

Chronic Cough... and a bit about COPD



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DISCLOSURE

I have no financial relationships that might constitute a conflict of interest.





“The art of medicine is amusing the patient while nature cures the disease.”

- Voltaire



Classification

Acute cough

~ maximum of 3 weeks

Subacute cough

~ 3 to 8 weeks

Chronic Cough

~ more than 8 weeks

Why is cough important?... To society:

- Most common reason to consult a PCP
- Antitussive drug sales USA >\$4 billion/yr
- Chronic cough (>8wk): 12% population
- 10-38% of out-patients referrals

HRQOL: The LCQ

Physical

Chest pains

Sputum

Tired

Paints/fumes

Sleep

Frequency

Hoarse Voice

Energy

Psychological

Embarrassed

Anxious

In control

Frustrated

Fed up

Serious illness

Other people

Social

Conversation

Annoy family

Job

Enjoyment



Medical & Science

LCQ

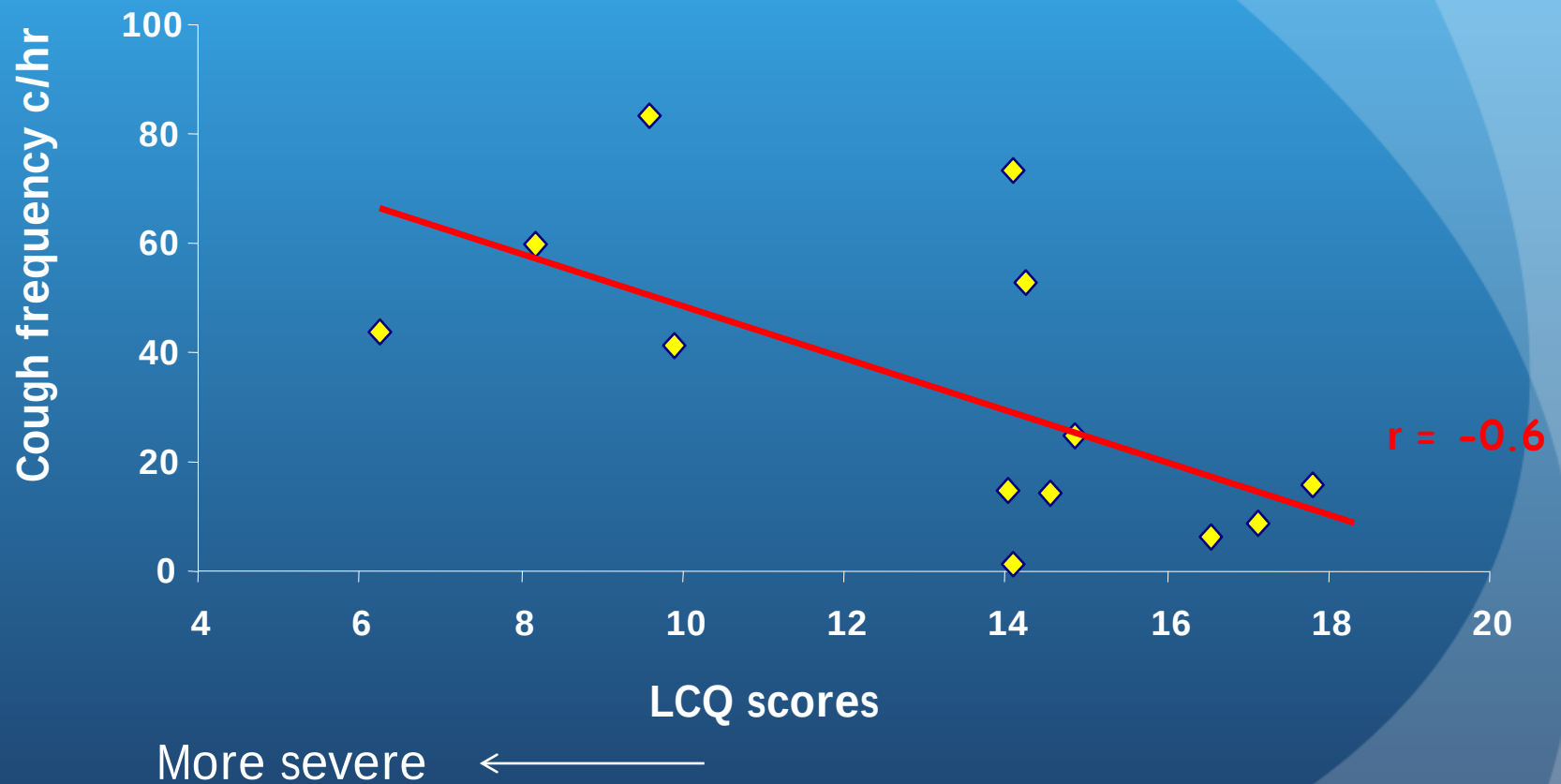
means

Leicester Cough Questionnaire

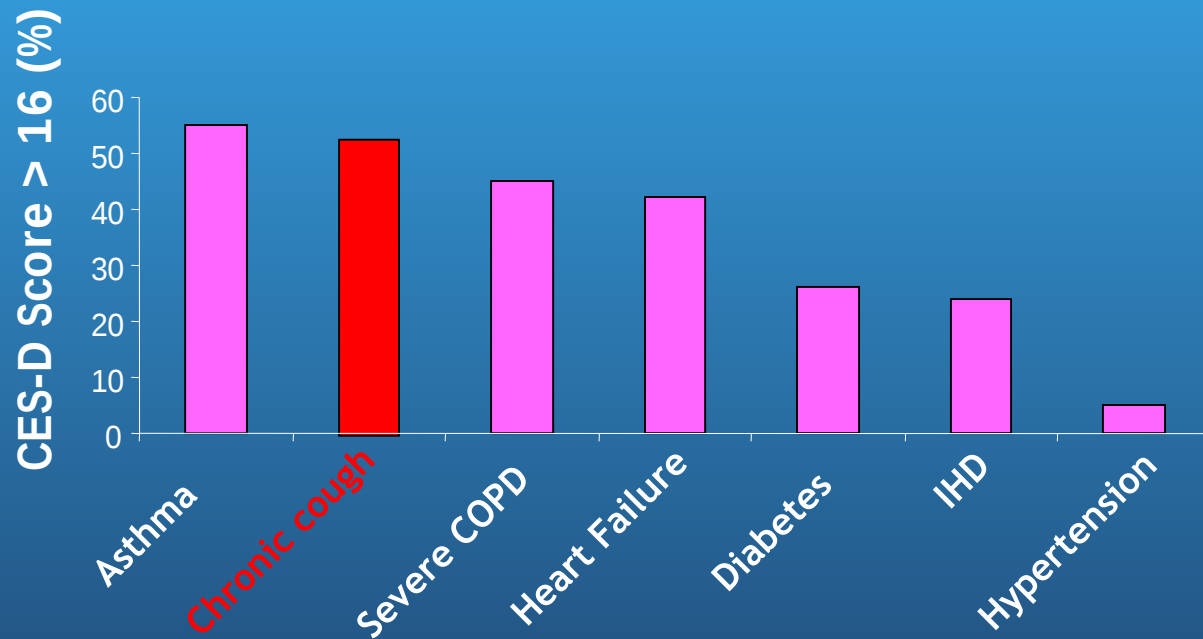
by acronymsandslang.com

Birring S et al, Thorax 2003; 58:339-343

Cough frequency & QOL



Depressive symptoms in chronic cough

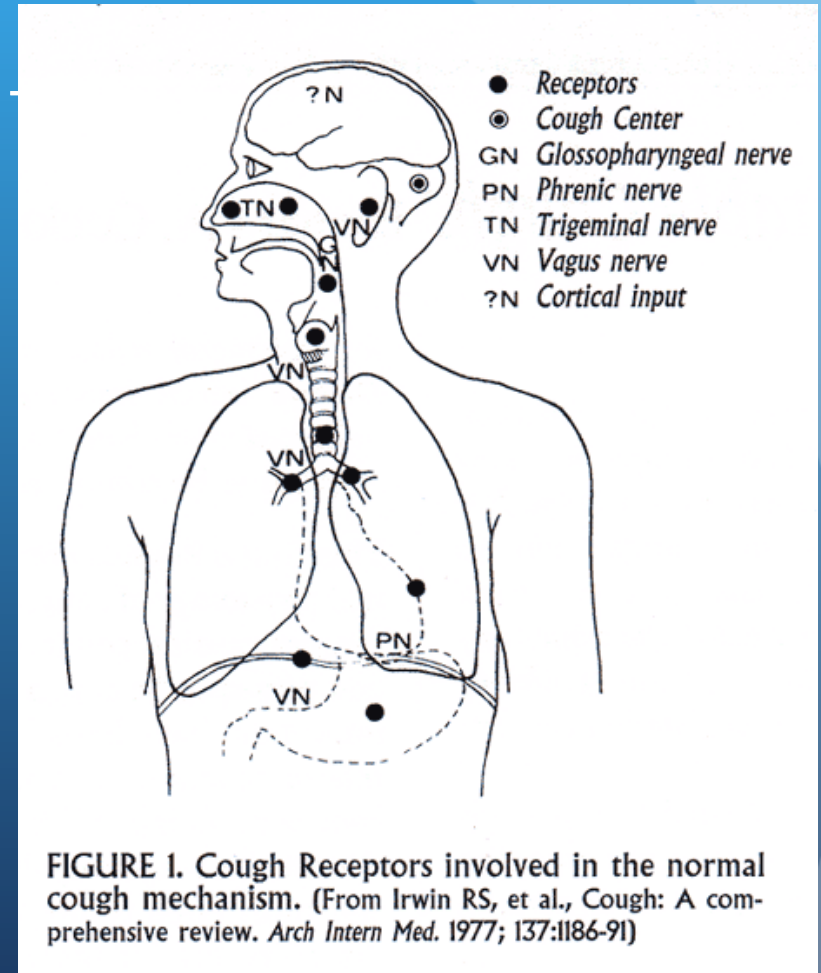


Adverse impact of chronic cough

Worried about serious illness	77%
Concerned something is wrong	72%
Frequent nausea	56%
Exhaustion	54%
Others think something is wrong with me	53%
Embarrassment	49%
Self-consciousness	46%
Difficulty speaking on the telephone	39%
Urine incontinence	30%
Absence from work	11%

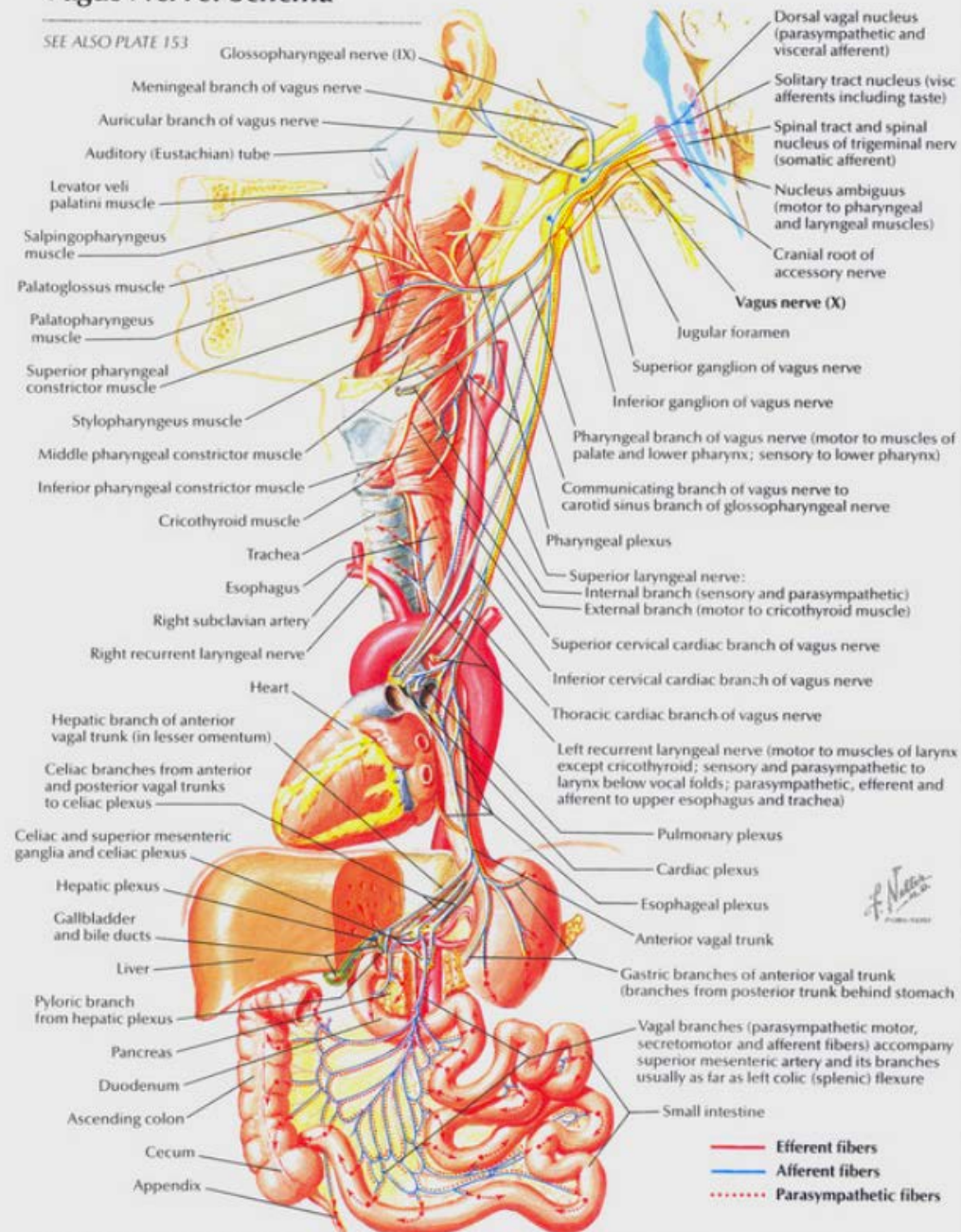
Cough Reflex: Afferent pathway

- Major afferent pathways:
- Stimuli arise from:
 - Nose (Trigeminal)
 - Larynx (Superior Laryngeal N)
 - Vagus:
 - Ear (Arnold's nerve)
 - Tracheobronchial tree
 - Heart
 - Pericardium
 - Esophagus



Vagus Nerve: Schema

SEE ALSO PLATE 153



ACE-Inhibitors:

“Déjà vu all over again” (-Yogi Berra)

- Roughly 10% of individuals treated with ACE inhibitors
- May be more common in women and Asians (50%)
- Accumulation of bradykinins and Substance P.
- Maybe also accumulation of bronchoconstrictive thromboxane
- Onset usually 1-2 weeks, but may be delayed (6-12 months)
- Usually resolves in about a week, but may take months

Take Home Message...

“In immunocompetent patients with chronic cough and a normal CXR finding who are nonsmokers and are not receiving therapy with an ACE inhibitor,

the diagnostic approach should focus on the detection and treatment of UACS (formerly called PNDS), asthma, NAEB, or GERD, alone or in combination.

This approach is most likely to result in a high rate of success in achieving cough resolution.”

Causes of Chronic Cough (90-95%)

- Upper airway cough syndrome (UACS)
- Asthma
- Gastroesophageal reflux (GERD)
- Nonasthmatic eosinophilic bronchitis (NEAB)

92-100%
immunocompetent
non-smokers with
normal chest X-ray

Upper Airway Cough Syndrome

- Most common cause in adults

UACS:

Myriad of rhinosinus conditions

- PNDS
- Allergic rhinitis
- Nonallergic rhinitis
 - Vasomotor rhinitis
 - Nonallergic rhinitis with eosinophilia (NARES)
 - Occupational
 - Postinfectious
 - Pregnancy
 - Rhinitis medicamentosa (topical decongestant overuse)
- Sinusitis (bacterial and fungal)

Upper Airway Cough Syndrome

- History:
 - Need to frequently clear throat
 - Tickle in throat
 - Sensation of dripping into throat
 - Nasal symptoms
- Physical Exam:
 - Secretions in nose or oropharynx
 - Cobblestone of mucosa



Treatment

- Oral (1st generation) antihistamine/decongestant x 3-5 weeks
- +/- Intranasal decongestant: e.g. oxymetazoline 2 sprays each nostril bid x 3 days only
- Antibiotics selectively, for sinusitis
- Can often convert to more standard/less expensive/more convenient/less sedating therapy (newer antihistamine alone, nasal CS, allergy shots) once better

Asthma

- Second most common cause of chronic cough
- Clues :
 - Episodic wheezing, dyspnea , cold or exercise induced
 - Reversible airflow obstruction
 - Bronchial hyperresponsiveness (test only if needed)
- “Confirmed” by resolution of cough with asthma treatment

Cough Variant Asthma

- 30% of patients presenting with chronic cough that was due to asthma had cough as their ONLY symptom
- Clues:
 - nocturnal cough, exercise induced, after allergen exposure
- Bronchoprovocation test (Methacholine challenge):
 - NEGATIVE PREDICTIVE VALUE EXCELLENT
 - Negative test excludes asthma
 - ...but does not rule out steroid-responsive cough (NAEB)

ASTHMA/Cough Variant Asthma

Treatment

- Inhaled corticosteroid
- ICS/LABA combination > 8 weeks
- Leukotriene receptor antagonist

GERD-associated cough = #3

Two mechanisms:

- Distal esophageal acid stimulates vagus nerve
- Laryngopharyngeal reflux (LPR)
 - Microaspiration of esophageal contents into the laryngopharynx and tracheobronchial tree
- NEITHER mechanism always associated with heartburn

GERD

- Suspect GERD when...
 - Heartburn or
 - Sour taste in mouth (Waterbrash)
 - Globus or tickle (LPR)
 - Reflux can be demonstrated by:
 - 24-hour pH-impedance monitoring
 - Barium x-ray
- Cough is only symptom in 40-75% of patients

GERD: Life-style modifications

- Stop smoking
- Avoid alcohol
- Lose weight
- Elevate HOB
- Small meals
- Avoid fatty/acidic foods
- Avoid caffeine
- Avoid – tight clothes, eating < 4 hrs pre-bed, recumbency < 3 hrs post meal

Treatment

- Antacid therapy ≥ 2 months :
 - Proton pump inhibitor (high dose)
 - H2 blockers less effective
- Motility therapy:
 - Metoclopramide

Surgery is last resort

Non-Asthmatic Eosinophilic Bronchitis (NAEB)

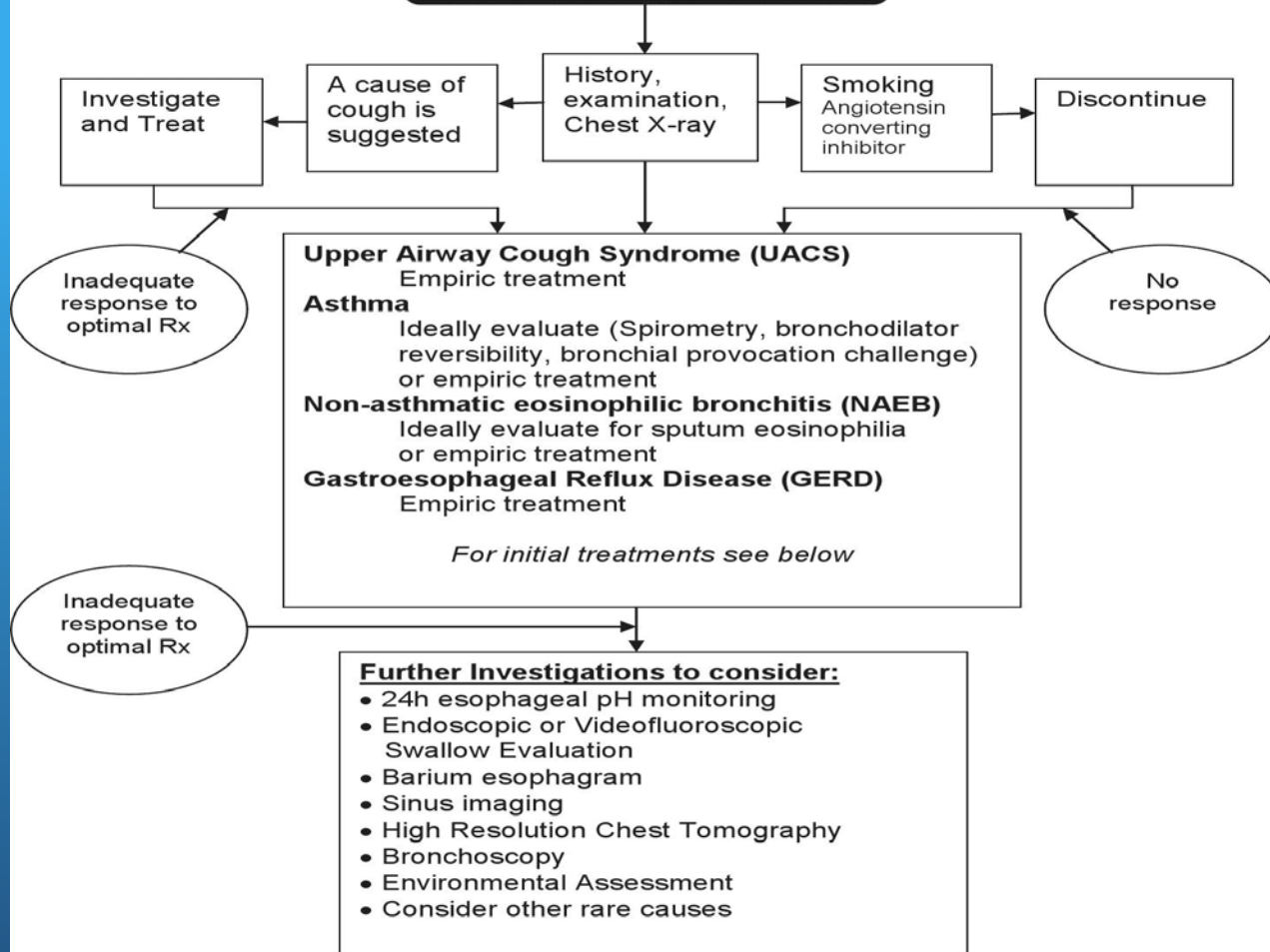
- Eosinophilic airway inflammation WITHOUT variable airflow obstruction or airway hyperresponsiveness
- **Diagnostic tests:**
 - Spirometry: normal
 - Methacholine challenge: normal
 - Sputum or BAL eosinophilia: >3% eosinophils
- **Diagnostic/Therapeutic trial:**
 - Characteristically resistant to bronchodilator but responds ICS
 - Confirmed diagnosis if responds to ICS, usually > 4 weeks

Other causes (5-10%)

-
- Bronchiectasis
 - Bronchiolitis
 - Bronchogenic carcinoma
 - COPD
 - Foreign body
 - Interstitial Lung Disease
 - Neuromuscular disease

-
- Pertussis
 - Psychogenic cough (?)
 - Sarcoidosis
 - Tracheoesophageal fistula
 - Tuberculosis
 - Zenker diverticulum
 - Chronic Cough
Hypersensitivity syndrome

Chronic Cough



Important General Considerations

Optimize therapy for each diagnosis
Check compliance
Due to possibility of multiple causes
maintain all partially effective treatments

Initial Treatments

UACS- Antihistamine/decongestant
Asthma- Inhaled corticosteroids, Bronchodilators, Leukotriene-receptor antagonist
NAEB- Inhaled corticosteroids
GERD- Proton pump inhibitor, diet/lifestyle changes

Chronic Cough Hypersensitivity Syndrome

- “psychogenic cough”
- “tic cough”

- **Laryngeal Sensory Neuropathy**

- LN responsible for causing the sensation/urge to cough in affected patients

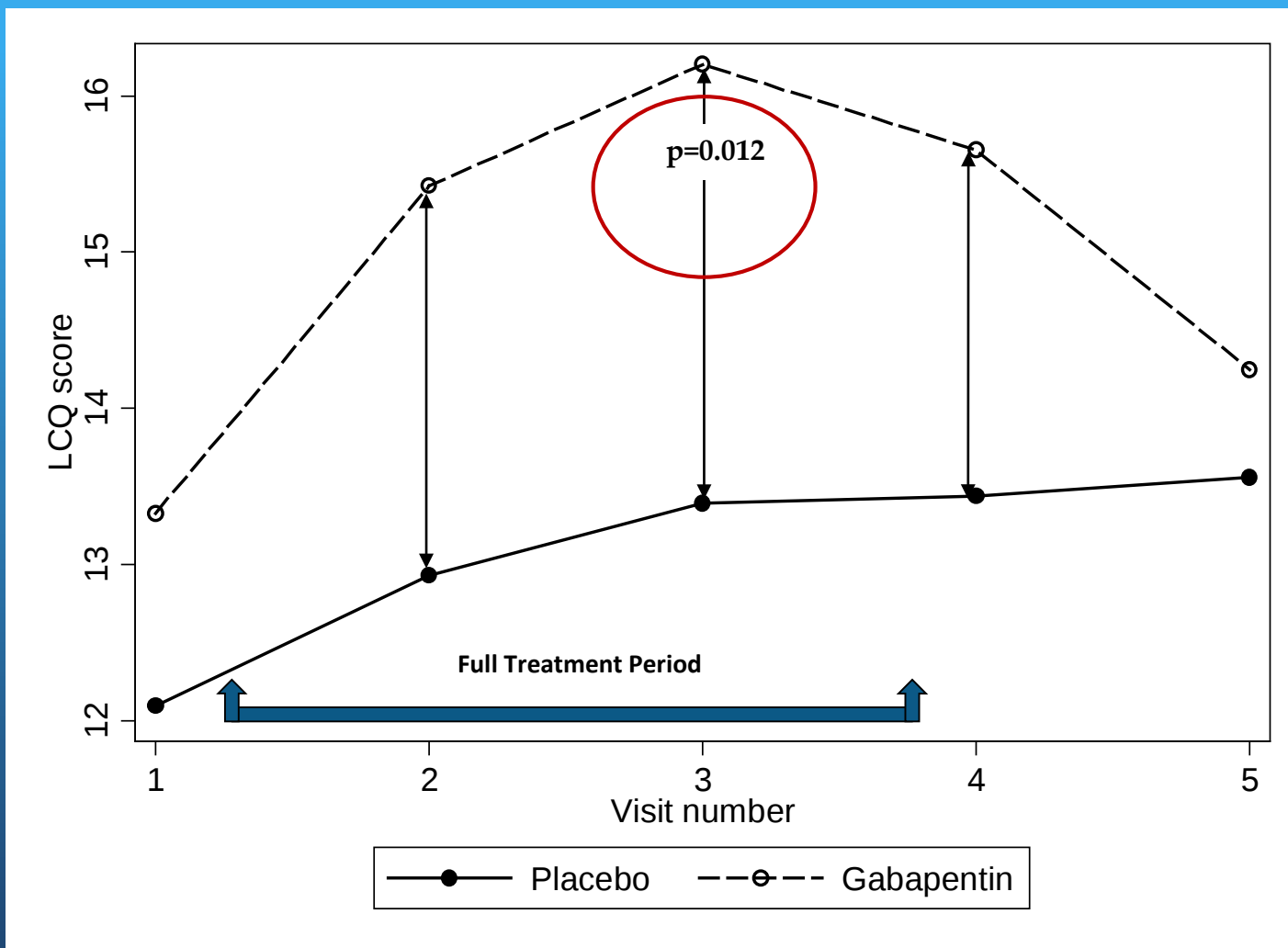
- SELSAP (Surface Evoked Laryngeal Sensory Action Potential)

- testing of the Superior Laryngeal Nerve

Cough Suppression Physiotherapy

- **Education** (avoid triggers, no benefit of excessive cough)
- **Laryngeal hygiene** (reduce alcohol/caffeine, sips water, avoid mouth breathing, correct abnormal breathing pattern+ VCD)
- **Cough control** (chew sweets, forced swallow, huff, distraction)
- **Counselling** (reinforcement of techniques, modify behaviour, address adverse symptoms such as incontinence)

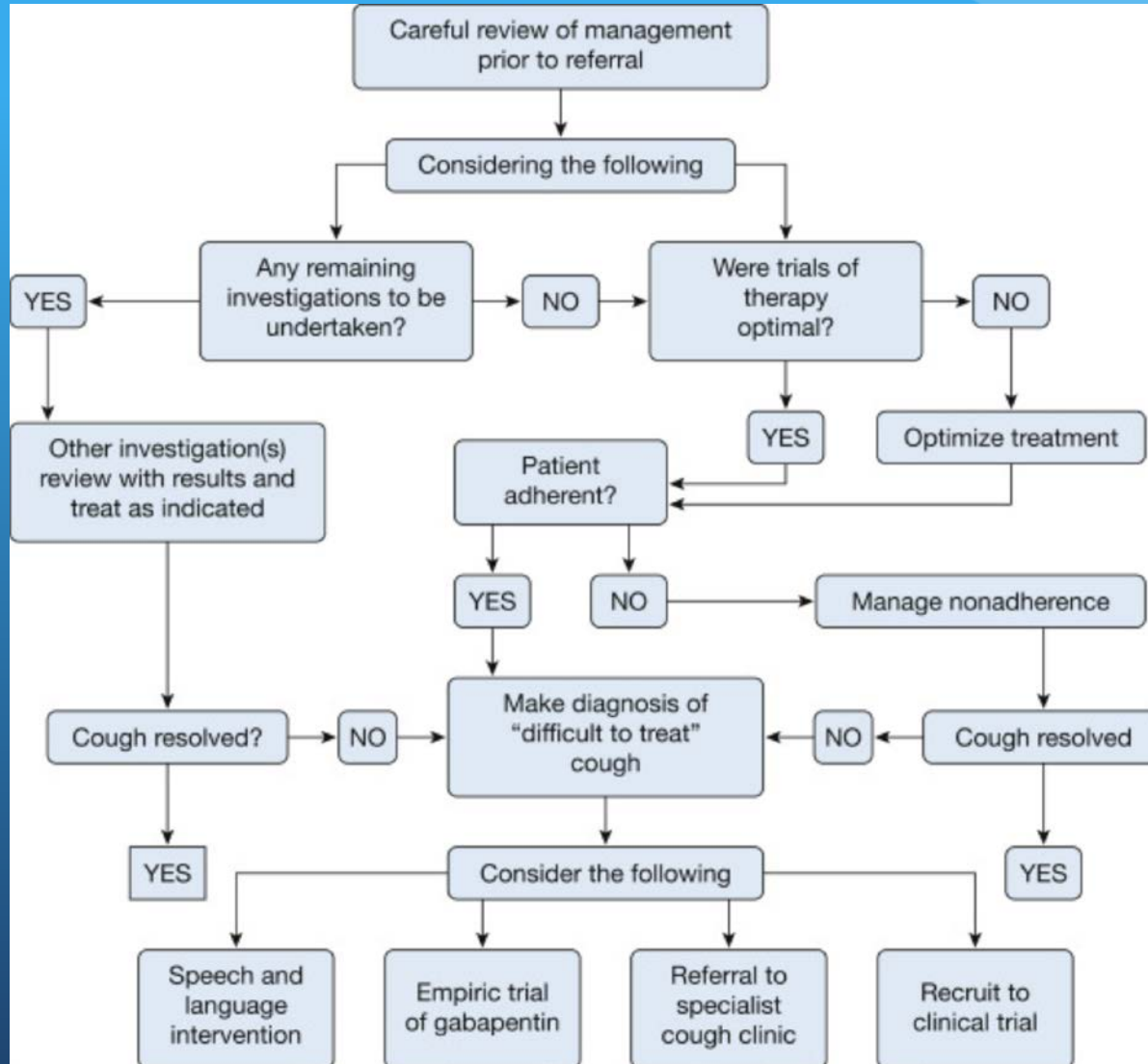
Gabapentin: randomised controlled trial



Unexplained Chronic Cough (UCC)

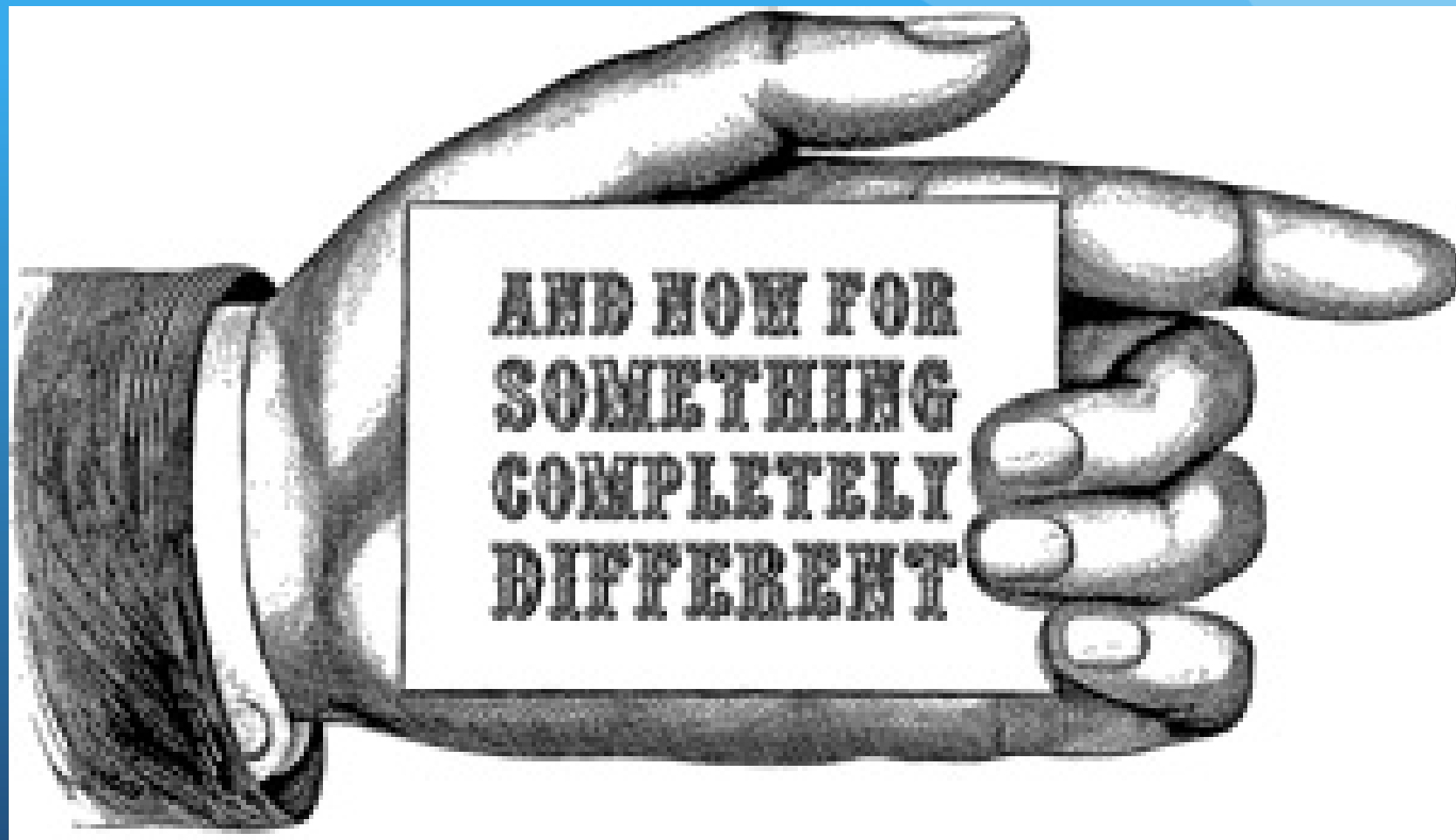
- Cough > 8 weeks persists unexplained despite investigation and treatment.
- Test for bronchial hyperresponsiveness and eosinophilic bronchitis, or a therapeutic corticosteroid trial (ungraded consensus-based statement).
- Therapeutic trial of multimodality speech pathology therapy (Grade 2C).
- If negative tests for bronchial hyperresponsiveness and eosinophilia (sputum eosinophils, exhaled nitric oxide), inhaled corticosteroids should not be prescribed (Grade 2B).
- Conduct a trial of gabapentin if risks < benefits. Reassess at 6 months (Grade 2C).
- If a negative symptoms and workup for GERD, the PPIs should not be prescribed (Grade 2C).

Unexplained chronic cough



Recommended
Gabapentin dose:

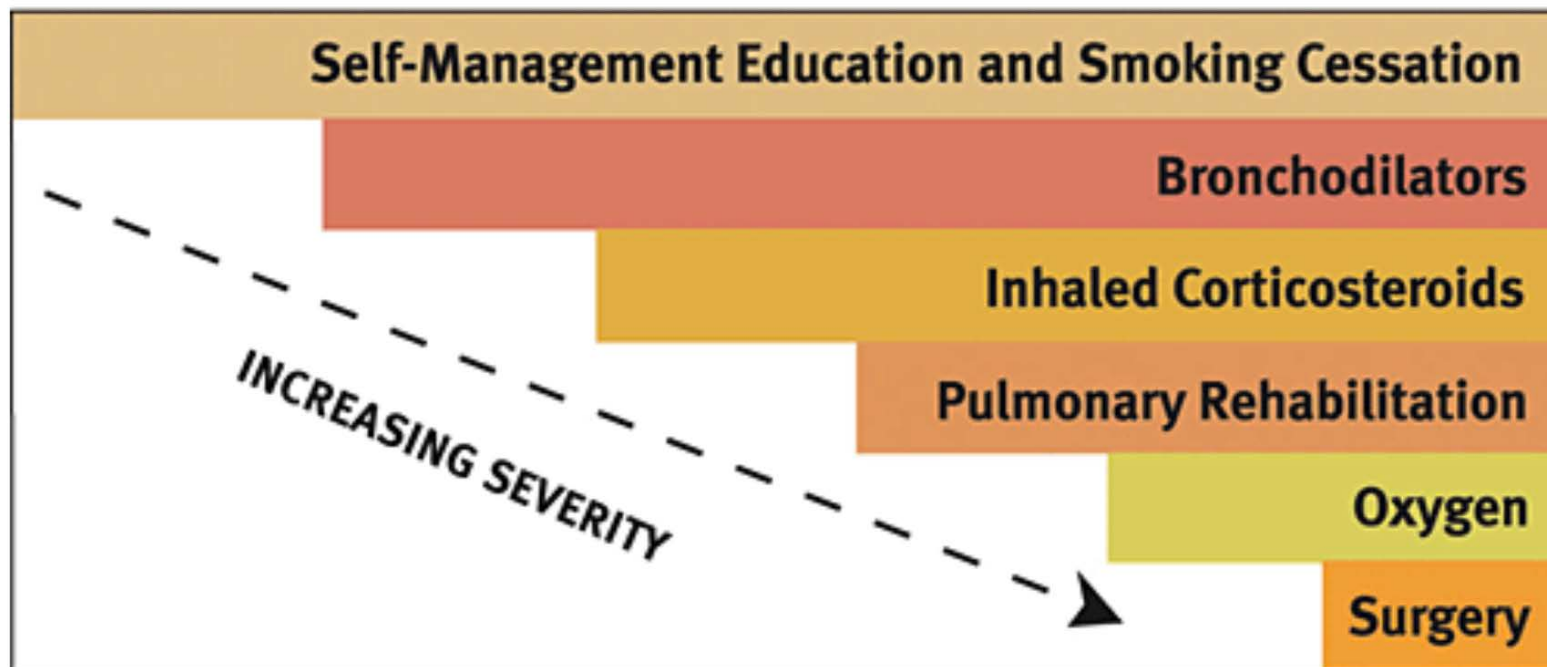
300 mg qHS
To
900 mg BID



Is this the making of a 21st Century physician?



TREATMENT OPTIONS FOR COPD



COPD:

Treatments that Improve Survival

- Quit smoking !!!!
- Use oxygen continuously if:
 - $pO_2 < 55$
 - $P_{O_2} 55 - 59$ if polycythemia or pulmonary hypertension
- Lung Transplantation
- Lung Volume Reduction
 - If predominantly upper lobe and low exercise capacity
- Lung Cancer Screening

BODE Index

Table. Variables and cutoff values for points 0 to 3 in the BODE index computation.

	Point on BODE index*			
	0	1	2	3
FEV ₁ (% of predicted)	≥65	50–64	36–49	≤35
Distance walked in 6 minutes (m)	≥350	250–349	150–249	≤149
Dyspnea scale score	0–1	2	3	4
Body mass index measure	>21	≤21	—	—

*Values range from 0 (best) to 10 (worst)

Source: Adapted from the Body-mass Index, Airflow Obstruction, Dyspnea, and Exercise Capacity Index in Chronic Obstructive Pulmonary Disease*

- **APPROXIMATE 4 YEAR SURVIVAL INTERPRETATION**
- 0-2 Points: 80%
- 3-4 Points: 67%
- 5-6 Points: 57%
- 7-10 Points: 18%

Modified MRC Dyspnoea Scale (mMRC)

Grade 0: Breathless on strenuous exercise

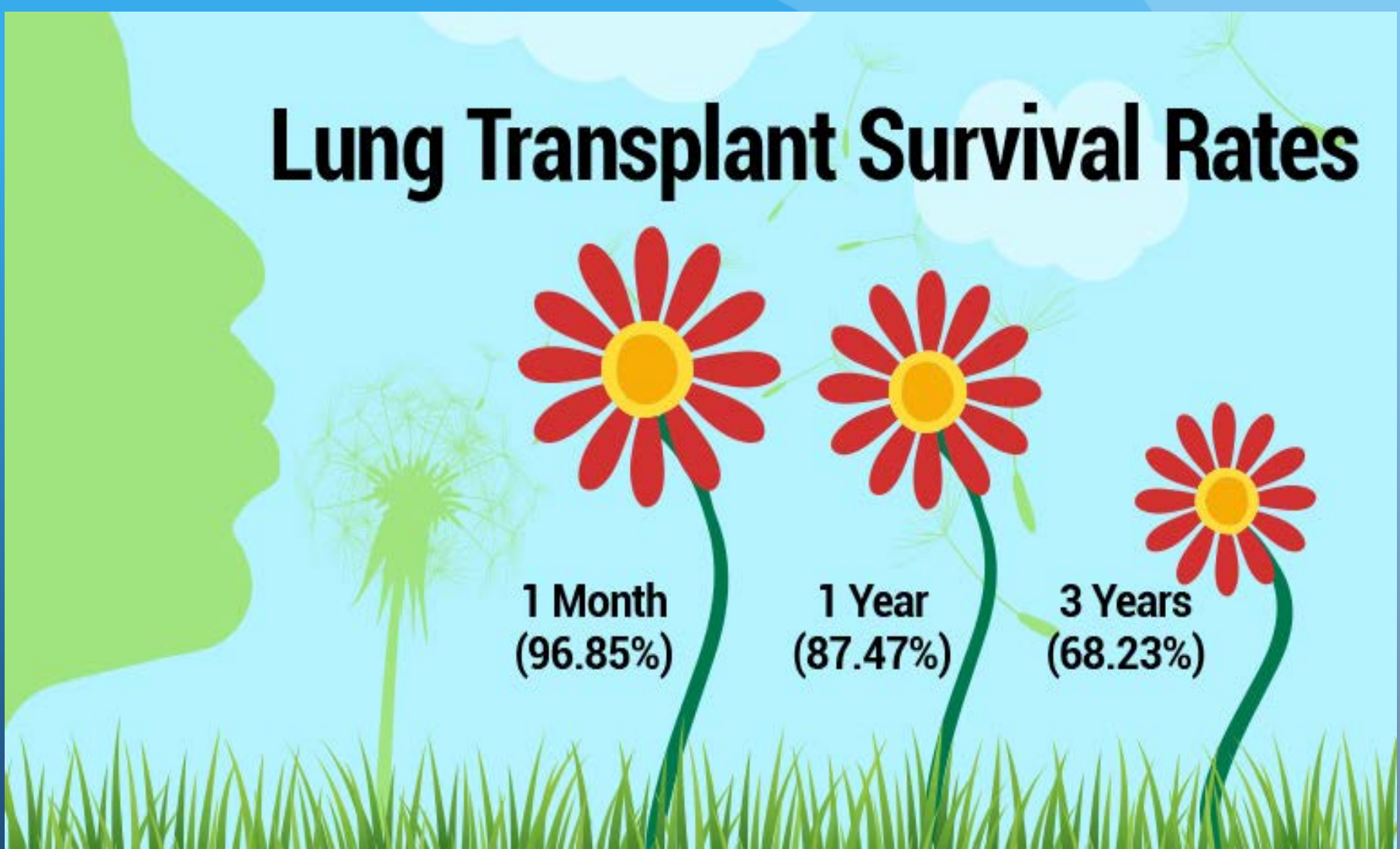
Grade 1: Short of breath when hurrying or walking up a slight hill

Grade 2: Walk slower than others or stop when walking at own pace on level ground

Grade 3: Stop every 100m or after a few minutes

Grade 4: Too breathless to leave the house or breathless on washing/dressing

Lung Transplant Survival Rates

An infographic titled "Lung Transplant Survival Rates" set against a light blue sky with white clouds and a green grassy field at the bottom. On the left, a green silhouette of a person's head is shown in profile, blowing a dandelion seed. Three dandelions are depicted: a faded seed head on the left, and two vibrant red flowers with yellow centers on the right. The first flower is labeled "1 Month (96.85%)", the second "1 Year (87.47%)", and the third "3 Years (68.23%)". The dandelion seeds are shown drifting from left to right, symbolizing the progression of time and survival.

**1 Month
(96.85%)**

**1 Year
(87.47%)**

**3 Years
(68.23%)**

About 55% at 5 years

Lung Transplantation for COPD: Candidacy

Usually 65 or younger, with progressive disease despite aggressive care, BODE 5-6 or above and:

- FEV1 < 25% of predicted (without reversibility)
- and/or
 - PaCO₂ > 55 mmHg
 - Pulmonary Hypertension with progressive deterioration (cor pulmonale)
- Preference to patients with:
 - Elevated PaCO₂, cor pulmonale and O₂ dependence

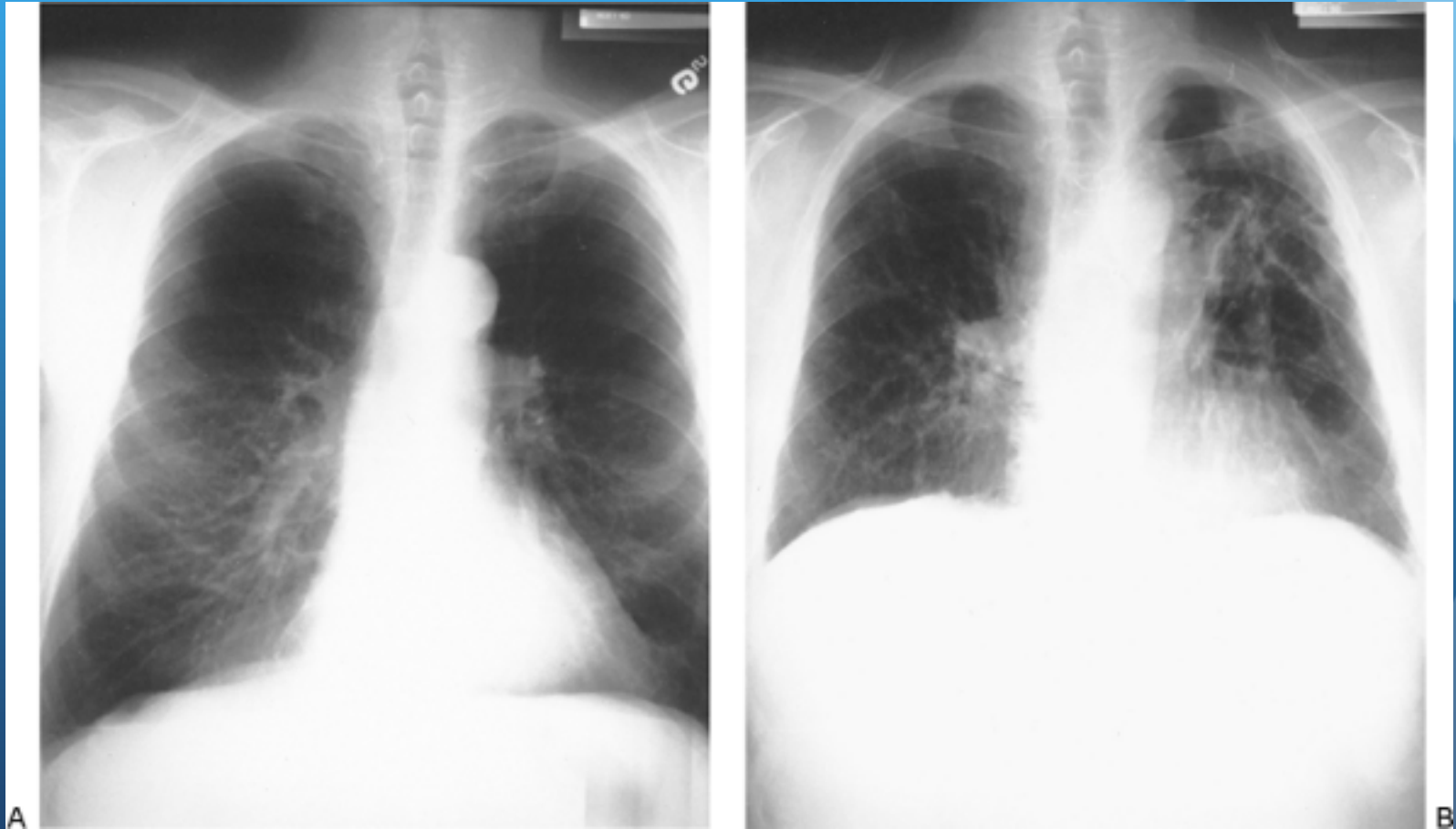
Lung Cancer Screening

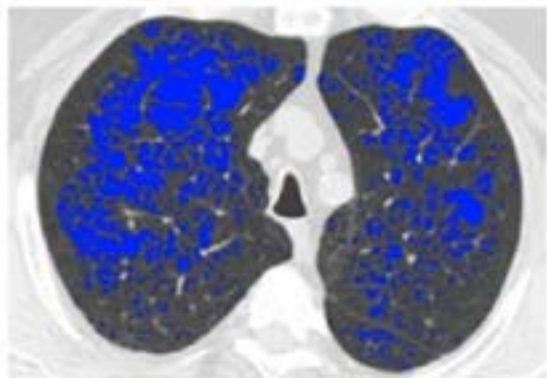
- National Lung Screening Trial (NLST)
- Low dose CT chest (LDCT)
- Roughly 1/5th radiation of conventional CT
 - 15 Chest X-rays
 - 50 cross country flights
 - 6 months of natural background radiation

Lung Cancer Screening: CMS approved

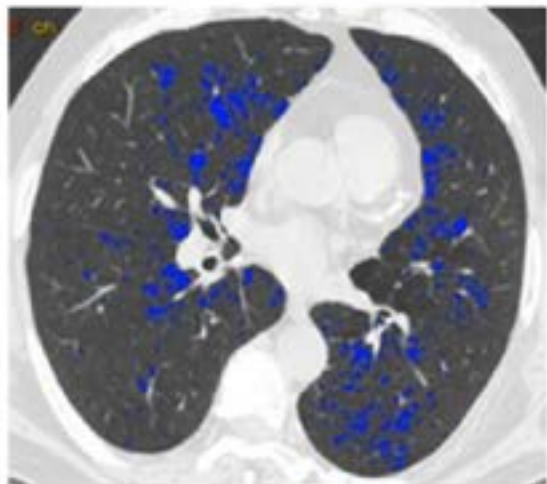
- **96% of (+) LDCT findings prove NOT to be cancer
- Reduces lung cancer mortality by 20%
 - 3 fewer deaths/1000 people screened
- Reduces all cause mortality by 6.7%
- Current recommendation = Yearly LDCT chest:
 - Age 55-77
 - 30 pack-years or more
 - Smoking within the past 15 years

Lung Volume Reduction Surgery (LVRS)

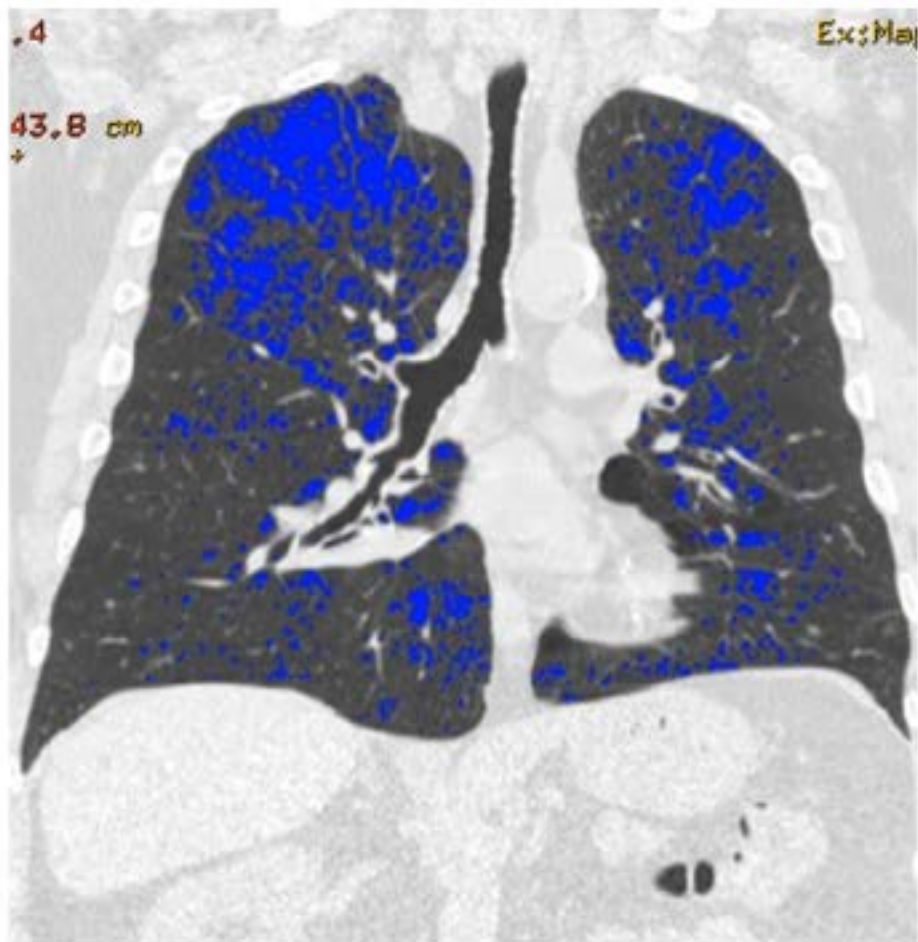




(a)



(b)



(c)

LVRS survival curves

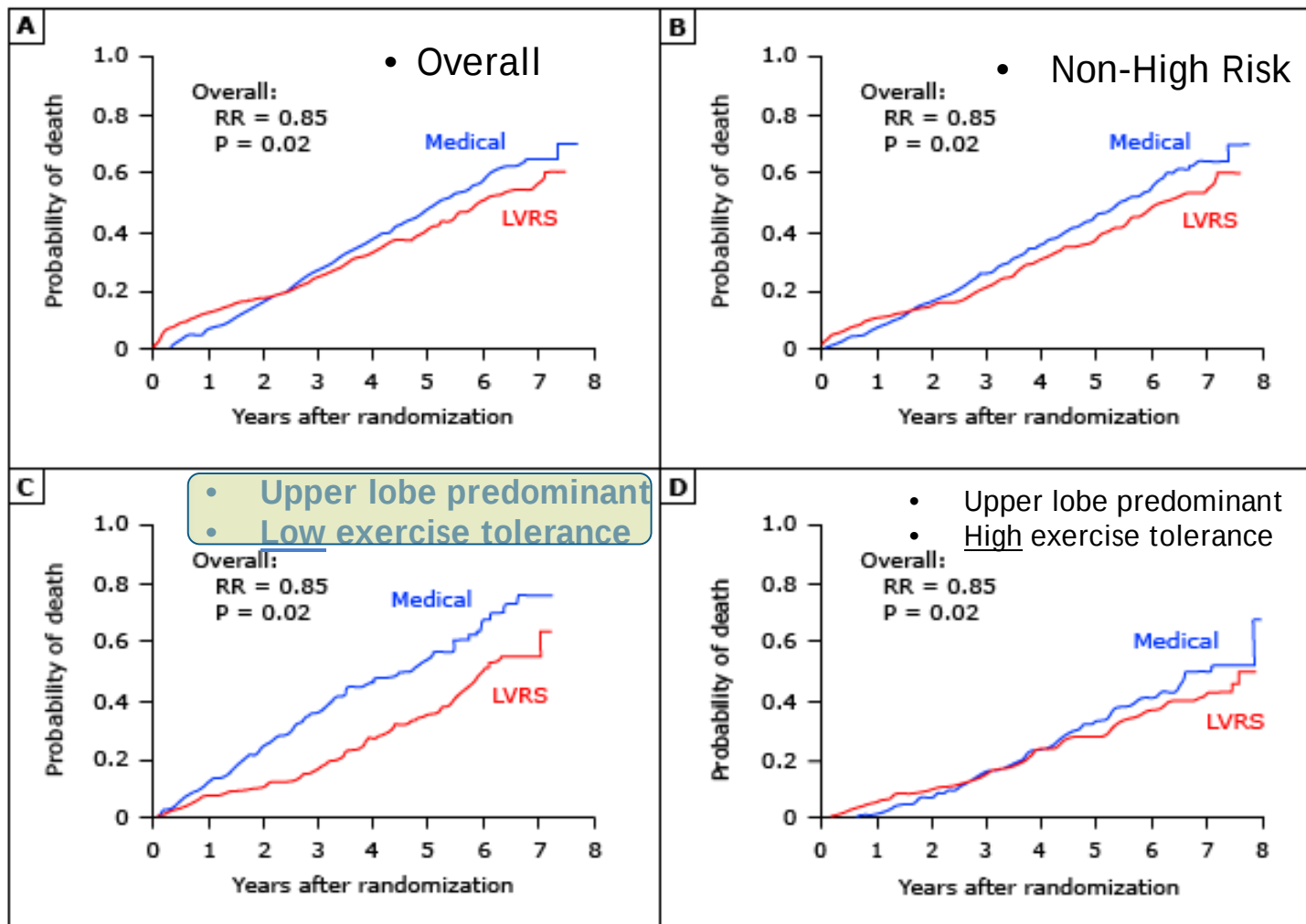


Table 2. Efficacy of Different Approaches to Decreasing Risk for Exacerbations

	Efficacy	Support	References
Non-pharmacologic Interventions			
Smoking Cessation	Supported	Large-scale observational study	66
Pulmonary Rehabilitation	Supported	Small-scale clinical studies	68, 69
Vaccination Against Pneumococcal and Influenza Virus Infection	Very strongly supported	Multiple clinical trials and meta-analyses	70-74
Pharmacotherapy			
LABA	Very strongly supported	Meta-analyses and multiple clinical trials	13, 76
LAMA	Very strongly supported	Meta-analyses and multiple clinical trials	57, 79, 80, 82, 83
LABA + LAMA vs. Monotherapy	Supported for LABA + LAMA vs LAMA monotherapy	Clinical trial	132
ICS Monotherapy	Supported	Meta-analysis, benefit limited to patients with FEV ₁ <50%	91
ICS + LABA vs ICS or LABA monotherapy	Very strongly supported	Multiple clinical trials	56, 94
Triple Combination Therapy vs. Components	Variable results	Small-scale clinical trials provide conflicting results; meta-analysis indicates no significant benefit; large-scale observational study supports	102-105, 133
Systemic Treatments			
Roflumilast	Very strongly supported as add-on treatment to bronchodilators	Multiple large-scale clinical trials and meta-analysis FEV ₁ < 50%, chronic bronchitis and > 3 exacerbations/y	106-109
Macrolides/Quinolones	Strongly supported	Supported by large-scale clinical trials	116, 117
Statins	Supported	Supported by multiple observational studies, but no controlled trials to date	121, 122

ICS = inhaled corticosteroid, LABA = long-acting β_2 -agonist LAMA = long-acting muscarinic antagonist



Combination Inhalers

SAMA

(Short-Acting Muscarinic Antagonist)

SABA

(Short-Acting Beta2-Agonist)

LAMA

(Long-Acting Muscarinic Antagonist)

LABA

(Long-Acting Beta2-Agonist)

Corticosteroid and LABA

SAMA and SABA



LAMA and LABA

Additional Medications

MDI = Metered Dose Inhaler

Currently FDA approved for COPD

	Mechanism of action	Dosing
Tiotropium	LAMA	Daily
Aclidinium	LAMA	Twice daily
Umeclidinium	LAMA	Daily
Salmeterol	LABA	Twice daily
Formoterol	LABA	Twice daily
Indacaterol	LABA	Daily
Olodaterol	LABA	Daily
Umeclidinium/vilanterol	LAMA/LABA	Daily
Salmeterol/fluticasone	ICS/LABA	Twice daily
Budesonide/formoterol	ICS/LABA	Twice daily
Fluticasone furoate/ vilanterol	ICS/LABA	Daily

Tiotropium/olodaterol

LAMA/LABA

Daily

Global Initiative for Chronic **O**bstuctive **L**ung **D**isease



PROGETTO MONDIALE BPCO
STRATEGIA GLOBALE PER LA DIAGNOSI,
IL TRATTAMENTO E LA PREVENZIONE DELLA
BRONCOPNEUMOPATIA CRONICA
OSTRUTTIVA

Revisione 2014

GOLD staging of COPD

Stage 1	Mild COPD	FEV ₁ at least 80% of normal
Stage 2	Moderate COPD	FEV ₁ between 50% and 80% of normal
Stage 3	Severe COPD	FEV ₁ between 30% and 50% of normal
Stage 4	Very Severe COPD	FEV ₁ below 30% of normal

Global Strategy for Diagnosis, Management and Prevention of COPD

Assessment of COPD

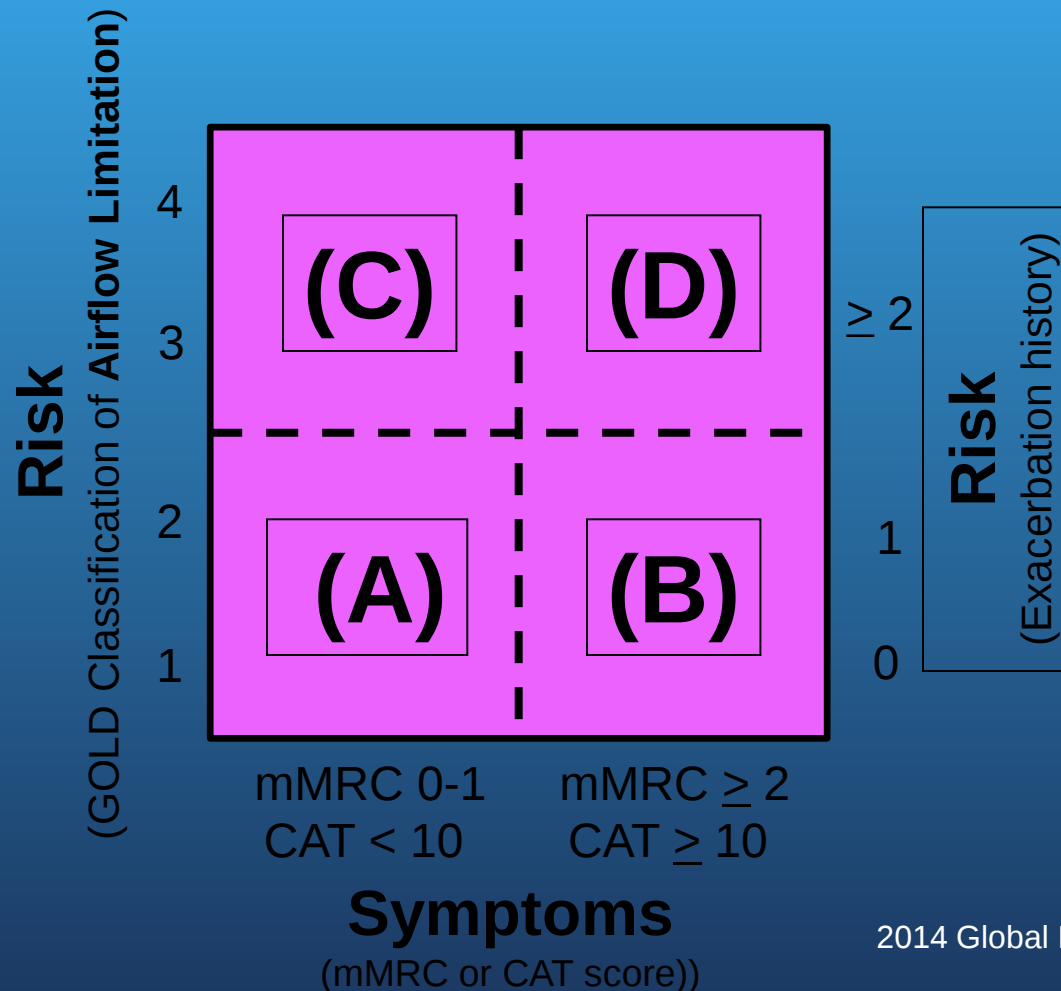
Assess symptoms : CAT, mMRC

Assess degree of airflow limitation using spirometry

Assess risk of exacerbations

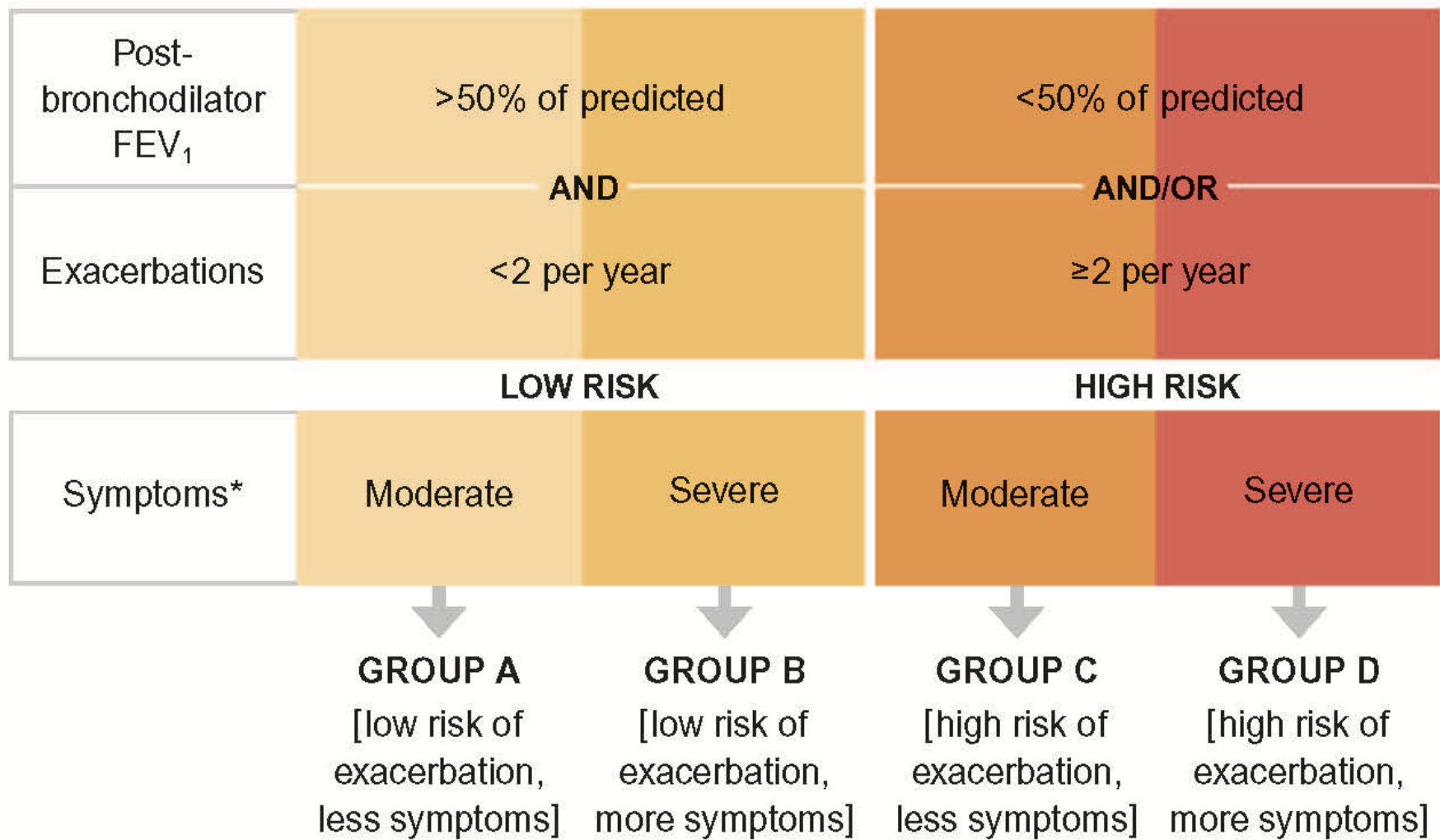
Assess comorbidities

Combined Assessment of COPD



Patient is now in one of four categories:

- A: Less symptoms, low risk
- B: More symptoms, low risk
- C: Less symptoms, high risk
- D: More symptoms, high risk



Pharmacologic Therapy RECOMMENDED FIRST CHOICE

		Exacerbations per year			
		≥ 2	1	0	
GOLD 4	C	ICS + LABA or LAMA	ICS + LABA and/or LAMA		
	D				
GOLD 3					
GOLD 2	A	SAMA <i>prn</i> or SABA prn	LABA or LAMA		
GOLD 1	B				
		mMRC 0-1 CAT < 10	mMRC ≥ 2 CAT > 10		

Group A**Group B****Group C****Group D****First line therapy**[Short-acting
 β -agonist PRN]

—OR—

[Short-acting
anticholinergic PRN][Long-acting
 β -agonist]

—OR—

[Long-acting
anticholinergic][Inhaled corticosteroid
+ long-acting
 β -agonist]

—OR—

[Long-acting
anticholinergic][Inhaled corticosteroid
+ long-acting
 β -agonist]

—OR—

[Inhaled corticosteroid
+ long-acting
 β -agonist +
long-acting
anticholinergic]*Add short-acting bronchodilators as rescue medication as needed***Optional alternative therapies:****Group A:** [Short-acting β -agonist + short-acting anticholinergic] **or** [long-acting β -agonist] **or** [long-acting anticholinergic]**Group B:** [Long-acting β -agonist + long-acting anticholinergic]**Group C:** [Inhaled corticosteroid + long-acting anticholinergic] **or** [long-acting β -agonist + long-acting anticholinergic]
or [long-acting β -agonist/long-acting anticholinergic + PDE4 inhibitor for chronic bronchitis]**Group D:** [PDE4 Inhibitor added to first line therapy for chronic bronchitis]

Group A

Group B

Group C

Group D

Smoking cessation

Reduce occupational and environmental exposures

Exercise/physical therapy

Good nutrition

Influenza and pneumococcal vaccines

Pulmonary rehabilitation

Pulmonologist referral

Address end of life decision making

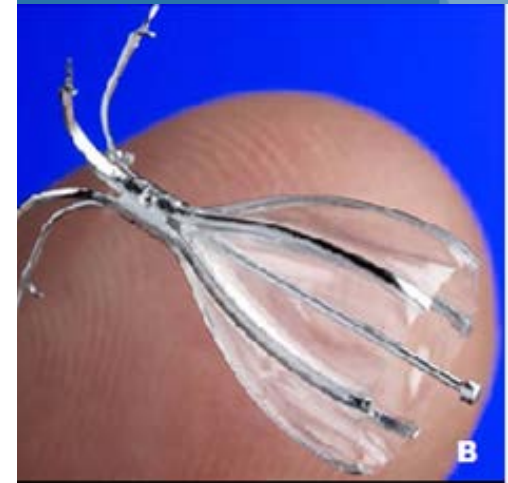
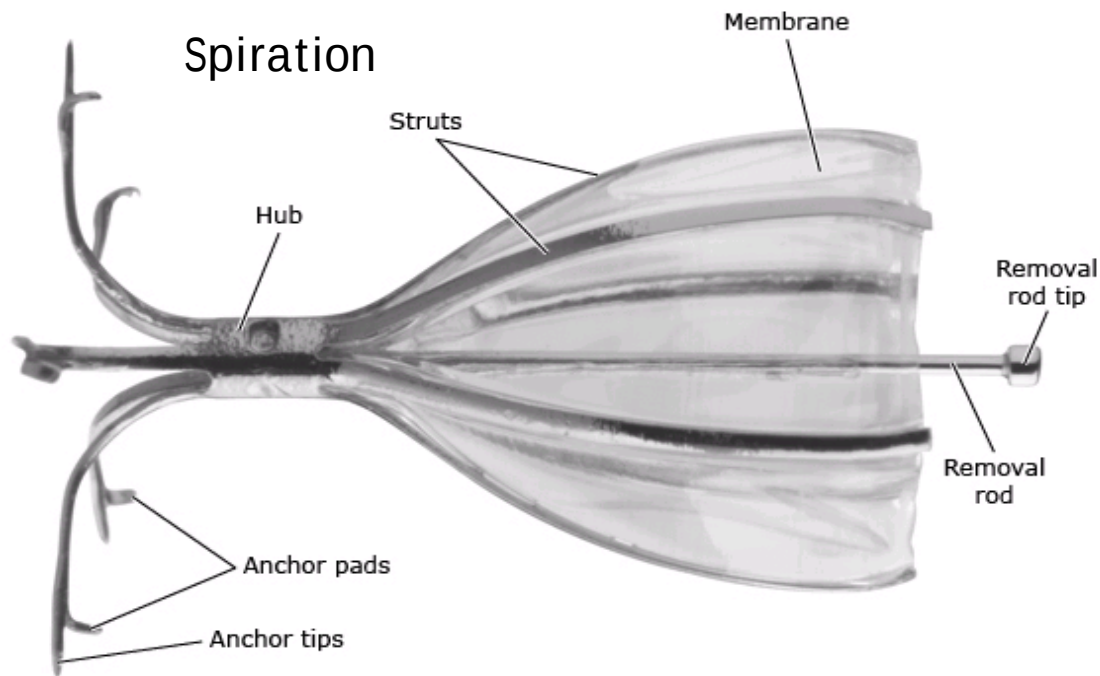
**Consider surgery
in selected patients**

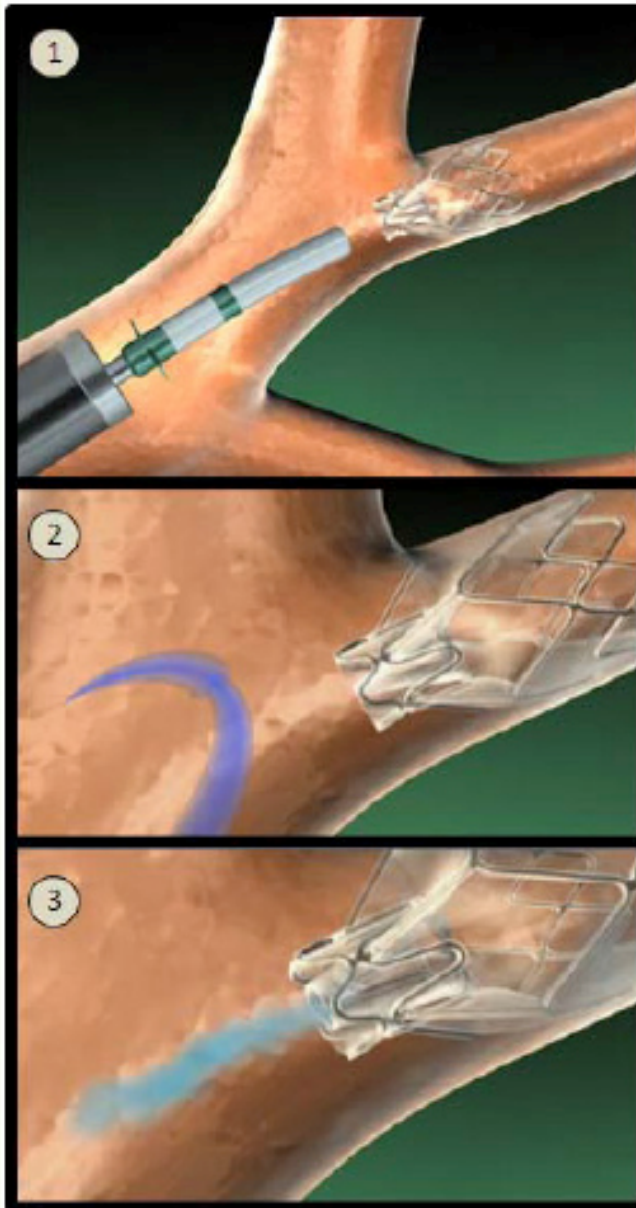
On the horizon.....



Endobronchial LVRS

- Valves
- Coils
- Biologics (thrombin/fibrin/polymers)
- Thermal ablation





Endobronchial Valves are delivered to the target airway via a delivery catheter placed through the working channel of the bronchoscope (Panel 1). Multiple valves are placed to completely isolate the diseased, hyperinflated target lobe.

Upon inspiration, the unidirectional valve at the center of the device blocks air from entering the target lobe (Panel 2).

Upon exhalation, air and fluids escape through the valve (Panel 3).

*Art courtesy of the
New England Journal of Medicine*

Regenerative therapy for COPD?

- Inducing endogenous stem cells to proliferate and differentiate in situ
 - Retinoids (all-trans-retinoic acid)
 - Others...
- Adding differentiated stem cells
 - Stem cells differentiated to Type II pneumocytes in vitro
 - Embryonic stem cells
 - Autologous (mesenchymal) stem cells
 - Adverse effects: Sarcomas and Fibrosis

????????????

CALL TOLL FREE
(888) 494-5910



Stem Cell Therapy for Lung Disease

*Breathe easier Arizona.
The Lung Institute is here!*

See if you qualify!

First Name

Last Name

Email

Phone

Select Disease

☒ I would like to receive the Lung Institute email newsletter.

Find Out More

By submitting this form, I am agreeing to the [LI Internet Privacy Disclosure](#).

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Stem Cell Therapy

Lung Diseases

Use your own stem cells to promote healing from lung disease.

Stem cells can promote healing in the lungs and slow the progression of chronic lung disease. The procedure has no chance of rejection and is minimally invasive.

At the Lung Institute, we provide treatment for the following diseases:

**THANK
YOU**

Robert.Aaronson@tmcaz.com

PDF

In Patients with FEV₁/FVC < 0.70:

Gold 1:	Mild	FEV ₁ ≥ 80% predicted
Gold 2:	Moderate	50% ≤ FEV ₁ < 80% predicted
Gold 3:	Severe	30% ≤ FEV ₁ < 50% predicted
Gold 4:	Very Severe	FEV ₁ < 30% predicted

Patient	Characteristic	Spirometric Classification	Exacerbations per year	mMRC	CAT
A	Low Risk Less Symptoms	GOLD 1-2	≤ 1	0 - 1	< 10
B	Low Risk More Symptoms	GOLD 1-2	≤ 1	≥ 2	≥ 10
C	High Risk Less Symptoms	GOLD 3-4	≥ 2	0 - 1	< 10
D	High Risk More Symptoms	GOLD 3-4	≥ 2	≥ 2	≥ 10
Patient Group	RECOMMENDED FIRST CHANCE	ALTERNATIVE CHOICE	OTHER POSSIBLE TREATMENTS		
A	SA anticholinergic prn or SA beta ₂ -agonist prn	LA anticholinergic or LA beta ₂ -agonist or SA anticholinergic and SA beta ₂ -agonist	Theophylline		
B	LA anticholinergic or LA beta ₂ -agonist	LA anticholinergic and LA beta ₂ -agonist	SA beta ₂ -agonist <i>and/or</i> SA anticholinergic Theophylline		
C	LA anticholinergic or ICS + LA beta ₂ -agonist	LA anticholinergic and LA beta ₂ -agonist or LA anticholinergic and PDE-4 Inhibitor or LA beta ₂ -agonist and PDE-4 Inhibitor	SA beta ₂ -agonist <i>and/or</i> SA anticholinergic Theophylline		
D	LA anticholinergic <i>and/or</i> ICS + LA beta ₂ -agonist	LA anticholinergic and ICS + LA beta ₂ -agonist or ICS + LA beta ₂ -agonist and PDE-4 Inhibitor or LA anticholinergic and LA beta ₂ -agonist or LA anticholinergic and PDE-4 Inhibitor	Carbocystine SA beta ₂ -agonist <i>and/or</i> SA anticholinergic Theophylline		

PDF

Your name:

Today's date:



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** (1) (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	