

He is still Short of Breath
Is there any new puffer?

Saidul Ansary

Mr S C

66 yr. old retired Engineer for pre op elective assessment

“I am fine but Anaesthetist said I need to see you”.

I am little bit SOB, “not much”.

Accompanied Mrs S.C “he too SOB, can’t do much”.

Cont.

B/G Hx:

- Poorly controlled Psoriatic arthritis on biologics
- HTN
- Hyper cholesterolaemia
- Elevated BMI
- On elective list for Rt TKR

Anaesthetist found him to be puffed after walking in to the room
Was wheezy and desaturating down to 93% in preadmission clinic.

Central Booking Number
 1300 780 239

☐ Dr. Bill Burke - 038617AH

☐ Dr. Tim McDonald - 033175BH

Test Comments: Good patient effort & cooperation. The results of this test meet the ATS standards for acceptability and repeatability. Puffer technique was Ok, some further pointers given regarding use of a spacer.

 Patient: CHEIMARDINOV, Saiar Date: 29/03/2016
 DOB: 28/08/1950 Age: 65 Gender: Male Race: <Unspecifi
 Height: 167.00 Cms Weight: 92.60 Kgs BMI: 33.2
 Smoker: Cigarette How Long: 17.5 Quit: 0.1
 Clinical Details: ?COPD. Pre-op
 Referring Doctor: ANSARY, Saidal
 Family Doctor: Coples to GROSS, Michael
 Respiratory Scientist: JH

	Pre-Bronch			Post Bronch			
	<u>Actual</u>	<u>Pred</u>	<u>% Pred</u>	<u>SD</u>	<u>LLN</u>	<u>Actual</u>	<u>% Chng</u>
---- SPIROMETRY ----							
FVC (L)	*2.65	3.50	*75	0.51	2.92	*2.80	+5
FEV1 (L)	*1.69	2.74	*61	0.43	2.29	*1.97	+16
FEV1/FVC (%)	*64	78		7	65	70	+9
FEF 25% (L/sec)	*1.82	7.14	*25	1.57	5.96	*4.98	+172
FEF 75% (L/sec)	*0.40	1.27	*31	0.71	1.06	*0.64	+59
FEF 25-75% (L/sec)	*1.00	2.28	*43	0.90	1.90	*1.44	+44
FEF Max (L/sec)	*4.93	7.84	*62	1.24	6.55	*6.11	+23
FIVC (L)	2.33					2.88	+23
FIF Max (L/sec)	4.50					4.14	-7
---- LUNG VOLUMES ----							
SVC (L)	2.96	3.50	84	0.51	2.92		
IC (L)	2.71	2.97	91		2.48		
ERV (L)	*0.25	0.53	*46		0.44		
TGV (L)	3.08	3.18	96	0.72	2.54		
RV (Pleth) (L)	2.83	2.40	117	0.41	1.92		
TLC (Pleth) (L)	5.79	6.15	94	0.79	4.92		
RV/TLC (Pleth) (%)	*49	40		5	32		
Trapped Gas (L)							
---- DIFFUSION ----							
DLCOunc (ml/min/mmHg)	28.41	24.46	116	4.21	19.57		
DLCOcor (ml/min/mmHg)		24.46		4.21	19.57		
DL/VA (ml/min/mmHg/L)	*5.68	3.98			3.18		
VA (L)	*5.00	6.15	*81	0.79	5.14		



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Test Comments: Good patient effort & cooperation. The results of this test meet the ATS standards for acceptability and repeatability. Resp meds Symbicort.

ID: CHES280850MCSC

Patient: CHEIMARDINOV, Saiar

Date: 20/02/2017

DOB: 28/08/1950 Age: 66 Gender: Male Race: <Unspecifi

Height: 167.00 Cms Weight: 92.60 Kgs BMI: 33.2

Smoker: How Long: Quit:

Clinical Details: Asthma/Ex-smoker ?progress on inhalers

Referring Doctor: Ansary, S

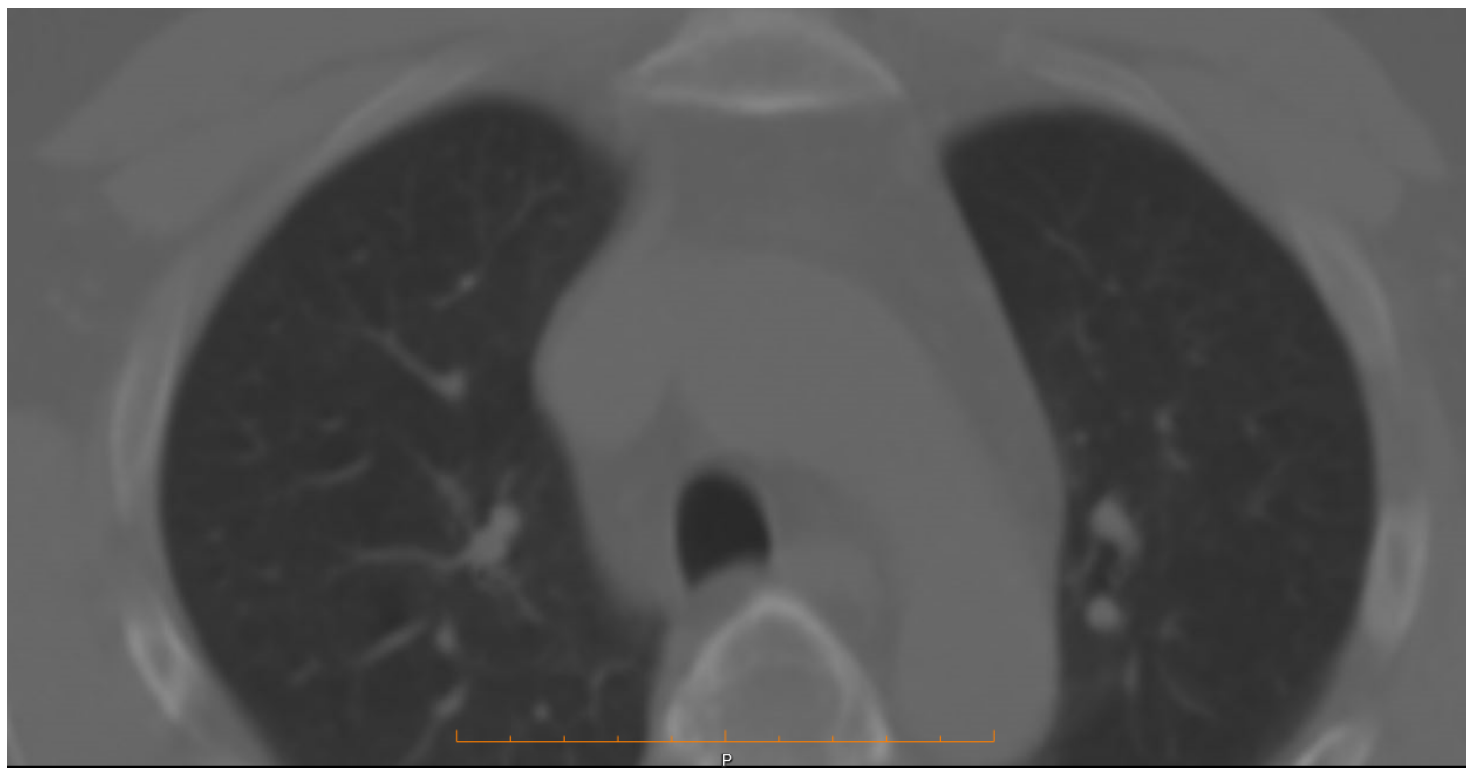
Family Doctor: Copies to:

Respiratory Scientist: JH

	Pre-Bronch			Post Bronch			
	<u>Actual</u>	<u>Pred</u>	<u>%Pred</u>	<u>SD</u>	<u>LLN</u>	<u>Actual</u>	<u>% Chng</u>
---- SPIROMETRY ----							
FVC (L)	*2.78	3.47	*80	0.51	2.90	*2.69	-3
FEV1 (L)	*1.83	2.71	*67	0.43	2.26	*1.82	+0
FEV1/FVC (%)	66	78		7	65	68	+3
FEF 25% (L/sec)	*2.39	7.11	*33	1.57	5.94	*3.23	+35
FEF 75% (L/sec)	*0.55	1.25	*44	0.71	1.04	*0.39	-28
FEF 25-75% (L/sec)	*1.21	2.24	*53	0.89	1.87	*0.98	-19
FEF Max (L/sec)	*5.84	7.76	*75	1.24	6.48	*6.10	+4
FIVC (L)	2.76					2.40	-13
FIF Max (L/sec)	3.27					3.51	+7

Diagnosis?

Asthma
COPD





COPD Definition



- ▶ Chronic Obstructive Pulmonary Disease (COPD) is a common, **preventable** and **treatable** disease that is characterized by persistent **respiratory symptoms** and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.

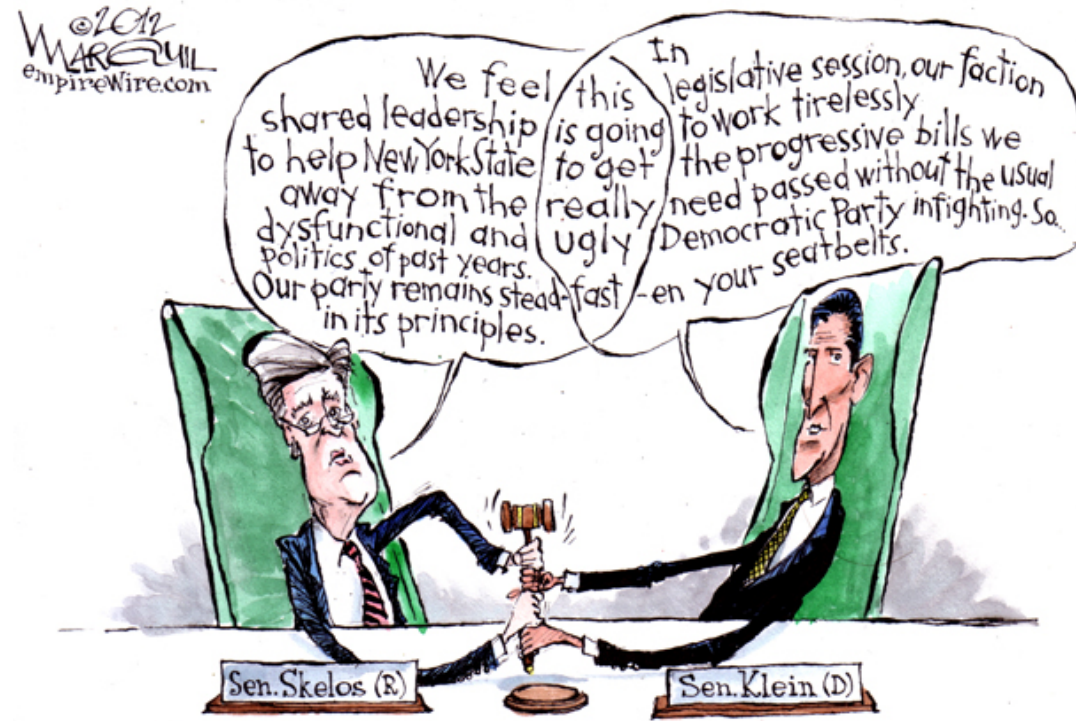


Definition of asthma

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

2017 update

Overlap





The Asthma–COPD Overlap Syndrome

Dirkje S. Postma, M.D., Ph.D., and Klaus F. Rabe, M.D., Ph.D.
N Engl J Med 2015; 373:1241-1249 [September 24, 2015](#)

Pharmacotherapy

The goal of treatment

- Not just **symptom relief**

It also includes:

- An attempt to improve lung function
- Slow the loss of lung function
- To prevent exacerbations
- Most medications for COPD/Asthma are administered by inhalation
 - Standard therapy consists of inhaled bronchodilators
 - Either β -agonists or antimuscarinics (anticholinergics), and ICS/LABA or Combination product
 - Oral agents, less commonly are, methylxanthines (e.g., theophylline, non-selective PDE4), Selective phosphodiesterase-4 inhibitors (e.g., roflumilast), and corticosteroids (prednisone or prednisolone, as maintenance)

Type	Common medicines	Pharmacological class	Function
Manually actuated pMDI	<i>Airomir Inhaler</i> (salbutamol)	SABA	Reliever
	<i>APO-Salbutamol Inhaler</i> (salbutamol)	SABA	
	<i>Asmol CFC-Free Inhaler</i> (salbutamol)	SABA	
	<i>Ventolin CFC-Free Inhaler</i> (salbutamol)	SABA	
	<i>Symbicort Rapihaler</i> (budesonide plus formoterol)*	ICS + LABA	
	<i>Alvesco Metered-dose Inhaler</i> (ciclesonide)	ICS	Preventer
	<i>Flixotide Junior/Flixotide Inhaler</i> (fluticasone propionate)	ICS	
	<i>Flutiform Metered-dose Inhaler</i> (fluticasone propionate plus formoterol)	ICS + LABA	
	<i>Intal CFC-Free Inhaler/IntalForte CFC-Free Inhaler</i> (sodium cromoglycate)	Cromone	
	<i>Qvar</i> (beclometasone)	ICS	
	<i>Seretide MDI</i> (fluticasone propionate plus salmeterol)	ICS + LABA	
	<i>Symbicort Rapihaler</i> (budesonide plus formoterol)	ICS + LABA	
	<i>Tilade CFC-Free</i> (nedocromil sodium)	Cromone	
	<i>Atrovent Metered Aerosol</i> (ipratropium)	SAMA	Other bronchodila

Breath-actuated pressurised	<i>Airomir Autohaler</i> (salbutamol)	SABA	Reliever
MDI	<i>Qvar Autohaler</i> (beclometasone)	ICS	Preventer

DPI (multi-dose)	<i>Bricanyl Turbuhaler</i> (terbutaline sulfate)	SABA	Reliever
	<i>Symbicort Turbuhaler</i> (budesonide plus formoterol)*	ICS + LABA	
	<i>Arnuity Ellipta</i> (fluticasone furoate)	ICS	Preventer
	<i>Breo Ellipta</i> (fluticasone furoate plus vilanterol)	ICS + LABA	
	<i>Flixotide Accuhaler</i> (fluticasone propionate)	ICS	
	<i>Pulmicort Turbuhaler</i> (budesonide)	ICS	
	<i>Seretide Accuhaler</i> (fluticasone propionate plus salmeterol)	ICS + LABA	
	<i>Symbicort Turbuhaler</i> (budesonide plus formoterol)	ICS + LABA	
	<i>Anoro Ellipta</i> (umeclidinium plus vilanterol)	LAMA + LABA	Other bronchodilator
	<i>Bretaris Genuair</i> (aclidinium)	LAMA	
	<i>Brimica Genuair</i> (aclidinium plus formoterol)	LAMA + LABA	
	<i>Incruse Ellipta</i> (umeclidinium)	LAMA	
	<i>Oxis Turbuhaler</i> (formoterol)	LABA	
	<i>Serevent Accuhaler</i> (salmeterol)	LABA	

Dry powder inhaler (capsule)	<i>Onbrez Breezhaler</i> (indacaterol)	LABA	Other bronchodilator
	<i>Seebri Breezhaler</i> (glycopyrronium)	LAMA	
	<i>Spiriva Handihaler</i> (tiotropium)	LAMA	
	<i>Ultibro Breezhaler</i> (glycopyrronium plus indacaterol)	LAMA + LABA	
Mist inhaler	<i>Spiolto Respimat</i> (tiotropium plus olodaterol)	LAMA + LABA	Other bronchodilator
	<i>Spiriva Respimat</i> (tiotropium)	LAMA	

History of **advances** in COPD Therapy

There has been significant advances

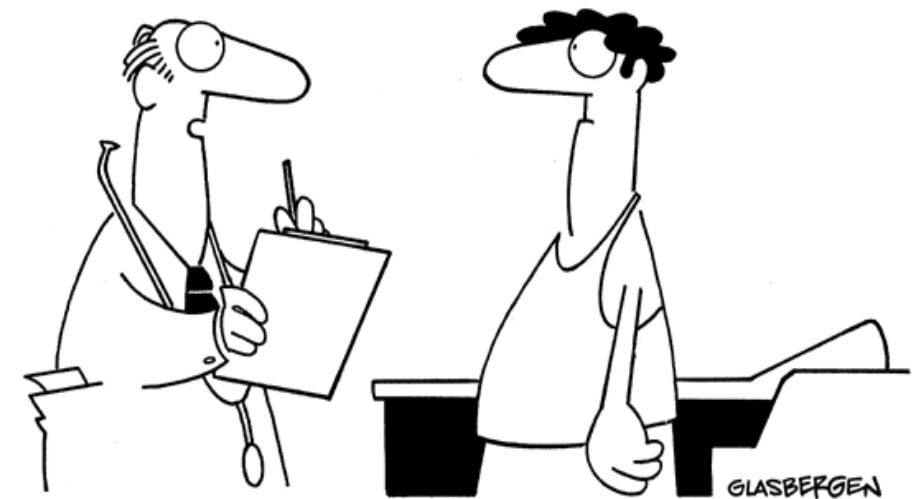
- In the technology of devices

- In formulations for inhaled drugs in the past 50 years

Therapy

The most important treatment is quit smoking; smoking cessation can slow the rate at which lung function is lost and can diminish symptoms

Copyright 2004 by Randy Glasbergen.
www.glasbergen.com



**"If smoking relaxes you, then don't quit.
Being dead is very relaxing."**

Advances in Inhalational Therapy

Now there are many pharmaceutical categories that have been shown to improve outcomes in COPD/Asthma




Often there are many choices within each drug class, and a variety of ways to progress through a therapeutic algorithm

The GOLD and GINA guidelines provide a framework for making these decisions



Which inhaler(s) do you use for Chronic Obstructive Pulmonary Disease (COPD)?

LAMAs: Long-acting muscarinic antagonists		LABAs: Long-acting β_2 -agonists		LABA/LAMA inhalers		Combination medicines Inhaled corticosteroid/Long-acting β_2 -agonist	
	Bretaris® Genuair®†		Foradile® Aerolizer®^		Anoro® Ellipta®†		Breco® Ellipta®†
	Incruse® Ellipta®†		Onbrez® Breezhaler®^		Ultibro® Breezhaler®^		Seretide® Accuhaler®†
	Seebri® Breezhaler®^		Serevent® Accuhaler®†				Seretide® MDI†
	Spiriva® HandiHaler®*						Symbicort® Rapihaler™#
Short-acting reliever medicines							Symbicort® Turbuhaler®#
	Airomir™ Autohaler†	Airomir™ Inhaler†	Asmol® Inhaler‡	Atrovent® Metered Aerosol*	Bricanyl® Turbuhaler®§		

LAMAs: Long-acting muscarinic antagonists		LABAs: Long-acting β_2 -agonists		LABA/LAMA inhalers		Combination medicines Inhaled corticosteroid/Long-acting β_2 -agonist	
	LAMA -Aclidinium Bretaris® Genuair®†		LABA Foradile® Aerolizer®^		LABA/LAMA U/V Anoro® Ellipta®†		LABA/ICs Breco® Ellipta®†
	LAMA, umc Incruse® Ellipta®†		LABA Onbrez® Breezhaler®^		LABA/LAMA ind/GP Ultibro® Breezhaler®^		LABA/ICs Seretide® Accuhaler®†
	LAMA Seebri® Breezhaler®^		LABA Serevent® Accuhaler®†				LABA/ICs Seretide® MDI†
	LAMA Spiriva® HandiHaler®*						LABA/ICs Symbicort® Rapihaler™#
							LABA/ICs Symbicort® Turbuhaler®#
SAMA							
							
Airomir™ Autohaler†	Airomir™ Inhaler†	Asmol® Inhaler‡	Atrovent® Metered Aerosol*	Bricanyl® Turbuhaler®§	Ventolin® Inhaler†		



LAMAs: Long-acting muscarinic antagonists	
	LAMA -Aclidinium Bretaris® Genuair® ^{††}
	LAMA, umc Incruse® Ellipta® ^{††}
	LAMA, Gp Seebri® Breezhaler® ^{††}
	LAMA Spiriva® HandiHaler® [†]

LABAs: Long-acting β_2 -agonists	
	LABA Foradile® Aerolizer® ^{††}
	LABA Onbrez® Breezhaler® ^{††}
	LABA Serevent® Accuhaler® ^{††}

LABA/LAMA inhalers	
	LABA/LAMA U/V Anoro® Ellipta® ^{††}
	LABA/LAMA ind/GP Ultibro® Breezhaler® ^{††}
	LABA/LAMA, Efmt/Acid Brimica® Genuair® ^{††}

Combination medicines Inhaled corticosteroid/Long-acting β_2 -agonist	
	LABA/ICs Breo® Ellipta® ^{††}
	LABA/ICs Seretide® Accuhaler® ^{††}
	LABA/ICs Seretide® MDI [†]
	LABA/ICs Symbicort® Rapihaler™ ^{††}
	LABA/ICs Symbicort® Turbuhaler® ^{††}

Short-acting reliever medicines					
					
Airomir™ Autohaler[†]	Airomir™ Inhaler[†]	Asmol® Inhaler[‡]	Atrovent® Metered Aerosol[*]	Bricanyl® Turbuhaler®[‡]	Ventolin® Inhaler[†]

SABA

SABA

Choice of medications/Guidelines for Tx

Formerly, medication decisions were based primarily on severity of airflow obstruction; guidelines now, as exemplified by GOLD

GOLD Classification of Severity of Airflow Limitation in COPD, Based on Post-Bronchodilator FEV₁

In Patients with FEV₁ /FVC < 0.70

GOLD 1: mild FEV₁ ≥ 80% predicted

GOLD 2: moderate 50% ≤ FEV₁ < 80% predicted

GOLD 3: severe 30% ≤ FEV₁ < 50% predicted

GOLD 4: very severe FEV₁ < 30% predicted

COPD, chronic obstructive pulmonary disease; FEV₁, forced expiratory volume in 1 second.

Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2014



"Your breathing test results would be normal ...
if you were 3'8" and 150 years old."

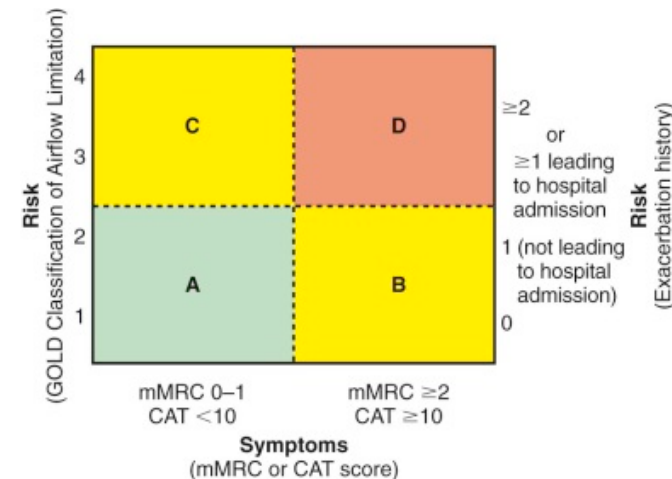
Choice of medications/Guidelines for Tx

Based on an assessment of the severity of airflow obstruction, symptoms, frequency and severity of exacerbations, and patient's functional limitation, as well as on the availability and local cost of medications guidelines now emphasize a metric that includes obstruction (GOLD grade), based on FEV₁ percent predicted (table)

Symptoms (based on either the Medical Research Council dyspnea scale or the COPD Assessment Test)

Risk of exacerbations

Using this tool, patients can be categorized into class A, B, C, or D, and GOLD provides specific treatment recommendations for each category



GOLD classification system

How is your COPD? Take the COPD Assessment Test (CAT)

This questionnaire will help you and your healthcare professional measure the impact COPD (Chronic Obstructive Pulmonary Disease) is having on your wellbeing and daily life. Your answers and test score, can be used by you and your healthcare professional to help improve the management of your COPD and get the greatest benefit from treatment.

If you wish to complete the questionnaire by hand on paper, [please click here](#) and then print the questionnaire.
If you complete the questionnaire on-line, for each question below, click your mouse to place a mark (X) in the box that best describes you currently.

Example: I am very happy 0 X 2 3 4 5 I am sad

I never cough

012345

I cough all the time

SCORE

I have no phlegm (mucus) in my chest at all

012345

My chest is full of phlegm (mucus)

My chest does not feel tight at all

012345

My chest feels very tight

When I walk up a hill or one flight of stairs I am not breathless

012345

When I walk up a hill or one flight of stairs I am very breathless

I am not limited doing any activities at home

012345

I am very limited doing activities at home

I am confident leaving my home despite my lung condition

012345

I am not at all confident leaving my home because of my lung condition

I sleep soundly

012345

I don't sleep soundly because of my lung condition

I have lots of energy

012345

I have no energy at all

CLICK TO GET YOUR TOTAL SCORE!

Score	Impact Level
<10	Low
10-20	Medium
>20	High
>30	Very high

Stepwise pharmacological management of stable COPD

Patient Group	Recommended First choice	Alternative Choice	Other Possible Treatments †
A	SAMA prn or SABA prn	LAMA or LABA or SABA and SAMA	Theophylline
B	LAMA or LABA	LAMA and LABA	SABA and/or SAMA Theophylline
C	ICS + LABA or LABA	LAMA and LABA or LABA and PDE4-inh. or LABA and PDE4-inh.	SABA and/or SAMA Theophylline
D	ICS + LABA and/or LABA	ICS and LABA and LAMA or ICS and LABA and PDE4- inh. or LABA and LABA or LABA and PDE4-inh.	C arboxysteine SABA and / or SAMA Theophylline

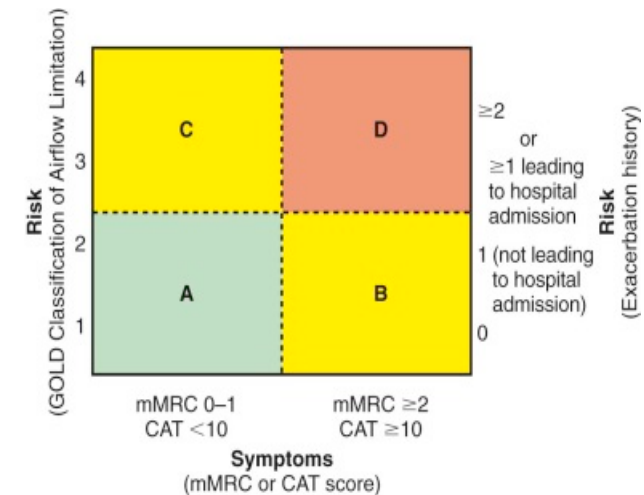
In Patients with $FEV_1 / FVC < 0.70$

GOLD 1: mild $FEV_1 \geq 80\%$ predicted

GOLD 2: moderate $50\% \leq FEV_1 < 80\%$ predicted

GOLD 3: severe $30\% \leq FEV_1 < 50\%$ predicted

GOLD 4: very severe $FEV_1 < 30\%$ predicted



Stepwise pharmacological management of stable

	MILD	MODERATE	SEVERE
Typical Symptoms	<ul style="list-style-type: none"> few symptoms breathless on moderate exertion recurrent chest infections little or no effect on daily activities 	<ul style="list-style-type: none"> increasing dyspnoea breathless walking on level ground increasing limitation of daily activities cough and sputum production exacerbations requiring oral corticosteroids and/or antibiotics 	<ul style="list-style-type: none"> dyspnoea on minimal exertion daily activities severely curtailed experiencing regular sputum production chronic cough exacerbations of increasing frequency and severity
Lung Function	FEV ₁ ≈ 60-80% predicted	FEV ₁ ≈ 40 -59% predicted	FEV ₁ < 40% predicted
Non-Pharmacological Interventions Management of stable COPD should centre around supporting smoking patients to quit. Encouraging physical activity and maintenance of a normal weight range are also important. Pulmonary rehabilitation is recommended in symptomatic patients.	RISK REDUCTION Check smoking status, support smoking cessation, recommend annual influenza and pneumococcal vaccine according to immunisation handbook		
	OPTIMISE FUNCTION Encourage physical activity, review nutrition, provide education, develop GP management plan and initiate regular review		
	CONSIDER CO-MORBIDITIES especially osteoporosis, coronary disease, lung cancer, anxiety and depression		
	REFER TO PULMONARY REHABILITATION and consider psychosocial needs, agree written action plan		
			Consider oxygen therapy, surgery, palliative care and advanced care directives
Pharmacological Interventions The aim of pharmacological treatment may be to treat symptoms (e.g. breathlessness) or to prevent deterioration (either by decreasing exacerbations or by reducing decline in quality of life) or both. A stepwise approach is recommended, irrespective of disease severity, until adequate control has been achieved.	CHECK DEVICE USAGE TECHNIQUE AND ADHERENCE AT EACH VISIT - Up to 90% of patients don't use devices correctly		
	SHORT-ACTING RELIEVER MEDICATION: Short-acting beta ₂ -agonist (SABA) or short-acting muscarinic antagonist (SAMA). Refer to Table 1 overleaf.		
	SYMPTOM RELIEF: Long-acting muscarinic antagonist (LAMA) and/or long-acting beta ₂ -agonist (LABA). Refer to Table 1 overleaf. These medicines may also help to prevent exacerbations. **SEE PRECAUTIONS 1-3**		
	EXACERBATION PREVENTION: When FEV ₁ <50% predicted AND 2 or more exacerbations in the previous 12 months, consider commencing inhaled corticosteroid (ICS)/LABA combination therapy. **SEE PRECAUTIONS**		
			Consider low dose theophylline

In Patients with FEV₁ /FVC < 0.70

GOLD 1: mild FEV₁ ≥ 80% predicted

GOLD 2: moderate 50% ≤ FEV₁ < 80% predicted

GOLD 3: severe 30% ≤ FEV₁ < 50% predicted

GOLD 4: very severe FEV₁ < 30% predicted

REFERENCE: 1 Lung Foundation Australia. Stepwise management of stable COPD. 2016

ssion of the Sisters of the Little Company of Mary

Typical Symptoms

MILD	MODERATE	SEVERE
<ul style="list-style-type: none"> few symptoms breathless on moderate exertion recurrent chest infections little or no effect on daily activities 	<ul style="list-style-type: none"> increasing dyspnoea breathless walking on level ground increasing limitation of daily activities cough and sputum production exacerbations requiring oral corticosteroids and/or antibiotics 	<ul style="list-style-type: none"> dyspnoea on minimal exertion daily activities severely curtailed experiencing regular sputum production chronic cough exacerbations of increasing frequency and severity

Lung Function

FEV ₁ ≈ 60-80% predicted	FEV ₁ ≈ 40 -59% predicted	FEV ₁ < 40% predicted
-------------------------------------	--------------------------------------	----------------------------------

Non-Pharmacological Interventions

Management of stable COPD should centre around supporting smoking patients to quit. Encouraging physical activity and maintenance of a normal weight range are also important. Pulmonary rehabilitation is recommended in symptomatic patients.

RISK REDUCTION Check smoking status, support smoking cessation, recommend annual influenza and pneumococcal vaccine according to immunisation handbook

OPTIMISE FUNCTION Encourage physical activity, review nutrition, provide education, develop GP management plan and initiate regular review

CONSIDER CO-MORBIDITIES especially osteoporosis, coronary disease, lung cancer, anxiety and depression

REFER TO PULMONARY REHABILITATION and consider psychosocial needs, agree written action plan

Consider oxygen therapy, surgery, palliative care and advanced care directives

Pharmacological Interventions

The aim of pharmacological treatment may be to treat symptoms (e.g. breathlessness) or to prevent deterioration (either by decreasing exacerbations or by reducing decline in quality of life) or both. A stepwise approach is recommended, irrespective of disease severity, until adequate control has been achieved.

CHECK DEVICE USAGE TECHNIQUE AND ADHERENCE AT EACH VISIT - Up to 90% of patients don't use devices correctly

SHORT-ACTING RELIEVER MEDICATION: Short-acting beta₂-agonist (SABA) or short-acting muscarinic antagonist (SAMA). Refer to Table 1 overleaf.

SYMPTOM RELIEF: Long-acting muscarinic antagonist (LAMA) and/or long-acting beta₂-agonist (LABA). Refer to Table 1 overleaf. **These medicines may also help to prevent exacerbations. **SEE PRECAUTIONS 1-3****

EXACERBATION PREVENTION: When FEV₁ <50% predicted AND 2 or more exacerbations in the previous 12 months, consider commencing inhaled corticosteroid (ICS)/LABA combination therapy. ****SEE PRECAUTIONS4****

Consider low dose theophylline

Based on COPD-X Plan: Australian and New Zealand Guidelines for the Management of COPD; Australian Therapeutic Guidelines.

FEBRUARY 2016

PRECAUTIONS:

- 1 An assessment should be undertaken to exclude asthma or check if asthma and COPD co-exist before initiating LABA monotherapy. LABA monotherapy should not be used when asthma and COPD co-exist.
- 2 Once a LAMA is commenced, ipratropium (a SAMA) should be discontinued.
- 3 If starting a fixed dose LAMA/LABA combination inhaler, discontinue existing inhalers containing a LAMA or LABA. Refer to Table 1 overleaf.
- 4 If starting an ICS/LABA combination inhaler, discontinue existing inhalers containing a LABA. Refer to Table 1 overleaf.

Advocacy • Awareness • Education • Support • Research

 Lung Foundation Australia
 PO Box 1949
 Milton Qld 4064
 Free call: 1800 654 301
 Website: www.lungfoundation.com.au



LAMAs: Long-acting muscarinic antagonists	
	LAMA -Aclidinium Bretaris® Genuair®†
	LAMA, umc Incruse® Ellipta®†
	LAMA, Gp Seebri® Breezhaler®‡
	LAMA Spiriva® HandiHaler®*

LABAs: Long-acting β_2 -agonists	
	LABA Foradil® Aerolizer®‡
	LABA Onbrez® Breezhaler®‡
	LABA Serevent® Accuhaler®†

LABA/LAMA inhalers	
	LABA/LAMA U/V Anoro® Ellipta®†
	LABA/LAMA ind/GP Ultibro® Breezhaler®‡
	LABA/LAMA, Efmt/Acid Brimica® Genuair®‡

Combination medicines Inhaled corticosteroid/Long-acting β_2 -agonist	
	LABA/ICs Breo® Ellipta®†
	LABA/ICs Seretide® Accuhaler®†
	LABA/ICs Seretide® MDI†
	LABA/ICs Symbicort® Rapihaler™‡
	LABA/ICs Symbicort® Turbuhaler®‡

Short-acting reliever medicines					
					
Airomir™ Autohaler*	Airomir™ Inhaler‡	Asmol® Inhaler‡	Atrovent® Metered Aerosol*	Bricanyl® Turbuhaler®‡	Ventolin® Inhaler†

SABA

SABA

Evince for LAMA

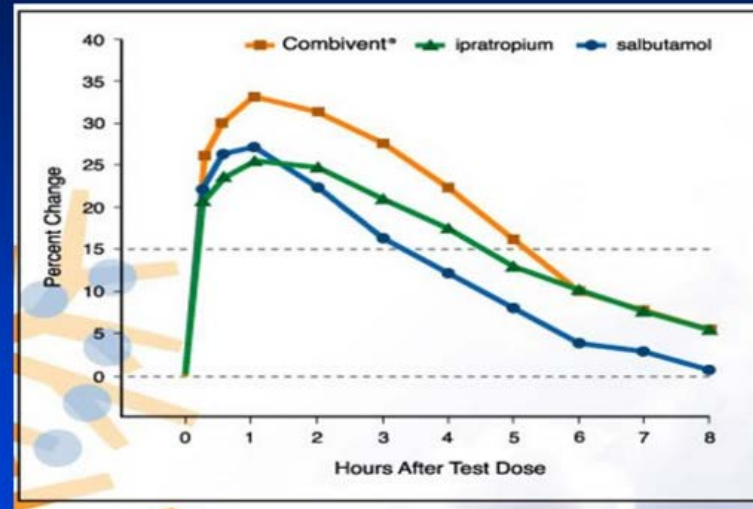
(tiotropium, aclidinium, umeclidinium, and glycopyrronium)

UPLIFT(Understanding Potential Long-Term Impacts on Function with [Tiotropium](#)-identified no significant safety issues with the use of tiotropium, n=6000, over 4 years; N Engl J Med. 2008;359(15):1543

CONCLUSIONS: In patients with COPD, therapy with tiotropium was associated with improvements in lung function, quality of life, and exacerbations during a 4-year period but did not significantly reduce the rate of decline in FEV

What Happens if we combine them?

Combination Therapy



Chest 1997;112:1514-21

Combo?

Combination Therapy

TABLE 1. Bronchodilators: combination versus monotherapy

Combination	PFTs	Symptoms	Exacerbations	Mortality	Side Effects
SABA + SAAC	↑	↓	↓	-	-
SABA + theophylline	↑	↓	+/-	+/-	↑
LABA + SAAC	↑	↓	?	?	-
LABA + theophylline	↑	↓	?	?	+/-
LAAC + SABA	↑	↓	?	?	-
LAAC + LABA	↑	↓	?	?	-

Definition of abbreviations: LAAC = long-acting anticholinergic; LABA = long-acting β -agonist; PFT = pulmonary function tests; SAAC = short-acting anticholinergic; SABA = short-acting β -agonist.

James F. Donohue

Evidence for LAMA/LABA combo

Aclidinium bromide and formoterol fumarate as a fixed-dose combination in COPD: pooled analysis of symptoms and exacerbations from two six-month, multicentre, randomised studies (ACLIFORM and AUGMENT); [Respir Res.](#) 2015 Aug 2;16:92. doi: 10.1186/s12931-015-0250-2. N=3394

CONCLUSIONS: Aclidinium/formoterol 400/12 µg significantly improves 24-hour symptom control compared with placebo, in patients with moderate to severe COPD. Furthermore, aclidinium/formoterol 400/12 µg reduces the frequency of exacerbations compared with placebo.

Evidence for LAMA/LABA combo

Long-acting beta2-agonist *in addition to tiotropium* versus either tiotropium or long-acting beta2-agonist alone for chronic obstructive pulmonary disease; [Farne HA](#), [Cates CJ](#).

The review included 10 trials on 10,894 participants, mostly recruiting participants with moderate or severe COPD

This meta-analysis found that treatment with tiotropium plus LABA resulted in improvements in health-related quality of life and increased FEV1 compared to either agent alone

Cochrane Database Syst Rev. 2015 Oct 22;10:CD008989

Which LAMA/LABA combo to use?

Comparative efficacy of fixed-dose combinations of long-acting muscarinic antagonists and long-acting β 2-agonists: a systematic review and network meta-analysis; *Schlueter, Gonzalez-Rojas, Baldwin, Groenke, Voss*.

A meta-analysis of 27 randomized controlled trials found **no differences** in efficacy and safety of LAMA/LABA fixed-dose combinations for patients with moderate-to-very severe COPD; *Ther Adv Respir Dis*.2016 Jan 8

Screened, a total of 27 trials from 26 publications

30,361 subjects were eligible for inclusion in the NMA

Non-significant differences were seen in most analyses **comparing efficacy, exacerbations and discontinuation rates** of included LAMA/LABA FDCs

- Acclidinium/formoterol 400/12 μ g (Brimica), glycopyrronium/indacaterol 110/50 μ g (Ultibro), tiotropium + olodaterol 5/5 μ g, umeclidinium/vilanterol 62.5/25 μ g (Anoro)

CONCLUSION: All LAMA/LABA FDCs were found to **have similar efficacy and safety**




Definitive assessment of the relative efficacy of different treatments can only be performed through direct comparison in **head-to-head RCTs**

In the absence of such data, **this indirect comparison may be of value in clinical and health economic decision-making**



LAMAs: Long-acting muscarinic antagonists	
	LAMA -Aclidinium Bretaris® Genuair®†
	LAMA, umc Incruse® Ellipta®†
	LAMA Seebri® Breezhaler®‡
	LAMA Spiriva® HandiHaler®*

LABAs: Long-acting β_2 -agonists	
	LABA Foradil® Aerolizer®^
	LABA Onbrez® Breezhaler®^
	LABA Serevent® Accuhaler®†

LABA/LAMA inhalers	
	LABA/LAMA U/V Anoro® Ellipta®†
	LABA/LAMA ind/GP Ultibro® Breezhaler®^
	LABA/LAMA, Efmt/Acid Brimica® Genuair®‡/ 12 microgram inhalation powder Acidinium / Formoterol fumarate dihydrate * containing 60 doses Almirall

Combination medicines Inhaled corticosteroid/Long-acting β_2 -agonist	
	LABA/ICs Breo® Ellipta®†
	LABA/ICs Seretide® Accuhaler®†
	LABA/ICs Seretide® MDI†
	LABA/ICs Symbicort® Rapihaler™*
	LABA/ICs Symbicort® Turbuhaler®‡

Short-acting reliever medicines					
					
Airomir™ Autohaler*	Airomir™ Inhaler‡	Asmol® Inhaler‡	Atrovent® Metered Aerosol*	Bricanyl® Turbuhaler®‡	Ventolin® Inhaler†

SABA

SABA

Combo LABA/ICS

TORCH⁺ (TOwards a Revolution in COPD Health)

Combo significantly improves some outcomes compared to placebo, long-acting beta agonists alone, inhaled glucocorticoids alone, or long-acting anticholinergics alone

- Support for these conclusions comes from the two largest trials of combination therapy

TORCH -randomized, double-blind trial comparing salmeterol at a dose of 50 microg plus fluticasone propionate at a dose of 500 microg twice daily (combination regimen), administered with a single inhaler-combo, with placebo, salmeterol alone, or fluticasone propionate alone for a period of 3 years

The primary outcome was death from any cause for the comparison between the combination regimen and placebo; the frequency of exacerbations, health status, and spirometric values were also assessed.

RESULTS: Of 6112 patients in the efficacy population, 875 died within 3 years after the start of the study treatment.

All-cause mortality rates were 12.6% in the combination-therapy group,

15.2% in the placebo group,

13.5% in the salmeterol group, and

16.0% in the fluticasone group.

CONCLUSIONS: The reduction in death from all causes among patients with COPD in the combination-therapy group did not reach the predetermined level of statistical significance (i.e primary endpoint was not met). **There were significant benefits in all other outcomes among these patients**

- N Engl J Med. 2007;356(8):775; Calverley PM, Anderson JA, Celli B, Ferguson GT, Jenkins C, Jones PW, Yates JC, Vestbo J, TORCH investiga

Combo LABA/ICS

INSPIRE (Investigating New Standards for Prophylaxis in Reducing Exacerbations)

LABA/ICS vs. Tiotropium

A total of 1,323 patients (mean age, 64 yr, post-bronchodilator FEV1, >39% predicted), randomized, double-blind, double-dummy parallel study for 2-years

No difference in frequency of exacerbations or quality of life when patients with severe COPD given salmeterol/fluticasone 50/500 mcg twice daily or tiotropium 18 mcg daily

No difference in exacerbation rate between two groups. However,

- Salmeterol/fluticasone associated with exacerbations requiring antibiotics
- Tiotropium associated with exacerbations requiring oral steroids
- There was an unexpected finding of lower deaths in salmeterol/fluticasone propionate-treated (Combo=3%, Tiotropium alone 6%)

- Wedzicha JA, Calverley PM, Seemungal TA, Hagan G, Ansari Z, Stockley RA; Am J Respir Crit Care Med. 2008;177(1):19, INSPIRE Investigators

New era of therapy

Combo LAMA/LABA better than LABA/ICS combo

Systematic review, 10 studies (9,609 patients, Combo-umeclidinium/vilanterol (Anoro) is superior to the each agent alone, tiotropium (alone), as well as Combo->salmeterol/fluticasone in patients with moderate to severe COPD- 8/1/15

Findings: Once-daily inhaled UMEC/VIL showed superior efficacy compared with its monocomponents, tiotropium-alone, and Salmeteropol/fluticasone combination in patients with moderate to severe COPD

Combo LAMA/LABA better than LABA/ICS combo

Respir Med. 2015 Jul;109(7):870-81; Donohue JF1, Worsley S2, Zhu CQ3, Hardaker L4, Church A5

Improvements in lung function with umeclidinium/vilanterol versus fluticasone propionate/salmeterol in patients with moderate-to-severe COPD and infrequent exacerbations.

Combo umeclidinium (LAMA)/vilanterol (LABA) **versus** Combo salmeterol/fluticasone (LABA/ICS) was used

Umeclidinium/vilanterol (LAMA/LABA) demonstrated clinically meaningful improvements in lung function compared to salmeterol/fluticasone (LABA/ICS)

Once-daily UMEC/VI 62.5/25 mcg over 12 weeks resulted in statistically significant, clinically meaningful improvements in lung function compared to twice-daily FP/SAL 250/50 mcg

In patients with moderate-to-severe COPD with infrequent exacerbations, both treatments improved dyspnea and QoL

Choice of device

Selection of a device should be guided by patient factors

- Patient preference
- Ability of the patient to use the device

Potential patient factors that can influence device choice:

Dexterity

Lung function

Age

Cognition

Risk of adverse effects

General health status

Previous device experience

Patient preference

There has not been found to be any difference in therapeutic efficacy between DPI and pMDI type inhalers except patient with very low FEV1

Correct use of inhaler device

The majority of patients do not use inhaler devices correctly
Only approximately 10% of patients use correct technique

Basheti IA, Bosnic-Anticevich SZ-Faculty of Pharmacy, University of Sydney, Australia, 2008

Bosnic-Anticevich, S. Z., Sinha, H., So, S., Reddel, H. K. Metered-dose inhaler technique: the effect of two educational interventions delivered in community pharmacy over time. *The Journal of asthma-2010*











High rates of incorrect inhaler use have been reported (in Asthma & COPD), even among regular users

- Italian study by: Melani AS, Bonavia M *et al.* Inhaler mishandling remains common in real life and is associated with reduced disease control. *Respir Med.* 2011; 105: 930-8

Critical mistakes were widely distributed among users

- 12% for MDIs, 35% for Diskus[®] and HandiHaler[®] and 44% for Turbuhaler[®]
- Independent of the inhaler, they found

The strongest association between inhaler misuse and older age ($p = 0.008$), lower schooling ($p = 0.001$) and **lack of instruction received for inhaler technique by health caregivers ($p < 0.001$)**

Regardless of the type of inhaler device prescribed, patients are unlikely to use inhalers correctly

- They need clear instruction
- Need a physical demonstration
- Need their inhaler technique checked regularly

National Asthma Council Australia. *Inhaler technique for people with asthma or COPD*. National Asthma Council Australia, Melbourne, 2016

Device-specific checklists

Produced by NPS Medicinewise in collaboration with the National Asthma Council Australia

Further information about the resource can be found on the
<http://www.nps.org.au>

Device	Clinically effective inspiratory flow
Accuhaler®	30–90 l/min [†]
Autohaler®	30–60 l/min [†]
Clickhaler®	15–60 l/min [†]
Easi-Breathe®	20–60 l/min [†]
HandiHaler® (using adapter)	20–60 l/min [‡]
pMDI	25–60 l/min [†]
Turbohaler®	30–90 l/min [†]
[†] Data taken from from Clement Clarke Ltd, UK.	
[‡] Data taken from [63].	

Common errors with pMDI

Failing to shake the inhaler before actuating

Holding the inhaler in wrong position

Failing to exhale fully before actuating the inhaler

Actuating the inhaler too early or during exhalation (the medicine may be seen escaping from the top of the inhaler)

Actuating the inhaler too late while inhaling

Actuating more than once while inhaling

Inhaling too rapidly (especially kids)

Multiple actuations without shaking between doses

Common errors for DPIs

Error with positioning while loading the dose

- Horizontal for *A/H* and vertical for *T/H*

Failing to exhale fully before inhaling

Failing to inhale completely

Inhaling too slowly (kids/elderly) and weakly (elderly)

Exhaling into the device mouthpiece before or after inhaling

Failing to close the inhaler after use

Using past the expiry date or when empty

Other/miscellaneous problems include

Poor dexterity (e.g. osteoarthritis, stroke, muscle weakness)

Incomplete seal around the mouthpiece of an inhaler or spacer

Suboptimal inspiratory flow for the inhaler type (low FEV1)

Not using a spacer when needed

Musk issues (kids)

Cost of poor inhaler technique

Incorrect technique

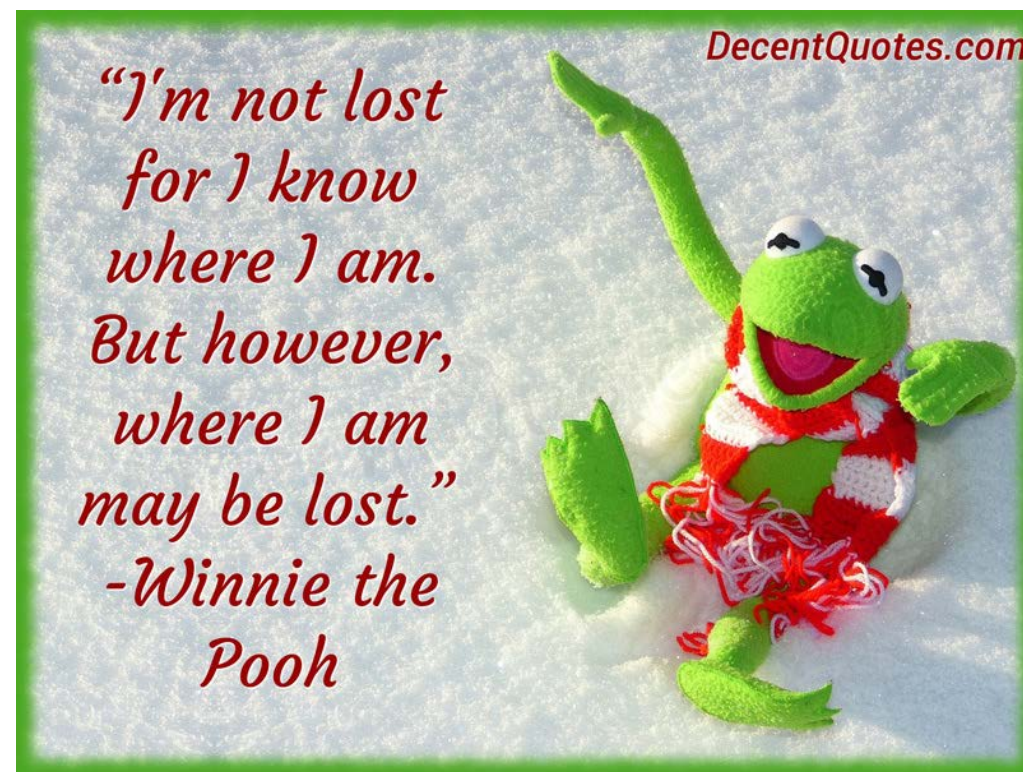
- Caused 50% increased risk of hospitalisation
- Increased emergency department visits and increased use of oral corticosteroids due to flare-ups
- It can lead to poor asthma symptom control and overuse of relievers and preventers

It has been associated with worse outcomes in asthma and COPD

Correcting patients' inhaler technique has been shown to improve asthma control, asthma-related quality of life and lung function

Compliance monitoring





Takeaway

Bronchodilators are the first-line Pharmacotherapy

- Pharmacotherapy is no longer for symptom relief only. They improve exercise capacity, improve quality of life, improve **performance** and reduce exacerbations
- **There is strong emerging evidence for Combination inhalers**
- Choice of medications is based in part on the availability of medication and the patient's response
- Choice of device should be individualized
- Guidelines including GOLD/GINA have proposed stepwise treatment algorithm, based on a combination of airflow obstruction (spirometry), symptoms, and risk of future exacerbations

Thank you