COPD 2009

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COPD 2009

Overview
Exacerbations
The Importance of Co-morbidities
COPD vs Asthma
What's New

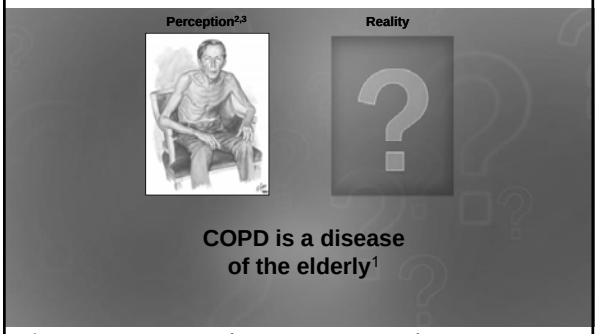
Definition of COPD

COPD is a preventable and treatable disease state that is

- Characterized by airflow limitation that is not fully reversible
- Usually progressive
- Associated with an abnormal inflammatory response of the lungs to noxious particles or gases
- Primarily caused by cigarette smoking
- Related to systemic consequences

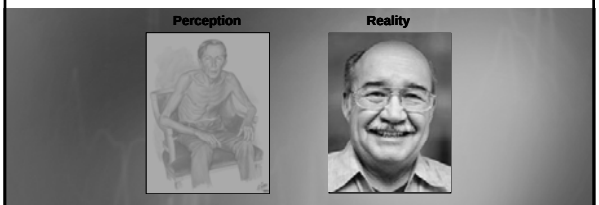
Celli et al. *Eur Respir J.* 2004;23:932-946.

Who is the COPD Patient?



[1]Tinkelman, et al. *Am J Manag Care*. 2003;9:767-771. [2]Rennard SI. *New Engl J Med*. 2004;350:965-966. [3]Kleinschmidt P. Chronic obstructive pulmonary disease and emphysema. Available at http://www.emedicine.com.

COPD in Younger Patients is on the Rise



- COPD afflicts the working age population
- ~ 50% of COPD patients are younger than age 65[3]
- Patients < 65 accounted for 67% of COPD office visits and 43% of hospitalizations[2]
- COPD is as common as asthma and diabetes in population aged 45-64[1]

[1]Mannino, et al. *MMWR*. 2002;51(6 suppl):1-16. [2]Sin, et al. *Am J Respir Crit Care Med*. 2002;165:704-707. [3]Tinkelman, et al. *Am J Manag Care*. 2003;9:767-771.

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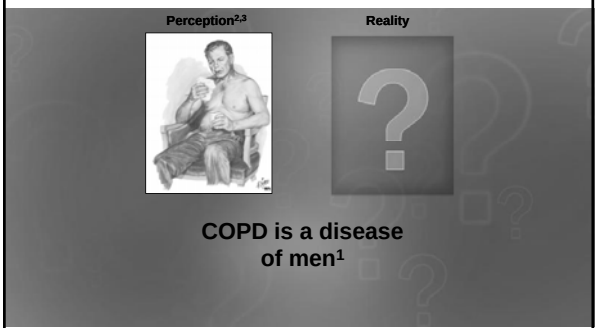
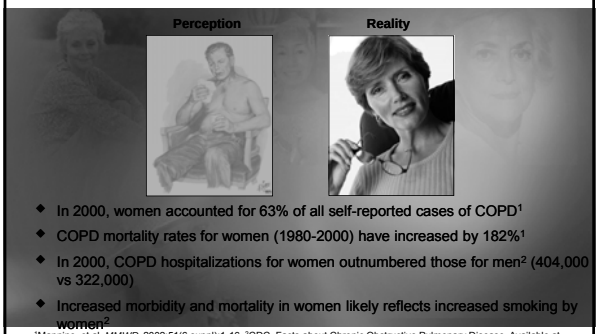


[1]Chapman KR. *Clin Chest Med*. 2004;25:331-334. [2]Rennard SI. *New Engl J Med*. 2004;305:965-966. [3]Kleinschmidt P. Chronic obstructive pulmonary disease and emphysema. Available at http://www.emedicine.com.

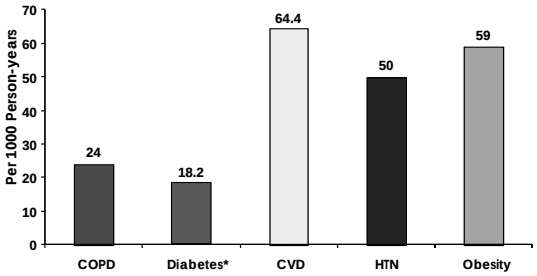
COPD in women is on the rise



- In 2000, women accounted for 63% of all self-reported cases of COPD[1]
- COPD mortality rates for women (1980-2000) have increased by 182%[1]
- In 2000, COPD hospitalizations for women outnumbered those for men[2] (404,000 vs 322,000)
- Increased morbidity and mortality in women likely reflects increased smoking by women[2]

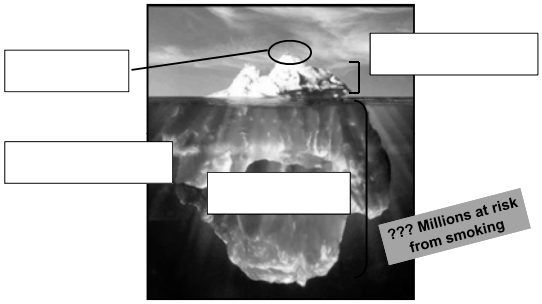
[1]Mannino, et al. *MMWR*. 2002;51(6 suppl):1-16. [2]CDC. Facts about Chronic Obstructive Pulmonary Disease. Available at http://www.cdc.gov. Netter illustrations used with permission from Icon Learning Systems, a division of MediMedia USA, Inc. All rights reserved.

COPD Is as Prevalent as Many Other Chronic Diseases Treated in Primary Care



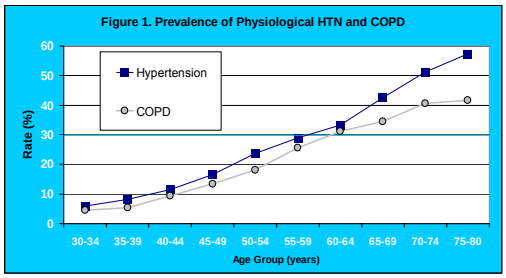
**All About Diabetes.* American Diabetes Association Web site. http://www.diabetes.org. 90% to 95% of Americans with diabetes have type 2 diabetes. AHA. *Heart Disease and Stroke Statistics—2004 Update.* Dallas, TX: AHA; 2003.
Frequently asked questions on overweight and obesity. CDC Web site. http://www.cdc.gov/nccdphp/dnpa/obesity/faq.htm#adults.

Clinical COPD Is Just the Tip of the Iceberg



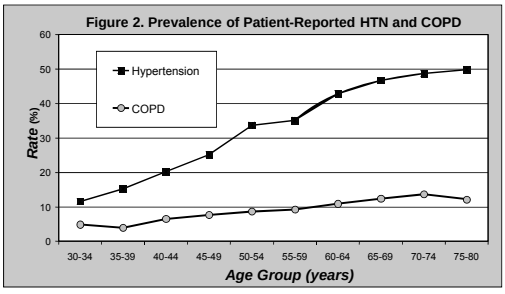
*Repeated exacerbations and hospitalizations.
Mannino et al. *MMWR Morb Mortal Wkly Rep*. 2002;51(SS-6):1-16.

Prevalence in NHNES III



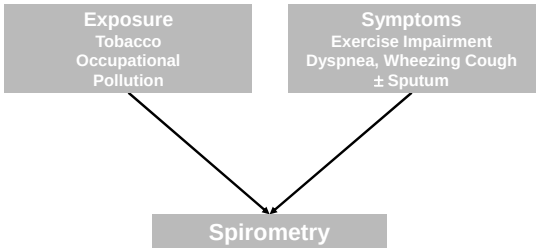
Celli et al ATS 2004

Prevalence in NHNES III



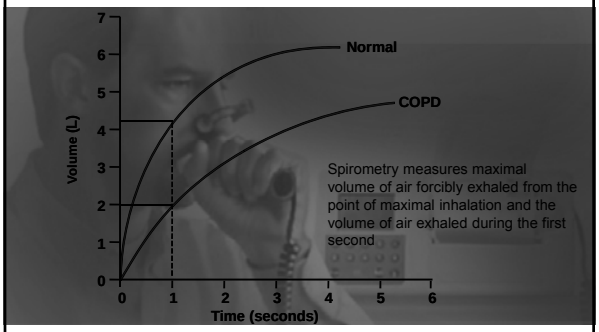
Celli et al ATS 2004

When to Perform Spirometry: Diagnosis of COPD (GOLD Guidelines)



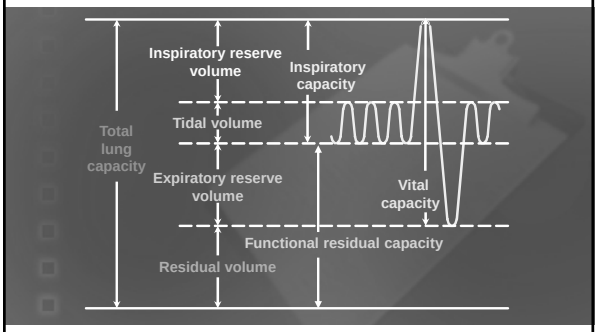
Executive Summary: Global Strategy for the Diagnosis, Management, and Prevention of COPD Updated 2005. Available at: http://www.goldcopd.com/Guidelineitem.asp?l1=2&l2= 1&intId=996. Accessed June 6, 2006 (A).

Spirometry Measurement in COPD

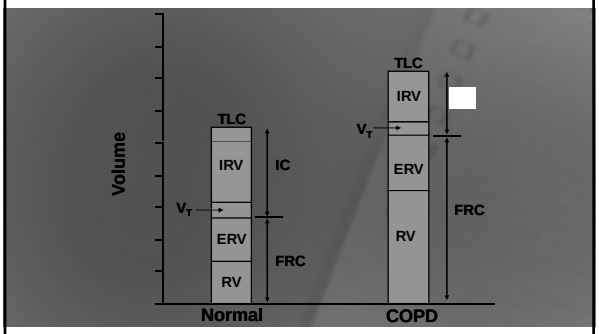


Adapted from Weinberger SE. Disturbances of Respiratory Function. In: Fauci AS et al (eds.) *Harrison's Principles of Internal Medicine*. Vol 2; 14th edition. NY: McGraw-Hill; 1998:1410.

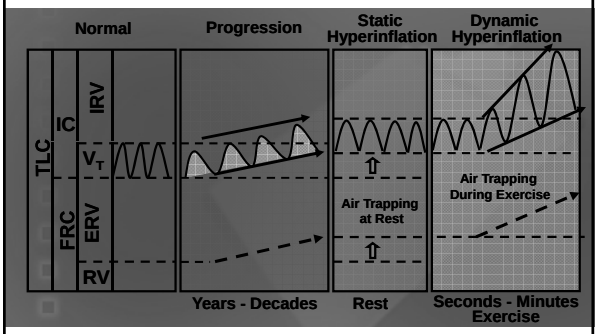
Lung Volume Terminology

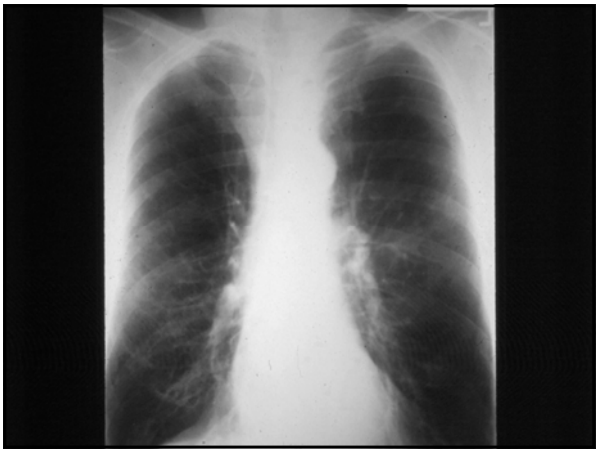


Comparison of Lung Volume Parameters

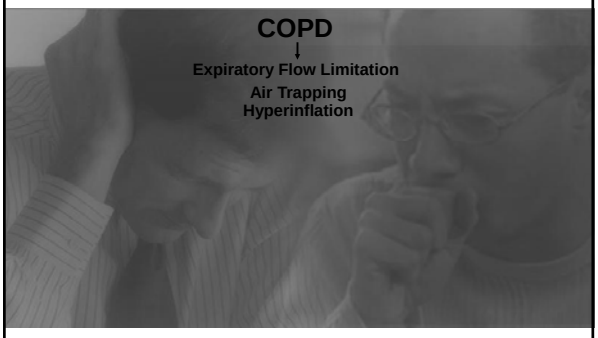


Effects of Exercise on Hyperinflation



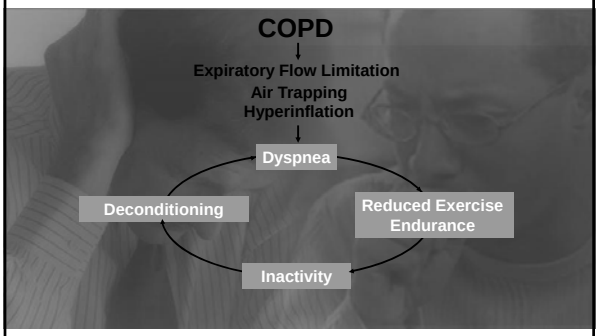


Damaging Cycle of COPD



Adapted from Global Initiative for Chronic Obstructive Lung Disease (GOLD) Executive Summary. Updated 2003. Available at: http://www.goldcopd.com

Damaging Cycle of COPD



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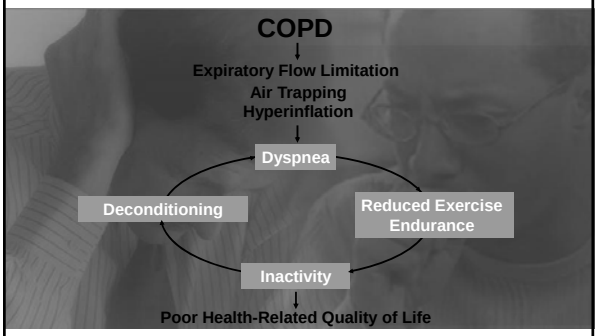

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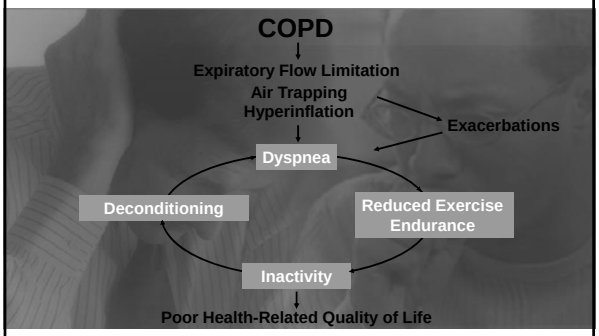

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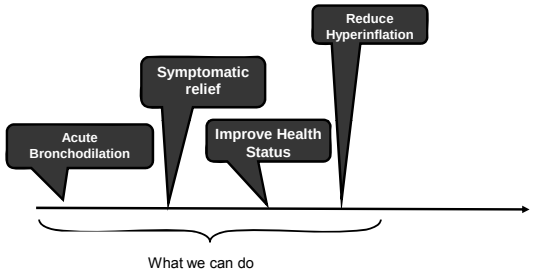
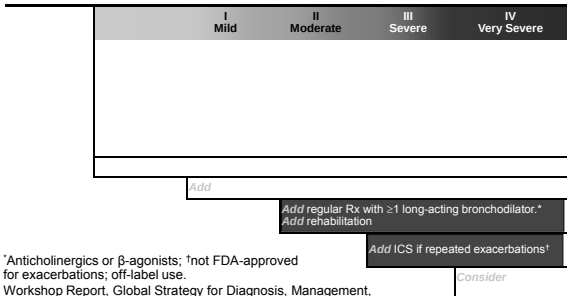
An abbreviated history of COPD therapy



Therapy Based on Staging of COPD



*Anticholinergics or β-agonists; †not FDA-approved for exacerbations; off-label use.
Workshop Report, Global Strategy for Diagnosis, Management, and Prevention of COPD – 2005 Update. Available at: http://www.goldcopd.com/Guidelineitem.asp?l1=2&l2=1&intId=989. Accessed June 6, 2006 (A).

Effects of Bronchodilators on Clinical Outcomes in Patients With COPD

*Although the results from a number of drug studies are not uniform, many of the drugs studied provide these results. N/A=evidence not available.
Adapted from Celli et al. *Eur Respir J*. 2004;23:932-946.

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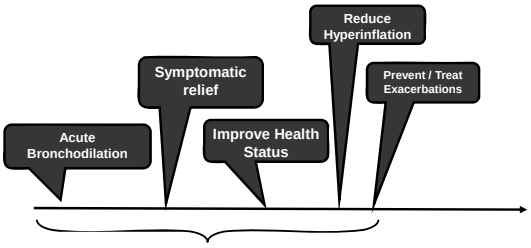


COPD Exacerbations

Defined as an acute change in dyspnea, cough and/or sputum sufficient enough to warrant therapy change[1]

In a 12-month observational study (n=127), 77% of patients reported having at least one exacerbation[2*]

The prevention of exacerbations is recognized as a key goal in COPD disease state management[3]

***Based on diary records of symptom-defined and healthcare-defined exacerbations.**

1. American Thoracic Society/European Respiratory Society. *Standards for the diagnosis and management of patients with COPD* [Internet]. Version 1.2. www.thoracic.org/go/copd. Accessed April 30, 2008.
2. O'Reilly, et al. *Prim Care Respir J.* 2006;15:346-353.
3. Global Initiative for Chronic Obstructive Lung Disease. *Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease* – Updated 2007. www.goldcopd.org. Accessed April 30, 2008.

The Majority of Healthcare Costs for Managing COPD Are Associated With Exacerbations

In 2005, there were approximately 721,000 hospitalizations due to COPD[1]

Average costs (2001 data) for a COPD-related[2]:

- Emergency Department Visit—$571
- Hospitalization ranged from
  - $5,997 (standard hospitalization) to
  - $36,743 (ICU plus intubation)

50%-75% of all COPD costs are for services associated with exacerbations[3]

1. American Lung Association. *Trends in chronic bronchitis and emphysema: morbidity and mortality*. December 2007. www.lungusorg. Accessed April 30, 2008.
2. Stanford R, et al. *Treat Respir*2006;5:343-349.
3. American Thoracic Society/European Respiratory Society. *Standards for the diagnosis and management of patients with COPD* [Internet]. Version 1.2. www.thoracic.org/go/co Accessed April 30, 2008.

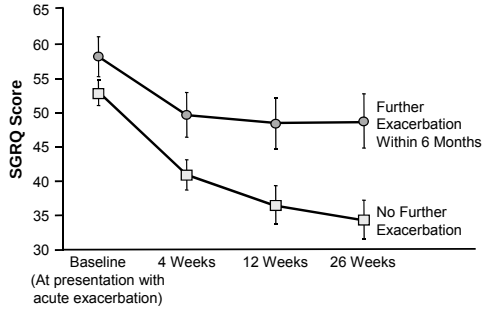
Outcomes of AECOPD

In ICU patients	Hospital mortality	20%-24%
In hospitalized patients	Hospital mortality	2.5%-10%
In ER patients	Relapse (repeat ER visit)	22%-32%
In outpatients	Treatment failure rate	13%-33%

Treatment failure is defined as not responsive to initial treatment(s).
Outcomes = health utilizations.

Seneff et al. *JAMA*. 1995;274:1852-1857 (B); Murata et al. *Ann Emerg Med*. 1991;20:125-129 (B); Adams et al. *Chest*. 2000;117:1345-1352 (B); Patil et al. *Arch Intern Med*. 2003;163:1180-1186; Ai-Ping et al. *Chest*. 2005;128:518-524 (B).

Health Status Changes Following an Exacerbation



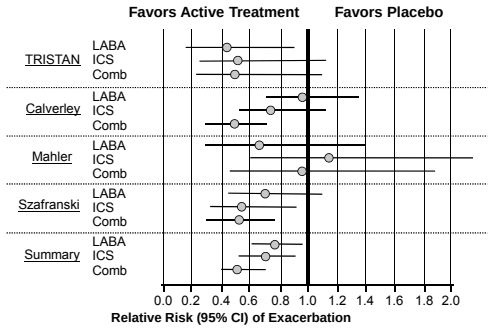
Spencer et al. *Thorax*. 2003;58:589-593 (A).

Prevention of Acute Exacerbations in COPD

COPD Exacerbations Preventative Measures

- Long acting bronchodilators
- Inhaled corticosteroids
- Phosphodiesterase inhibitors
- Mucolytics/Antioxidants
- Immunizations-influenza vaccine pneumococcal vaccine
- OM-85(Broncho-vaxim)
- Macrolides
- Case management
- Lung Volume Reduction Surgery

Prevention of AECOPD Additive Drug Effects



Adapted from Sin et al. *JAMA*. 2003;290:2301-2312.

COPD Exacerbations Preventative Measures

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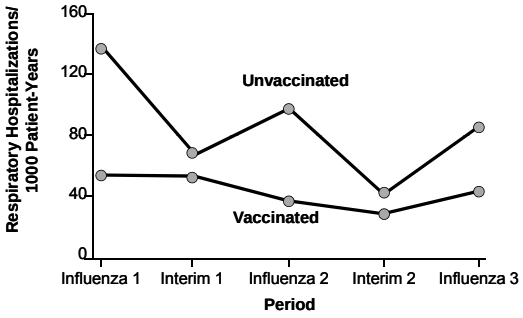
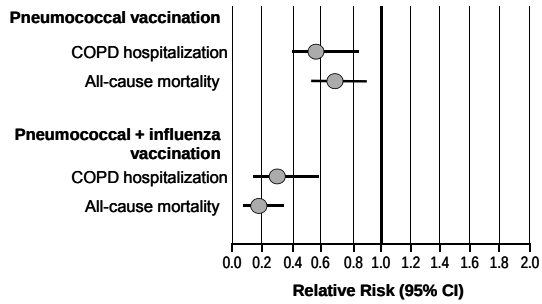
Prevention of COPD Exacerbations: Influenza Vaccination



Nichol et al. *Ann Intern Med*. 1999;130:397.

Prevention of COPD Exacerbations: Pneumococcal and Influenza Vaccination



Nichol et al. *Arch Intern Med*. 1999;159:2437-2442.

COPD Exacerbations Preventative Measures

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Management of Acute Exacerbations in COPD

Bronchodilators in Acute Exacerbations of COPD

- Initiate or increase dose of short-acting inhaled beta$_2$-agonists (eg, albuterol)
- Add anticholinergic (eg, ipratropium) if no prompt response
- Role of methylxanthines (aminophylline, theophylline) is controversial: some benefits as third-line drug, but side effects and drug interactions
- Delivery method (nebulization or metered dose) can be individualized

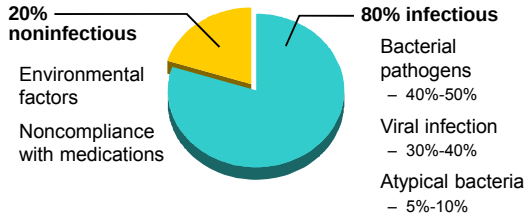
NIH/NHLBI. Global Initiative for Chronic Obstructive Lung Disease ("GOLD"), Updated 2003.

Systemic Corticosteroids in Acute Exacerbations of COPD

- Corticosteroids shorten recovery time, help restore lung function
- Add to bronchodilators if baseline FEV_1 is <50% predicted
- Dosage, length of treatment, administration, and setting have varied widely
- 2-week course as beneficial as 8-week course
- 3-day course not as beneficial as 10-day course
- GOLD-recommended regimen: 30-40 mg prednisolone for 10-14 days
- Common side effect: hyperglycemia (mostly in patients with type 2 diabetes)

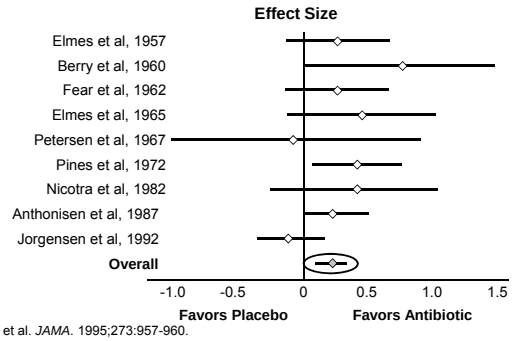
NIH/NHLBI. Global Initiative for Chronic Obstructive Lung Disease ("GOLD"), Updated 2003
Niewoehner DE et al. *N Engl J Med*. 1999;340:1941-1947.
Snow V et al. *Ann Intern Med*. 2001;134:595-599.

AECOPD: Etiology of AECOPD



Sethi et al. *Chest*. 2000;117:380-385.

COPD Exacerbations: Antibiotic Therapy



Saint et al. *JAMA*. 1995;273:957-960.

Antibiotics in Acute Exacerbations

- Beneficial in patients with 2 or more symptoms: worsening dyspnea, increased sputum volume, increased sputum purulence
- Patients with severe exacerbations and/or severe underlying COPD are most likely to benefit
- Traditional regimen: 3-14 days of tetracycline, amoxicillin, or trimethoprim-sulfamethoxazole
- Choice of agent should reflect local patterns of antibiotic sensitivity among *S pneumoniae, H influenzae,* and *M catarrhalis*
- Exacerbations have been linked to new strains of these organism

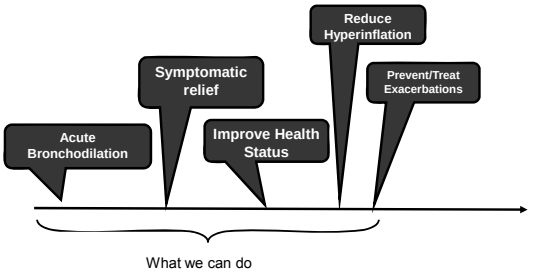
Anthonisen NR et al. *Ann Intern Med*. 1987;106:196-204.
Snow V et al. *Ann Intern Med*. 2001;134:595-599.
Sethi S et al. *N Engl J Med*. 2002;347:465-471.

NPPV in Acute Exacerbations of COPD

- Tight-fitting mask with bilevel positive airway pressure
- Early-care alternative to endotracheal tube or tracheostomy
- Physiologic improvements: increases pH, reduces $PaCO_2$
- Symptomatic improvements: reduces severity of breathlessness
- Decreases intubation rate, mortality rate, and hospital length of stay
- NPPV: now a standard of care in acute exacerbations…but still controversial in severe stable COPD
- Unresolved issues: efficacy in "real-world" settings, costs, ideal patients

NIH/NHLBI. Global Initiative for Chronic Obstructive Lung Disease ("GOLD"), Updated 2003.
Mehta S et al. *Am J Respir Crit Care Med*. 2001;163:540-577.
Hill NS. *Resp Care*. 2004;49:72-87.

An abbreviated history of COPD therapy



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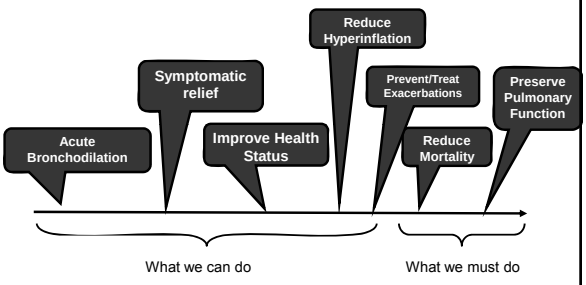
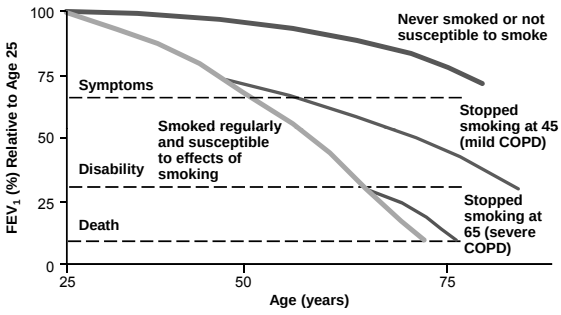
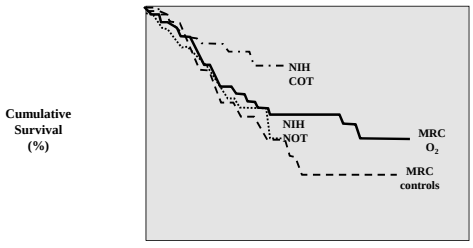


Lung Function Over Time

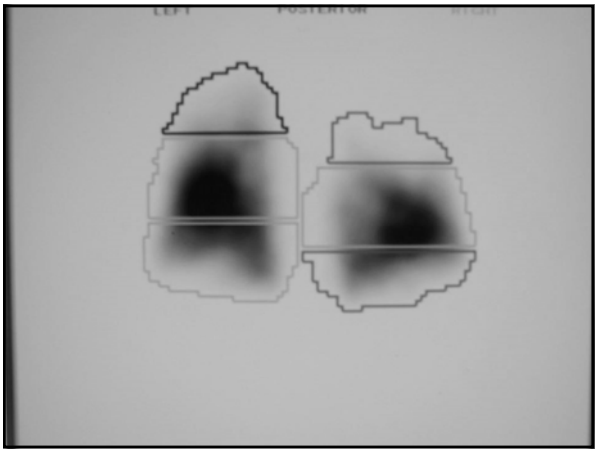


Adapted from Fletcher et al. *BMJ.* 1977;1:1645-1648 (B).

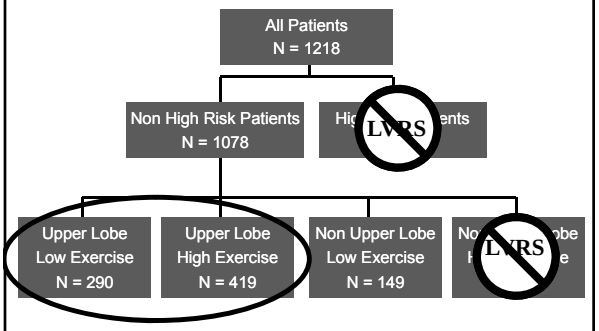
Oxygen reduces mortality in COPD patients with resting hypoxemia



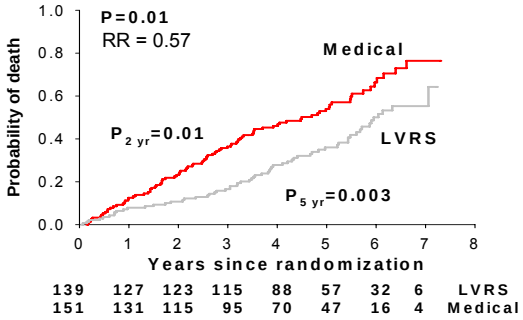
COT = continuous oxygen therapy; NOT = nocturnal oxygen therapy; MRC controls = no oxygen therapy; MRC = domiciliary oxygen therapy.
Flenley DC. *Resp Care*. 1983;2S:876.



Lung volume reduction surgery is appropriate in subgroups of COPD



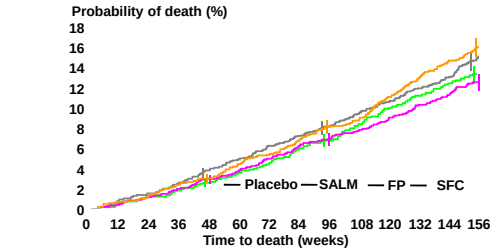
Mortality
Upper Lobe / Low Exercise



Alpha one Replacement Therapy Product Comparison

* Minimum release specific activity. Actual specific activities for all drugs are much higher.
† Limited and not promoted

TORCH: All-cause mortality at 3 years



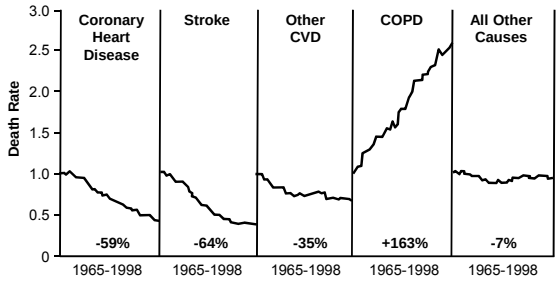
Number alive	1524	1464	1399	1293
	1533	1487	1426	1339
	1521	1481	1417	1316
	1534	1487	1409	1288

Vertical bars are standard errors

Calverley et al. *N Engl J Med* 2007;356:775.

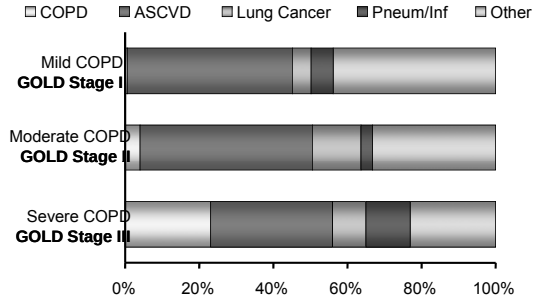
COPD: The Importance of Co-morbidities

Percent Change in Age-Adjusted US Death Rates



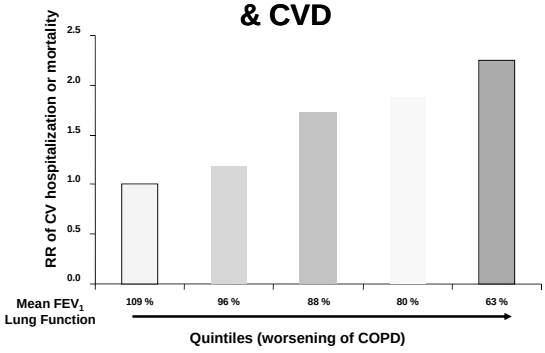
GOLD. Available at: http://www.goldcopd.org/OtherResourcesItem.asp?l1=2&l2=2&intId=969. Accessed July 13, 2006 (A).

What Do COPD Patients Die From?



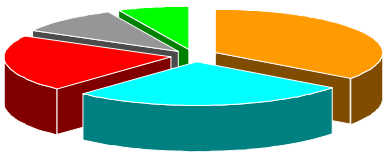
Mannino et al. *Thorax.* 2003;58:388-393.

The Relationship Between COPD & CVD



NHANES 1; N=1,861

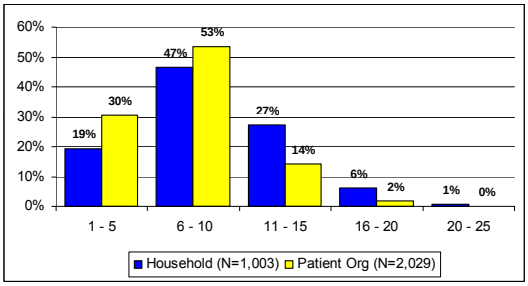
Overall causes of death in TORCH as adjudicated by the Clinical Endpoint Committee



Calverley et al. *N Engl J Med* 2007;356:775.

Unapproved Use
Not For Affirmative Use

Total Number of Co-Morbidities

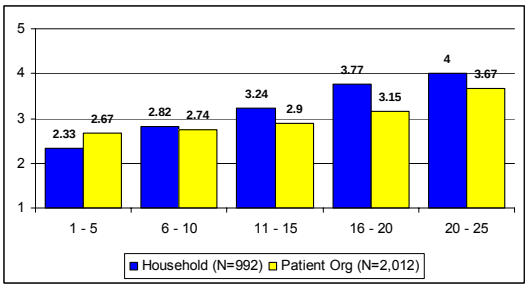


p < .001 58

COPD and Co-morbidities

- Arthritic Pains- 70%
- GERD- 63%
- Sinus Disease- 58%
- Heart Disease- 54%
- Hypertension- 52%
- Hyperlipidemia- 51%
- Depression- 38%
- Cataract- 32%
- Osteoporosis- 30%
- Sleep apnea- 20%
- Diabetes- 18%

Degree of Dyspnea grouped by # of Co-Morbidities



60

COPD : A Systemic Disease
The Importance of Inflammation

COPD: The Role of Inflammation

Ongoing Lung Inflammation

↓

Systemic Inflammation

↓

End Organ Damage

COPD vs Asthma

COPD vs Asthma: Definitions

COPD

A preventable and treatable disease characterized by airflow limitation that is not fully reversible

Airflow limitation is usually progressive and may be associated with an abnormal inflammatory response of the lungs to noxious particles or gases

Asthma

A chronic inflammatory disorder of the airways with an associated increase in airway hyperresponsiveness

Recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning

Usually associated with widespread but variable airflow obstruction often reversible either spontaneously or with treatment

ATS/ERS, http://www.thoracic.org/sections/publications/statements/pages/respiratory-disease-adults/copd1-45.html; www.ginasthma.org. The Global Initiative for Asthma: Available at: www.ginasthma.org. Accessed: July 31, 2006.

Asthma vs COPD
History

Asthma

- Atopy
- Sensitizing agents
- Family History
- Childhood or young adult onset
- Intermittent wheeze/symptoms

COPD

- Smoking history
- Noxious agents
- Later onset
- Progressive symptoms

Asthma vs COPD
Inflammatory Markers

Asthma

- Cells- eosinophils, + macrophages, mast cells
- CD4 T-lymphocytes
- Mediators-histamine, IL-4, IL-5, IL-13
- Effects all airways, little fibrosis, epithelial shedding

COPD

- Cells- neutrophils, lymphocytes, +++macrophages
- CD8 T-lymphocytes
- Mediators-LTb_4, IL-8, TNF-alpha
- Effects-peripheral airways, lung destruction, fibrosis and sqaumous metaplasia

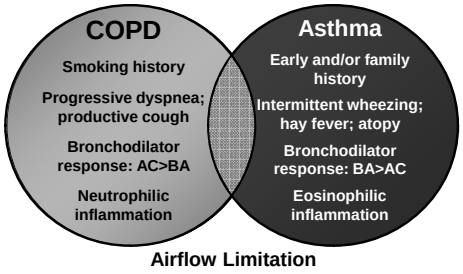
Asthma vs COPD Physiologic Responses

Asthma	COPD
Reversible	Partially reversible
Bronchodilator response BA>AC	Bronchodilator response AC>BA
Steroid responsive	+/- Steroid effect
+/- Dynamic hyperinflation with exacerbations	Progressive static and dynamic hyperinflation
Normal DLCO	Reduced DLCO in emphysema

Asthma vs COPD Therapy

Asthma	COPD
ICS- first line therapy	Bronchodilators- first line therapy
Smoking asthmatics less responsive	Add ICS if recurrent exacerbations
Add bronchodilators-Beta agonists	ICS not first line therapy unless overlap
Leukotriene modifiers	+/- Theophyllines
+/- Theophyllines	

Clinical Overlap Between COPD and Asthma

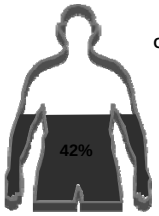


Adapted by Christopher B. Cooper, MD.
Barnes. *Chest.* 2000;117:10-14 (C); Balmes et al, for the American Thoracic Society. *Am J Respir Crit Care Med*. 2003;167:787-797 (C).

COPD Misdiagnosis Is Common in Women

Hypothetical male patient with COPD symptoms

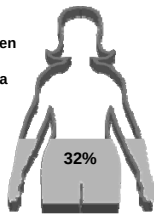
Diagnosed as COPD by 42% of physicians



COPD symptoms in women were most commonly misdiagnosed as asthma

Hypothetical female patient with COPD symptoms

Diagnosed as COPD by 32% of physicians



Miravitlles et al. *Arch Bronconeumol.* 2006;42:3-8.

COPD: What's New

COPDGENE

6000 with COPD

4500 current or former smokers without COPD

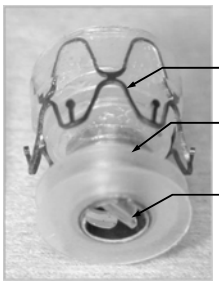
30% African Americans

CT scans, spirometry pre and post, genetic studies

Minimally Invasive Lung Volume Reduction

Bronchoscopic Valves

Emphasys Endobronchial Valve ™

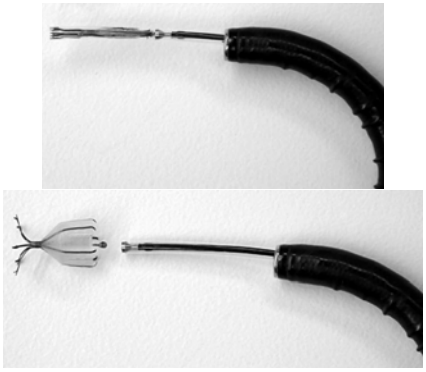


Valve Design

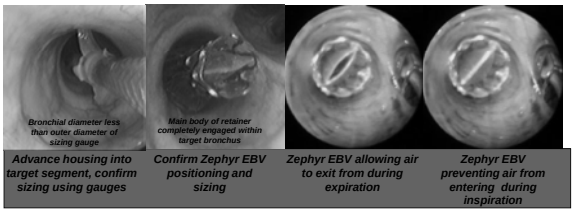
- **Self-expanding retainer**
  - stabilizes device in airway
- **Flexible seals**
  - conform to bronchial wall
  - prevent air leak around valve
- **One-way valve**
  - blocks inspiration
  - allows mucus clearance

Investigational device only. Not currently approved for sale.

Spiration intra-bronchial valve



EBV Procedure Overview



Advance housing into target segment, confirm sizing using gauges

Confirm Zephyr EBV positioning and sizing

Zephyr EBV allowing air to exit from during expiration

Zephyr EBV preventing air from entering during inspiration

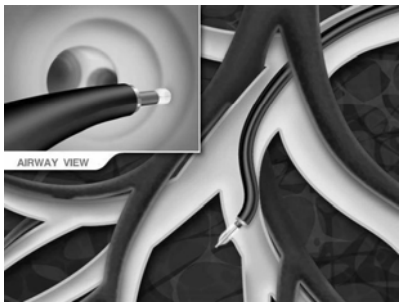
Pre-procedure

24 hours post-procedure

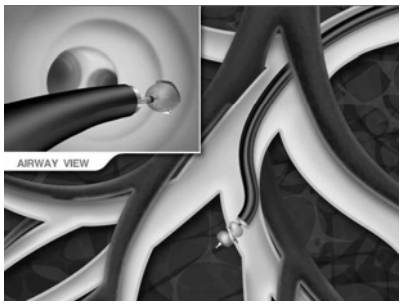
Minimally Invasive Lung Volume Reduction

Bronchoscopic Stent Placements

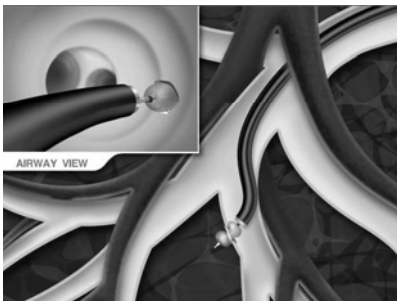
Airway Bypass Procedure



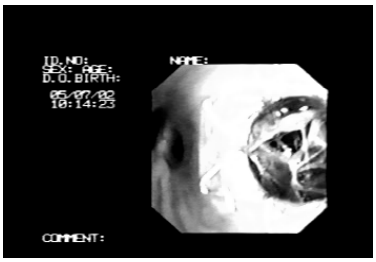
Airway Bypass Procedure



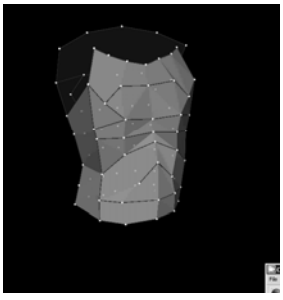
Airway Bypass Procedure



Airway Bypass Procedure



OPTICAL ELECTRONIC PLETHYSMOGRAPHY OEP



COPD 2009

Treatable and Preventable
Together We Can Make a Difference