IS IT ASTHMA?

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Disclosures

- I receive research funds from CIHR.

- I have not received any financial or in kind contributions from PHARMA in the last 8 years.

- Therefore, the opinions I express are my own.

Learning objectives

- To be aware of the differential diagnosis of common presentations of asthma such as dyspnea, cough and noisy breathing.

- To be aware of which factors in the clinical history are suggestive that respiratory symptoms are likely to be indicative of asthma.

- To recognize the importance of the objective confirmation of the diagnosis of asthma.

- To know what results of objective testing are suggestive that respiratory symptoms are likely to be indicative of asthma.
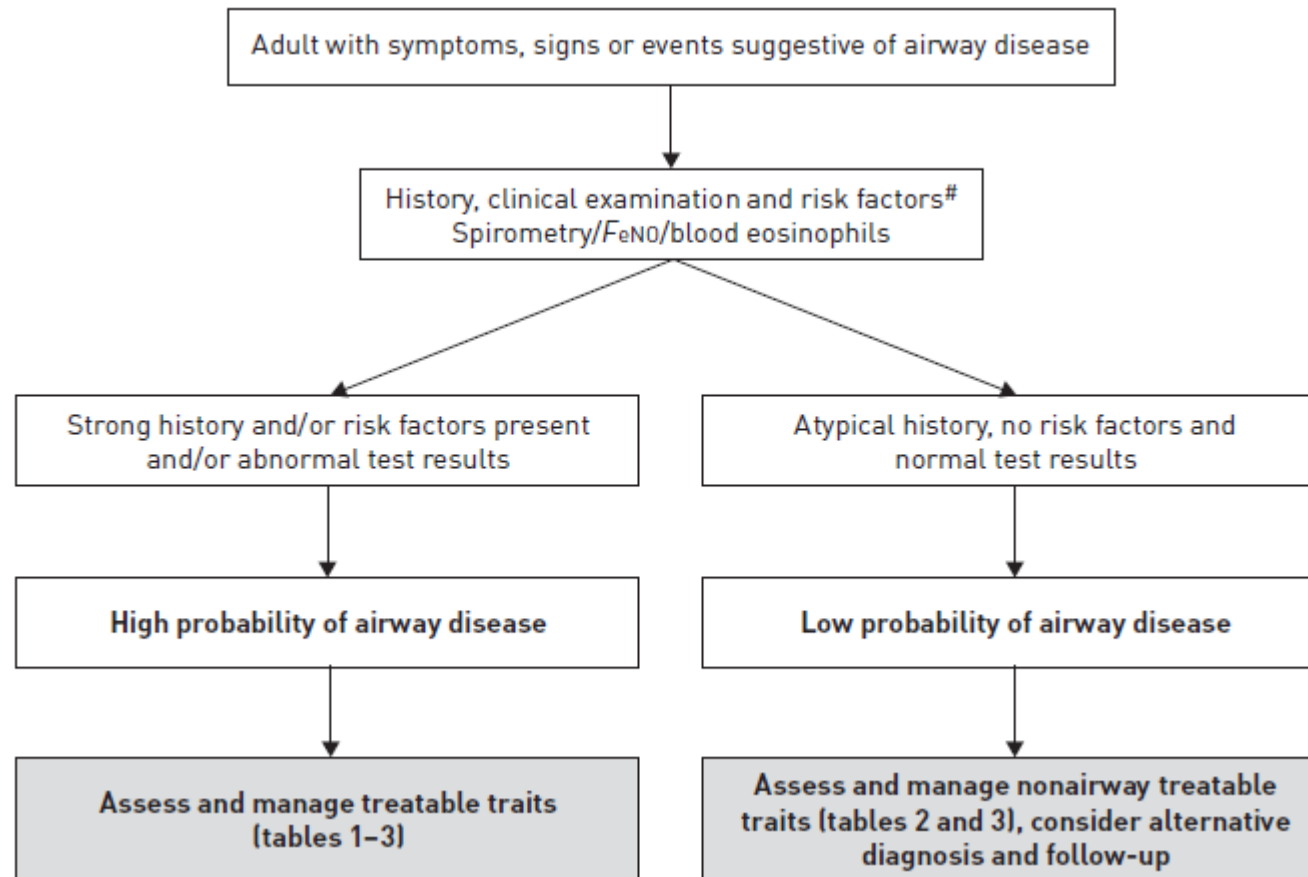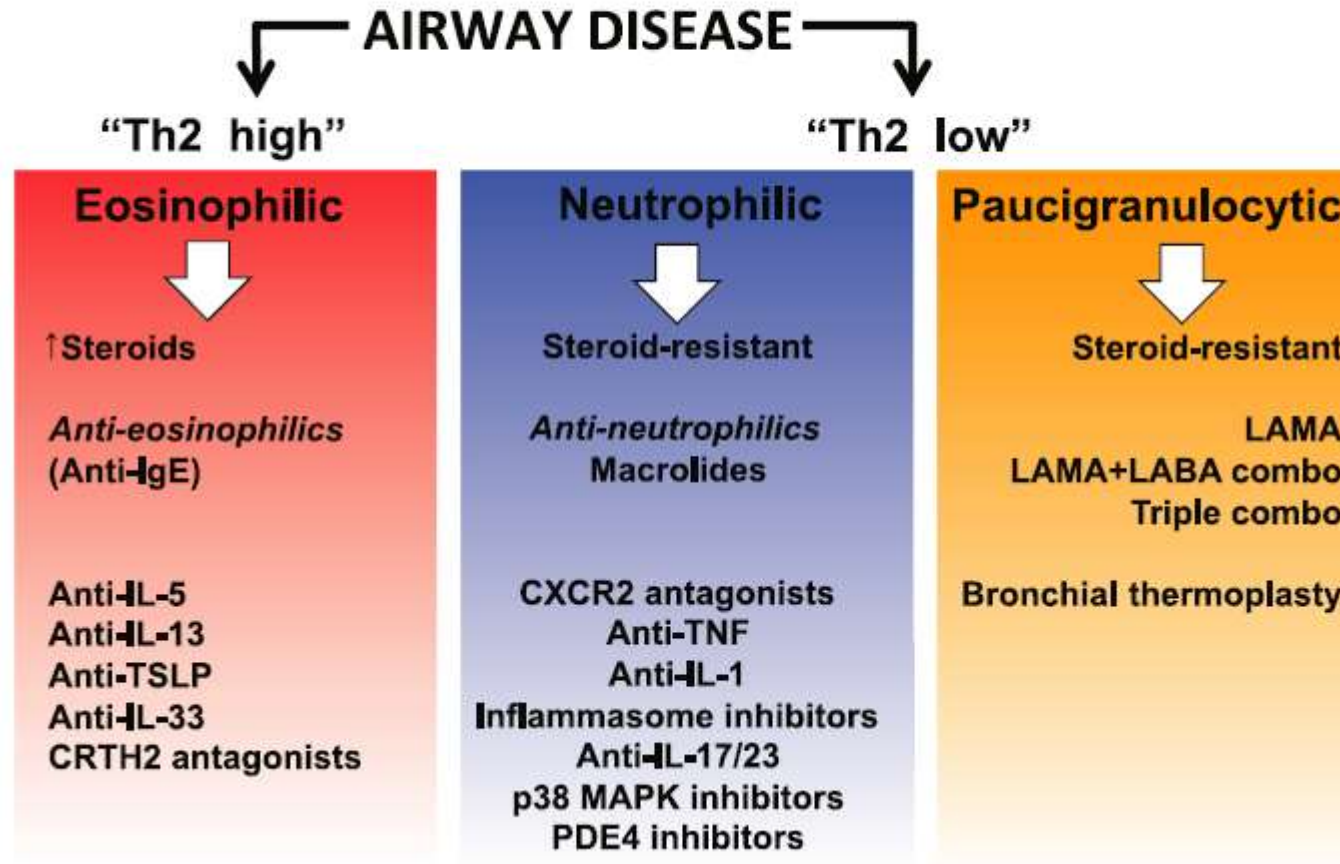
Case presentation

- A 27 year-old man, IT specialist, occasional vaper of cannabis, presents with the complaint of dyspnea on exertion. He describes difficulty keeping up with his team mates during recreational hockey.

- His girlfriend tells him his breathing is noisy at times. He will experience a productive cough for up to 4-6 weeks following a URTI.

- He has no known allergies. He has never had a severe attack of dyspnea requiring urgent consultation.

- On exam: VS are normal; BMI is 30; there may be some wheezing during forced expiration.

- IS IT ASTHMA?

Treatable traits: toward precision medicine of chronic airway diseases

Alvar Agusti[1], Elisabeth Bel[2], Mike Thomas[3], Claus Vogelmeier[4], Guy Brusselle[5,6], Stephen Holgate[7], Marc Humbert[8], Paul Jones[9], Peter G. Gibson[10], Jørgen Vestbo[11], Richard Beasley[12] and Ian D. Pavord[13]

Treatable traits: a label-free, precision medicine approach to the diagnosis and management of chronic airway diseases

Asthma Diagnosis

- Audible wheezing is not a good indicator of asthma.

- Significant airways obstruction may be present in the absence of wheezing on auscultation.

- The diagnosis of asthma requires the demonstration of variable airways obstruction.

Reevaluation of Diagnosis in Adults With Physician-Diagnosed Asthma

Shawn D. Aaron, MD; Katherine L. Vandemheen, MScN; J. Mark FitzGerald, MD; Martha Ainslie, MD; Samir Gupta, MD; Catherine Lemière, MD; Stephen K. Field, MD; R. Andrew McIvor, MD; Paul Hernandez, MD; Irvin Mayers, MD; Sunita Mulpuru, MD; Gonzalo G. Alvarez, MD; Smita Pakhale, MD; Ranjeeta Mallick, PhD; Louis-Philippe Boulet, MD; for the Canadian Respiratory Research Network
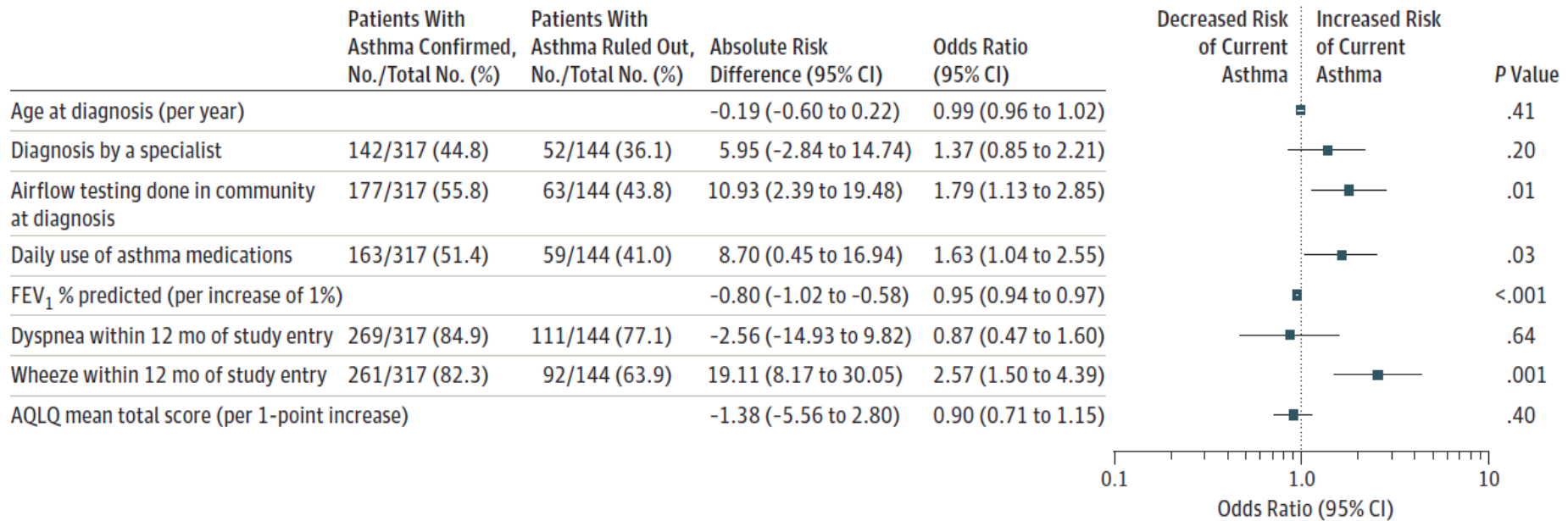
Subjects underwent extensive diagnostic algorithm including a one year follow-up without treatment to rule out current asthma.

Table 1. Baseline Characteristics of Individuals Whose Diagnosis of Current Asthma Was Confirmed or Ruled Out (continued)

| Characteristic | Current Asthma | | Absolute Difference (95% CI)[a] |
	Confirmed (n = 410)	Ruled Out (n = 203)	
Patients with symptoms as assessed using ECRHS, No. (%)			
During past 12 mo			
Dyspnea	354 (86.3)	157 (77.3)	9.0 (2.4 to 15.6)
Wheeze	337 (82.2)	137 (67.5)	14.7 (7.3 to 22.1)

Figure 3. Adjusted Odds Ratios and Absolute Risk Differences for Determinants of Current Asthma

	Patients With Asthma Confirmed, No./Total No. (%)	Patients With Asthma Ruled Out, No./Total No. (%)	Absolute Risk Difference (95% CI)	Odds Ratio (95% CI)	P Value
Age at diagnosis (per year)			-0.19 (-0.60 to 0.22)	0.99 (0.96 to 1.02)	.41
Diagnosis by a specialist	142/317 (44.8)	52/144 (36.1)	5.95 (-2.84 to 14.74)	1.37 (0.85 to 2.21)	.20
Airflow testing done in community at diagnosis	177/317 (55.8)	63/144 (43.8)	10.93 (2.39 to 19.48)	1.79 (1.13 to 2.85)	.01
Daily use of asthma medications	163/317 (51.4)	59/144 (41.0)	8.70 (0.45 to 16.94)	1.63 (1.04 to 2.55)	.03
FEV_1 % predicted (per increase of 1%)			-0.80 (-1.02 to -0.58)	0.95 (0.94 to 0.97)	<.001
Dyspnea within 12 mo of study entry	269/317 (84.9)	111/144 (77.1)	-2.56 (-14.93 to 9.82)	0.87 (0.47 to 1.60)	.64
Wheeze within 12 mo of study entry	261/317 (82.3)	92/144 (63.9)	19.11 (8.17 to 30.05)	2.57 (1.50 to 4.39)	.001
AQLQ mean total score (per 1-point increase)			-1.38 (-5.56 to 2.80)	0.90 (0.71 to 1.15)	.40

Decreased Risk of Current Asthma — Increased Risk of Current Asthma

0.1 — 1.0 — 10

Odds Ratio (95% CI)

Aaron JAMA 2017

To confirm asthma:

- Bronchodilator response; how much is enough? *15% improvement in FEV1*

- Peak flow variability; how much is enough? *20% within day variability*

- Methacholine bronchoprovocation; *drop in FEV1 of 20% in subjects with normal spirometry.*

Spirometry – Volume/Time Curve

Measured (····)

FEV$_1$ = 2.0 (67% pred.)

FVC = 3.6 (90% pred.)

FEV$_1$/FVC = 0.56

Predicted (——)

FEV$_1$ = 3.0

FVC = 4.0

FEV$_1$/FVC = 0.75
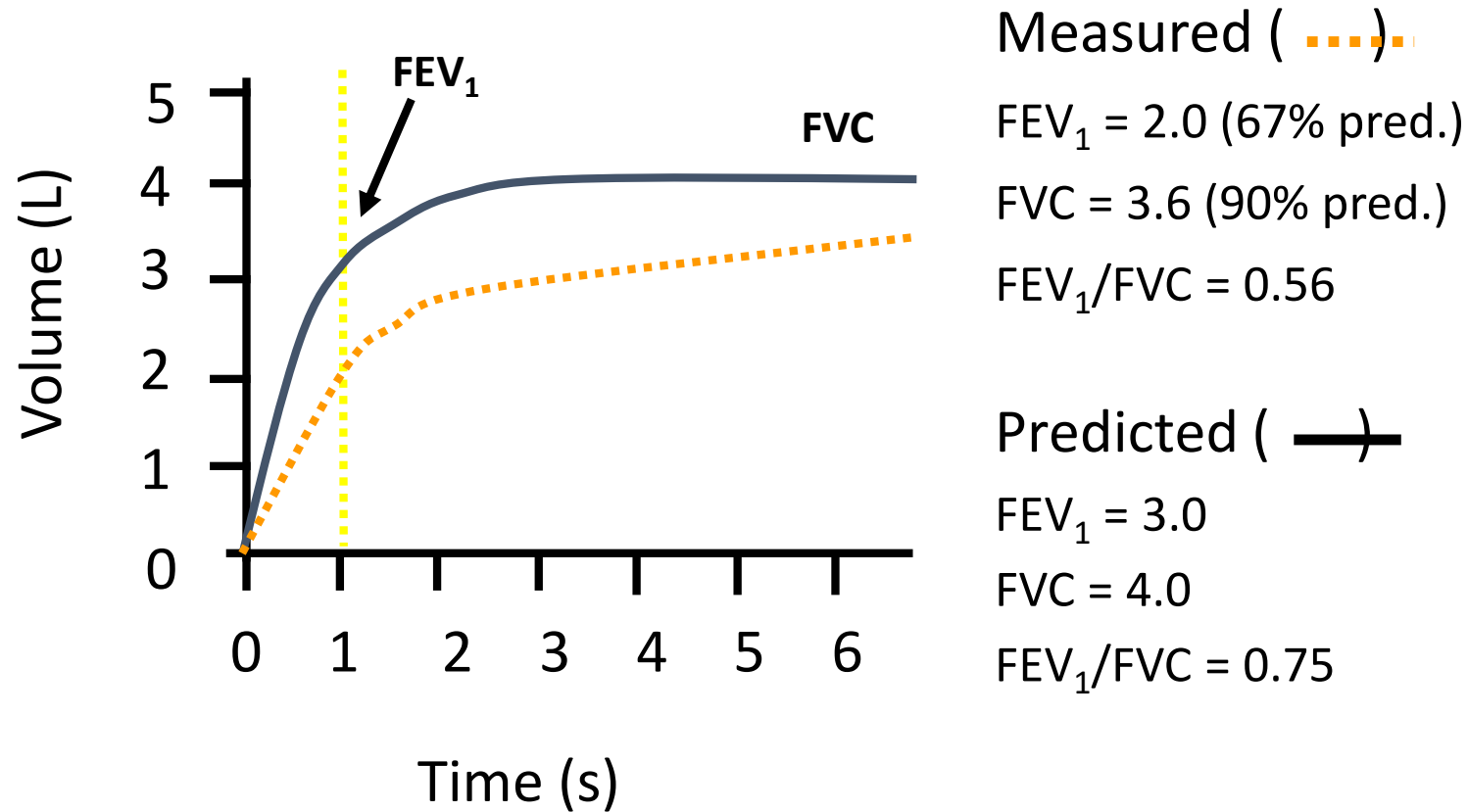
Asthma more likely if:

- If present in direct family members
- History of infantile eczema
- Allergy to indoor aeroallergens such as dust mite, pets, cockroach
- Female
- Typical triggers: *exercise in cold air (running for bus at -25 Celsius)
   *laughter
                        *new pet

- However, but poor LRs; not very helpful in the individual patient

Common causes of dyspnea other than asthma:

- Hyperventilation
- Anemia
- Heart disease
- Anxiety
- Deconditioning

Causes of wheeze other than asthma:

- Obesity
- Vocal cord dysfunction (Inducible Laryngeal obstruction)
- Upper airway tumour
- Airway tumour or foreign body
- Bronchomalacia

A

Flow (liters/sec)

Volume (liters)

B

C

Flow (liters/sec)

Volume (liters)
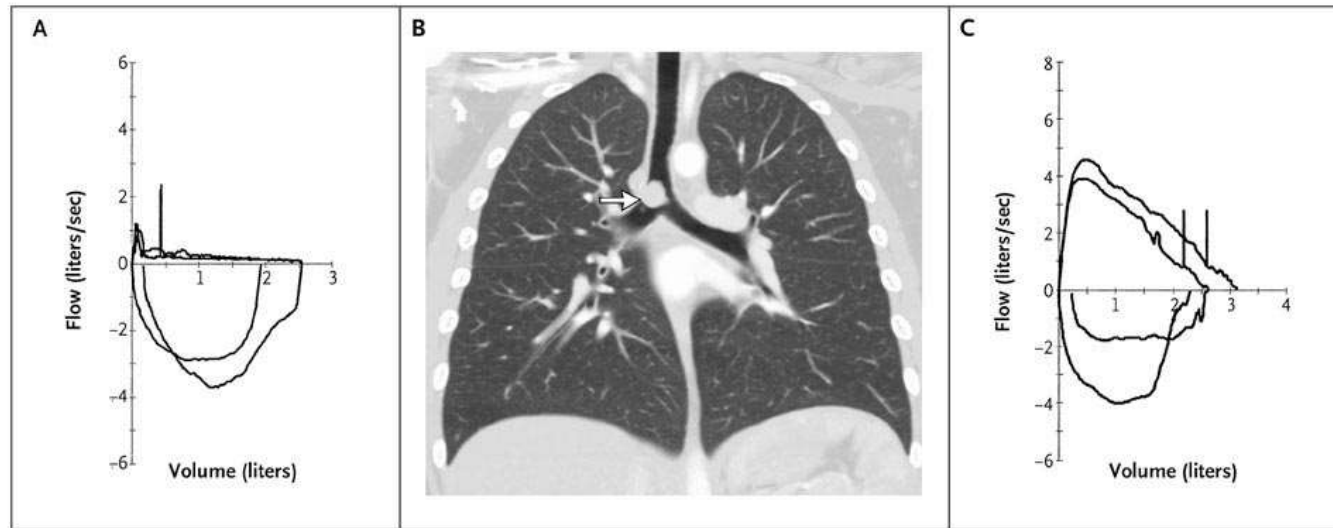
Differential diagnosis of a persistent cough

- Sinus disease with post-nasal drip (chronic upper airway cough)
- GERD
- VCD
- ACEi

Auxiliary testing

- *FeNO (expired nitric oxide) > 50*

- Blood eosinophils (300 or 4%)
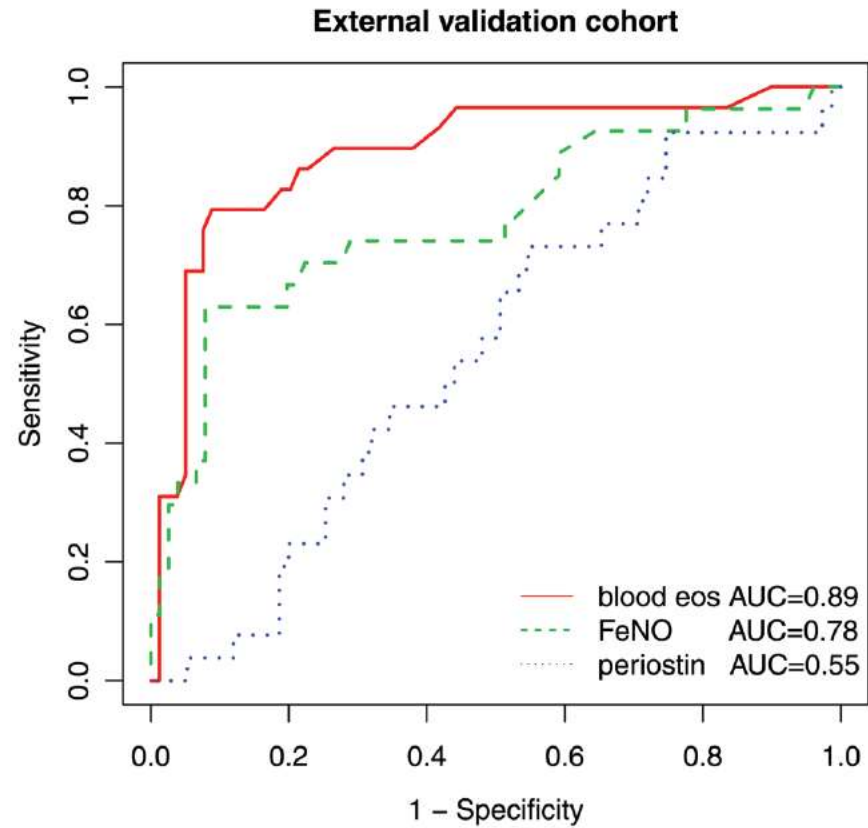
External validation cohort

Figure 1 Receiver operating characteristics curve analyses of the sensitivity and the specificity of blood eosinophils (eos), FE_{NO} and serum periostin (in-house) for the diagnosis of eosinophilic inflammation. AUC, area under the curve.

Mrs L.

- 34yo woman with ? asthma

- Migraines: can take Propanolol?

- Hx of recurrent bronchitis

- SOBOE x 1 year, coughs & wheezes if runs, unable to train, air hunger

- Allergy to pets & dust (no pets @ home)

- Chronic rhinitis

- FEV1: 2.69 normal

- PBE: 100

- FeNO: 11

- Given Ventolin pre-exercise, Nasonex + f/u with Metha

Mrs L.

- Metacholine: negative

- Symptoms likely hyperventilation: booked for breathing exercises

  FeNO along with blood and spirometry were indicator of low asthma probability (confirmed with Metacholine) despite symptoms being suggestive.

Box 3-5A
Adults & adolescents 12+ years

Personalized asthma management:
Assess, Adjust, Review response

REVIEW RESPONSE
Symptoms
Exacerbations
Side-effects
Lung function
Patient satisfaction
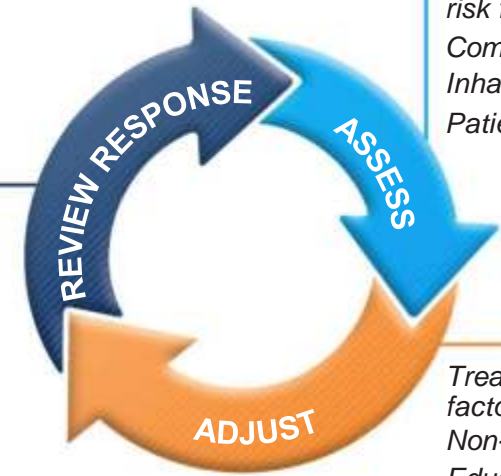
ASSESS
Confirmation of diagnosis if necessary
Symptom control & modifiable
risk factors (including lung function)
Comorbidities
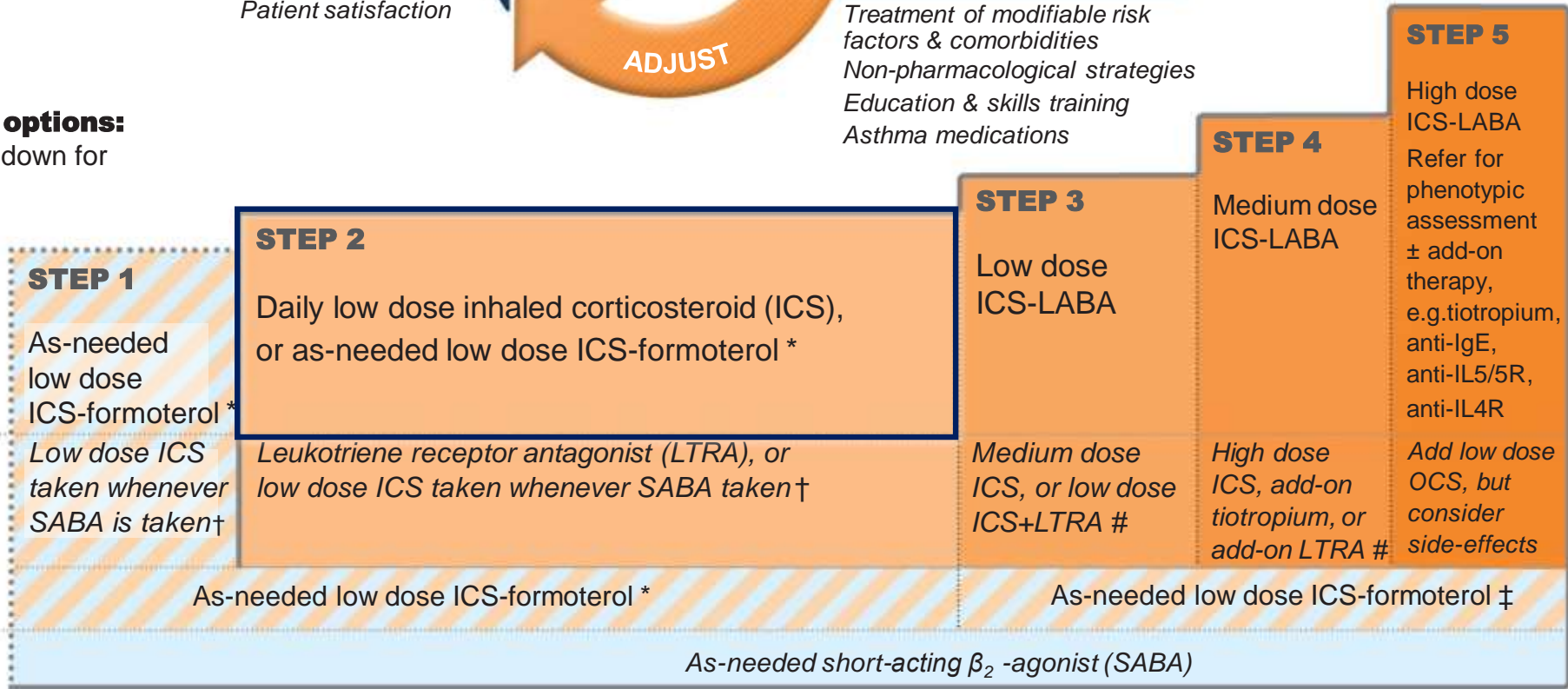Inhaler technique & adherence
Patient goals

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

Asthma medication options:
Adjust treatment up and down for
individual patient needs

PREFERRED CONTROLLER
to prevent exacerbations
and control symptoms

	STEP 1	**STEP 2**	**STEP 3**	**STEP 4**	**STEP 5**
PREFERRED CONTROLLER	As-needed low dose ICS-formoterol *	Daily low dose inhaled corticosteroid (ICS), or as-needed low dose ICS-formoterol *	Low dose ICS-LABA	Medium dose ICS-LABA	High dose ICS-LABA Refer for phenotypic assessment ± add-on therapy, e.g.tiotropium, anti-IgE, anti-IL5/5R, anti-IL4R
Other controller options	*Low dose ICS taken whenever SABA is taken†*	*Leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken†*	*Medium dose ICS, or low dose ICS+LTRA #*	*High dose ICS, add-on tiotropium, or add-on LTRA #*	*Add low dose OCS, but consider side-effects*

PREFERRED RELIEVER

As-needed low dose ICS-formoterol *   As-needed low dose ICS-formoterol ‡

Other reliever option

As-needed short-acting β₂ -agonist (SABA)

* Off-label; data only with budesonide-formoterol (bud-form)
† Off-label; separate or combination ICS and SABA inhalers

‡ Low-dose ICS-form is the reliever for patients prescribed
 bud-form or BDP-form maintenance and reliever therapy
Consider adding HDM SLIT for sensitized patients with
 allergic rhinitis and FEV >70% predicted

GINA 2019 – landmark changes in asthma management

- For safety, GINA no longer recommends SABA-only treatment for Step 1
  - This decision was based on evidence that SABA-only treatment increases the risk of severe exacerbations, and that adding any ICS significantly reduces the risk
- GINA now recommends that all adults and adolescents with asthma should receive symptom-driven or regular low dose ICS-containing controller treatment, to reduce the risk of serious exacerbations
  - This is a population-level risk reduction strategy, e.g. statins, anti-hypertensives

Trial of Therapy

- Budesonide/Formoterol 200mcg; one inhalation as needed.

QUESTIONS?