Asthma - the basics and beyond

Ian Yang

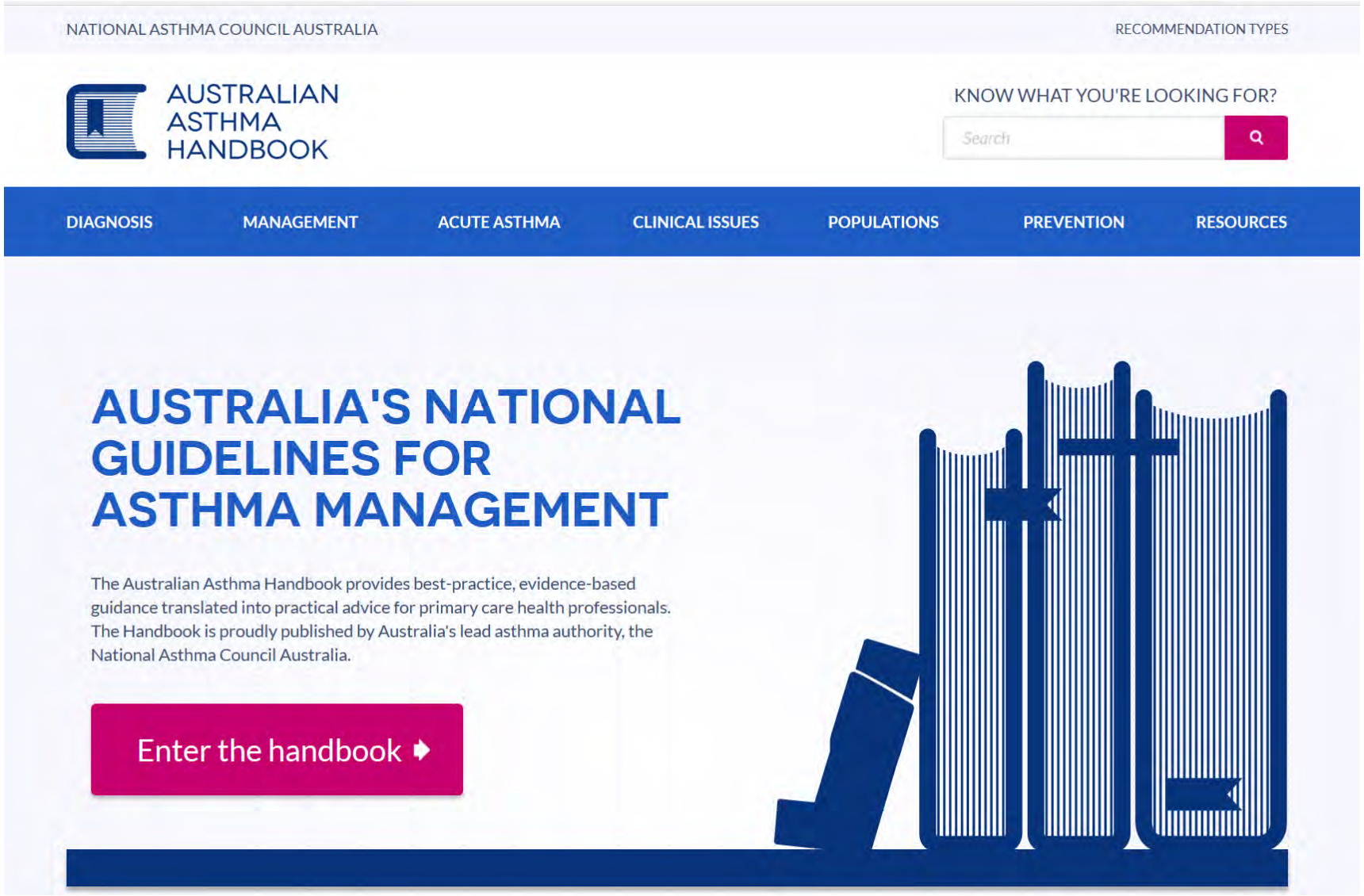
Director, Thoracic Medicine, The Prince Charles Hospital

Professor, Faculty of Medicine, The University of Queensland

Queensland Government

THE UNIVERSITY OF QUEENSLAND
AUSTRALIA

Australian Asthma Handbook



Australian Asthma Handbook v2.0, 2019

https://www.asthmahandbook.org.au/

Asthma diagnosis and initial management

Ms A

50 y.o.

- Dry cough, intermittent chest tightness and mild wheeze for 2 months
- Variable exertional breathlessness
- No specific triggers

Rhinosinusitis

Hiatus hernia

Current smoker - 15-50 years old,
10 per day, ~17 pack years

O/E chest clear

Spirometry

Pre-bronchodilator

FEV_1	2.07	81% predicted
VC	3.63	99% predicted

Post-bronchodilator

FEV_1	2.40	16% increase
VC	3.66	

Diagnosis?

Initial management?

Diagnosing asthma in adults

A working definition of asthma

Asthma is a chronic lung disease, which can be controlled but not cured.

In clinical practice, asthma is defined by the presence of **both** the following:

- excessive variation in lung function ('**variable airflow limitation**', i.e. variation in expiratory airflow that is greater than that seen in healthy people)
- **respiratory symptoms** (e.g. wheeze, shortness of breath, cough, chest tightness) that **vary over time** and may be present or absent at any point in time.

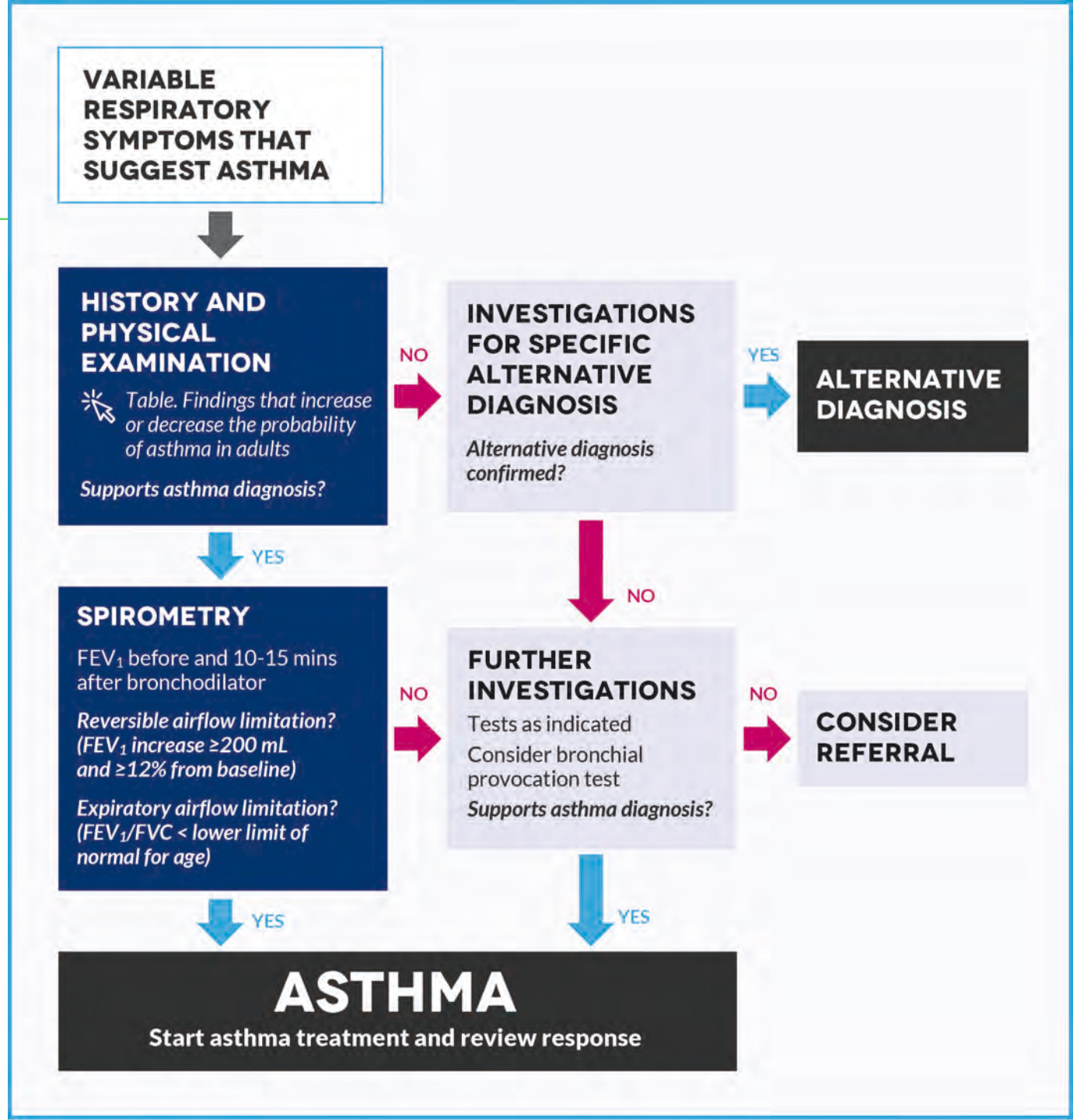
Untreated asthma is usually characterised by chronic inflammation involving many cells and cellular elements, airway hyperresponsiveness, and intermittent airway narrowing (due to bronchoconstriction, congestion or oedema of bronchial mucosa, mucus, or a combination of these).

Steps in the diagnosis of asthma in adults

There is no single reliable test ('gold standard') and there are no standardised diagnostic criteria for asthma.

The diagnosis of asthma is based on:

- history
- physical examination
- considering other diagnoses
- documenting variable airflow limitation.



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Pathogenesis of asthma

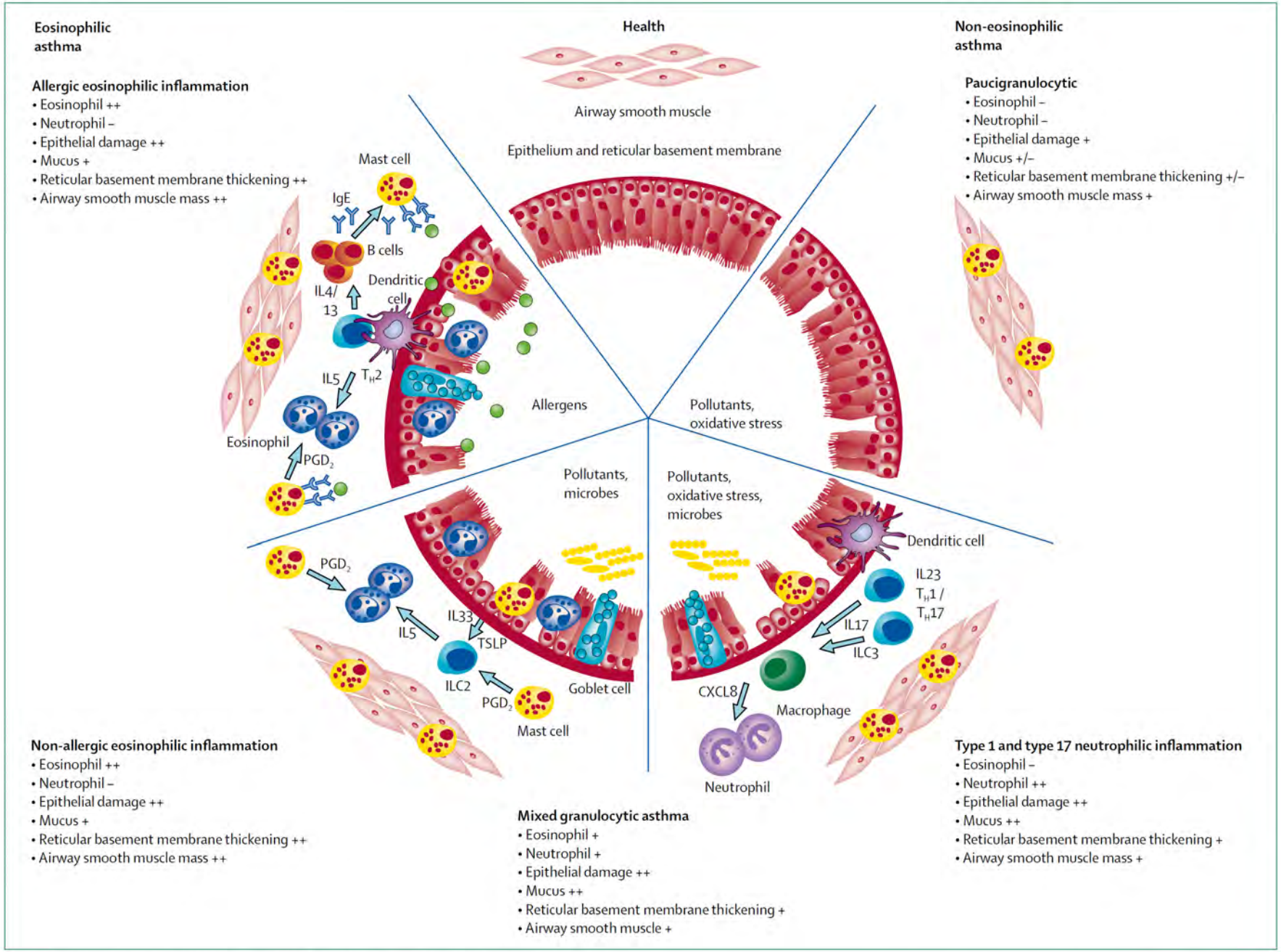


Figure 2: **Mechanisms and characteristic pathological features of asthma immunopathology**
Features are divided into eosinophilic (allergic and non-allergic), non-eosinophilic (neutrophilic type 1 and type 17 and paucigranulocytic), and mixed granulocytic inflammation. Reproduced from Russell and Brightling,[12] by permission of Portland Press. IL=interleukin. T_H=T helper. PDG_2=prostaglandin D2. TSLP=thymic stromal lymphopoietin. ILC2=type 2 innate lymphoid cells. CXCL8=C-X-C motif chemokine ligand 8. ILC2=type 3 innate lymphoid cells.

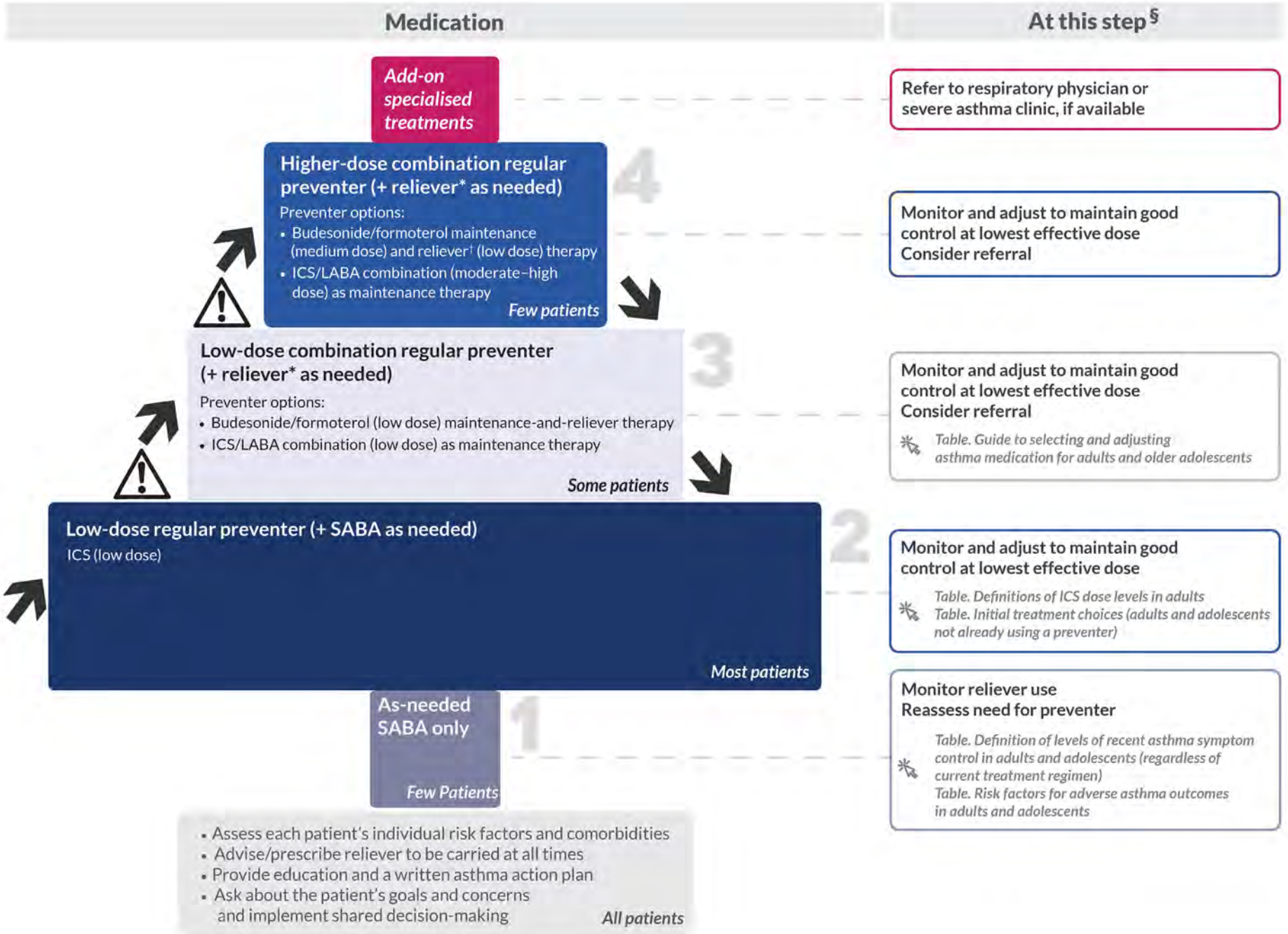
Papi *et al*. Lancet 2018;391:783-800

Asthma management

Asthma management in adults is based on:

- confirming the diagnosis
- assessing asthma control (recent asthma symptom control and risk factors)
- identifying management goals in collaboration with the patient
- choosing initial treatment appropriate to recent asthma symptom control, risk factors and patient preference
- reviewing and adjusting drug treatment periodically
- providing information, skills and tools for self-management, including:
  - training in correct inhaler technique
  - information and support to maximise adherence
  - a written asthma action plan
  - information about avoiding triggers, where appropriate
- managing flare-ups when they occur
- managing comorbid conditions that affect asthma or contribute to respiratory symptoms
- providing advice about smoking, healthy eating, physical activity, healthy weight and immunisation

Australian Asthma Handbook v2.0, 2019



Australian Asthma Handbook 2019

STEPWISE MANAGEMENT OF STABLE CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

	MILD	MODERATE	SEVERE
Typical symptoms	few symptoms breathless on moderate exertion recurrent chest infections little or no effect on daily activities	breathless walking on level ground increasing limitation of daily activities cough and sputum production exacerbations requiring oral corticosteroids and/or antibiotics	breathless on minimal exertion daily activities severely curtailed experiencing regular sputum production chronic cough exacerbations of increasing frequency and severity
Typical lung function	**FEV_1 ≈ 60-80% predicted**	**FEV_1 ≈ 40-59% predicted**	**FEV_1 < 40% predicted**
Non-pharmacological interventions	**RISK REDUCTION** Check smoking status, support smoking cessation, recommend annual influenza vaccine and pneumococcal vaccine according to immunisation handbook		
	OPTIMISE FUNCTION Encourage regular exercise and physical activity, review nutrition, provide education, develop GP management plan and written COPD action plan (and initiate regular review)		
	CONSIDER CO-MORBIDITIES especially cardiovascular disease, anxiety, depression, lung cancer and osteoporosis		
	REFER symptomatic patients to pulmonary rehabilitation		
		Consider oxygen therapy for hypoxaemia, surgery, bronchoscopic interventions, palliative care services and advanced care planning	
Stepwise pharmacological interventions (inhaled medicines)*	**START with short-acting relievers:** (used as needed)		
	SABA (short-acting beta$_2$-agonist) OR **SAMA** (short-acting muscarinic antagonist)		
	ADD long-acting bronchodilators: **LAMA** (long-acting muscarinic antagonist) OR **LABA** (long-acting beta$_2$-agonist) Single inhaler dual therapy (**LAMA/LABA**) may be suitable		
		CONSIDER adding ICS (inhaled corticosteroids) FEV$_1$ <50% predicted AND ≥two exacerbations in last 12 months AND significant symptoms despite LAMA and LABA therapy*	**ICS/LABA** and **LAMA** Single inhaler triple therapy (**ICS/LAMA/LABA**) may be suitable
	Assess and optimise inhaler device technique at each visit		

REFER PATIENTS TO LUNG FOUNDATION AUSTRALIA FOR INFORMATION AND SUPPORT - FREECALL 1800 654 301

Lung Foundation Australia has a range of resources to promote understanding of COPD and assist with management.

Based on The COPD-X Plan: Australian and New Zealand Guidelines for the Management of COPD and COPD-X Concise Guide for Primary Care

*Refer to PBS criteria: www.pbs.gov.au

Register at www.copdx.org.au to receive an alert when the COPD-X Guidelines are updated

Lung Foundation Australia

1800 654 301 | Lungfoundation.com.au

Green tick indicates therapies that can be used together

			SABA	SAMA	LAMA	LABA	LABA/ LAMA	ICS/ LABA	ICS/ LAMA/ LABA
SABA	salbutamol (Ventolin™, Airomir™, Asmol™)	terbutaline (Bricanyl™)		✓	✓	✓	✓	✓	✓
SAMA	ipratropium (Atrovent™)		✓			✓		✓	
LAMA	tiotropium (Spiriva™) glycopyrronium (Seebri™)	aclidinium (Bretaris™) umeclidinium (Incruse™)	✓			✓		✓	
LABA	salmeterol (Serevent™) formoterol (Oxis™, Foradile™)	indacaterol (Onbrez™)	✓	✓	✓				
LABA/ LAMA	indacaterol/glycopyrronium (Ultibro™) umeclidinium/vilanterol (Anoro™)	tiotropium/olodaterol (Spiolto™) aclidinium/formoterol (Brimica™)	✓						
ICS/LABA	fluticasone propionate/salmeterol (Seretide™) fluticasone propionate/salmeterol (SalplusF™/ Cipla™) budesonide/formoterol (Symbicort™)	budesonide/formoterol (DuoResp™) fluticasone furoate/vilanterol (Breo™)	✓	✓	✓				
ICS/LAMA/ LABA	fluticasone furoate/umeclidinium/ vilanterol (Trelegy™)		✓						

Relievers

SABA: Short-acting beta$_2$-agonists

Ventolin® MDI *salbutamol*

Asmol® MDI *salbutamol*

Airomir™ Autohaler® *salbutamol*

Bricanyl® Turbuhaler® *terbutaline*

SAMA: Short-acting muscarinic antagonist

Atrovent® MDI *ipratropium*

Maintenance

LAMAs: Long-acting muscarinic antagonists

Spiriva® HandiHaler® *tiotropium*

Spiriva® Respimat® *tiotropium*

Incruse® Ellipta® *umeclidinium*

Seebri® Breezhaler® *glycopyrronium*

Bretaris® Genuair® *aclidinium*

LAMA/LABA combinations

Ultibro® Breezhaler® *indacaterol/ glycopyrronium*

Spiolto® Respimat® *tiotropium/ olodaterol*

Anoro® Ellipta® *umeclidinium/ vilanterol*

Brimica® Genuair® *aclidinium/ formoterol*

LABAs: Long-acting beta$_2$-agonists

Onbrez® Breezhaler® *indacaterol*

Foradile® Aerolizer® *formoterol*

Oxis® Turbuhaler® *formoterol*

Serevent® Accuhaler® *salmeterol*

ICS/LABA combinations

Symbicort® Rapihaler™ *budesonide/formoterol*

Symbicort® Turbuhaler® *budesonide/formoterol*

Seretide® Accuhaler® *fluticasone propionate/ salmeterol*

Seretide® MDI *fluticasone propionate/ salmeterol*

DuoResp® Spiromax® *budesonide/formoterol*

Breo® Ellipta® *fluticasone furoate/ vilanterol*

Fluticasone + Salmeterol Cipla®/SalplusF® MDI *fluticasone propionate/ salmeterol*

ICS: Inhaled corticosteroids (for patients with COPD and Asthma)

Flixotide® MDI *fluticasone propionate*

Flixotide® Accuhaler® *fluticasone propionate*

Alvesco® MDI *ciclesonide*

Pulmicort® Turbuhaler® *budesonide*

QVAR® MDI *beclometasone*

ICS/LABA combination

Flutiform® MDI *fluticasone propionate/ formoterol*

ICS/LAMA/LABA combination

Trelegy® Ellipta® *fluticasone furoate/ umeclidinium/ vilanterol*

Flare Up Medicines

1. Antibiotics (Refer to Therapeutic Guidelines: Antibiotic: www.tg.org.au)
2. Oral steroids (prednisone, prednisolone)

Notes

- Handihaler, Breezhaler and Aerolizer devices require a capsule to be loaded into the device. All other devices are preloaded.
- Where possible, metered dose inhalers (MDI) should be used with a spacer
- ICS monotherapy is not indicated for COPD without co-existing asthma
- **Shaded = PBS listed for asthma only**

Watch inhaler device technique videos on your device through ZAPPAR

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CONCISE CLINICAL REVIEW

Underdiagnosis and Overdiagnosis of Asthma

Shawn D. Aaron[1], Louis Philippe Boulet[2], Helen K. Reddel[3], and Andrea S. Gershon[4]

[1]The Ottawa Hospital Research Institute, University of Ottawa, Ottawa, Ontario, Canada; [2]Institut de Cardiologie et de Pneumologie de Québec, Université Laval, Québec, Québec, Canada; [3]Woolcock Institute of Medical Research, Sydney, Australia; and [4]Department of Medicine, The University of Toronto, Toronto, Ontario, Canada

Underdiagnosis

Under-reporting of symptoms

Poor socioeconomic status

Overdiagnosis

Lack of variable airflow obstruction

Unrecognised sustained clinical remission of symptoms

- Canadian study: 613 patients – 30% had no features of current asthma on extensive workup and could discontinue asthma inhalers

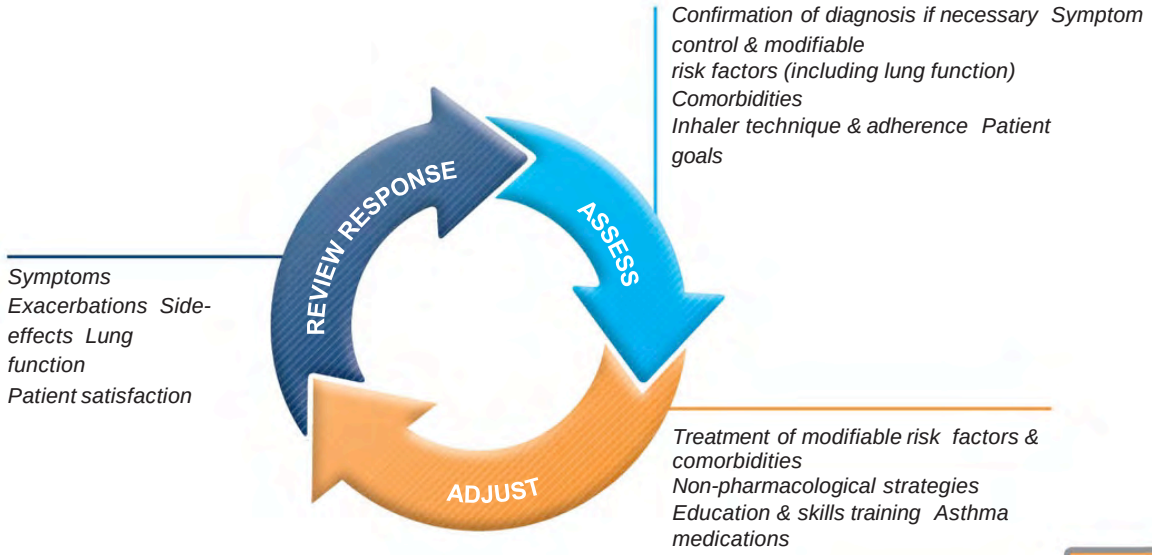
Aaron *et al*. JAMA 2017;317:269-279

Aaron *et al*. Am J Respir Crit Care Med 2018;198:1012-1020

Box 3-5A

Adults & adolescents 12+ years

Personalized asthma management: Assess, Adjust, Review response



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

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms	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 β_2 -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

Note: At June 2019 – as needed ICS/LABA alone is not available on PBS for asthma

The NEW ENGLAND JOURNAL of MEDICINE

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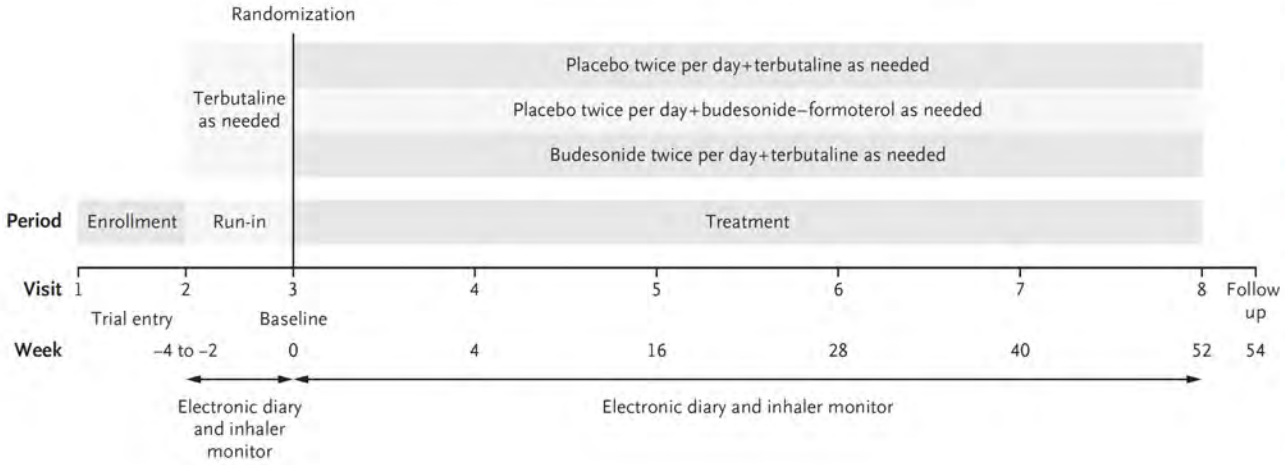
Inhaled Combined Budesonide–Formoterol as Needed in Mild Asthma

Paul M. O'Byrne, M.B., J. Mark FitzGerald, M.D., Eric D. Bateman, M.D., Peter J. Barnes, M.D., Nanshan Zhong, Ph.D., Christina Keen, M.D., Carin Jorup, M.D., Rosa Lamarca, Ph.D., Stefan Ivanov, M.D., Ph.D., and Helen K. Reddel, M.B., B.S., Ph.D.



RESULTS

A total of 3849 patients underwent randomization, and 3836 (1277 in the terbutaline group, 1277 in the budesonide–formoterol group, and 1282 in the budesonide maintenance group) were included in the full analysis and safety data sets. With respect to the mean percentage of weeks with well-controlled asthma per patient, budesonide–formoterol was superior to terbutaline (34.4% vs. 31.1% of weeks; odds ratio, 1.14; 95% confidence interval [CI], 1.00 to 1.30; P=0.046) but inferior to budesonide maintenance therapy (34.4% and 44.4%, respectively; odds ratio, 0.64; 95% CI, 0.57 to 0.73). The annual rate of severe exacerbations was 0.20 with terbutaline, 0.07 with budesonide–formoterol, and 0.09 with budesonide maintenance therapy; the rate ratio was 0.36 (95% CI, 0.27 to 0.49) for budesonide–formoterol versus terbutaline and 0.83 (95% CI, 0.59 to 1.16) for budesonide–formoterol versus budesonide maintenance therapy. The rate of adherence in the budesonide maintenance group was 78.9%. The median metered daily dose of inhaled glucocorticoid in the budesonide–formoterol group (57 μg) was 17% of the dose in the budesonide maintenance group (340 μg).

CONCLUSIONS

In patients with mild asthma, as-needed budesonide–formoterol provided superior asthma-symptom control to as-needed terbutaline, assessed according to electronically recorded weeks with well-controlled asthma, but was inferior to budesonide maintenance therapy. Exacerbation rates with the two budesonide-containing regimens were similar and were lower than the rate with terbutaline. Budesonide–formoterol used as needed resulted in substantially lower glucocorticoid exposure than budesonide maintenance therapy. (Funded by AstraZeneca; SYGMA 1 ClinicalTrials.gov number, NCT02149199.)

Note: At June 2019 – as needed ICS/LABA alone is not available on PBS for asthma

Asthma/COPD overlap

Mr B

72 y.o.

- Exertional breathlessness up hills
- Cough and dark green sputum
- No wheeze, occasional left chest pain
- No recent chest infections
- Triggers: pollen

Rhinosinusitis. Childhood asthma.

IHD – STEMI, PCI

Former smoker - 15-68 years old,
15 per day, ~30 pack years

O/E chest – reduced breath sounds

Fractional exhaled nitric oxide (FeNO): elevated at 35 parts per billion (RR<25)

Spirometry

Pre-bronchodilator

FEV_1	1.40	43% predicted
VC	3.89	100% predicted

Post-bronchodilator

FEV_1	1.56	18% increase
VC	4.36	

CXR – mild hyperinflation

CT chest – moderate emphysema

FBC – eosinophils: normal

IgE – 300: elevated

Alpha1-antitrypsin level 1.70: normal.

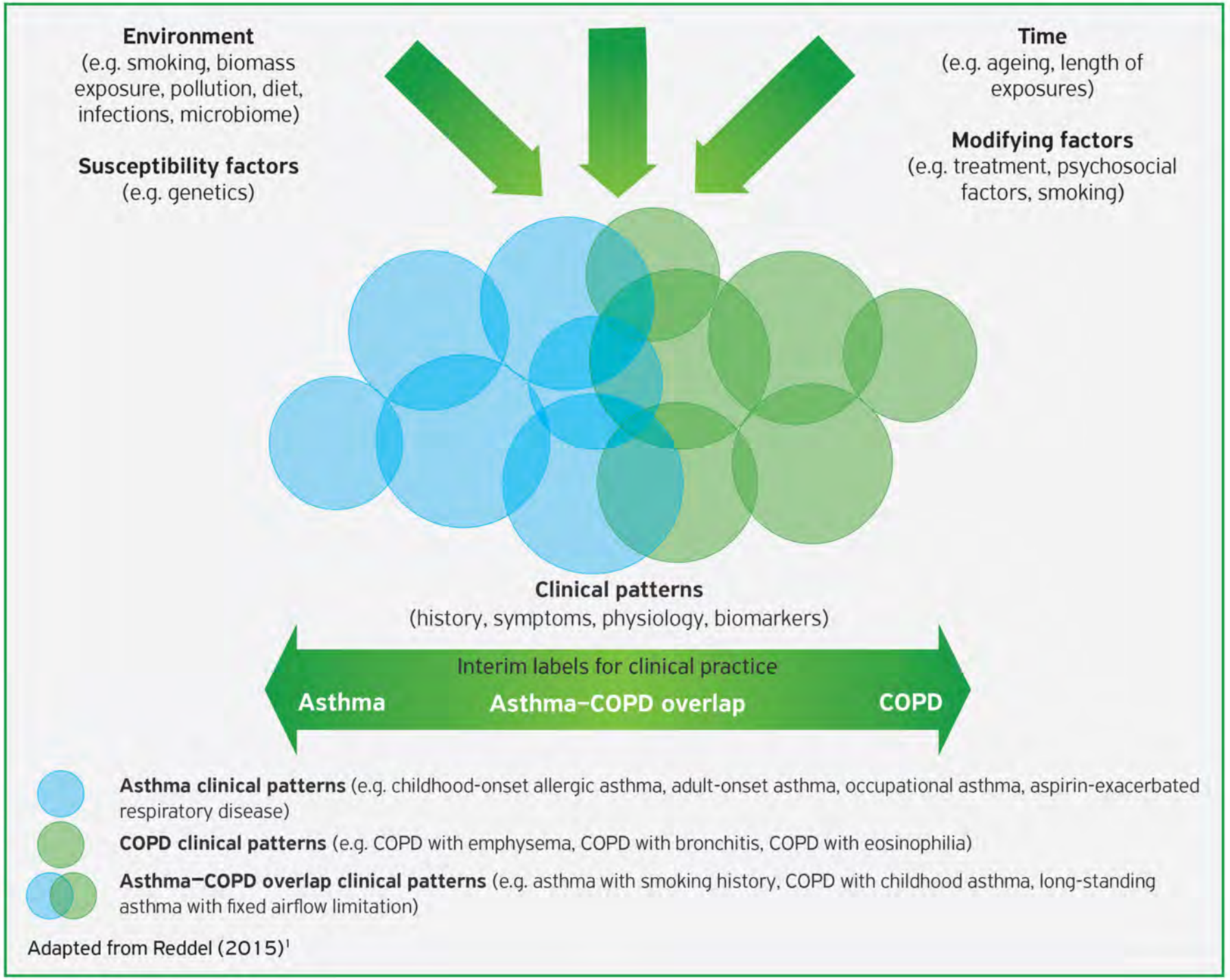
Diagnosis? Initial management?

Asthma-COPD overlap

Position paper:

National Asthma Council and Lung Foundation Australia

https://www.nationalasthma.org.au/living-with-asthma/resources/health-professionals/information-paper/asthma-copd-overlap



Diagnosis and initial treatment of asthma, COPD and asthma-COPD overlap (ACO)

A joint project of GINA and GOLD

UPDATED 2017

GINA Global Strategy for Asthma Management and Prevention

GOLD Global Strategy for Diagnosis, Management and Prevention of COPD

Definitions

Asthma

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation. [GINA 2017]

COPD

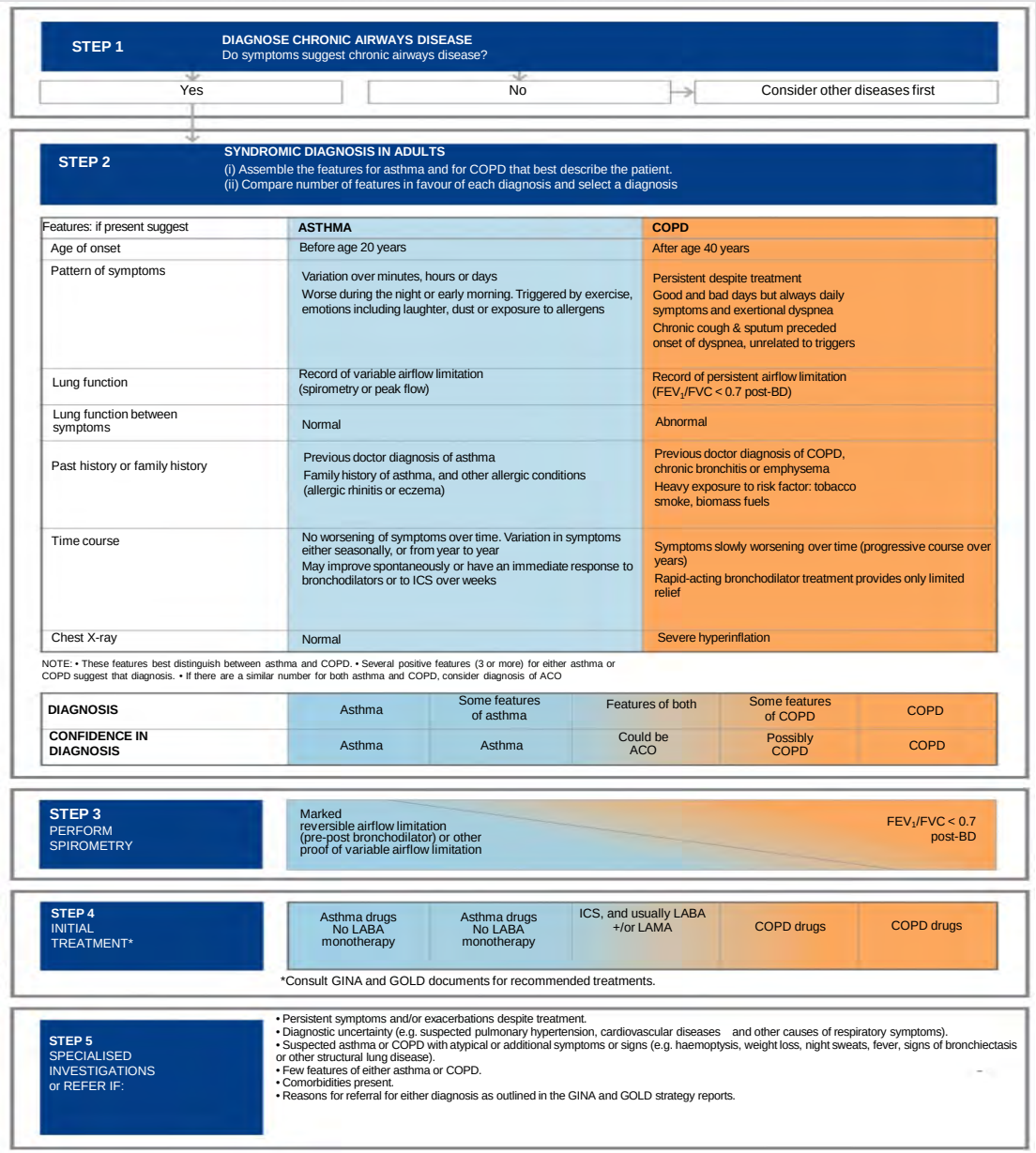
Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases. [GOLD 2017]

Asthma-COPD overlap [not a definition, but a description for clinical use]

Asthma-COPD overlap (ACO) is characterized by persistent airflow limitation with several features usually associated with asthma and several features usually associated with COPD. Asthma-COPD overlap is therefore identified in clinical practice by the features that it shares with both asthma and COPD.

This is not a definition, but a description for clinical use, as asthma-COPD overlap includes several different clinical phenotypes and there are likely to be several different underlying mechanisms.

Stepwise approach to diagnosis and initial treatment



STEP 1 — DIAGNOSE CHRONIC AIRWAYS DISEASE
Do symptoms suggest chronic airways disease?

Yes → **STEP 2**

No → Consider other diseases first

STEP 2 — SYNDROMIC DIAGNOSIS IN ADULTS
(i) Assemble the features for asthma and for COPD that best describe the patient.
(ii) Compare number of features in favour of each diagnosis and select a diagnosis

Features: if present suggest	ASTHMA	COPD
Age of onset	Before age 20 years	After age 40 years
Pattern of symptoms	Variation over minutes, hours or days Worse during the night or early morning. Triggered by exercise, emotions including laughter, dust or exposure to allergens	Persistent despite treatment Good and bad days but always daily symptoms and exertional dyspnea Chronic cough & sputum preceded onset of dyspnea, unrelated to triggers
Lung function	Record of variable airflow limitation (spirometry or peak flow)	Record of persistent airflow limitation (FEV_1/FVC < 0.7 post-BD)
Lung function between symptoms	Normal	Abnormal
Past history or family history	Previous doctor diagnosis of asthma Family history of asthma, and other allergic conditions (allergic rhinitis or eczema)	Previous doctor diagnosis of COPD, chronic bronchitis or emphysema Heavy exposure to risk factor: tobacco smoke, biomass fuels
Time course	No worsening of symptoms over time. Variation in symptoms either seasonally, or from year to year May improve spontaneously or have an immediate response to bronchodilators or to ICS over weeks	Symptoms slowly worsening over time (progressive course over years) Rapid-acting bronchodilator treatment provides only limited relief
Chest X-ray	Normal	Severe hyperinflation

NOTE: • These features best distinguish between asthma and COPD. • Several positive features (3 or more) for either asthma or COPD suggest that diagnosis. • If there are a similar number for both asthma and COPD, consider diagnosis of ACO

DIAGNOSIS	Asthma	Some features of asthma	Features of both	Some features of COPD	COPD
CONFIDENCE IN DIAGNOSIS	Asthma	Asthma	Could be ACO	Possibly COPD	COPD

STEP 3 PERFORM SPIROMETRY

Marked reversible airflow limitation (pre-post bronchodilator) or other proof of variable airflow limitation → FEV_1/FVC < 0.7 post-BD

STEP 4 INITIAL TREATMENT*

Asthma drugs No LABA monotherapy	Asthma drugs No LABA monotherapy	ICS, and usually LABA +/or LAMA	COPD drugs	COPD drugs

*Consult GINA and GOLD documents for recommended treatments.

STEP 5 SPECIALISED INVESTIGATIONS or REFER IF:

- Persistent symptoms and/or exacerbations despite treatment.
- Diagnostic uncertainty (e.g. suspected pulmonary hypertension, cardiovascular diseases and other causes of respiratory symptoms).
- Suspected asthma or COPD with atypical or additional symptoms or signs (e.g. haemoptysis, weight loss, night sweats, fever, signs of bronchiectasis or other structural lung disease).
- Few features of either asthma or COPD.
- Comorbidities present.
- Reasons for referral for either diagnosis as outlined in the GINA and GOLD strategy reports.

For an adult who presents with respiratory symptoms:

1. Does the patient have chronic airways disease?
2. Syndromic diagnosis of asthma, COPD and overlap
3. Spirometry
4. Commence initial therapy
5. Referral for specialized investigations (if necessary)

GINA 2017, Box 5-4

Step 1 – Does the patient have chronic airways disease?

- Clinical history: consider chronic airways disease if
  - Chronic or recurrent cough, sputum, dyspnea or wheezing, or repeated acute lower respiratory tract infections
  - Previous doctor diagnosis of asthma and/or COPD
  - Previous treatment with inhaled medications
  - History of smoking tobacco and/or other substances
  - Exposure to environmental hazards, e.g. airborne pollutants
- Physical examination
  - May be normal
  - Evidence of hyperinflation or respiratory insufficiency
  - Wheeze and/or crackles

Step 1 – Does the patient have chronic airways disease?

- Radiology (CXR or CT scan performed for other reasons)
  - May be normal, especially in early stages
  - Hyperinflation, airway wall thickening, hyperlucency, bullae
  - May identify or suggest an alternative or additional diagnosis, e.g. bronchiectasis, tuberculosis, interstitial lung disease, cardiac failure
- Screening questionnaires
  - Designed to assist in identification of patients at risk of chronic airways disease
  - May not be generalizable to all countries, practice settings or patients
  - See GINA and GOLD reports for examples

Step 2 – Syndromic diagnosis of asthma, COPD and asthma-COPD overlap

- Assemble the features that, **when present**, most favor a diagnosis of typical asthma or typical COPD
- Compare the number of features on each side
  - If the patient has ≥3 features of either asthma or COPD, there is a strong likelihood that this is the correct diagnosis
- Consider the level of certainty around the diagnosis
  - Diagnoses are made on the weight of evidence
  - The absence of any of these features does not rule out either diagnosis, e.g. absence of atopy does not rule out asthma
  - When a patient has a similar number of features of both asthma and COPD, consider the diagnosis of asthma-COPD overlap

STEP 2 — SYNDROMIC DIAGNOSIS IN ADULTS

(i) Assemble the features for asthma and for COPD that best describe the patient.
(ii) Compare number of features in favour of each diagnosis and select a diagnosis

Features: if present suggest -	ASTHMA	COPD
Age of onset	❑ Before age 20 years	❑ After age 40 years
Pattern of symptoms	❑ Variation over minutes, hours or days ❑ Worse during the night or early morning ❑ Triggered by exercise, emotions including laughter, dust or exposure to allergens	❑ Persistent despite treatment ❑ Good and bad days but always daily symptoms and exertional dyspnea ❑ Chronic cough & sputum preceded onset of dyspnea, unrelated to triggers
Lung function	❑ Record of variable airflow limitation (spirometry or peak flow)	❑ Record of persistent airflow limitation (FEV_1/FVC < 0.7 post-BD)
Lung function between symptoms	❑ Normal	❑ Abnormal
Past history or family history	❑ Previous doctor diagnosis of asthma ❑ Family history of asthma, and other allergic conditions (allergic rhinitis or eczema)	❑ Previous doctor diagnosis of COPD, chronic bronchitis or emphysema ❑ Heavy exposure to risk factor: tobacco smoke, biomass fuels
Time course	❑ No worsening of symptoms over time. Variation in symptoms either seasonally, or from year to year ❑ May improve spontaneously or have an immediate response to bronchodilators or to ICS over weeks	❑ Symptoms slowly worsening over time (progressive course over years) ❑ Rapid-acting bronchodilator treatment provides only limited relief
Chest X-ray	❑ Normal	❑ Severe hyperinflation

NOTE: • These features best distinguish between asthma and COPD. • Several positive features (3 or more) for either asthma or COPD suggest that diagnosis. • If there are a similar number for both asthma and COPD, consider diagnosis of ACO

DIAGNOSIS	Asthma	Some features of asthma	Features of both	Some features of COPD	COPD
CONFIDENCE IN DIAGNOSIS	Asthma	Asthma	Could be ACO	Possibly COPD	COPD

Step 3 - Spirometry

- Essential if chronic airways disease is suspected
  - Confirms chronic airflow limitation
  - More limited value in distinguishing between asthma with fixed airflow limitation, COPD and asthma-COPD overlap
- Measure at the initial visit or subsequent visit
  - If possible measure before and after a trial of treatment
  - Medications taken before testing may influence results
- Peak expiratory flow (PEF)
  - Not a substitute for spirometry
  - Normal PEF does not rule out asthma or COPD
  - Repeated measurement may confirm excessive variability, found in asthma or in some patients with asthma-COPD overlap

Step 3 - Spirometry

Spirometric variable	Asthma	COPD	Overlap
Normal FEV_1/FVC pre- or post-BD	Compatible with asthma	Not compatible with diagnosis (GOLD)	Not compatible unless other evidence of chronic airflow limitation
Post-BD FEV_1/FVC <0.7	Indicates airflow limitation; may improve	Required for diagnosis by GOLD criteria	Usual in asthma-COPD overlap (ACO)
FEV_1 ≥80% predicted	Compatible with asthma (good control, or interval between symptoms)	Compatible with GOLD category A or B if post-BD FEV_1/FVC <0.7	Compatible with mild ACO
FEV_1<80% predicted	Compatible with asthma. A risk factor for exacerbations	Indicates severity of airflow limitation and risk of exacerbations and mortality	Indicates severity of airflow limitation and risk of exacerbations and mortality
Post-BD increase in FEV_1 >12% and 200mL from baseline (reversible airflow limitation)	Usual at some time in course of asthma; not always present	Common in COPD and more likely when FEV_1 is low	Common in ACO, and more likely when FEV_1 is low
Post-BD increase in FEV_1 >12% and 400mL from baseline	High probability of asthma	Unusual in COPD. Consider ACO	Compatible with diagnosis of ACO

GINA 2017, Box 5-3

Step 4 – Commence initial therapy

- Initial pharmacotherapy choices are based on both efficacy and safety
- If syndromic assessment suggests asthma as single diagnosis
  - Start with low-dose ICS
  - Add LABA and/or LAMA if needed for poor control despite good adherence and correct technique
  - Do not give LABA alone without ICS
- If syndromic assessment suggests COPD as single diagnosis
  - Start with bronchodilators or combination therapy
  - Do not give ICS alone without LABA and/or LAMA
- If differential diagnosis is equally balanced between asthma and COPD, i.e. asthma-COPD overlap
  - Start treatment as for asthma, pending further investigations
  - Start with ICS at low or moderate dose
  - Usually also add LABA and/or LAMA, or continue if already prescribed

Step 4 – Commence initial therapy

- For all patients with chronic airflow limitation:
  - Treat modifiable risk factors including advice about smoking cessation
  - Treat comorbidities
  - Advise about non-pharmacological strategies including physical activity, and, for COPD or asthma-COPD overlap, pulmonary rehabilitation and vaccinations
  - Provide appropriate self-management strategies
  - Arrange regular follow-up
- See GINA and GOLD reports for details

Step 5 – Refer for specialized investigations if needed

- Refer for expert advice and extra investigations if patient has:
  - Persistent symptoms and/or exacerbations despite treatment
  - Diagnostic uncertainty, especially if alternative diagnosis (e.g. TB, cardiovascular disease) needs to be excluded
  - Suspected airways disease with atypical or additional symptoms or signs (e.g. hemoptysis, weight loss, night sweats, fever, chronic purulent sputum). Do not wait for a treatment trial before referring
  - Suspected chronic airways disease but few features of asthma, COPD or asthma-COPD overlap
  - Comorbidities that may interfere with their management
  - Issues arising during on-going management of asthma, COPD or asthma-COPD overlap

Step 5 – Refer for specialized investigations if needed

Investigation	Asthma	COPD
DLCO	Normal or slightly elevated	Often reduced
Arterial blood gases	Normal between exacerbations	In severe COPD, may be abnormal between exacerbations
Airway hyperresponsiveness	Not useful on its own in distinguishing asthma and COPD. Higher levels favor asthma	
High resolution CT scan	Usually normal; may show air trapping and increased airway wall thickness	Air trapping or emphysema; may show bronchial wall thickening and features of pulmonary hypertension
Tests for atopy (sIgE and/or skin prick tests)	Not essential for diagnosis; increases probability of asthma	Conforms to background prevalence; does not rule out COPD
FENO	If high (>50ppb) supports eosinophilic inflammation	Usually normal. Low in current smokers
Blood eosinophilia	Supports asthma diagnosis	May be found during exacerbations
Sputum inflammatory cell analysis	Role in differential diagnosis not established in large populations	

Asthma exacerbations

Ms C – acute presentation

TRIAGE NURSE SUMMARY:
1/7 INCREASED SOB

HAS TAKEN OWN VENTOLIN NEBS AND PUFFER WITH MINIMAL RELIEF

PMHX ASTHMA - HOSPITAL ADM. NIL ICU ADM.

A: Patent. **B**: Spont, speaking in full sentences, SaO2 97% RA, RR 24. **C**: warm, pink, dry, reg radial pulse, HR 125. **D**: alert, denies pain. **Wheezing+++**

What *management* should be initiated?

A. Discharge home immediately, as anxiety is the main cause
B. Diuretics to treat heart failure
C. Intubation and mechanical ventilation in the Intensive Care Unit
D. Primary assessment of asthma severity, with early use of bronchodilators
E. Spirometry before any treatment starts, since baseline lung function needs to be known in the Emergency Department

‘Asthma attack’

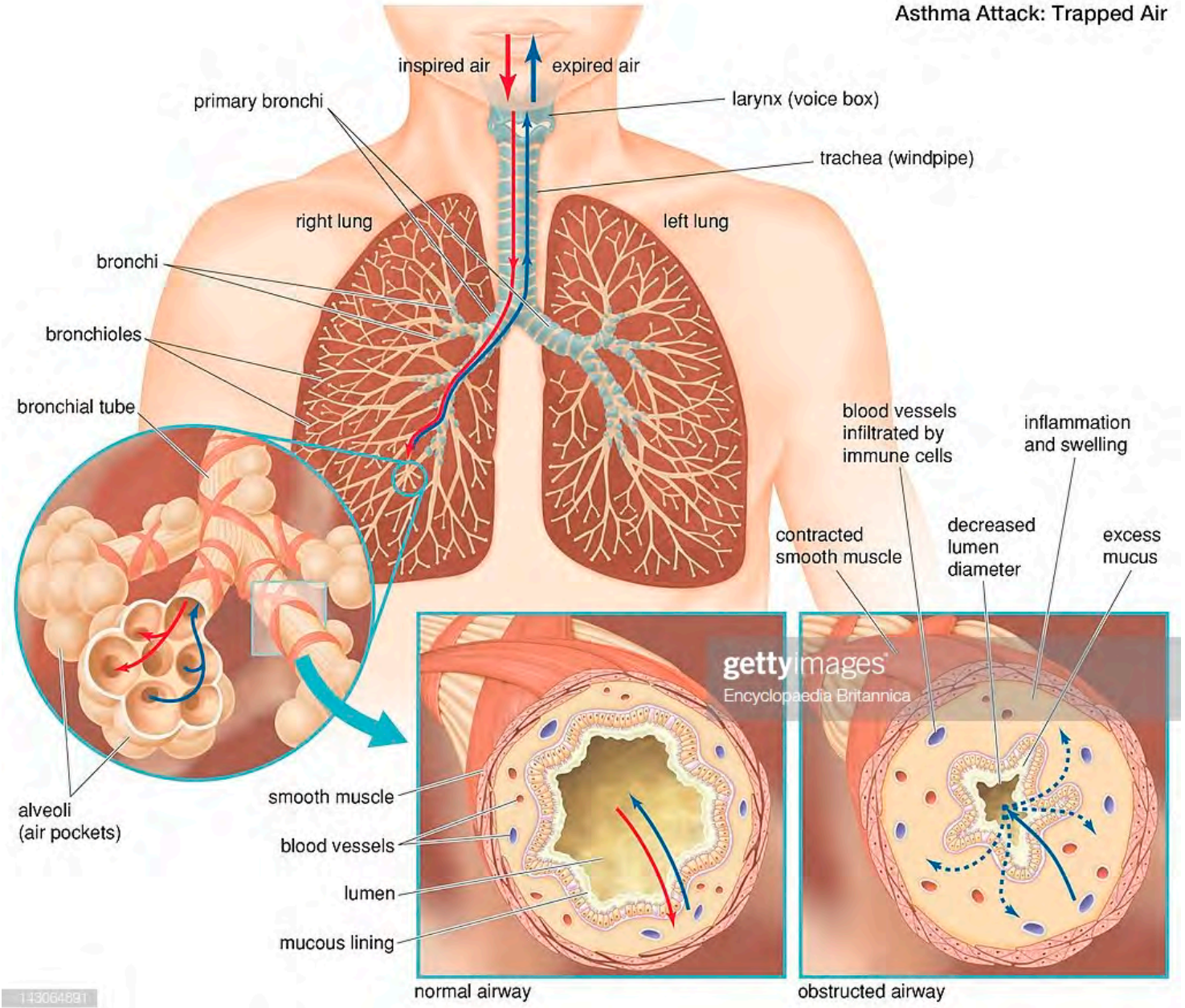
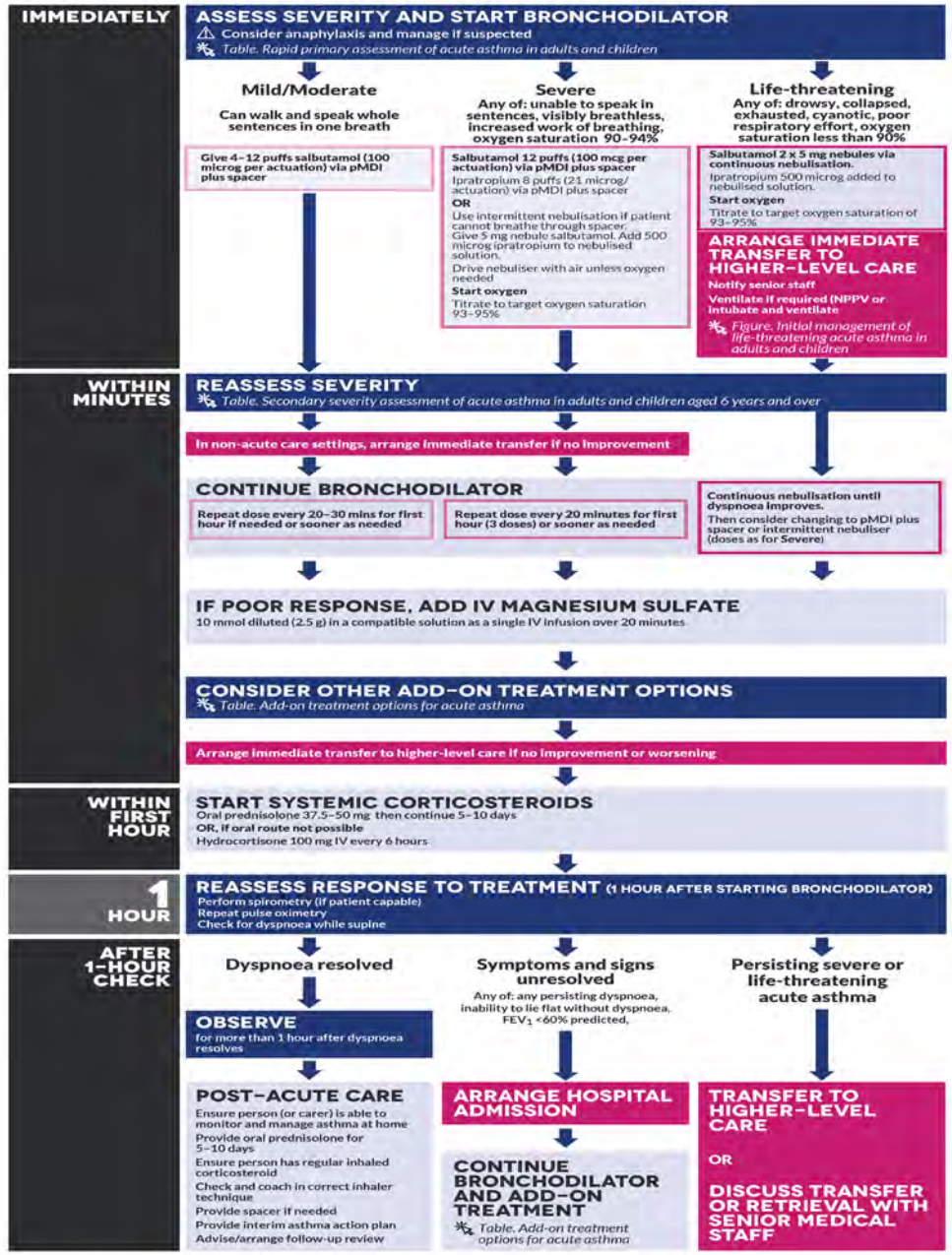


Figure. Managing acute asthma in adults



For more details on the initial management of life-threatening acute asthma, see Initial management of life-threatening acute asthma in adults and children

Australian Asthma Handbook v2.0, 2019

Primary assessment

Complete a rapid primary assessment and start initial treatment

- Make a rapid clinical assessment with the person in a sitting position
- Measure pulse oximetry while the person is breathing air (unless life-threatening)
- Start bronchodilator immediately, according to severity and age

Mild/Moderate	*Severe*	*Life-threatening*
Can walk, speak whole sentences in one breath (For young children: can move around, speak in phrases) Oxygen saturation >94%	**Any** of these findings: • Use of accessory muscles of neck or intercostal muscles or 'tracheal tug' during inspiration or subcostal recession ('abdominal breathing') • Unable to complete sentences in one breath due to dyspnoea • Obvious respiratory distress • Oxygen saturation 90–94%	**Any** of these findings: • Reduced consciousness or collapse • Exhaustion • Cyanosis • Oxygen saturation <90% • Poor respiratory effort, soft/absent breath sounds

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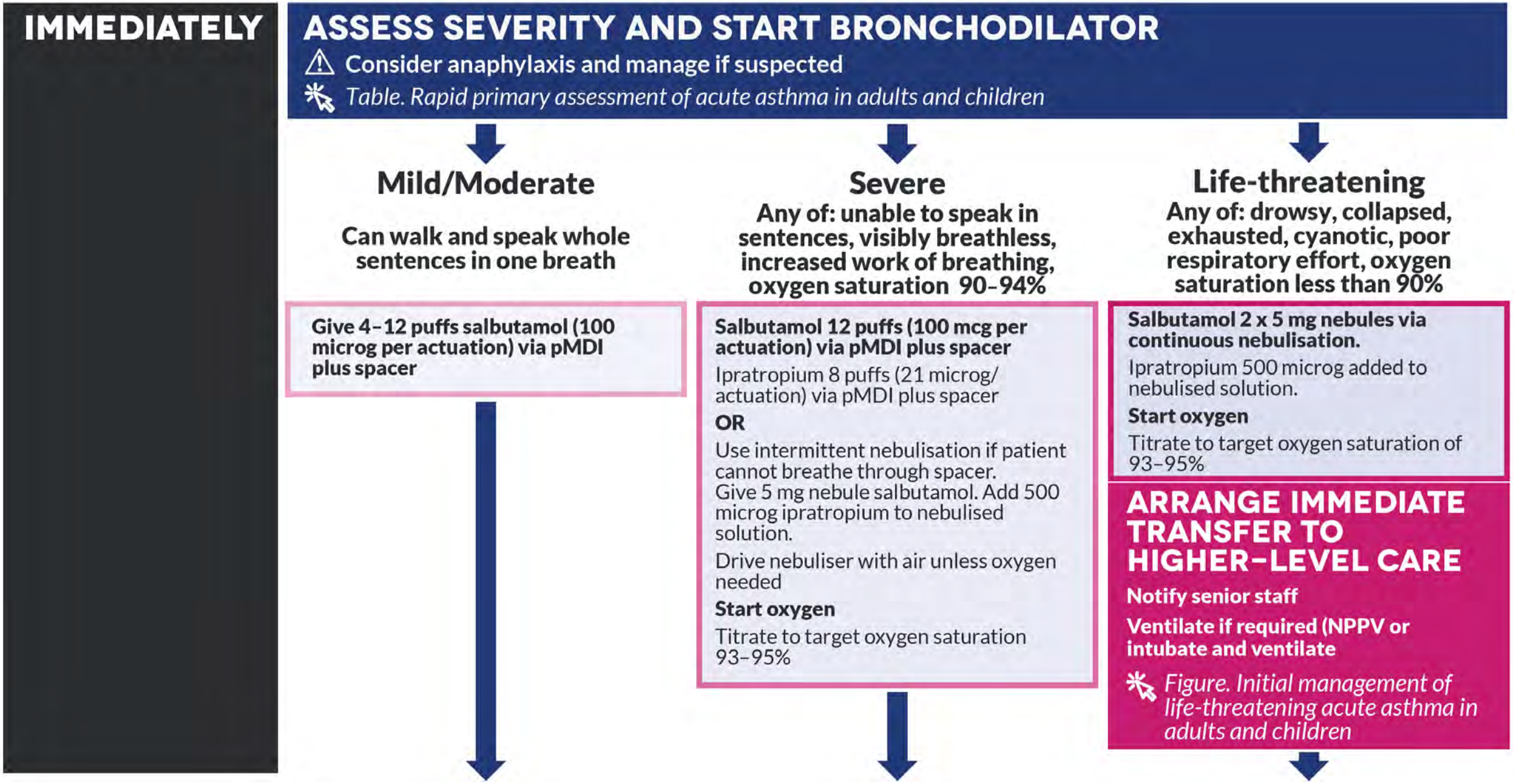


Australian Asthma Handbook v2.0, 2019

Ms C – ED assessment

ED RMO assessment (11pm)

16yo F
Presented with 1/7 of increased dyspnoea and wheeze. B/g of asthma
Reports using salbutamol, 3 puffs every 5 minutes today since waking up to minimal relief
2/7 history of "hayfever' - runny nose, dry cough, sneezing
Has an asthma action plan, however it is with the GP. No copy at home

PMHx:
Asthma
- rare asthmatic attacks. Nil hospital admissions although has had previous ED presentations
Eczema

Med:
Salbutamol PRN
Should be on Seretide 2puff BD, however has been non-compliant

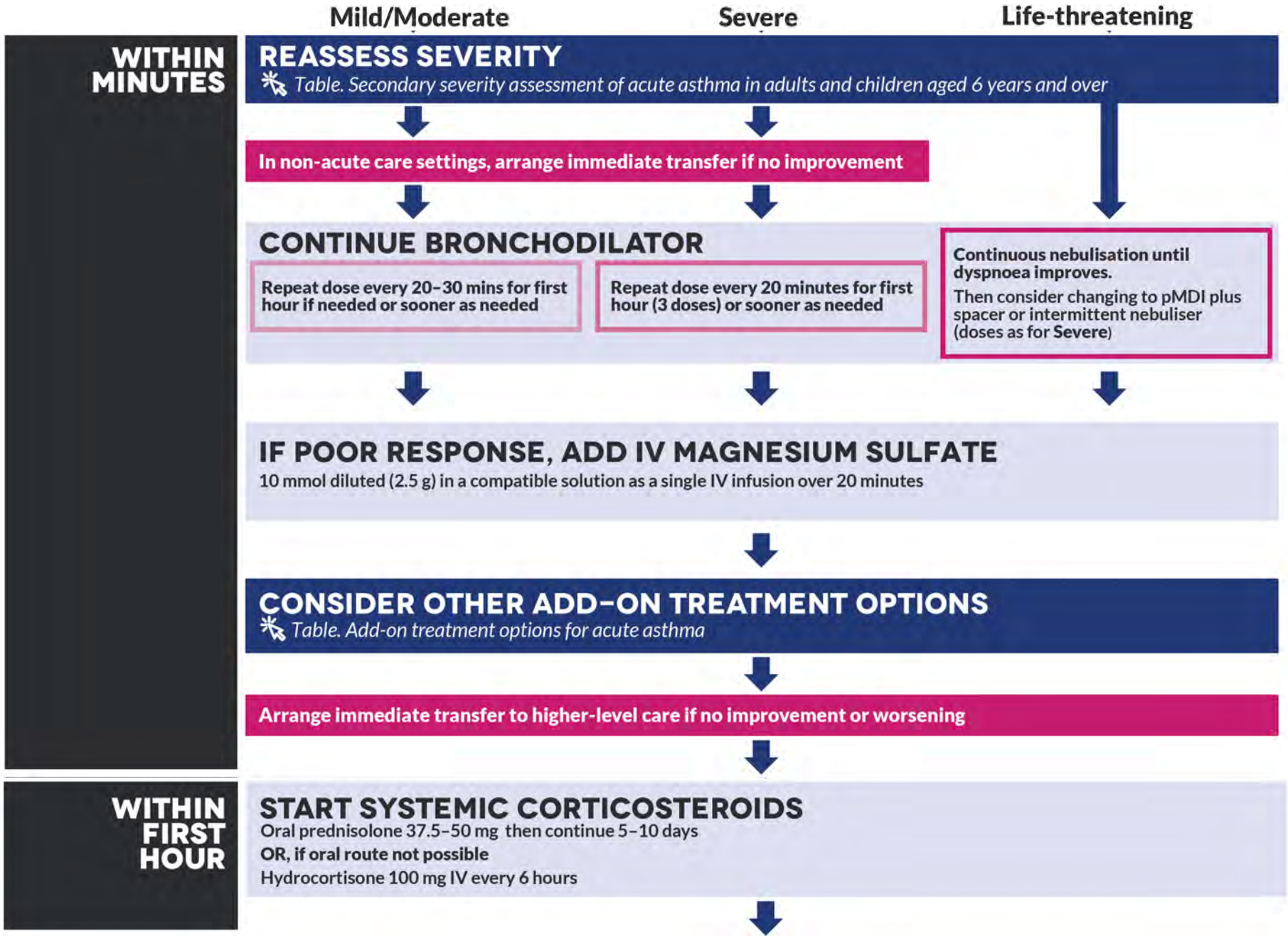
NKDA

Ms C – ED assessment

Social hx:
Lives w family
Studying at school
Non-smoker

O/E:
HR 125, BP 141/115, 96% RA, RR 24, GCS 15
Increased BMI
Speaking in normal sentences
Nil obvious accessory muscle use
Chest - generalised insp and exp wheeze bilaterally
Pulses regular, warm peripherally bilat

Imp: Exacerbation of asthma



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Secondary assessment

Complete a brief history, including:

- reliever taken for this episode (dose, number of doses, time of last dose)
- current asthma medicines (regular and as-needed, including type of devices used)
- assessment of adherence to preventer (if prescribed)
- what triggered this episode, if known (e.g. allergies, immediate hypersensitivity, medicines, respiratory infections)
- coexisting heart or lung disease, including chronic obstructive pulmonary disease
- assess smoking status and exposure to second-hand smoke

Corticosteroids

For adults with acute asthma:

Start systemic corticosteroids within 1 hour of presentation (unless contraindicated), regardless of severity at initial assessment

- Give starting dose of oral **prednisolone** 37.5–50 mg, then repeat each morning on second and subsequent days (total 5–10 days)
- It is usually not necessary to taper the dose unless the duration of treatment exceeds 2 weeks

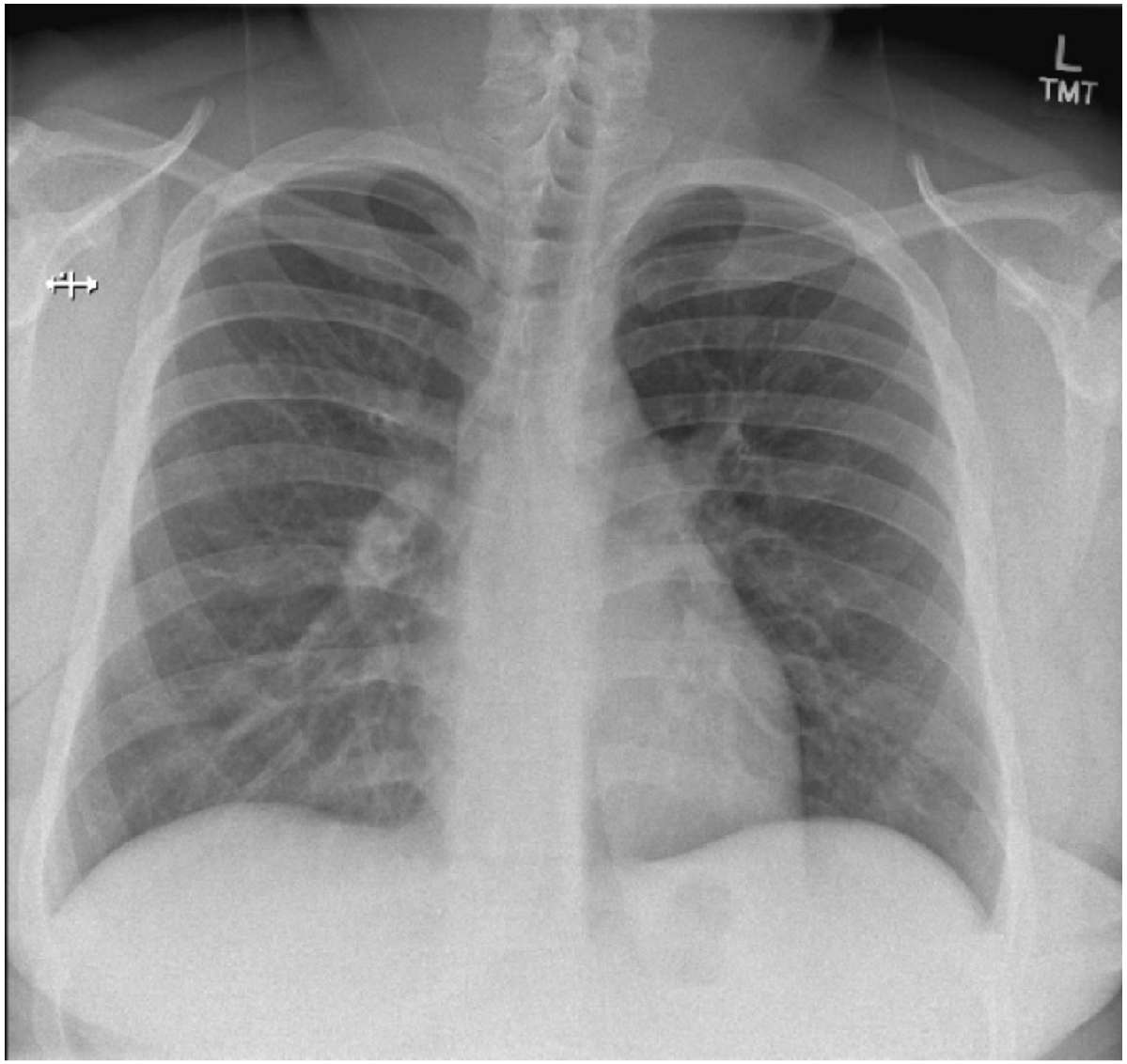
If corticosteroids cannot be given orally, give **IV hydrocortisone** 4 mg/kg (maximum 100 mg) every 6 hours for 24 hours then reduce over next 24 hours or switch to oral prednisolone

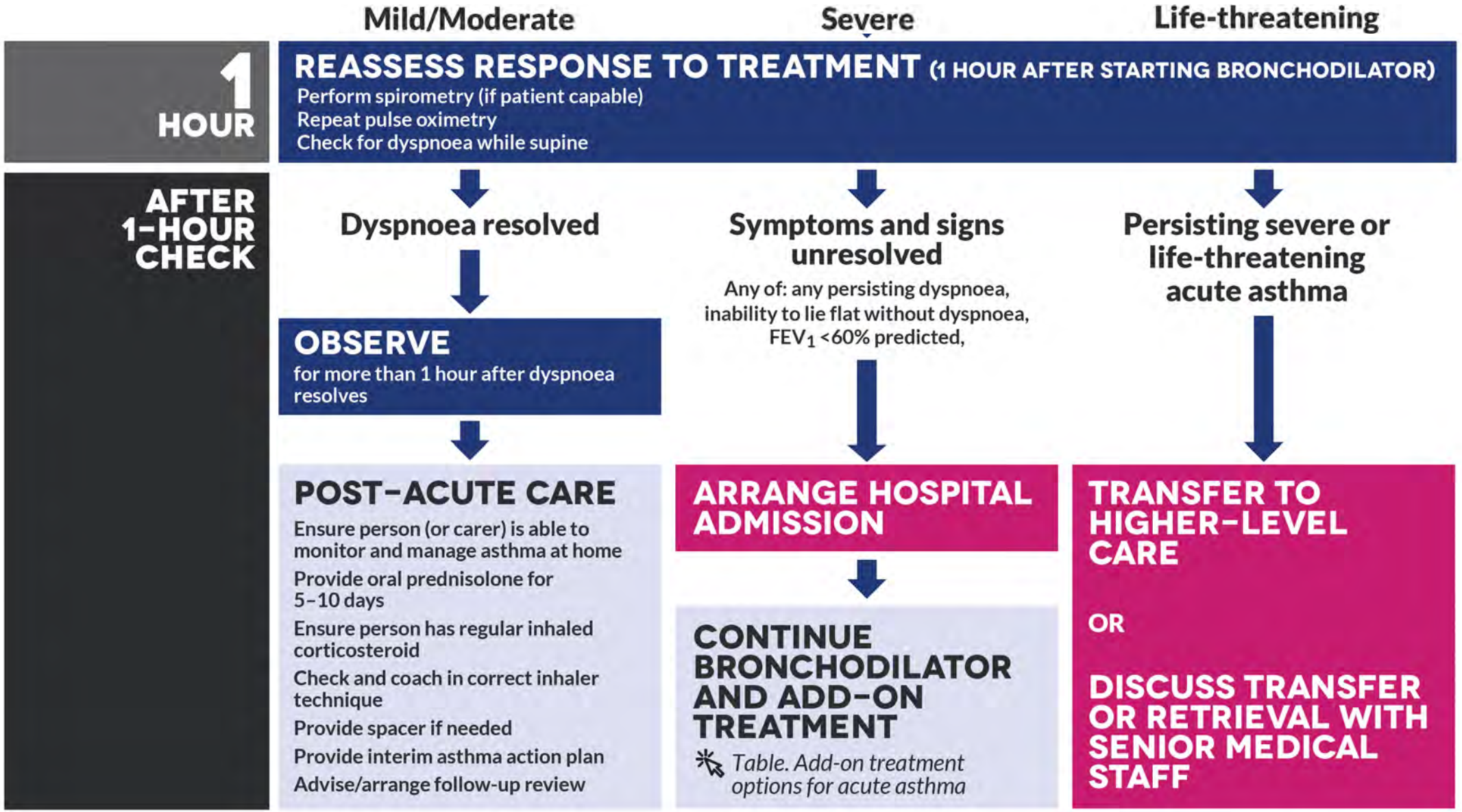
Ms C – investigations and treatment

salbutamol MDI 100 microg, 9 puffs via spacer
ipratropium MDI 21 microg, 8 puffs via spacer
prednisolone PO 50 mg

20 min later:
salbutamol MDI 100 microg, 12 puffs via spacer
20 min later:
salbutamol MDI 100 microg, 12 puffs via spacer
iptratropium MDI 21 microg, 8 puffs via spacer

2 hr later:
salbutamol neb 5mg
salbutamol neb 5mg (*20 min later*)
salbutamol neb 5mg (*20 min later*)
ipratropium neb 250 mcg





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Add-on treatment for life-threatening asthma

- Inhaled ipratropium bromide - MDI, or nebulised (500 mcg)
- IV magnesium sulfate - 10 mmol infusion over 20 min
- IV salbutamol (in ED or ICU) - 200 microg over 1 min, then 5 microg/min (and increasing)
- IV aminophylline
- IM or IV adrenaline - 0.3 to 0.5 mg IM, or 50 mcg IV slow injection, or infusion
- Non-invasive positive pressure ventilation
- Intubation and mechanical ventilation

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Ms C - progress

Issues:

1. Asthma – since primary school years
2. Suboptimal adherence – intermittent use of ICS/LABA (salmeterol/fluticasone = Seretide)
3. Obesity – BMI 40

Progress:

- Admitted to Short Stay ED unit; brought back to Acute ED
- Admitted to Thoracic Ward – bronchodilators; 5 days of oral steroids
- Recommenced on regular ICS/LABA
- Reviewed by asthma nurse educator, dietitian, physiotherapist, pharmacist, thoracic medical team
- Discharged home after 3 day admission; GP review arranged

Management of mild-moderate exacerbations

Self-management – based on patient's written **asthma action plan**

Increase **reliever** use to control symptoms

Keep taking regular **preventer** during a flare-up (even if needing oral corticosteroids)

Prescribe an increase in **preventer** and/or a course of **oral corticosteroids** (37.5–50 mg for 5–10 days) for patients with (any of):

- acute asthma symptoms that recur within 3 hours of taking a rapid-onset $beta_2$ agonist reliever
- increasing difficulty breathing over one or more days
- night-time asthma symptoms that interfere with sleep over more than one night in a row
- peak flow below a pre-defined level (for those monitoring peak flow each day; level determined based on individual’s personal best and history of peak flow levels before and during flare-ups)

Australian Asthma Handbook v2.0, 2019

SUMMARY of acute asthma management

- Emergency assessment
- If asthma, start bronchodilators
- Assess severity, trigger factors, differential diagnoses
- Use oral or IV steroids early
- Monitor response
- Escalate treatment if needed
- Decide on admission or discharge
- Plan for longer term asthma management

Check Australian Asthma Handbook for more details, assessment tools and evidence

Severe asthma and biologic therapy

Ms D

72 y.o.

- Asthma since childhood
- Worsening cough and exertional breathlessness
- 5 courses of prednisolone in 12 mth
- No specific triggers

Rhinosinusitis. GORD. Never smoker

Seretide MDI 250 mcg 2 bd via spacer

Alvesco MDI 160 mcg 2 mane via spacer

Tried Spiriva, montelukast, Tilade

O/E chest – expiratory wheezes

Spirometry

Pre-bronchodilator

FEV_1	1.45	75% predicted
VC	2.57	91% predicted

Post-bronchodilator

FEV_1	1.81	29% increase
VC	2.55	

FBC – eosinophils 1.10: elevated

IgE – 20: normal

Diagnosis?

Management?

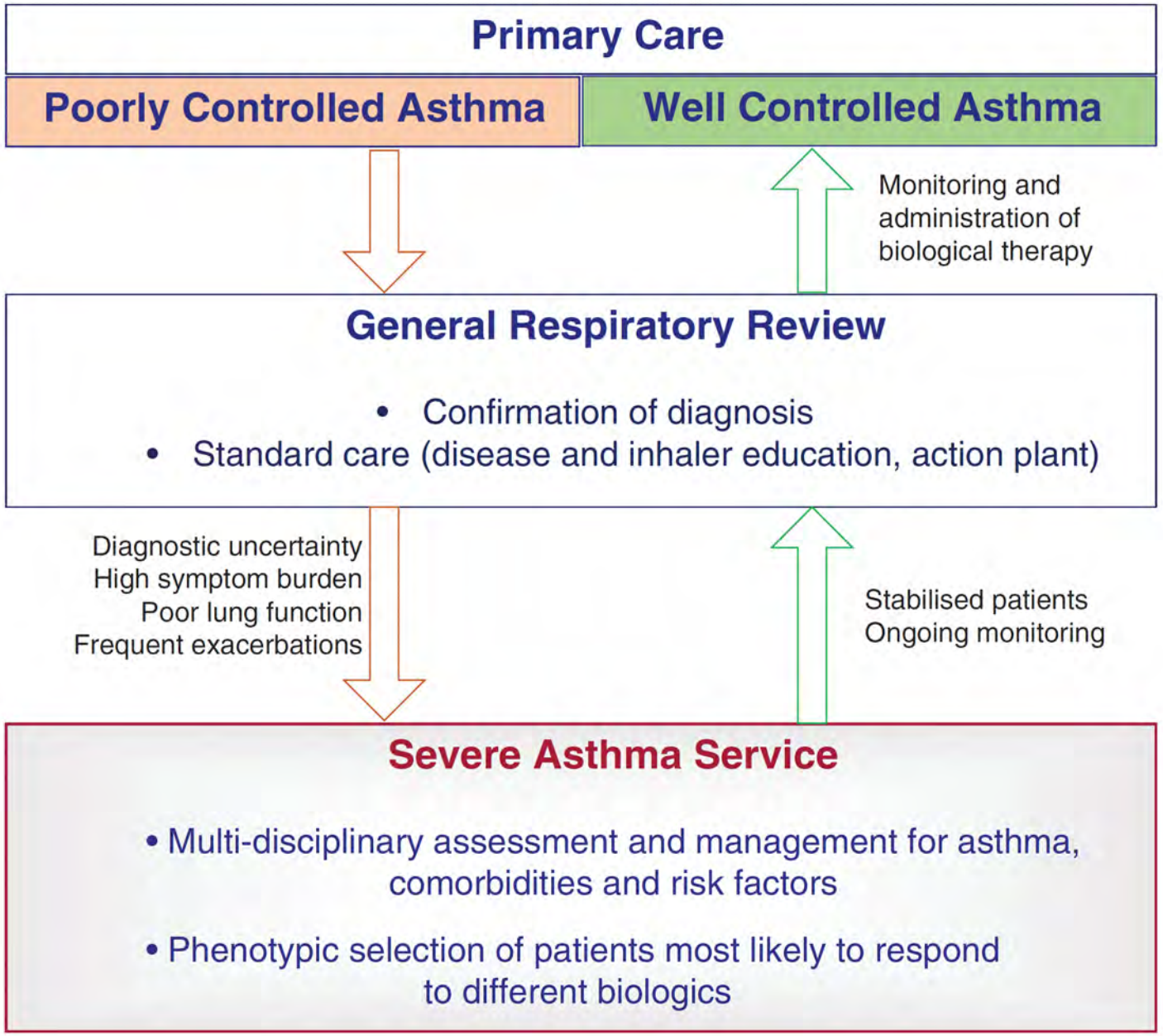
Severe asthma

Severe asthma is defined as:

- asthma that remains uncontrolled despite regular treatment with high-dose inhaled corticosteroids plus long-acting beta$_2$ agonist, or with maintenance oral corticosteroids, or
- asthma that requires this level of treatment (Step 4) to prevent it becoming uncontrolled.

If a patient continues to experience **poor control of asthma**, frequent flare-ups, or poor quality of life due to asthma, despite regular treatment with a high dose of an inhaled corticosteroid plus a long-acting beta$_2$ agonist, make a full assessment to rule out common problems (including poor inhaler technique and suboptimal adherence) before applying the label of severe asthma.

Severe asthma model of care



Chung *et al*. Intern Med J 2018;48:1536-1541

Severe asthma in primary care (1)

3 The role of primary care in the multidimensional model of care for asthma

Assessment of airway pathology

Is it asthma?	• Confirm history is compatible • Obtain spirometry for evidence of variable airflow limitation: ▸ training available through asthma foundations, NAC Australia, ALF; online resources also available* ▸ consider external referral for spirometry
Is it severe asthma?	• Definition: ▸ high dose ICS plus one other maintenance therapy, or oral corticosteroid for > 50% of the previous year required to keep asthma under control; or ▸ uncontrolled asthma despite such therapies • If severe, respiratory physician referral recommended
Is the asthma controlled?	• Definition: ▸ no nocturnal or early morning symptoms ▸ no limitation of activities ▸ daytime symptoms ≤ 2 days per week ▸ need for reliever ≤ 2 days per week • More than two exacerbations per year • Assess at every opportunity with specific questioning • Consider use of validated questionnaires (eg, ACQ or ACT)† • If not controlled, review and escalate therapy, as below, followed by referral to respiratory physician

Chung *et al*. MJA 2018;209(2 Suppl): S34-S40

Severe asthma in primary care (2)

Management	
Is inhaler therapy optimised?	• Escalate maintenance therapy as required in stepwise manner according to guideline recommendation:[3] ▸ low dose ICS ▸ low dose ICS/LABA ▸ medium /high dose ICS/LABA • Assess adherence and inhaler technique, and address as required. Ask: ▸ how often the patient is actually taking their maintenance therapy ▸ what makes it difficult to take ▸ what makes it easier to take • Consider use of trained practice nurse, pharmacists, asthma educator from asthma foundations, online resource such as videos and patient resource from NAC Australia
Asthma action plan[3]	• Should explain: ▸ what patient should do when well ▸ how to recognise worsening symptoms ▸ what patient should do when symptoms worsen
Smoking cessation advice	• Provide advice and support for smoking cessation (eg, through motivational interviewing, opportunistic counselling, pharmacotherapy, QUIT line)

Chung *et al*. MJA 2018;209(2 Suppl): S34-S40

Severe asthma in primary care (3)

Ongoing coordinated care	
Comorbidities	• Review and manage common contributory comorbidities (eg, GORD, obesity, anxiety and depression, allergic rhinitis) • Consider specialist referral and coordinate care for assessment and management of complex comorbidities (eg ,vocal cord dysfunction, dysfunctional breathing, OSA and bronchiectasis) • Coordinate community allied health professional involvement as required (eg, dietitian, clinical psychologist)
Targeted therapies	• Assist with ongoing administration of biological therapies once patient is stabilised by respiratory physician ▸ appropriate GP training and support can be provided by treating respiratory physician or Centre of Excellence in Severe Asthma
Collaboration between primary and specialist care	• Refer back to treating respiratory physician in event of: ▸ deterioration in asthma symptom control after a period of stability ▸ frequent exacerbations ▸ deteriorating lung function ▸ intolerance or adverse effects to therapies • Respiratory physician may support GPs by providing streamlined re-referral pathways • Communication between primary and specialist care may be improved by increased use of eHealth records

ACQ = Asthma Control Questionnaire. ACT = Asthma Control Test. ALF = Australian Lung Foundation. GORD = gastroesophageal reflux disease. ICS = inhaled corticosteroid. LABA = long-acting β-agonist. NAC = National Asthma Council. OSA = obstructive sleep apnoea. * For example, www.toolkit.severeasthma.org.au. † See www.asthmahandbook.org.au/resources/tools/control-questionnaires (Sources: ACT, QualityMetric and GlaxoSmithKline. ACQ, Juniper EF, O'Byrne PM, Guyatt GH, et al. Development and validation of a questionnaire to measure asthma control. *Eur Respir J* 1999; 14: 902-907).

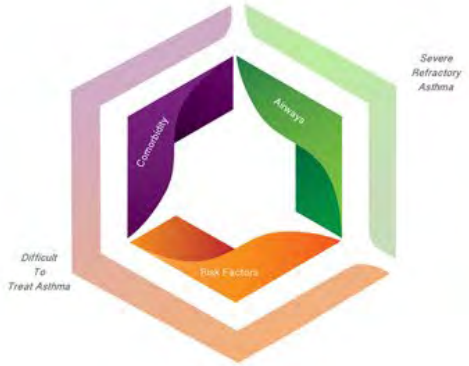
Chung *et al*. MJA 2018;209(2 Suppl): S34-S40

Severe asthma toolkit

SEVERE ASTHMA TOOLKIT

Home About Specific Populations

What is Severe Asthma? | Diagnosis & Assessment | Management | Medications | Co-Morbidities | Living with Severe Asthma | Establishing a Clinic | Paediatrics | Resources



What is Severe Asthma >

Diagnosis & Assessment >

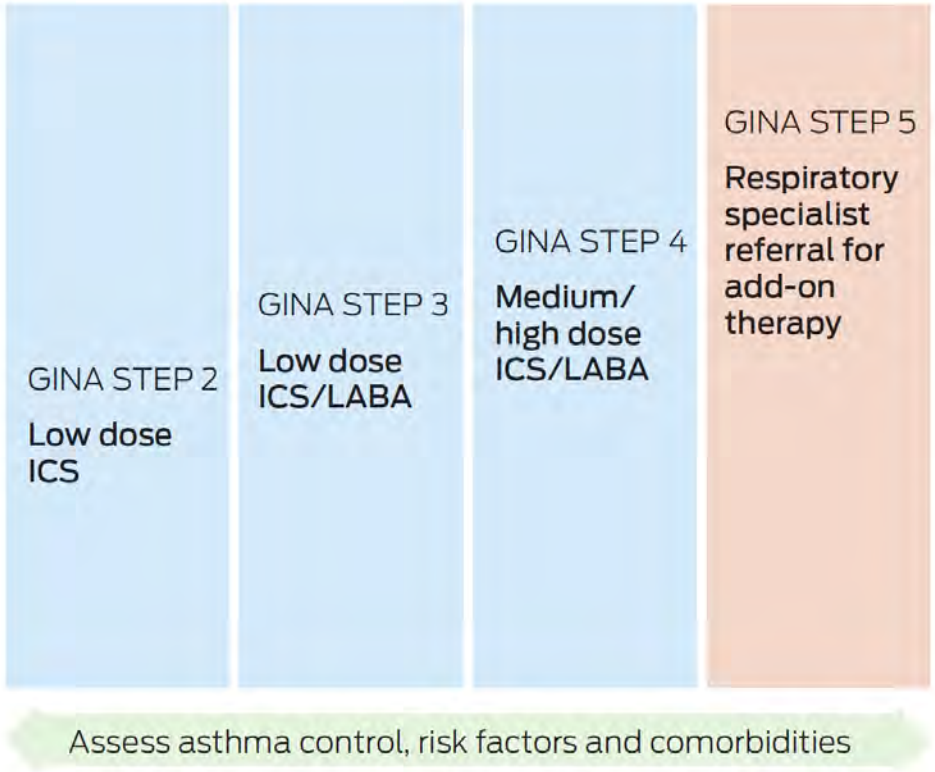
Management >

Medications >

NHMRC Centre for Research Excellence in Severe Asthma https://www.severeasthma.org.au/

Add-on therapies for severe asthma

1 Stepwise treatment of asthma, showing possible add-on therapies for particular asthma phenotypes



Possible add-on therapies

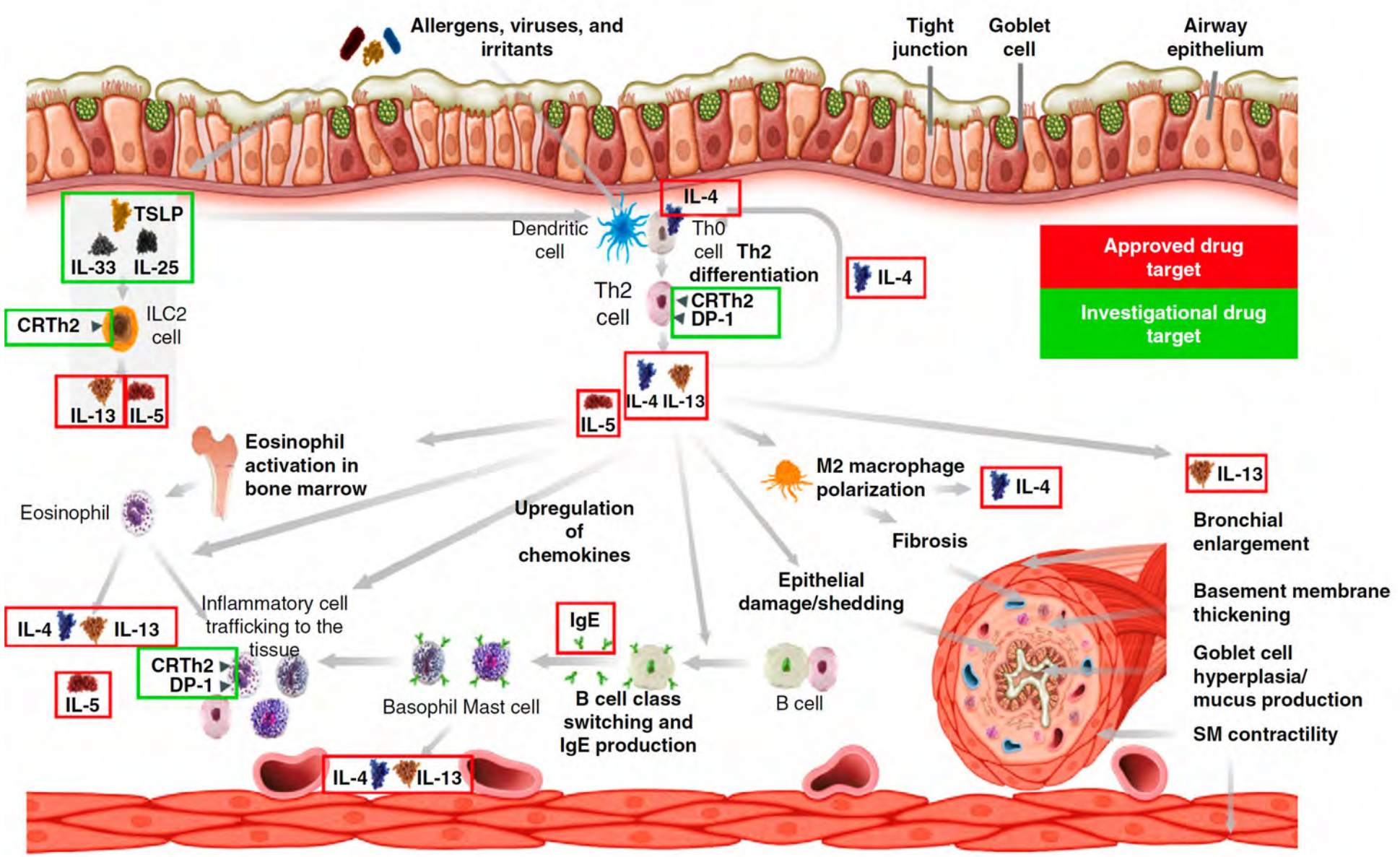
Therapy	Phenotype
LAMA (eg, tiotropium mist inhaler)	Exacerbation despite optimised ICS/LABA
Leukotriene antagonist (eg, montelukast)	Asthma with aspirin sensitivity
Antifungal*†	ABPA or fungal sensitivity
Macrolides*†	Uncontrolled asthma despite optimised ICS/LABA
Biologicals Anti-IgE (omalizumab) Anti-IL-5 (mepolizumab, benralizumab†, reslizumab†)	 Severe atopic asthma Severe eosinophilic asthma
Bronchial thermoplasty	Unknown
Continuous oral corticosteroid	Uncontrolled asthma

* non-TGA approved in Australia † non-PBS funded in Australia

ABPA = allergic bronchopulmonary aspergillosis. GINA = Global Initiative for Asthma.[2] IL-5 = interleukin-5. ICS = inhaled corticosteroids. LABA = long-acting β2-agonists. LAMA = long-acting anti-muscarinic antagonists. PBS = Pharmaceutical Benefits Scheme. TGA = Therapeutic Goods Administration.

Upham *et al*. MJA 2018;209 (2 Suppl):S22-S27

Biologic therapy - mechanisms



McGregor *et al*. Am J Respir Crit Care Med 2018;199:433-445

Biologic therapy for severe asthma

Anti-IgE

omalizumab (Xolair)

SC every 2-4 wk

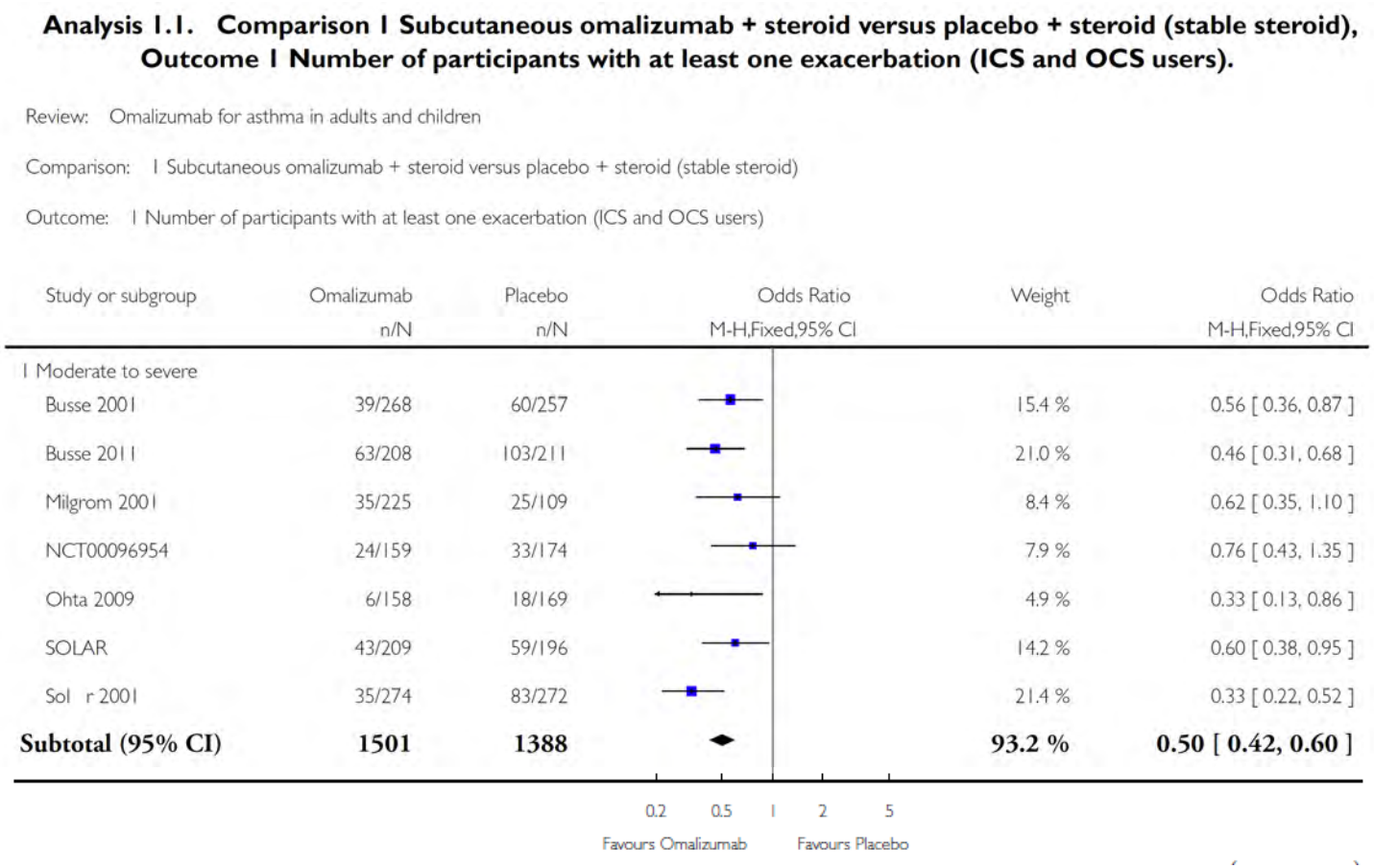
Anti-interleukin-5 (IL-5) (anti-eosinophilic)

mepolizumab (Nucala)

SC every 4 wk

benralizumab (Fasenra)

SC every 4 wk then 8 wk



Analysis 1.1. Comparison 1 Subcutaneous omalizumab + steroid versus placebo + steroid (stable steroid), Outcome 1 Number of participants with at least one exacerbation (ICS and OCS users).

Review: Omalizumab for asthma in adults and children

Comparison: 1 Subcutaneous omalizumab + steroid versus placebo + steroid (stable steroid)

Outcome: 1 Number of participants with at least one exacerbation (ICS and OCS users)

Study or subgroup	Omalizumab n/N	Placebo n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 Moderate to severe					
Busse 2001	39/268	60/257		15.4 %	0.56 [0.36, 0.87]
Busse 2011	63/208	103/211		21.0 %	0.46 [0.31, 0.68]
Milgrom 2001	35/225	25/109		8.4 %	0.62 [0.35, 1.10]
NCT00096954	24/159	33/174		7.9 %	0.76 [0.43, 1.35]
Ohta 2009	6/158	18/169		4.9 %	0.33 [0.13, 0.86]
SOLAR	43/209	59/196		14.2 %	0.60 [0.38, 0.95]
Sol r 2001	35/274	83/272		21.4 %	0.33 [0.22, 0.52]
Subtotal (95% CI)	**1501**	**1388**		**93.2 %**	**0.50 [0.42, 0.60]**

0.2 0.5 1 2 5

Favours Omalizumab Favours Placebo

~50% reduction in exacerbation rates

Normansell *et al*. Cochrane Database Syst Rev 2014;CD003559

Biologic therapy for severe asthma

Anti-IgE

omalizumab (Xolair)

SC every 2-4 wk

Anti-interleukin-5 (IL-5)

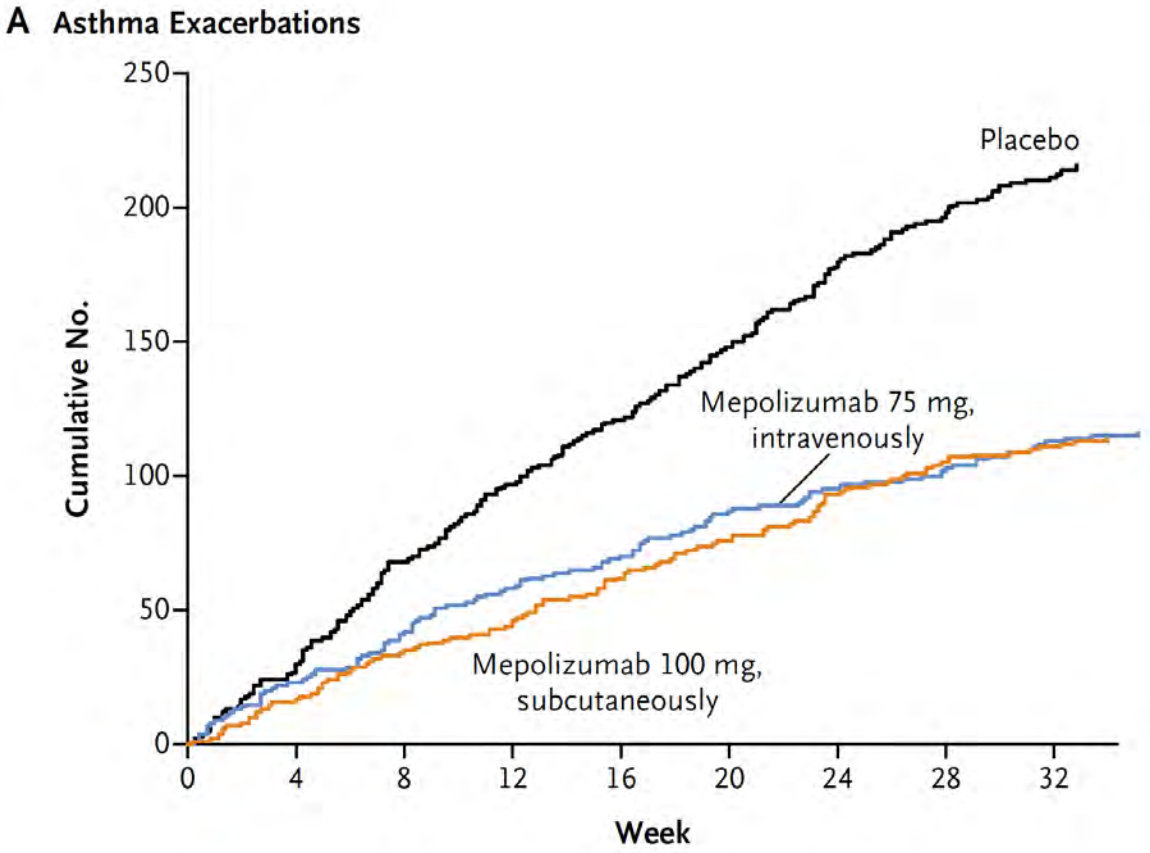
(anti-eosinophilic)

mepolizumab (Nucala)

SC every 4 wk

benralizumab (Fasenra)

SC every 4 wk then 8 wk



~53% reduction in exacerbation rates

~50% reduction in oral steroids

Bel *et al*. New Engl J Med 2014;371:1189-97

Ortega *et al*. New Engl J Med 2014;371:1198-1207

Biologic therapy for severe asthma

Anti-IgE

omalizumab (Xolair)

SC every 2-4 wk

Anti-interleukin-5 (IL-5)

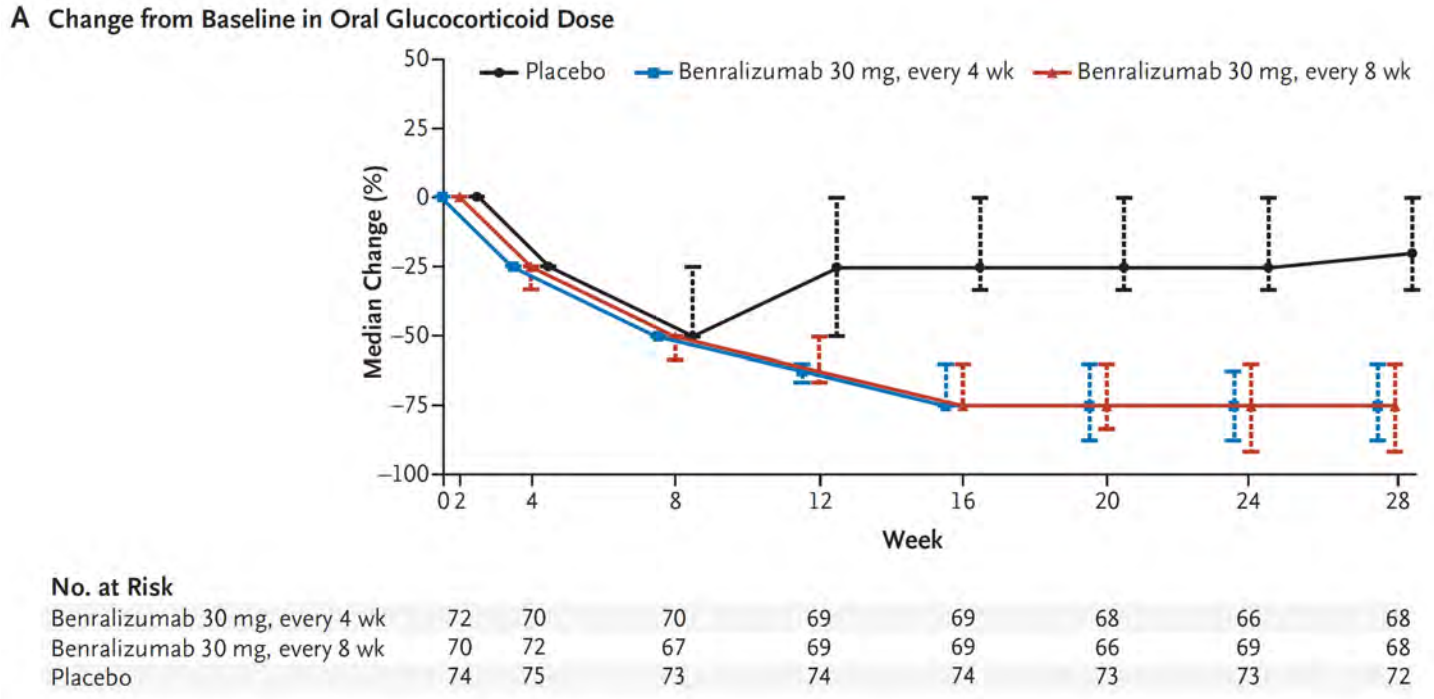
(anti-eosinophilic)

mepolizumab (Nucala)

SC every 4 wk

benralizumab (Fasenra)

SC every 4 wk then 8 wk



~75% reduction in oral steroid dose
~55% reduction in exacerbation rates

Nair *et al*. New Engl J Med 2017;376:2448-2458

Biologic therapy – practice tips

Practice tips

- Add-on treatment for uncontrolled severe eosinophilic asthma or severe allergic asthma
- Hospital authority script prescribed by specialist
  - initiation (6 months) then continuation (6 months) – required to meet PBS criteria
- First 3 doses in hospital, then primary care/community
- Rare incidence of anaphylaxis
  - resuscitation facilities
  - recommend Epipen
  - observe after subcutaneous injection for specified time

    1 to 2 hr initially, 30 min subsequently
- Continue inhaled preventer medications

Effect of azithromycin on asthma exacerbations and quality of life in adults with persistent uncontrolled asthma (AMAZES): a randomised, double-blind, placebo-controlled trial

Peter G Gibson, Ian A Yang, John W Upham, Paul N Reynolds, Sandra Hodge, Alan L James, Christine Jenkins, Matthew J Peters, Guy B Marks, Melissa Baraket, Heather Powell, Steven L Taylor, Lex E X Leong, Geraint B Rogers, Jodie L Simpson

Lancet 2017; 390: 659–68

Findings Between June 12, 2009, and Jan 31, 2015, 420 patients were randomly assigned (213 in the azithromycin group and 207 in the placebo group). Azithromycin reduced asthma exacerbations (1·07 per patient-year [95% CI 0·85–1·29]) compared with placebo (1·86 per patient-year [1·54–2·18]; incidence rate ratio [IRR] 0·59 [95% CI 0·47–0·74]; p<0·0001). The proportion of patients experiencing at least one asthma exacerbation was reduced by azithromycin treatment (127 [61%] patients in the placebo group *vs* 94 [44%] patients in the azithromycin group, p<0·0001). Azithromycin significantly improved asthma-related quality of life (adjusted mean difference, 0·36 [95% CI 0·21–0·52]; p=0·001). Diarrhoea was more common in azithromycin-treated patients (72 [34%] *vs* 39 [19%]; p=0·001).

Interpretation Adults with persistent symptomatic asthma experience fewer asthma exacerbations and improved quality of life when treated with oral azithromycin for 48 weeks. Azithromycin might be a useful add-on therapy in persistent asthma.

Note: Maintenance therapy in asthma is not an approved indication for azithromycin

Summary

Diagnosis and treatment

- Variable symptoms
- Variable airflow obstruction
- Inhaled steroids, bronchodilators
- Trigger avoidance, action plan

Asthma and COPD

- Overlapping features of both asthma and COPD on history and spirometry
- Inhaled steroids, long-acting bronchodilators

Exacerbations

- Assess acute severity and start bronchodilators
- Early use of systemic steroids for exacerbations and acute asthma

Severe asthma

- Check diagnosis, optimise management, treat comorbidities
- Consider add-on therapy including tiotropium, montelukast, biologic therapy (anti-IgE, anti-IL5)