Inhalers and Beyond: Navigating Therapeutic Advances and Holistic Care in Asthma & COPD Management

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- Astra-Zeneca
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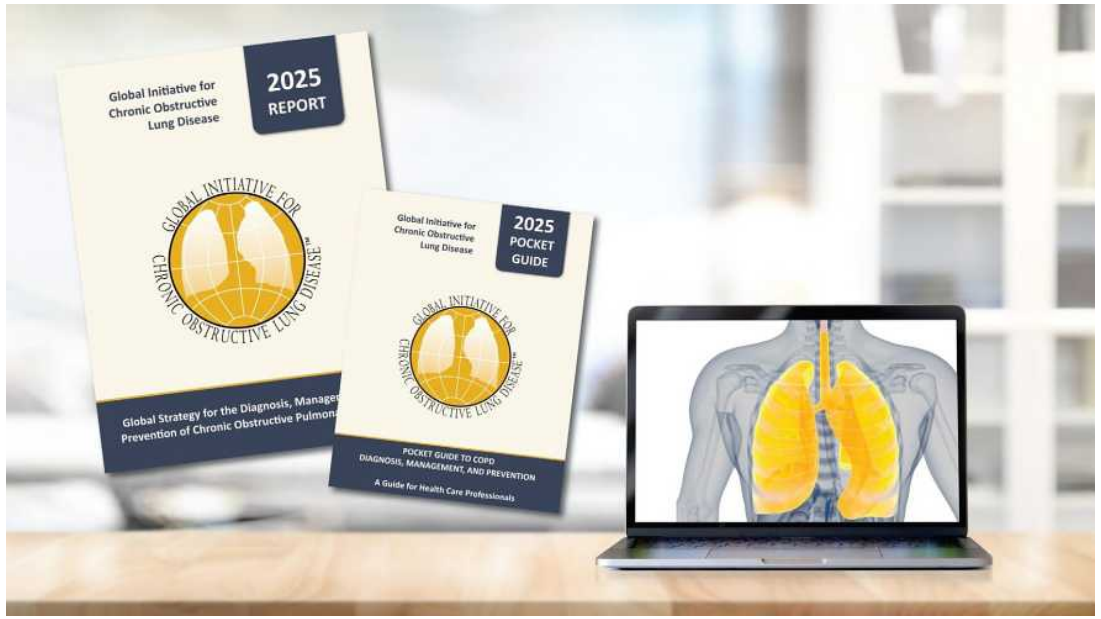
- Fresenius
- Gambro
- GE Healthcare
- GSK
- Hospira
- Medtronic
- Moderna
- Novartis
- Pfizer
- Sanofi-Aventis

Key reference sources

Global Initiative for Asthma (GINA) Strategy Report 2024

Global Initiative for Chronic Obstructive Lung Disease (GOLD) Report 2025

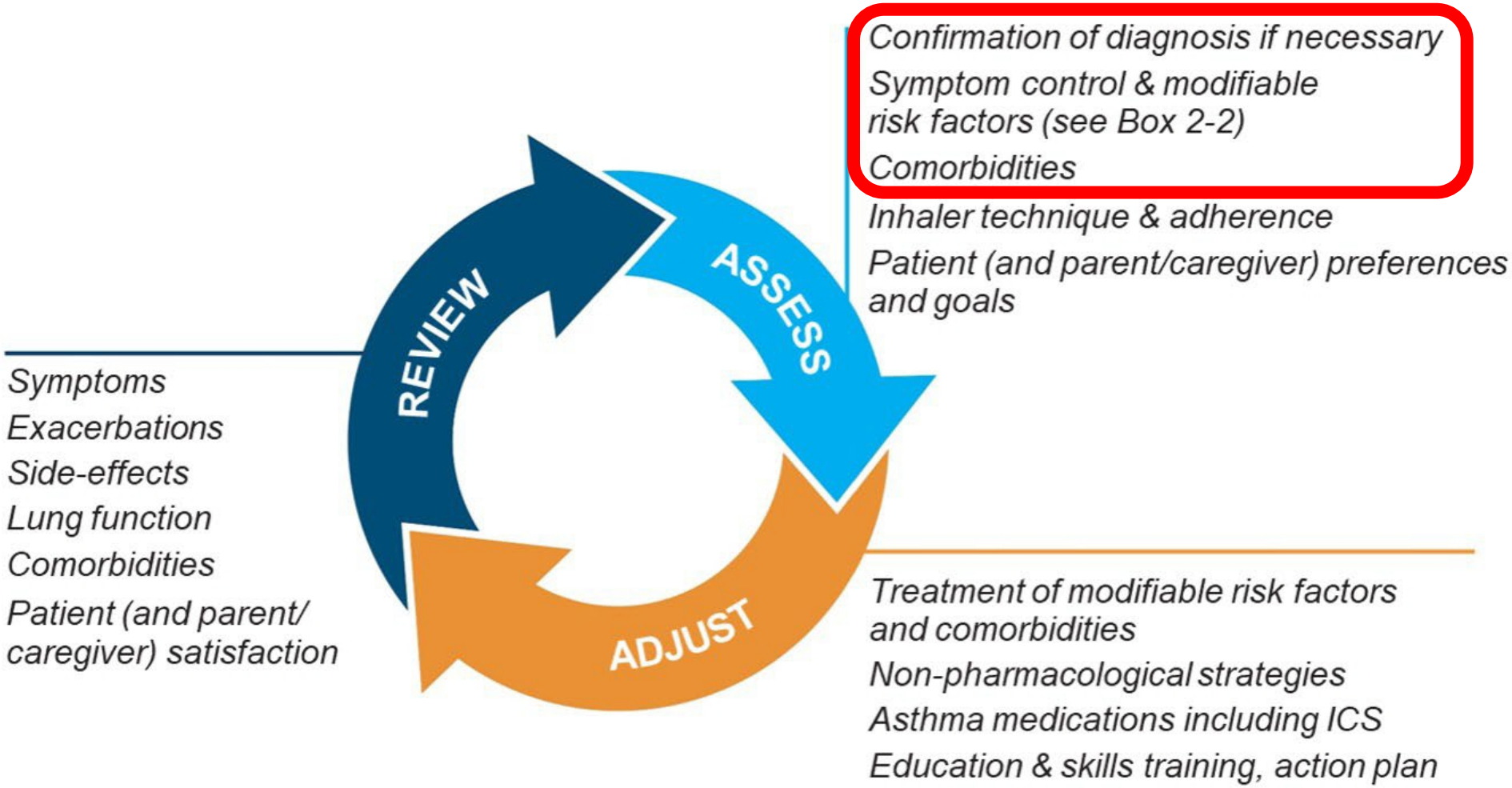


60-year-old man

- Smoker
- Delivery driver
- **Asthma** since childhood
- Diagnosed with **COPD** 1 year ago (post-BD FEV1/FVC was 60%)
- On salmeterol-fluticasone propionate 50/250 1 puff BD **for asthma**
- Seeing his GP for routine follow-up
- **Troubled by dyspnea and decreased exercise tolerance over the past 2 months**
- **How should his GP approach this case?**

Case study courtesy of speaker

Asthma treatment is not ‘set and forget’, and not just medications



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Not all that wheezes is asthma

Special considerations for asthma diagnoses	List of non-asthma diagnoses
• Allergic rhinitis, allergic conjunctivitis and atopic eczema • Allergic bronchopulmonary aspergillosis • Eosinophilic granulomatosis with polyangiitis • Exercise-induced asthma • Work-related asthma	• Benign or malignant masses, lymph nodes, or vascular rings causing central airway obstruction • Bronchiectasis • Bronchitis or pneumonia • Carcinoid syndrome • Cardiac ischemia, valvular heart disease, or heart failure • Chronic obstructive pulmonary disease • Endobronchial tuberculosis • Eosinophilic pneumonia • Foreign body inhalation • Interstitial lung disease • Paradoxical vocal cord motion • Parasitic infection with pulmonary involvement • Relapsing polychondritis • Tracheal stenosis or tracheobronchomalacia • Vocal cord mass or paralysis

See, Singapore Family Physician 2018

Differential diagnosis of COPD

Differential Diagnosis of COPD

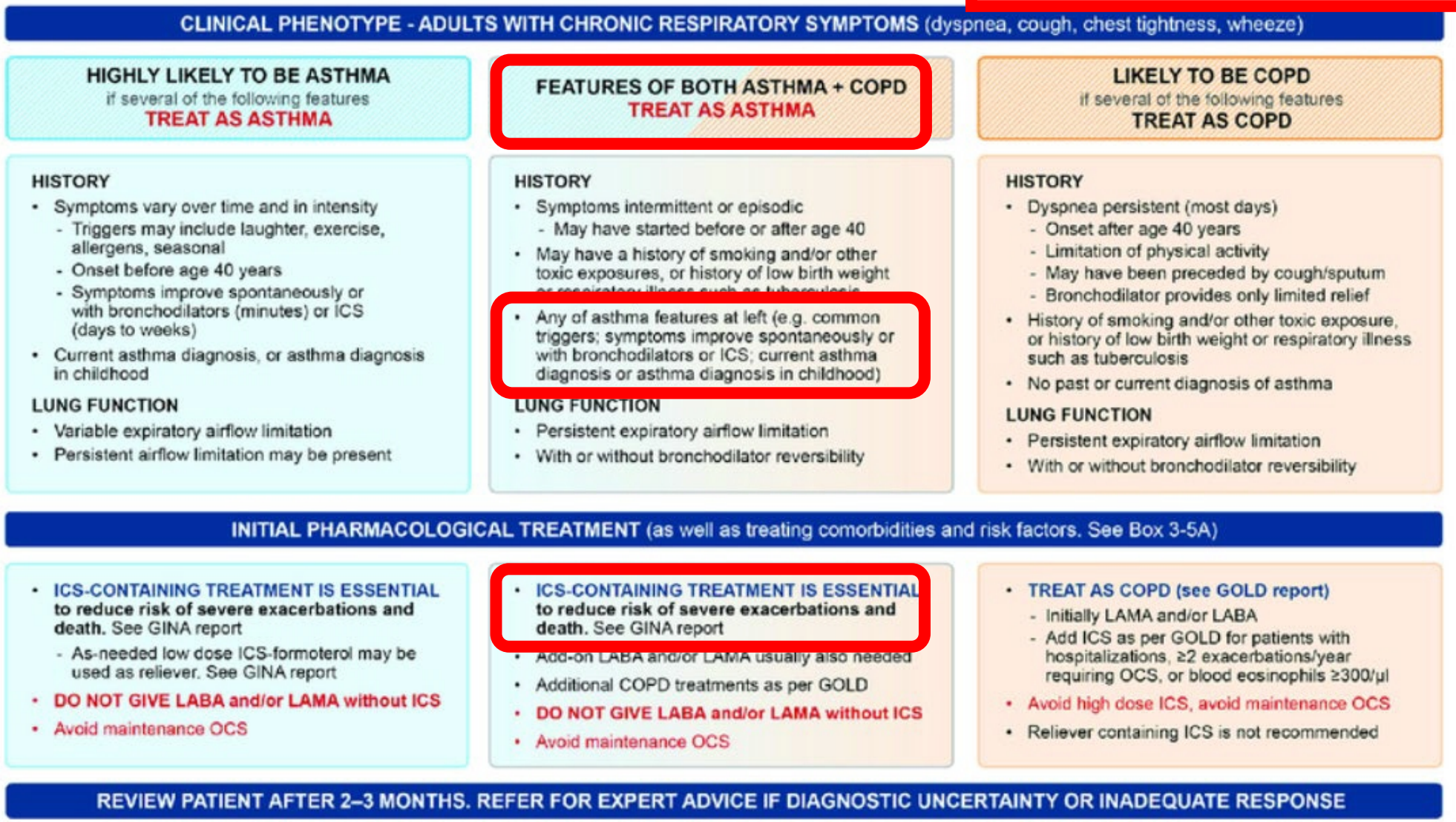
Figure 2.3

Diagnosis	Suggestive Features
COPD	Symptoms slowly progressive History of tobacco smoking or other risk factors
Asthma	Variable airflow obstruction Symptoms vary widely from day to day Symptoms worse at night/early morning Allergy, rhinitis, and/or eczema also present Often occurs in children Family history of asthma
Congestive heart failure	Chest X-ray shows dilated heart, pulmonary edema Pulmonary function tests indicate volume restriction, not airflow obstruction
Bronchiectasis	Large volumes of purulent sputum Commonly associated with bacterial infection Chest X-ray/HRCT shows bronchial dilation
Tuberculosis	Onset at all ages Chest X-ray shows lung infiltrate Microbiological confirmation High local prevalence of tuberculosis
Obliterative bronchiolitis	Can occur in children Seen after lung or bone marrow transplantation HRCT on expiration shows hypodense areas
Diffuse panbronchiolitis	Predominantly seen in patients of Asian descent Most patients are male and nonsmokers Almost all have chronic sinusitis Chest X-ray & HRCT show diffuse small centrilobular nodular opacities & hyperinflation

These features tend to be characteristic of the respective diseases, but are not mandatory. For example, a person who has never smoked may develop COPD (especially in LMICs where other risk factors may be more important than cigarette smoking).

GOLD 2025

COPD with asthma features (*not* "eosinophilic COPD")



GINA 2024

Causes of COPD

Proposed Taxonomy (Etiotypes) for COPD

Figure 1.2

Classification	Description
Genetically determined COPD (COPD-G)	Alpha-1 antitrypsin deficiency (AATD) Other genetic variants with smaller effects acting in combination
COPD due to abnormal lung development (COPD-D)	Early life events, including premature birth and low birthweight, among others
Environmental COPD	
Cigarette smoking COPD (COPD-C)	• Exposure to tobacco smoke, including *in utero* or via passive smoking • Vaping or e-cigarette use • Cannabis
Biomass and pollution exposure COPD (COPD-P)	Exposure to household pollution, ambient air pollution, wildfire smoke, occupational hazards
COPD due to infections (COPD-I)	Childhood infections, tuberculosis-associated COPD, HIV-associated COPD
COPD & asthma (COPD-A)	Particularly childhood asthma
COPD of unknown cause (COPD-U)	

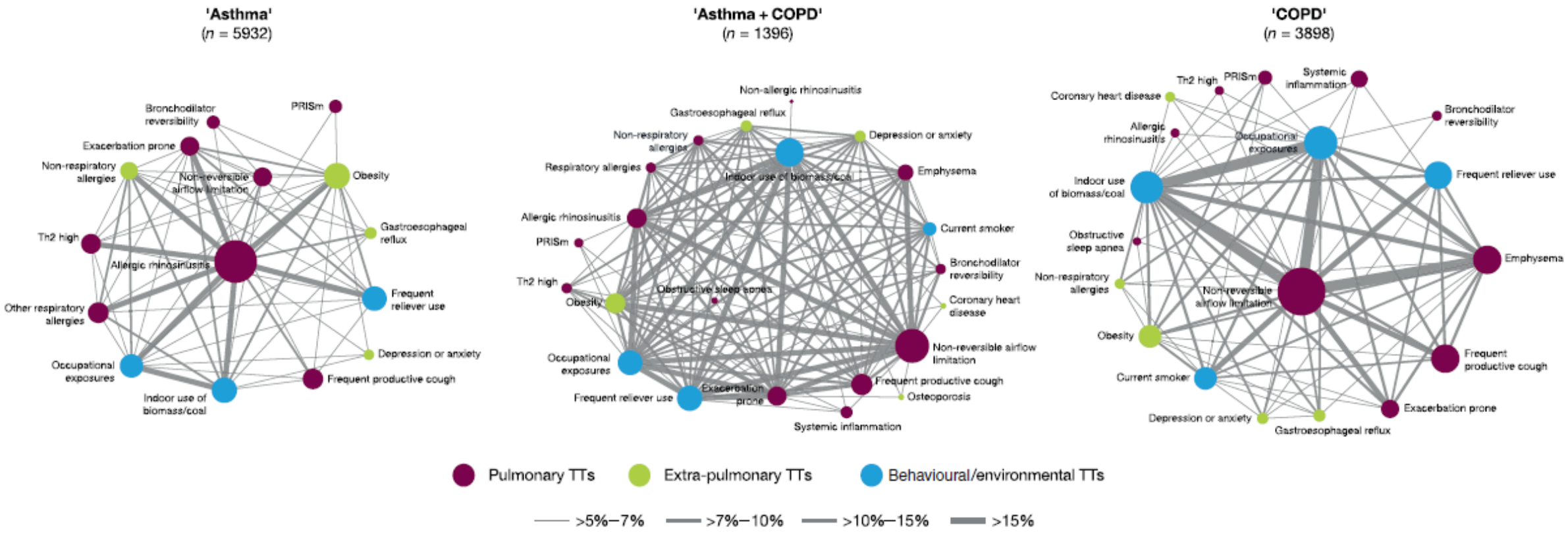
*Adapted from Celli et al. (2022) and Stolz et al. (2022)

Asthma vs. COPD: Primary care implications

Relationship	Pharmacotherapy implications
Asthma OR COPD	Asthma needs ICS. COPD may not need ICS
COPD with asthma features	**Treat as asthma** and include ICS
Co-existing asthma AND COPD	**Treat as asthma** and include ICS

GINA, 2024

Treatable traits: NOVELTY study



Agusti, Respirology 2022

Treatable traits for chronic lung diseases

Treatable Traits

Specific traits with specific trait markers

Targeted by specific therapies

Methods and Findings

58 studies from PubMed and Embase selected

Promising model in improving care in chronic respiratory diseases

Further trials should be conducted to evaluate clinical utility

5 Main Themes

Physiological Traits

Biochemical Traits

Microbiological Traits

Psychosocial Traits

Comorbidity Traits

Lee, Cells 2021

Allergic Rhinitis and Its Impact on Asthma

TABLE I. Classification of treatments used in patients with allergic rhinitis[6]

T1	Nonsedating H_1-antihistamine (oral, intranasal, and ocular), leukotriene receptor antagonists, or cromones (intranasal and ocular)
T2	INCSs
T3	INCSs + intranasal azelastine
~~T4~~	~~Oral corticosteroid as a short course and an add-on treatment~~
T5	Consider referral to a specialist and allergen immunotherapy

ARIA, JACI 2020

AR: Effect of INCS on FEV1

INCS spray vs Placebo

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Agondi 2008	2.41	0.56	16	2.41	0.54	14	11.4%	0.00 [-0.72, 0.72]
Corren 1992	3.17	0.21	10	2.88	0.16	8	5.7%	1.46 [0.38, 2.53]
Henriksen 1984	80	15	17	84	19	19	13.1%	-0.23 [-0.88, 0.43]
Kersten 2012	88.2	12.5	12	86.6	13.4	13	9.8%	0.12 [-0.67, 0.90]
Sandrini 2003	94	10.25	7	89.78	13.71	9	6.5%	0.32 [-0.67, 1.32]
Stelmach 2005	2.78	0.52	19	2.69	0.67	19	13.7%	0.15 [-0.49, 0.78]
* Thio 2000	114	10	11	102	16	10	7.7%	0.87 [-0.03, 1.78]
Thio 2000a	102.8	8	25	100.4	5.3	24	16.3%	0.35 [-0.22, 0.91]
Thio 2000b	103.1	5.5	23	100.4	5.3	24	15.7%	0.49 [-0.09, 1.07]
Total (95% CI)			140			140	100.0%	0.31 [0.04, 0.58]

Heterogeneity: $\tau^2 = 0.03$; $\chi^2 = 10.01$, df = 8 ($P = 0.26$); $I^2 = 20\%$

Test for overall effect: $Z = 2.23$ ($P = 0.03$)

Lohia, Allergy 2013

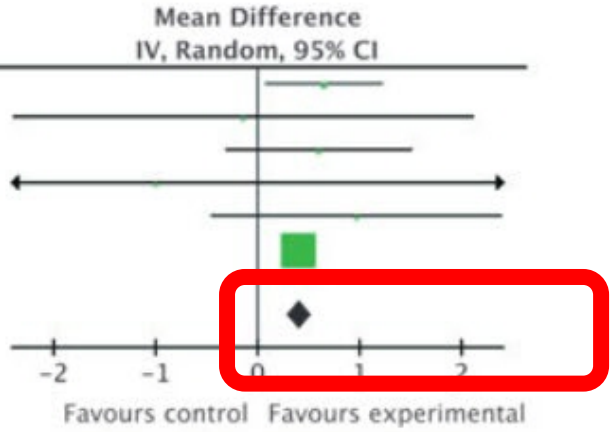
*Data from two separate studies reported as one publication. Data extracted from three parallel experimental arms: Thio 2000 (200 μ g FP aqueous nasal spray vs placebo); Thio 2000a (200 μ g FP aqueous nasal spray vs placebo); Thio 2000b (400 μ g BDP aqueous nasal spray vs placebo).

AR: Effect of INCS on asthma symptoms and rescue medication use

INCS spray vs Placebo

Study or Subgroup	Favours experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Agondi 2008	3.77	0.56	16	3.12	0.97	14	4.1%	0.65 [0.07, 1.23]
Corren 1992	3.22	2.6879	10	3.36	2.2062	8	0.3%	-0.14 [-2.40, 2.12]
Henriksen 1984	8.5	0.798	17	7.9	1.7555	17	1.6%	0.60 [-0.32, 1.52]
Sandrini 2003	18	10.4293	7	19	5.9905	9	0.0%	-1.00 [-9.66, 7.66]
Stelmach 2005	2.2	1.89	19	1.23	2.55	19	0.7%	0.97 [-0.46, 2.40]
Watson 1993	2.4	0.2	21	2	0.2	21	93.3%	0.40 [0.28, 0.52]
Total (95% CI)			90			88	100.0%	0.42 [0.30, 0.53]

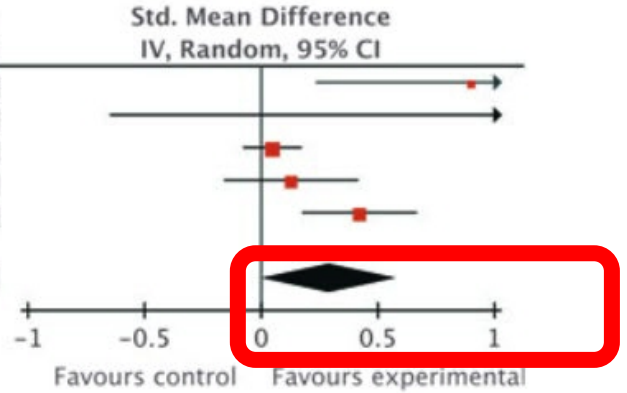
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 1.77$, df = 5 ($P = 0.88$); $I^2 = 0\%$
Test for overall effect: Z = 6.97 ($P < 0.00001$)



INCS spray vs Placebo

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI
Agondi 2008	0.9	0.34	12.1%	0.90 [0.23, 1.57]
Baiardini 2011	4.4	2.576	0.3%	4.40 [-0.65, 9.45]
Pedroletti 2008	0.0476	0.0641	33.3%	0.05 [-0.08, 0.17]
Reed 1988	0.1278	0.1469	26.1%	0.13 [-0.16, 0.42]
* Stelmach 2005	0.4211	0.1255	28.1%	0.42 [0.18, 0.67]
Total (95% CI)			100.0%	0.29 [0.01, 0.58]

Heterogeneity: $\tau^2 = 0.06$; $\chi^2 = 14.82$, df = 4 ($P = 0.005$); $I^2 = 73\%$
Test for overall effect: Z = 1.99 ($P = 0.05$)



*Data extracted from two parallel experimental arms: Stelmach 2005 (400 µ g BDP aqueous nasal spray with placebo MDI vs placebo nasal spray with placebo MDI); Stelmach 2005a (400 µ g BDP aqueous nasal spray with 1000 µ g BDP MDI vs placebo nasal spray with 1000 µ g BDP MDI).

Lohia, Allergy 2013

AR vs. CRS: Treatment

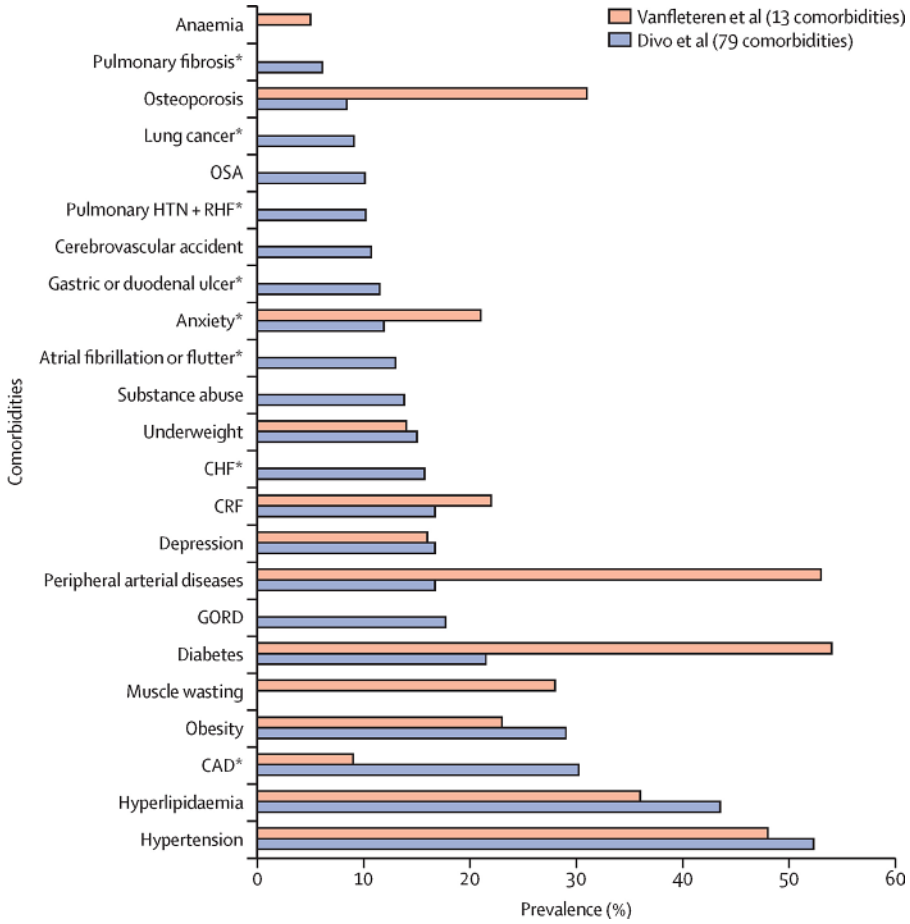
TREATMENT	Allergic rhinitis (hay fever)	Chronic rhinosinusitis (CRS)
Reduce exposure to triggers, such as grass or dust	Yes	Yes
Steroid nasal spray	Yes	Yes
Saline (salt) nasal sprays or rinses	Yes	Yes
Antihistamines	Yes Nasal sprays work better than tablets	May not work
Combined steroid and antihistamine nasal sprays	Yes	Yes
Oral steroids	No	Sometimes (short course only)
Allergen immunotherapy (Desensitisation)	Often works	May not work
Monoclonal Antibodies	No	May work if there are nasal polyps
Antibiotics	No	Sometimes
Surgery	No	May be needed

allergyfacts.org.au

COPD and CV disease

GOLD 2025

COPD and multimorbidity = “Syndemic”



Fabbri, Lancet RM 2023

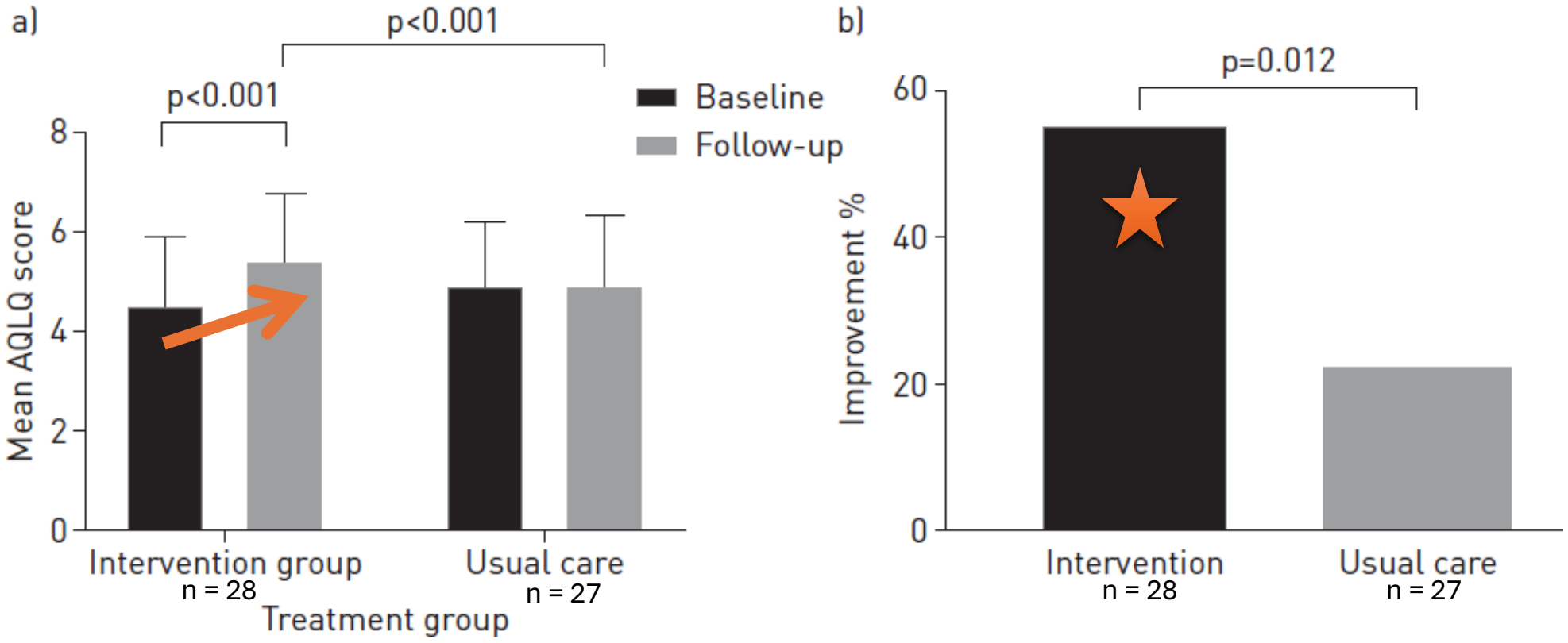
Triggers for asthma and COPD

Variable	%		p-value
	Asthma (n = 779)	COPD (n = 129)	
No. of trigger factors*	3 (2–4)	0 (0–1)	< 0.001
≥ 1	93.8	42.6	< 0.001
≥ 2	81.4	17.8	< 0.001
≥ 3	60.9	11.6	< 0.001
Trigger factor			
Dust	63.2	16.3	< 0.001
Heavy rain (cold and wet weather)	32.5	17.1	< 0.001
Upper respiratory tract infection	29.5	9.3	< 0.001
Anxiety/anger/depression	23.1	7.0	< 0.001
Heavy traffic fumes	20.2	0.8	< 0.001
Citrus fruits	19.9	1.6	< 0.001
Air-conditioning	19.1	3.1	< 0.001
Tobacco smoke	15.7	2.3	< 0.001
Hot weather	14.9	12.4	0.503
Incense smoke	14.8	1.6	< 0.001
Laughter	11.2	1.6	< 0.001
Household pets	10.0	0	< 0.001
Perfume	9.5	0.8	< 0.001
Flowers/pollen	6.3	0	0.001
Alcohol	5.1	0.8	0.021
Gastro-oesophageal reflux (i.e. heartburn)	5.1	0.8	0.021
Medication	3.3	0	0.04
Chemical exposure at work	3.2	2.3	0.786
Household pests†	2.1	0	0.148
Others‡	14.4	2.3	< 0.001

*Data presented as median (interquartile range). †Includes cockroaches, flies and moth[illegible]. ‡Includes bathing, fatigue, insufficient sleep, crowded places and overeating.

See, SMJ 2016

Treatable traits for asthma management



McDonald, Eur Respir J 2020

Treatable traits for COPD management

Courtesy of speaker

Smoking cessation: ACE Clinical Guidance

ACE Clinical Guidance 2025

Smoking cessation: HPB's "I Quit Programme"

Courtesy of speaker

Vaccinations

Asthma (GINA 2024)

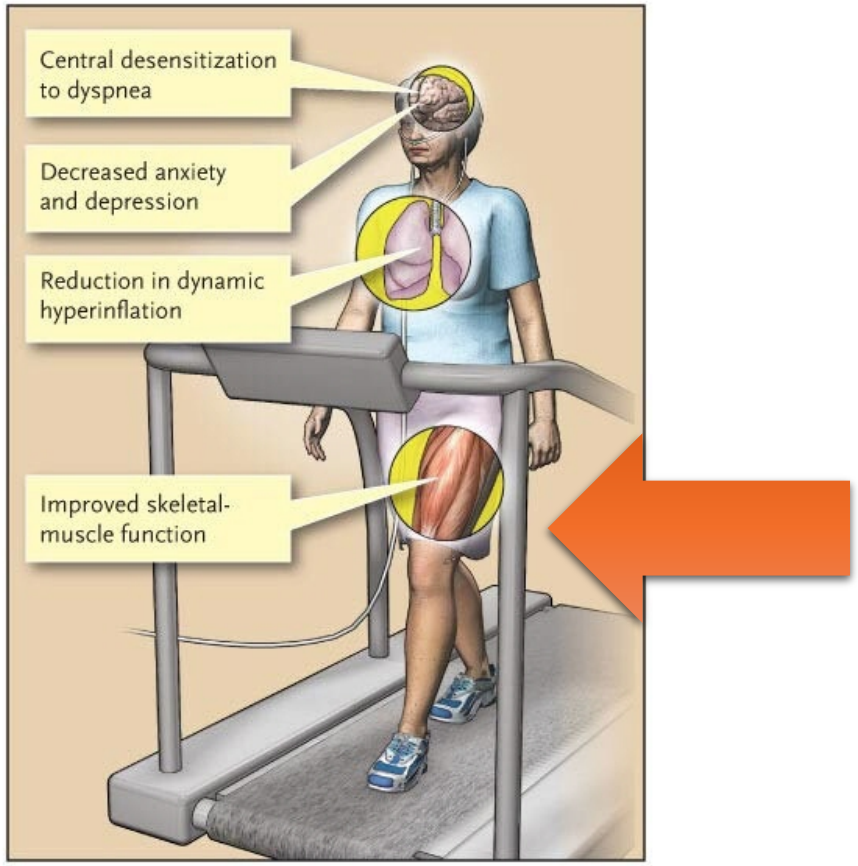
- Influenza
- COVID-19
- RSV (≥ 60 years old)
- KIV Pneumococcal
- KIV Pertussis (Tdap)

COPD (GOLD 2025)

- Influenza
- COVID-19
- RSV (≥ 60 years old)
- Pneumococcal
- Pertussis (Tdap) (if not done in adolescence)
- Zoster (>50 years old)

KIV, Keep in view.

Walking in pulmonary rehabilitation



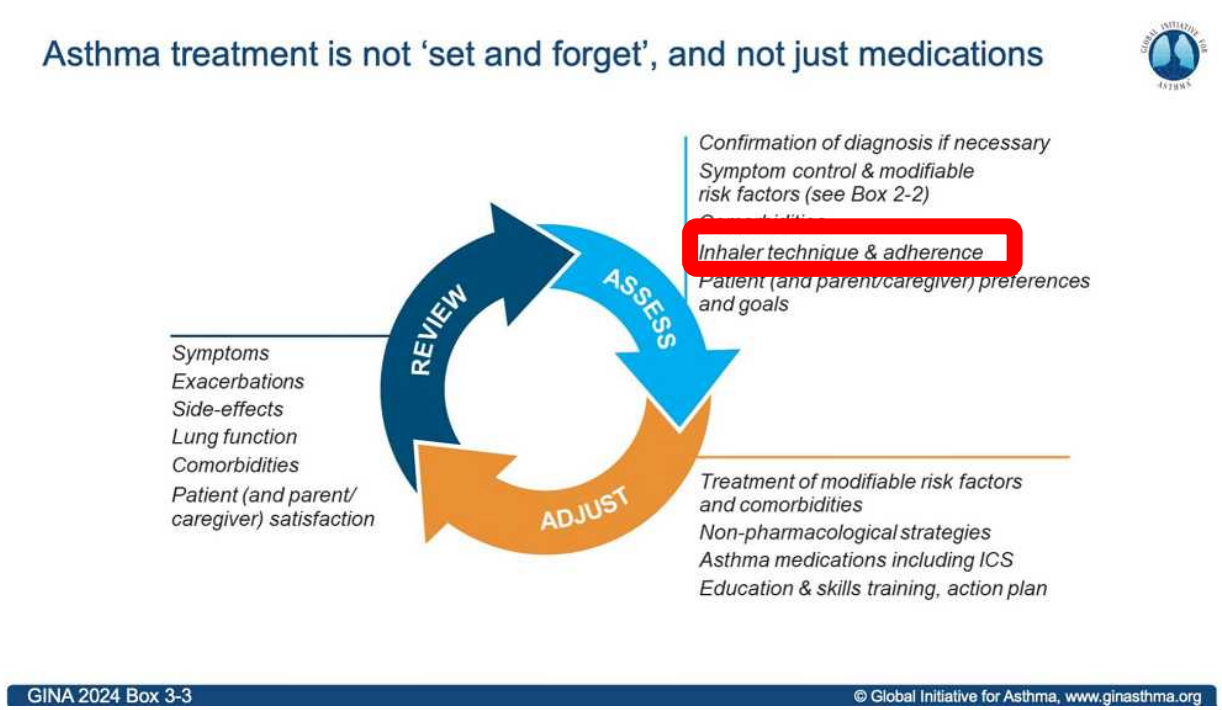
Casaburi, NEJM 2009

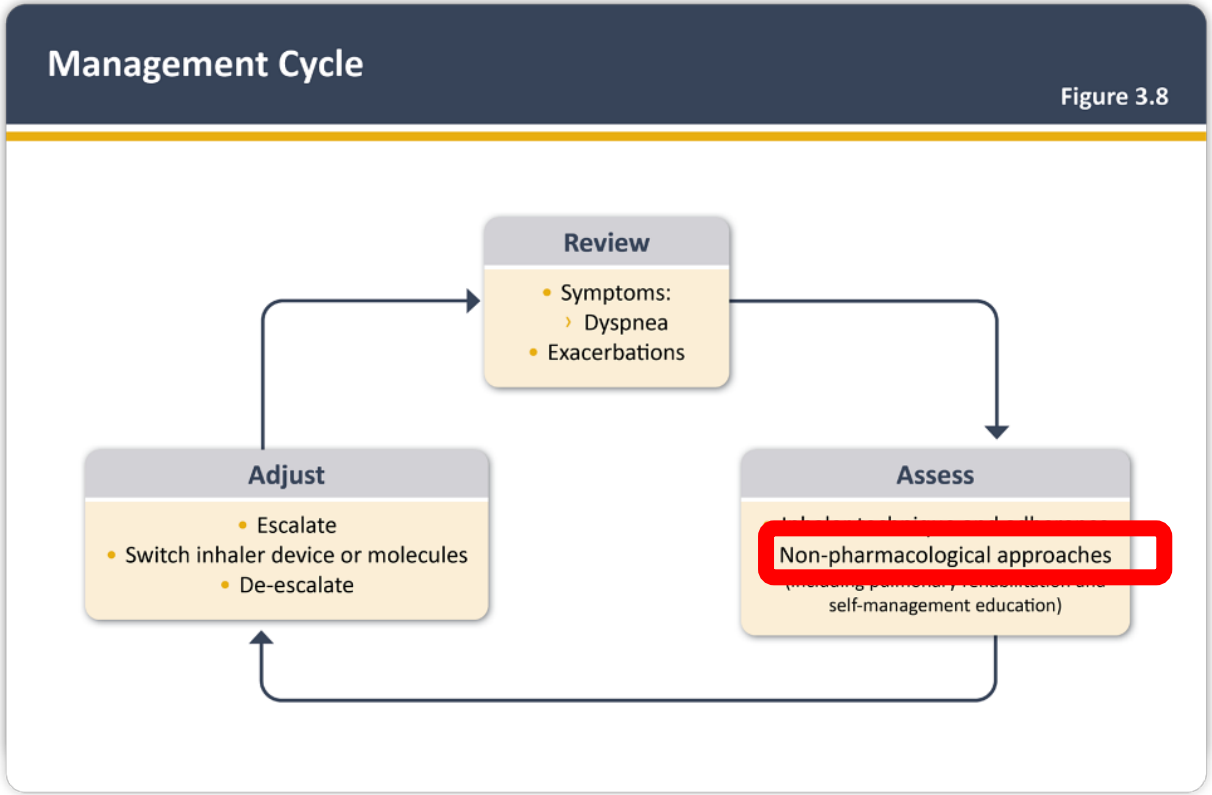
- Exercise training does not enhance lung function in COPD but significantly increases exercise tolerance, reduces dyspnea, and improves quality of life by reversing muscle deconditioning and boosting aerobic function in **walking muscles**.
- Training **lowers ventilatory demand and respiratory rate** during heavy exertion, reducing dynamic hyperinflation, easing breathing, and allowing more time for expiration. It also appears to centrally desensitize patients to dyspnea, though the mechanism is unclear.
- Greater exercise capacity leads to increased daily activity and a **sense of mastery, contributing to reduced anxiety and depression**.

Walking goals & self-management

Courtesy of speaker

Asthma and COPD management cycles





GINA 2024; GOLD 2025

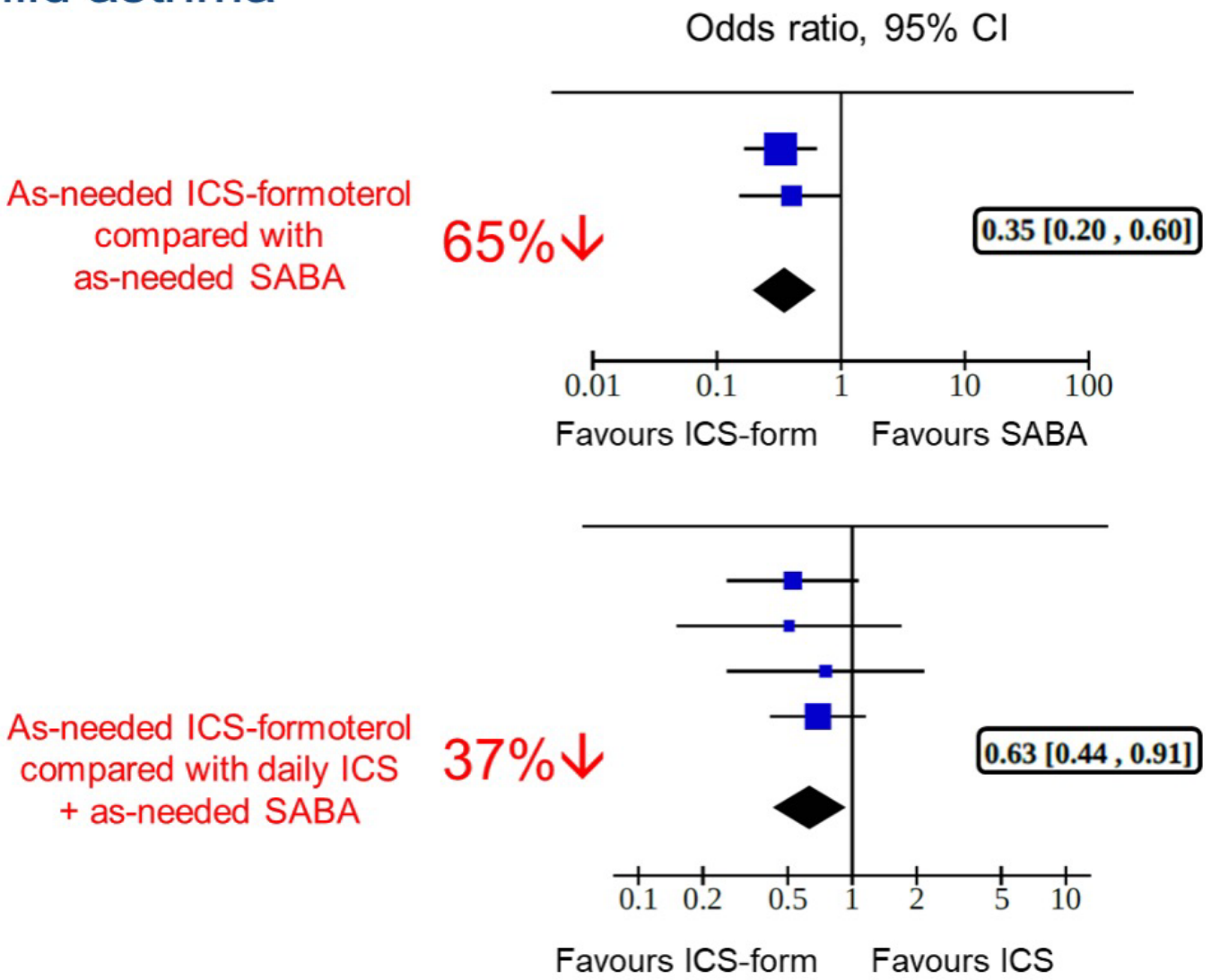
Types of nonadherence

Table 3 Matching adherence interventions to the type of nonadherence

Type of nonadherence	Adherence interventions
Erratic	Simplify and tailor regimen Implement behavioral strategies such as cueing (eg, storing medication next to toothbrush), reminders and reinforcement Self-monitoring and support, with monitoring from others
Unwitting	Review of adherence behavior Written or visual medication plans Patient education in disease management
Intelligent	Patient education and counseling Negotiate therapy Link therapy with personal goals

Lareau, Int J COPD 2010

As-needed-only ICS-formoterol reduces emergency visits and hospitalisations in patients with mild asthma



From Crossingham et al, Cochrane Database Syst Rev 2021 (n=9565)

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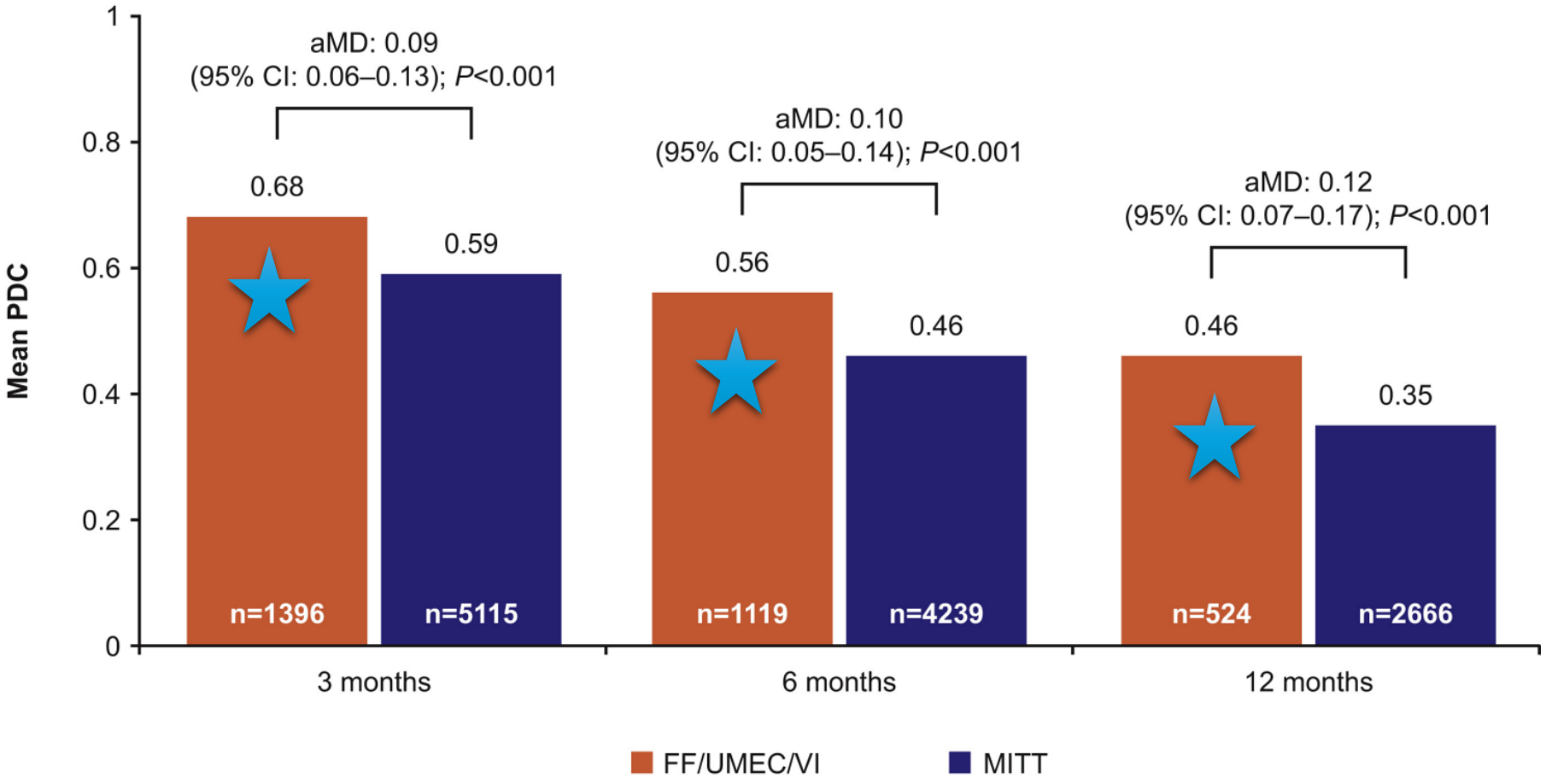
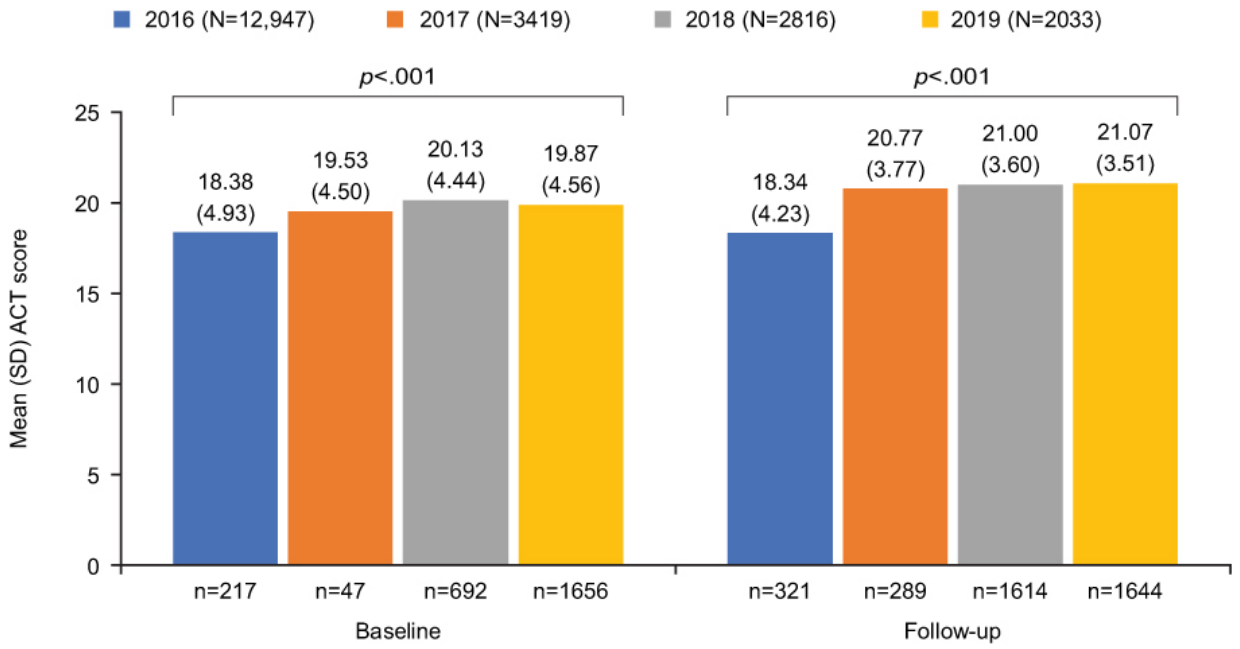
Inhaler adherence: SITT vs. MITT



Busse, J Allergy Clin Immunol Pract 2022

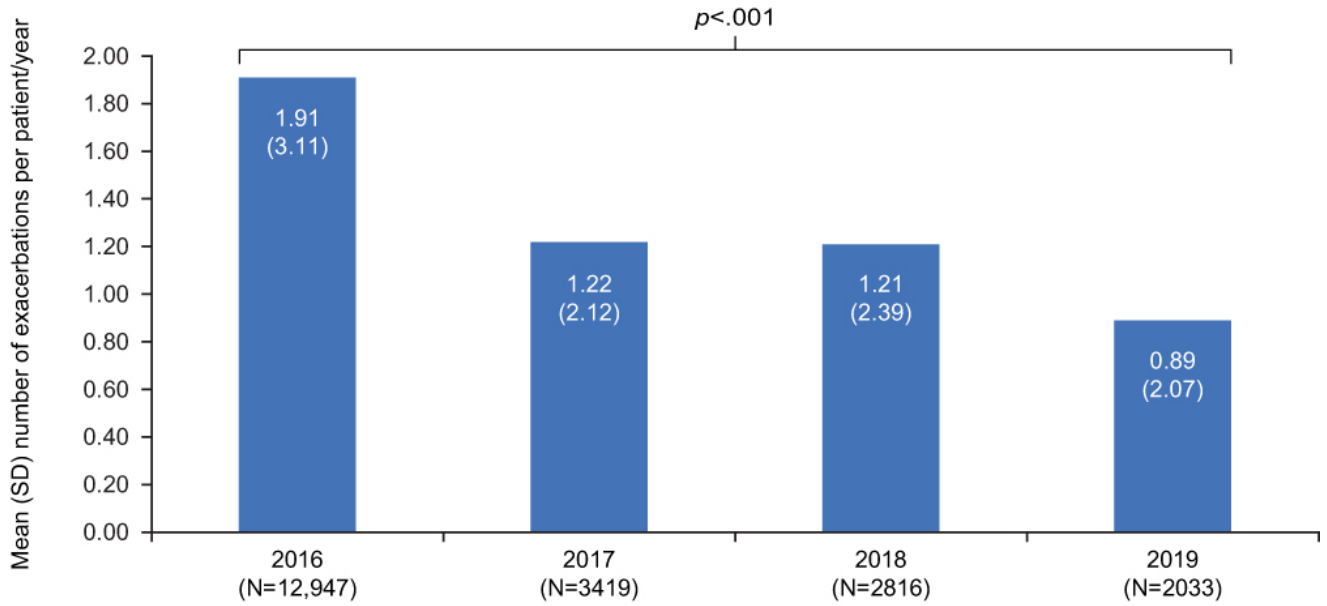
Outcomes for Singapore adults ≥18y



ACT score <20, n (%)	2016 (N=12,947)	2017 (N=3419)	2018 (N=2816)	2019 (N=2033)	*p* value
Baseline	n=217 112 (51.6)	n=47 16 (34.0)	n=692 233 (33.8)	n=1656 596 (36.2)	<.001
Follow-up	n=321 171 (53.3)	n=289 85 (29.4)	n=1614 430 (26.6)	n=1644 433 (26.3)	<.001

Koh, Pragmat Obs Res 2024

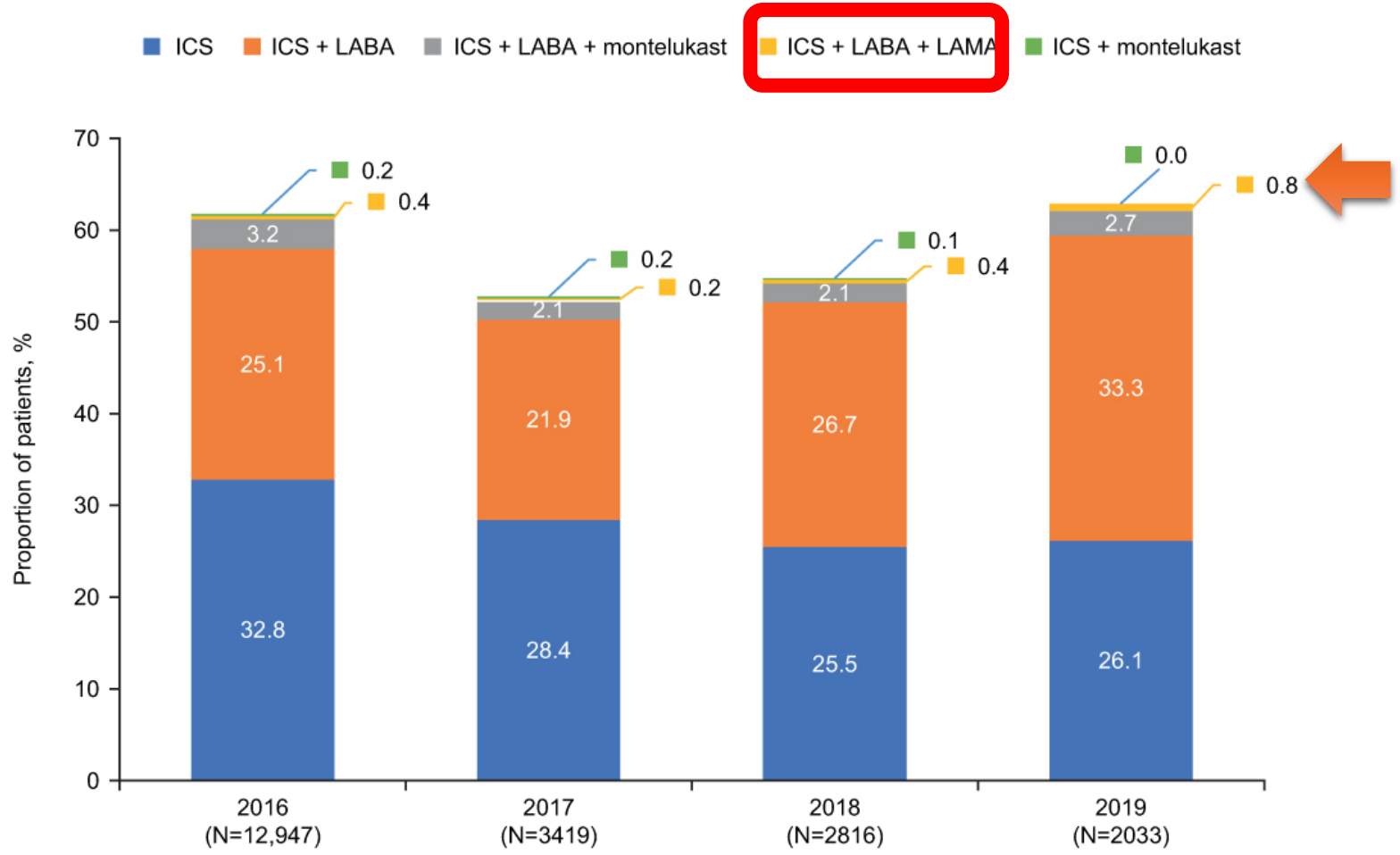
Outcomes for Singapore adults ≥18y



Exacerbations per year, n (%)	2016 (N=12,947)	2017 (N=3419)	2018 (N=2816)	2019 (N=2033)
0	5994 (46.3)	1883 (55.1)	1724 (61.2)	1490 (73.3)
1	403 (3.1)	122 (3.6)	100 (3.6)	86 (4.3)
2	255 (2.0)	99 (2.9)	93 (3.3)	61 (3.0)
>2	6295 (48.6)	1315 (38.5)	899 (31.9)	396 (19.5)

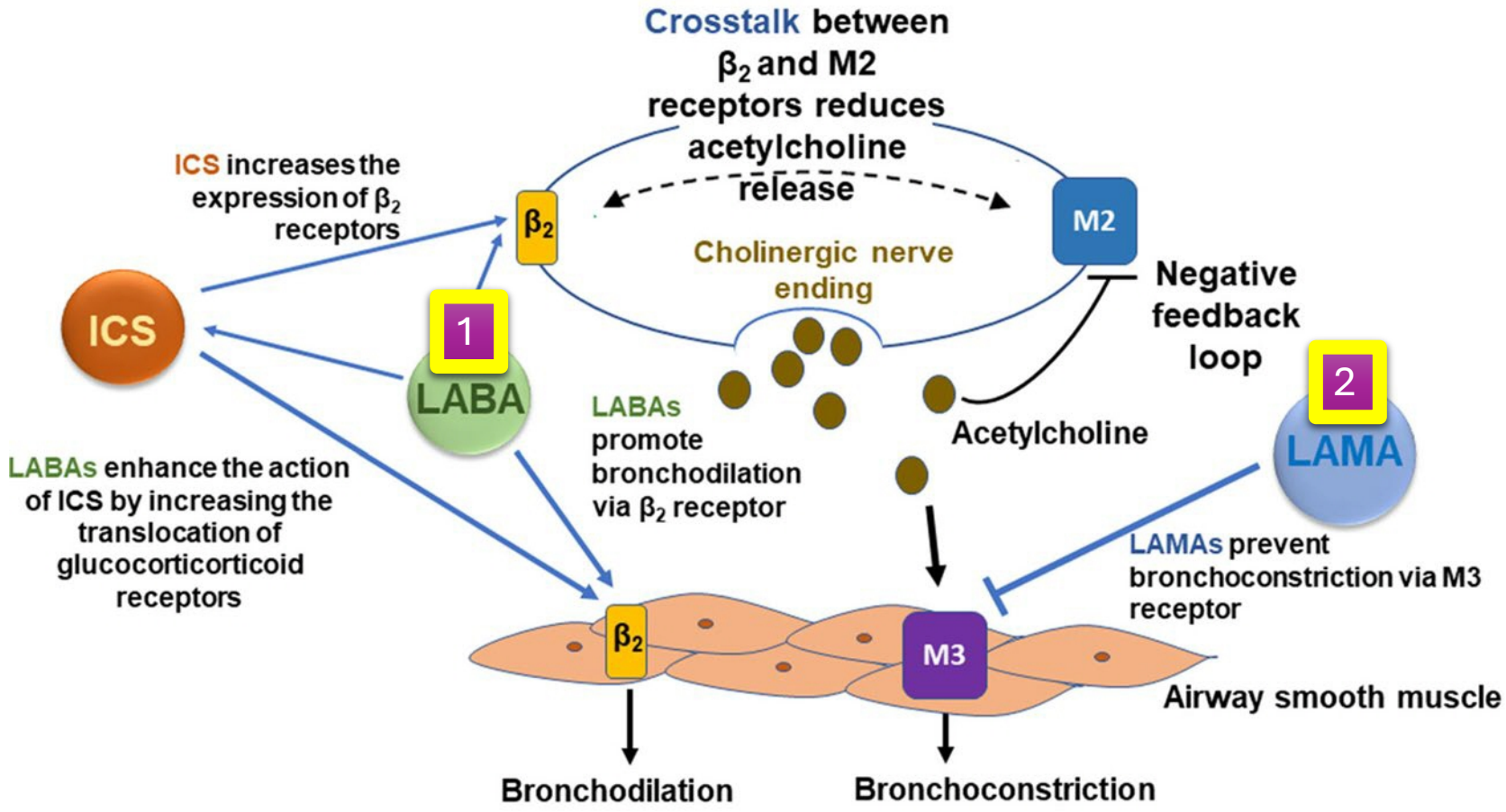
Koh, Pragmat Obs Res 2024

Inhaler prescription for Singapore adults ≥18y



Koh, Pragmat Obs Res 2024

LABA and LAMA for treating asthma

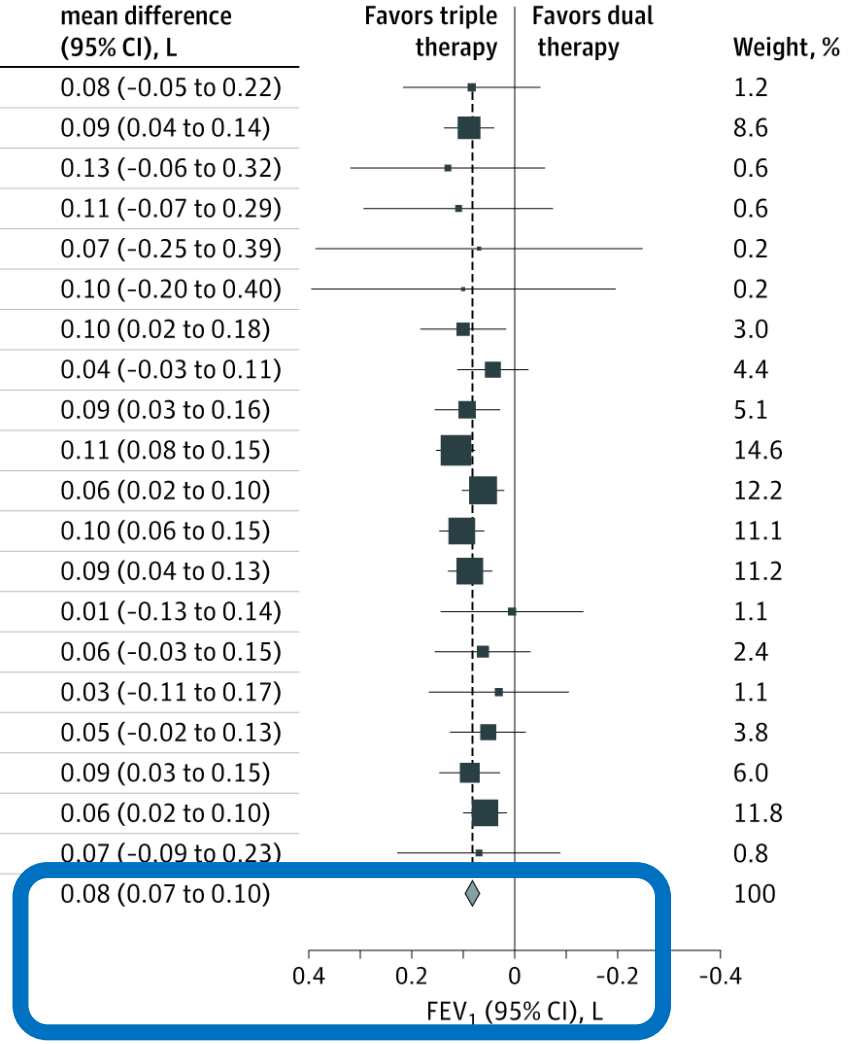


Mechanistic Action of ICS, LABA and LAMA

Wadhawan, Public Health Chall 2022

LAMA **added to LABA-ICS** ↑lung function

Source	Triple therapy No.	Triple therapy FEV_1, mean (SD), L	Dual therapy No.	Dual therapy FEV_1, mean (SD), L	FEV_1, mean difference (95% CI), L	Weight, %
Hamelmann et al,[50] 2017	256	0.31 (0.78)	132	0.23 (0.55)	0.08 (-0.05 to 0.22)	1.2
Hoshino et al,[51] 2018	29	0.11 (0.08)	30	0.02 (0.11)	0.09 (0.04 to 0.14)	8.6
Ishiura et al,[52] 2019	17	0.20 (0.28)	17	0.07 (0.29)	0.13 (-0.06 to 0.32)	0.6
Ishiura et al,[53] 2020	19	0.10 (0.29)	19	-0.01 (0.29)	0.11 (-0.07 to 0.29)	0.6
Jabbal et al,[47] 2017	14	0.15 (0.43)	14	0.08 (0.43)	0.07 (-0.25 to 0.39)	0.2
Jabbal et al,[54] 2020	16	0.21 (0.43)	16	0.11 (0.42)	0.10 (-0.20 to 0.40)	0.2
Kerstjens et al,[48] 2011	67	0.15 (0.25)	33	0.05 (0.17)	0.10 (0.02 to 0.18)	3.0
Kerstjens et al,[46] 2012[a]	237	0.13 (0.39)	222	0.09 (0.37)	0.04 (-0.03 to 0.11)	4.4
Kerstjens et al,[46] 2012[a]	216	0.16 (0.34)	232	0.06 (0.35)	0.09 (0.03 to 0.16)	5.1
Kerstjens et al,[55] 2020[a]	614	0.45 (0.37)	1213	0.34 (0.42)	0.11 (0.08 to 0.15)	14.6
Kerstjens et al,[55] 2020[a]	614	0.39 (0.35)	602	0.33 (0.38)	0.06 (0.02 to 0.10)	12.2
Lee et al,[56] 2020[a]	803	0.13 (0.44)	400	0.02 (0.31)	0.10 (0.06 to 0.15)	11.1
Lee et al,[56] 2020[a]	804	0.16 (0.44)	403	0.08 (0.31)	0.09 (0.04 to 0.13)	11.2
Pearl Therapeutics,[57] 2017	702	0.13 (1.77)	193	0.13 (0.32)	0.01 (-0.13 to 0.14)	1.1
Ohta et al,[58] 2015	228	0.14 (0.41)	57	0.08 (0.29)	0.06 (-0.03 to 0.15)	2.4
Singh et al,[59] 2014	152	0.14 (0.70)	49	0.11 (0.28)	0.03 (-0.11 to 0.17)	1.1
Szefler et al,[49] 2017	263	0.19 (0.43)	130	0.14 (0.31)	0.05 (-0.02 to 0.13)	3.8
Virchow et al,[45] 2019[a]	826	0.24 (0.71)	547	0.16 (0.41)	0.09 (0.03 to 0.15)	6.0
Virchow et al,[45] 2019[a]	557	0.18 (0.36)	553	0.13 (0.36)	0.06 (0.02 to 0.10)	11.8
Zhang et al,[62] 2018	40	0.75 (0.44)	40	0.68 (0.26)	0.07 (-0.09 to 0.23)	0.8
Overall: $I^2 = 0\%$	6474		4902		0.08 (0.07 to 0.10)	100

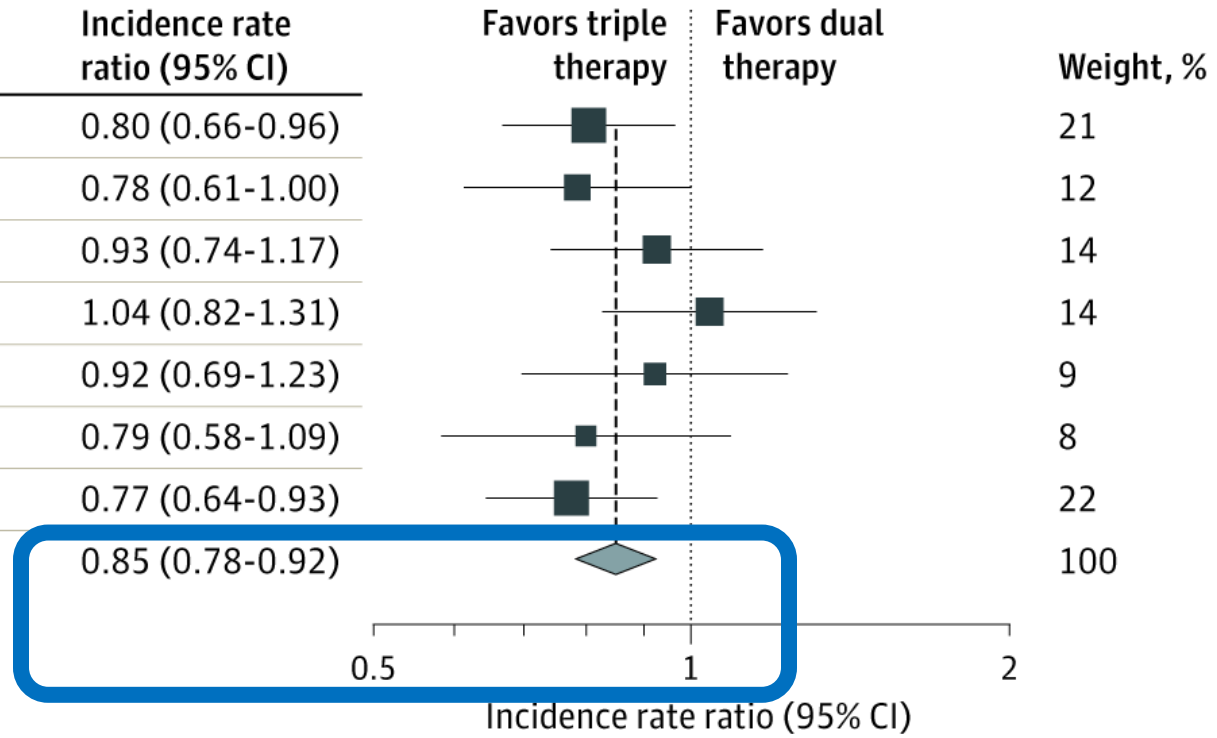


Kim, JAMA 2021

LAMA **added to LABA-ICS** ↓exacerbations

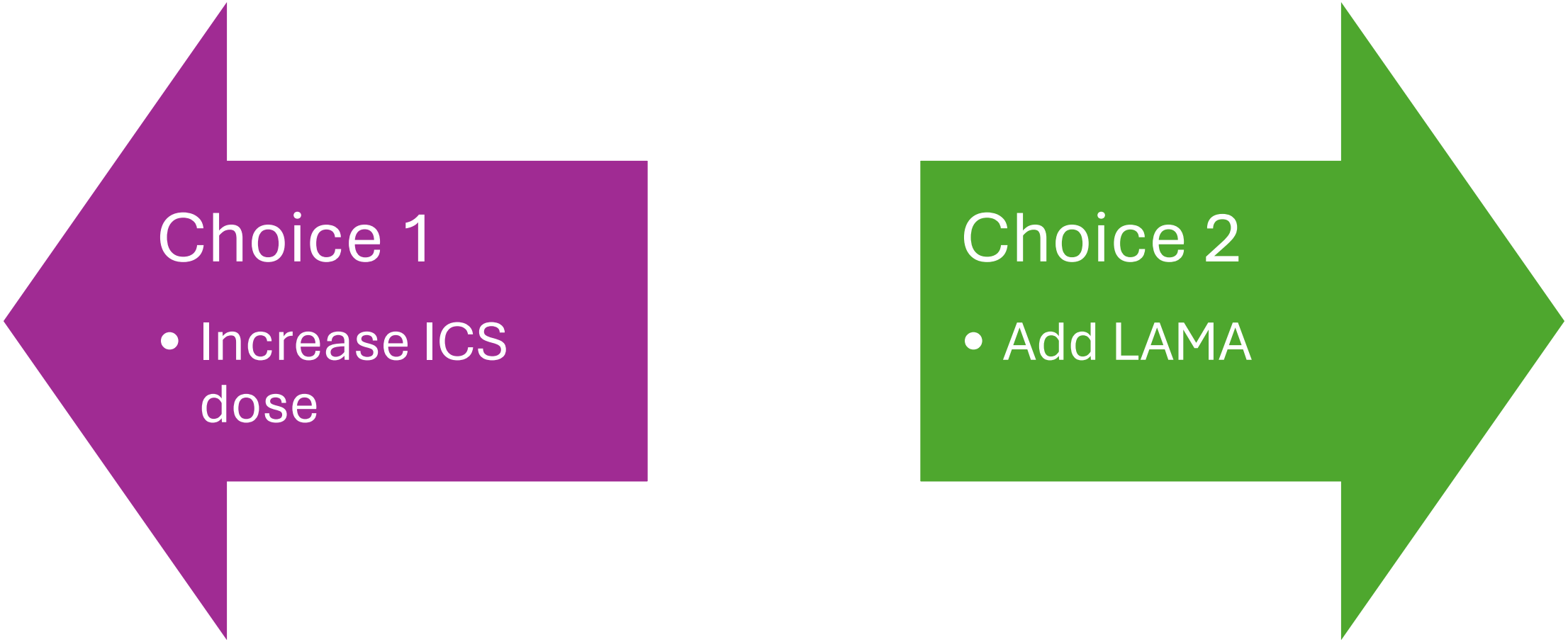
A Incidence rate ratio of exacerbations

Source	Mean annualized exacerbation rate[a] Triple	Dual	Incidence rate ratio (95% CI)	Weight, %
Kerstjens et al,[46] 2012	0.53	0.66	0.80 (0.66-0.96)	21
Kerstjens et al,[55] 2020[b]	0.26	0.33	0.78 (0.61-1.00)	12
Kerstjens et al,[55] 2020[b]	0.38	0.41	0.93 (0.74-1.17)	14
Lee et al,[56] 2020[b]	0.38	0.41	1.04 (0.82-1.31)	14
Lee et al,[56] 2020[b]	0.39	0.38	0.92 (0.69-1.23)	9
Pearl Therapeutics,[57] 2017	0.44	0.55	0.79 (0.58-1.09)	8
Virchow et al,[45] 2019	0.27	0.35	0.77 (0.64-0.93)	22
Overall: $I^2 = 0\%$			0.85 (0.78-0.92)	100



Kim, JAMA 2021

What can help guide clinicians in managing asthmatics who are uncontrolled on ICS-LABA?



Courtesy of speaker

Dose-response curve for ICS (FTC) in asthma

Table 2 Doses of fluticasone (μg/day) at which 80% and 90% of the maximum effect is achieved, as derived from a negative exponential model*

Outcome measure	80% of maximum effect achieved	90% of maximum effect achieved
FEV_1	146	209
Morning PEF	172	247
Evening PEF	175	251
Use of rescue medication	71	102
Major exacerbations	108	155
Night awakenings	135	193

*The effect obtained with 1000 μg/day of fluticasone was considered to be the "maximum effect" for the purposes of this analysis.
FEV_1=forced expiratory volume in one second; PEF=peak expiratory flow.

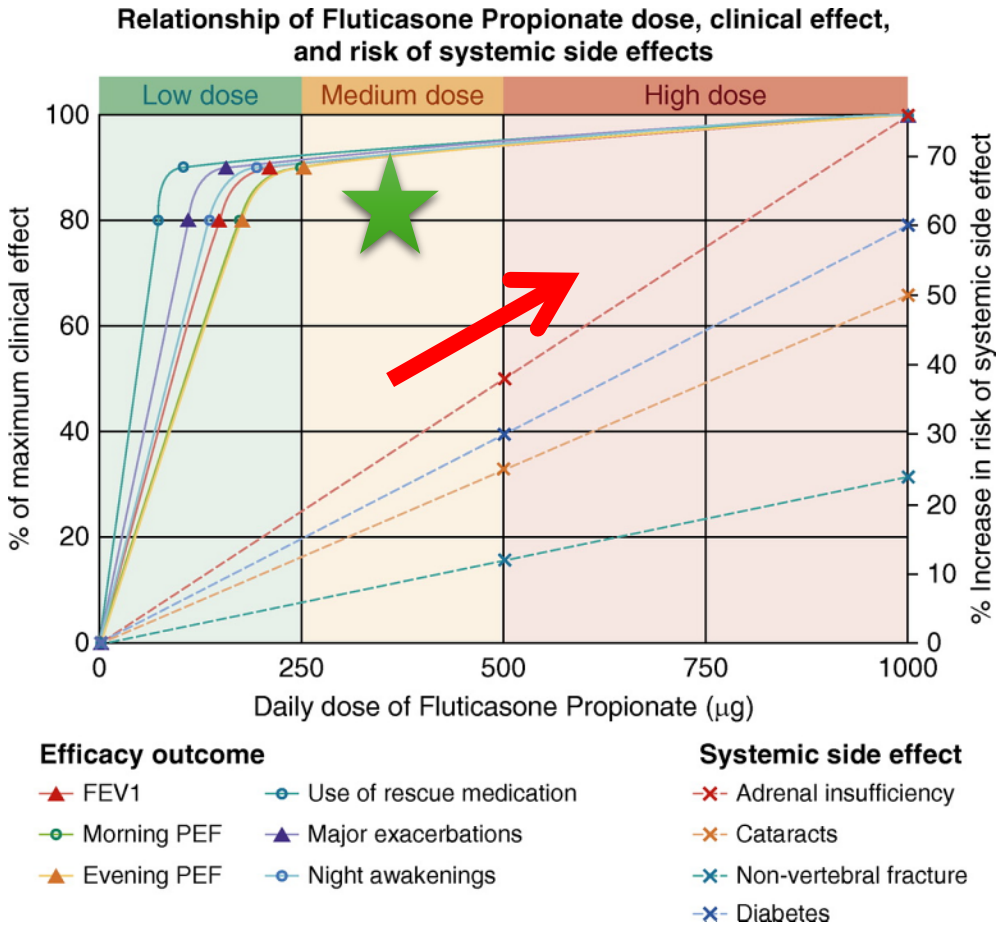
Table 3 Estimates of dose of fluticasone (μg/day) giving peak effect and effect on mean change in outcome measure

		Fixed effects model		Random effects model	
Outcome measure	R^2	Dose of peak effect	Mean change (95% CI)	Dose of peak effect	Mean change (95% CI)
FEV_1 (l)	35%	568	0.62 (0.24 to 1.00)	628	0.70 (0.24 to 1.17)
Morning PEF (l/min)	48%	600	44 (19.5 to 68.5)	633	50 (14.5 to 86.1)
Evening PEF (l/min)	49%	590	52 (8.6 to 95.0)	657	51 (12.6 to 89.7)
β agonist use (puffs/day)	35%	560	–1.98 (–3.00 to –0.93)	574	–2.36 (–4.05 to –0.66)

FEV_1=forced expiratory volume in one second; PEF=peak expiratory flow.

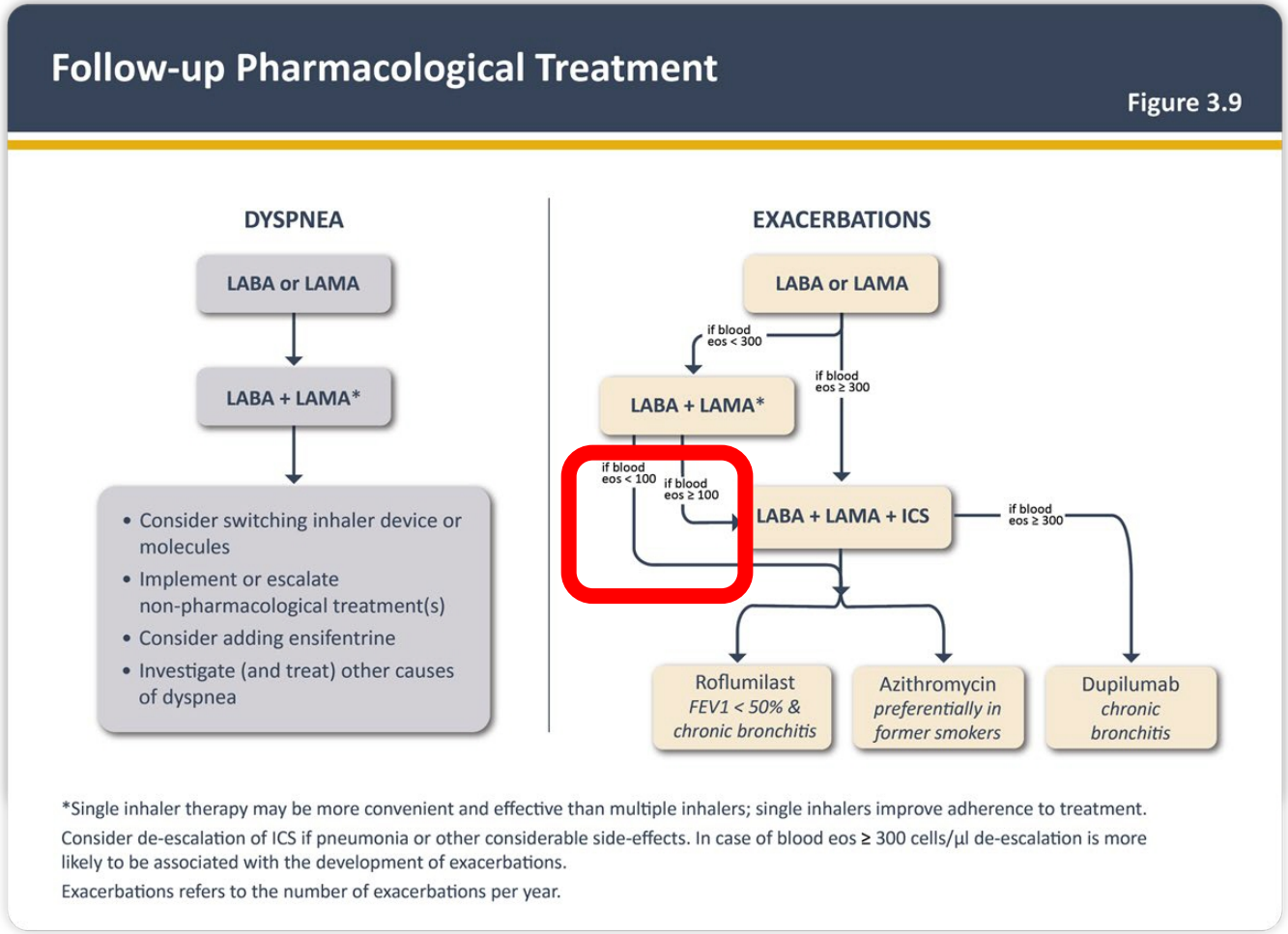
Holt, BMJ 2001

Dose-related benefits/risks for ICS in asthma



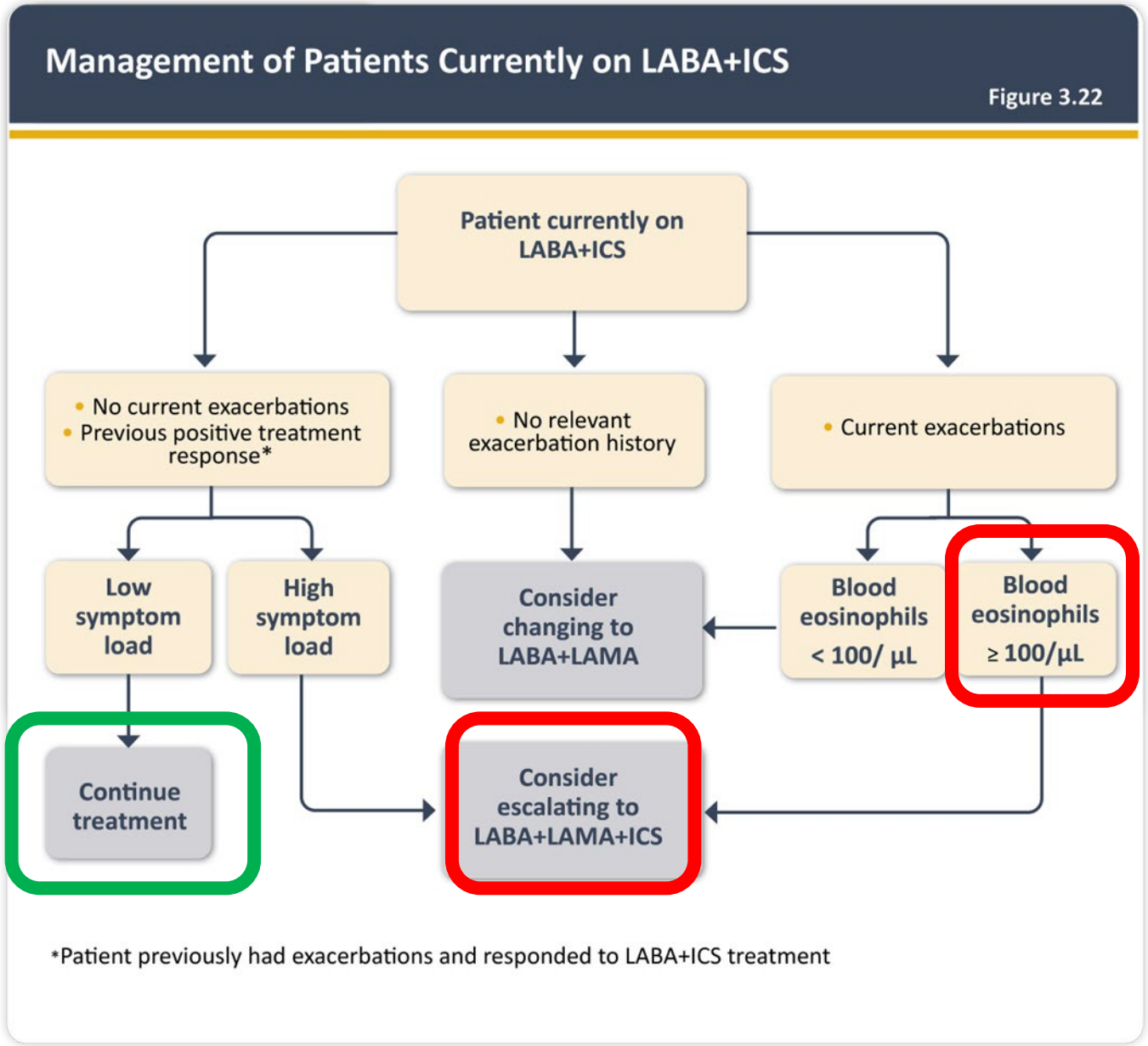
Beasley, AJRCCM 2019

COPD: Add ICS to LAMA-LABA if exacerbation+ & eos ≥100/µL



GOLD 2025

COPD: Add LAMA to LABA-ICS if exacerbation+ & eos ≥100/µL



GOLD 2025

Triple therapy reduces COPD mortality

Evidence Supporting a Reduction in Mortality with Pharmacotherapy and Non-pharmacotherapy in COPD Patients Figure 3.17

Therapy	RCT*	Treatment effect on mortality	Patient characteristics
Pharmacotherapy			
LABA+LAMA+ICS[1]	Yes	Single inhaler triple therapy compared to dual LABD therapy relative risk reduction: IMPACT: HR 0.72 (95% CI: 0.53, 0.99)[1a] ETHOS: HR 0.51 (95% CI: 0.33, 0.80)[1b]	Symptomatic people with a history of frequent and/or severe exacerbations
Non-pharmacological Therapy			
Smoking cessation[2]	Yes	HR for usual care group compared to intervention group (smoking cessation) HR 1.18 (95% CI: 1.02, 1.37)[2]	Asymptomatic or mildly symptomatic
Pulmonary rehabilitation[3#]	Yes	Old trials: RR 0.28 (95% CI 0.10, 0.84)[3a] New trials: RR 0.68 (95% CI 0.28, 1.67)[3b]	Hospitalized for exacerbations of COPD (during or ≤ 4 weeks after discharge)
Long-term oxygen therapy[4]	Yes	NOTT: ≥ 19 hours of continuous oxygen vs ≤ 13 hours: 50% reduction[4a] MRC: ≥ 15 hours vs no oxygen: 50% reduction[4b]	PaO_2 ≤ 55 mmHg or < 60 mmHg with *cor pulmonale* or secondary polycythemia
Noninvasive positive pressure ventilation[5]	Yes	12% in NPPV (high IPAP level) and 33% in control HR 0.24 (95% CI 0.11, 0.49)[5]	Stable COPD with marked hypercapnia
Lung volume reduction surgery[6]	Yes	0.07 deaths/person-year (LVRS) vs 0.15 deaths/person-year (UC) RR for death 0.47 (p = 0.005)[6]	Upper lobe emphysema and low exercise capacity

*RCT with pre-specified analysis of the mortality outcome (primary or secondary outcome); #Inconclusive results likely due to differences in pulmonary rehabilitation across a wide range of participants and settings.

1. a) IMPACT trial (Lipson et al. 2020) and b) ETHOS trials (Martinez et al. 2021); 2.Lung Health Study (Anthonisen et al. 2005); 3. a) Puhan et al. (2011) and b) Puhan et al. 2016; 4. a) NOTT (NOTT, 1980) and b) MRC (MRC, 1981); 5. Kohlein trial (Kohlein et al. 2014); 6. NETT trial (Fishman et al. 2003)

ICS: inhaled corticosteroid; IPAP: inspiratory positive airway pressure; LABA: long-acting beta$_2$-agonist; LABD: long-acting bronchodilator; LAMA: long-acting anti-muscarinic; LTOT: long-term oxygen therapy; NPPV: noninvasive positive pressure ventilation; LVRS: lung volume reduction surgery; UC: usual treatment control group.

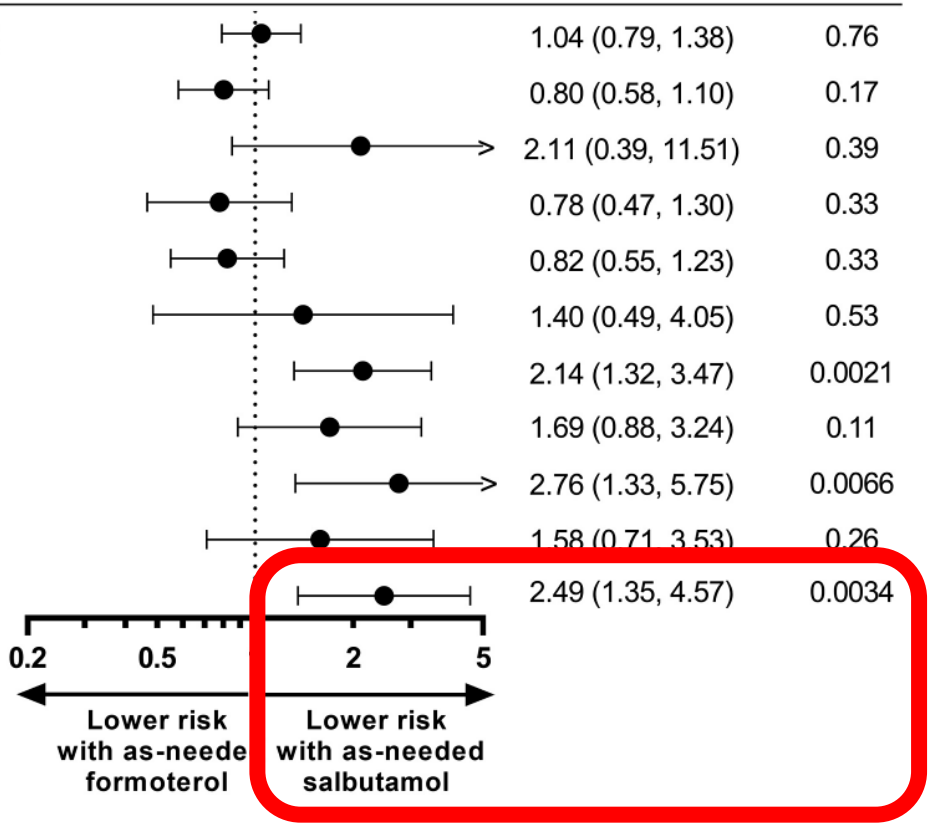
Evidence Supporting a Reduction in Mortality with Pharmacotherapy and Non-pharmacotherapy in COPD Patients Figure 3.17

Therapy	RCT*	Treatment effect on mortality	Patient characteristics
Pharmacotherapy			
LABA+LAMA+ICS[1]	Yes	Single inhaler triple therapy compared to dual LABD therapy relative risk reduction: IMPACT: HR 0.72 (95% CI: 0.53, 0.99)[1a] ETHOS: HR 0.51 (95% CI: 0.33, 0.80)[1b]	Symptomatic people with a history of frequent and/or severe exacerbations

Reliever for non-formoterol maintenance therapy

Patients receiving maintenance ICS-salmeterol at study entry

Variable	As-needed formoterol n (%)	As-needed salbutamol n (%)	OR (95% CI)	p-value
Total SAE and/or DAE	105 (6.6)	106 (6.3)	1.04 (0.79, 1.38)	0.76
Serious adverse events	70 (4.4)	91 (5.4)	0.80 (0.58, 1.10)	0.17
Deaths	4 (0.3)	2 (0.1)	2.11 (0.39, 11.51)	0.39
Asthma-related SAE	26 (1.6)	35 (2.1)	0.78 (0.47, 1.30)	0.33
Non asthma-related SAE	44 (2.8)	56 (3.4)	0.82 (0.55, 1.23)	0.33
Cardiovascular-related SAE	8 (0.5)	6 (0.4)	1.40 (0.49, 4.05)	0.53
Discontinuation due to AE	50 (3.1)	25 (1.5)	2.14 (1.32, 3.47)	0.0021
Asthma-related DAE	24 (1.5)	15 (0.9)	1.69 (0.88, 3.24)	0.11
Non asthma-related DAE	26 (1.6)	10 (0.6)	2.76 (1.33, 5.75)	0.0066
DAE due to SAE	15 (0.9)	10 (0.6)	1.58 (0.71, 3.53)	0.26
DAE due to non SAE	35 (2.2)	15 (0.9)	2.49 (1.35, 4.57)	0.0034



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RELIEF (post-hoc), JACI Pract 2023

Reliever for non-formoterol maintenance therapy

The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Albuterol–Budesonide Fixed-Dose Combination Rescue Inhaler for Asthma

Papi A et al. DOI: 10.1056/NEJMoa2203163

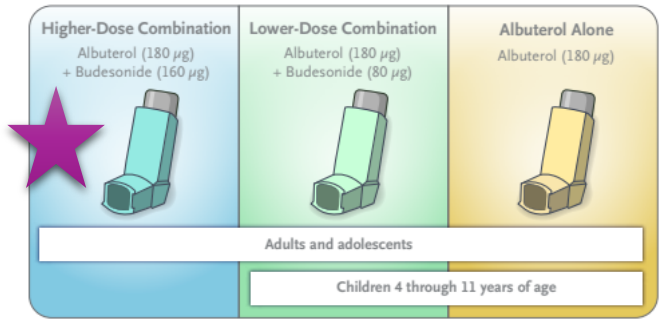
CLINICAL PROBLEM

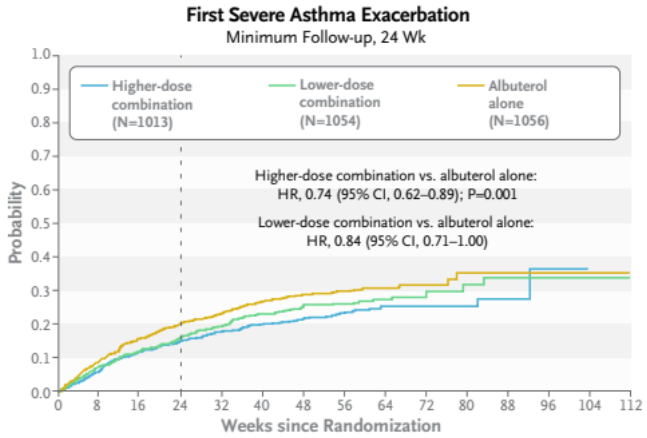
Patients typically treat acute asthma symptoms with short-acting β_2-agonist (SABA) rescue therapy. However, SABAs do not treat inflammation, leaving patients at risk for severe exacerbations. Whether rescue therapy with a fixed-dose combination of a SABA (albuterol) plus a glucocorticoid (budesonide) can improve outcomes is unknown.

CLINICAL TRIAL

Design: A multinational, phase 3, double-blind, randomized trial evaluated the safety and efficacy of as-needed use of a fixed-dose combination of albuterol and budesonide, as compared with albuterol alone, in patients with uncontrolled moderate-to-severe asthma receiving inhaled glucocorticoid-containing maintenance therapy.

Intervention: Adults and adolescents were randomly assigned to receive, on an as-needed basis, 180 μg of albuterol plus 160 μg of budesonide, 180 μg of albuterol plus 80 μg of budesonide, or 180 μg of albuterol; the treatments were delivered through a single metered-dose inhaler. Children 4 through 11 years of age were assigned only to the lower-dose combination group or the albuterol-alone group. Participants continued their baseline glucocorticoid-containing maintenance therapies. The primary efficacy end point was the first severe asthma exacerbation in a time-to-event analysis.





MANDALA, NEJM 2022

60-year-old man

- Smoker
- Delivery driver
- **Asthma** since childhood
- Diagnosed with **COPD** 1 year ago (post-BD FEV1/FVC was 60%)
- On salmeterol-fluticasone propionate 50/250 1 puff BD **for asthma**
- Seeing his GP for routine follow-up
- **Troubled by dyspnea and decreased exercise tolerance over the past 2 months**
- **How should his GP approach this case?**

Case study courtesy of speaker

Summary: Holistic care for asthma and COPD

Review non-inhaler-related issues

- **Diagnosis**
- **Comorbidity** (e.g., AR/CRS, IHD)
- **Psychosocial treatable traits** (including environmental and work-related triggers)
- **Preventive healthcare**: Smoking cessation, walking (e.g., 30min/day), vaccinations

Review inhaler-related issues

- **Adherence/technique**
- **Uncontrolled asthma**: Add **LAMA** to LABA-ICS if ICS dose is mid-high already
- **Uncontrolled COPD**: Add **ICS** to LAMA-LABA if baseline eosinophils ≥100/μL
- Consider **combination inhalers**

kaychoongsee@nus.edu.sg

Succinct Safety Information

Relvar Ellipta

Contraindications: Severe milk-protein allergy, or hypersensitivity to the active substance(s) or any of the excipients. Warnings & Precautions: Not for acute asthma symptoms or acute exacerbation in COPD. Therapy should not be stopped without physician supervision. Paradoxical bronchospasm may occur. Caution advised in patients with severe cardiovascular disease, pulmonary tuberculosis, chronic or untreated infections, with moderate to severe hepatic impairment, diabetes mellitus, and for co-administration with strong CYP3A4 inhibitors. Systemic effects may occur at high doses. Consider risk factors for pneumonia before prescription, and re-evaluate treatment if pneumonia occurs. Avoid concurrent use of non-selective and selective beta-blockers. Adverse Reactions: Very common - Headache, nasopharyngitis; Common -pneumonia, upper respiratory tract infection, bronchitis, influenza, candidiasis of mouth and throat, oropharyngeal pain, sinusitis, pharyngitis, rhinitis, cough, dysphonia, abdominal pain; arthralgia, back pain, fractures, and pyrexia. Please refer to the full prescribing information for more details.

Full PI available on request. Version abbrev GDS12/IPI12 (SI)

Relvar Ellipta was developed in collaboration with INNOVIVA

Succinct Safety Information

Trelegy Ellipta

Contraindications: Hypersensitivity to the active substances or to any of the excipients (lactose monohydrate and magnesium stearate) or patients with severe milk-protein allergy. Warnings & Precautions: Asthma: Should not be used to treat acute asthma symptoms or an acute exacerbation in COPD for which a short-acting bronchodilator is required. COPD: Should not be used to treat an acute exacerbation in COPD for which a short-acting bronchodilator is required. Patients should not stop therapy with Trelegy Ellipta, in asthma or COPD, without physician supervision since symptoms may recur after discontinuation. Discontinue Trelegy if paradoxical bronchospasm occurs and institute alternative therapy if necessary. Cardiovascular effects, such as cardiac arrhythmias e.g. atrial fibrillation and tachycardia, may be seen after the administration of muscarinic receptor antagonists or sympathomimetics, use with caution in patients with unstable or life-threatening cardiovascular disease. Monitor patients with moderate to severe hepatic impairment for systemic corticosteroid-related adverse reactions and the 100/62.5/25 micrograms dose should be used. Systemic effects may occur, particularly at high doses for long periods, but much less likely than with oral corticosteroids. Possible systemic effects include HPA suppression, decrease in bone mineral density, cataract, glaucoma, central serous chorioretinopathy and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression. Use with caution in patients with urinary retention, narrow angle glaucoma, pulmonary tuberculosis or with chronic or untreated infections. hyperglycaemia and severe hepatic impairment. Consider risk factors for pneumonia in patients with COPD before prescribing, and re-evaluate treatment if pneumonia occurs. Adverse Reactions: Very Common: Nasopharyngitis. Common: Urinary tract infection, sinusitis, pharyngitis, upper respiratory tract infection, headache, cough, oropharyngeal pain, dysphonia, constipation, pneumonia, bronchitis, rhinitis, influenza, candidiasis of mouth and throat, arthralgia, back pain, viral respiratory tract infection. Uncommon: dry mouth, dysgeusia, atrial fibrillation, supraventricular tachyarrhythmia, tachycardia, fractures.

Version number: GDS12/IPI13a (SI)

Trelegy 200 is not licensed for COPD in Singapore.

For Full Prescribing Information, scan QR codes.

Seretide Accuhaler:

Relvar Ellipta:

Trelegy Ellipta:

Flixotide Evohaler:

Only Seretide Accuhaler 50/500mcg is indicated for COPD in Singapore.
Flixotide Evohaler is not licensed for tthe treatment of COPD in Singapore.