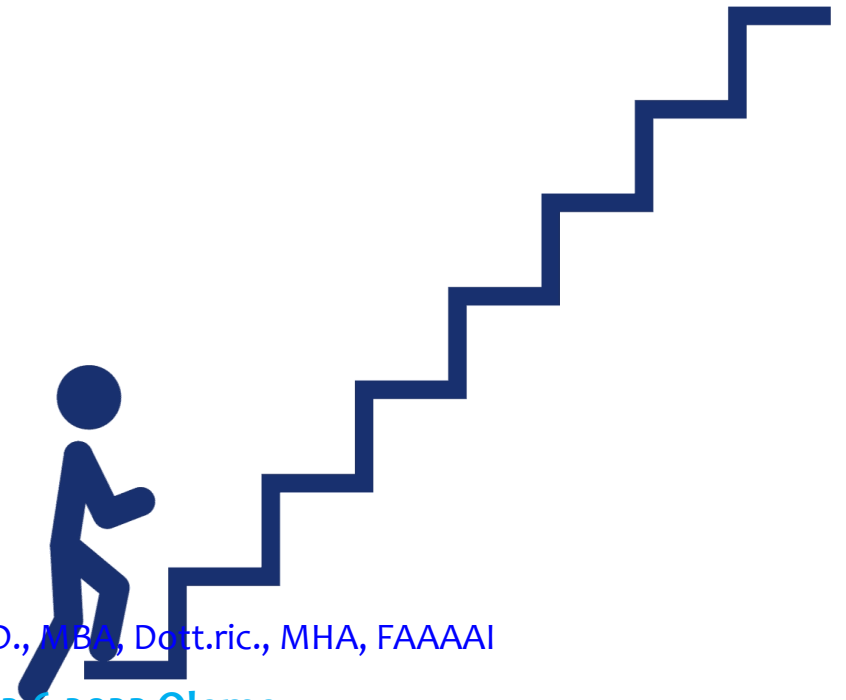


# REMISIA

*ako nový (a dosiahnuteľný)  
cieľ v liečby bronchiálnej astmy*

prof. MUDr. Mgr. **Miloš Jeseňák**, PhD., MBA, Doct.ric., MHA, FAAAAI

Setkání mladých alergológů a pneumológů – 1.-3.6.2023 Olomou



# Vyhlásenie o potenciálnom konflikte záujmov

Člen Advisory board	Novartis • Abbvie • Takeda • Merck Sharp & Dohme • Chiesi • Pfizer • ALK • Stallergen Greer • Kalvista • SOBI • Moderna • AstraZeneca
Medicínsky konzultant	Novartis • Abbvie • Takeda • Merck Sharp & Dohme • CSL Behring • SOBI • ALK • Imunoglukan • AstraZeneca
Spolupráca na výskumných úlohách	Novartis • Abbvie • Takeda • Pharming • BioCryst • Imunoglukan • Octapharma
Iná spolupráca (prednáška, články)	Novartis • BerlinChemie Menarini • Abbvie • Takeda • MerckSharp & Dohme • ALK • Stallergenes Greer • Imunoglukan • CSL Behring • Moderna • Pfizer • Chiesi • Worwag • Schwabe • IBSA Slovakia • Angelini • Glenmark • Zentiva • Sanofi

Príjem peňažného alebo nepeňažného plnenia v príslušnom kalendárnom roku

**Táto prednáška bola podporená spoločnosťou Chiesi Slovakia s.r.o.**

Účelom prednášky nie je reklama liekov.

Jej účelom je výlučne zdieľanie výsledkov klinických štúdií, výmena skúseností z klinickej praxe a podpora odbornej medicínskej diskusie.

# THE ROYAL SOCIETY OF MEDICINE



# Bronchiálna astma

*Dva základné piliere patogenézy*

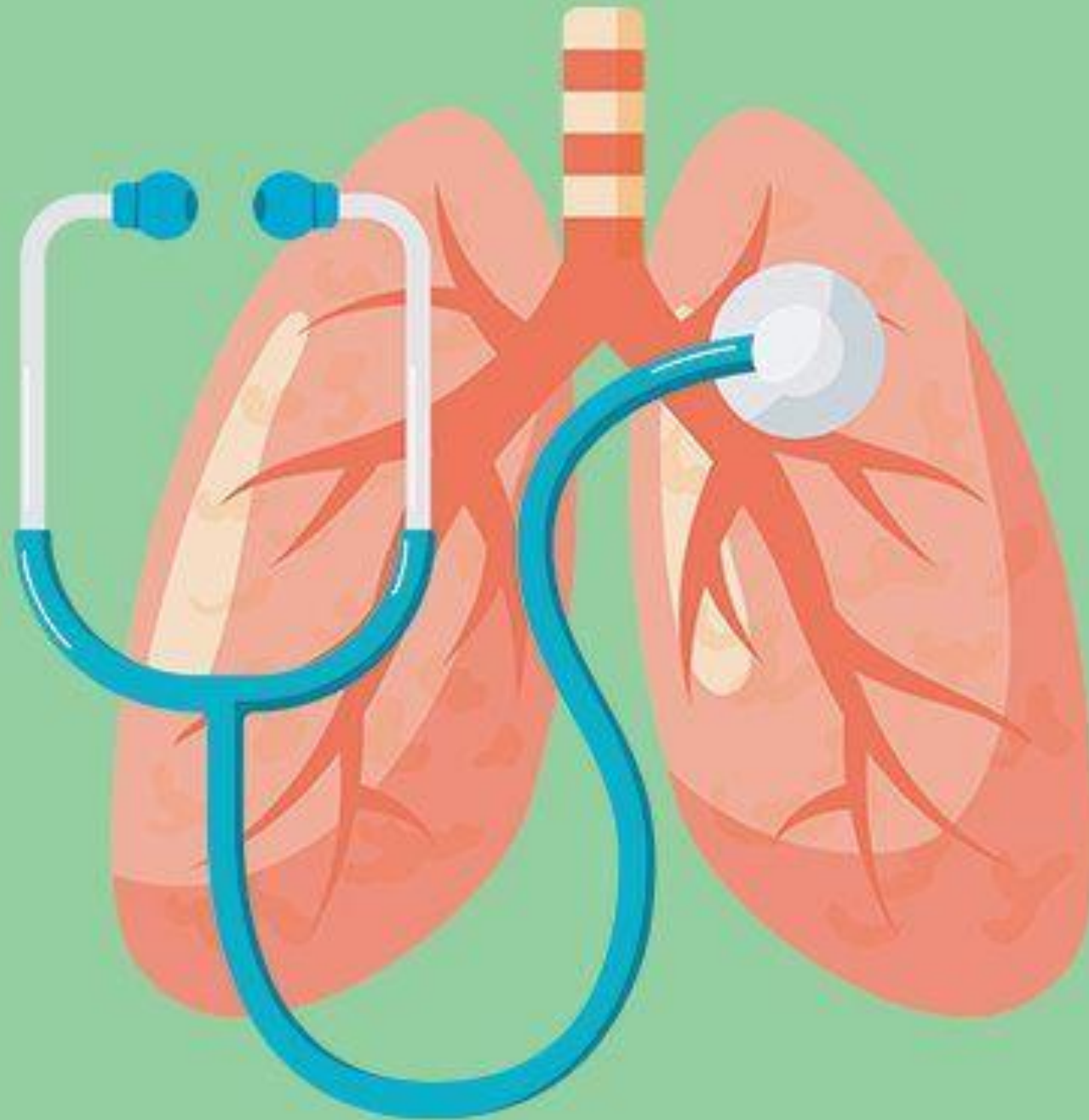


**Chronický zápal**  
v dýchacích cestách  
(malé a stredné DC)

**Bronchiálna**  
**hyperreaktivita**  
(špecifická, nešpecifická)

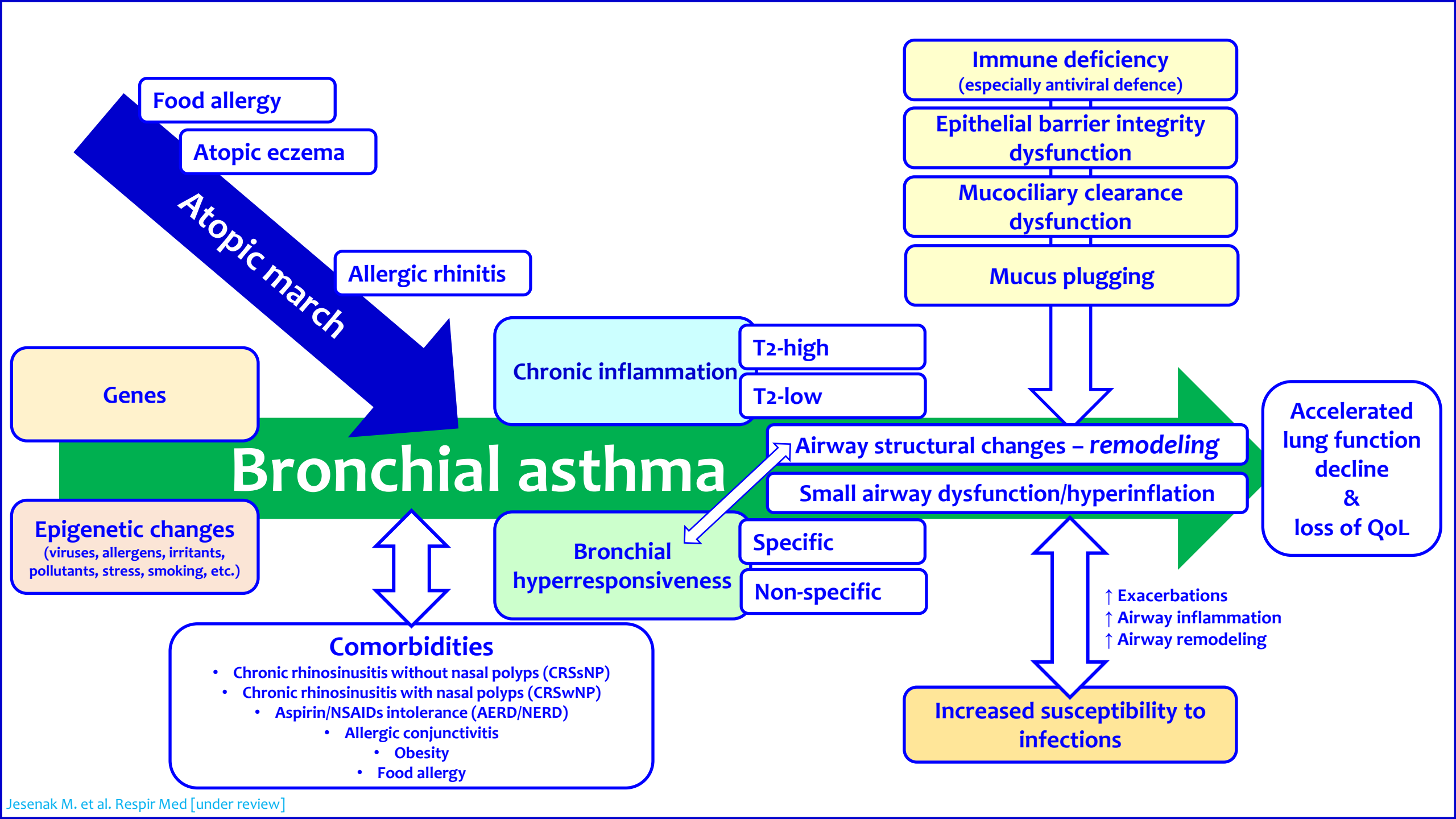
**10%**

**dospelej  
populácie**

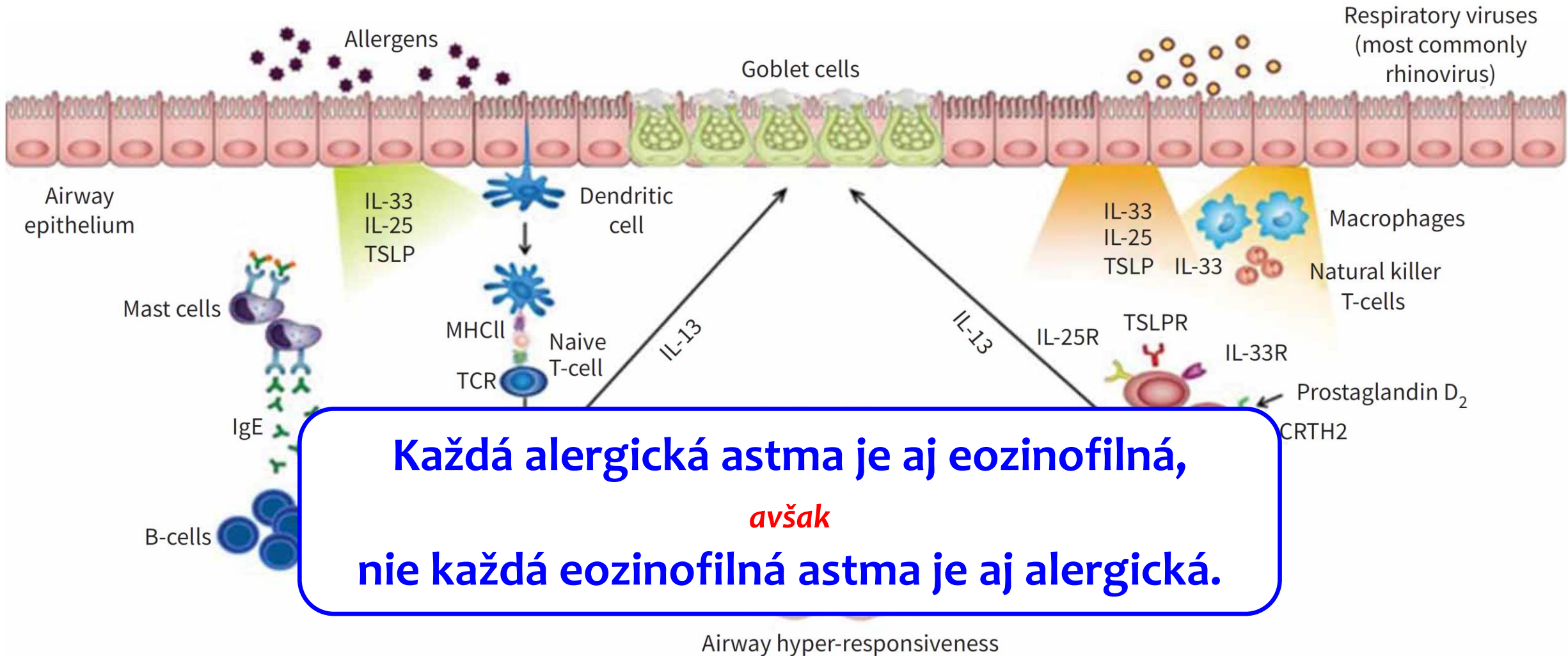


**~6%**

**t'ážká  
astma**



# Ťažká bronchiálna astma mechanizmy

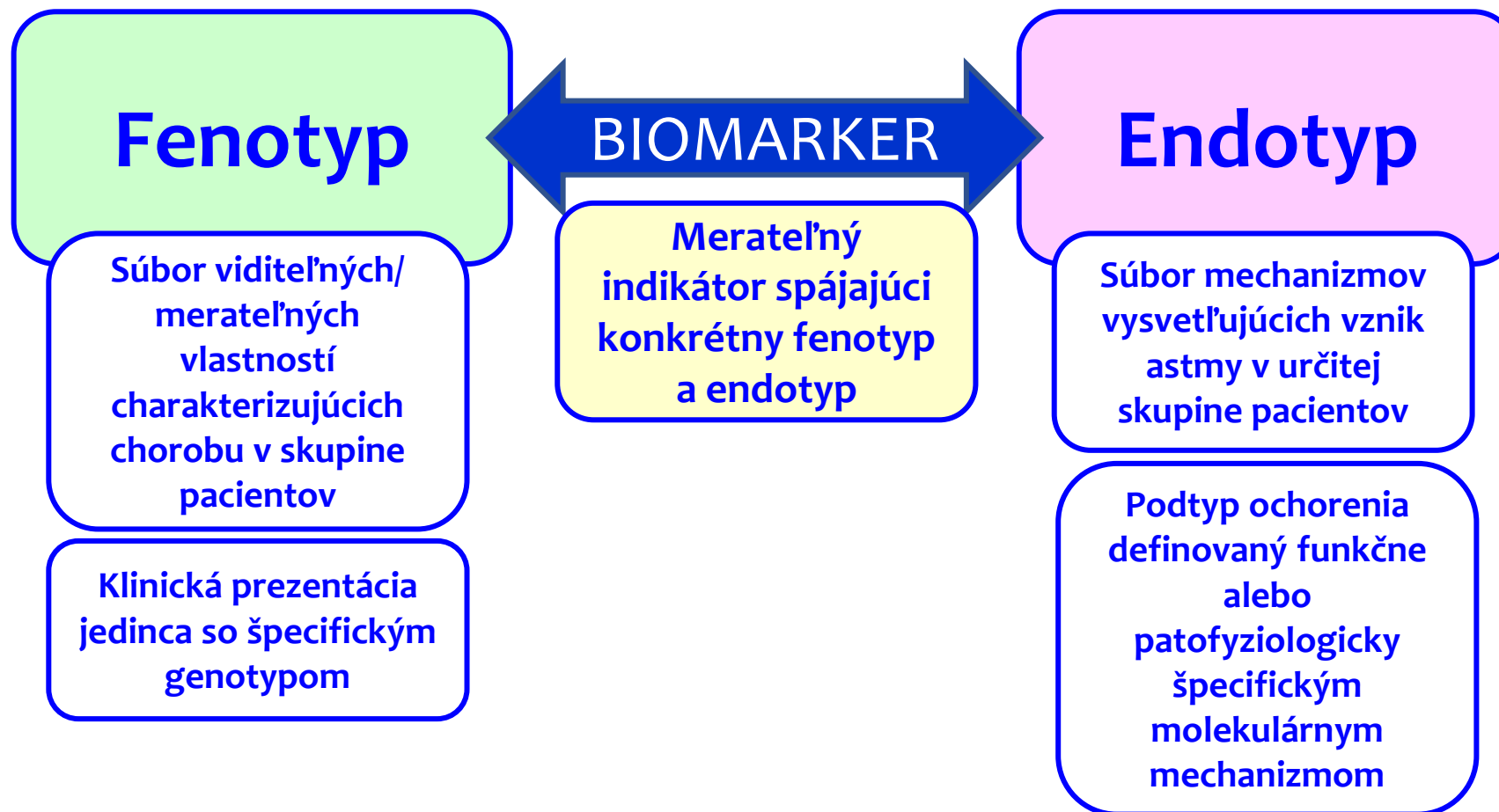


**Alergický eozinofilný zápal**

**Nealergický eozinofilný zápal**

# Bronchiálna astma

## Nomenklatúra a kľúčové termíny



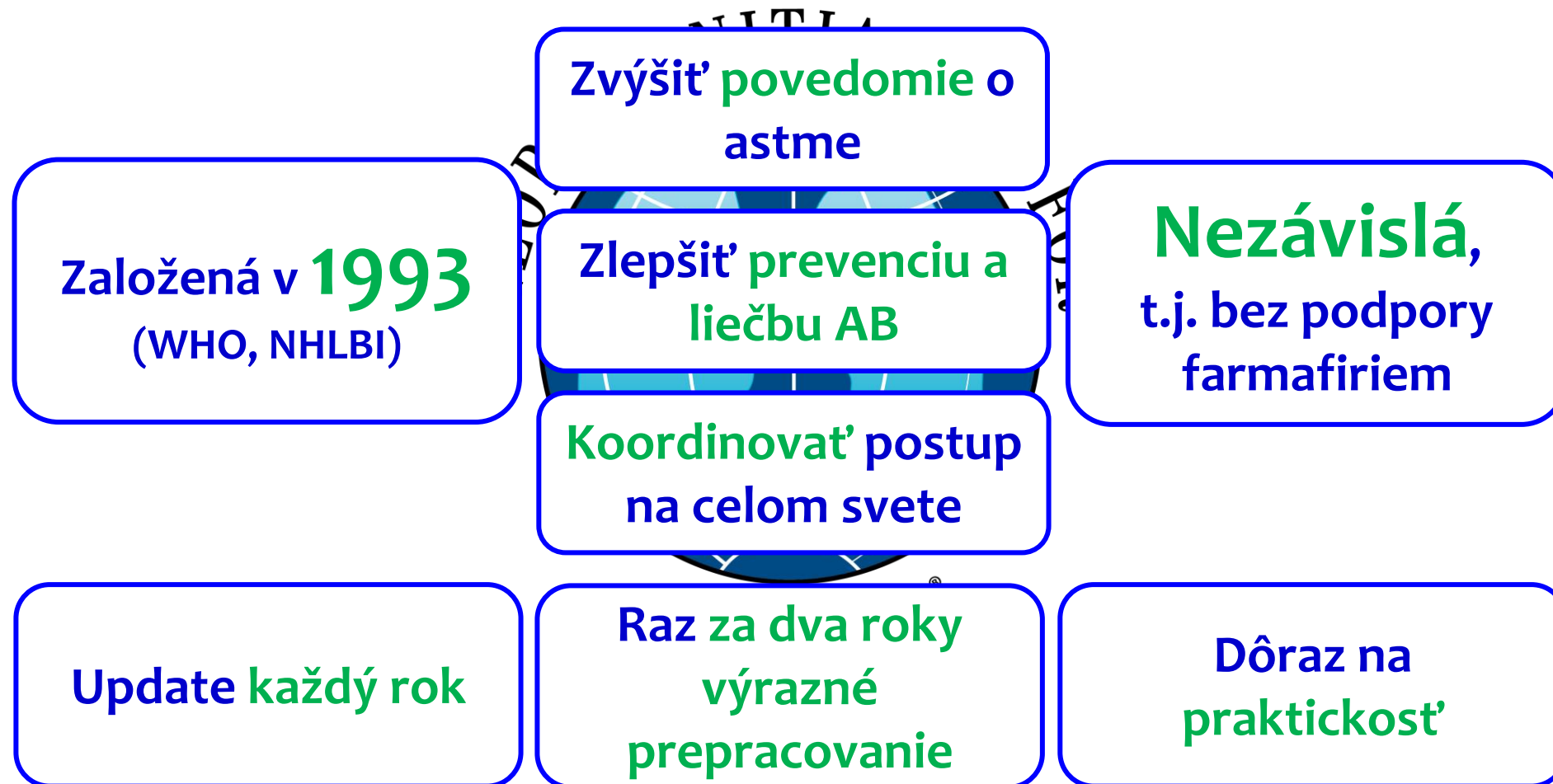




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FOR ASTHMA**

# Astma a GINA 2021

## Zopár zaujímavostí z histórie



# GINA =

globálna a komplexná stratégia  
*pre manažment astmy*

Založená na EBM

Adaptácia na  
lokálne podmienky

Modifikovaná  
podľa dostupnosti  
liekov

**PLEASE NOTE**

**Pozn.: postupy odporúčané  
v GINA **nemusia korešpondovať**  
*s SPC prípravkov***

# GINA

**nerozlišuje** medzi  
*intermitentnou &*  
*ľahkou perzistujúcou*  
*astmou*

# GINA 2023

**dôraz na dôslednosť pri**  
***stanovení iniciálnej dg. astmy***

Vylúčenie iných  
podobných stavov

Určenie komorbidít

Stanovenie  
fenotypu/endotypu

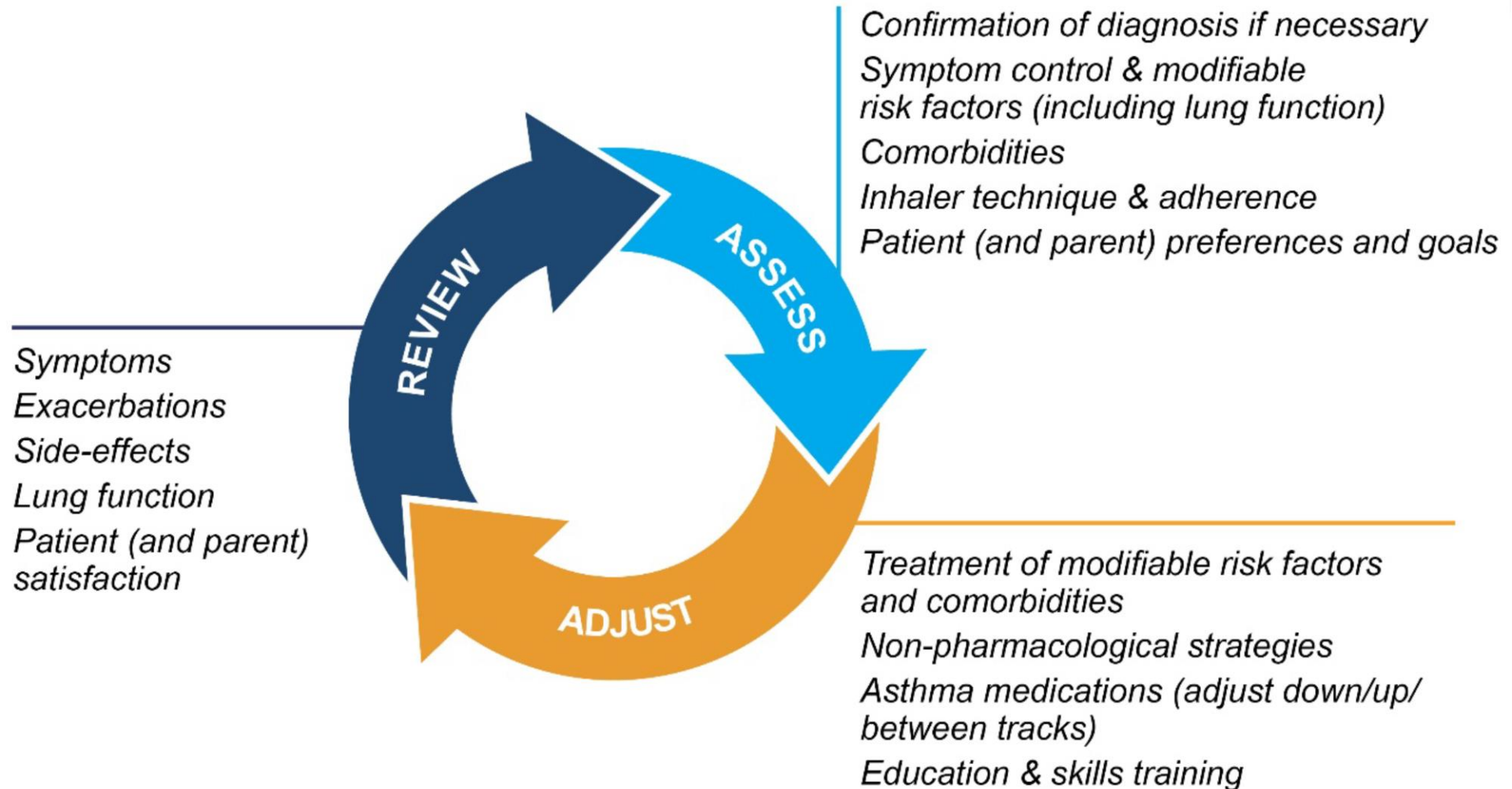
# Bronchiálna astma

## Ciele liečby



# Astma a GINA 2023

## Základný princíp





# Bronchial asthma

## *New challenges and aims*

Age

Course of disease

Structural changes

## Early treatment intervention:

Halt the  
disease  
progression

↑ likelihood to  
achieve  
disease  
remission

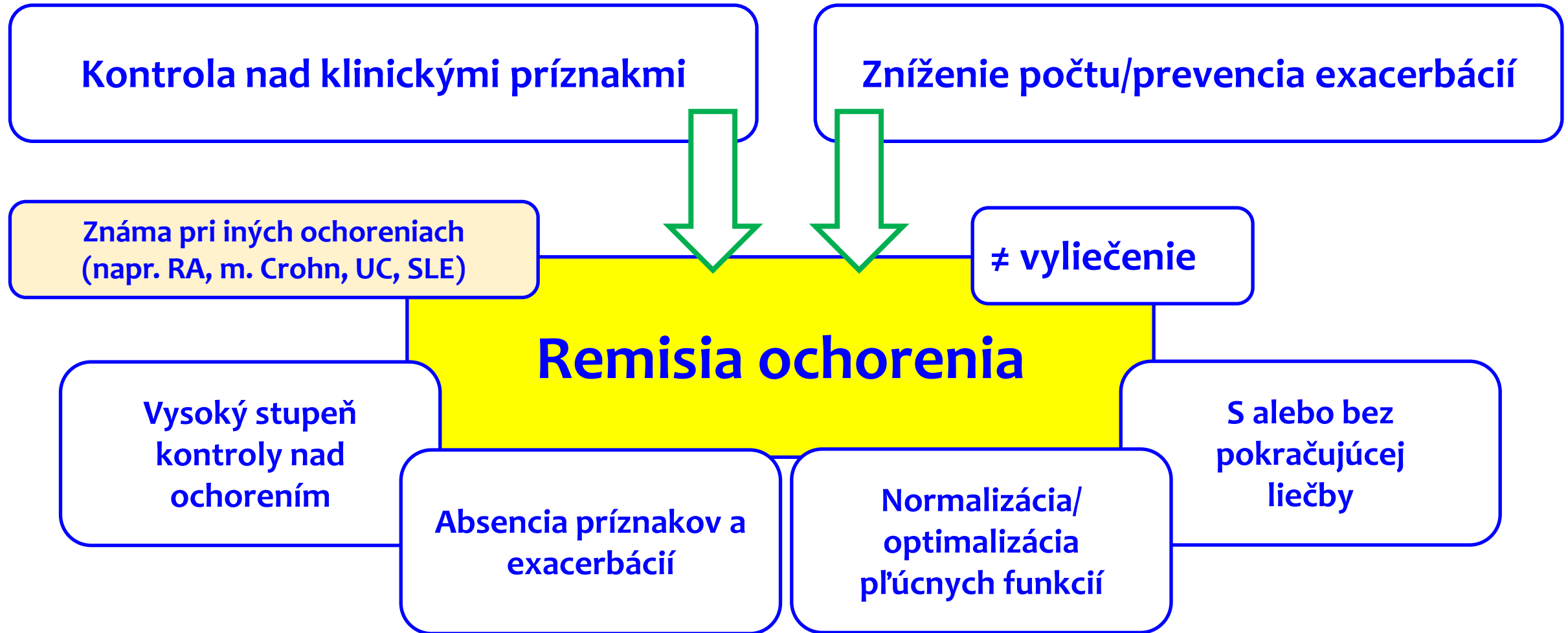
↑ QoL

Improve lung  
functions

Revert  
remodeling  
changes

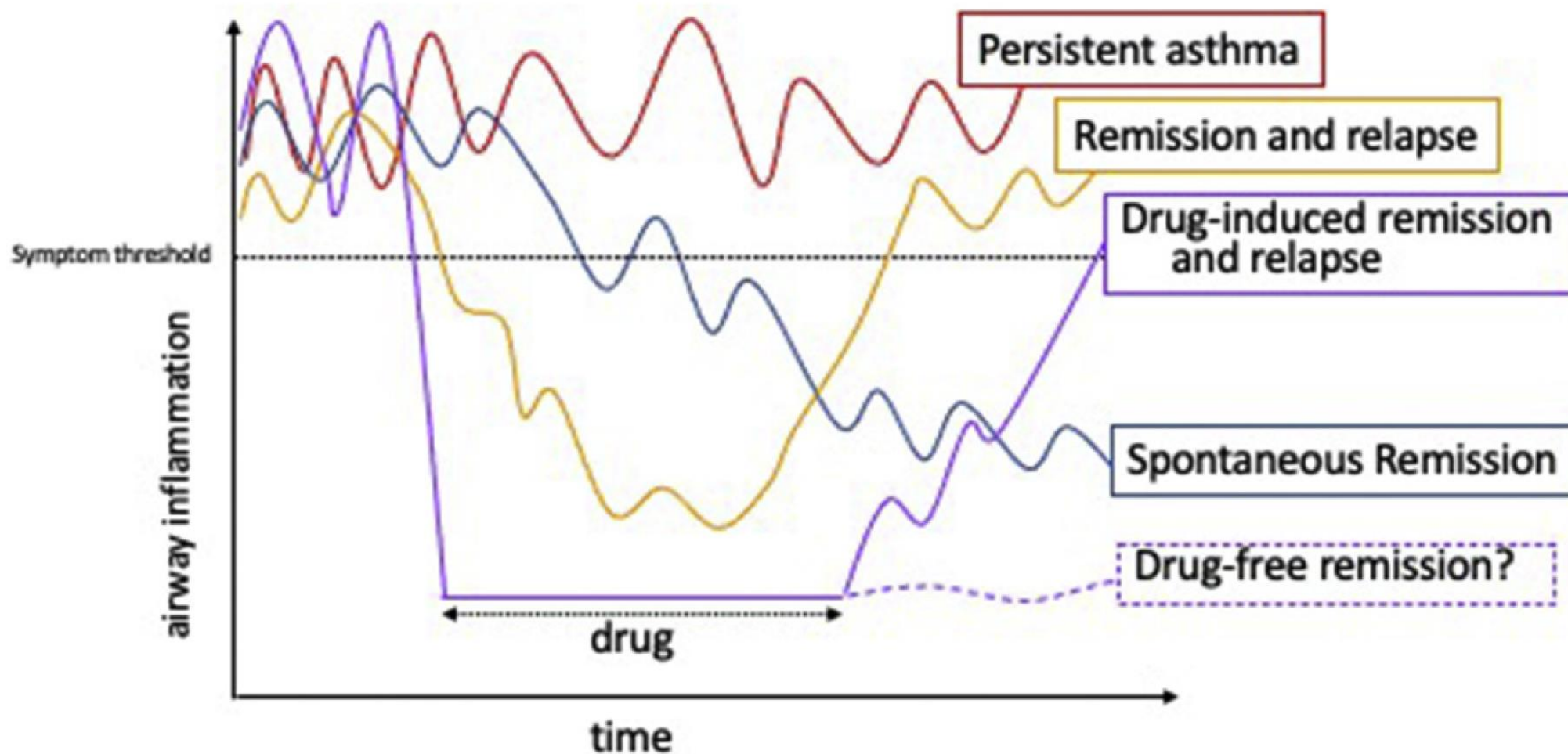
# Bronchiálna astma

## Zameranie liečby



# Bronchiálna astma

*Je možné dosiahnuť remisiu bez potreby liečby?*



# Prevalencia remisie

Dospelá populácia:

1 – 17 %

2 – 52 %

Lahké formy  
astmy

Mladší vek

Lepšie pľúcne  
funkcie

Lepšia  
dlhodobá  
kontrola

Skorší  
začiatok  
ochorenia

Kratšie  
trvanie  
ochorenia

Miernejšia  
BHR

Menej ko-  
morbidít

Skončenie  
fajčenia

Bez anamnézy  
fajčenia

## Clinical Remission on Treatment

### For $\geq 12$ months:

- Sustained absence of significant asthma symptoms based on validated instrument, **and**
- Optimization and stabilization of lung function, **and**
- Patient and HCP agreement regarding disease remission, **and**
- No use of systemic corticosteroid therapy for exacerbation treatment or long-term disease control

## Clinical Remission off Treatment

Same criteria maintained without asthma treatment for  $\geq 12$  months

## Complete Remission on Treatment

### Clinical remission plus the following:

- Current, objective evidence of the resolution of previously documented asthma-related inflammation (eg, reduced blood or sputum eosinophil counts, FENO, and/or other relevant measures), **and**
- In appropriate research settings: Current negative bronchial hyperresponsiveness

## Complete Remission off Treatment

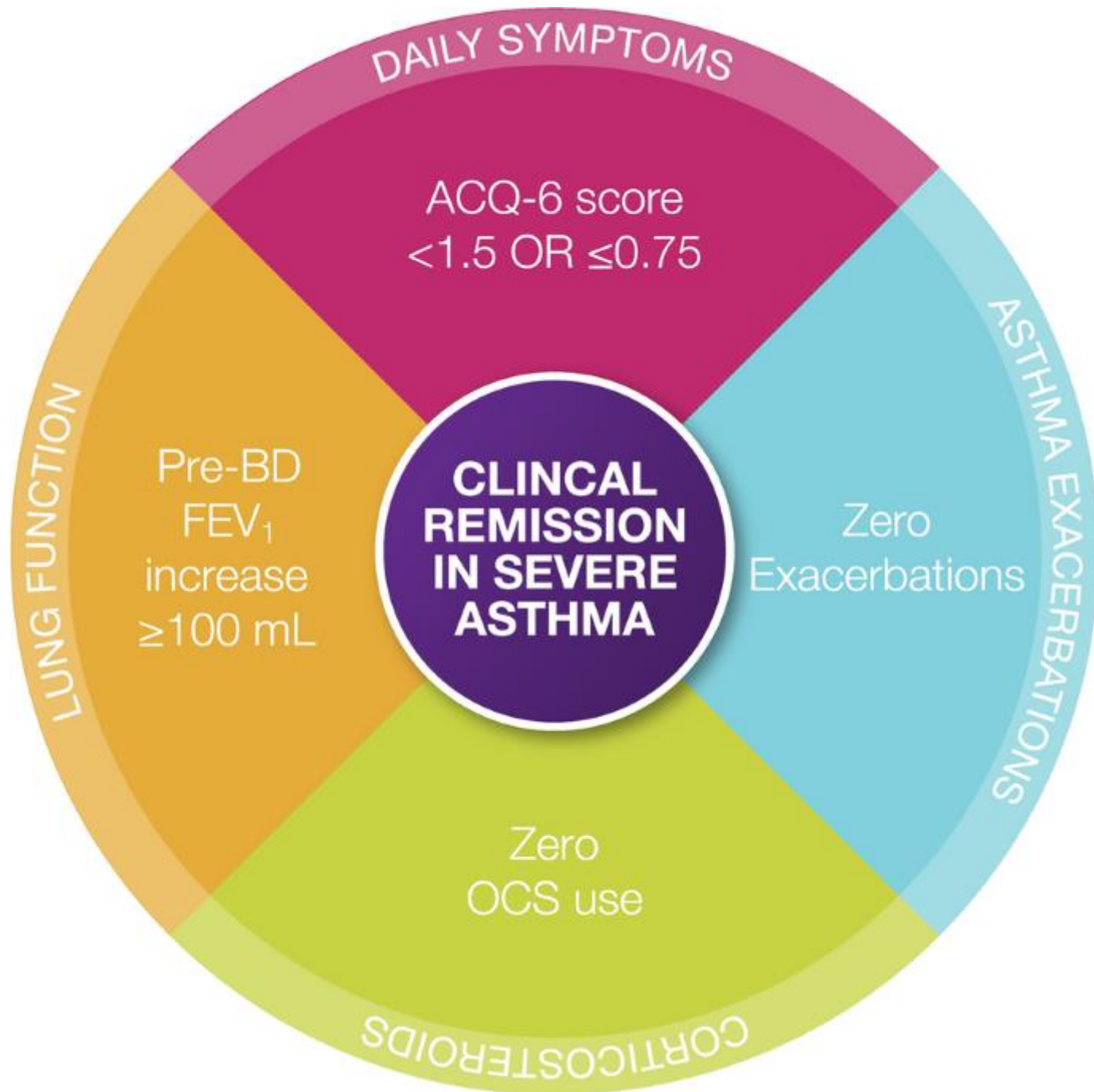
Same criteria maintained without asthma treatment for  $\geq 12$  months

# Klinická vs. kompletná *remisia*

Normalizácia ev. stabilizácia  
patofyziologického podkladu

Symptomatická remisia

Niektoré terapeutiká majú kapacitu navodiť  
remisiu u časti pacientov  
(najmä biologiká ev. azitromycín)



# Klinická vs. kompletná *remisia*

Type	Criteria	Assessments
<b>Clinical remission</b>	No symptoms  No exacerbations  Optimisation of lung function	Sustained absence of significant asthma symptoms established using a validated instrument (e.g. ACQ score $\leq 1$ or ACT score $\geq 20$ ); the use of relievers is not permitted during the remission period  The use of systemic corticosteroids for exacerbation treatment is not permitted during the remission period; hospitalisation or emergency department visit or unscheduled doctor visit for asthma exacerbation management are also not permitted during the remission period  Example: post-bronchodilator $FEV_1 \geq 80\%$ predicted
<b>Complete remission</b>	Clinical remission plus normalisation of underlying pathology	No evidence of current inflammation established using either blood eosinophil count ( $< 300 \text{ cells} \cdot \mu\text{L}^{-1}$ ), sputum eosinophil count ( $< 3\%$ ) or $F_{ENO}$ ( $< 40 \text{ ppb}$ ) [97, 98]; other measures of underlying pathology may include a negative bronchial hyperresponsiveness test (e.g. histamine or methacholine provocation tests) or degree of subepithelial fibrosis (subepithelial thickness)



Biologics	Form	Target	Biological effects	Effects on airway remodeling
Omalizumab	Humanized IgG1- $\kappa$ mAb	IgE	<ul style="list-style-type: none"> <li>• <math>\downarrow</math> circulating total IgE</li> <li>• Downregulation of Fc<math>\epsilon</math>RI receptors on basophils, mast cells, and DCs</li> </ul>	<ul style="list-style-type: none"> <li>• <math>\uparrow</math> FEV<sub>1</sub></li> <li>• <math>\downarrow</math> RBM thickness</li> <li>• <math>\downarrow</math> airway wall thickness in CT</li> <li>• <math>\downarrow</math> fibronectin deposition</li> <li>• Prevents IgE-mediated ECM deposition in vitro</li> </ul>
Reslizumab	Humanized IgG4- $\kappa$ mAb	IL-5	Blockage of IL-5/IL-5R binding	<ul style="list-style-type: none"> <li>• <math>\uparrow</math> FEV<sub>1</sub></li> </ul>
Mepolizumab	Humanized IgG1- $\kappa$ mAb	IL-5	Blockage of IL-5/IL-5R binding	<ul style="list-style-type: none"> <li>• <math>\uparrow</math> FEV<sub>1</sub></li> <li>• <math>\downarrow</math> airway eosinophils and TGF-<math>\beta</math>1<sup>+</sup> eosinophils</li> <li>• <math>\downarrow</math> tenascin expression</li> </ul>
Benralizumab	Humanized IgG1- $\kappa$ mAb	IL-5 receptor (IL-5R $\alpha$ )	$\downarrow$ eosinophils and basophils via antibody-dependent cell-mediated cytotoxicity (ADCC)	<ul style="list-style-type: none"> <li>• <math>\uparrow</math> FEV<sub>1</sub></li> <li>• <math>\downarrow</math> airway eosinophils</li> <li>• <math>\downarrow</math> ASM mass</li> </ul>
Dupilumab	Human IgG4 mAb	IL-4 receptor $\alpha$ chain (IL-4R $\alpha$ )	<ul style="list-style-type: none"> <li>• Blockage of IL-4/IL-4R<math>\alpha</math> binding</li> <li>• Blockage of IL-13/IL-4R<math>\alpha</math> binding</li> </ul>	<ul style="list-style-type: none"> <li>• <math>\uparrow</math> FEV<sub>1</sub></li> <li>• prevents eosinophil infiltration into lung tissue in a mouse model of asthma</li> </ul>
Tezepelumab	Human IgG2- $\lambda$ mAb	TSLP	Blockage of TSLP/TSLPR binding	<ul style="list-style-type: none"> <li>• <math>\uparrow</math> FEV<sub>1</sub></li> <li>• <math>\downarrow</math> airway eosinophils</li> <li>• <math>\downarrow</math> AHR to mannitol</li> <li>• <math>\downarrow</math> airway inflammation</li> <li>• <math>\downarrow</math> TGF-<math>\beta</math>1</li> <li>• <math>\uparrow</math> CT scan-determined lumen area</li> </ul>

A top-down view of a wooden desk. In the center is a white spiral-bound notebook with the text "Take-home message" written in a black serif font. A hand on the right holds a black pen, positioned as if about to write. To the left, another hand rests on a silver laptop. The desk is cluttered with office supplies: two green binder clips, two yellow paper clips, and a black pen cap are scattered around the notebook. A red mug with a green rim is partially visible in the top right corner.

Take-home  
message

# Asthma Remission

## What is asthma remission?

A high level of disease control – the absence of signs and symptoms of asthma for  $\geq 12$  months

## Types of asthma remission

Types	Either on or off treatment:
Clinical remission	<ul style="list-style-type: none"><li>No symptoms</li><li>No attacks</li><li>Optimisation of lung function</li></ul>
Complete remission	<ul style="list-style-type: none"><li>Clinical remission plus normalisation of underlying pathology</li></ul>

## Prevalence

Spontaneous remission in adult asthma patients

**2–52%**

## Potential treatments to induce remission

### Biologics

- Highly effective in eosinophilic asthma



### Macrolides

- Treat eosinophilic and non-eosinophilic asthma



### Treatable traits approach

- Many underlying treatable traits contribute to the multifaceted aetiology of asthma
  - Identifying and treating all underlying traits may improve asthma outcomes



## Early intervention

- People accumulate health and psychological issues over time, including iatrogenic issues
- Timely targeted intervention might halt asthma progression



**Remisia = nový aspekt  
manažmentu AB**

**Remisia a remodelácia**

**Remisia  $\neq$  vyliečenie**  
(hoci je k tomu blízko)

**Niektoré vybrané lieky**  
(biologiká, azitromycín,  $\uparrow$ dávka ICS)

**Nové štúdie zamerané na  
tento aspekt**

**Remisia je známy fenomén  
z iných zápalových  
ochorení**

**Remisia s alebo bez liečby**

**Remisia = nový cieľ v  
liečba astmy**

**Aplikácia liečby v skorších  
štádiách AB?**



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1993-2023

• *Proud to be celebrating the 30<sup>th</sup> year of GINA* •

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