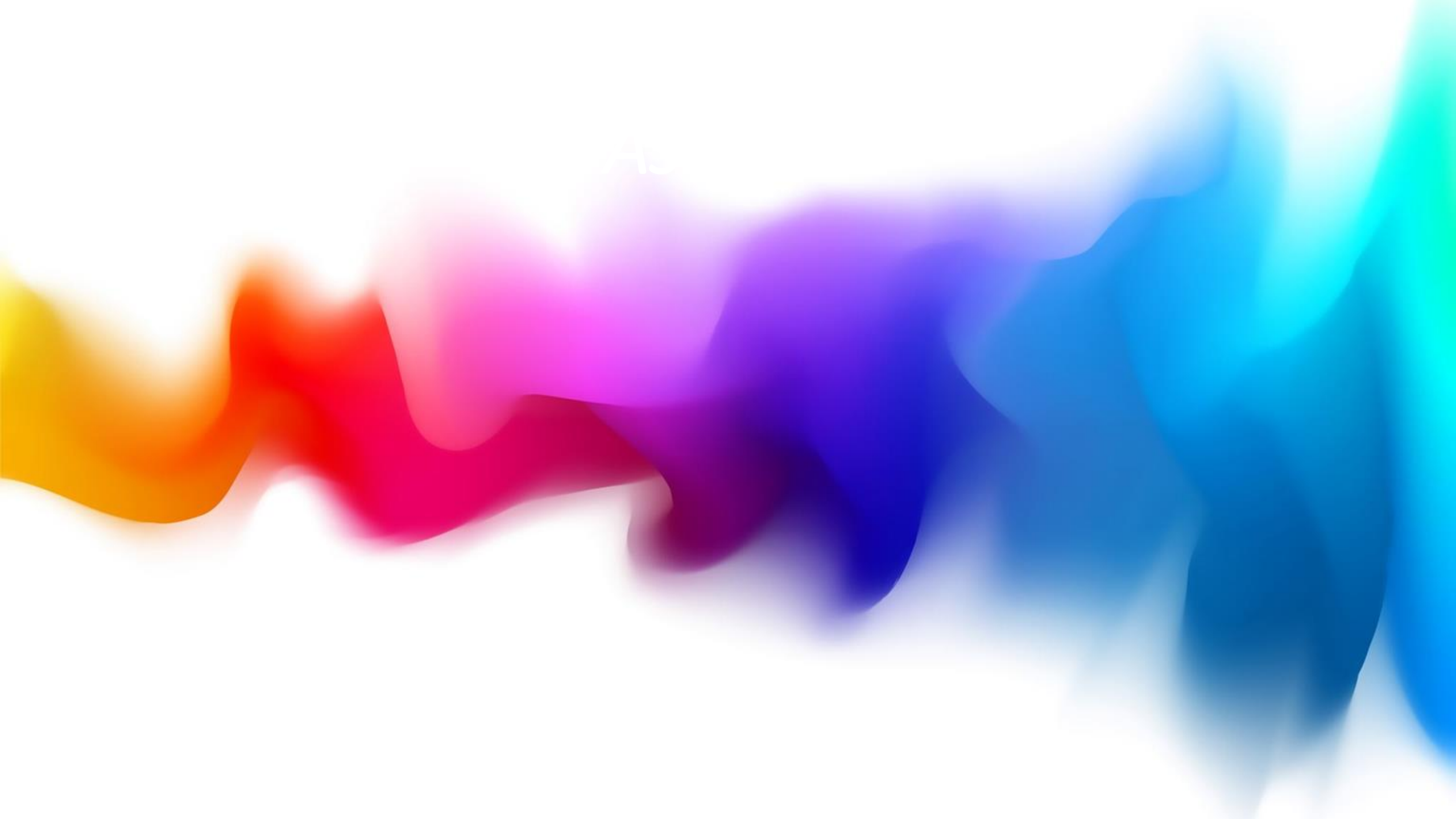
- ***Day > 2 days/ wk,***
- ***Night*** 0-4 y/o : 1-2 /mo
- 5y/o :3-4/mo
- ***Activity : nl***
- ***FEV1/FVC.>80%***

Asthma severity, moderate

- ***Day ; > daily symptom***
- ***Night*** 0-4 y/o : 3-4 /mo
- 5y/o :1/wk
- ***Activity : some limitation***
- ***FEV1 60-80%***
- ***FEV1/FVC : 5-11y/o; 75-80%***
- ***>12y/o***

Asthma severity, sever

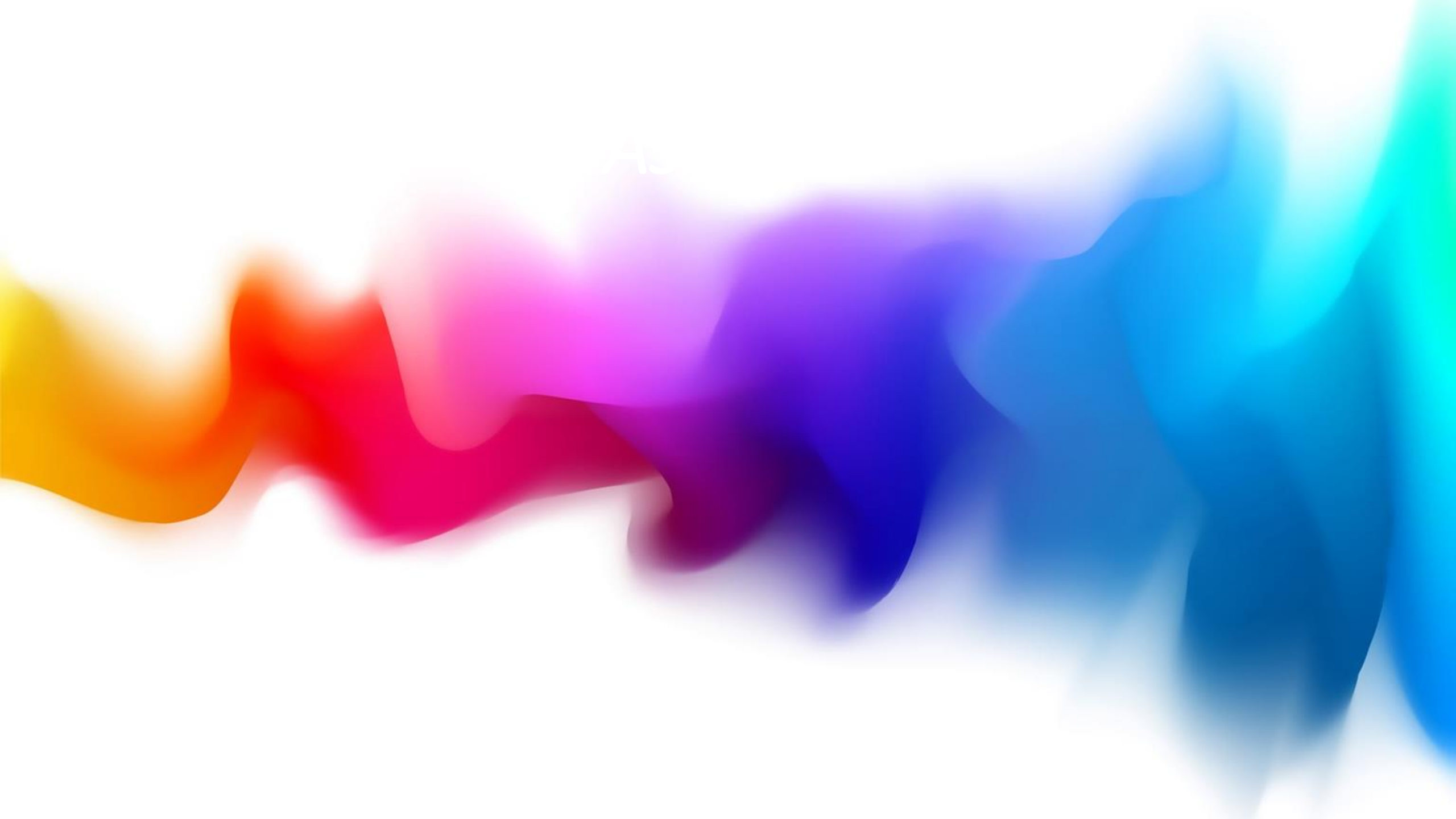
- ***Day > throughout the day***
- ***Night*** 0-4 y/o : 1 /wk
- 5y/o :often
- ***Activity : extreme limitation***
- ***FEV1 <60%***
- ***FEV1/FVC 5-11y/o 75%***
- ***>12y/o***



RISK

- Exacerbation
- ***Intermittent*** : 0-4y/o: 0-1/year,
- >5y/o : 1/y

- ***MILD and more*** :
- 0-4y/o: 2/6mo or
  >=4wheeze /y, more than 1 day with high risk for asthma
- , >5y/o : >= 2/year



Well Controlled

- ***Symptom <= 2/week. 1 in a day***
- ***Night 0-4y/o <=1/mo***
- ***5-11Y/o <=1/mo***
- ***>=12y/o <= 2/mo, , <= 2 days /wk***
- ***Nl activity***
- ***FEV1>80%***
- ***Risk 0-4 y/o 0-1/year***
- ***>5 y/o 0-1/y***

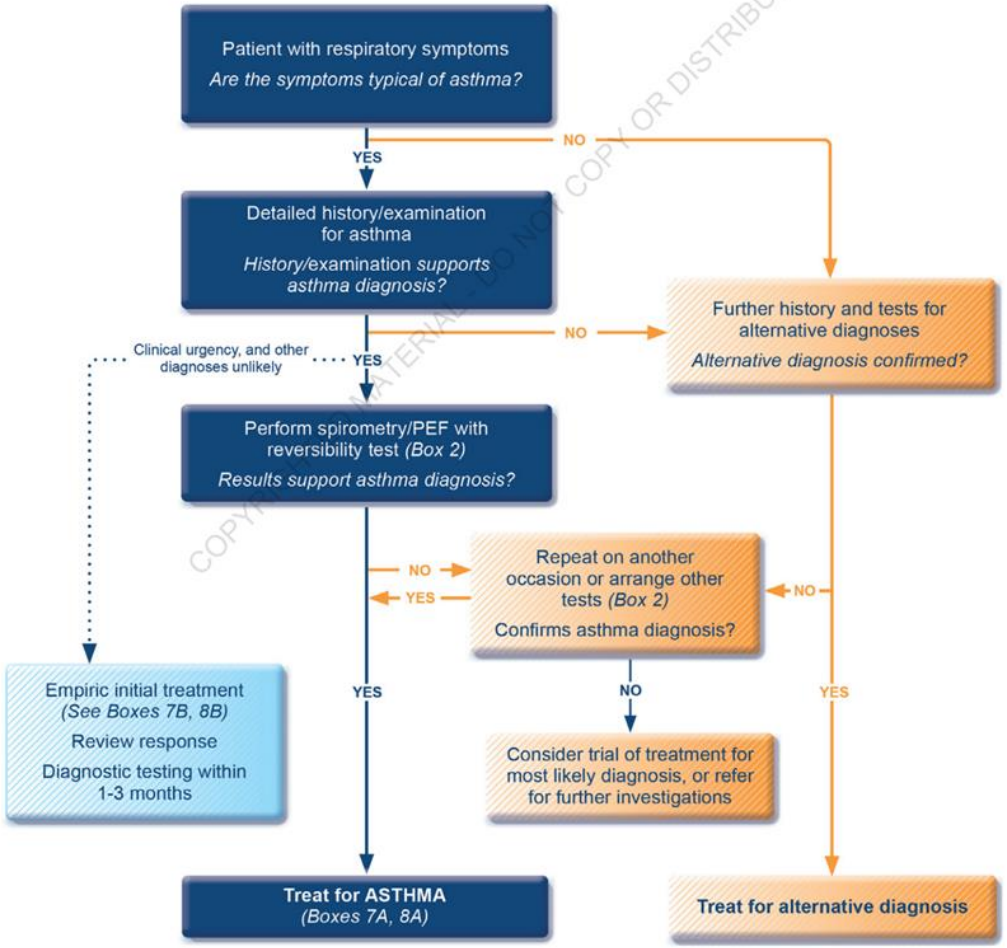
Not Well Controlled

- ***Symptom > 2/week. Or multiple***
- ***Night 0-4y/o >1/mo***
- ***5-11Y/o >= 2/mo***
- ***>=12y/o 1-3/wk, , > 2 days /wk***
- ***Activity: some limitation***
- ***FEV1, 60-80%***
- ***Risk 0-4 y/o 2-3/year***
- ***>5 y/o >2/y***

Poor Controlled

- ***Symptom , throughout the day***
- ***Night , several times***
- ***Activity: extreme limitation***
- ***FEV1, <60%***
- ***Risk 0-4 y/o >3/year***
- ***>5 y/o***

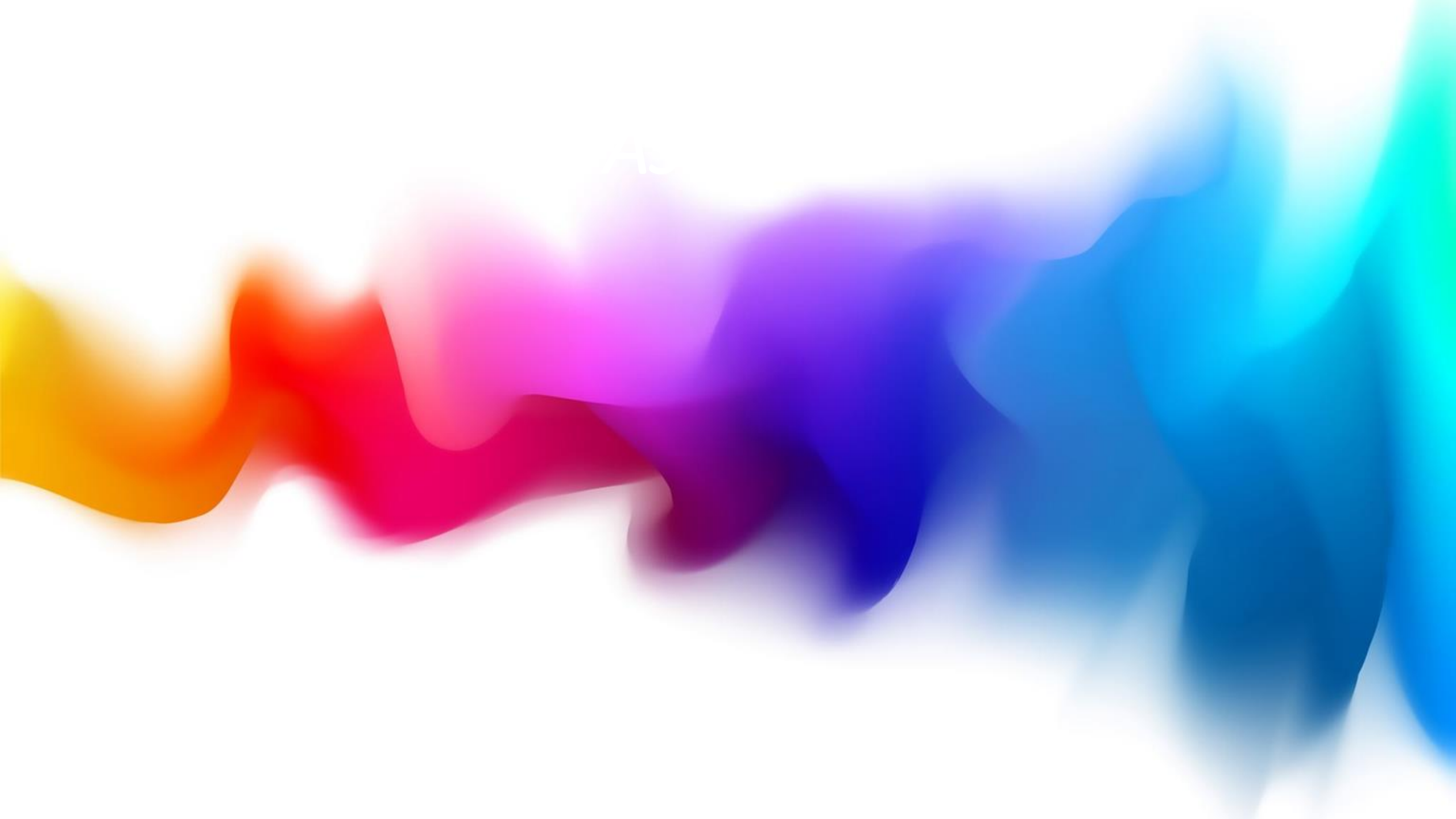
Box 1. Diagnostic flow-chart for asthma in clinical practice



The **diagnosis of asthma** should be confirmed, and the evidence documented in the patient's medical record, preferably before starting

Asthma treatment

- ***Effective treatment***
- ***avoid troublesome symptoms during day and night***
- ***need little or no reliever medication***
- ***have productive physically active lives***
- ***have normal or near normal lung function***
- ***avoid serious asthma flare up***

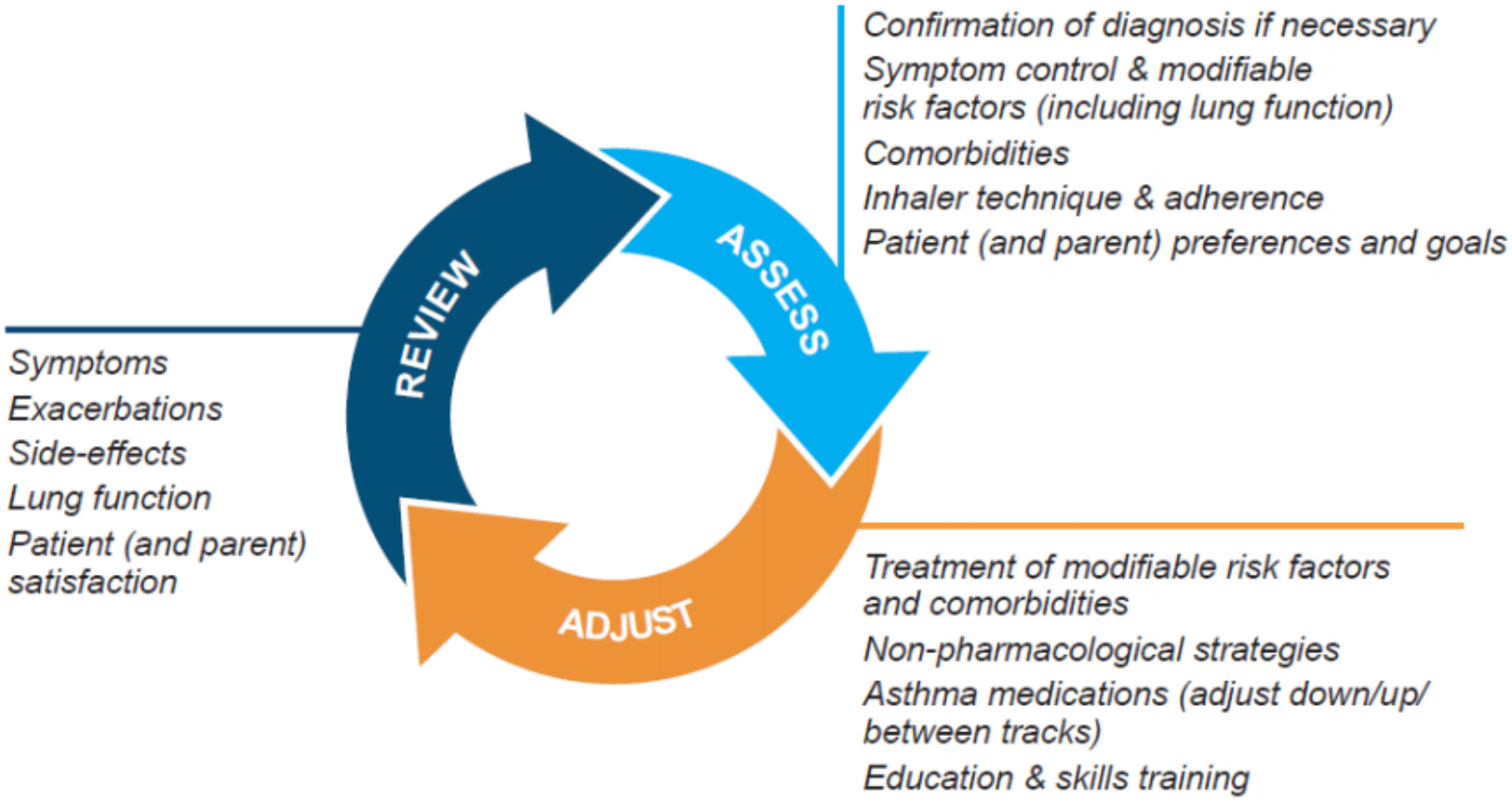


GLOBAL INITIATIVE FOR ASTHMA

ASTHMA MANAGEMENT AND PREVENTION

for adults and children older than 5 years

The aim of asthma management is to prevent exacerbations and asthma deaths, and to relieve and control symptoms



- ***Every patient should have reliever:***

  1) low dose ICS- formoterol (preferred) :decrease attack

  2) SABA

Gina: no recommend SABA without ICS

1-although short term relief ,but no protect from severe attack

2- prolonged use: severe attack

- *GINA; all adults and adolescents : ICS containing inhaler for control and exacerbation*
- *adult and adolescence : mild asthma :*

  as needed low ICS- Formoterol (preferred) or:

  a regular low ICS + as needed SABA.
- *WHY? ; -Decrease death - decrease patient reliance on SABA early in course - SABA only treatment;*

  increase exacerbation ,decrease lung function
- *- regular use of SABA: allergic response+ airway inflammation, decrease response to SABA when is needed*
- *>3 canister in Year: more severe exacerbation*
- *>12 canister in year: death*

- ***For the best outcome ICS containing treatment should be initiated as soon as possible after the diagnosis of asthma is made because:***

- patient even mild asthma can have severe exacerbation

- low dose ICS reduces asthma hospital hospitalization and death

- low dose ICS is very effective in preventing severe exacerbation

- reduce symptom, improve lung function

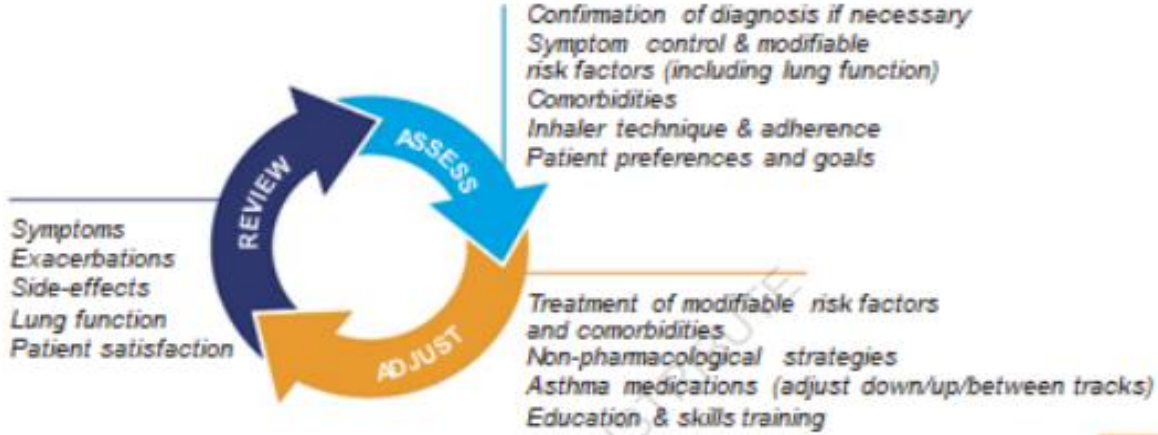
- prevent exercise IA even in asthma

- early treatment with low dose ICS: better lung function after a severe exacerbation in long-term

Box 7A. The GINA asthma treatment strategy – adults and adolescents

Adults & adolescents 12+ years

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



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

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

RELIEVER: As-needed low-dose ICS-formoterol

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

STEP 1	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 phenotypic assessment ± anti-IgE, anti-IL5/5R, anti-IL4R Consider high dose ICS-LABA

RELIEVER: As-needed short-acting β2-agonist

Other controller options for either track

	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; add low dose OCS but consider side-effects*

- ***For most adults or adolescents with asthma: treatment can be started at a step 2 with either***

  -as needed low dose ICS- Formoterol (preferred) or :

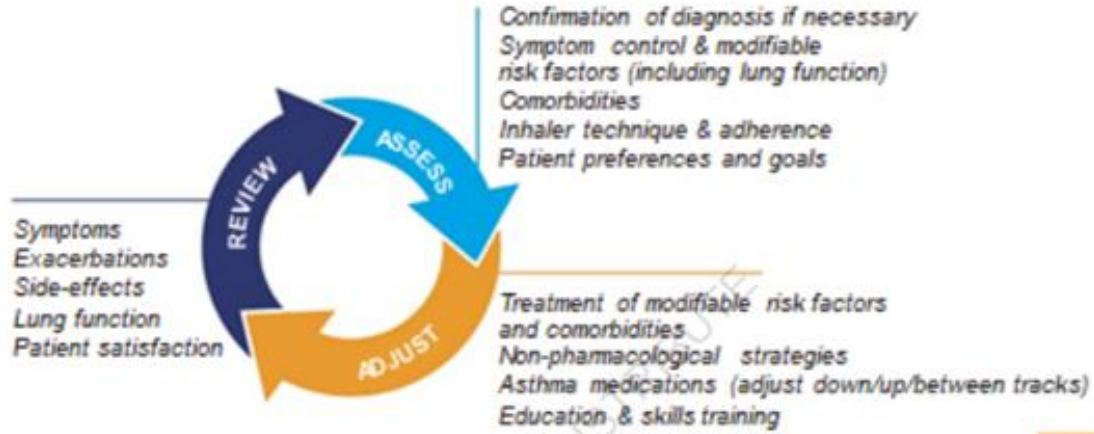
  -regular daily low dose ICS with as needed SABA

- ***Track 1: reliever is as needed low dose ICS- formoterol inhaler***
- ***: when a patient at any treatment is this has asthma symptoms they use low dose ICS-Formeterol in a single inhaler for symptom relief***
- ***in a step 3-5 patients also take ICS-Formoterol as their regular daily treatment***
- ***This is called maintenance and reliever therapy(MART)***
- ***Track2: the reliever is as needed SABA***
- ***This is an alternative approach when track one is not possible or is not preferred by a patient who has no exacerbation on their current therapy***
- ***in a step one the patient takes a SABA and a low dose ICS together for symptoms relief when symptoms occur either in combination inhaler or with the ICS taken right after the SABA***
- ***in step 2-5 SABA alone is used for symptom relief and the patient takes ICS containing controller medication regularly everyday***

Box 7A. The GINA asthma treatment strategy – adults and adolescents

Adults & adolescents 12+ years

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



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

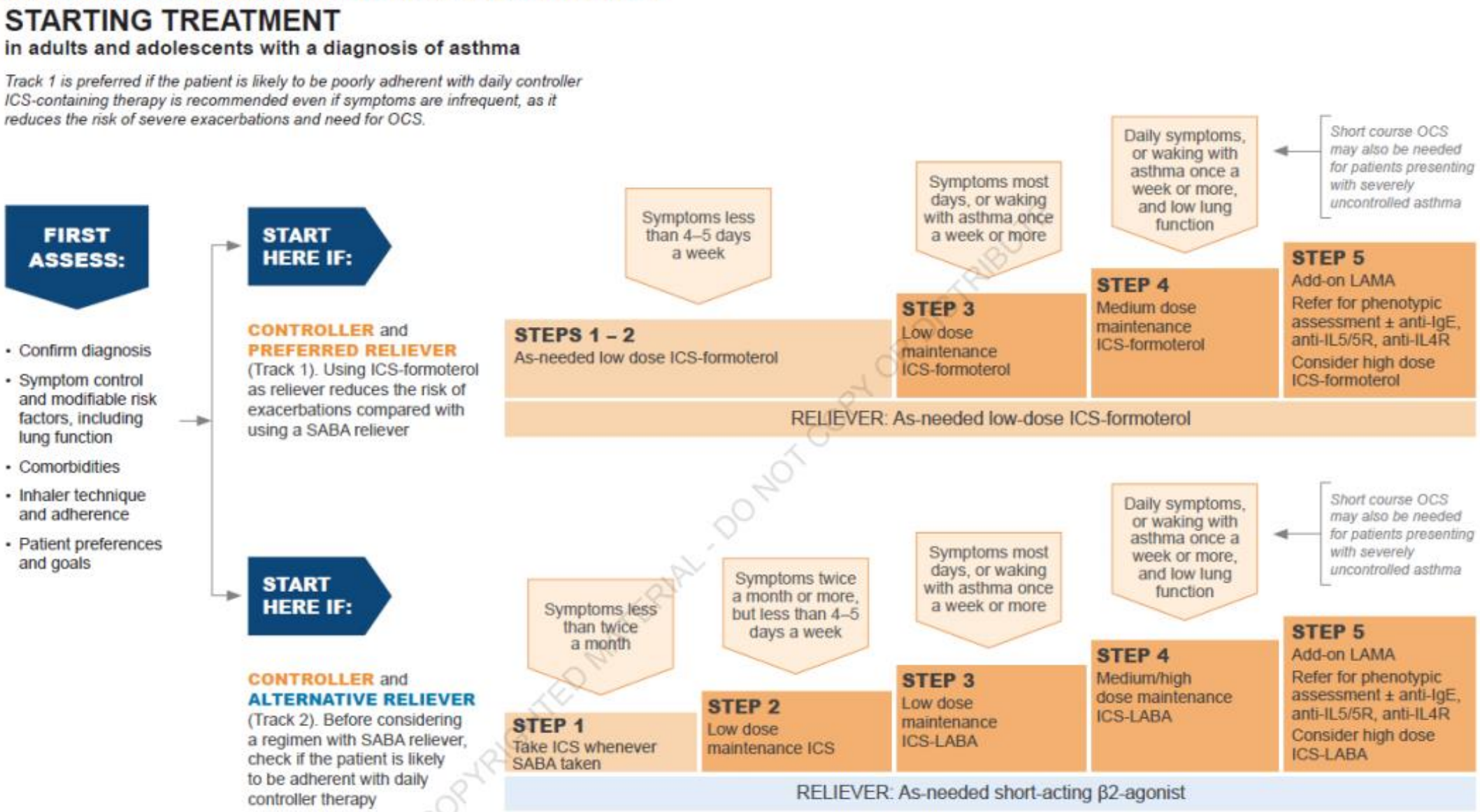
STEPS 1 – 2	STEP 3	STEP 4	STEP 5
As-needed low dose ICS-formoterol	Low dose maintenance ICS-formoterol	Medium dose maintenance ICS-formoterol	Add-on LAMA Refer for phenotypic assessment ± anti-IgE, anti-IL5/5R, anti-IL4R Consider high dose ICS-formoterol
RELIEVER: As-needed low-dose ICS-formoterol			

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

STEP 1	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 phenotypic assessment ± anti-IgE, anti-IL5/5R, anti-IL4R Consider high dose ICS-LABA
RELIEVER: As-needed short-acting β2-agonist				

Other controller options for either track				
	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; add low dose OCS but consider side-effects*

Box 7B. Initial treatment: adult or adolescents with a diagnosis of asthma

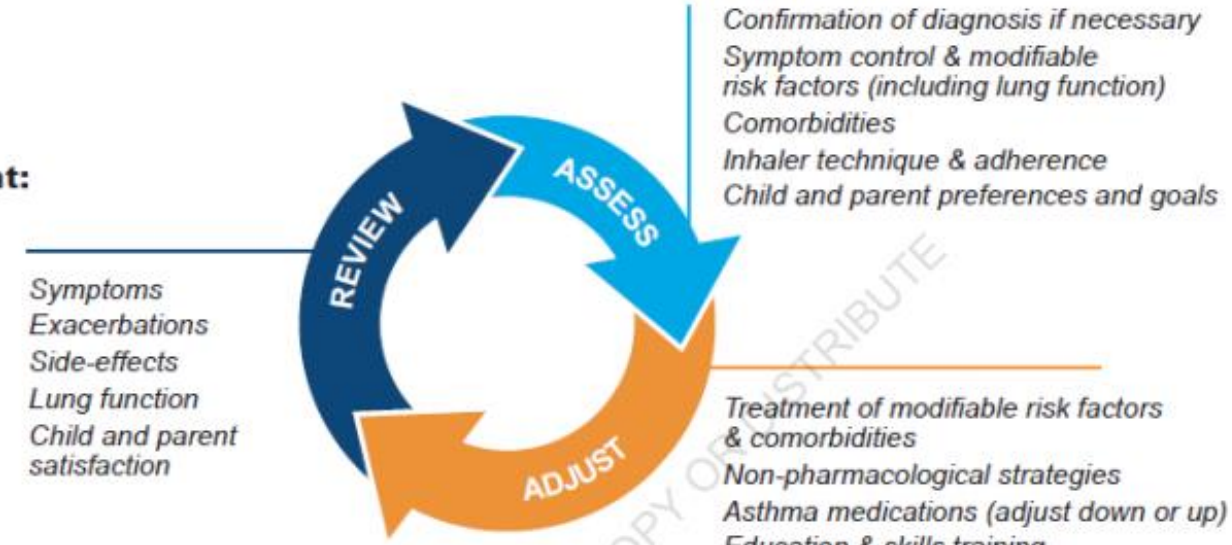


ICS: inhaled corticosteroid; SABA: short-acting beta$_2$-agonist

For initial asthma treatment in children 6–11 years, see Box 8B (p.28). For more details about treatment recommendations including supporting evidence, and clinical advice about implementation in different populations see the full GINA 2021 report (www.ginasthma.org). For more details about Step 5 add-on therapies, see Chapter 3E of the GINA report, or the GINA 2021 Pocket Guide on Difficult to Treat and Severe Asthma, and check eligibility criteria with local payers.

Children 6-11 years

Personalized asthma management:
Assess, Adjust, Review

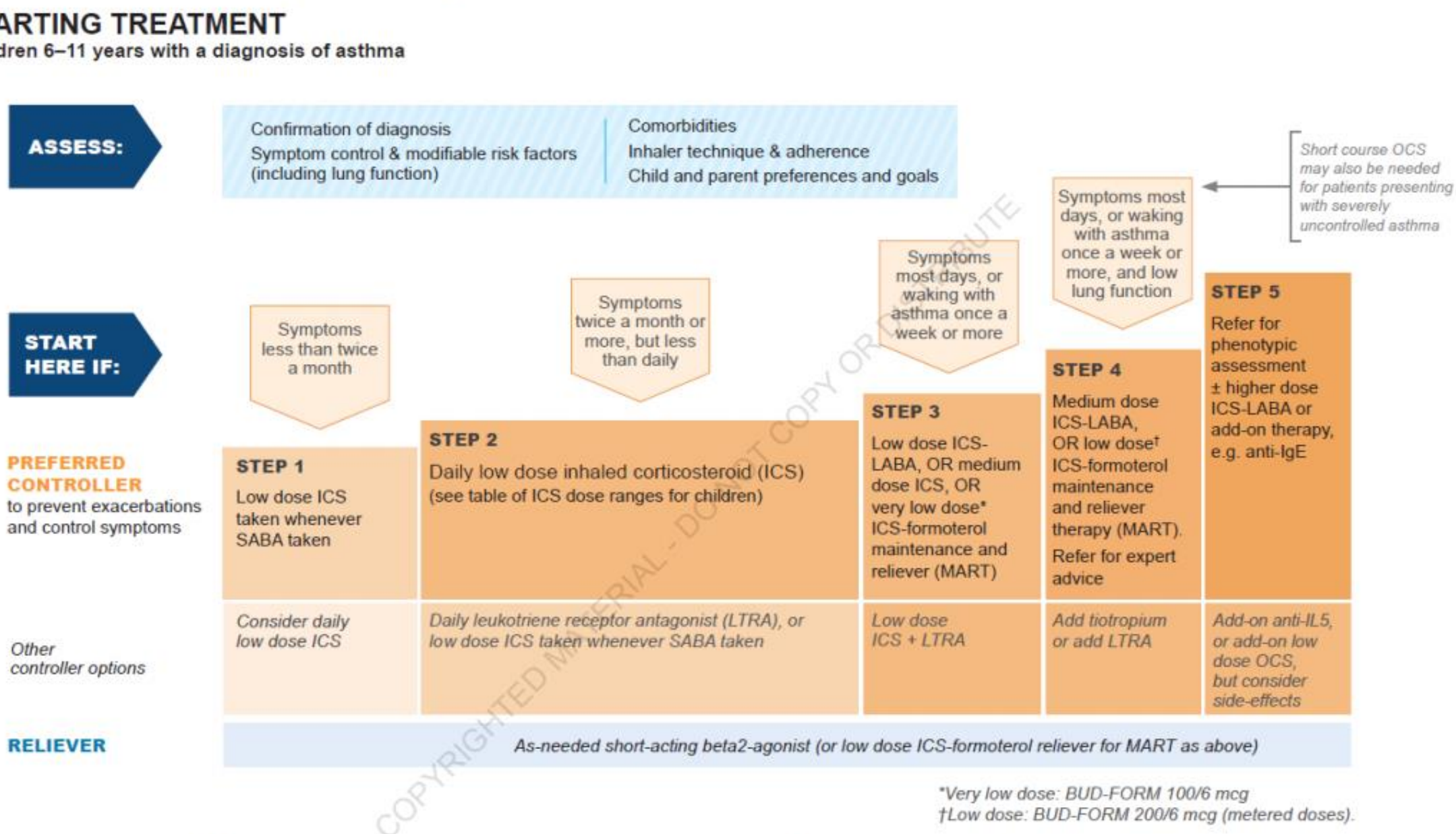


Asthma medication options:
Adjust treatment up and down for individual child's needs

	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 (MART)	Medium dose ICS-LABA, OR low dose† ICS-formoterol maintenance and reliever therapy (MART). Refer for expert advice	Refer for phenotypic assessment ± higher dose ICS-LABA or add-on therapy, e.g. anti-IgE
Other controller options	*Consider daily low dose ICS*	*Daily leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken*	*Low dose ICS + LTRA*	*Add tiotropium or add LTRA*	*Add-on anti-IL5, or add-on low dose OCS, but consider side-effects*
RELIEVER	*As-needed short-acting beta2-agonist (or ICS-formoterol reliever for MART as above)*				

*Very low dose: BUD-FORM 100/6 mcg
†Low dose: BUD-FORM 200/6 mcg (metered doses).

Box 8B. Initial treatment: children 6–11 years with a diagnosis of asthma



associated with an increased risk of local and systemic side-effects.

Adults and adolescents Inhaled corticosteroid	Total daily ICS dose (mcg) Low	Medium	High
BDP (pMDI*, HFA)	200–500	>500–1000	>1000
BDP (DPI or pMDI, extrafine particle, HFA)	100–200	>200–400	>400
Budesonide (DPI or pMDI*, 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*, HFA)	100–250	>250–500	>500
Mometasone furoate (DPI)	Depends on DPI device		
Mometasone furoate (pMDI*, HFA)	200–400		400

Children 6-11 years Inhaled corticosteroid	Total daily ICS dose (mcg) Low	 Medium	 High
BDP (pMDI*, HFA)	100–200	>200–400	>400
BDP (pMDI, extrafine particle, HFA)	50–100	>100–200	>200
Budesonide (DPI)	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*, HFA)	50–100	>100–200	>200
Mometasone furoate (pMDI*, HFA)	100		200

BDP: beclometasone dipropionate; DPI: dry powder inhaler; HFA: hydrofluoroalkane

For patients whose asthma is not well-controlled on a particular treatment, adherence, inhaler technique and comorbidities should be checked before considering a different medication in the same step, or before stepping up.

STEP 1. Preferred treatment for adults and adolescents: low dose ICS-formoterol taken as needed for symptom relief (Track 1)

Step 1 recommendations are for:

- Initial asthma treatment for patients with symptoms less than twice a month and no exacerbation risk factors, a group that is rarely studied
- Step-down treatment for patients whose asthma is well-controlled on Step 2 treatment

- The historic distinction between so-called ‘intermittent’ and ‘persistent’ asthma is arbitrary. With as-needed ICS-formoterol, a large reduction in risk of severe exacerbations was seen compared with as-needed SABA, even in patients with SABA use twice a week or less at baseline.

- It is important to avoid the conflicting messages from the past in which patients were initially told to use SABA for symptom relief but then (despite this treatment being effective from their perspective) they were told that they needed to take a daily controller to reduce their SABA use and prevent exacerbations. Starting treatment with SABA alone trains the patient to regard SABA as their primary asthma treatment.

The usual dose of as-needed budesonide-formoterol in mild asthma is one inhalation of 200/6 mcg (delivered dose 160/4.5) taken whenever needed for symptom relief, or before exercise if needed. The maximum recommended dose in a single day is a total of 72 mcg formoterol (54 mcg metered dose). However, in the mild asthma studies, patients rarely needed this much, and average usage was only 3–4 inhalations per week.

Daily low dose ICS had been suggested by GINA since 2014 in Step 1 to reduce the risk of severe exacerbations. It is no longer recommended as patients with symptoms less than twice a month are unlikely to take ICS regularly, leaving them exposed to the risks of SABA-only treatment.

STEP 2. Preferred treatment for adults and adolescents: low dose ICS-formoterol taken as needed for symptom relief (Track 1)

As-needed low dose ICS-formoterol taken for symptom relief: the evidence to date in mild asthma is with low dose budesonide-formoterol.

- Compared with as-needed SABA alone, as-needed ICS-formoterol reduces severe exacerbations by 60-64%
- Compared with daily low dose ICS, as-needed budesonide-formoterol reduces severe exacerbations to the same or greater extent as daily low dose ICS, with a very small or no difference in symptom control.

Alternative Step 2 treatment for adults and adolescents: daily low dose ICS plus as-needed SABA (Track 2)

There is a large body of evidence from RCTs and observational studies showing that the risks of severe exacerbations, hospitalizations and mortality are substantially reduced with regular low dose ICS. Symptoms and exercise-induced bronchoconstriction are also reduced. Severe exacerbations are halved even in patients with symptoms 0–1 days a week.

Other controller options at Step 2

- *Low dose ICS taken whenever SABA is taken,* either in combination or

- *Leukotriene receptor antagonists (LTRA)* are less effective than regular ICS, particularly for preventing exacerbations. There is a boxed warning about the risk of serious mental health effects with montelukast.

For purely seasonal allergic asthma, evidence is needed. Current advice is to start ICS at the start of the allergen season and cease 4 weeks after end of exposure.

Step 2 treatment for children 6-11 years

The preferred controller option for children at Step 2 is regular low dose ICS with as-needed SABA (see Box 9, p.30 for ICS dose ranges in children). Other options include taking low dose ICS whenever SABA is taken, using separate inhalers. Daily LTRA is less effective for exacerbation reduction.

STEP 3. Preferred treatment for adults and adolescents: low dose ICS-formoterol maintenance and reliever therapy (Track 1)

Before considering a step-up in treatment, check adherence, inhaler technique and comorbidities.

The preferred Step 3 option is low dose ICS-formoterol as both maintenance and reliever treatment (MART). In patients with or without a history of severe exacerbations, this reduces the risk of severe exacerbations compared with maintenance ICS-LABA or higher dose ICS or conventional best practice with as-needed SABA, with a similar level of symptom control.

The maximum recommended dose of ICS-formoterol in a single day is a *total* of 48 mcg formoterol for BDP-formoterol (36 mcg delivered dose), and 72mcg formoterol for budesonide-formoterol (54 mcg delivered dose).

Alternative Step 3 treatment for adults and adolescents: maintenance low dose ICS-LABA plus as-needed SABA (Track 2)

For patients whose asthma is uncontrolled on low dose ICS, low dose combination ICS-LABA reduces severe exacerbations by about 20%, and lung function is higher, with little difference in reliever use.

Other controller options for adults and adolescents: Medium dose ICS, or low dose ICS plus LTRA. For adult patients with rhinitis who are allergic to house dust mite, consider adding sublingual immunotherapy (SLIT), provided FEV_1 is >70% predicted.

Preferred Step 3 treatment for children 6-11 years

After checking inhaler technique and adherence, and treating modifiable risk factors, there are three preferred options for children:

- Medium dose ICS with as-needed SABA
- Low dose ICS-LABA, with as-needed SABA. Combination ICS-LABA is non-inferior to ICS alone for severe exacerbations, with no difference in symptom control or reliever use
- Maintenance and reliever therapy with a very low dose of budesonide-formoterol (100/6 mcg once-daily, 80/4.5 mcg delivered dose) showed a large reduction in severe exacerbations in children compared with the same dose of ICS-formoterol or higher dose of ICS.

Individual children's responses vary, so each of these options may be tried before considering a step-up.

STEP 4. Preferred treatment for adults and adolescents: *Medium* ***dose ICS-formoterol as maintenance and reliever therapy (Track 1)***

At a group level, most benefit from ICS is obtained at low dose, but individual ICS responsiveness varies, and some patients whose asthma is uncontrolled on Step 3 treatment despite good adherence and correct technique may benefit from increasing the maintenance ICS dose to medium.

For MART, the maintenance dose can be increased to medium (e.g. double the number of inhalations) but the reliever is still low dose ICS-formoterol. Maximum recommended dose in a single day is the same as in Step 3.

Alternative Step 4 treatment for adults and adolescents: medium or high dose ICS-LABA with as-needed SABA (Track 2)

Some patients whose asthma is uncontrolled or who have frequent exacerbations on low dose ICS-LABA despite good adherence and correct technique may benefit from medium dose ICS-LABA, if maintenance and reliever therapy is not available.

Other Step 4 controller options for adults and adolescents include add-on LAMA for patients ≥18 years (≥6 years for tiotropium by mist haler) in separate or combination ('triple') inhalers. This modestly improves lung function, and sometimes exacerbations, but not symptoms. Before considering add-on LAMA for patients with exacerbations, increase ICS dose to at least medium, or switch to maintenance and reliever therapy. For adult patients with rhinitis and asthma who are allergic to house dust mite, consider adding SLIT, provided FEV_1 is >70% predicted.

Preferred Step 4 treatment for children (6-11 years): Options include increasing the dose of maintenance ICS-LABA to medium; for maintenance and reliever therapy, the maintenance dose may be increased to 100/6 mcg twice daily (metered dose 80/4.5 mcg). If asthma is not well-controlled with medium dose ICS, continue controller, and refer for expert advice.

STEP 5. Refer for phenotypic investigation ± add-on treatment

Patients with uncontrolled symptoms and/or exacerbations despite Step 4 treatment should be assessed for contributory factors, have their treatment optimized, and be referred for expert assessment including severe asthma inflammatory phenotype, and potential add-on treatment. The **GINA Pocket Guide on Difficult to Treat and Severe Asthma v2.0 2019** provides a decision tree and practical guide for assessment and management in adults and adolescents. Sputum-guided treatment, if available, improves outcomes in moderate-severe asthma.

Add-on treatments in Step 5 include LAMA for patients ≥18 years (≥6 years for tiotropium) in separate or combination ('triple') inhalers, anti-IgE (SC omalizumab, ≥6 years) for severe allergic asthma, and anti-IL5 (SC mepolizumab, ≥6 years, or IV reslizumab, ≥18 years) or anti-IL5R (SC benralizumab, ≥12 years) or anti-IL4R (SC dupilumab, ≥12 years) for severe eosinophilic asthma. See glossary (p.46) and check local eligibility criteria for specific add-on therapies. Add-on azithromycin three days/week reduces exacerbations, but antibiotic resistance increases. There is no evidence about initiating MART in patients on Step 5 add-on treatment, but for a patient on MART, switching the reliever back to SABA may increase exacerbation risk.

Other options: Some patients may benefit from low dose OCS but long-term systemic side-effects are common and serious.

Stepping up asthma treatment

Asthma is a variable condition, and periodic adjustment of controller treatment by the clinician and/or patient may be needed.

- *Sustained step-up (for at least 2–3 months)*: if symptoms and/or exacerbations persist despite 2–3 months of controller treatment, assess the following common issues before considering a step-up
  - incorrect inhaler technique
  - poor adherence
  - modifiable risk factors, e.g. smoking
  - are symptoms due to comorbid conditions, e.g. allergic rhinitis
- *Short-term step-up (for 1–2 weeks)* by clinician or by patient with written asthma action plan (p.42), e.g. during viral infection or allergen exposure
- *Day-to-day adjustment by patient* with as-needed low dose ICS-formoterol for mild asthma, or ICS-formoterol as maintenance and reliever therapy. This is particularly effective in reducing severe exacerbations.

- *A stepping down when asthma is well controlled after 3 months*
- *find the lowest treatment that control asthma and minimum side effects*
- *appropriate time(no URI, no travel, no pregnancy)*
- *risk factor*
- *step down: decrease ICS 25 to 50% at 2 -3 months interval*
- *if asthma is well controlled then: as needed low dose ICS-Formeterol is a step down option*
- *do not completely stop ICS in adults or adolescence with asthma unless this is needed temporary to confer their diagnosis of asthma*

Stepwise approach in 5 y-o and younger

Step 2	***step3***	***step 4***
• ** ***dialy low dose ICS***	****double low dose ICS***	****continue controller***
• *LTA, intermittent ICS*	*low ICS+LA*	*LTA,add intermittent ICS*
• ***Reliever SABA***……		
• ***Infrequent viral wheeze***	3 ***attack /y-***	
	not asthma, but wheeze every 6- wks	

Advise on asthma in covid-19 pandemic

- ***not increase risk of infection or severe covid-19 in well controlled asthma but increase in person who receives oral corticosteroid for asthma***
- ***in 2020 decrease in asthma exacerbation because of hand washing ,mask, physical distance***
- ***advised to continue ICS and OCS if prescribed***
- ***very dangerous to stop the OCS suddenly***
- ***avoid nebulizer because of risk of transmission of infection to health worker and patient***
- ***avoid spirometry during pandemic***
- ***covid vaccination***
- ***influenza vaccination***