

## Internal Medicine Update: The Pleiotropic Effects of Statins in COPD

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## Risk reduction benefit from observational studies

Reference	Cohort	Sample size	RR Reduction	OR (95% CI)
Mancini et al	COPD	19720	47% risk reduction for death, or MI	0.53 (0.42 – 0.62)
Frost et al	COPD	76232	38% risk reduction for death following hospitalization 81% risk reduction for death with COPD exacerbation	0.62 (0.43 – 0.91) 0.19 (0.08 – 0.47)
Farwell et al	US veterans	483733	55% risk reduction of lung cancer with statin use	0.45 (0.42 – 0.48)

Janda s et al. Chest 2009;136:734-743

Young RB et al. Postgrad Med J 2009;85:414-421

## “Potential benefits of statins on morbidity and mortality in chronic obstructive pulmonary disease: a review of the evidence”

R P Young, R Hopkins and T E Eaton

This is a review of evidence ... the benefits of statins in COPD patients

Postgrad Med J 2009;85:414-421

## Randomized control trial

- Lee et al. Placebo vs pravastatin in COPD
  - randomized, double-blinded, parallel
  - N = 125 (clinically stable COPD patients)
  - pravastatin 40mg over 6 months

Results:

- increased exercise time by 54% (pravastatin group)
- decreased C-reactive protein
- decrease interleukin-6
- slight increase in FEV1 %

## Background

- Reduced FEV1 is an important independent predictor of CV death in COPD
- Pulmonary and systemic inflammation
- Statins have anti-inflammatory effects in lungs and arteries
- Non-randomized studies show benefits in COPD patients taking statins
- Reduced risk of lung cancer
- ??? Consider statin use in COPD patients

## Why is this important?

COPD ....

- Affects 15 million Americans
- Fourth leading cause of death in US
- Results in more than 500,000 hospitalizations/yr
- Second leading cause of missed work days
- Only major health problem in which mortality has been increasing over past 20 years
- Death rate 10x greater than that for asthma

Bang, Chest 1993, Desai, MMWR CDC Surveillance Summary 1999

## Definition of COPD

*“Disease state characterized by airflow limitation that is no longer fully reversible and is usually progressive.... This results in a chronic inflammatory response in the walls and lumen of the airways.”*

Gold Guidelines, 2008. www.goldcopd.com

## Causes of Death in COPD

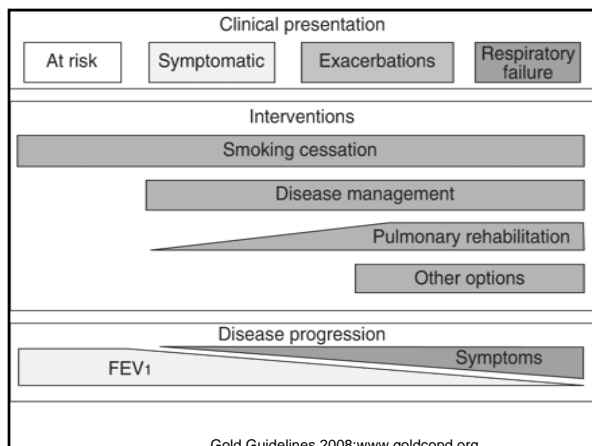
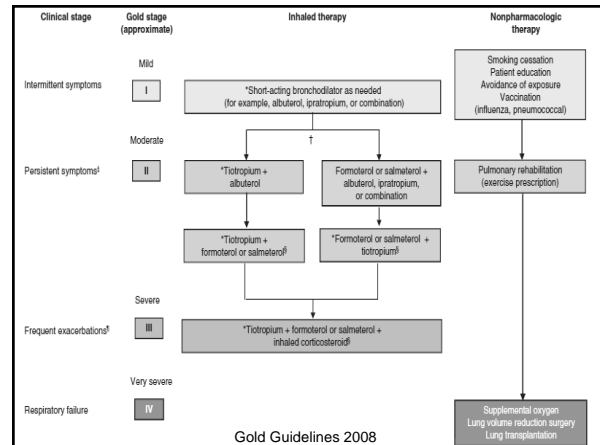
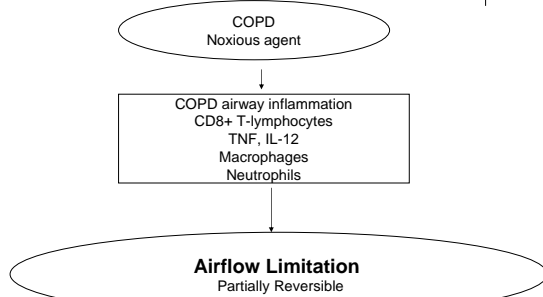
- COPD is the fourth leading cause of death
- Coronary artery disease (20 – 50% deaths)
- Respiratory failure (10 – 30% deaths)
- Lung cancer (20 – 30% deaths)
- Stroke

\*\* collectively these accounts for over 80% of deaths in COPD \*\*\*

Young RP et al. Postgrad Med J 2009;85:414-421

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## Cellular and Molecular Presentation



## COPD and Systemic Inflammation

- Association of c-reactive protein and severity of COPD
- Inflammation is exaggerated by but not dependent on cigarette smoking
- Pollutant exposure
- Genetics

Young RP et al. Postgrad Med J 2009;85:414-421

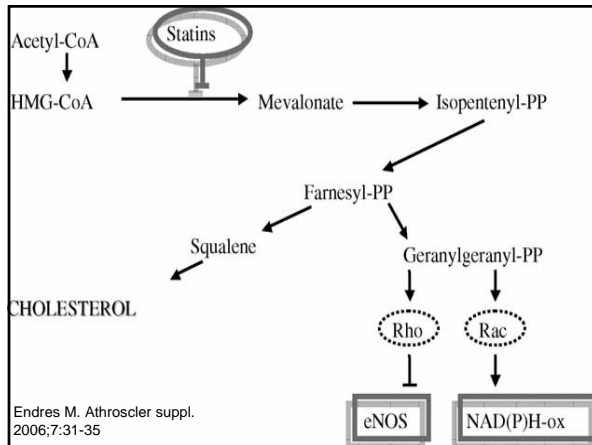
## Statins and Anti-inflammatory Effects

- Reduction in serum cholesterol
- Reduction of mortality and morbidity in CAD
  - primary and secondary prevention studies show an association with a relatively 30% reduction in mortality
- Immunomodulatory effects
  - attenuate the inflammatory effects of smoking on the lung

Young RP et al. Postgrad Med J 2009;85:414-421

## What does this mean??

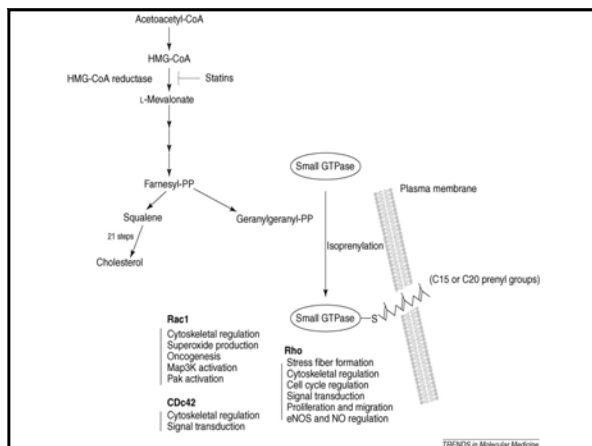
- Statins have anti-inflammatory and immunomodulatory effects
- There is "compelling evidence" but RCT are needed
- There have been 9 studies looking at statins in COPD (8 observational studies and one RCT)
- Benefits: improved lung function, improved exercise capacity, decreased exacerbations, decreased hospitalizations, COPD-related mortality
- Data not sufficient to justify routine clinical use of statins for COPD patients
- Evidence is sufficient to justify large randomized controlled prospective studies



## RCT in the pipeline

- Effects of statins on lung function: atorvastatin vs. matched placebo
- Effects of statin therapy on c-reactive protein levels in patients with COPD: simvastatin
- Effects of rosuvastatin therapy in patients with stable COPD: rosuvastatin vs. placebo
- Lovastatin as a potential modulator of apoptosis in COPD: lovastatin vs. placebo
- Simvastatin in COPD: simvastatin vs. placebo

[www.ClinicalTrials.gov](http://www.ClinicalTrials.gov), access 9/19/09



**STAY TUNED ....**

**QUESTIONS??**

## References



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