Respiratory Updates

Curtis Addison *MD, FRCPC* (Respirology, Interventional Pulmonology)

Pan-Northern Clinical Rounds

March 3, 2021

Learning Objectives

1. To describe the appropriate treatment of patients diagnosed with COVID-19.

2. Demonstrate the appropriate way to diagnose and treat COPD.

3. Identify how to manage acute exacerbations of COPD in the outpatient and hospital settings.

4. To explain indications for referral to respirology including identifying expanded respirology services in Northeastern Ontario.

Disclosure of Affiliations, Financial Support, and Mitigating Bias

Speaker Name: Dr. Curtis Addison

Affiliations: Honoraria: AstraZeneca (Train-the-Trainer)

Financial Support: Dr. Addison has received payment from AstraZeneca, whose products are being discussed in this program

Mitigating Potential Bias: Respiratory medications are being discussed in terms of their pharmacologic class and device

Hydroxychloroquine

Patients Diagnosed with COVID-19

1. Ensure the patient is placed on appropriate precautions.
   "…minimum of Droplet and Contact Precautions" *PHAC*
   Centre-specific Infection Control policies, up to/including N95/helmets, double-gloving
2. Supportive care
3. Careful search for and treatment of comorbid disease
4. COVID-19 treatments

Treatment	Mechanism	Evidence (April 17, 2020)	Evidence (February 2021)
Hydroxychloroquine		Reduced in-vitro activity[1] Small *nonrandomized* CT in mild COVID-19: slightly faster time to improvement in cough, fever and CXR.[2]	RCT-No significant difference in mean reduction of viral load, hospitalization, time to complete resolution of symptoms.[6]
+ azithromycin		Nonrandomized trial, reduced virus carriage at day 6.[2]	RCT-No improvement in clinical status at 15 days.[7]
Remdesivir	Nucleotide analogue (prevents viral replication)	in-vitro activity[3] Animal studies in SARS and MERS-CoV[4] Case series	RCT-Reduced time to recovery. No reduction in mortality or need for IMV.[8]
Lopinavir-ritonavir	Protease inhibitors (prevents viral replication)	RCT severe COVID-19, no change in time to clinical improvement, improved mortality trend[5]	RCT-No improvement in 28-day mortality or need for IMV[9]
Tocilizumab	Anti-IL6 Reduced “cytokine storm”	Case reports	Preliminary unpublished data, 2 RCTs: reduced 28-day mortality[10]; reduced in-hospital mortality
Convalescent plasma	Antibodies	Case series	No mortalty benefit in severe disease.11 Reduced severe respiratory disease in outpatients.12

References for Investigational Treatments

1. Yao et al. In Vitro Antiviral Activity and Projection of Optimized Dosing Design of Hydroxychloroquine for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). *Clin Infect Dis*. **2020**. doi: 10.1093/cid/ciaa237

2. Gautret et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *Int J Antimicrob Agents*. **2020**. doi.org/10.1016/j.ijantimicag.2020.105949

3. Wang et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res.* **2020**; 30(*3*) 269-271. doi: 10.1038/s41422-020-0282-0

4. Sheahan et al. Broad-spectrum antiviral GS-5734 inhibits both epidemic and zoonotic coronaviruses. Sci Transl Med. **2017**; 9(*396*). doi: 10.1126/scitranslmed.aal3653

5. Cao et al. A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19. N Engl J Med. 2020. doi: 10.1056/NEJMoa2001282

References for Investigational Treatments

6. Mitjà, O. et al. Clin. Infect. Dis. 2020. DOI: 10.1093/cid/ciaa1009 [Online]
7. Cavalcanti, A.B. et al. *N. Engl. J. Med.* **2020**; 383:2041-205. DOI: 10.1056/NEJMoa2019014
8. Beigel, J.H. N Engl J Med. 2020;383(19):1813. DOI: 10.1056/NEJMoa2007764
9. Horby, P.W. et al. *Lancet*. **2020**;396(10259):1345-1352. DOI: 10.1016/S0140-6736(20)32013-4.
10. Preliminary results manuscript: RECOVERY_Tocilizumab_MainPaper_medRxiv (1253)
11. Piechotta V, et al. *Cochrane Database Syst. Rev*. **2020**;7(7):CD013600. doi: 10.1002/14651858.CD013600.pub2. Update in: Cochrane Database Syst Rev. 2020 Oct 12;10:CD013600. PMID: 32648959; PMCID: PMC7389743.

Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a living systematic review - PubMed (nih.gov)

Outpatients

- Monoclonal antibodies
  - Use in context of clinical trial
    - ***Bamlanivumab alone (BLAZE-1)***
      - Phase 2/3 showed trend toward reduced ED visits or hospitalizations
    - Bamlanivumab-etesevimab (BLAZE-1)
      - Phase 3 RCT, 1035 outpatients, unpublished preliminary data:
      - Reduced hospitalization or death (2% vs 7 %)
    - Casirivimab-imdevimab
      - RCT, 799 outpatients patients, unpublished, preliminary results:
        - Fewer medical visits (2.8% vs 6.5%)
        - Fewer ED visits (3% vs 9%)
- Convalescent plasma
  - RCT 160 patients, Adults ≥ 75 or ≥ 65 with at least one specific comorbidity
  - Reduced severe respiratory disease (16% vs 32%)

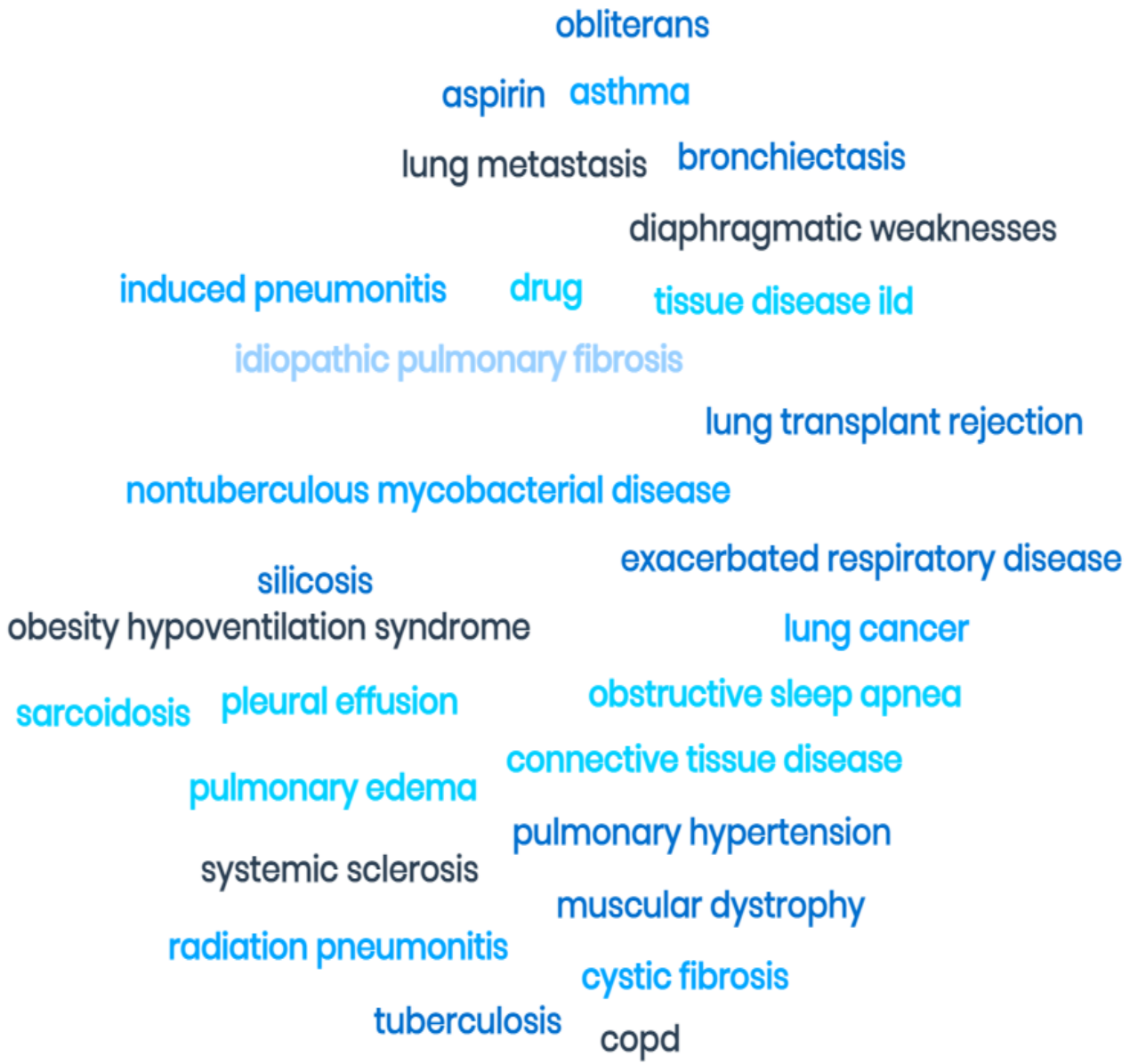
Severe disease

- Remdesivir
- Dexamethasone
- Tocilizumab: require high-flow O2 or IMV within 48 hours of ICU admission

COVID-19

- Lessons to learn from the pandemic:
  - The differential of COVID-19 is extremely broad
  - Many patients with “suspected COVID-19” have an alternative diagnosis with highly effective treatment
  - Don’t routinely use unproven treatments
  - Don’t abandon high-value care due to infection control concerns
  - Don’t withhold life-saving therapy due to infection control concerns
  - Don’t restrict prescribing of medications with strong evidence-based indications for common conditions
  - There are unintended consequences when using fear to change public behaviour

Diseases in Respirology



COPD:
A Guide to Assessment and Management

Definition

- Respiratory disorder largely caused by smoking
- Progressive, partially reversible airway obstruction and lung hyperinflation, systemic manifestations, and increasing frequency and severity of exacerbations
- Post-bronchodilator $FEV_1/FVC < 70\ \%$

Definition – GOLD 2021

- Common, preventable and treatable disease
- Persistent respiratory symptoms and airflow limitation
- Due to airway and/or alveolar abnormalities
- Usually caused by exposure to noxious particles or gases
- Influenced by host factors including abnormal lung development

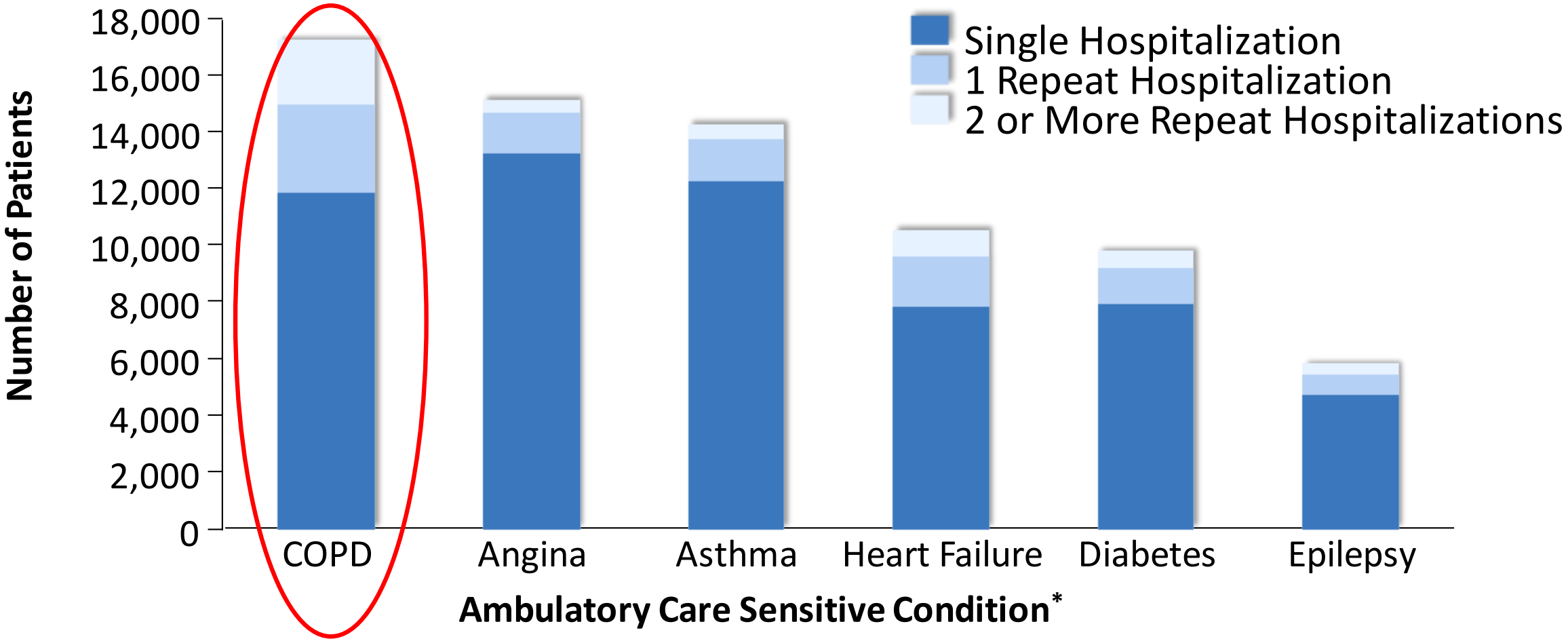
Epidemiology

- 3rd leading cause of death worldwide (WHO)
- Prevalence:
  - 3.9 % men, 4.8 % women in Canada (probably COPD, by health-care professional reporting)
  - Studies suggest up to 50 % undiagnosed
  - 30-70 % no or suboptimal treatment

  - Highest rate of hospital admissions among major chronic illnesses in Canada[1]

[1] Information CIfH. Health Indicators. Ottawa: CIHI; 2008, 2008

COPD: A Leading Cause of Hospital Admissions

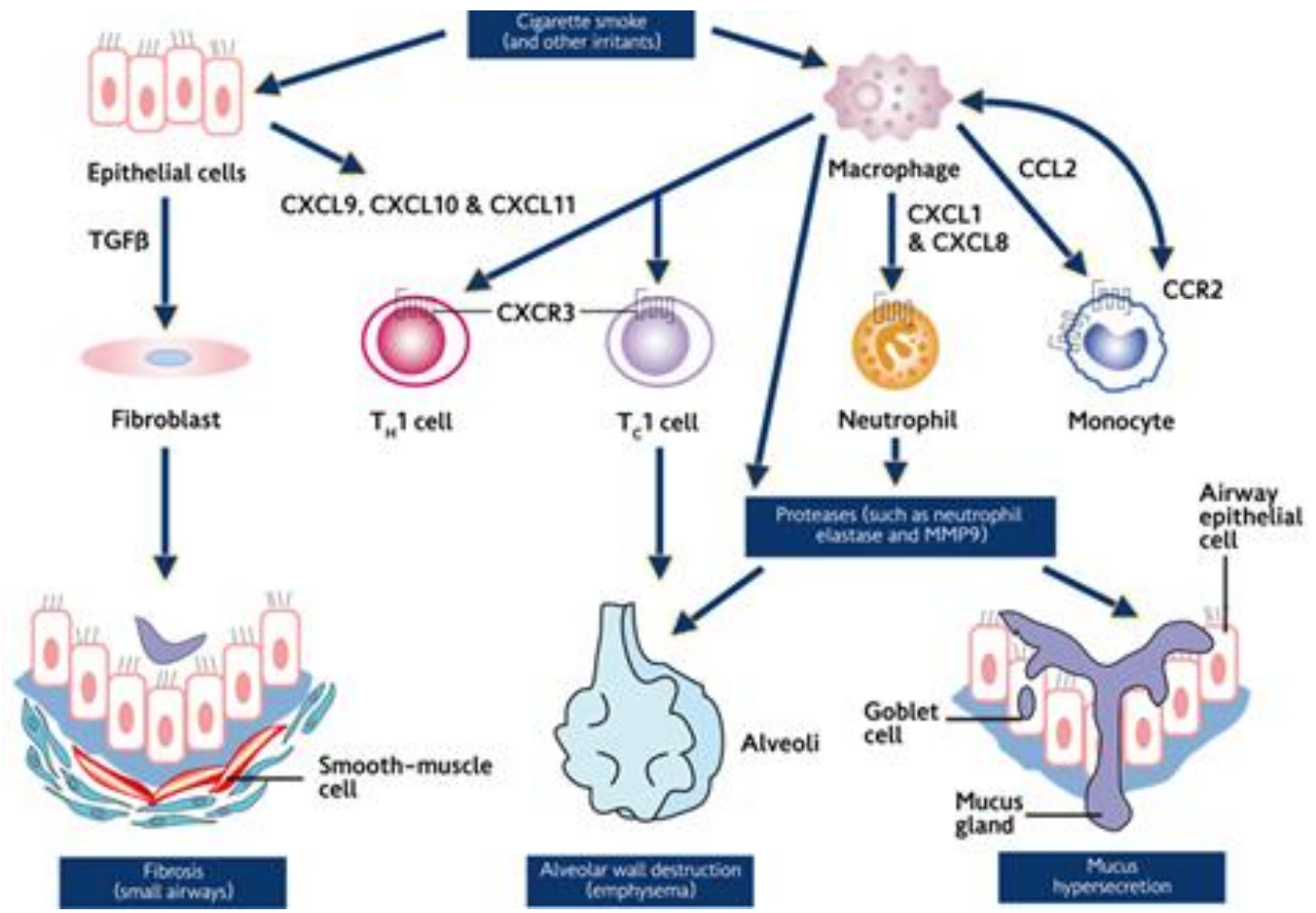


*An ambulatory care sensitive condition is a condition that is normally manageable on an outpatient basis

Data are for the Canadian population, excluding Quebec Canadian Institute for Health Information. Health Indicators 2008. Ottawa: CIHI; 2008.

Pathophysiology

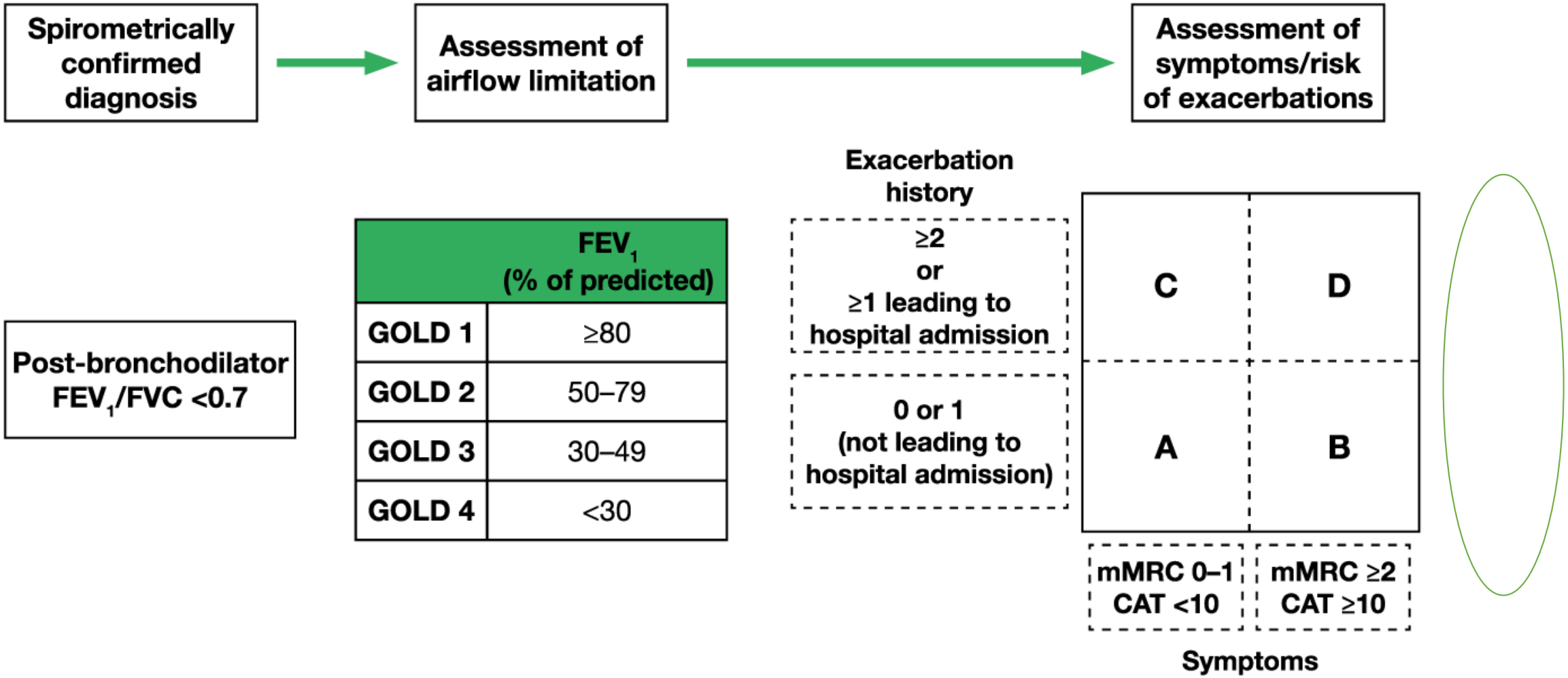
- Airway inflammation
  - Persists long after stimulus is removed
- edema, remodelling with fibrosis, secretions
- Compression by overinflated alveoli
- Emphysematous destruction leading to loss of tethering of airways



Diagnosis

- Targeted screening:
  - Canadian Lung Associations suggests:
    - current or ex-smokers AND
      - Regular coughing
      - Regular phlegm
      - Dyspnea with simple chores
      - Wheezing on exertion or at night
      - Frequent colds that last longer than others
- Spirometry:
  - GOLD Criteria:
    - $FEV_1/FVC < 70\ \%$

GOLD 2017 “Refined ABCD Assessment Tool”



FEV_1=forced expiratory volume in the first second; FVC=forced vital capacity; mMRC=modified Medical Research Council; CAT=COPD assessment test.

Evaluation

1. Smoking history (pack-years), current smoking, occupational exposures
2. Comprehensive Assessment of Symptoms

The Modified Medical Research Council (MMRC) Dyspnoea Scale

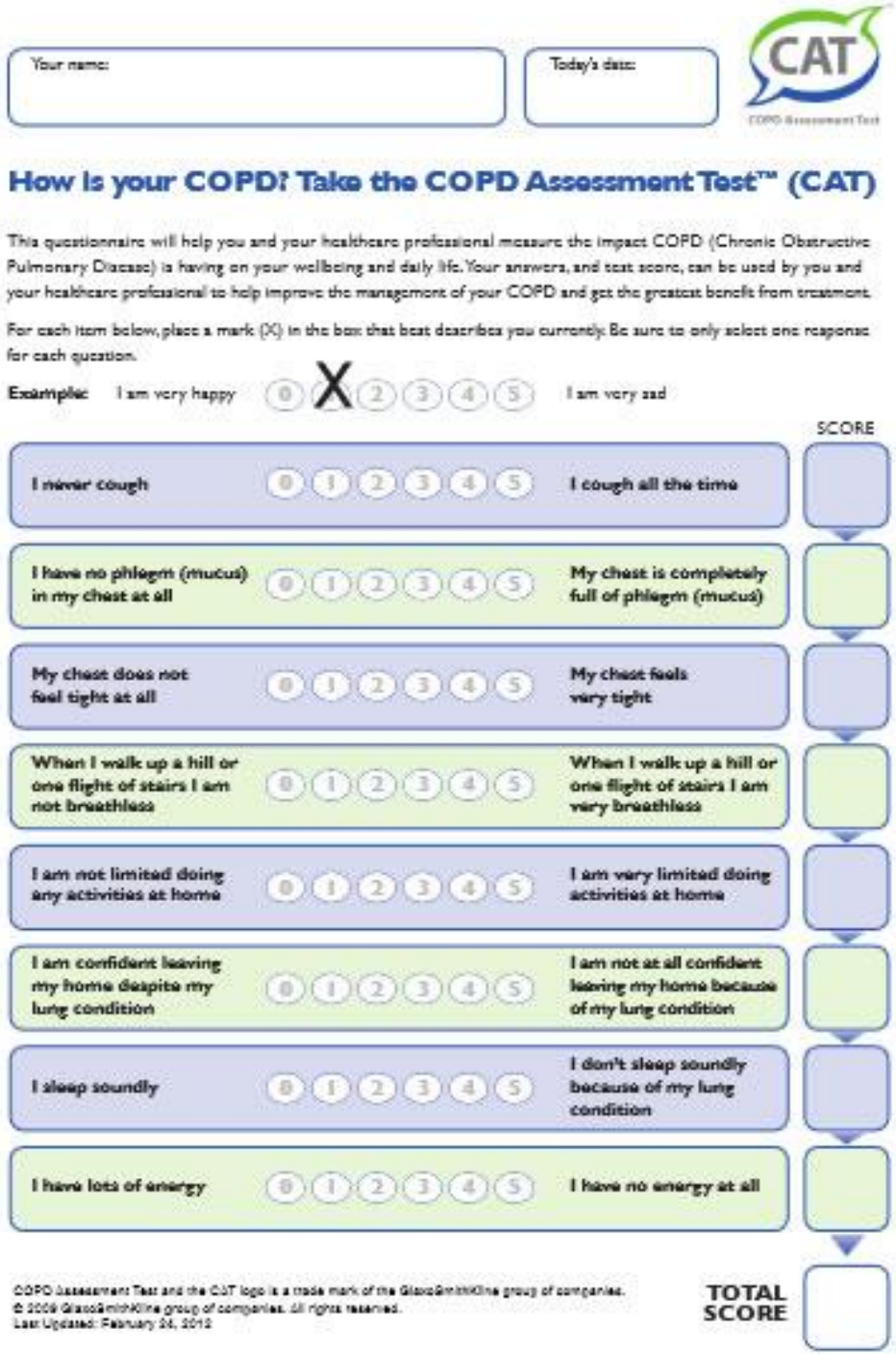
Grade of dyspnoea	Description
0	Not troubled by breathlessness except on strenuous exercise
1	Shortness of breath when hurrying on the level *or* walking up a slight hill
2	Walks slower than people of the same age on the level because of breathlessness *or* has to stop for breath when walking at own pace on the level
3	Stops for breath after walking about 100 m *or* after a few minutes on the level
4	Too breathless to leave the house *or* breathless when dressing or undressing

Predicts future mortality

Correlates well with other measures of health status

CAT

- Comprehensive assessment
- Feasible for clinical use



Your name:

Today's date:

CAT
COPD Assessment Test

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.

For each item below, place a mark (X) in the box that best describes you currently. Be sure to only select one response for each question.

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

		SCORE
I never cough	0 1 2 3 4 5	I cough all the time
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)
My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	When I walk up a hill or one flight of stairs I am very breathless
I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition
I have lots of energy	0 1 2 3 4 5	I have no energy at all
		TOTAL SCORE

Last Updated: February 24, 2012

Evaluation

3. Frequency and Severity of exacerbations
    - Antibiotic/steroid requirements
    - Number of hospitalizations
4. Assessment of complications
    - Right-sided volume overload (cor pulmonale)
    - Malnutrition
5. Assessment of Comorbidities
    - Heart disease
    - Lung cancer
    - Osteoporosis
    - Mood/anxiety disorders
6. Current medical treatment
    - Ask about inhaled therapy specifically
    - Home O_2 therapy
    - Immunizations: pneumococcal, influenza
    - Pulmonary rehabilitation

Alpha-1 Antitrypsin Deficiency

	GOLD 2017	CTS 2012 Position Statement
Screening	All patients with COPD	COPD and either: • Age < 65 • Smoking < 20 pack·years (Grade 1A)
Treatment (A1AT augmentation)	All patients with progressive lung disease	COPD • FEV1 25-80 % predicted • Nonsmoking or exsmoking • Emphysema • A1AT ≤ 11 µmol/L • Optimal pharmacological and nonpharmacological therapy (Grade 2B – CT lung density; Grade 2C – mortality)

Management

1. Education
2. **Smoking Cessation (A)**
3. Inhaled therapy (A)
4. Azithromycin (A)
5. Roflumilast (A)
6. Mucolytics (B)
7. Vaccinations: pneumococcal (B) and **annual influenza** (B)
8. Written Action Plan
9. Pulmonary Rehabilitation (A)
   - Most effective therapy for improving symptoms, exertional tolerance, and quality of life
   - Indications: stable, symptomatic: reduced activity and increased dyspnea despite optimal medical management, post-exacerbation
10. **Oxygen therapy (A)**
11. NIPPV (B)
12. Nutritional Support (B)
13. Lung volume reduction surgery (A)
    - Ambulatory, symptomatic patients with upper-lobe predominant emphysema, low post-rehab exercise tolerance
14. Bronchoscopic interventions (B)
15. Lung transplantation (C)
    - FEV_1 less than 25 %, Pco_2 > 55 mmHg, or pulmonary hypertension with deterioration
16. Palliation

My COPD Action Plan _____ Date _____
Patient's Copy (Patient's Name)

Canadian Respiratory Guidelines

COPD Treatable. Preventable.

This is to tell me how I will take care of myself when I have a COPD flare-up.

My goals are _____

_____

My support contacts are _____ and _____
(Name & Phone Number) (Name & Phone Number)

My Symptoms	I Feel Well	I Feel Worse	I Feel Much Worse URGENT
I have sputum.	My usual sputum colour is: _____	Changes in my sputum, for **at least** 2 days. *Yes* ☐ *No* ☐ OR	My symptoms are not better after taking my flare-up medicine for 48 hours.
I feel short of breath.	When I do this: _____ _____	More short of breath than usual for **at least** 2 days. *Yes* ☐ *No* ☐	I am very short of breath, nervous, confused and/or drowsy, and/or I have chest pain.

My Actions	Stay Well	Take Action	Call For Help
	I use my daily puffers as directed.	If I checked 'Yes' to one or both of the above, I use my **prescriptions** for COPD flare-ups.	I will call my support contact and/or see my doctor and/or go to the nearest emergency department.
	If I am on oxygen, I use _____L/min.	I use my daily puffers as usual. If I am **more** short of breath than usual, I will take ___ puffs of _____ up to a **maximum** of ___ times per day.	**I will dial 911.**
		I use my breathing and relaxation methods as taught to me. I pace myself to save energy.	**Important information:** I will tell my doctor, respiratory educator, or case manager **within 2 days** if I had to use any of my flare-up prescriptions. I will also make follow-up appointments to review my COPD Action Plan twice a year.
		If I am on oxygen, I will increase it from ___ L/min to ___ L/min.	

Notes:

THE LUNG ASSOCIATION™ L'ASSOCIATION PULMONAIRE

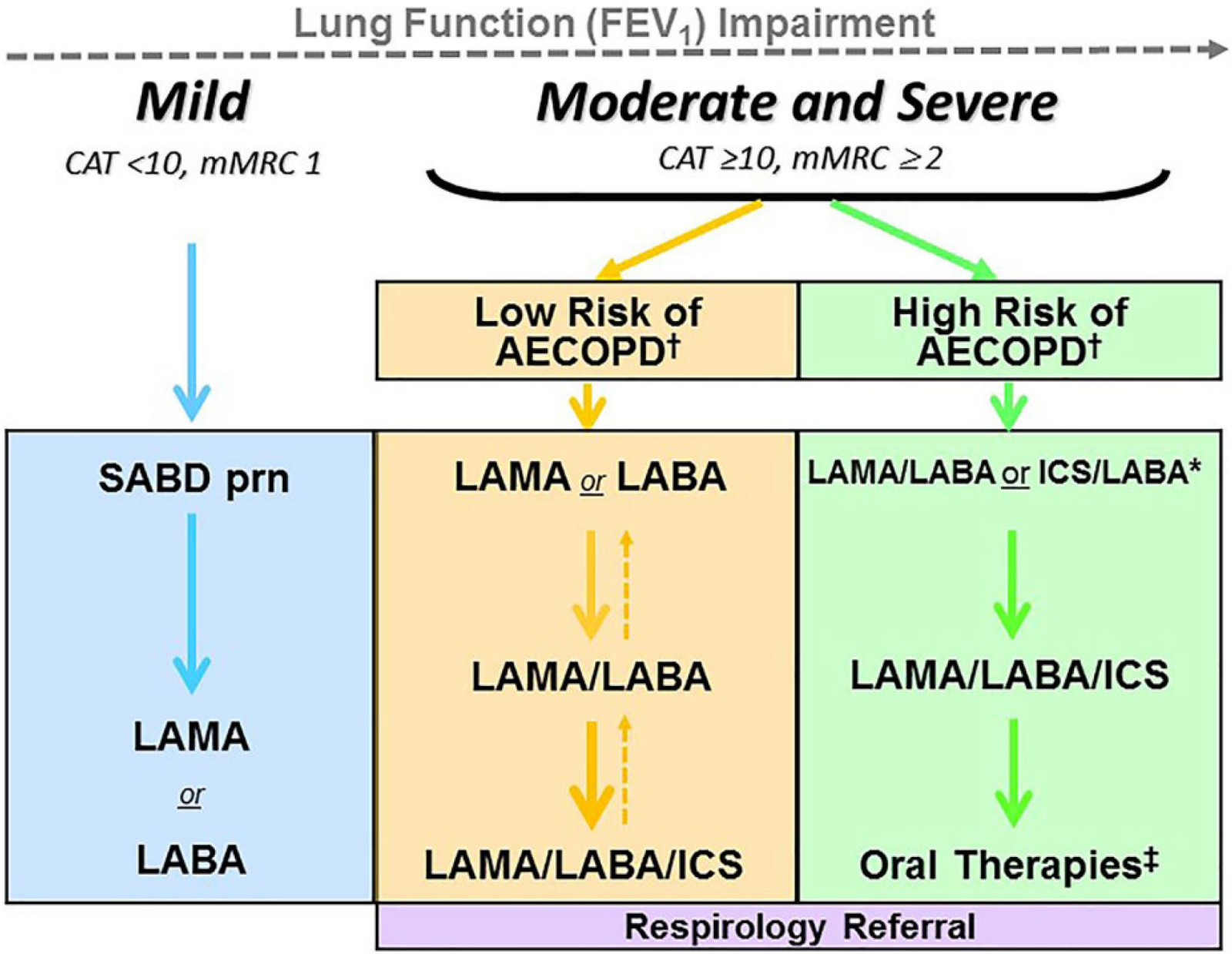
CANADIAN THORACIC SOCIETY SOCIÉTÉ CANADIENNE DE THORACOLOGIE

Produced in collaboration with the *COPD & Asthma Network of Alberta (CANA)*.
The Canadian Thoracic Society (CTS) acknowledges the past contributions of *Living well with COPD* and the *Family Physician Airways Group of Canada*.

Oxygen Therapy

- Indications:
  - $PaO_2 \leq 55$ mmHg
  - $PaO_2 \leq 60$ mmHg plus one of:
    - Ankle edema
    - Cor pulmonale
    - Polycythemia (Hct > 56 %)

CTS Guidelines 2019



Management of Exacerbations

- Bronchodilators
- Antibiotics for purulent exacerbations (1A)
- Systemic corticosteroids for purulent exacerbations (1A)
  - Prednisone 40 mg po daily for 5 days
- NIV for severe exacerbations with pH <7.30
- Intubate patients with severe exacerbations and classical "contraindications" to NIV

Respiratory MEDICATIONS

lung health starts now — lung health foundation

RELIEVERS

Short-Acting Beta2-Agonist (SABA)

Airomir®†◊
(salbutamol) *Valeant*
Strength: 100mcg
Capacity: 200 actuations/canister, 100 actuations for hospital pack

Bricanyl® Turbuhaler®*†
(terbutaline) *AstraZeneca*
Strength: 0.5mg
Capacity: 100 or 200 doses/device

Ventolin® HFA *†◊
(salbutamol) *GlaxoSmithKline§*
Strength: 100mcg
Capacity: 200 actuations/canister

Ventolin® Diskus®*†
(salbutamol) *GlaxoSmithKline§*
Strength: 200mcg
Capacity: 60 blisters/device

Salbutamol HFA generic products such as:
Apo-Salvent® *Apotex*, Salbutamol HFA *Sanis*, Novo-Salbutamol HFA *Teva*

Short-Acting Muscarinic Antagonist (SAMA) (Anti-cholinergic)

Atrovent® HFA†◊
(ipratropium) *Boehringer Ingelheim*
Strength: 20mcg
Capacity: 200 actuations/canister

CONTROLLERS / MAINTENANCE

Inhaled Corticosteroids (ICS)

Alvesco®*◊
(ciclesonide) *AstraZeneca*
Use: OD or BID
Strength: 100mcg, 200mcg
Capacity: 120 actuations/canister

Arnuity™ Ellipta®*
(fluticasone furoate)
GlaxoSmithKline§
Use: OD
Strengths: 100mcg, 200mcg
Capacity: 14 or 30 blisters/device

Asmanex® Twisthaler®*
(mometasone) *Merck*
Use: OD or BID
Strength: 100mcg, 200mcg, 400mcg
Capacity: 30 (100 & 400mcg) or 60 (200 & 400mcg) doses/device

Flovent® HFA*◊
(fluticasone propionate)
GlaxoSmithKline§
Use: BID
Strength: 50mcg, 125mcg, 250mcg
Capacity: 120 actuations/canister

Flovent® Diskus®*
(fluticasone propionate)
GlaxoSmithKline§
Use: BID
Strength: 100mcg, 250mcg, 500mcg
Capacity: 60 blisters/device

Pulmicort® Turbuhaler®*
(budesonide) *AstraZeneca*
Use: BID
Strength: 100mcg, 200mcg, 400mcg
Capacity: 200 doses/device

Qvar™*◊
(beclomethasone) *Valeant*
Use: BID
Strength: 50mcg, 100mcg
Capacity: 200 actuations/canister

Long-Acting Bronchodilators also known as: Long-Acting Beta2-Agonist (LABA)

Foradil®*† via Aerolizer®
(formoterol) *Novartis*
Use: BID
Strength: 12mcg
Capacity: 60 capsules/carton

Onbrez® Breezhaler®†
(indacaterol) *Novartis*
Use: OD
Strength: 75mcg
Capacity: 10 or 30 capsules/carton

Serevent® Diskus®*†
(salmeterol) *GlaxoSmithKline§*
Use: BID
Strength: 50mcg
Capacity: 60 blisters/device

Oxeze® Turbuhaler®*
(formoterol) *AstraZeneca*
Use: BID
Strength: 6mcg, 12mcg
Capacity: 60 doses/device

Combination ICS/LABA

Advair® Diskus®*†
(fluticasone propionate/salmeterol)
GlaxoSmithKline§
Use: BID
Strength: 100/50mcg, 250/50mcg, 500/50mcg
Capacity: 28 or 60 blisters/device

Advair®*◊
(fluticasone propionate/salmeterol)
GlaxoSmithKline§
Use: BID
Strength: 125/25mcg, 250/25mcg
Capacity: 120 actuations/canister

Breo® Ellipta®*†
(fluticasone furoate/vilanterol) *GlaxoSmithKline§*
Use: OD
Strength: 100/25mcg*†, 200/25mcg*
Capacity: 14 or 30 blisters/device

Symbicort® Turbuhaler®*†
(budesonide/formoterol)
AstraZeneca
Use: OD or BID
Strength: 100/6 mcg, 200/6mcg (FORTE)
Capacity: 120 doses/device

Zenhale®*◊
(mometasone/formoterol)
Merck
Use: BID
Strength: 100/5mcg, 200/5mcg
Capacity: 120 actuations/canister

Wixela® Inhub®*†
(fluticasone propionate/salmeterol) *Mylan Inc.*
Use: BID
Strength: 100/50mcg, 250/50mcg, 500/50mcg
Capacity: 60 blisters/device

Other Fluticasone/salmeterol products:
pms-Fluticasone propionate/Salmeterol DPI

Combination LAMA/LABA

Anoro™ Ellipta®†
(umeclidinium/vilanterol)
GlaxoSmithKline§
Use: OD
Strength: 62.5/25mcg
Capacity: 7 or 30 blisters/device

Duaklir™ Genuair®†
(aclidinium/formoterol) *AstraZeneca*
Use: BID
Strength: 400mcg/12mcg
Capacity: 60 actuations/device

Inspiolto™ Respimat®†
(tiotropium/olodaterol)
Boehringer Ingelheim
Use: OD
Strength: 2.5/2.5mcg per actuation
Capacity: 28 or 60 actuations/cartridge

Ultibro®Breezhaler®†
(indacaterol/glycopyrronium) *Novartis*
Use: OD
Strength: 110mcg/50mcg
Capacity: 6 or 30 capsules/carton

Long-Acting Muscarinic Antagonist (LAMA) also known as: Long-Acting Anticholinergic (LAAC)

Incruse™ Ellipta®†
(umeclidinium) *GlaxoSmithKline§*
Use: OD
Strength: 62.5mcg
Capacity: 7 or 30 blisters/device

Seebri® Breezhaler®†
(glycopyrronium) *Novartis*
Use: OD
Strength: 50mcg
Capacity: 10 or 30 capsules/carton

Spiriva®† via HandiHaler®
(tiotropium) *Boehringer Ingelheim*
Use: OD
Strength: 18mcg
Capacity: 10 or 30 capsules/carton

Spiriva®*† Respimat®
(tiotropium)
Boehringer Ingelheim
Use: OD
Strength: 2.5mcg/actuation
Capacity: 28 or 60 actuations/cartridge

Tudorza® Genuair®†
(aclidinium) *AstraZeneca*
Use: BID
Strength: 400mcg
Capacity: 30 or 60 actuations/device

Combination ICS/LABA/LAMA

Trelegy® Ellipta®
(fluticasone furoate/umeclidinium/vilanterol) *GlaxoSmithKline§*
Use: OD
Strength: 100/62.5/25mcg
Capacity: 7 or 30 blisters/canister

Combination SAMA/SABA

Combivent® Respimat®†
(ipratropium/salbutamol) *Boehringer Ingelheim*
Use: QID
Strength: 20/100mcg
Capacity: 120 actuations/cartridge
Product monograph recommends:
1 inhalation 4 times/day for COPD

Additional Medications

- **Leukotriene Receptor Antagonists (LTRA)*:** Accolate® (zafirlukast) *AstraZeneca*, Singulair® (montelukast) *Merck*
- **IL-5 Inhibitor*:** Cinqair™* (reslizumab) *Teva*, Nucala®* (mepolizumab) *GlaxoSmithKline§*, Fasenra® (benralizumab) *AstraZeneca*
- **Anti-IgE*:** Xolair® (omalizumab) *Novartis*
- **Oral Corticosteroid (Oral Corticosteroids)*†:** Prednisone *e.g. Apotex, Teva, Jaapharm, Pro Doc Ltée*
- **Methylxanthines†:** (aminophylline, oxtriphylline, theophylline)
- **Phosphodiesterase-4 inhibitor†:** Daxas®† (roflumilast) *AstraZeneca*
- **Macrolides†:** e.g. Azithromycin
- **Mucolytic†:** oral N-acetylcysteine

◊**Note:** The addition of a valved-holding chamber (spacer) with a pMDI is helpful in improving coordination, reducing side effects and increasing drug delivery and deposition (CTS 2010 Asthma Guidelines—respiratoryguidelines.ca)

Acronyms: OD = Once daily, BID = Twice Daily, QID = Four times daily **Symbols:** *Indicated for the treatment of Asthma, †Indicated for the treatment of COPD, ◊Indicated for use with a valved-holding chamber (spacer).

This is not a complete list of respiratory medications. **Please refer to the respective product monographs for detailed information on indications, contraindications, adverse events, dosing and administration and patient selection.** Health Canada Drug Product Database: https://health-products.canada.ca/dpd-bdpp/index-eng.jsp This chart is provided for information purposes only. Medications are listed in alphabetical order.

Version: February 2021 Electronic most-updated version can be accessed at https://hcp.lunghealth.ca/clinical-tools/ This document was created and developed in partnership with the Primary Care Asthma Program (PCAP) and the Ontario Lung Association © ASTH0011

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 3, 2018 VOL. 378 NO. 18

Once-Daily Single-Inhaler Triple versus Dual Therapy in Patients with COPD

David A. Lipson, M.D., Frank Barnhart, D.V.M., Noushin Brealey, M.D., Jean Brooks, M.Sc., Gerard J. Criner, M.D., Nicola C. Day, Ph.D., Mark T. Dransfield, M.D., David M.G. Halpin, M.D., MeiLan K. Han, M.D., C. Elaine Jones, Ph.D., Sally Kilbride, M.Sc., Peter Lange, M.D., David A. Lomas, M.D., Ph.D., Fernando J. Martinez, M.D., Dave Singh, M.D., Maggie Tabberer, M.Sc., Robert A. Wise, M.D., and Steven J. Pascoe, M.B., B.S., for the IMPACT Investigators

Triple-combined inhaler

- Population: COPD, age ≥ 40, CAT ≥10 + FEV1 <50% OR 2 mod or 1 severe exacerbation
- Primary outcome: Mod-severe exacerbations
  - 0.91/yr vs 1.07/yr (ICS/LABA) vs 1.21 (LABA/LAMA) (p<0.001)
- Secondary outcomes:
  - FEV_1 +97 mL (ICS/LABA), +54 mL (LABA/LAMA)
  - SGRQ decrease by ≥ 4 points
    - (42% vs 34% (ICS/LABA) vs 34% (LABA/LAMA)
- Protocol-defined other outcomes:
  - Death from any cause (HR 0.58, p=0.01)

Cochrane Library

Cochrane Database of Systematic Reviews

Non-invasive ventilation for the management of acute hypercapnic respiratory failure due to exacerbation of chronic obstructive pulmonary disease (Review)

Osadnik CR, Tee VS, Carson-Chahhoud KV, Picot J, Wedzicha JA, Smith BJ

NIV for AECOPD

- 17 randomised controlled trials involving 1264 participants
- NIV
  - **decreased the risk of mortality by 46%** (RR 0.54, 95% CI 0.38-0.76)
  - **decreased the risk of needing endotracheal intubation by 65%** (RR 0.36, 95% CI 0.28-0.46)

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Non-invasive ventilation versus usual medical care for management of acute hypercapnic respiratory failure due to exacerbation of chronic obstructive pulmonary disease (overall effects)

Patient or population: Patients admitted to hospital with acute hypercapnic respiratory failure due to an exacerbation of chronic obstructive pulmonary disease (COPD)
Setting: Acute inpatient
Intervention: Non-invasive ventilation
Comparison: Usual care

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with usual care - Overall	Risk with NIV				
Mortality	183 per 1000	99 per 1000 (70 to 139)	RR 0.54 (0.38 to 0.76)	854 (12 RCTs)	⊕⊕⊕◯ MODERATE[a]	Downgraded owing to risk of bias for some included studies
Need for endotracheal intubation	341 per 1000	123 per 1000 (95 to 157)	RR 0.36 (0.28 to 0.46)	1105 (17 RCTs)	⊕⊕⊕◯ MODERATE[a]	Downgraded owing to risk of bias for some included studies
Length of hospital stay (days)	Mean length of hospital stay (days) was 17.5	MD 3.39 lower (5.93 lower to 0.85 lower)	-	888 (10 RCTs)	⊕⊕⊕◯ MODERATE[a,b]	Downgraded owing to risk of bias and inconsistency of findings for some included studies

***The risk in the intervention group** (and its 95% confidence interval) is based on assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)

CI: confidence interval; OR: odds ratio; RR: risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Respirology Referral

- COPD and increased symptoms, young age at onset, or exacerbations
- Uncontrolled asthma despite ICS/LABA therapy
- Undiagnosed lung disease
- Undiagnosed dyspnea without suspicion for heart failure or coronary artery disease
- Mediastinal lymphadenopathy NYD
- Sarcoidosis
- Non-group 2 pulmonary hypertension
  - (secondary to left heart disease)
- Respiratory failure
- Neuromuscular disease (e.g. ALS)
- Hemoptysis
- Pleural effusion
- Preoperative respiratory consultation
- Local care for lung transplantation

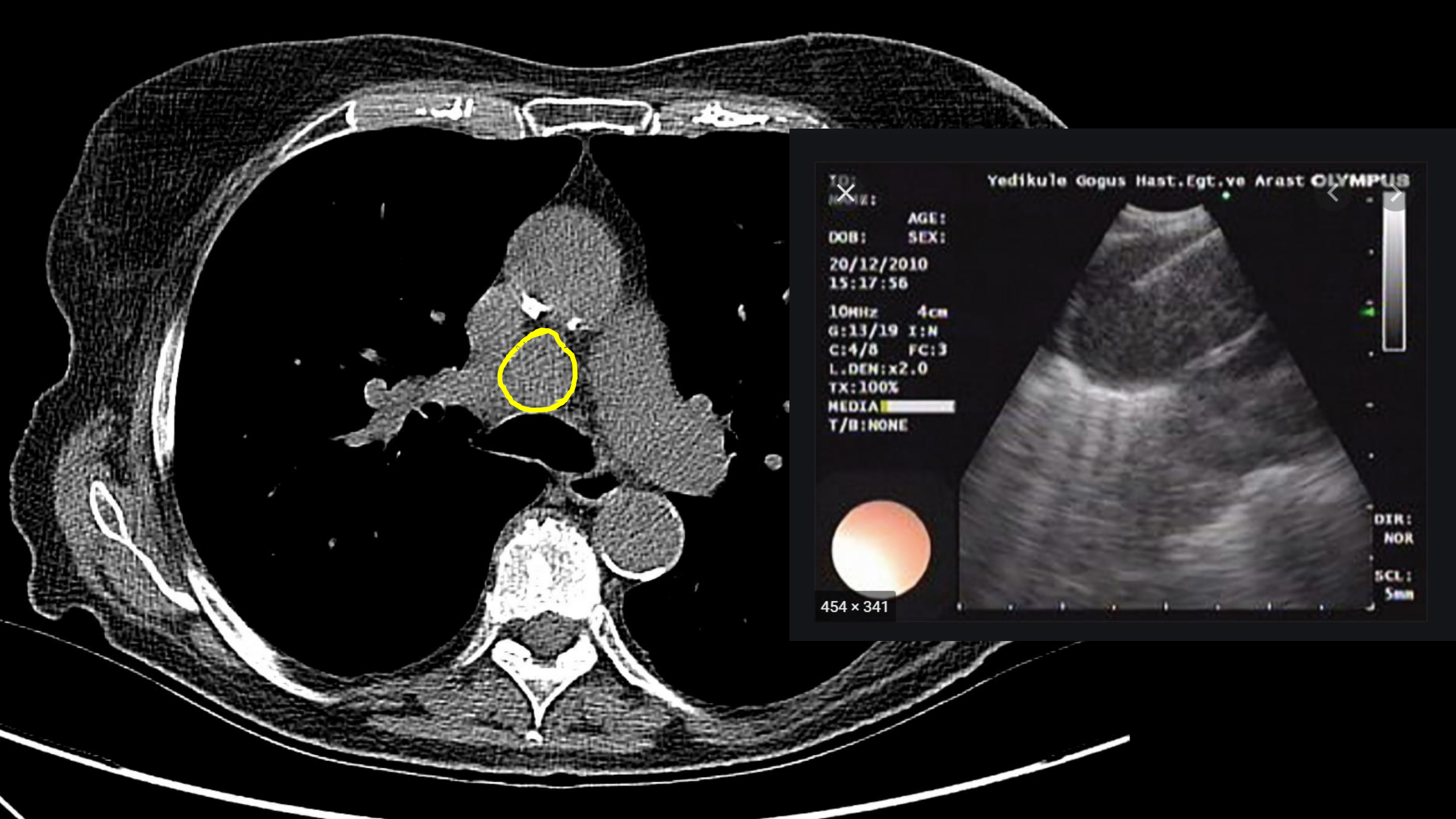
What I don’t do

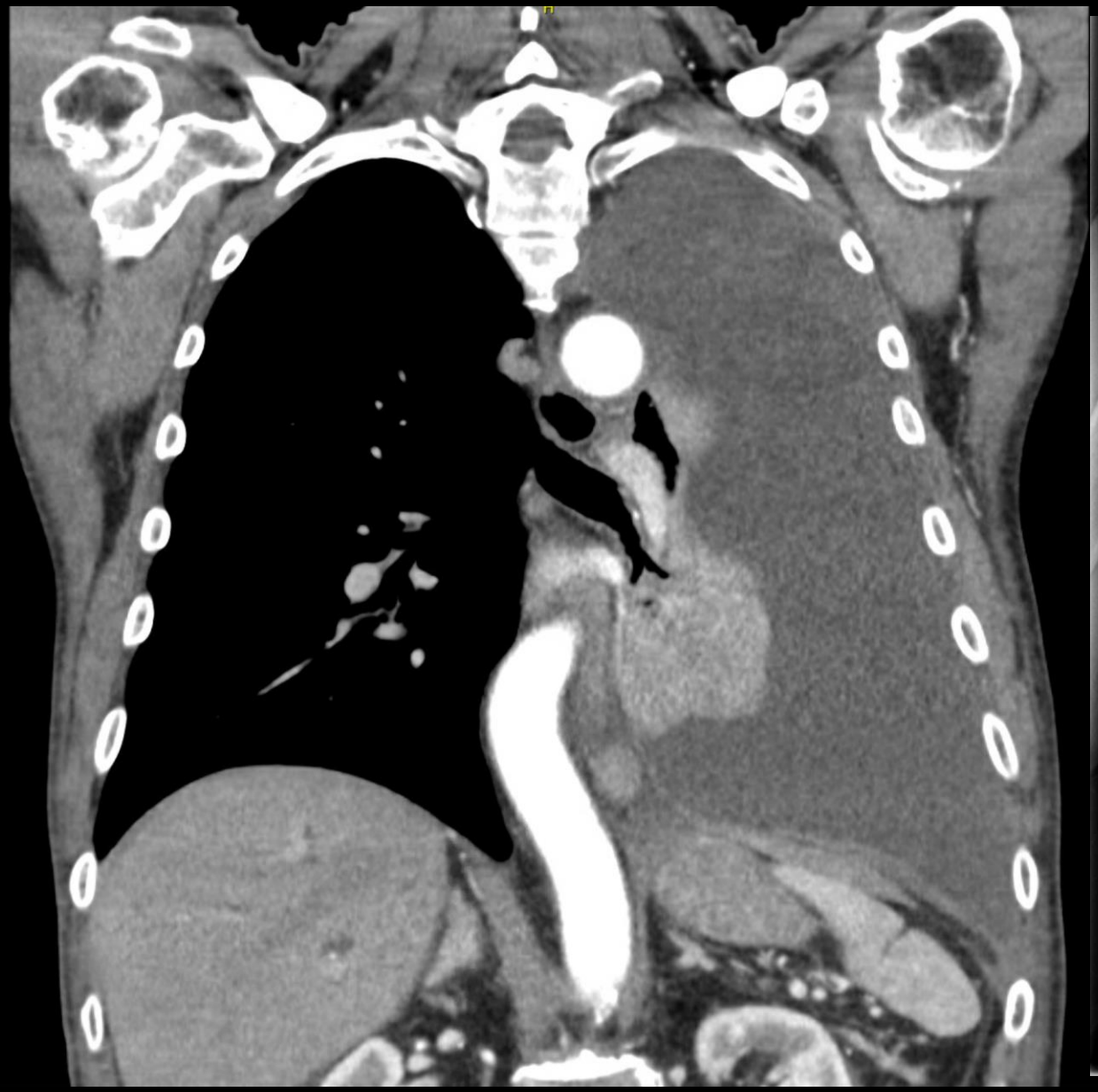
- Sleep Medicine
  - (consults provided by Dr. Chandy, Dr. Dales, and Dr. Alewan – refer through the Sleep Lab at HSN)

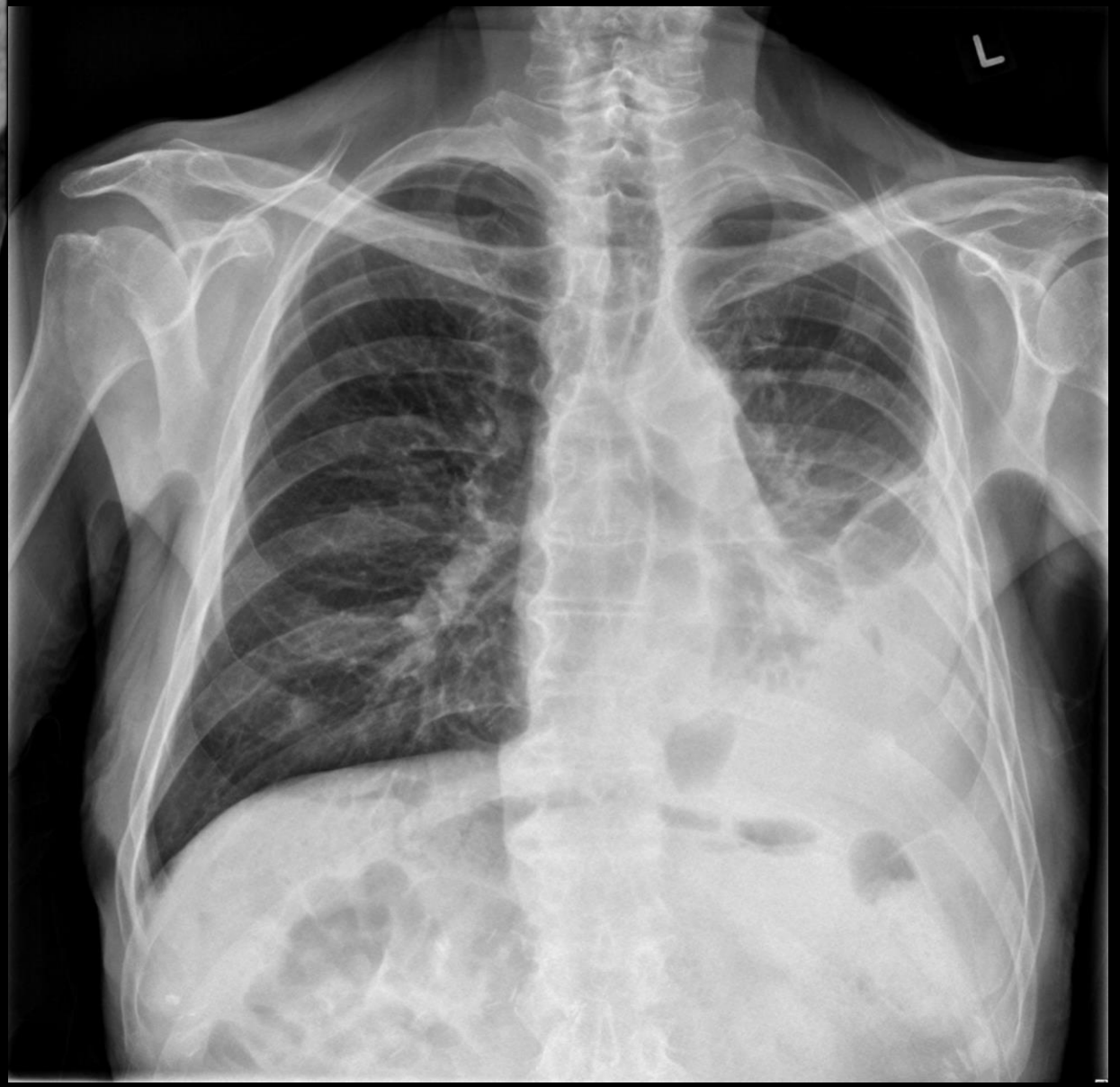
Introduction to Interventional Pulmonology

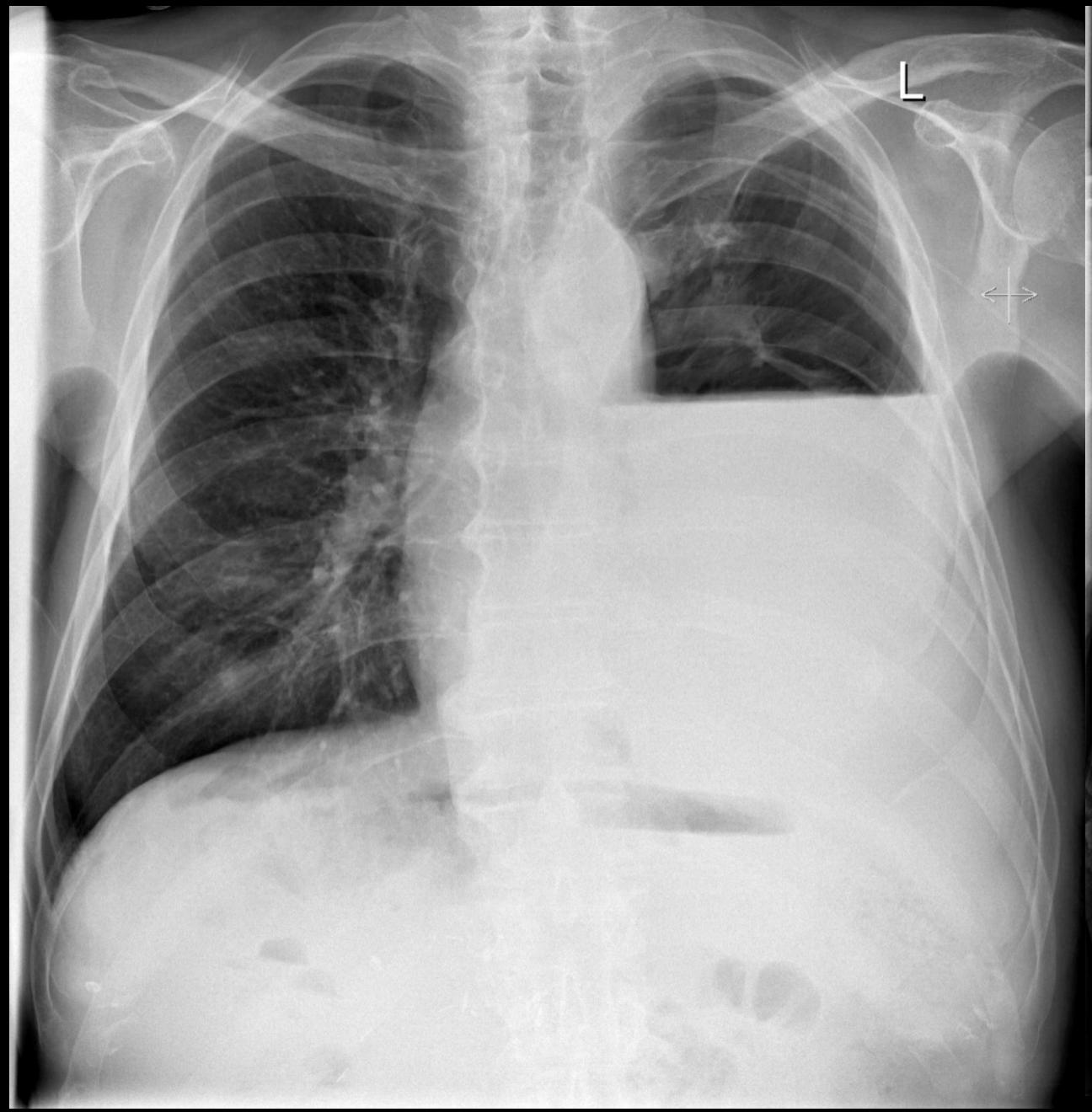
- Use of advanced airway and pleural procedures for diagnosis and treatment of diseases of the airways, lungs, and pleura
- Procedures:
  - Endobronchial ultrasound (Linear EBUS)
  - Transbronchial and endobronchial biopsies
  - Tunnelled indwelling pleural catheter (IPC) insertion
  - Debulking or dilatation of short-segment obstructive lesions
  - Medical Pleuroscopy
  - Endobronchial stents
  - Endobronchial valves
  - Bronchial thermoplasty
  - Radial EBUS

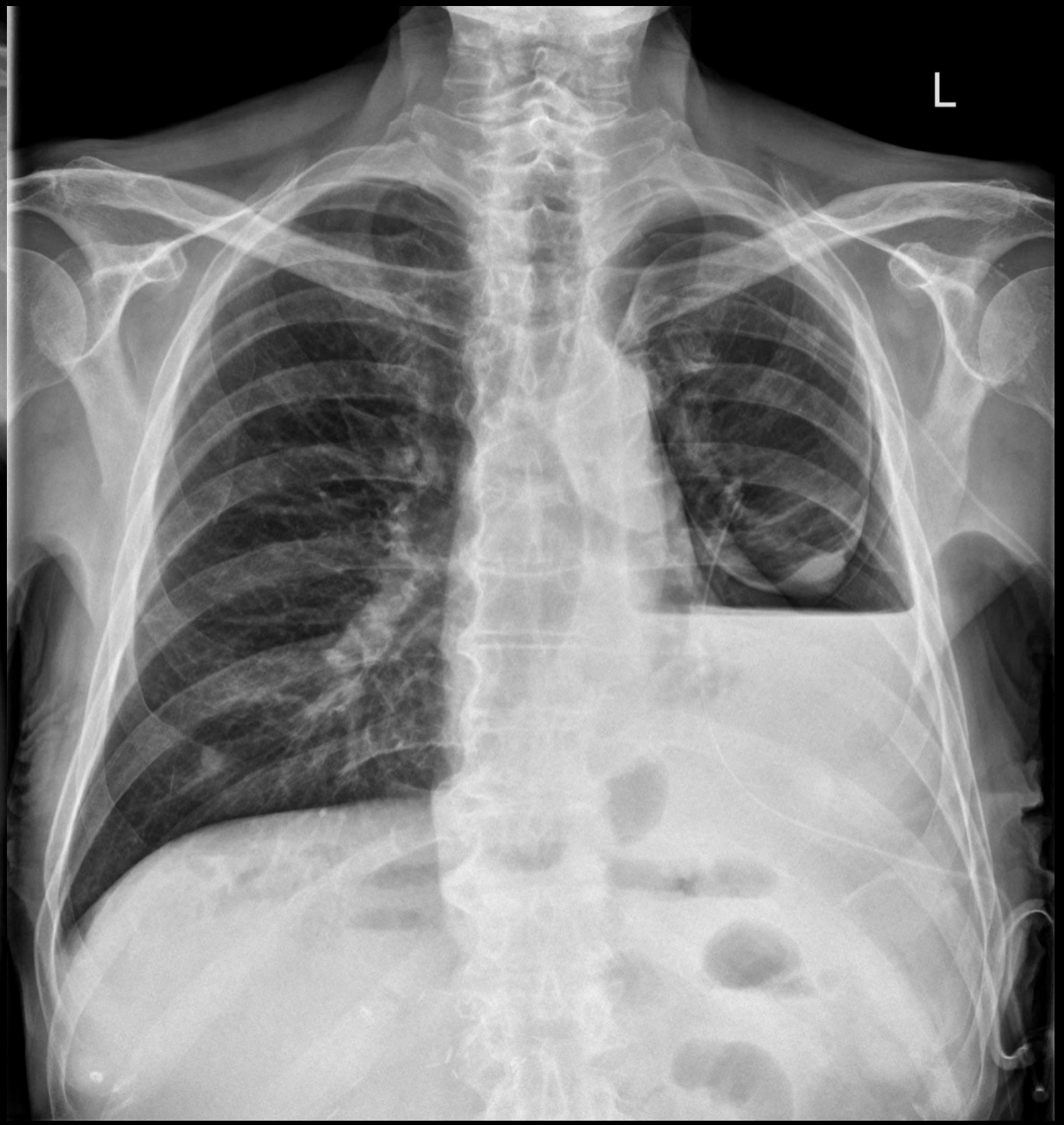
Currently available at HSN


Yedikule Gogus Hast.Egt.ve Arast
OLYMPUS
AGE:
DOB: SEX:
20/12/2010
15:17:56
10MHz 4cm
G:13/19 I:N
C:4/8 FC:3
L.DEN:x2.0
TX:100%
MEDIA
T/B:NONE
DIR:
NOR
SCL:
5mm
454 × 341

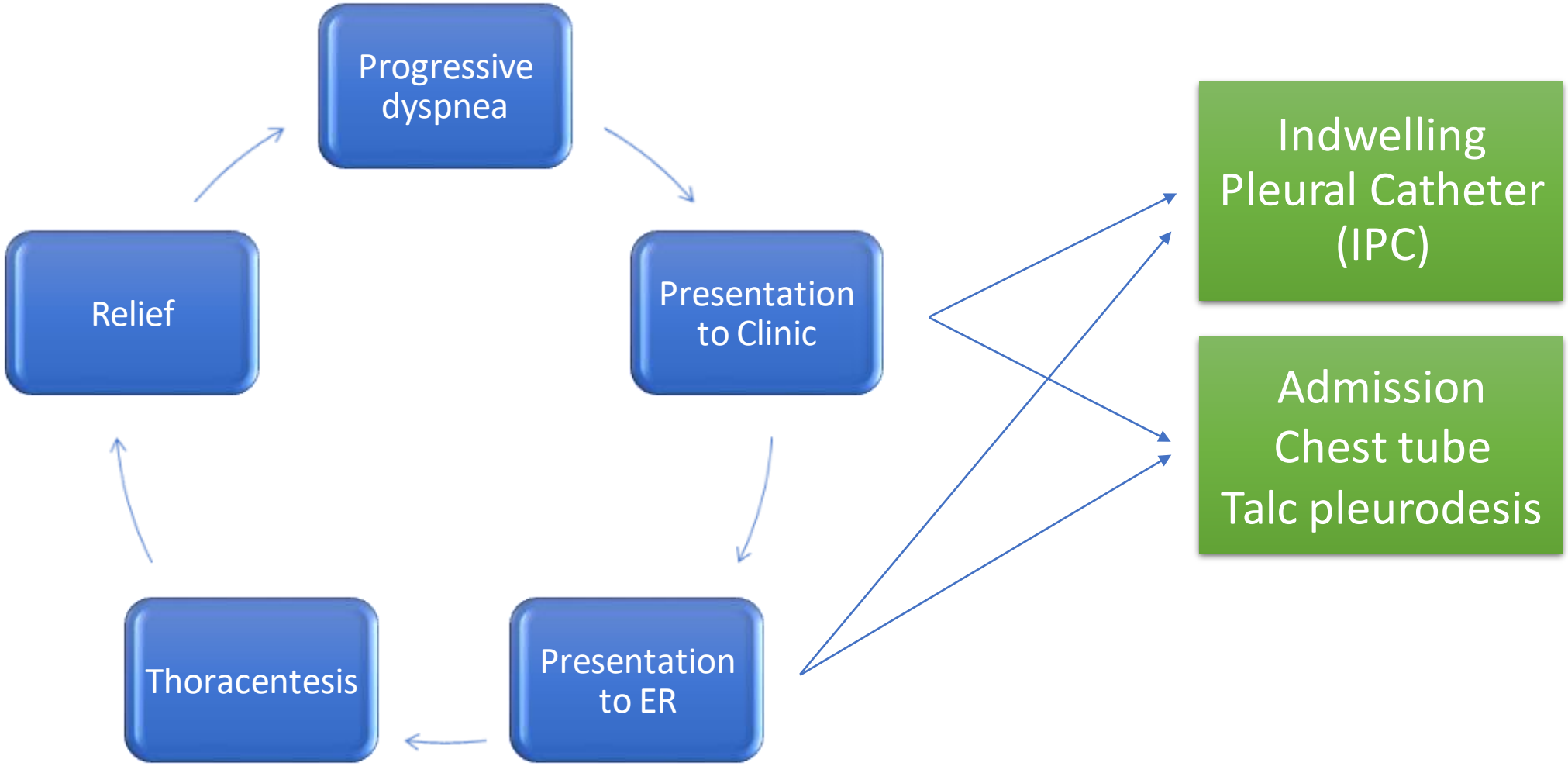


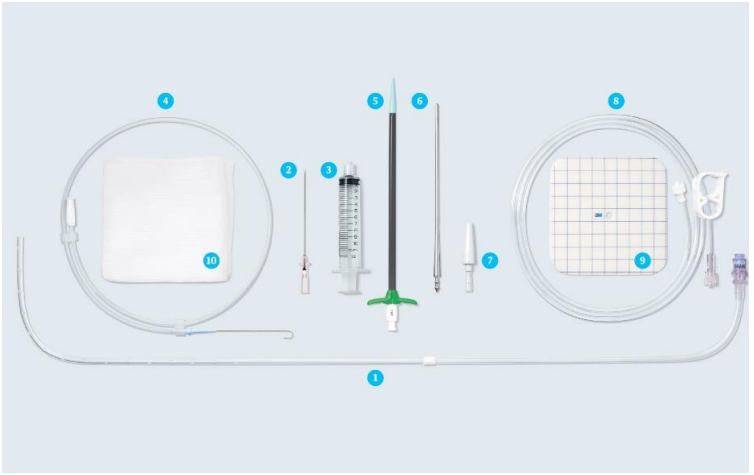

L


L


L

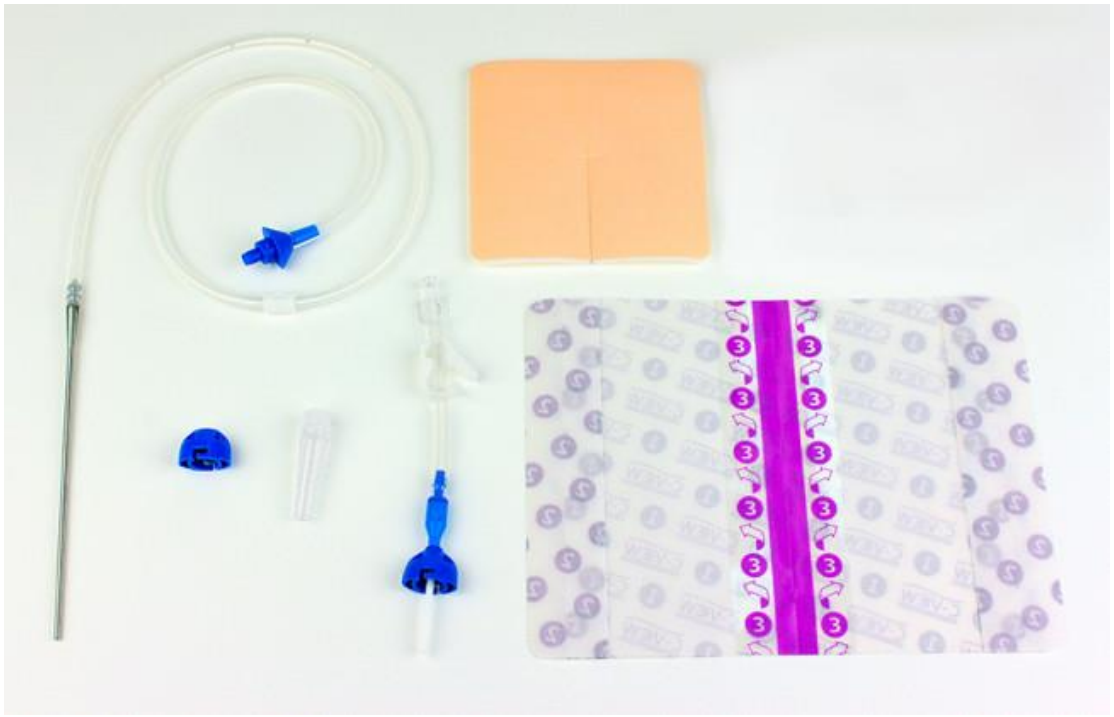
Natural History of Malignant Pleural Effusions





ASEPT® Pleural Drainage System

PleurX™ Drainage System



Rocket™ IPC

Aspira® Drainage System

Choosing Wisely Canada

1. Don't initiate long-term maintenance inhalers in stable patients with suspected COPD if they have not had confirmation of post-bronchodilator airflow obstruction with spirometry.

2. Don't perform CT screening for lung cancer among patients at low risk for lung cancer.

3. Don't perform chest computed tomography (CT angiography) or ventilation-perfusion scanning to evaluate for possible pulmonary embolism in patients with a low clinical probability and negative results of a highly sensitive D-dimer assay.

4. Don't treat adult cough with antibiotics even if it lasts more than 1 week, unless bacterial pneumonia is suspected (mean viral cough duration is 18 days).

5. Don't initiate medications for asthma (e.g., inhalers, leukotriene receptor antagonists, or other) in patients ≥ 6 years old who have not had confirmation of reversible airflow limitation with spirometry, and in its absence, a positive methacholine or exercise challenge test, or sufficient peak expiratory flow variability.

6. Don’t use antibiotics for acute asthma exacerbations without clear signs of bacterial infection.

Take-Home Messages

- The differential of “symptoms of COVID-19” is extremely broad
- A careful search for alternative or comorbid respiratory disease is likely to result in high-value care
- Confirm suspected COPD with pre-/post-bronchodilator spirometry
- Don’t miss asthma
- Refer patients with uncontrolled airway disease or undiagnosed dyspnea
- Interventional techniques are available at HSN including EBUS, transbronchial biopsies, and indwelling pleural catheters