

# ***COPD and COMORBIDITIES***

## ***Why All The Worry ?***

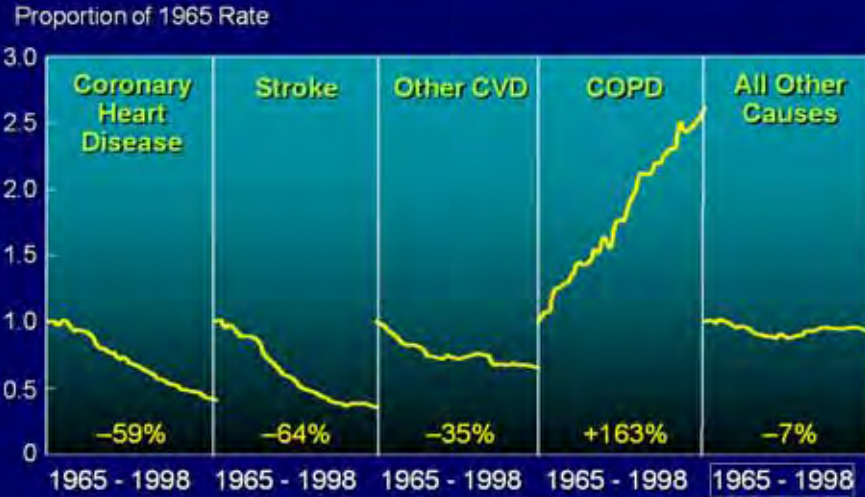
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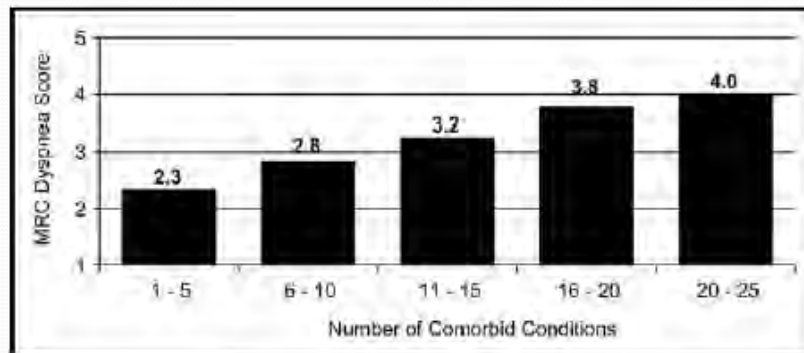
## **Brian Carlin, MD Disclosures**

- Speakers' bureau
  - Glaxo Smith Kline
  - Boehringer Ingelheim
  - Philips Respironics
  - Forest
  - Breathe Technologies
  - PneumRx
- Organizational
  - National Lung Health Education Program (Chair)
  - National Board for Respiratory Care

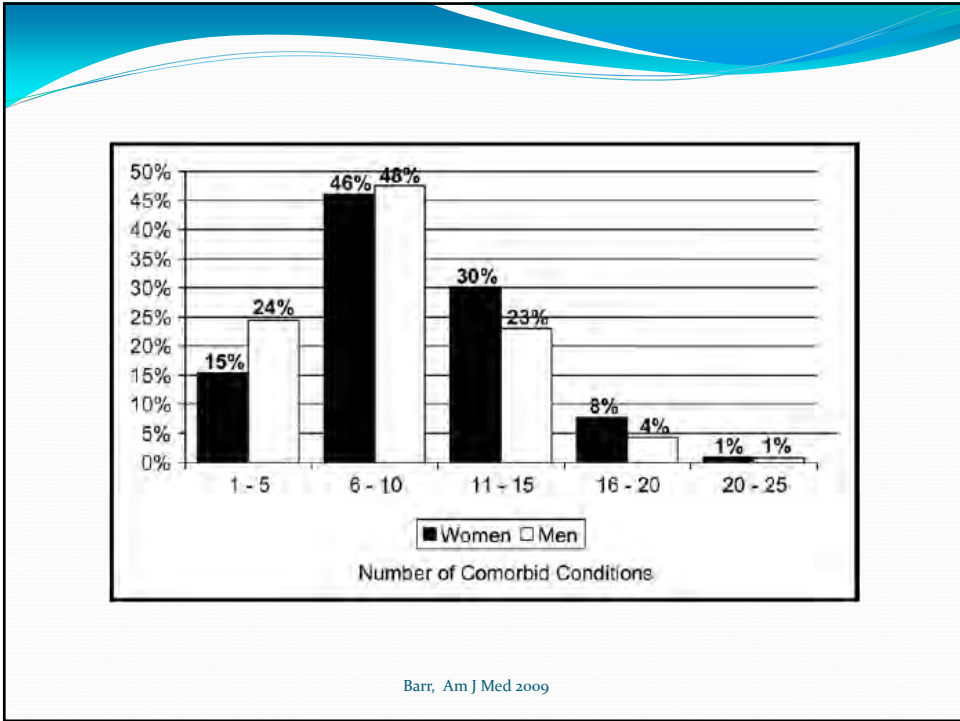
## Percent Change in Age-Adjusted Death Rates, U.S., 1965-1998



Source: NHLBI/NIH/DHHS



Barr, Am J Med 2009

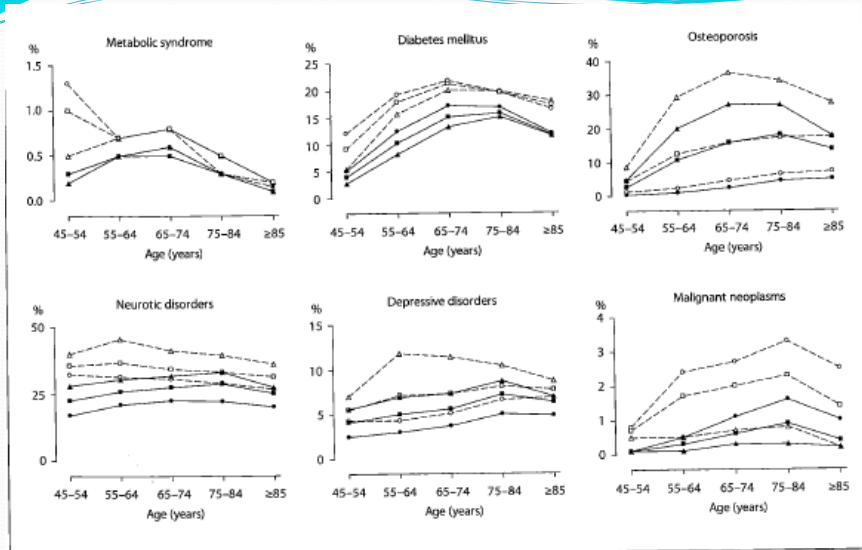


## Comorbidities and COPD

- What you might expect ?
- Write down three comorbidities that you might expect to see ?

# COPD

- Airflow limitation
  - Airway inflammation
  - Remodeling
  - Emphysema
  
- Systemic manifestations
  - Cardiovascular compromise
  - Malnutrition
  - Skeletal muscle dysfunction
  - Osteoporosis
  - Anemia
  - Gastro esophageal reflux
  - Depression, anxiety



**Fig. 2.** People with (□○△) and without COPD (■●▲) who reported other selected comorbidities by age group and gender (% of the examined population). ■ □ = Total; ● ○ = men; ▲ △ = women.

Cazzola, Respiration 2010

## Impact of Comorbidities and COPD

- HRQL
- Utilization of healthcare resources
- Response to pulmonary rehabilitation
- Mortality

## Impact of Comorbidities and COPD

Putcha, J COPD 2013

- Self reported dx of COPD (n=843, NHANES data)
- Higher number of concurrent chronic conditions
- Inverse relationship (QOL and comorbidities)
- Those particularly more detrimental
  - CHF
  - DM
  - CAD
  - Arthritis
  - Asthma
  - Depressive symptoms
  - Obesity
  - Urinary incontinence



## Systemic Inflammation

- Spillover, parallel, or other relation (??)
- Related to accelerated decline in lung function
- Components
  - Cytokines
  - Acute phase proteins
  - Circulating cells

## Systemic Factors

- Overt malnutrition
- Loss of muscle mass
- Anemia
- Osteoporosis
- Cardiovascular compromise
- Evaluation
  - BODE
  - HRQL questionnaires

## Muscle Dysfunction / Malnutrition

- Main systemic side effects of COPD
- Loss of fat-free muscle mass
- Associated with
  - Reduced exercise capacity
  - Morbidity
  - Need for mechanical ventilatory support
  - Increase hospitalization rate
  - Mortality

## Muscle Dysfunction Mechanisms

- Poorly understood
- Inactivity a key factor
  - Diaphragm v. quadriceps
- Complex process
  - Control of substrate and protein metabolism
  - Changes in muscle cell regeneration, apoptosis

## Muscle Dysfunction Mechanisms

- Systemic inflammation is an important factor
  - NF-kB activation results in muscle loss
- Enhanced oxidative stress
  - Increased reactive oxygen species
  - Reduced antioxidant capacity
    - Increase muscle proteolysis
    - Inhibit muscle-specific protein expression
    - Increase muscle cell apoptosis

## Muscle Dysfunction Treatment

- Pulmonary rehabilitation
  - Improves exercise capacity
  - Increases oxidative enzymes in mitochondria
- Never returns to normal
- Medications (??)
- Nutritional supplements (??)



## Muscle Dysfunction

### What Should I Do?

- Recognize as cause

## Normocytic Anemia

- High prevalence in COPD (15-30%)
- Polycythemia rare (6%)
- Independent predictor of mortality
- Erythropoietin resistance
- Treatment effects unknown

## Normocytic Anemia

- Linked in COPD
  - Health status
  - Exercise intolerance
  - Hospital readmit rate
  - Mortality
  - Proinflammatory cytokines

## Anemia

Divo, AJRCCM 2012

- 321 pts with COPD (admitted to PR)
- Anemia (hgb <12,13) 20%
- Polycythemia 8%
- Anemia
  - Higher CRP levels
  - Lower BMD
- Polycythemia
  - Lower % of men
  - Lower proportion of low muscle mass

# Anemia

Divo, AJRCCM 2012

## KEY FINDINGS

- No difference in disease related outcomes
- Only 3% reported anemia (i.e. underdiagnosis)

# Anemia

## What Should I Do?

- Consider anemia
- Obtain CBC

## Osteoporosis

- High prevalence
  - Osteoporosis
  - Low bone mineral density
- TORCH study
  - Over 50% patients had osteoporosis/osteopenia
- Patients with GOLD IV – 75 % prevalence
- High for males
- Relationship with functional status is unknown

## Osteoporosis Mechanisms

- Advanced age
- Poor mobility
- Smoking
- Poor nutrition
- Low BMI
- High doses of steroids (inhaled, oral)



## Osteoporosis Treatment

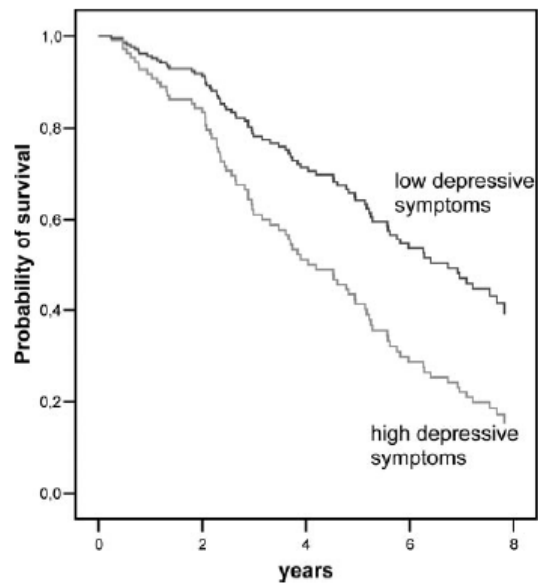
- Measure BMD
- Medical therapy (bisphosphonate)

## Osteoporosis What Should I Do ?

- Bone mineral density test
- Vitamin D
- Calcium
- Bisphosphonate

# Depression

- Frequently associated with COPD
  - 42% incidence
- Similar symptoms
- Often undiagnosed



DeVoogd, Chest 2009

## Depression Mechanisms

- Unknown
- Multifactorial
  - Genetic factors
  - Smoking
  - “reactive” due to declining health
  - Aging
  - Hypoxemia
  - Systemic inflammation

## Depression Therapy

- Antidepressants
- Pulmonary rehabilitation
- Psychotherapy
- Anti-inflammatory (?)

## Depression

### What Should I Do?

- Screening
- Appropriate referral

## Lung Cancer

- 3-4 times more likely to develop
- Increase in women



## Lung Cancer Mechanisms

- Increased inflammation and oxidative stress
- NF-kappa beta activation
- Promotion of tumor angiogenesis
- Other factors
  - Transcription factor nuclear factor
  - Epidermal growth factor receptors

## Lung Cancer What Should I Do?

- High index of suspicion
- Radiographic studies
  - Chest Xray
  - Computed tomography scan

## Diabetes

- Increased prevalence in patients with COPD
  - Even in mild disease
  - Doubtful due to steroid use
  - Insulin resistance
    - Cytokine induced
    - Plasma CRP, TNF-alpha

## Diabetes

### What Should I Do ?

- Ask about symptoms (e.g. polyuria, polydipsia)
- Obtain serum glucose, hemoglobin a-1 C level

## Sleep Disordered Breathing

- OSA - 20% have COPD
- COPD - 10% have OSA
- Both share several comorbidities
  - Endothelial dysfunction
  - Cardiac failure
  - Diabetes
  - Metabolic syndrome

## COPD and OSA

Marin, AJRCCM 2010

- Results
  - Compared to COPD only group
    - Overlap syndrome treated with CPAP
      - No increased risk for either outcome
    - Overlap syndrome not treated with CPAP
      - Higher mortality RR 1.79 (1.16-2.77 95% CI)
      - Exacerbation RR 1.70 (1.21-2.38 95% CI)

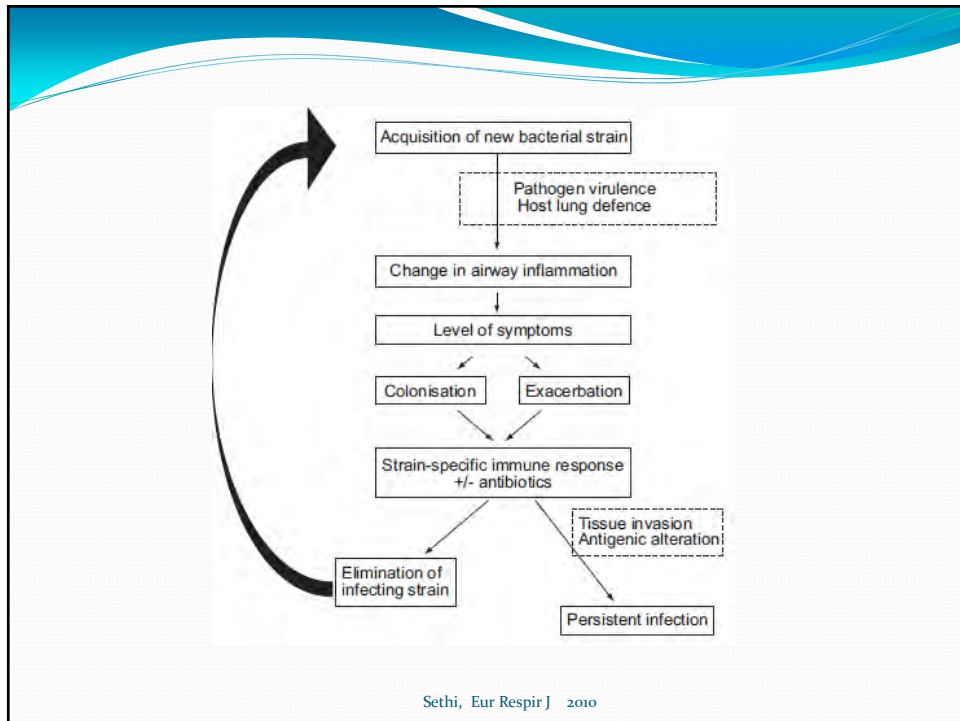
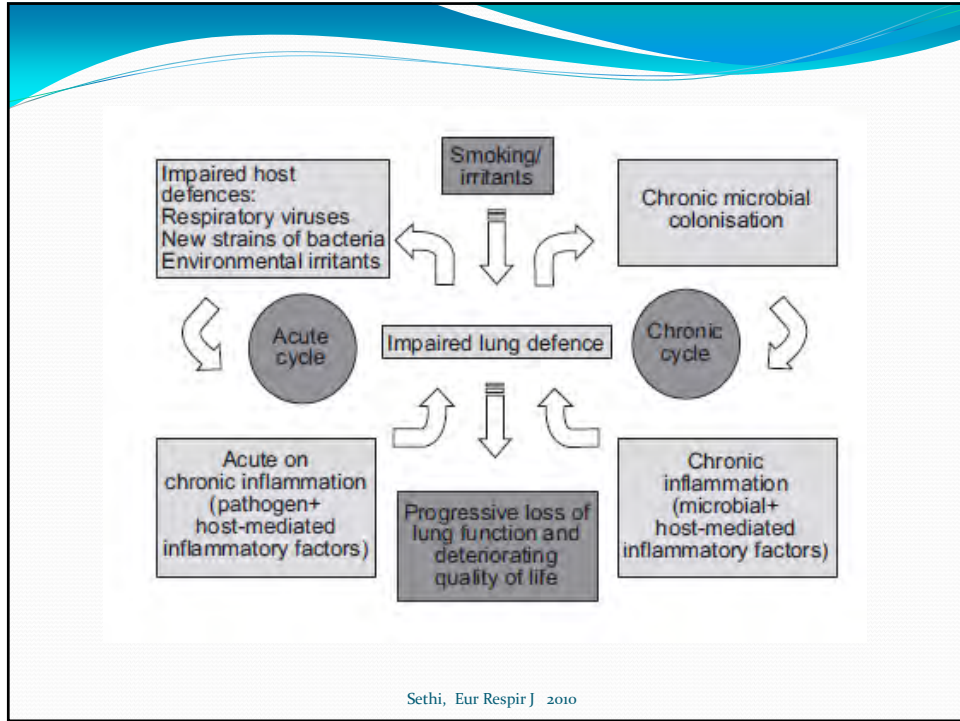
## Sleep Disordered Breathing Therapy

- Positive airway pressure
- Oral appliance
- Surgery
  - Posterior pharyngeal
  - Mandibular

## Sleep Disordered Breathing What Should I Do?

- Ask appropriate questions
  - Snoring
  - Daytime fatigue, sleepiness
- Screen
  - STOP-BANG
  - Epworth scale
  - Berlin questionnaire
  - Nocturnal oximetry

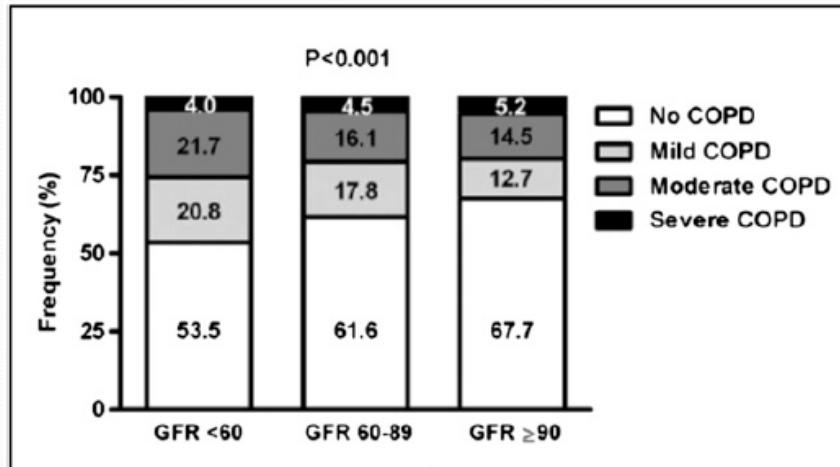




# Infection

## What Should I Do ?

- Monitor for change in symptoms
- Obtain sputum culture
- Initiate antimicrobial therapy



Nussbaumer-Ochsner, Chest 2011

## Renal Failure

### What Should I Do ?

- Awareness
- Obtain serum chemistries (SMA, BUN, Cr)

## Cardiovascular Disease

- CAD and atherosclerosis
- Heart failure
- Pulmonary arterial hypertension

## Cardiovascular Disease

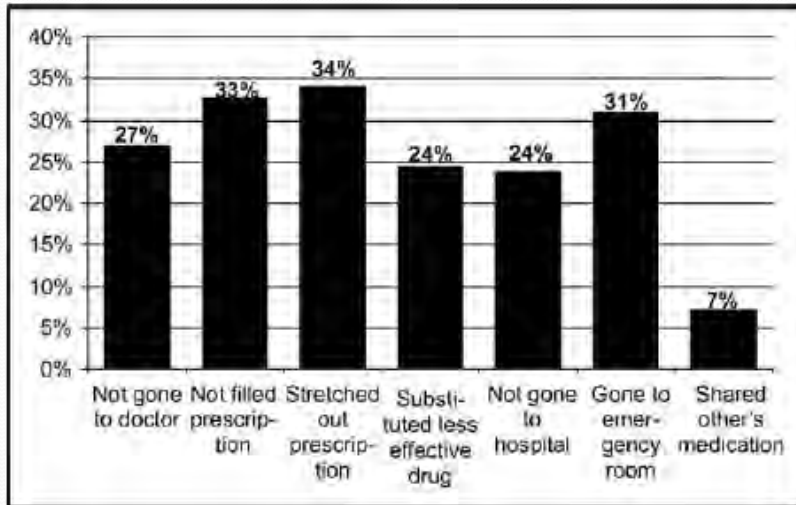
- Rest
- Exercise

Most Important Comorbidity ??

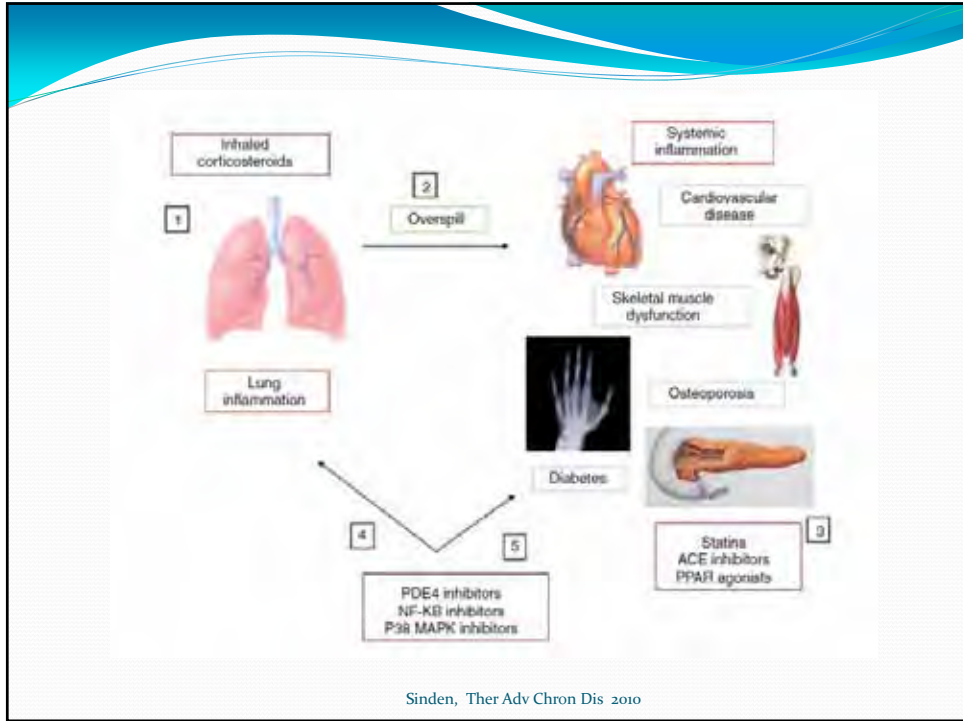


## Most Important Comorbidity ??

- Knowledge
- Adherence



Barr, Am J Med 2009

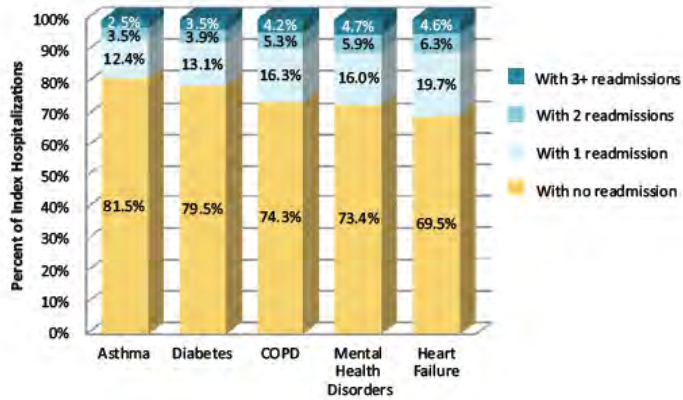


## IMPLICATIONS FOR THERAPY

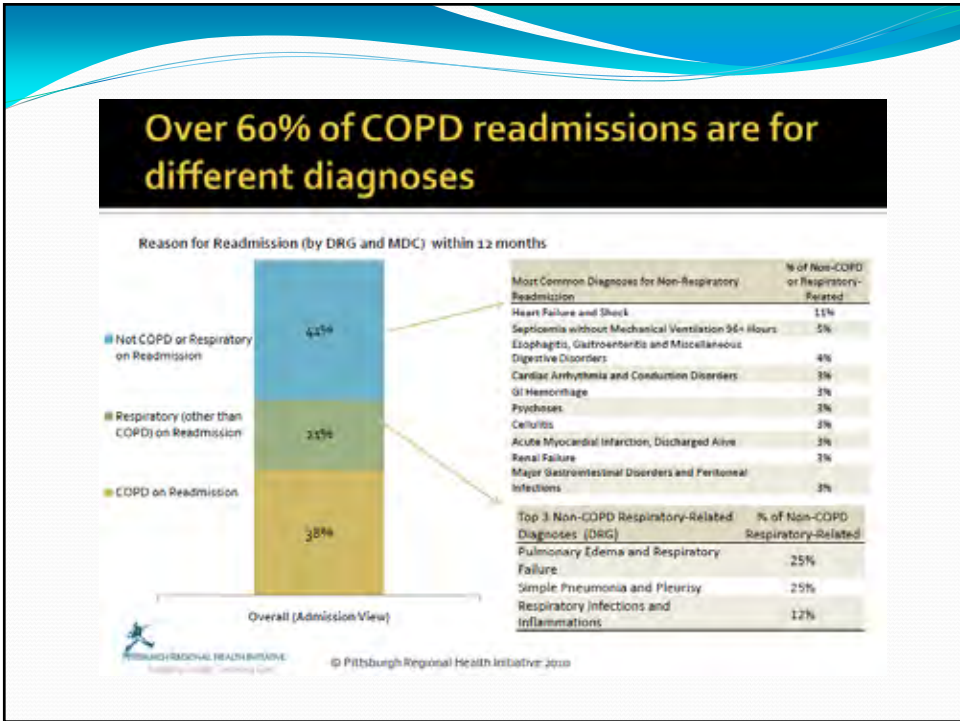
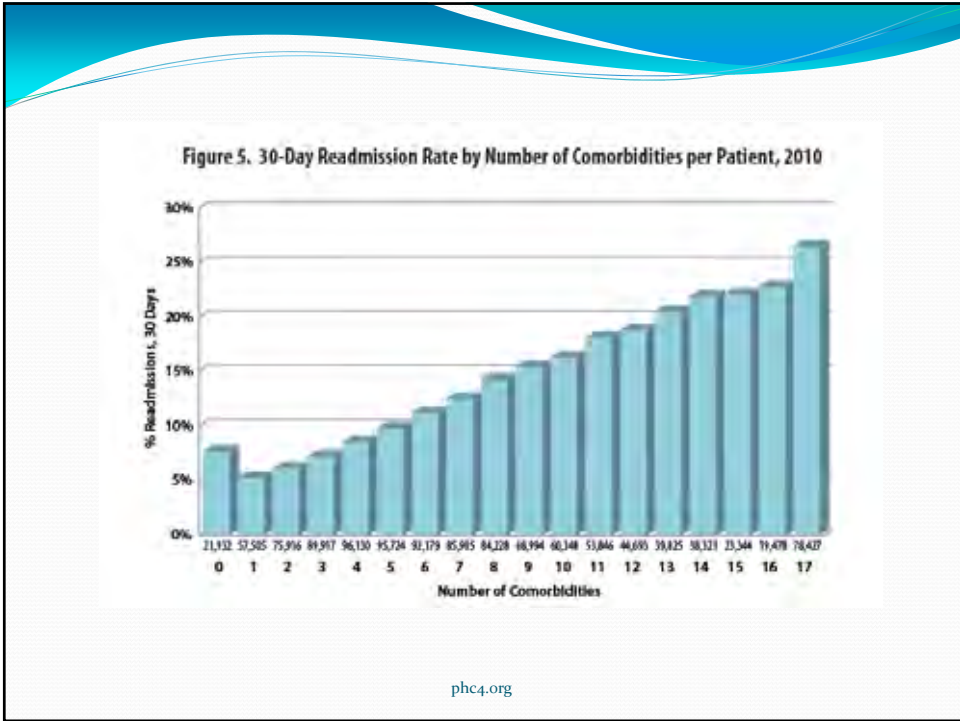
- Suppress pulmonary inflammation associated with systemic diseases
- Treatment
  - Systemic disease
  - Comorbid disease
- Knowledge and adherence

# Comorbidities and Readmissions

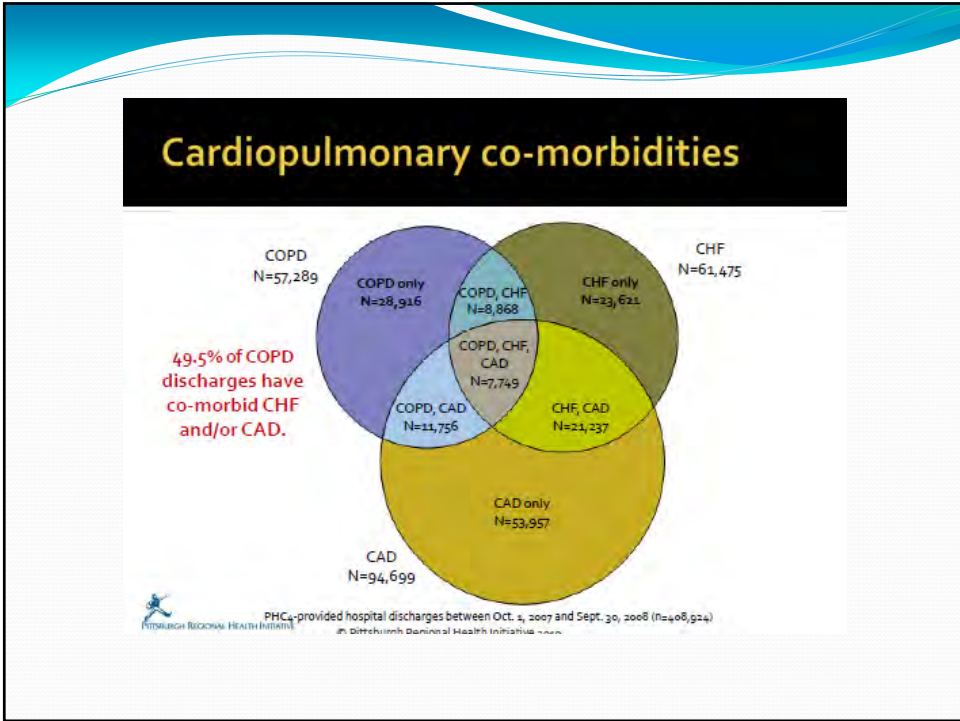
Figure 2. Common Chronic Conditions with a High Number of Readmissions for the Same Condition within One Year of Initial Discharge, 2009



phc4.org







**Table 2. Risk Factors Associated With Readmission Within 30 Days of CABG Surgery**

Variables	%	Logistic Regression Coefficient	Adjusted OR (95% CI)	p Value
<b>Patient characteristics</b>				
Age >70 yrs, n	—	0.0220	1.02 (1.01–1.03)	<0.0001
Female	26.46	0.2034	1.23 (1.16–1.29)	<0.0001
African American	7.23	0.1475	1.16 (1.01–1.32)	0.03
<b>BMI kg/m<sup>2</sup></b>				
≤30	62.86		1.00	
30.1–34.9	23.71	0.1276	1.14 (1.04–1.24)	0.004
35–40	8.98	0.2563	1.29 (1.17–1.43)	<0.0001
≥40	4.44	0.4812	1.62 (1.42–1.84)	<0.0001
<b>Pre-operative risk factors</b>				
Cerebrovascular disease	19.30	0.1053	1.11 (1.04–1.19)	0.002
Peripheral vascular disease	12.65	0.1882	1.21 (1.09–1.33)	0.0002
Shock	0.23	0.5800	1.79 (0.80–4.00)	0.16
CHF	10.84	0.2026	1.22 (1.10–1.36)	0.0002
COPD	19.92	0.2795	1.32 (1.24–1.41)	<0.0001
Extensive aortic atherosclerosis	6.39	0.1595	1.17 (1.06–1.30)	0.002
Diabetes	35.71	0.1714	1.19 (1.09–1.29)	<0.0001

Hannan et al, JACC 2011

## Comorbidities

- Screen
- Diagnose
- Treat

## COPD and COMORBIDITIES Summary

- Association with systemic inflammation
- Awareness of potential comorbidities
- Treatment of underlying inflammation, comorbidity

## REFERENCES

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