**COPD Overview** A Crawley, BSP © www.RxFiles.ca Sept 2015

## What is it?

- Progressive, partially reversible airway limitation
- Damage to the walls of the lungs → reduced elasticity → reduced ability of patient to exhale
- 4th leading cause of death in Canada; prevalence ~5%
- Primary cause (85% of cases) is smoking
- An estimated 15-20% of smokers develop COPD

Symptoms: Cardinal triad: dyspnea, chronic cough, and sputum production. Dyspnea is typically progressive, worsens with exercise, persistent; described as gasping. **Definitions:** Emphysema describes the damage to the lungs. Chronic bronchitis is defined as increased cough and sputum. Most COPD patients have features of both. Diagnosis: Spirometry post-bronchodilator FEV<sub>1</sub>/FVC < 0.7

Indicators: symptoms (dyspnea, cough, sputum), smoking history (10-20 pack-years or more), family history of COPD, environmental exposure to dust/chemicals. Screen for  $\alpha_1$ -antitrypsin deficiency in select patients (e.g. if atypical features, disease onset <45 years). Goals of therapy:  $\lor$  dyspnea,  $\land$  exercise tolerance,  $\land$  quality of life, &  $\sqrt{\phantom{a}}$  complications such as exacerbations & cor pulmonale. Comorbidities: common, especially depression and CV disease.

## Therapeutic Pearls / Nonpharmacologic Approach FOR ALL PATIENTS

- cannot demonstrate proper inhaler technique! Reassess at every visit.
- Establish individualized action plan e.g. respiratoryguidelines.ca/updated-cts-copd-action-plan
- Pulmonary rehab has proven benefits in symptomatic and recently hospitalized patients (NNT = 4 to prevent one hospitalization in patients with recent exacerbation)
- An estimated 50% of patients are non-adherent to COPD therapy and 50% of patients Encourage smoking cessation. Benefits (40% √ in both death & rate of lung function decline) apparent even in severe COPD ("never too late to quit!")

  - Pneumococcal vaccine recommended by guidelines (x1 dose, ?repeat in 5-10 years in severe COPD); however, only weak evidence of benefit available

An Approach to Treatment	Pharmacotherapy	General Agents	
STEP 1: Start short-acting bronchodilators.	SAMA ± SABA	• SABA: salbutamol ventolin, terbutaline BRICANYL • SAMA:	
Start here if: mild COPD, or \$ barriers to LAMA or LABA	<b>Benefit:</b> $\psi$ symptoms, may not $\psi$ AECOPD/hospitalizations	ipratropium ATROVENT ● Combo: salbutamol/ipratropium COMBIVENT	
STEP 2: Reassess inhaler technique.* Start long-acting a	ents. • LAMA + SABA PRN <u>or</u> LABA + SABA PRN ± SAMA PRN	LAMA: tiotropium spiriva, aclidinium TUDORZA, glycopyrronium	
Start here if: moderate to severe COPD	Benefit:   ✓ symptoms,   ✓ AECOPD/hospitalizations	SEEBRI, umecledinium INCRUSE • LABA: formoterol oxeze, salmeterol SEREVENT, indacaterol ONBREZ, olodaterol STRIVERDI	
Move here if: treatment failure in Step 1	LAMA often preferred as it may have 个 efficacy/tolerability vs LABA		
STEP 3: Poor symptom contr	• LAMA <u>&amp;</u> LABA + SABA PRN	• LAMA + LABA: single agent products as above, or	
Reassess inhaler technique*  Maximize broncho	ilator Benefit: Limited evidence vs LAMA alone; may ↓ symptoms	• LAMA + LABA combinations: aclidinium + formoterol DUAKLIR;	
Optimize long-acting agents. therapy first, since	AE are • Poor symptom control despite LAMA + LABA:	glycopyrronium + indacaterol истывко; tiotropium + olodaterol	
Move here if: treatment failure associated with ac	ing ICS LAMA + (ICS+LABA) + SABA PRN	INSPIOLTO; umecledinium + vilanterol ANORO	
in Step 2	<b>Benefit:</b> Limited evidence vs LAMA+LABA; possibly <b>√</b> symptoms		
► Frequent AECOPD	LAMA + (ICS+LABA) + SABA PRN	• LABA + ICS combinations: formoterol + budesonide	
(≥1 year):	Benefit: ICS+LABA	symbicort; salmeterol + fluticasone advair; vilanterol +	
	{If on LAMA+LABA+ICS⇒ option to stop ICS: similar exacerbation risk} wisdom	fluticasone BREO	
STEP 4: Reassess inhaler technique.* Specialist Referral.		• oxygen therapy • theophylline low dose UNIPHYL or roflumilast DAXAS • prophylactic azithromycin ZITHROMAX • n-acetylcysteine	

Move here if: COPD severe or unresponsive to therapy;  $\alpha_1$  antitrypsin deficiency; exacerbations severe/recurrent; respiratory failure; ? in diagnosis/management; symptoms disproportionate to FEV<sub>1</sub> \*Refer to a pharmacist or COPD Educator to review inhaler technique with the patient. Teaching sheets available online at www.RxFiles.ca & patient handouts at sk.lung.ca/health-professionals/resources/resptrec-resources

FEV <sub>1</sub>	MRC	Symptom/Disability	COPD Stage	
≥ 80%	1	Not troubled by breathlessness except with strenuous exercise.	At Risk	
≥ 60%	2	Short of breath when hurrying on the level or walking up a slight hill.	Mild	
F0 700/	3	Walks slower than most people of the same age on the level because of breathlessness, or has to stop for breath when walking at own pace on the level.		
50-79%	4	Stops for breath after walking about 100 meters (~ 1 block) or after a few minutes on the level.	Moderate	
30-49%	- 5	Too breathless to leave the house, or breathless when dressing or undressing.	Severe	
< 30%			Very Severe	

## Should I choose a LAMA or a LABA?

Both will improve symptoms; LAMAs (tiotropium) may be superior in ↓ exacerbations (but unclear if this applies to newer agents). LAMAs may also be better tolerated than LABAs (↓ withdrawal in RCTs). Often in clinical practice, LAMAs are the preferred starting point.

## Which LAMA / which LABA should I choose?

Consider: evidence (tiotropium, salmeterol, & formoterol are the most studied), devicespecific advantages (see Asthma & COPD: Inhalation Devices), adherence (once vs twice daily regimens), & onset (see COPD: Drug Comparison Chart). If a patient frequently makes mistakes using their device, re-educate or consider a switch to an alternate device.

Management of AECOPD (acute worsening of symptoms over >48 hours): • Initiate scheduled salbutamol and ipratropium; long-acting inhalers can be continued but should not replace short-acting bronchodilators. 2 Initiate prednisone 30-50mg po daily x 5 REDUCE - 10days. • Add antibiotic if both change in sputum purulence (colour) AND at least one of increased sputum volume or increased dyspnea vs baseline. Antibiotics should also be strongly considered if patient requires hospitalization. Antibiotic choice: amoxicillin, doxycycline. TMP/SMX, clarithromycin, azithromycin, cefuroxime, or cefprozil for low risk patients; amoxi-clav, levofloxacin, or moxifloxacin for high risk patients (high risk: severe COPD, coronary artery disease, chronic steroids, ≥ 4 exacerbations/yr, home oxygen, or recent antibiotics).

Prevention of AECOPD: optimization and adherence to meds; vaccinations (influenza, pneumococcal); avoid environmental triggers; smoking cessation; pulmonary rehab.

AE=adverse events AECOPD=acute exacerbation of COPD CV=cardiovascular DPI=dry powder inhaler FEV1=forced expiratory volume in 1 second FVC=forced expiratory vital capacity ICS=inhaled corticosteroid LABA=long-acting Beta2-Agonist LAMA=long-acting muscarinic antagonist TMP/SMX=trimethoprim/sulfamethoxazole

	0.5+2.5mg/2mL nebs; 20+100mcg soft mist Neb: 0.5/2.5mg (1 neb) inhaled QID prn [4 nebs]	evidence for combi	nation over a single agent (but commonly used)	\$ 113		
		and increased convenience vs using a LAMA + LABA in separate inhalers (but drug coverage for combo products varies)				
	Aclidinium + Formoterol <b>DUAKLIR</b> 400+12mcg DPI <b>✗</b> ⊗ <b>Genuair</b> : 400/12mcg (1 puff) inhaled twi	ice daily	Data for dual therapy is limited, but evidence suggests	\$ 98		
	Glycopyrronium + Indacaterol ULTIBRO 50+110mcg DPI	a statistically significant, although not clinicall significant. A in quality of life & lung function	a statistically significant, although not clinically significant, 个 in quality of life & lung function. SPARK	\$ 105		
Suc	Tiotropium + Olodaterol INSPIOLTO 2.5+2.5mcg soft mist X 🛇 💾 Respimat: 5/5mcg (2 puffs) inhaled once	e daily	Dual therapy is reasonable in patients poorly	\$ <mark>85</mark>		
ati	Umeclidinium + Vilanterol ANORO 62.5+25mcg DPI   Bellipta: 62.5/25mcg (1 puff) inhaled once	e daily	controlled on monotherapy.	\$ 107		
Ĕ		ombination: addition of ICS further $\Psi$ exacerbations vs LABA alone; useful in severe COPD if frequent exacerbations; withdrawal of ICS an option in some wisdow				
Ē	Formoterol + Budesonide SYMBICORT Turbuhaler: 12/400mcg (2 puffs) inhaled BID [24/800mcg]			\$ 110		
3	6+100, 6+200 mcg DPI <b>a Ø</b>		d & evidence to support, but some ambiguity in the evidence).			
	Formoterol + Mometasone ZENHALE HFA: 10/200mcg (2 puffs) inhaled BID	<ul> <li>Triple therapy (LAMA + LABA + ICS) is rational, but evidence is limited: may not</li></ul>		\$ 116		
	5+100, 5+200 mcg DPI X ⊗ (EDS asthma) Not officially approved for COPD					
	Salmeterol + Fluticasone propionate ADVAIR Diskus: 50/250mcg (1 puff) inhaled BID [100/1000mcg]			\$ 126		
	50+100, 50+250, 50+500 mcg DPI $\cong \mathscr{C}$ (ADVAIR HFA 25+125, 25+250mcg not officially COPD approval)		cer when using an MDI), $\uparrow$ risk of pneumonia [NNH = 16	[\$ 175]		
	Vilanterol + Fluticasone turoate BREO Ellipta: 25/100mcg (1 puff) inhaled once daily SUMMIT		A], may $\uparrow$ osteoporosis/fractures (conflicting evidence).	\$ 153		
	25+100mcg DPI	• BREO: fluticasone fu	rroate - more potent/longer lasting vs fluticasone propionate			
	Roflumilast DAXAS 500mcg tab X Ø PL 500mcg po once daily AE: diarrhea, nausea, HA, abd pain, N	√wt. Rare: depression,	: CB2, pricriodaro, pricriytorii	\$ 85		
e L	Theophylline LA, SR, UNIPHYL PL 200-400mg SR po daily	/DL AF. A LID resuses	☐ CYP 3A4,1A2: ↓theo: CBZ, phenytoin, rifampin, smoking	\$ 15 - 24		

Infrequently used due to AE/toxicity/DI. AE: ↑ HR, nausea, tremor

M: HR, CNS effects (insomnia, irritability), serum levels (<83 µmol/L)

100, 200, 300, (400°, 600°mg) UNIPHYL SR tabs

↑theo: allopurinol, cimetidine, ciprofloxacin,

erythromycin, febuxostat, fluvoxamine, norfloxacin,

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There is no evidence to suggest one device works better than another. Poor inhaler technique:  $\psi$  efficacy. Pt device dissatisfaction:  $\psi$  adherence. Choose device based on pros/cons below & patient preference.

beclomethasone QVAR olodaterol STRIVERDI HandiHaler: formoterol OXEZE salbutamol VENTOLIN aclidinium TUDORZA umecledinium INCRUSE salbutamol/ipratropium COMBIVENT tiotropium SPIRIVA formoterol/budesonide salmeterol SEREVENT aclidinium/formoterol DUAKLIR vilanterol/fluticasone BREO ciclesonide ALVESCO vilanterol/umecledinium fluticasone FLOVENT tiotropium SPIRIVA **SYMBICORT** salmeterol/fluticasone ADVAIR formoterol/mometasone tiotropium/olodaterol INSPIOLTO terbutaline BRICANYL **ANORO** ZENHALE Breezhaler: glycopyrronium SEEBRI salmeterol/fluticasone ADVAIR glycopyrronium/indacterol ULTIBRO ipratropium ATROVENT salbutamol VENTOLIN indacaterol ONBREZ **DEVICE** MDI Respimat HandiHaler, Breezhaler Turbuhaler **Diskus** Genuair Ellipta Delivers aerosolized Uses a spring to deliver a "soft Capsules containing medication Dry powder inhaler stream of medication mist" of medication over ~1.5 Description are pierced, containing a reservoir of Dry powder inhaler containing single dose blisters of medication. over ~0.2 seconds. seconds. then powder inside is inhaled. medication. Low inspiratory flow ≈ 20L/min required Breath-actuated: reduces need for hand-breath coordination Slower actuation may Rattling or whirring heard if Simple to use & less errors Simple to use; one Suitable for all ages. Few steps, easy to use Note: spacer strongly improve technique vs MDI capsule's contents inhaled (compared to HandiHaler or Breezhaler). during dose preparation vs step to open & load **DOSE COUNTER:** numbered recommended correctly. Can look to view HandiHaler dose. Sub-analysis of Dose is not lost even if DOSE COUNTER: by interval (frequency of empty capsules (and Breezhaler Provides visual (window RCT data: 95% of regardless of age (see base is twisted multiple displays exact number has clear capsules). comments below). interval varies by changes green  $\rightarrow$  red) & asthmatics able to use times: however dose of remaining doses Spacer with a mask medication); loading base Low inspiratory effort needed audible ("click") feedback correctly after only counter will no longer available for cognitive locks to signal empty **DOSE COUNTER:** each capsule when dose taken correctly one demonstration be accurate **Pros** impairment, frail, **COMBIVENT** Respimat has equals 1 dose; thus no dose In one study, majority of In one study, majority DOSE COUNTER: every < 5 years old, etc. cost advantage over counter required patients (80%) preferred of patients (>60%) 20<sup>th</sup> dose numbered to Can be used with **COMBIVENT** nebules. preferred Ellipta over Genuair over HandiHaler. give approximation of DOSE COUNTER: every mechanical ventilation **INSPIOLTO** Respimat has MDI. Diskus, or doses remaining 10<sup>th</sup> dose numbered: (e.g. in critical care cost advantage over other HandiHaler. LAMA/LABA combos. loading button locks to DOSE COUNTER: units) signal empty displays exact number Note: Pharmacies should pre-load the of remaining doses Respimat canister before dispensing with large numbers **DOSE COUNTER:** most • Tipping device before inhalation (e.g. upside down) can expel the dose Requires reasonable Multi-step process: may be devices lack dose strength to spring-load dose difficult to use for patients with • When empty, remaining • Short expiry date after No way to identify if Some patients may counter (exceptions: Incorrect rate of inhalation poor manual dexterity (eg: desiccant can still be removal from experience a bitter taste proper inspiratory **ADVAIR, ZENHALE)** results in cough arthritic hands, Parkinson's heard - patients may protective packaging: with aclidinium effort is being Spacer can be Not approved for kids or for disease) or cognitive impairment think there are doses left ADVAIR = 1 month: achieved cumbersome; use with a spacer Capsules are packaged in foil DOSE COUNTER: displays **SEREVENT** = 6 weeks Short expiry date (6) however, if using only New device to the market blisters; may be difficult to a "zero", but it can be - Exception: weeks) after removal at home in the limited real-world remove (for some) and are light difficult to tell when the **VENTOLIN** = 1 year from protective Cons morning/evening, experience and moisture sensitive indicator reaches this packaging additional burden is Requires priming (until mist Patients have been known to mark Medications for Diskus New device to the market - limited real-world low. is visible, then 3 more swallow capsules instead of Humidity/moisture (e.g. inhalers tend to be experience. Susceptible to freezing sprays) if **first time use** OR if inhaling them. exhaling into device, among the most Requires priming (x 4 not used for  $\geq$  21 days. Pieces of capsule may be inhaled storing in bathroom) can expensive in their class Requires priming (x 1 spray) sprays) if not used for if pierced more than once. clump drug in reservoir if not used for  $\geq$  3 days. ≥ 5 days • Requires sharp, forceful inhalation of breath to get full dose - some patients (e.g. < 5 years old, some COPD patients with severe symptoms) will be unable to achieve adequate flow rate.

COPD=chronic obstructive pulmonary disease MDI=metered dose inhaler RCT=randomized controlled trial

More inhalation devices listed & compared at www.rxfiles.ca

- Use a spacer with an MDI: ↑ drug delivery to lungs; ↓ need for hand-breath coordination; ↓ systemic absorption; ↓ local adverse effects e.g. hoarseness & thrush with corticosteroids, dry mouth with anticholinergics.
- If on more than one inhaler: (1) consider using the same device for all medications; (2) use the bronchodilator first & the anti-inflammatory last; (3) wait ~5 minutes between puffs of different medications.
- Nebulizer/compressor solution: (available for budesonide, ipratropium, salbutamol, and salbutamol/ipratropium) expensive without added benefit versus spacer except possibly in very young & very old, drug entering room air may 1 infection transmission, time consuming, & can affect eyes. Useful during exacerbations for patients in too much distress to use proper inhaler technique, but spacer preferred.
- General inhaler technique: (1) prepare dose, (2) breathe out, (3) inhale medication, (4) hold 10 seconds, (5) breathe out. (See RxFiles Inhaler Technique.) May take a second breath from dry powder devices to ensure the entire dose is inhaled. Rinsing mouth (and spitting) after anticholinergics and corticosteroids decreases side effects. Best to wait ~1 minute between puffs of the same medication.

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