FAMILY PHYSICIAN airways group

The role of primary care physicians in the management of severe asthma

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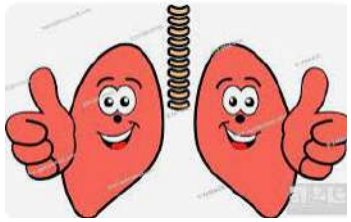
Presenter Disclosure

- **Faculty:** Alan Kaplan MD CCFP(EM) FCFP
- Chair Family Physician Airways Group of Canada
- Vice President, Respiratory Effectiveness Group
- Past Chair of Special Interest Focused Practice, College of Family Physicians in Respiratory Medicine.
- Honorary Professor of Primary Care Respiratory Research, OPRI
- Regional Primary Care Cancer Lead, Central Region, Ontario
- **Relationships with commercial interests:**
  - **Grants/Research Support:** none
  - **Speakers Bureau/Honoraria:** ALK, Astra Zeneca, Boehringer Ingelheim, GSK, Idorsia, Merck Frosst,, Moderna, Pfizer, Sanofi, Trudel, Valeo.
  - **Consulting Fees:** ALK**,** Astra Zeneca, GSK, Idorsia, Merck, Moderna, Pfizer, Sanofi, Trudel, Valeo
  - **Other:**

    Member of Health Canada Section on Allergy and Respiratory Therapeutics.

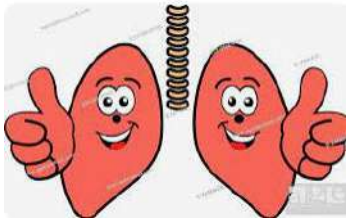
    Member of Public Health Agency of Canada section on Respiratory Surveillance



Disclosure of Financial Support

- **This program has received no financial support**
- **This program has received no in-kind support**

- **Potential for conflict(s) of interest:**
- **The speaker has received honoraria from multiple companies that make Asthma medications and vaccines**



Mitigating Potential Bias

Potential sources of bias identified in the preceding 2 slides have been mitigated as follows:

- Information/recommendations provided in the following program will be evidence- and/or guideline-based and opinions of the speaker will be identified as such.
- Current Canadian and International guidelines are referenced.

Objectives

- Define Severe Asthma
- Define the work up of uncontrolled asthma vs severe asthma
- Review the role of Family Medicine in patients with severe asthma
- Review severe asthma therapeutics

Defining Uncontrolled Asthma

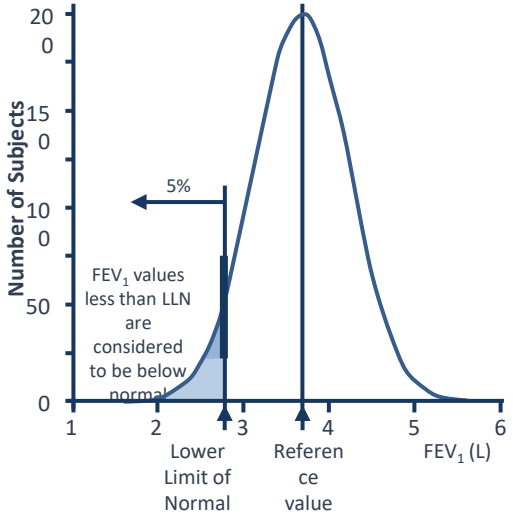
AT LEAST ONE OF THE FOLLOWING:

1) **POOR SYMPTOM CONTROL:** as per CTS asthma control criteria or other standardized questionnaires: ACQ consistently >1.5, ACT <20, or cACT <20

2) **FREQUENT SEVERE EXACERBATIONS**: two or more courses of systemic corticosteroids (3 days each) in the previous year

3) **SERIOUS EXACERBATIONS:** at least one hospitalization, intensive care unit (ICU) stay or mechanical ventilation in the previous year

4) **AIRFLOW LIMITATION:** after appropriate bronchodilator withhold FEV_1 <80% of personal best (or < the LLN, in the face of reduced FEV_1/FVC defined as less than the LLN)



ACQ, Asthma Control Questionnaire; ACT, Asthma Controlled Test; cACT, child Asthma Controlled Test; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; LLN, lower limit of normal; CTS, Canadian Thoracic Society

Adapted from FitzGerald JM et al. *Can J Respir Crit Car & Sleep Med*. 2017;1(4):199-221; Coates AL et al. *Can Respir J.* 2013;20(1):13-22.

Defining Severe Asthma

ASTHMA WHICH:

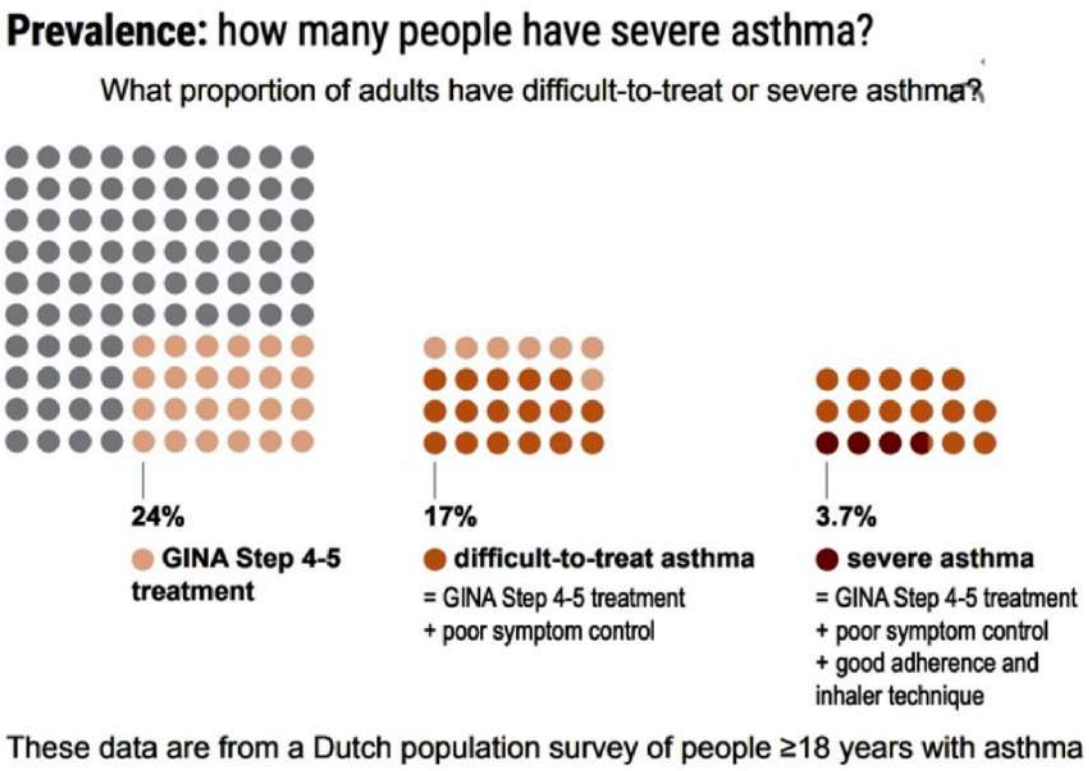
1. **REQUIRES TREATMENT** with high-dose ICS and a second controller for the previous year, OR

2. **SYSTEMIC CORTICOSTEROIDS** for 50% of the previous year to prevent it from becoming "uncontrolled"

3. **REMAINS "UNCONTROLLED"** despite this therapy

ICS, inhaled corticosteroids
Adapted from FitzGerald JM et al. *Can J Respir Crit Car & Sleep Med*. 2017;1(4):199-221.

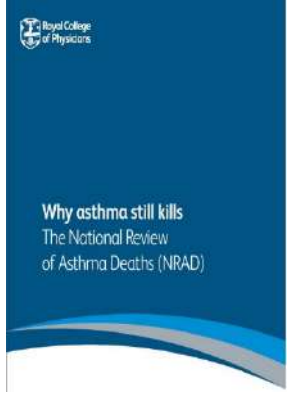
Prevalence of Difficult-to-Treat and Severe Asthma



Death is pretty severe!

But most asthmatic deaths do **not** occur in patients with Severe Asthma!

NRAD report reveals excessive prescribing of SABAs and under-prescribing of preventer medication



- The NRAD report was an investigation of recent asthma deaths in the UK by the Royal College of Physicians

Evidence of excessive prescribing of reliever medication

39% of patients who were on short-acting relievers at the time of death had been prescribed more than

12 short-acting reliever inhalers in the year before they died

4% had been prescribed more than **50** reliever inhalers

Evidence of under-prescribing of preventer medication

To comply with recommendations, most patients would usually need at least

12 preventer prescriptions per year

38% of patients on preventer inhalers* received fewer than **4** inhalers in the year leading up to their death…

and **80%** received fewer than 12 preventer inhalers

*Of those patients for which the number of prescriptions was known. Among 189 patients who were on short-acting relievers at the time of death, the number of prescriptions was known for 165. Among 168 patients on preventer inhalers at the time of death, either as stand-alone or in combination, the number of prescriptions was known for 128.

NRAD, National Review of Asthma Deaths; SABA, short-acting β_2-agonist

Royal College of Physicians. *Why Asthma Still Kills? The National Review of Asthma Deaths (NRAD)* [online] 2014. Available from: https://www.rcplondon.ac.uk/projects/outputs/why-asthma-still-kills [Last accessed: December, 2016].

Asthma Severity Classification – 2021

Severity	Treatment Required
Very mild	**Well-controlled** on PRN SABA
Mild	**Well-controlled** on: Low dose ICS (or leukotriene receptor antagonists (LTRA)) and PRN SABA or PRN bud/form
Moderate	**Well-controlled** on: Low dose ICS + second controller and PRN SABA or Moderate doses of ICS + second controller medication and PRN SABA or Low-moderate dose bud/formþPRN bud/form
Severe	High doses of ICS & second controller for the previous year or systemic steroids for 50% of the previous year to prevent it from becoming uncontrolled, or is uncontrolled despite this therapy

Yang CL, Hicks EA, Mitchell P, et al. 2021 Canadian Thoracic Society Guideline – A focused update on the management of very mild and mild asthma. *Canadian Journal of Respiratory, Critical Care, and Sleep Medicine*. Published online February 18, 2021:1-41. 10.1080/24745332.2021.1877043

Criteria for Well-Controlled Asthma

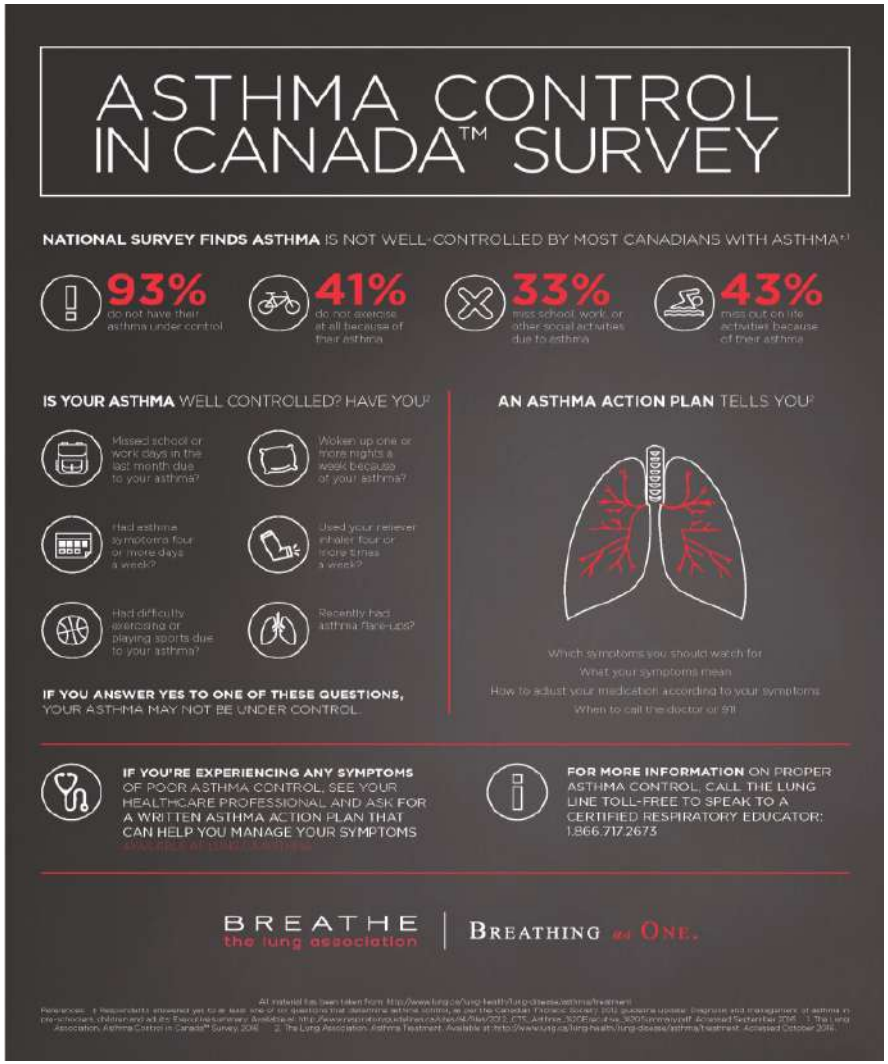
Symptom-related criteria of asthma control:

Criteria	New 2021 Value	Previous Value
Daytime symptoms	≤ 2 days per week	< 4 days per week
Nighttime symptoms	< 1 night per week & mild	≤ 1 night per week
Physical activity	Normal	
Exacerbations	Mild and infrequent*	
Missed school or work	None	
Reliever use (SABA or bud/form)	≤ 2 doses per week	< 4 doses per week

* Mild – no systemic steroids, ED visits or hospitalizations; Infrequent is subjective and dependent on quality-of-life impact

A patient who meets **ALL** of the above criteria = Well controlled Asthma

Asthma Control in Canada Survey, 2016



- 93% do not have their asthma under control
- 41% do not exercise at all because of their asthma
- 33% miss school, work, or social activities because of asthma
- 43% miss out on life activities due to asthma

The Asthma Control in Canada Survey, 2016. http://www.lung.ca/news/advocacy-tools/our-publications

Which of these is the most common reason for lack of asthma control?

A) Wrong diagnosis

B) Severe asthma

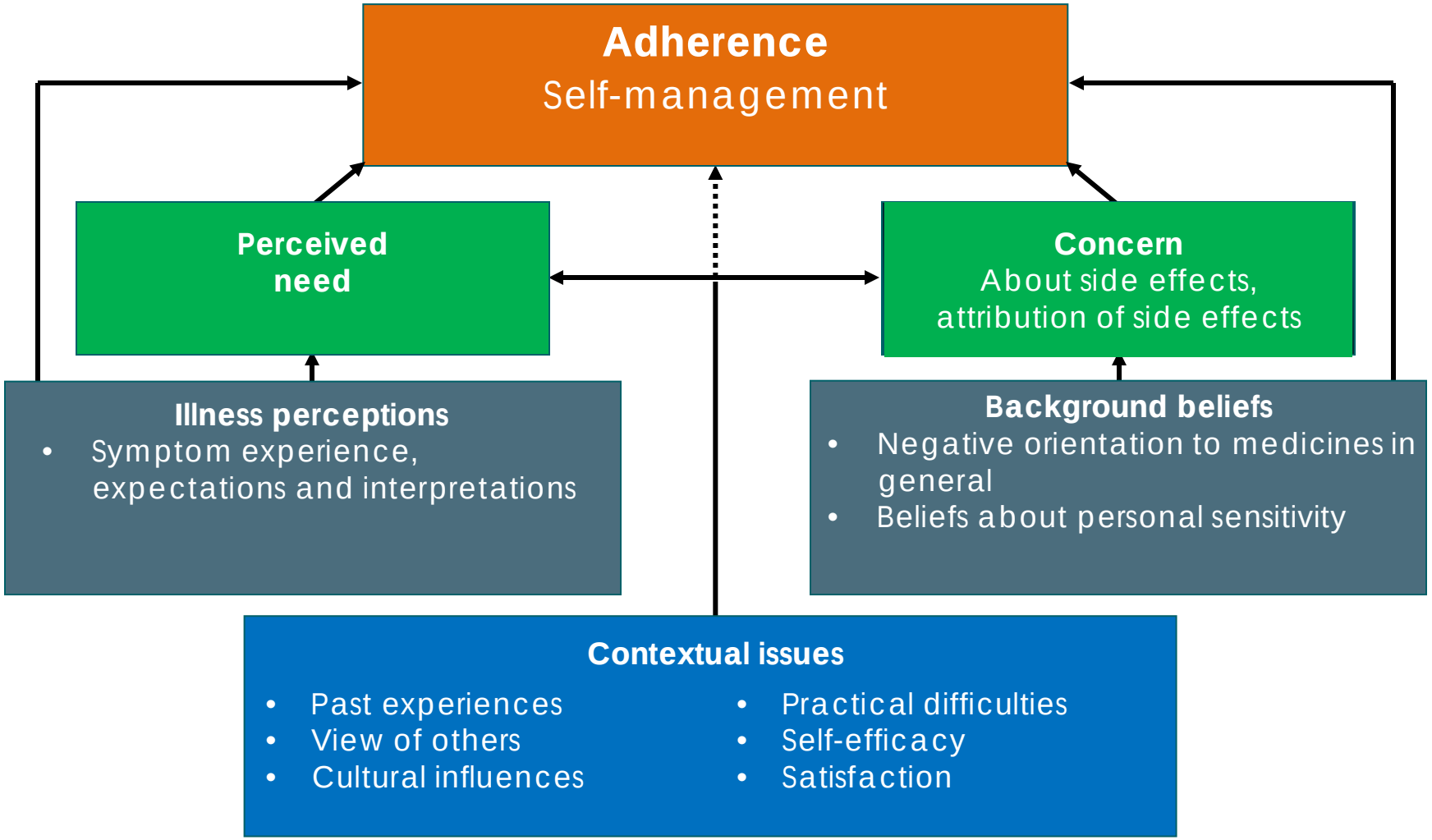
C) Inhaler technique incorrect

D) Comorbidities not managed

E) Adherence, lack of controllers

F) Continued trigger exposure

Factors affecting Adherence



CHEST

Horne R, *Chest* 2006;130(suppl):65S-72S

Patients undervalue control because:

A) They do not know any better
B) They do not care
C) They are not smart enough
D) Their Doctors have not told them
E) They cannot afford the medication

BMC Pulmonary Medicine

BioMed Central

Research article

Open Access

Features of asthma management: quantifying the patient perspective

John Haughney*[1], Monica Fletcher[2], Stephanie Wolfe[3], Julie Ratcliffe[4], Roger Brice[5] and Martyn R Partridge[6]

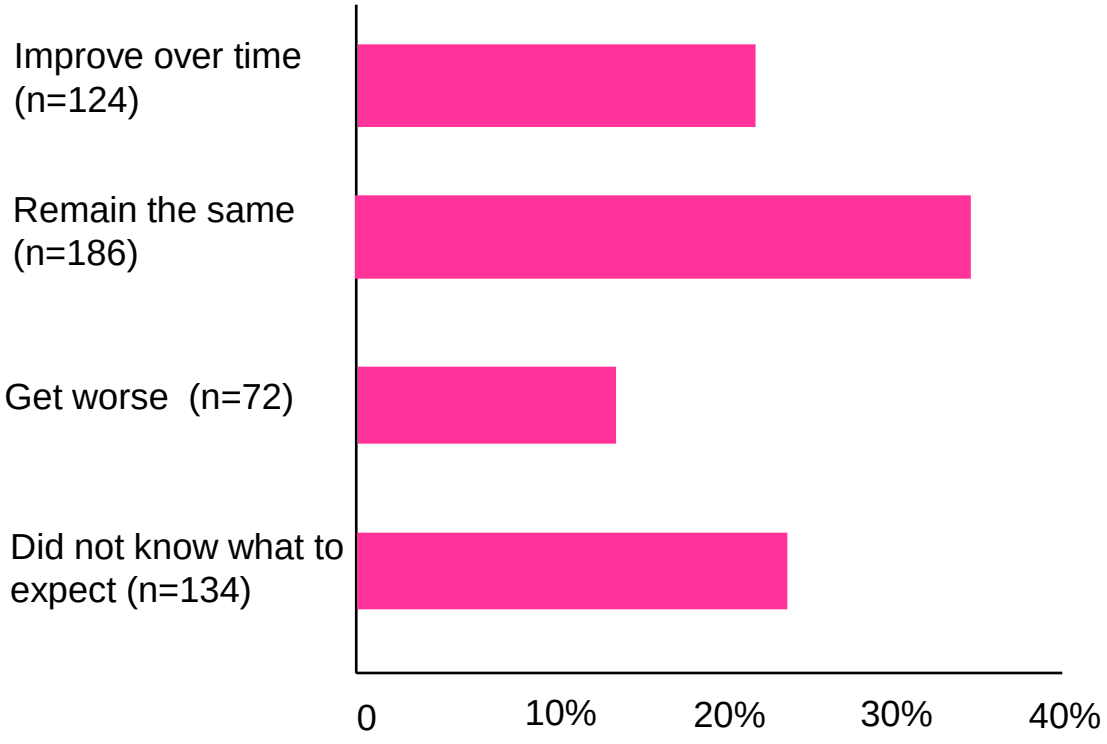
What is the patient perspective?

Putting patients first in asthma

Key findings and analysis of a nationwide survey of asthma patients

J Haughney, G Barnes, M Partridge J Cleland
Primary Care Respiratory Journal 2004; 13:28-35.

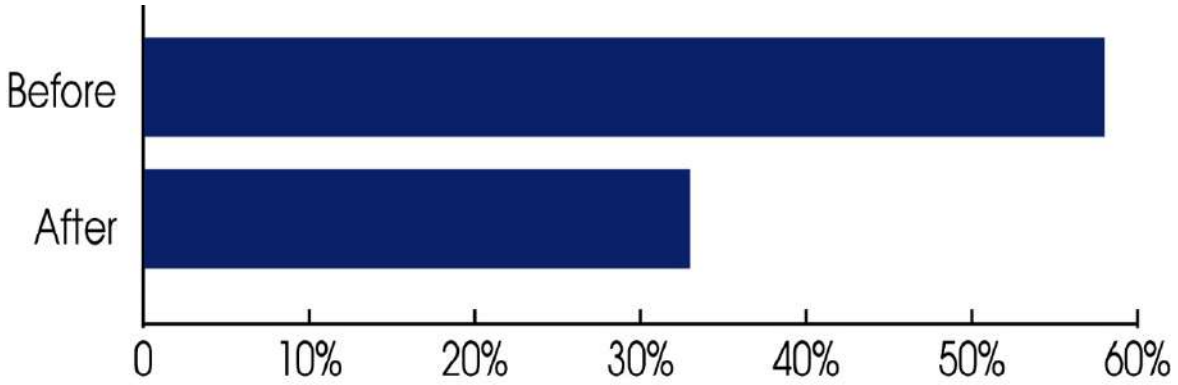
Patient expectations



Percentage of respondents related to patient expectations

Treatment guidelines

Percentage of respondents who said that they were very satisfied with the standard of their asthma management, before and after being shown international guidelines



"That can't be right. My treatment doesn't do that"

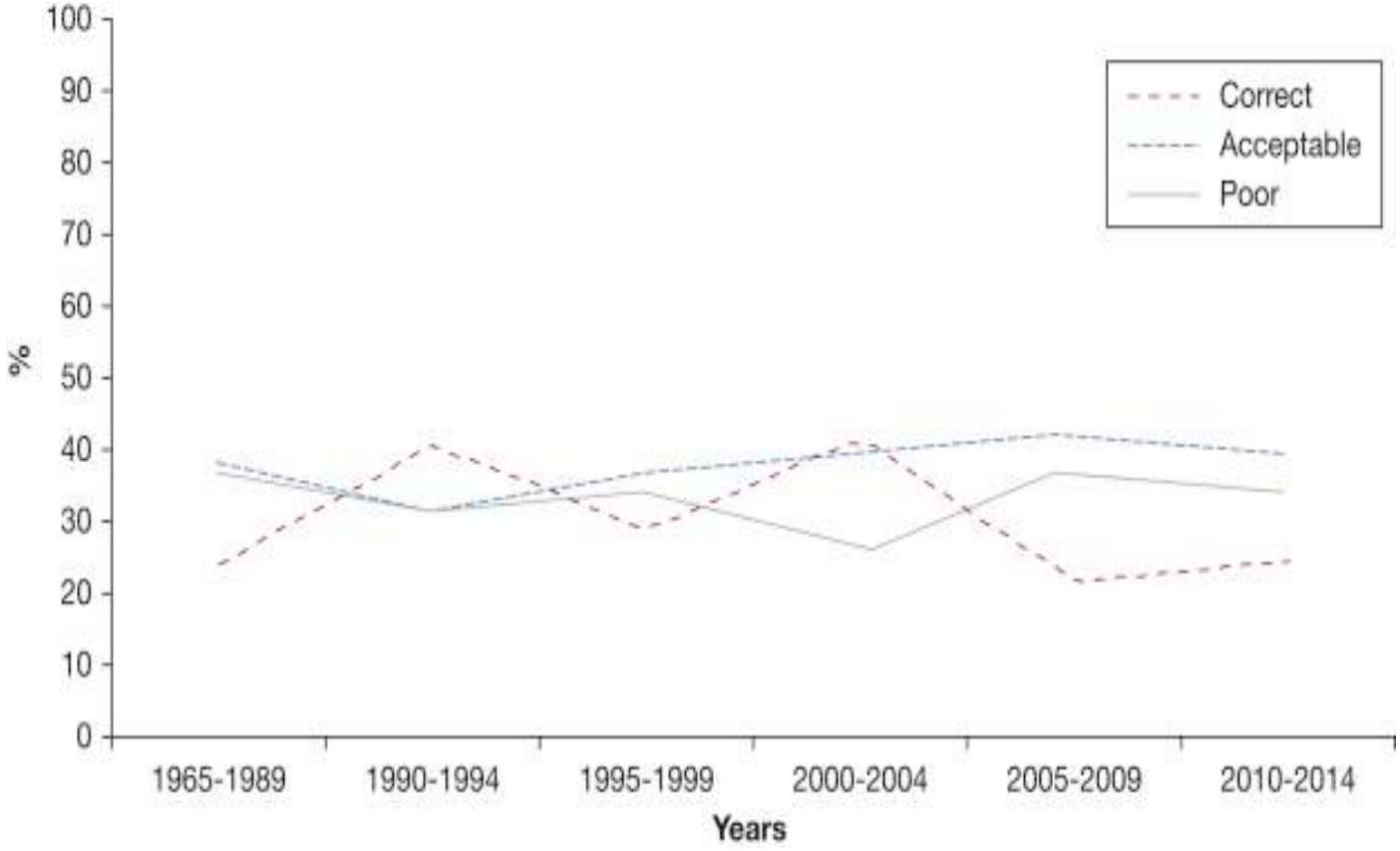
Management of asthma: What do patients want?

- Treatment as simple as possible
- Few inhalers
- Lowest dose of steroid to control symptoms
- Avoid hospitals when possible
- Minimise symptoms
- Self manage

Haughney J et al BMC Pulm Med 2007

The Importance of Assessing Inhaler Technique

Despite guidance for assessment of inhaler technique, inhaler technique has not improved in 40 years

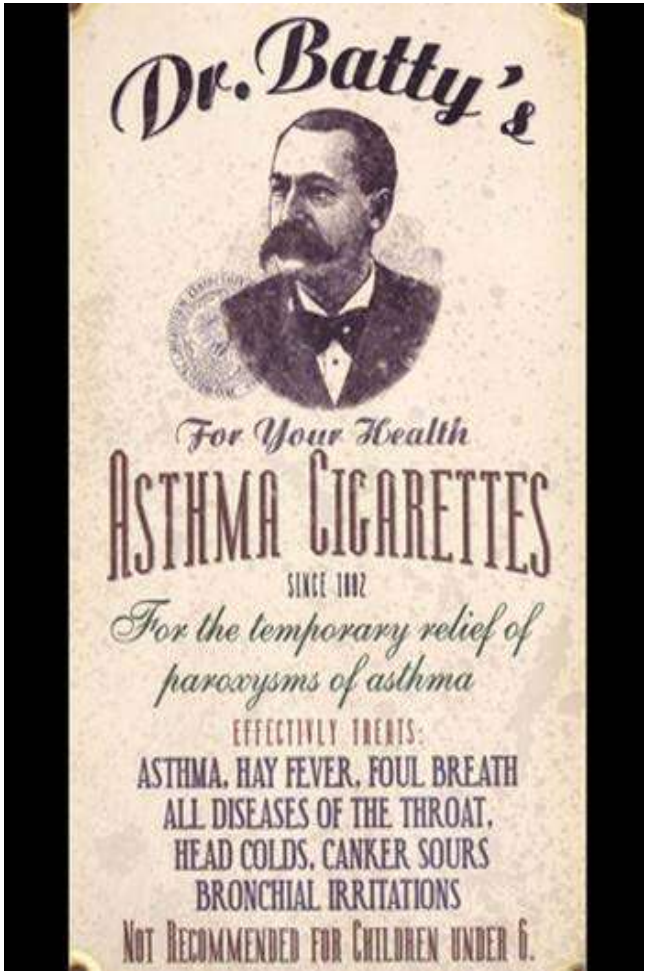


Sanchis J, et al. *Chest*. 2016;150(2):394-406.

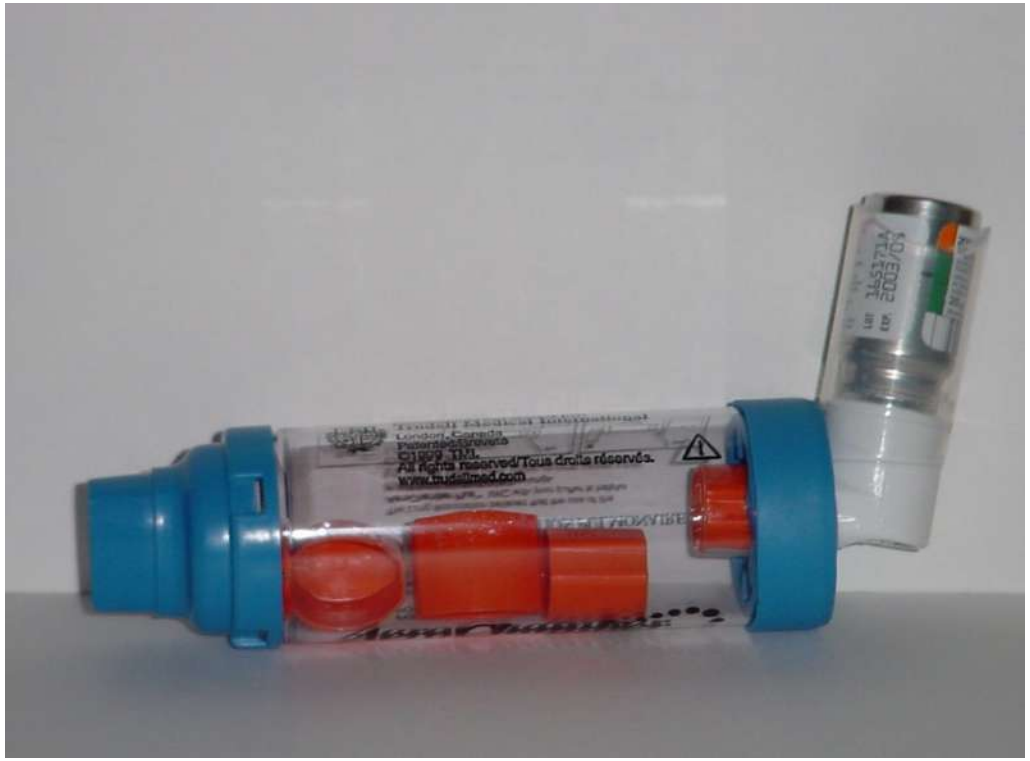
Inhaler technique

Technique for delivery is a barrier

Is this a better delivery device??



There are always technique issues, even with chambers…..



Thanks to Dr. Helen Ramsdale

Here is true inhaler technique!

For this patient, which is the right class of medication?

For these medications, which inhalers are currently available to the patient?

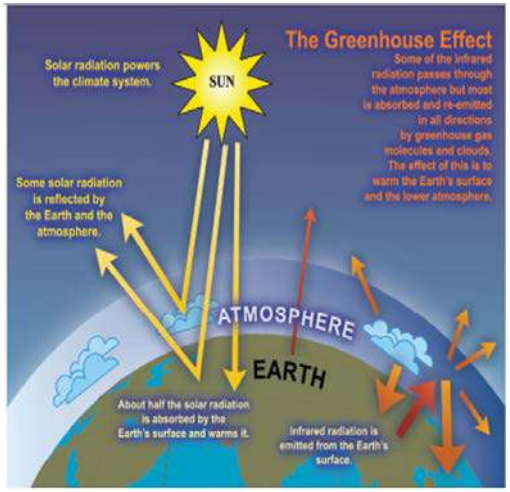
Which of these inhalers can the patient use correctly after training?

OPTIMAL INHALER SELECTION

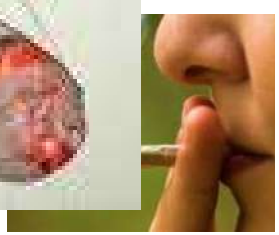
Safest and best for the patient and for the planet

Which of these inhalers has the lowest environmental impact?

Follow-up: Is the patient satisfied with the medication(s) and inhaler(s)?

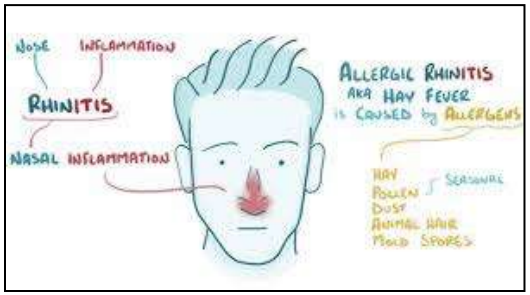


Triggers?

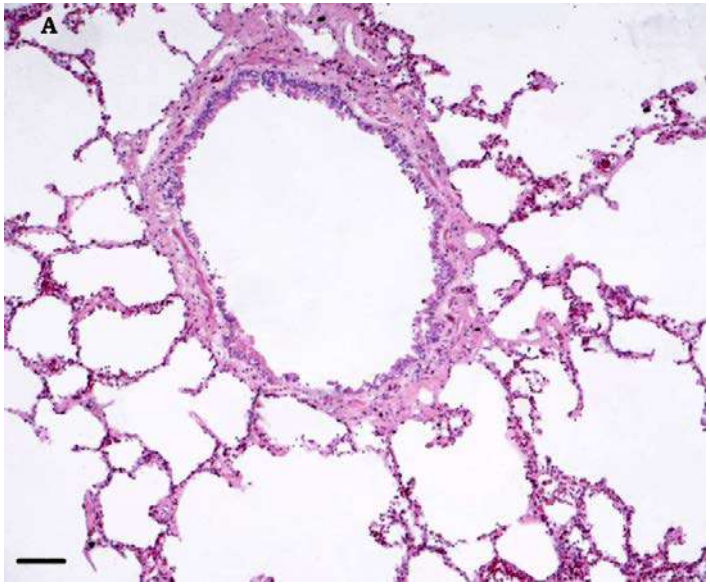



SORRY, BUT I CAN'T GO IN THERE. I'M ALLERGIC TO NUTS!
PROJECT MANAGEMENT OFFICE

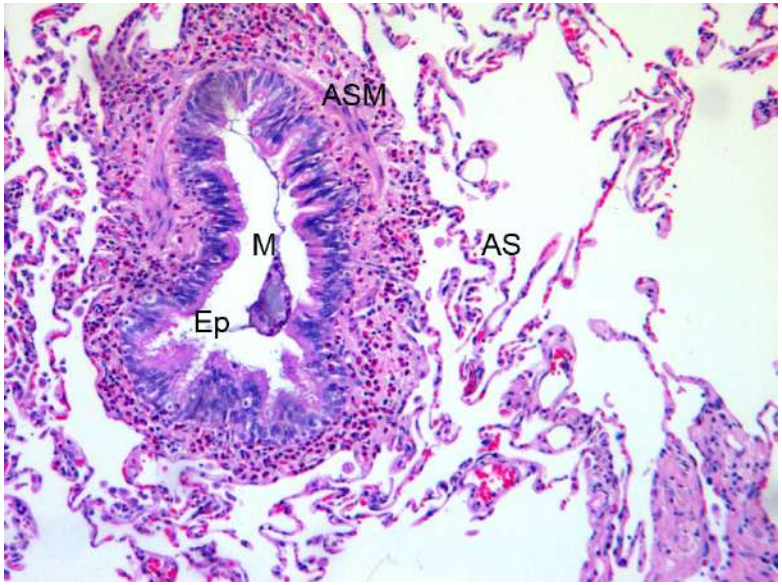
Comorbidities



What is Asthma? Airway inflammation in asthma



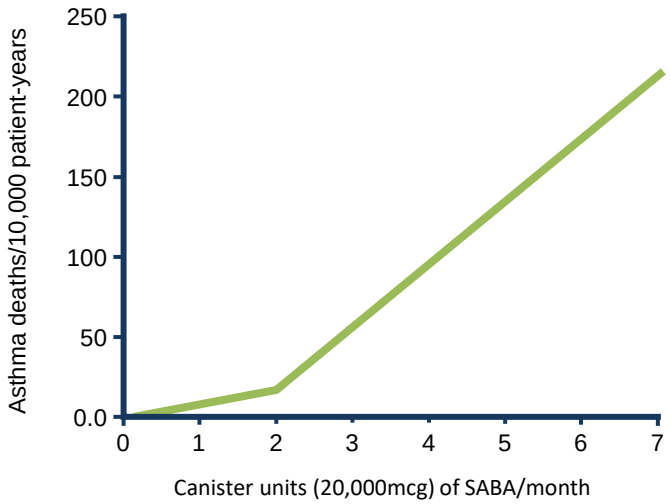
Normal



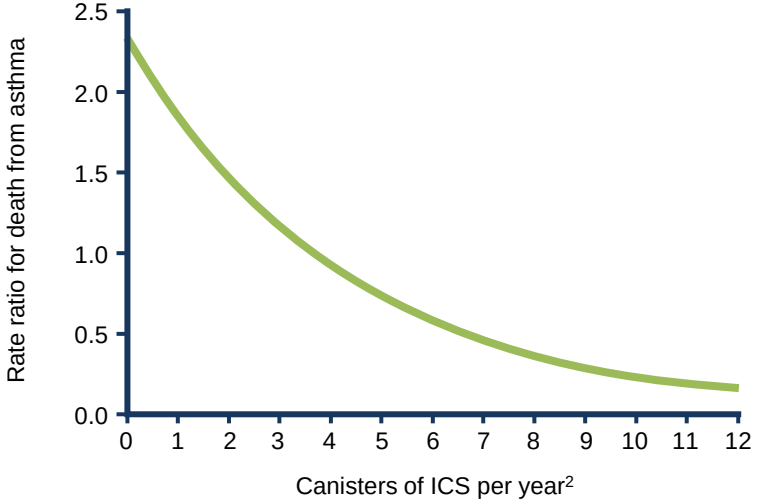
Asthma

Mauad T, et al. Am J Respir Crit Care Med 2004;170:857–62

A relationship exists between mortality and SABA or ICS use



Risk of asthma death was associated with rapid increase when >1–2 SABA canisters are used per month[1]

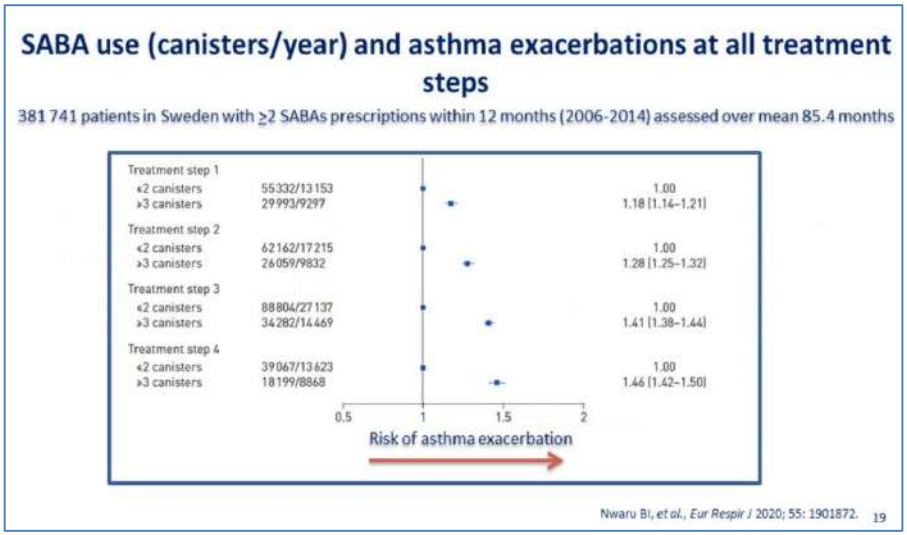


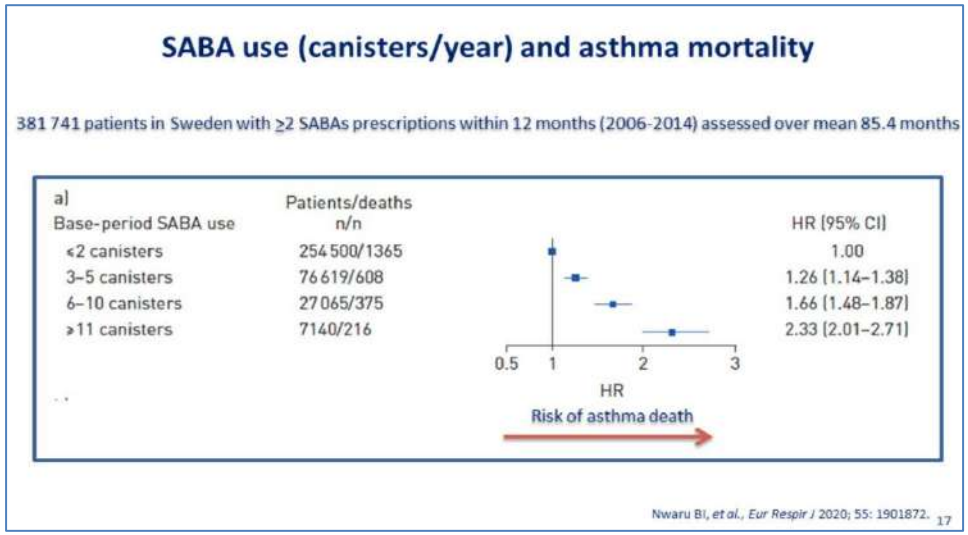
Use of ≥6 ICS canisters per year was associated with a 50% reduction in asthma mortality[2]

ICS, inhaled corticosteroids; SABA, short-acting β_2-agonist

1. Suissa S et al. *Am J Respir Crit Care Med* 1994;149:604–610; 2. Suissa S et al. *N Engl J Med* 2000;343:332–336

SABA Overuse (more than two cannisters per YEAR associated with bad outcomes





How many doses in two cannisters?

200 per cannister = 400

How many doses should you need in a year if you are controlled?

SABINA study concluded SABA are overused in Canada

NS

39%

SABA overuse

3067 patients

Met the definition of SABA overuse*

AB

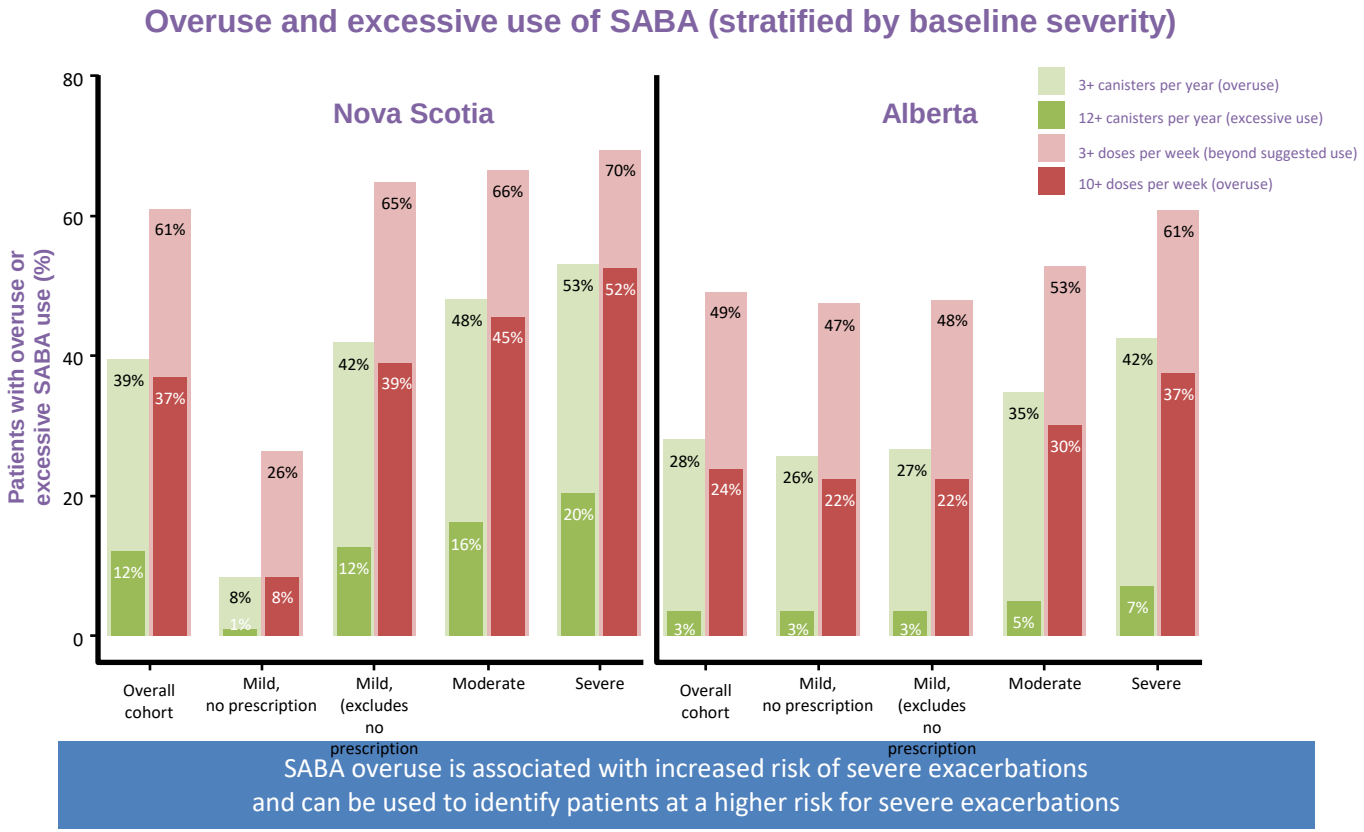
28%

SABA overuse

30,032 patients

Met the definition of SABA overuse*

*Defined as ≥3 canisters per year

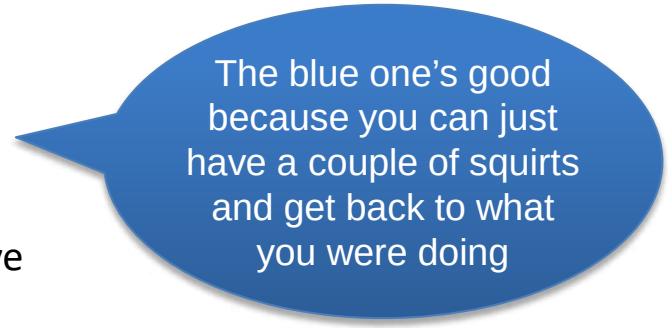


AB, Alberta; NS, Nova Scotia; SABA, short-acting beta agonist; SABINA, SABA in Asthma.

Noorduyn SG, Qian C, Johnston KM, et al. ERJ Open Res. 2022;8(3):00140-2022.

No More Treatment with inhaled short-acting beta$_2$-agonists (SABA) alone!!

- People with apparently mild asthma can have severe or fatal exacerbations *(Dusser, 2007)*
  - Up to 27% asthma deaths are in patients with occasional symptoms *(Bergstrom, 2008)*
  - Exacerbation triggers are unpredictable (viral, allergen, pollution, stress)
  - Even 4–5 **lifetime** OCS courses increase the cumulative risk of adverse events including osteoporosis, diabetes, cataract, heart failure, pneumonia *(Price et al, J Asthma Allerg 2018)*
- **Regular** use of SABA, even for 1–2 weeks, is associated with increased AHR, reduced bronchodilator effect, increased allergic response, increased eosinophils *(e.g. Cockcroft 2006)*
  - Can lead to a vicious cycle encouraging overuse
  - Over-use of SABA is associated with ↑ exacerbations and ↑ mortality *(e.g. Suissa 1994, Nwaru 2020)*
- Starting treatment with SABA **trains** the patient to regard it as their primary asthma treatment
  - Poor adherence with ICS is almost inevitable
- There is strong evidence for a more effective and safer alternative than SABA alone, or ICS with as-needed SABA



Cole et al, BMJ Open 2013

ASTHMA RIGHT CARE

International Primary Care Respiratory Group IPCRG work locally collaborate globally

SABA* RISK QUESTIONNAIRE (SRQ)

A questionnaire about risks associated with over reliance on blue RELIEVER INHALERS

This questionnaire is designed to help you and your healthcare professional to understand what you think about your traditional blue RELIEVER INHALER and whether you might be at risk of relying on it too much.

PART 1 Your views about your blue RELIEVER INHALER

1. Please circle the score that best represents your current view
2. Please write the number for each statement in the score box next to it
3. Please add up the numbers to get your total score
4. Share your score with your doctor/nurse or pharmacist

There are no right or wrong answers. We are interested in your views

									PART 1 SCORE
1 Using my blue **RELIEVER INHALER** to treat symptoms is the best way to keep on top of my asthma.	Strongly disagree	1	Disagree	2	Uncertain	3	Agree	4	Strongly agree 5	
2 I don't worry about asthma when I have my blue **RELIEVER INHALER** around.	Strongly disagree	1	Disagree	2	Uncertain	3	Agree	4	Strongly agree 5	
3 My blue **RELIEVER INHALER** is the only asthma treatment I can really rely on.	Strongly disagree	1	Disagree	2	Uncertain	3	Agree	4	Strongly agree 5	
4 The benefits of using my blue **RELIEVER INHALER** easily outweigh any risks.	Strongly disagree	1	Disagree	2	Uncertain	3	Agree	4	Strongly agree 5	
5 I prefer to rely on my blue **RELIEVER INHALER** than my **STEROID PREVENTER INHALER**.	Strongly disagree	1	Disagree	2	Uncertain	3	Agree	4	Strongly agree 5	

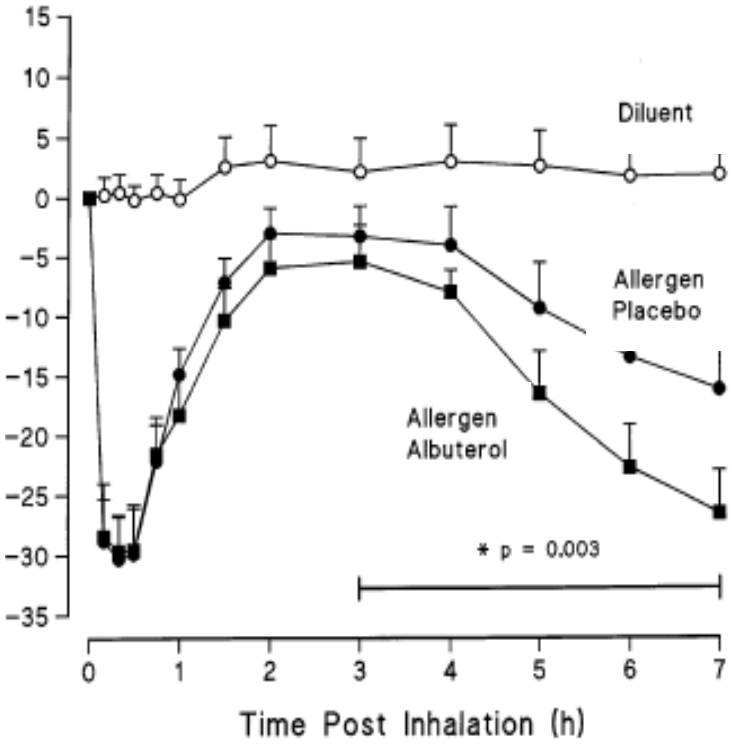
RELATIONSHIP WITH SABA??

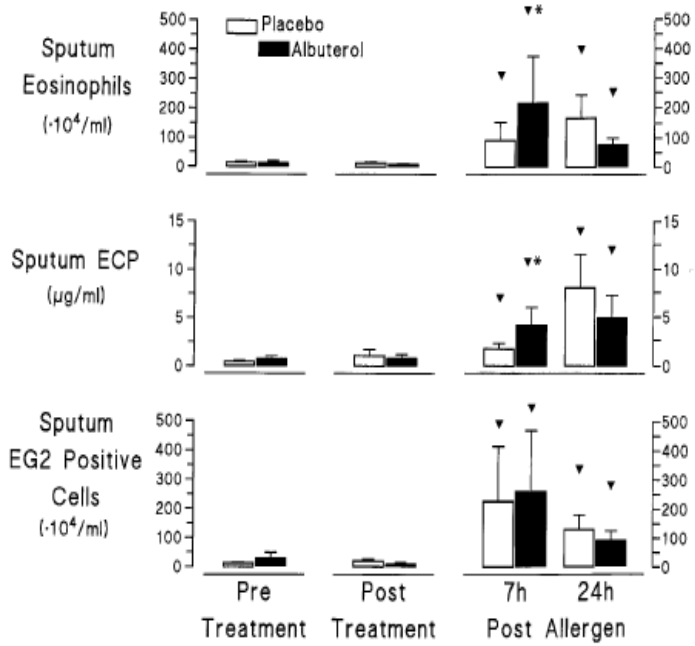
18–25:
High risk of over-reliance on your Blue Reliever Inhaler. Like many people, you seem to be relying on your Blue Reliever Inhaler a lot. If you are using it 3 or more times a week, this could be a sign that your asthma is not as well controlled as it could be. It's worth discussing your results with your doctor, nurse or pharmacist.

11–17:
Medium risk of over-reliance on your Blue Reliever Inhaler. Like many people, your Blue Reliever Inhaler is important to you, but you might be relying on it a bit too much. If you are using it 3 or more times a week, this could be a sign that your asthma is not as well controlled as it could be. It's worth discussing your results with your doctor, nurse or pharmacist.

10 or less:
Low risk of over-reliance on your Blue Reliever Inhaler. You do not appear to be over-relying on your Blue Reliever Inhaler. This is good news. Please keep reading to check that you don't have any of the other possible signs of poor asthma control.

Effect of regular inhaled albuterol on allergen-induced late responses and sputum eosinophils in asthmatic subjects





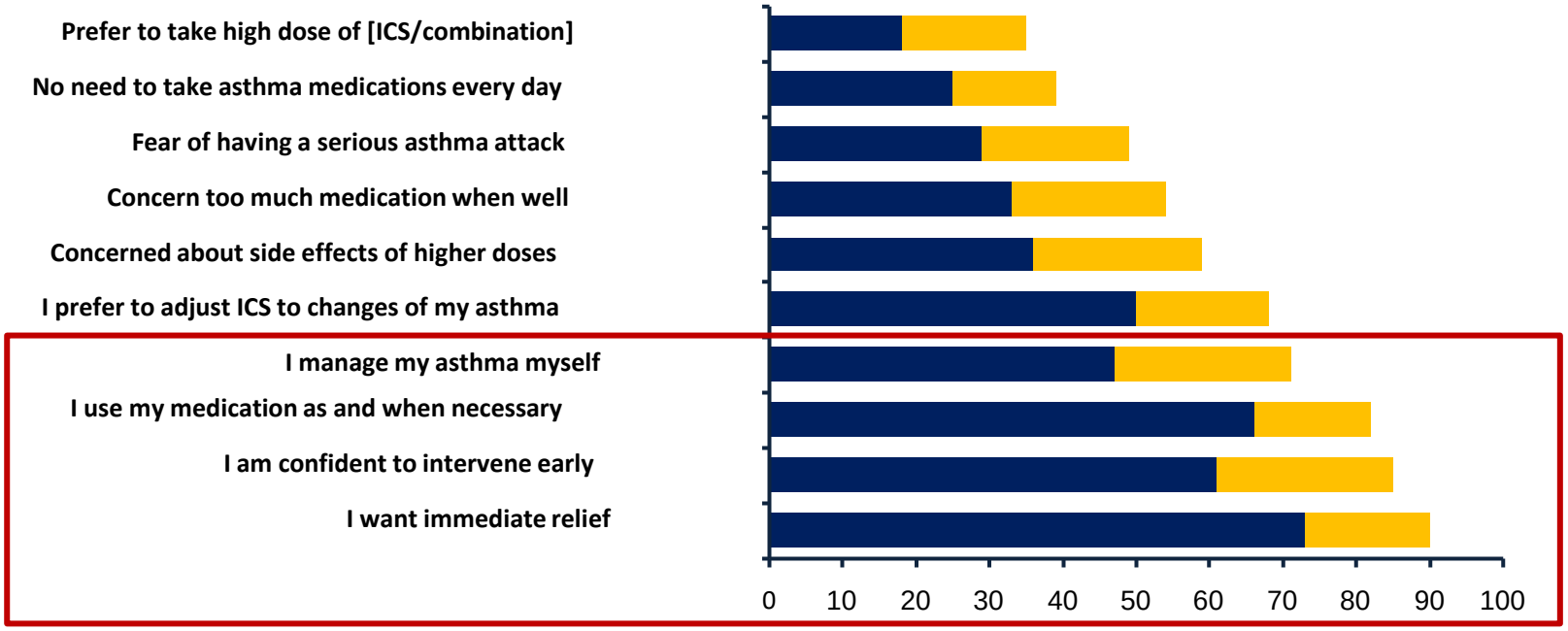
*Significant between albuterol vs placebo
▼Significant change vs baseline

Gauvreau GM, et al. Am J Respir Crit Care Med 1997;156:1738–45

Patients attitudes towards asthma management

Majority prefer some self-adjustment of treatment

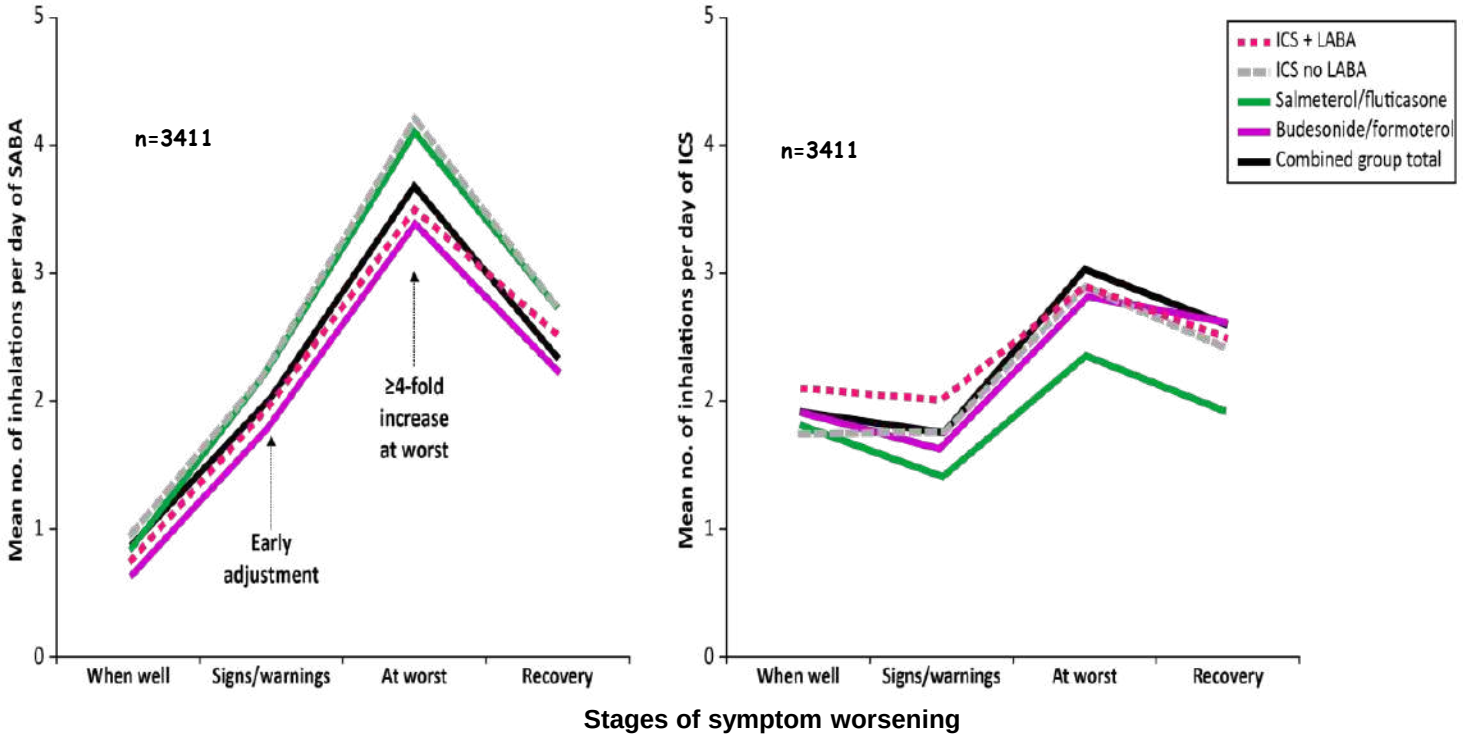
Proportion of patients that agree with each statement



(n=3,415)

Partridge MR *et al. BMC Pulmonary Medicine* 2006:6:13

If they have an action plan, do they use it?



Patients reported using their SABA immediately at the onset of symptoms, with ICS or ICS/LABA being increased later and to a lesser extent when symptoms were at their worst

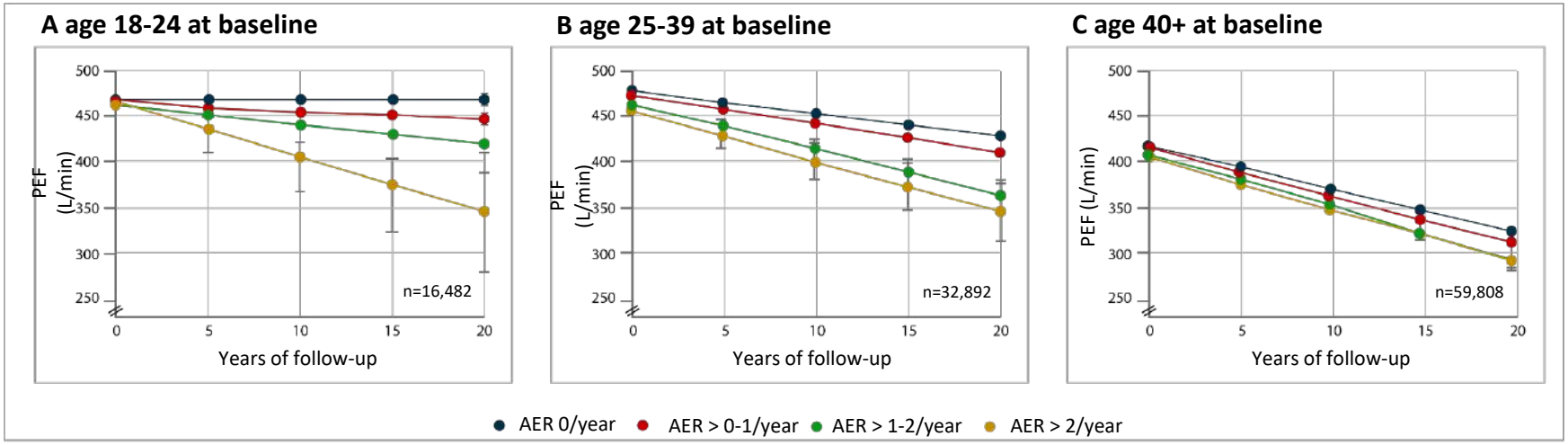
ICS, inhaled corticosteroids; INSPIRE, International Asthma Patient Insight Research; LABA, long-acting β_2-receptor agonist; SABA, short-acting β_2-receptor agonist

Partridge MR, et al. *BMC Pulm Med* 2006;6:13

Exacerbations are Bad

Harm from exacerbations, so Make sure each one is a learning experience to ensure that they do not happen again!!

Asthma Exacerbations Associated with Faster Lung Function Decline



Adjusted 20-year Peak Expiratory Flow (PEF) Trajectories (L/Year) by Annual Exacerbation Rate (AER) Stratified by Patient Age at Baseline

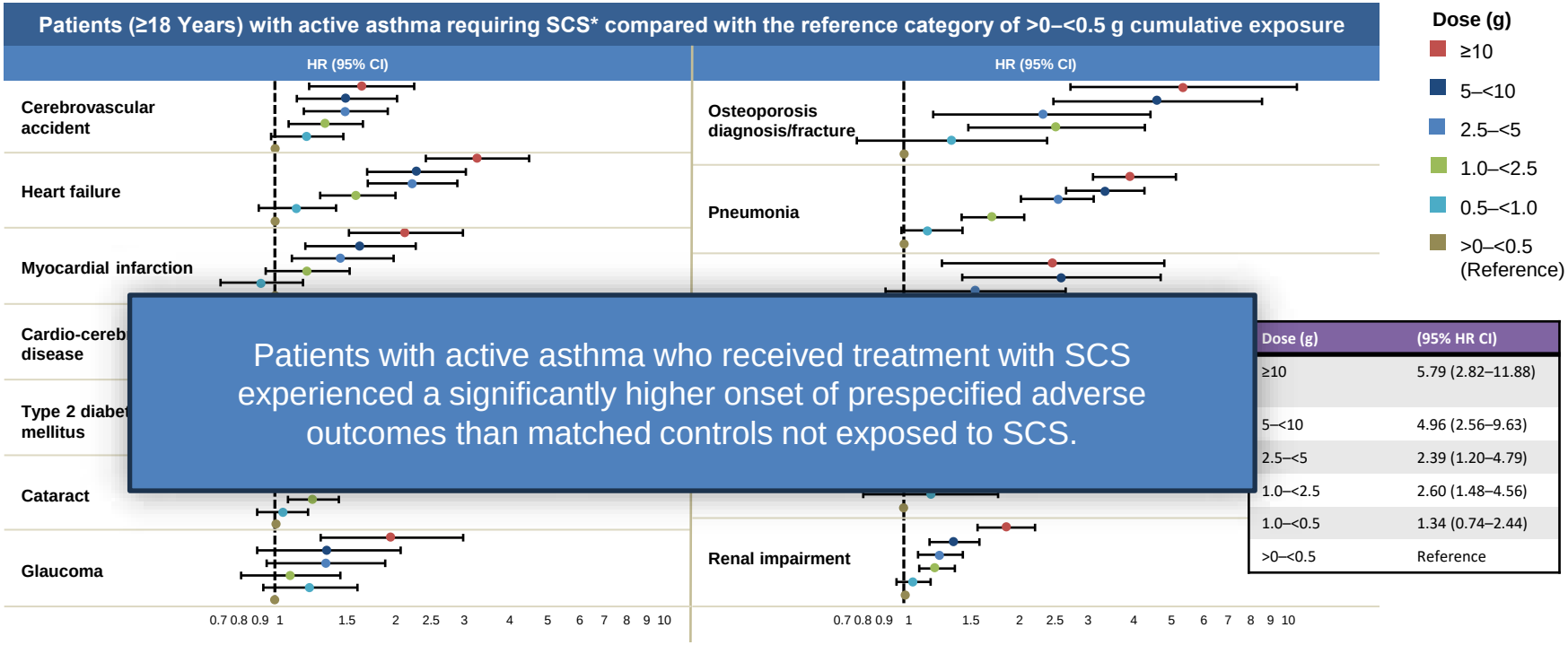
- This 20-year-long, UK-wide observational study of patients with active asthma managed in primary care demonstrates that asthma exacerbations are associated with faster lung function decline.
- Achieving better control decreases the likelihood of lung function decline in any age.

Early identification and intervention of patients with asthma is of value.

Soremekun S, et al. Thorax 2022;0:1–10.

Use of SCS is associated with adverse outcomes

A positive dose-response relationship was present between categorized, cumulative SCS exposure and adverse outcomes.



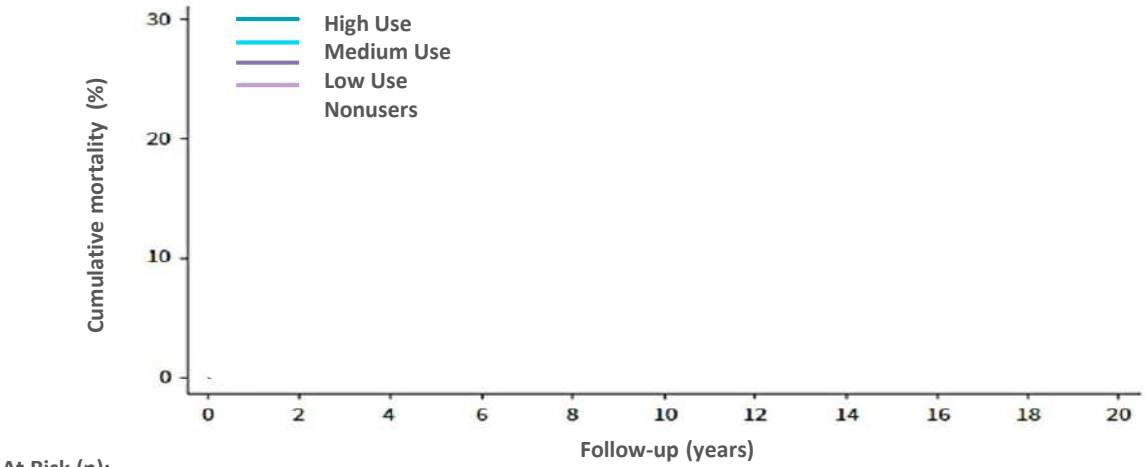
*Usually prescribed for oral administration.
CI, confidence interval; HR, hazard ratio; SCS, systemic corticosteroids.
Price DB, Trudo F, Voorham J, et al. J Asthma Allergy. 2018;11(suppl):193-204.

OCS Use in Asthma Management was Associated with Increased Risk of Mortality Among Adults with Asthma

OCS users (n=30,352) compared with nonusers (n=121,408) in a nationwide Danish asthma population.

Use stratified: low use ⩽500 mg, medium use >500–2000 mg and high use >2000 mg

OCS use in asthma management was associated with increased risk of comorbidities, mortality and unscheduled hospital visits.



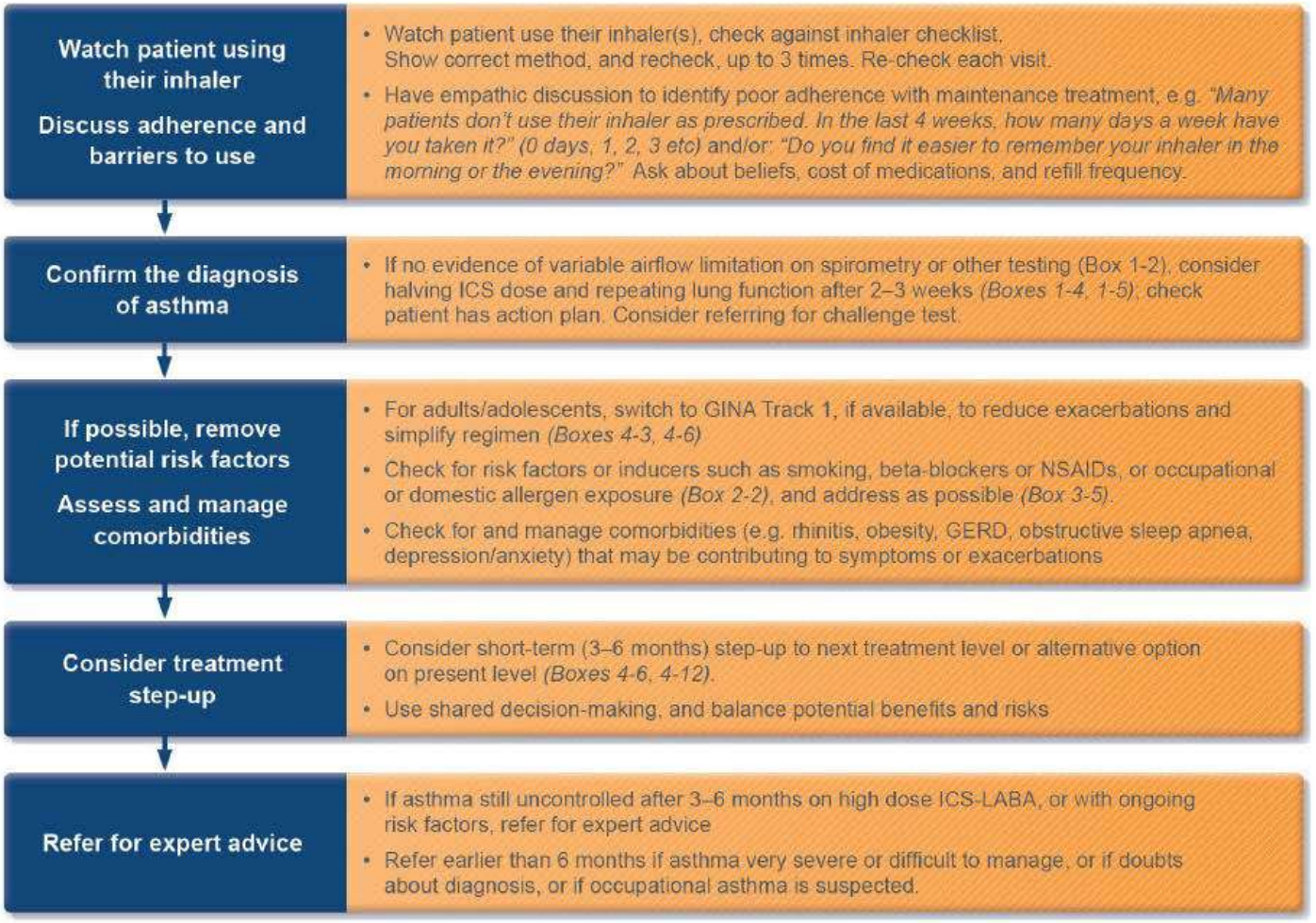
At Risk (n):										
Nonusers	121408	82908	55442	38565	26835	18587	12623	7974	4565	1873
Low use	28885	19550	14953	11693	8905	6569	4712	3116	1836	739
Medium use	487	4549	5000	4748	4189	3447	2719	1928	1195	549
High use	980	1745	2071	2196	2123	1941	1659	1303	881	437

OCS, Oral Corticosteroids

Skov IR, et al. Eur Respir J 2022; 60: 2103054

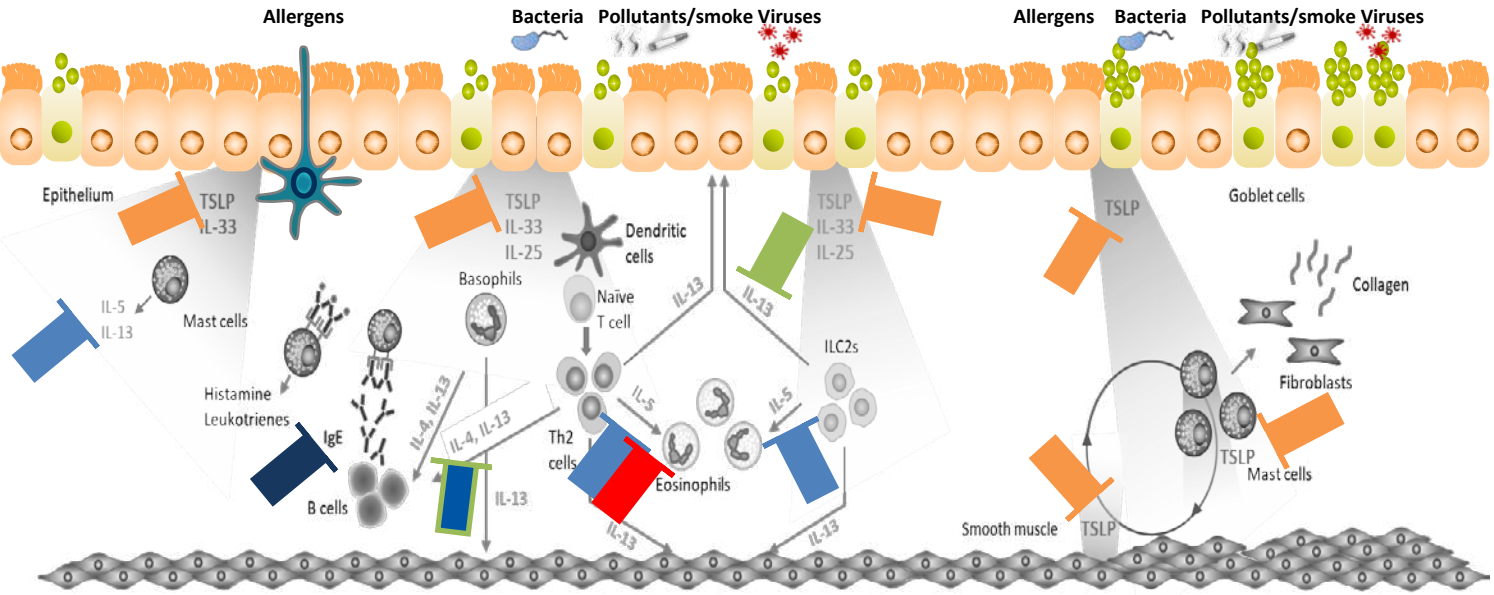
Review before referral..

Box 2-4. Investigating poor symptom control and/or exacerbations despite treatment



GINA 2019

Current biologics have different mechanisms of action



Select a molecule from the list to see its target

- Omalizumab (IgE)
- Mepolizumab (IL-5)
- Reslizumab (IL-5)
- Benralizumab (IL-5 Rα)
- Dupilumab (IL-4/IL-13)
- Tezepelumab (TSLP)

IgE, immunoglobulin E; IL, interleukin; TSLP, thymic stromal lymphopoietin

Figure adapted from Porsbjerg CM et al. Eur Respir J. 2020;56:2000260, Ishmael FT. J Am Osteopath Assoc. 2011;111(suppl 7):S11–S17 and Gauvreau GM et al. Expert Opin Ther Targets. 2020;24:777–792, which was based on Brusselle G, Bracke K. Ann Am Thorac Soc. 2014;11(suppl 5):S322–S328, Brusselle G et al. Nat Med. 2013;19:977–979 and Lambrecht BN, Hammad H. Nat Immunol. 2015;16:45–56. Mechanisms underlying non-eosinophilic inflammation in asthma and the relevance of TSLP and its potential effects on macrophages both require further elucidation. The information presented in this image has been simplified for illustration purposes only.

IgE, immunoglobulin E; IL, interleukin; ILC2, Type 2 innate lymphoid cell; Th, T helper; TSLP, thymic stromal lymphopoietin.

1. Gauvreau GM et al. Expert Opin Ther Targets. 2020;24:777–792; 2. Porsbjerg CM et al. Eur Respir J. 2020;56:2000260; 3. Roan F et al. J Clin Invest. 2019;129:1441–1451; 4. Menzies-Gow A et al. Respir Res. 2020;21:268.

Available biologics for severe asthma in Canada

Biologic (Target)[1]	Age indication	Frequency and administration	Other indication(s)
Omalizumab (IgE)	≥6 years	Subcutaneous (sc) injection every 2 to 4 weeks, based on body weight and serum IgE level	• CIU in patients ≥12 years old and severe CRSwNP in adults[2]
Mepolizumab (IL-5)	≥6 years	100 mg sc Q4W	• EGPA in adults ≥18 years old, severe CRSwNP in adults, HES in adults[3]
Reslizumab (IL-5)	≥18 years	Intravenous infusion 3 mg/kg Q4W	None specified
Benralizumab (IL-5 receptor α)	≥12 years	30 mg sc Q4W for the first 3 doses, then Q8W thereafter	None specified
Dupilumab (IL-4/IL-13)	≥6 years[4]	200 mg sc Q2W, with an initial loading dose of 400 mg or 300 mg Q2W with loading dose of 600 mg	Atopic dermatitis in patients ≥6 months, CRSwNP in patients ≥18 years old, eosinophilic esophagitis in patients ≥12 years old, and prurigo nodularis in patients ≥18 years old
Tezepelumab (TSLP)	≥12 years	210 mg sc Q4W	None specified

CRSwNP, chronic rhinosinusitis with nasal polyps; CIU, chronic idiopathic urticaria; EGPA, eosinophilic granulomatosis with polyangiitis; HES, hypereosinophilic syndrome; IL, interleukin; LABA, long-acting beta 2 agonist; PEF, peak expiratory flow; Q2W, every 2 weeks; Q4W, every 4 weeks; Q8W, every 8 weeks; SABA, short acting beta 2 agonist; TSLP, thymic stromal lymphopoietin.

1. FitzGerald JM et al. Can J Respir Crit Car & Sleep Med. 2017; 1(4):199-221. 2. XOLAIR® (omalizumab). Product monograph. Novartis Pharmaceuticals Canada Inc. Feb. 2024. 3. PrNUCALA (mepolizumab). Product monograph. GlaxoSmithKline Inc. Sept. 2022. 4. DUPIXENT® (dupilumab). Product monograph. Sanofi-Aventis Canada Inc. May 2024.

What test is not necessarily helpful for the referring physician to do while they are waiting for specialist appointment?

- A) Spirometry
- B) CBC
- C) FENO
- D) CT Chest
- E) Full PFTs
- F) Sputum eosinophils
- G) Serum IgE

What do you put in the referral letter?

How to Refer?

Key information to be included in a referral letter:

- Reason for referral (current concern)
- Criteria on which the original diagnosis was made
- Any measures of current control
- Conclusions of the structured approach (inhaler technique, adherence etc)
- Patient understanding of his/her condition
- Impact on quality of life
- Any concomitant atopic pathology and treatment
- Symptoms history, their exposures
- Other factors that may affect asthma management

IPCRG. Referral letter. https://www.google.com/search?client=firefox-b-1-d&q=IPCRG+referral+letter.

What do you do while waiting for the referral?

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https://doi.org/10.1080/24745332.2023.2237972

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CLINICAL RESPIRATORY REVIEW

OPEN ACCESS Check for updates

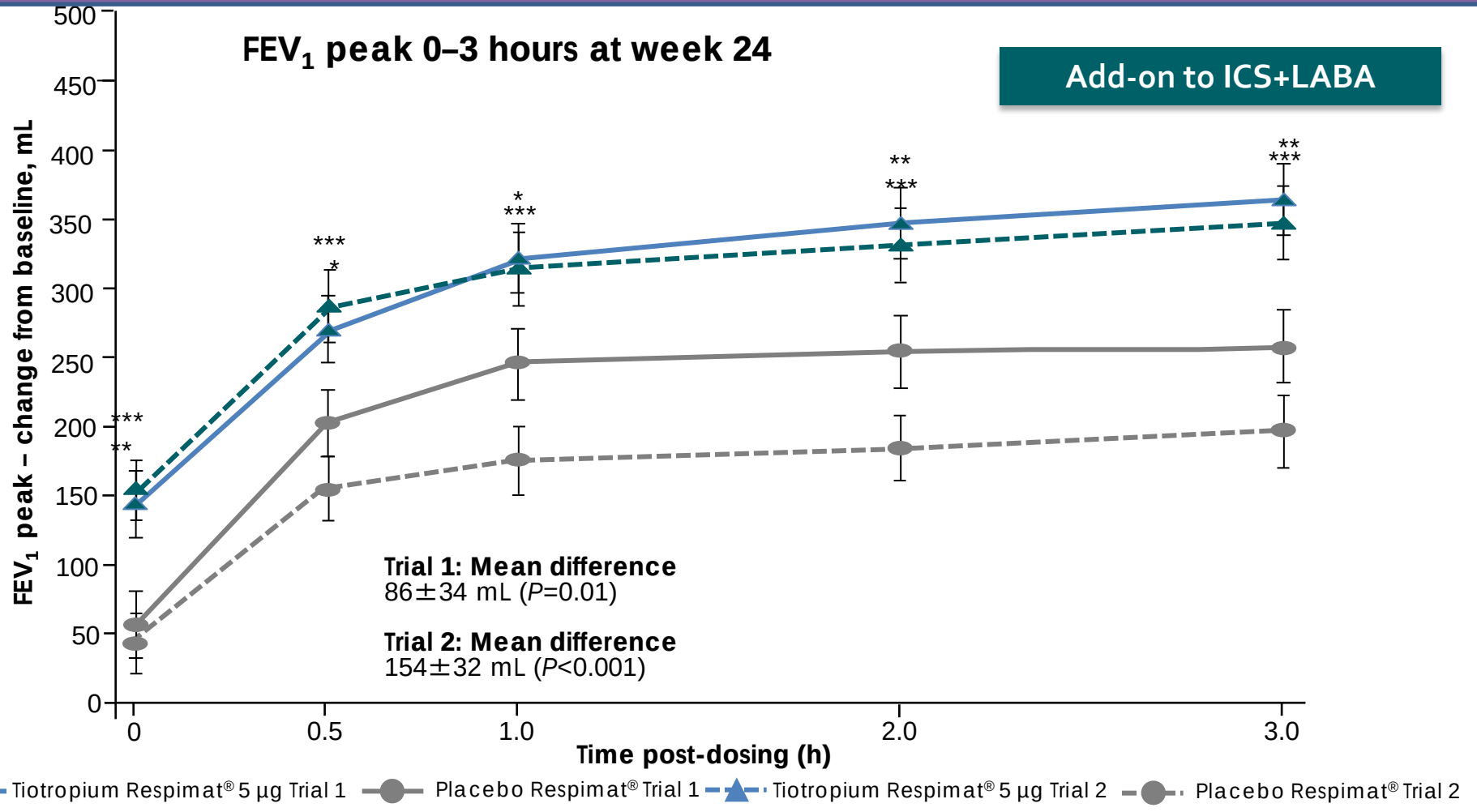
Triple inhaled therapy for asthma in Canada

Kenneth R. Chapman[a], Meyer Balter[b], Sacha Bhinder[c], Alan Kaplan[d], Andrew McIvor[e], Panayiota Papadopoulos[f] and Krystelle Godbout[g]

[a]Asthma & Airway Centre, University Health Network, University of Toronto, Toronto, Ontario, Canada; [b]Asthma Education Clinic, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, Canada; [c]Department of Medicine, Division of Respirology, Scarborough Health Network, Scarborough, Ontario, Canada; [d]Department of Family and Community Medicine, University of Toronto, Toronto, Ontario, Canada; [e]Firestone Institute for Respiratory Health, St. Joseph's Healthcare Hamilton, Ontario, Canada; [f]Valeo Pharma Inc, Kirkland, Québec, Canada; [g]Institut de Cardiologie et Pneumologie de Québec, Université de Laval, Québec City, Québec, Canada

Kenneth R. Chapman, Meyer Balter, Sacha Bhinder, Alan Kaplan, Andrew McIvor, Panayiota Papadopoulos & Krystelle Godbout (2023) Triple inhaled therapy for asthma in Canada, Canadian Journal of Respiratory, Critical Care, and Sleep Medicine, DOI: 10.1080/24745332.2023.2237972

Tiotropium Respimat® improves lung function in patients with uncontrolled asthma

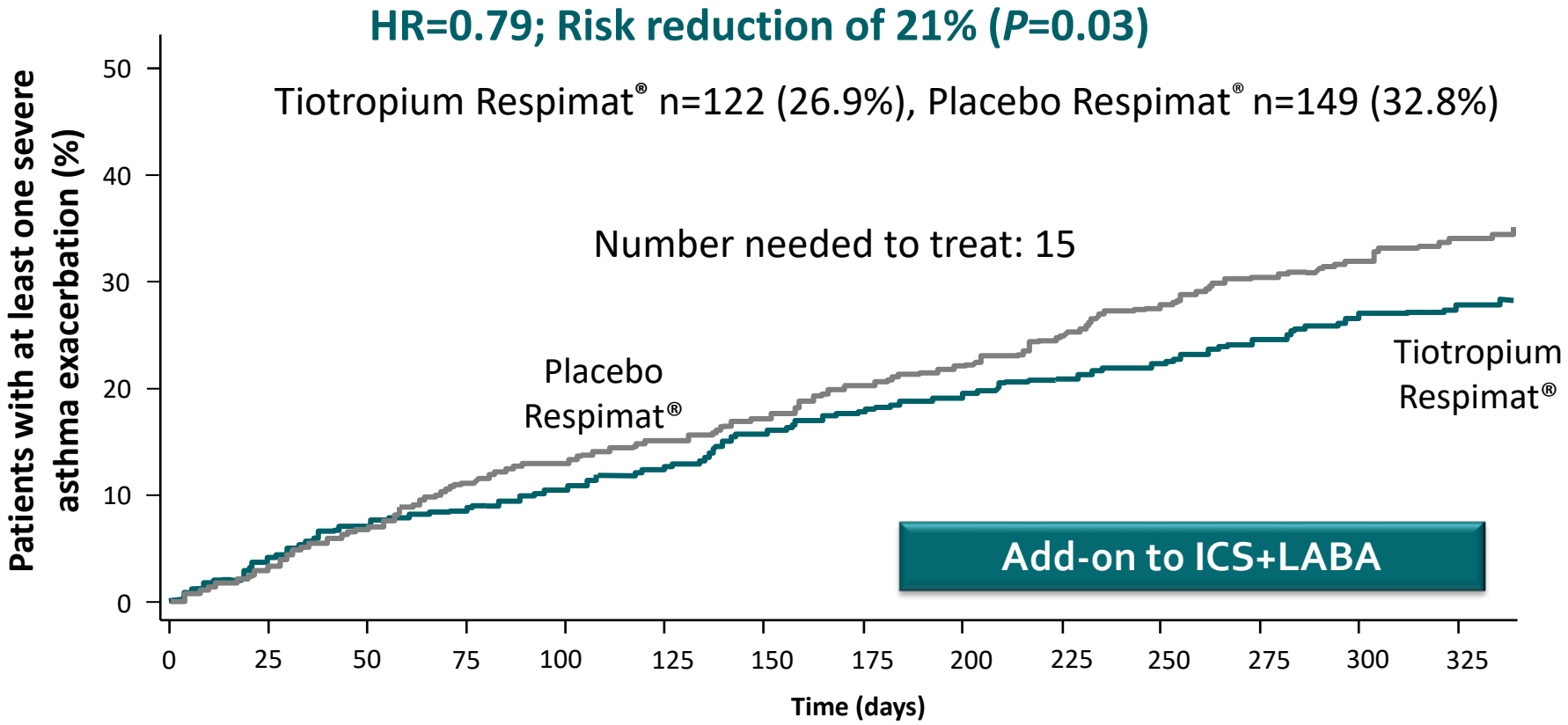


Kerstjens HAM et al. NEJM 2012;367:1198-1207.

FEV_1, forced expiratory volume in 1 second; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist. *P<0.05; **P<0.01; ***P<0.0001.

Error bars represent standard errors

Tiotropium Respimat® increases the time to first severe exacerbation



Patients at risk														
Placebo Respimat®	454	435	412	388	379	367	356	339	332	319	303	290	282	272
Tiotropium Respimat®	453	430	409	401	389	378	363	353	348	339	331	319	308	298

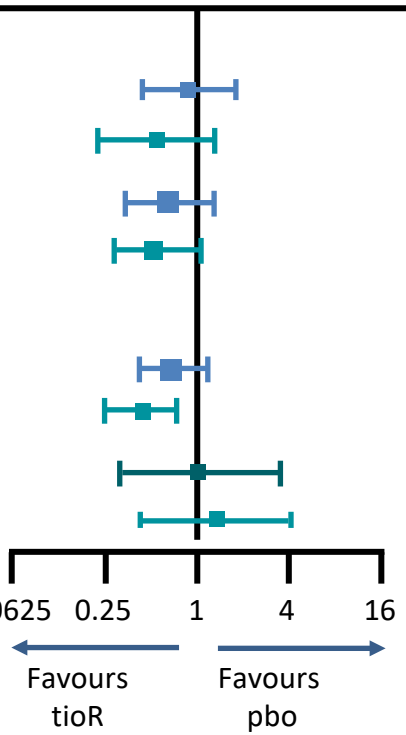
Kerstjens HAM et al. NEJM 2012;367:1198-1207.

HR, hazard ratio; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist

Time to first severe exacerbation with tiotropium Respimat® versus placebo: subgroup analysis by IgE and blood eosinophil status

MezzoTinA-asthma®[a]

Subgroup		Severe asthma exacerbation Patients, n (%) Active comparator	Pbo
Serum IgE			
≤430 µg/L	TioR 5 µg	13/190 (6.8)	
	TioR 2.5 µg	8/192 (4.2)	15/188 (8.0)
>430 µg/L	TioR 5 µg	17/319 (5.3)	
	TioR 2.5 µg	14/320 (4.4)	28/326 (8.6)
Blood eosinophils			
≤0.6×10^9/L	TioR 5 µg	25/406 (6.2)	
	TioR 2.5 µg	16/411 (3.9)	38/410 (9.3)
>0.6×10^9/L	TioR 5 µg	5/104 (4.8)	
	TioR 2.5 µg	6/103 (5.8)	5/107 (4.7)



Full analysis set. Pooled data

[a]Add-on to ICS (400–800 µg budesonide or equivalent); Cox regression analyses of interaction not performed for severe asthma exacerbations in MezzoTinA-asthma® because of the low incidence of events

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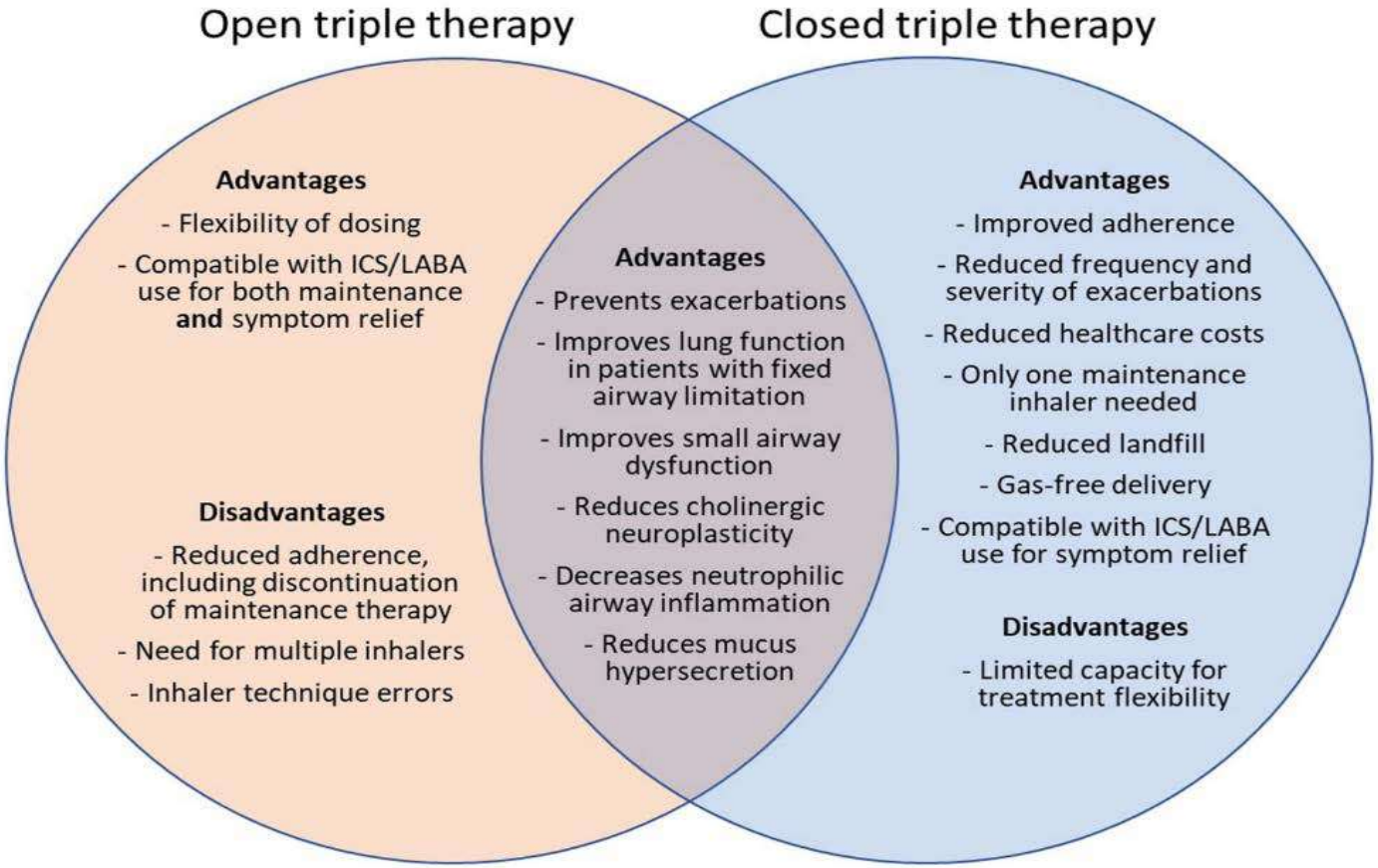
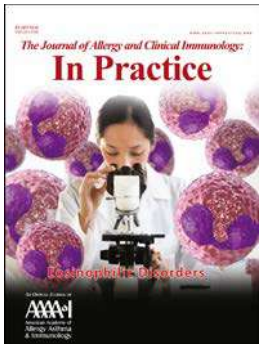


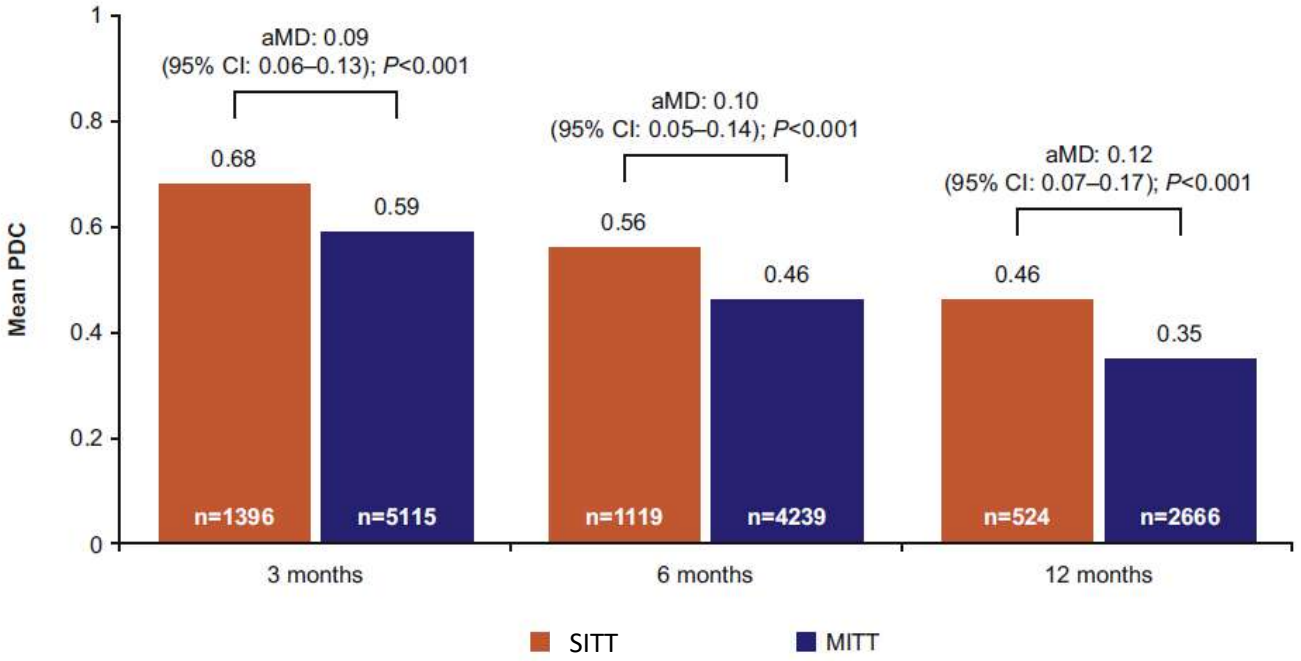
Kenneth R. Chapman, Meyer Balter, Sacha Bhinder, Alan Kaplan, Andrew McIvor, Panayiota Papadopoulos & Krystelle Godbout (2023) Triple inhaled therapy for asthma in Canada, Canadian Journal of Respiratory, Critical Care, and Sleep Medicine, DOI: 10.1080/24745332.2023.2237972

Original Article

Adherence and Persistence to Single-Inhaler Versus Multiple-Inhaler Triple Therapy for Asthma Management

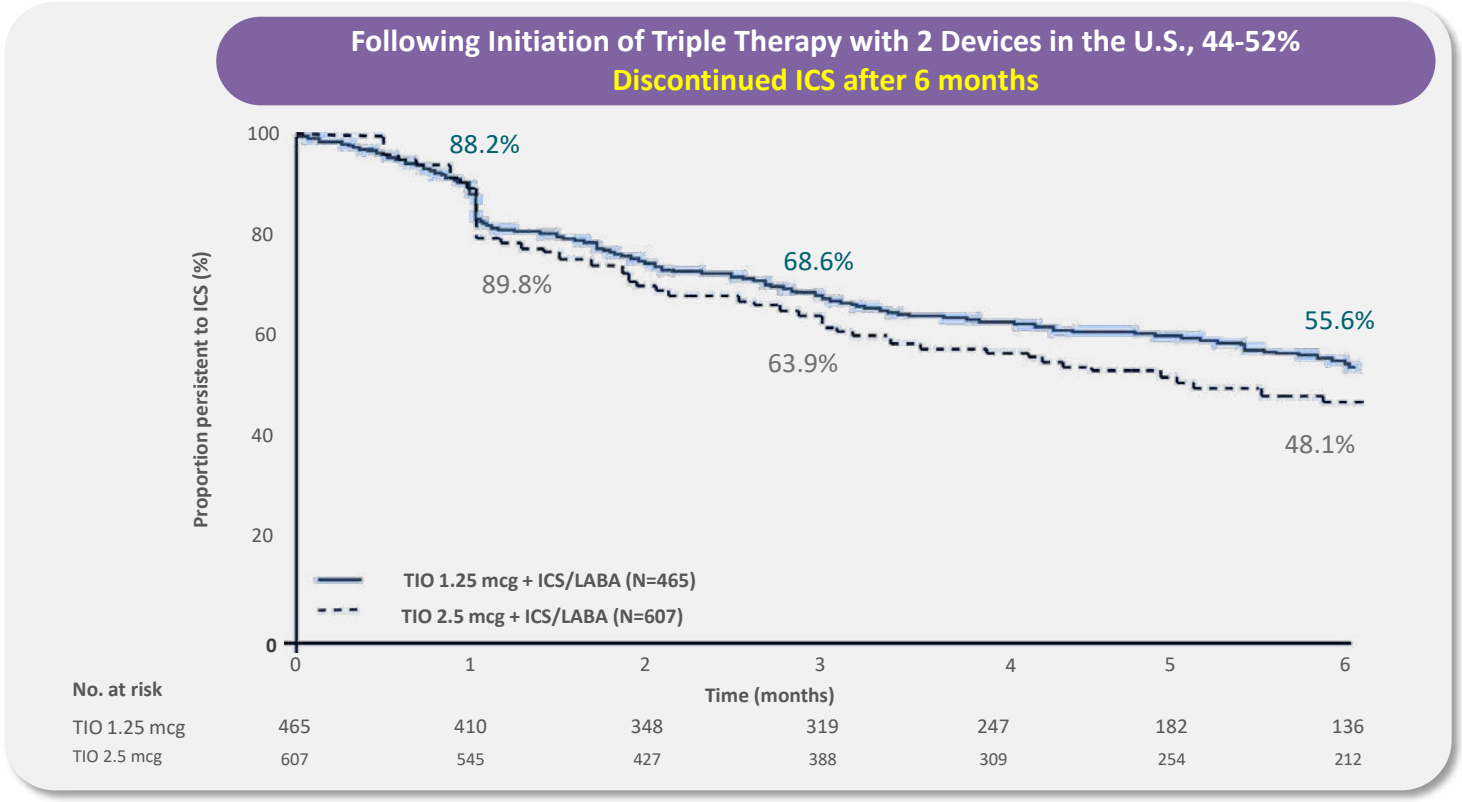
William W. Busse, MD[a], Carl B. Abbott, PharmD[b], Guillaume Germain, MSc[c], François Laliberté, MA[c], Sean D. MacKnight, MScPH[c], Young Jung, PhD[c], Mei Sheng Duh, MPH, ScD[d], and Carlyne M. Averell, SM, MS[b]
Madison, Wisc; Research Triangle Park, NC; Montréal, QC, Canada; and Boston, Mass





PDC, Proportion of Days Covered

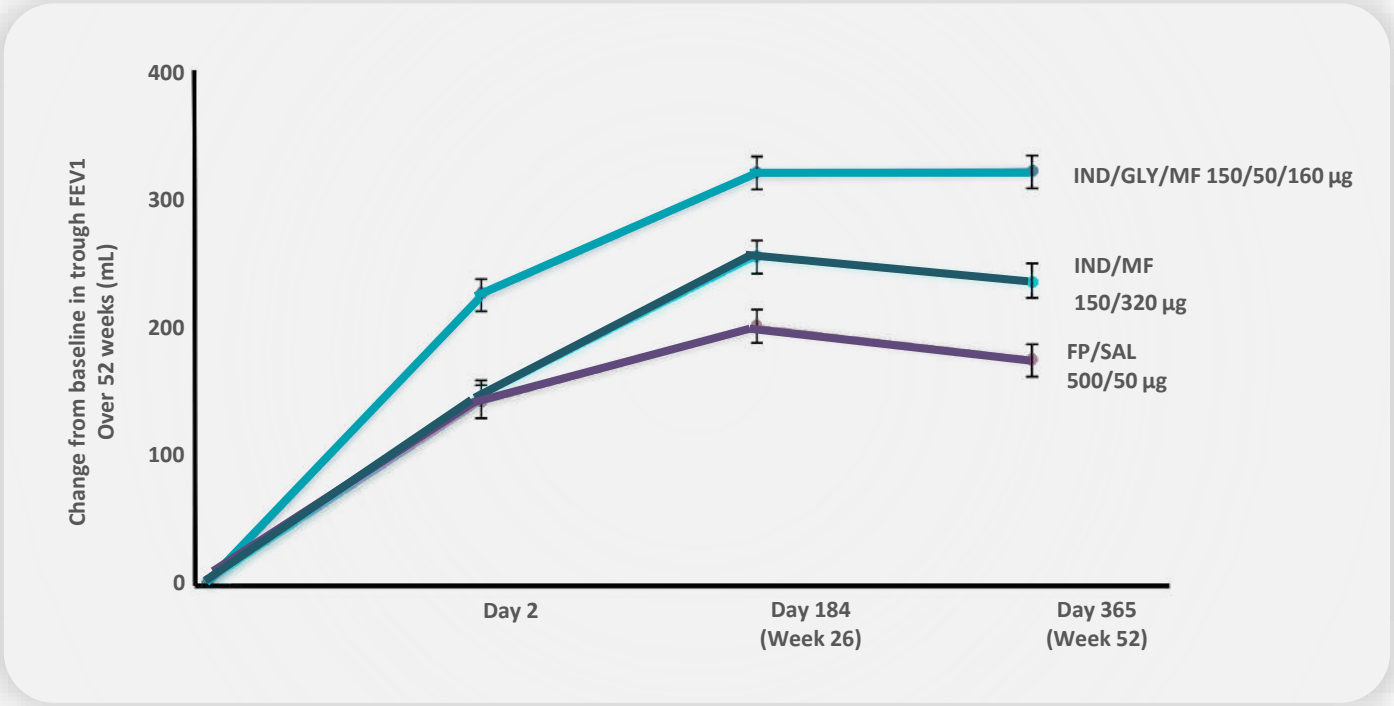
Adherence poor with two devices, and is it dangerous??



Averell et al. J Asthma Allergy. 2019; 12:309-321.

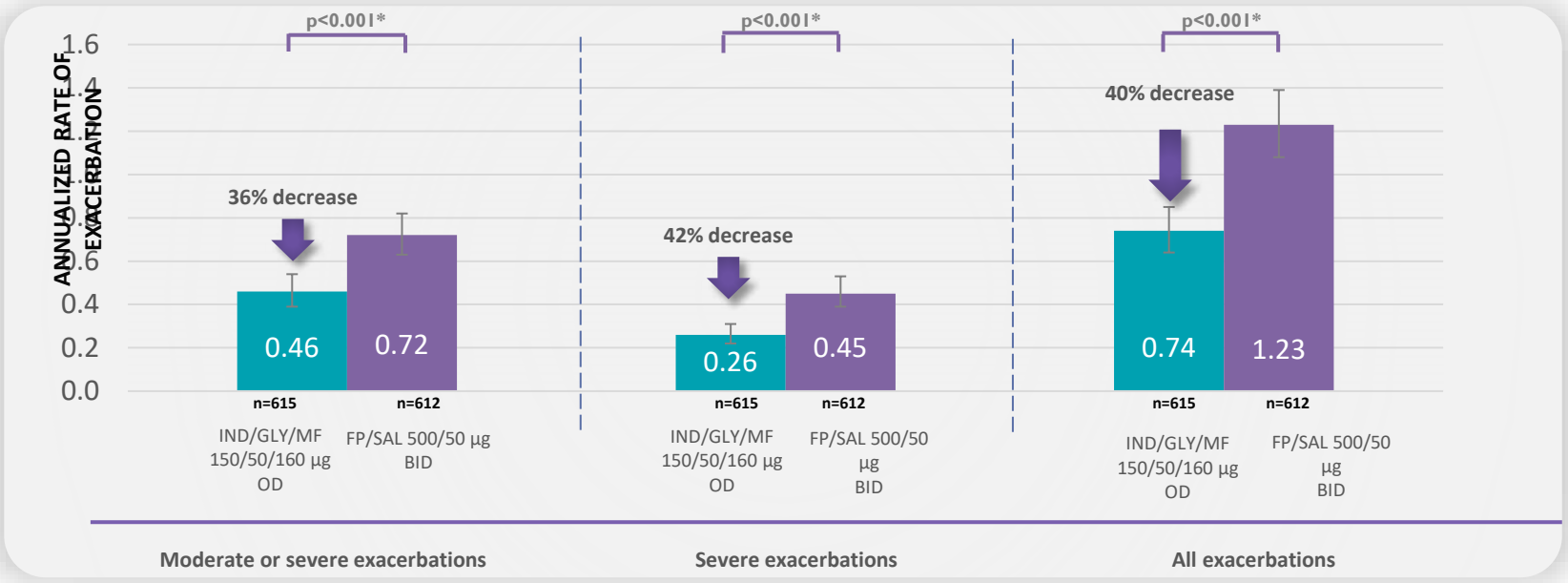
IRIDIUM

Sustained Improvement in Lung Function Over 52 Weeks (OD vs. BID)



Kerstjens HAM, et al. Lancet Respir Med. 2020;S2213-2600:30190-9.

Once Daily IND/GLY/MF Reduces Exacerbations vs. Twice Daily FP/SAL (ICS/LABA)



Significant reduction in exacerbations despite lesser ICS vs. Advair (160 µg MF vs. 1,000 µg FP)

FP, Fluticasone Propionate; GLY, Glycopyrronium bromide; IND, Indacaterol acetate; MF, Mometasone Furoate; SAL, Salmeterol

Kerstjens HAM, et al. Lancet Respir Med. 2020;S2213-2600:30190-9.

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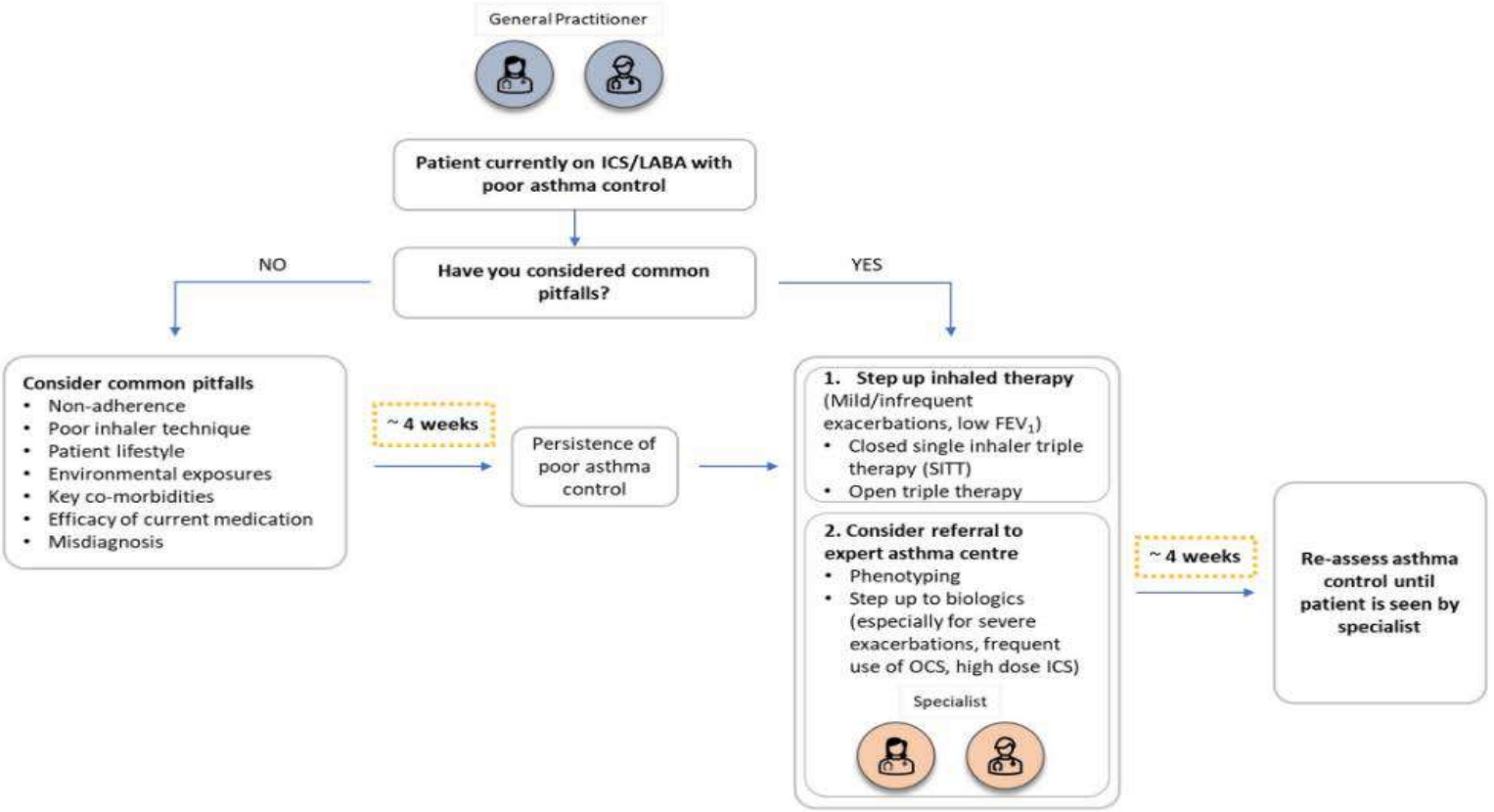
Figure 1 of 2

Figure 1. Schematic to assist decisions regarding whether to initiate triple inhaled therapy in patients with poor asthma control.



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Triple Therapies Approved for Asthma in Canada

Single Inhaler Triple Therapies (SITTs)

Mometasone furoate /Indacaterol/Glycopyrronium	Fluticasone furoate/ Vilanterol/Umeclidinium

ENERZAIR
Breezhaler
160/50/150 mcg

TRELEGY
Ellipta
100/62,5/25 mcg

TRELEGY
Ellipta
200/62,5/25 mcg

One inhalation once daily

Open Triple Therapy

ICS/LABA + Tiotropium (TIO)

ICS/LABA

\+

SPIRIVA
Respimat
2,5 mcg

Two TIO inhalations once daily (plus dosing schedule of existing ICS/LABA regimen)

ICS: inhaled corticosteroids, LABA: long-acting beta-agonist

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Triple therapy options:

Table 2 of 3

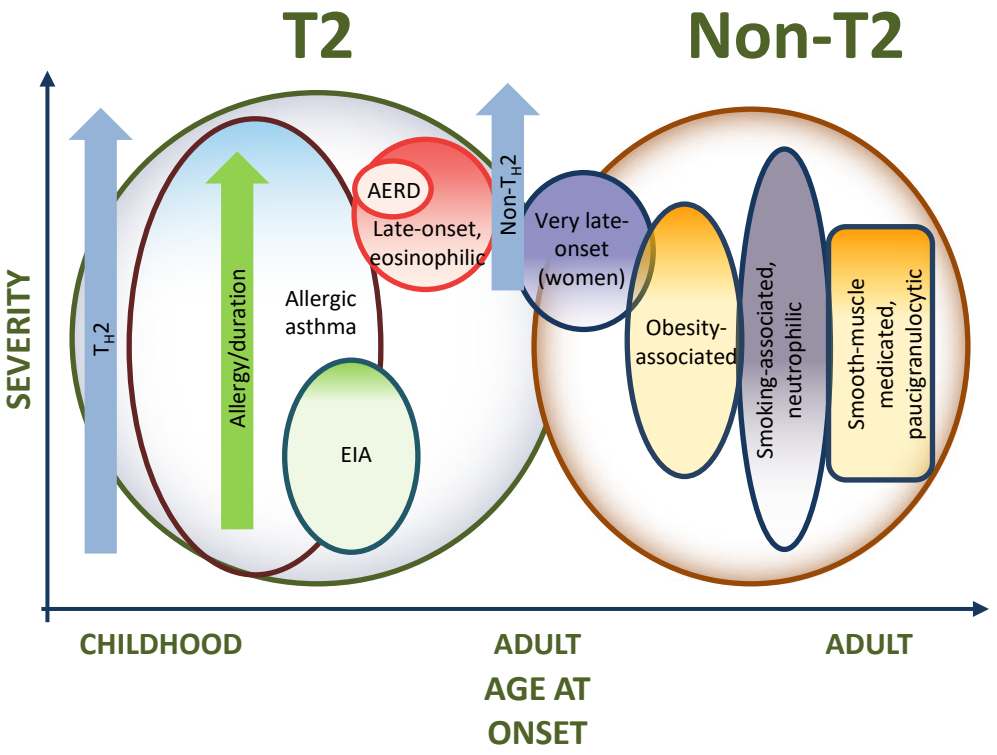
Table 2. Potential *inhaled-only*[a] step-up therapy fo… …dians with poor asthma control treated with ICS/LABA combination.

https://www.bcinhalers.ca/

Treatment	Administration		Dosing Frequency	Price Per Pack ($)[b]
Add-on inhaler to existing ICS/LABA therapy				
Tiotropium	Respimat® device (plus existing ICS/LABA inhaler(s))	2.5 µg (plus co… dose)	…re daily (plus dosing schedule for existing	TIO: 51.90 (QC)/54.86 (ON)/54.67 (AB) + MF/IND: 55.42 (QC, ON, AB)[c,d] FF/VI: 116.90 (QC)/154.73 (ON)/141.94 (AB)[c,d] TOTAL PRICE: MF/IND + TIO: 107.32 (QC)/110.28 (ON)/110.09 (AB) FF/VI + TIO: 168.80 (QC)/199.60 (ON)/164.76 (AB)
Single Inhaler Triple Therapies (SITTs)				
Indacaterol/glycopyrronium /mometasone furoate	Breezhaler® inhaler (powder hard capsules)	150 µg/50 µg/160 µg	One inhalation once daily	102.83 (QC, ON, AB)
Fluticasone furoate/ umeclidinium/vilanterol	Ellipta® inhaler (dry powder)	100 µg/62.5 µg/25 µg, and 200 µg/62.5 µg/25 µg	One inhalation once daily	132.20 (QC)/137.67 (ON, AB) Price not publicly available

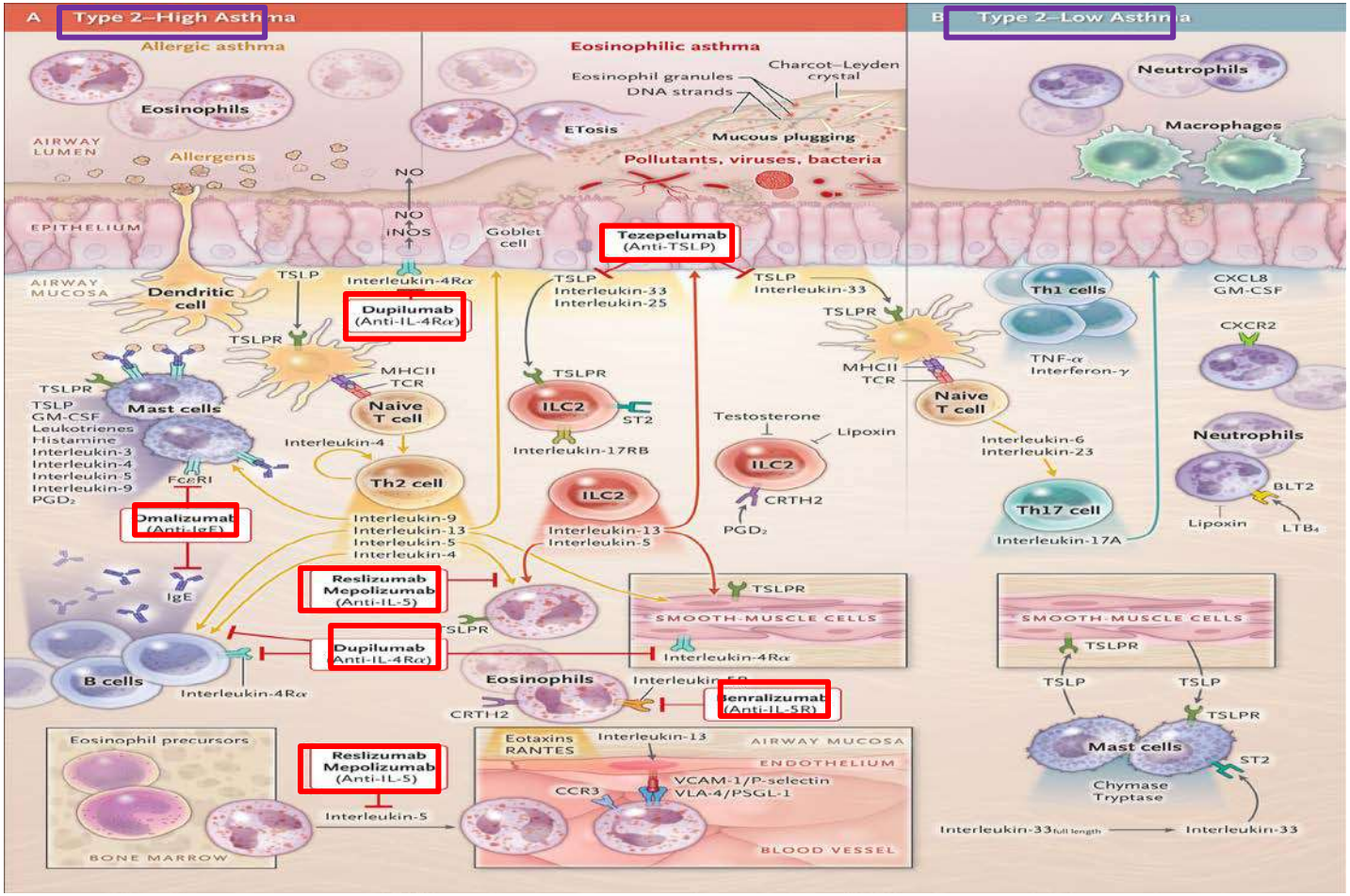
Kenneth R. Chapman, Meyer Balter, Sacha Bhinder, Alan Kaplan, Andrew McIvor, Panayiota Papadopoulos & Krystelle Godbout (2023) Triple inhaled therapy for asthma in Canada, Canadian Journal of Respiratory, Critical Care, and Sleep Medicine, DOI: 10.1080/24745332.2023.2237972

Heterogeneity of Asthma



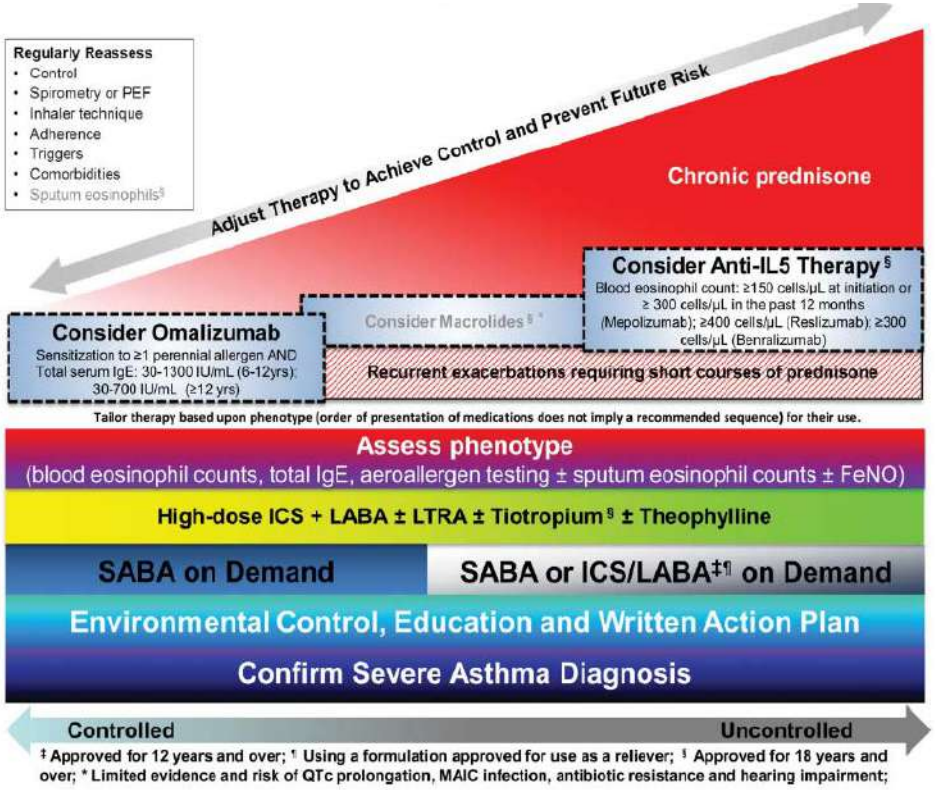
AERD, aspirin-exacerbated respiratory disease; EIA, exercise-induced asthma; T2, T helper cell type 2.
Adapted from Wenzel S. *Nat Med*. 2012;18(5):716-25; Lang DM. *Allergy Asthma Proc*. 2015;36;418-424; Barnes PJ, Woolcock AJ. *Eur Respir J.* 1998;12:1209-1218.

Airway Inflammation in Severe Asthma and Targets of Biologic Therapies.



GG Brusselle, GH Koppelman. N Engl J Med 2022;386:157-171.

Management of Severe Asthma CTS guidelines



FitzGerald JM et al. *Can J Respir Crit Car & Sleep Med*. 2017; 1(4):199-221.

2017, being updated this year!

GP OR SPECIALIST CARE

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

Consider referring to specialist or severe asthma clinic at any stage

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

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

1 Confirm the diagnosis (asthma/differential diagnoses)

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

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

3 Optimize management, including:

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

4 Review response after ~3-6 months

Is asthma still uncontrolled?

yes → DIAGNOSIS: *"Severe asthma"* → If not done by now, refer to a specialist, if possible

no → Consider stepping down treatment, OCS first (if used)

Does asthma become uncontrolled when treatment is stepped down?

yes → Restore previous dose

no → Continue optimizing management

Key

- decision, filters
- intervention, treatment
- diagnosis, confirmation

Eligibility Criteria for Biologic therapies

Criteria	Benralizumab (anti-eosinophilic)	Mepolizumab (anti-IL5)	Reslizumab (anti-IL5)	Dupilumab Anit IL4r/13	Tezepelumab Anti-TSLP
Indication	Add-on maintenance treatment of adult patients with severe eosinophilic asthma			Same	same
Exacerbations requiring OCS, ER or hospitalization, prior 12 months	≥2	≥2	≥1	≥1	≥2
Eosinophil count	No cutoff	≥150 cells/µL at visit 1 or ≥300 cells/µL in the past 12 months	≥400 cells/µL at baseline or visit 1	>150 or OCS	No cutoff
Inadequately controlled with ICS and an additional asthma controller(s) (e.g., LABA)	High-dose ICS: an equivalent of ≥500µg fluticasone propionate/day	High dose ICS: an equivalent of ≥1000 µg fluticasone propionate/day	Medium-to-high-dose ICS: an equivalent of ≥440 µg fluticasone propionate/day	Medium to High dose with controller	High dose (>500 fluticasone propionate

ER, emergency room; ICS, inhaled corticosteroid; IV, intravenous; LABA, long-acting beta agonist; OCS, oral corticosteroid; Q4W, once every 4 weeks; SC, subcutaneous

NUCALA® (mepolizumab) Product Monograph Oct. 2016; CINQAIR® (reslizumab) Product Monograph March 2017; FASENRA® (benralizumab) Product Monograph Feb 2018

Dupixent EAP criteria, Teze poruduct monograph.

Biologics for Severe Asthma

Route of Administration

Biologic	Target	Route of Administration	Dosing	At home?
Mepolizumab[a]	IL-5	SC	100 mg q4w	Yes
Benralizumab[b]	IL-5Rα	SC	30 mg q4w for first 3 doses; 30 mg q8w thereafter	Yes
Reslizumab[c]	IL-5	IV	3 mg/kg q4w	No
Dupilumab[d]	IL-4/IL-13	SC	In adult and adolescent patients ≥ 60 kg who take OCS or who also have AD: • 2 injections of 300 mg in 2 different sites, followed by one 300-mg injection q2w For all other patients with asthma: • 2 injections of 200 mg in 2 different sites, followed by one 200-mg injection q2w	Yes
Omalizumab[e]	IgE	SC	150-375 mg q2w to q4w; according to dosing calculation of 0.016 mg/kg/IU IgE in 4-wk period*	Yes, after a period of time

*Upper limits for patients with high IgE levels and increased weight exist.

a. EMA. EPAR: Nucala (mepolizumab). 2019; b. EMA. EPAR: Fasenra (benralizumab). 2019; c. EMA. EPAR: Cinqaero (reslizumab). 2019; d. EMA. EPAR: Supizent (dupilumab). 2019; e. Krings, JG, et al. *J Allergy Clin Immunol Pract.* 2019;7:1379-1392.

Tezepelumab	**Anti TSLP**	**SC**	**210 mg q 4 wk4 weeks**	**Yes**

What else should you consider prior to using biologics? COMORBIDITIES!

Type 2 asthma often coexists with other Type 2 inflammatory diseases

- Eosinophilic oesophagitis[1]
- Chronic spontaneous urticaria[5]
- Atopic dermatitis[1]
- Food allergy[1,2]
- CRSwNP[1]
- Allergic rhinitis[1]
- NSAID-ERD[3]
- Asthma[1]
- Eosinophilic COPD[1,4]

- COPD, chronic obstructive pulmonary disease; CRSwNP, chronic rhinosinusitis with nasal polyps; IgE, immunoglobulin E; IL, interleukin; NSAID-ERD, nonsteroidal anti-inflammatory drug–exacerbated respiratory disease.
- 1. Gandhi NA, et al. Nat Rev Drug Discov. 2016;15:35-50. 2.Bauer RN, et al. J Allergy Clin Immunol. 2015;135:312-323. 3. Kowalski ML, et al. Allergy. 2019;74:28-39. 4. Garudadri S, Woodruff PG. Ann Am Thorac Soc. 2018;15(suppl 4):S234-S238. 5. Fildan AP, Rajnoveanu RM, Cirjaliu R, et al. Exp Ther Med. 2021;22(5):1263.

Are Vaccinations OK?

Review Article

Guidance for Administering Biologics for Severe Asthma and Allergic Conditions

Delbert R. Dorscheid,[1] Jason K. Lee,[2] Warren Ramesh,[3] Mark Greenwald,[4] and Jaime Del Carpio[5]

2. Types of vaccines and whether to administer with a biologic [4, 5, 6, 8, 9, 45].

Vaccine type	Examples of available vaccines[a]	OK to receive a vaccine with continued biologic use?
Inactivated	Influenza, hepatitis A, rabies	✓
Live-attenuated	MMR, rotavirus, varicella	✓
		Except dupixent and cinqair[b]
mRNA	Pfizer-BioNTech COVID-19, Moderna COVID-19	✓
Conjugate, subunit, recombinant, polysaccharide	Hepatitis B, HPV, pneumococcal, meningococcal, shingles	✓
Toxoid	Diphtheria, tetanus	✓
Viral vector	Johnson & Johnson COVID-19, Oxford-AstraZeneca COVID-19, Verity Pharmaceuticals-Serum Institute of India COVID-19	✓

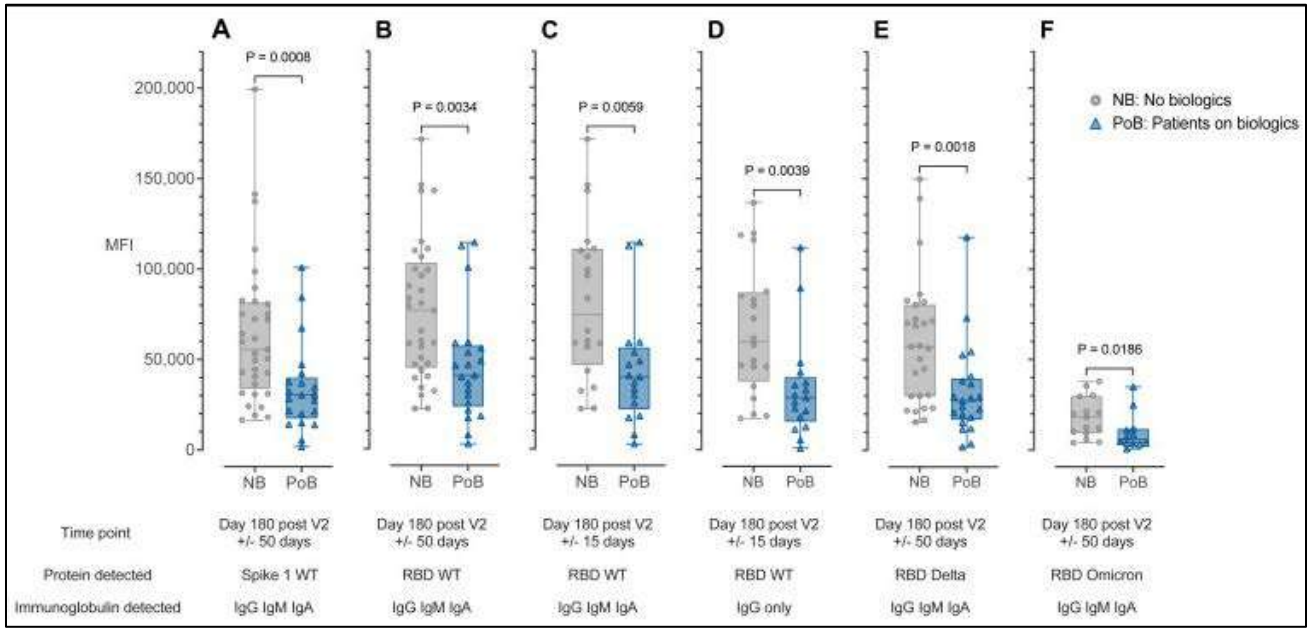
HPV: human papillomavirus; MMR: measles, mumps, and rubella; mRNA: messenger ribonucleic acid. [a]Table is not comprehensive; review all vaccine product information before administering. [b]Dupixent and Cinqair doses should be held for 1 month before the live vaccine administration and reinitiated at least 2 weeks postvaccination.

Dorscheid DR, Lee JK, Ramesh W, Greenwald M, Del Carpio J. Guidance for Administering Biologics for Severe Asthma and Allergic Conditions. Can Respir J. 2022 Sep 10;2022:9355606. doi: 10.1155/2022/9355606. PMID: 36124286; PMCID: PMC9482537.

But do biologics affect shot efficacy?

ARTICLE IN PRESS

Patients taking benralizumab, dupilumab, or mepolizumab have lower postvaccination SARS-CoV-2 immunity

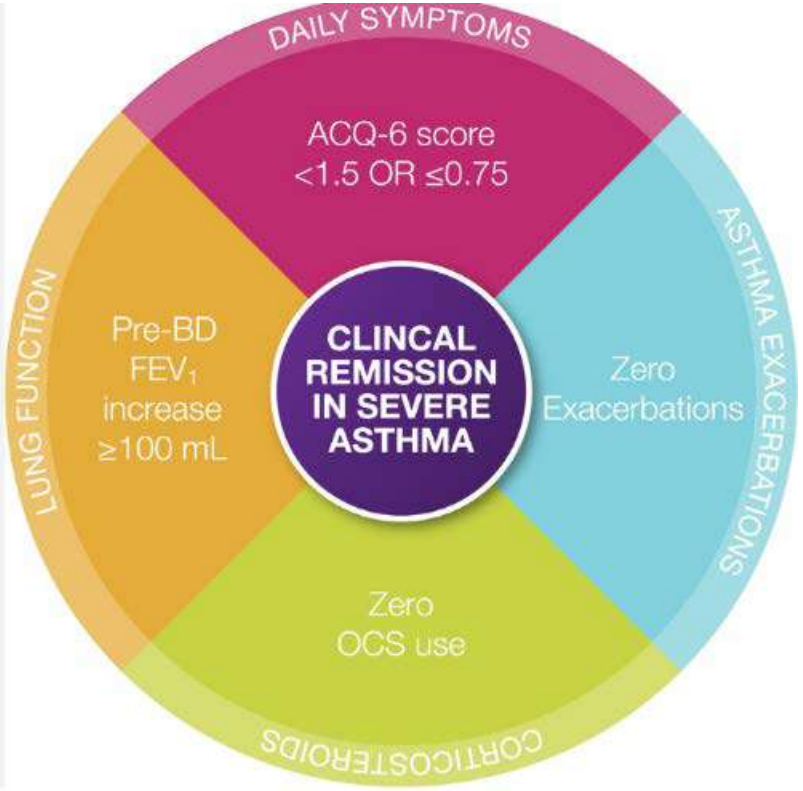


The patients in the [biologics] group had reduced SARS-CoV-2–specific antibody titers, neutralizing activity, and virus-specific B- and CD8 T-cell counts" 6 months after primary immunization to SARS-CoV-2,

Study limitations include possible confounding by age, body mass index, and use of high-dose inhaled corticosteroids, as well as imperfect matching between biologic and control groups.

Runnstrom MC, et al. Patients taking benralizumab, dupilumab, or mepolizumab have lower postvaccination SARS-CoV-2 immunity. J Allergy Clin Immunol. 2024 Jun 13:S0091-6749(24)00420-2. doi: 10.1016/j.jaci.2024.03.029. Epub ahead of print. PMID: 38878020.

It is time to rethink our Goals!



Menzies-Gow, A., Hoyte, F.L., Price, D.B. et al. Clinical Remission in Severe Asthma: A Pooled Post Hoc Analysis of the Patient Journey with Benralizumab. Adv Ther 39, 2065–2084 (2022). https://doi.org/10.1007/s12325-022-02098-1

How to find these patients in YOUR practices?

Asthma ReferID

Use this conversation guide to quickly identify adult asthma patients who may benefit from a specialist review

Consider review by a specialist if the patient answers 'yes' to any of the questions:

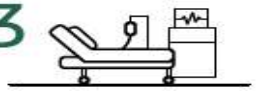
1

Has the patient used 2 or more courses of systemic corticosteroids (SCS) and/or is using maintenance SCS therapy over the past 12 months?

2

Has the patient had 2 or more emergency attendances /unscheduled visits due to asthma over the past 12 months?

3



Has the patient ever been intubated or admitted to an ICU (intensive care unit) or high dependency unit due to their asthma?

4

Has the patient used more than 3 SABA (short-acting beta2-agonist) inhalers in the past 12 months?

This ReferID guide has been developed by AstraZeneca in collaboration with five asthma experts: Dr. D. Jackson, Dr. J.W.H. Kocks, M. Al-Ahmad, MD, R. del Olmo, MD and Dr. Tan Tze Lee

The content of this guide is based upon the 2019 / 2020 Global Strategy for Asthma Management and Prevention reports - https://ginasthma.org

Veeva ID: Z4-22623. Date of preparation: March 2020. Date of expiry: 31 March 2022

Scan to access the digital version of ReferID.

For more information regarding ReferID, please email: support@asthmareferid.com

When you stop the biologic, the effect on exacerbations and asthma control deteriorates

EUROPEAN RESPIRATORY JOURNAL
ORIGINAL RESEARCH ARTICLE
W.C. MOORE ET AL.

Stopping *versus* continuing long-term mepolizumab treatment in severe eosinophilic asthma (COMET study)

Wendy C. Moore[1], Oliver Kornmann[2], Marc Humbert[3,4,5], Claude Poirier[6], Elisabeth H. Bel[7], Norihiro Kaneko[8], Steven G. Smith[9], Neil Martin[10,11], Martyn J. Gilson[12], Robert G. Price[13], Eric S. Bradford[9] and Mark C. Liu[14]

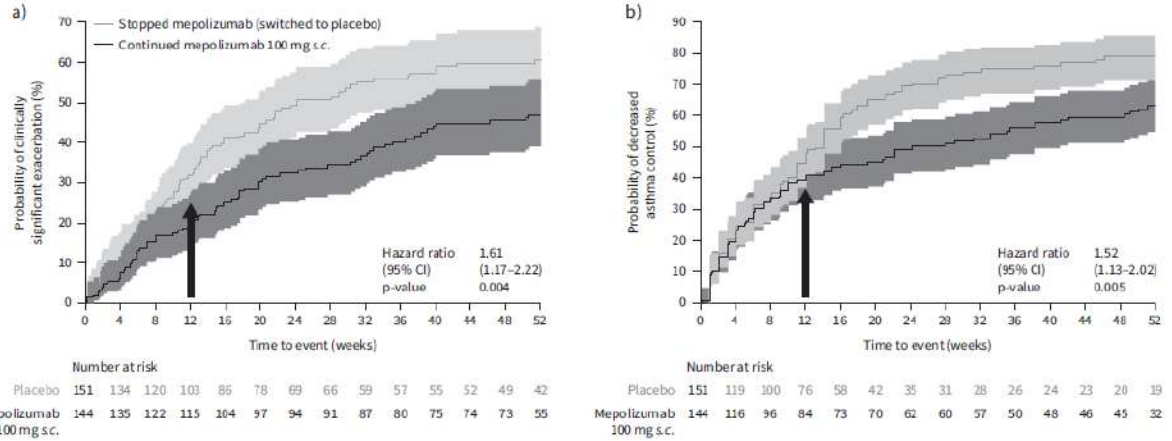


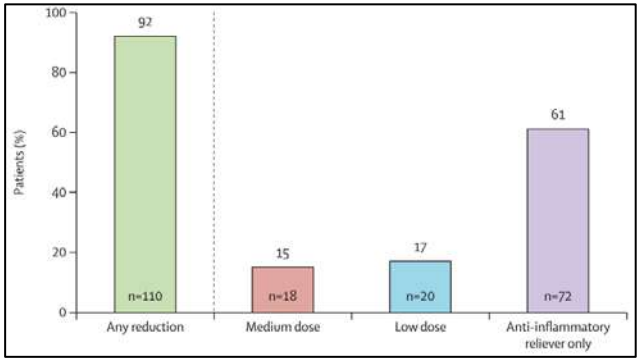
FIGURE 2 Kaplan–Meier cumulative incidence curve for time to first a) clinically significant exacerbation; and b) decrease in asthma control, defined as an increase from baseline in Asthma Control Questionnaire-5 score of ⩾0.5 units [15], and the associated hazard ratios (stopping/continuing mepolizumab) (on-treatment; Part C; blinded treatment). Week 0 represents 4 weeks following the last dose of open-label mepolizumab. Shaded areas represent 95% confidence intervals. Arrows indicate that the difference between groups was seen from week 12 onwards (16 weeks after the last dose of open-label mepolizumab).

Moore WC et al. European Resp J 2021:2100396

Reduction in Inhaled Medications After Good Responses to a Biologic

SHAMAL Study

Patients reporting reduction in ICS-formoterol maintenance dose at Week 32



92% of patients were able to successfully reduce their high-dose ICS, with more than 60% reducing to anti-inflammatory reliever only without a change in asthma control

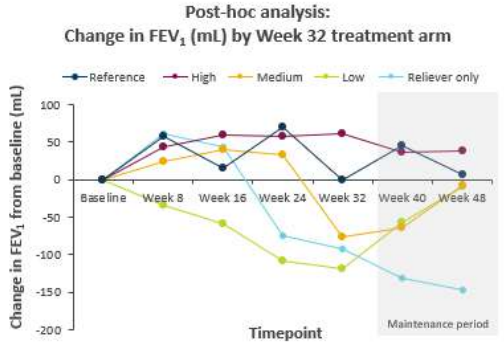
Rates of adverse events were similar between groups throughout the study.

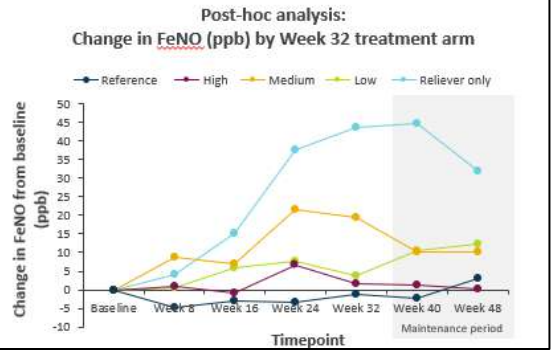
- 73% of patients in the reduction group had adverse events versus 83% in the reference group

These findings show that patients controlled on benralizumab can have meaningful reductions in ICS therapy while maintaining asthma control.

But reduction in lung function (often without symptoms) occurred when dose cut down to prn....

Changes in FEV_1 and FeNO during the study (post-hoc analysis)



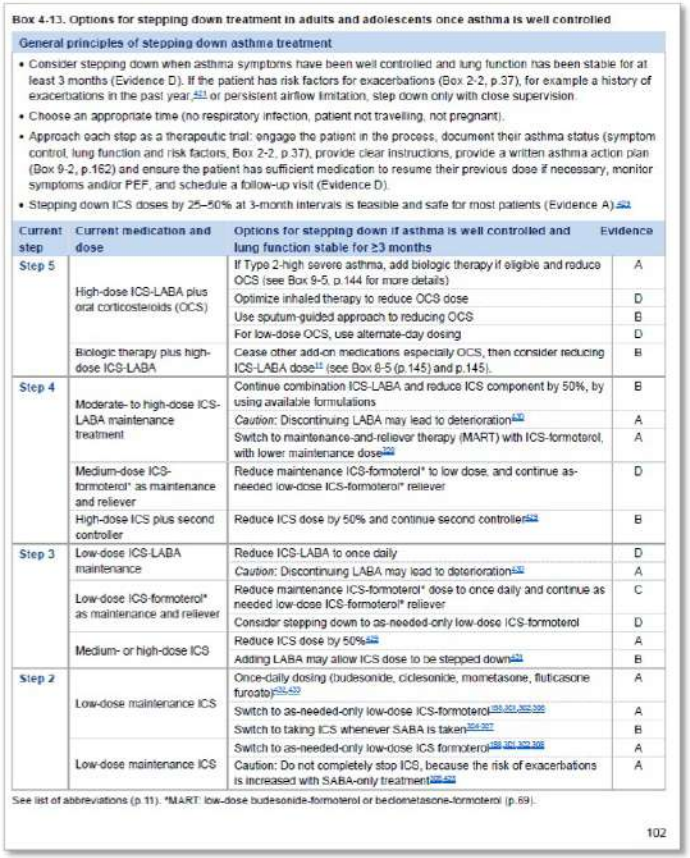


ACQ, asthma control questionnaire; ICS, inhaled corticosteroid; MART, maintenance and reliever therapy.

1. Jackson DJ, Heaney LG, Humbert M, et al. Lancet. 2024;403(10423):271-81.

Stepping down asthma treatment

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



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

General principles of stepping down asthma treatment

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

Current step	Current medication and dose	Options for stepping down if asthma is well controlled and lung function stable for ≥3 months	Evidence
Step 5	High-dose ICS-LABA plus oral corticosteroids (OCS)	If Type 2-high severe asthma, add biologic therapy if eligible and reduce OCS (see Box 9-5, p.144 for more details)	A
		Optimize inhaled therapy to reduce OCS dose	D
		Use sputum-guided approach to reducing OCS	B
		For low-dose OCS, use alternate-day dosing	D
	Biologic therapy plus high-dose ICS-LABA	Cease other add-on medications especially OCS, then consider reducing ICS-LABA dose[11] (see Box 8-5 (p.145) and p.145).	B
Step 4	Moderate- to high-dose ICS-LABA maintenance treatment	Continue combination ICS-LABA and reduce ICS component by 50%, by using available formulations	B
		Caution: Discontinuing LABA may lead to deterioration[430]	A
		Switch to maintenance-and-reliever therapy (MART) with ICS-formoterol, with lower maintenance dose[320]	A
	Medium-dose ICS-formoterol* as maintenance and reliever	Reduce maintenance ICS-formoterol* to low dose, and continue as-needed low-dose ICS-formoterol* reliever	D
	High-dose ICS plus second controller	Reduce ICS dose by 50% and continue second controller[429]	B
Step 3	Low-dose ICS-LABA maintenance	Reduce ICS-LABA to once daily	D
		Caution: Discontinuing LABA may lead to deterioration[430]	A
	Low-dose ICS-formoterol* as maintenance and reliever	Reduce maintenance ICS-formoterol* dose to once daily and continue as needed low-dose ICS-formoterol* reliever	C
		Consider stepping down to as-needed-only low-dose ICS-formoterol	D
	Medium- or high-dose ICS	Reduce ICS dose by 50%[429]	A
		Adding LABA may allow ICS dose to be stepped down[431]	B
Step 2	Low-dose maintenance ICS	Once-daily dosing (budesonide, ciclesonide, mometasone, fluticasone furoate)[335,433]	A
		Switch to as-needed-only low-dose ICS-formoterol[330-331,352-356]	A
		Switch to taking ICS whenever SABA is taken[304-307]	B
	Low-dose maintenance ICS	Switch to as-needed-only low-dose ICS formoterol[188-191,352-356]	A
		Caution: Do not completely stop ICS, because the risk of exacerbations is increased with SABA-only treatment[295-299]	A

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

102

Safety of Omalizumab in Pregnancy: EXPECT Registry

- Prospective, observational study of pregnant women exposed to ≥1 dose of omalizumab
  - Within 8 weeks prior to conception OR
  - Anytime during pregnancy
- 188/191 exposed during first trimester
- Small sample size

EXPECT results are consistent with pregnancy outcomes complicated by asthma.

The safety profile of omalizumab treatment during pregnancy must be weighed against the risks of uncontrolled asthma.

Omalizumab product monograph; Namazy J et al. *J Allergy Clin Immunol* 2015;135:407-12.

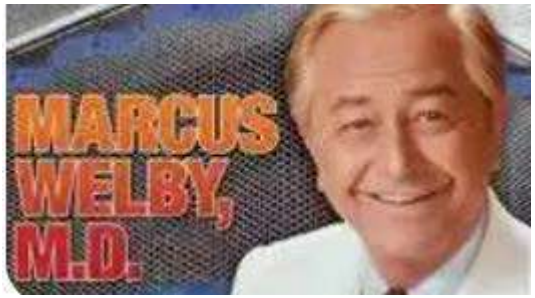
Safety of IL-5 Therapies in Pregnancy

- mAb are transported across the placenta in a linear fashion as pregnancy progresses
  - Any potential effect likely to be greater during 2nd and 3rd trimesters

- IL-5 (Benralizumab, Reslizumab, Mepolizumab)
  - No studies have been conducted in pregnant women
  - Registry has been established (http://mothertobaby.org/asthma)

What to do in Primary Care?

- **RECOGNIZE THESE PATIENTS IN YOUR PRACTICE (Refer ID)**
  - OCS harms
  - SABA overuse harms
- Take care of the basics
  - Diagnosis (spirometry!), adherence, technique, comorbidities, triggers
  - Aim higher, perfect control??
  - Severe is not the same as uncontrolled
- Consider some phenotyping: IgE, CBC, FENO
- ? Allergy testing
- Consider triple therapy while waiting for referral
- Consider mitigating OCS risk
  - Pneumonia risk
  - Bone health
  - Eye health
- Vaccinate appropriately
- Continue to support your patient
- REFER for biologics



So, what are OUR in Roles of Primary Care for Severe Asthma?

- If they are on asthma biologics
  - A) They are not immunocompromised wrt vaccinations
  - B) They should not stop their biologics when they feel better, and they will want to!
  - C) They should continue at least a low dose ICS even if/when they feel great!

I look forward to being able to assist you in your respiratory needs!

www.fpagc.com
for4kids@gmail.com