Statins in lung disease

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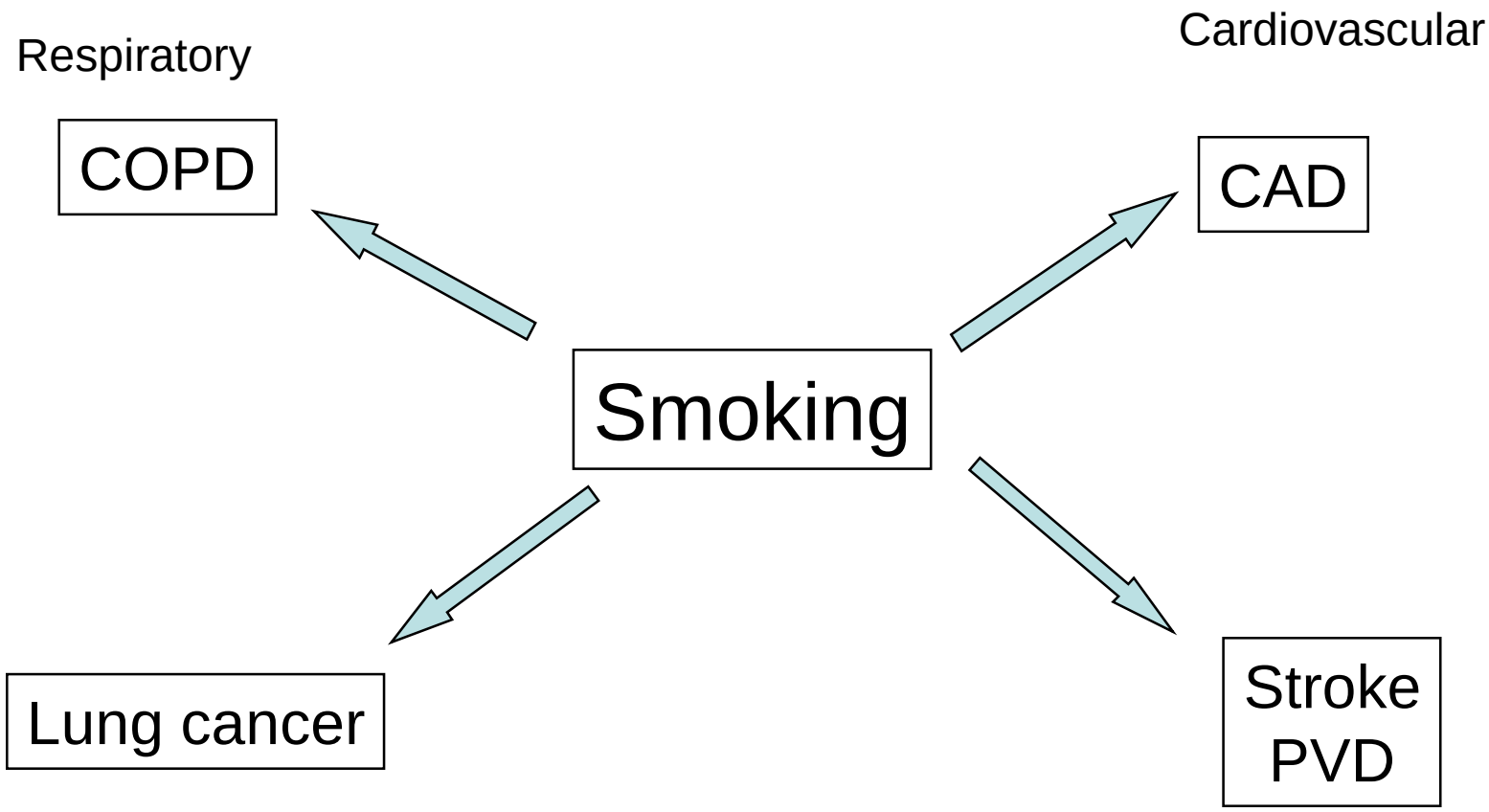
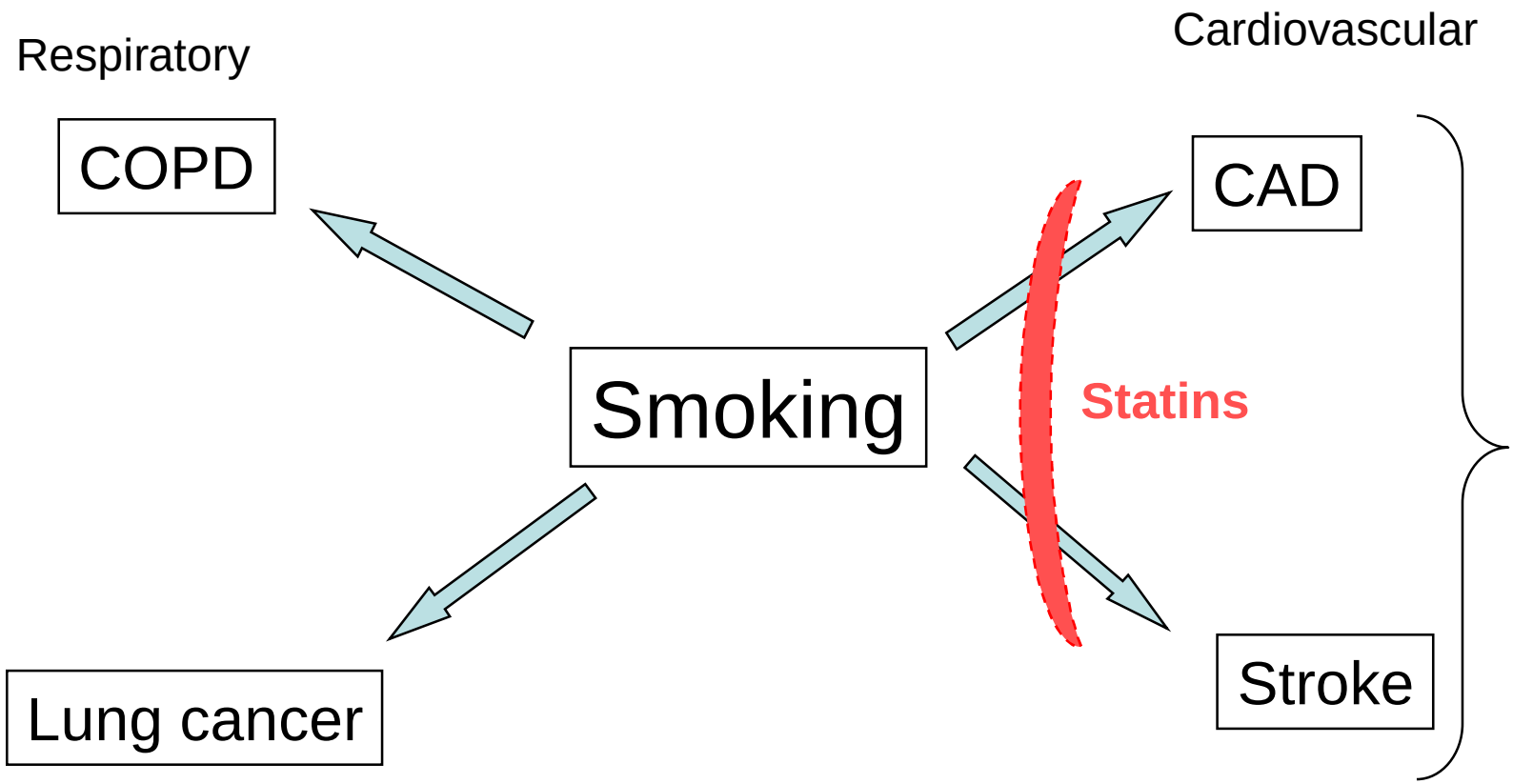
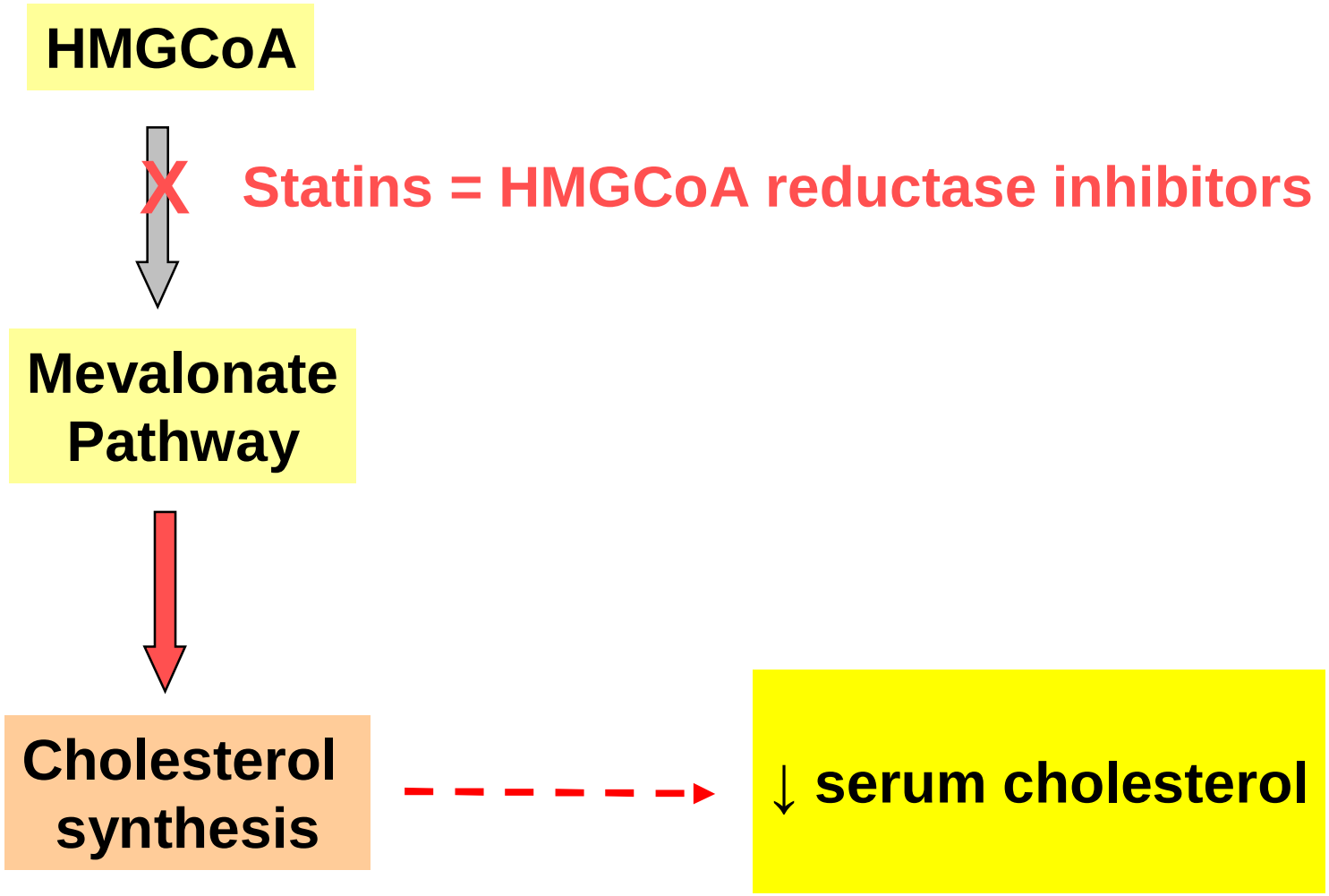
Smoking and its complications



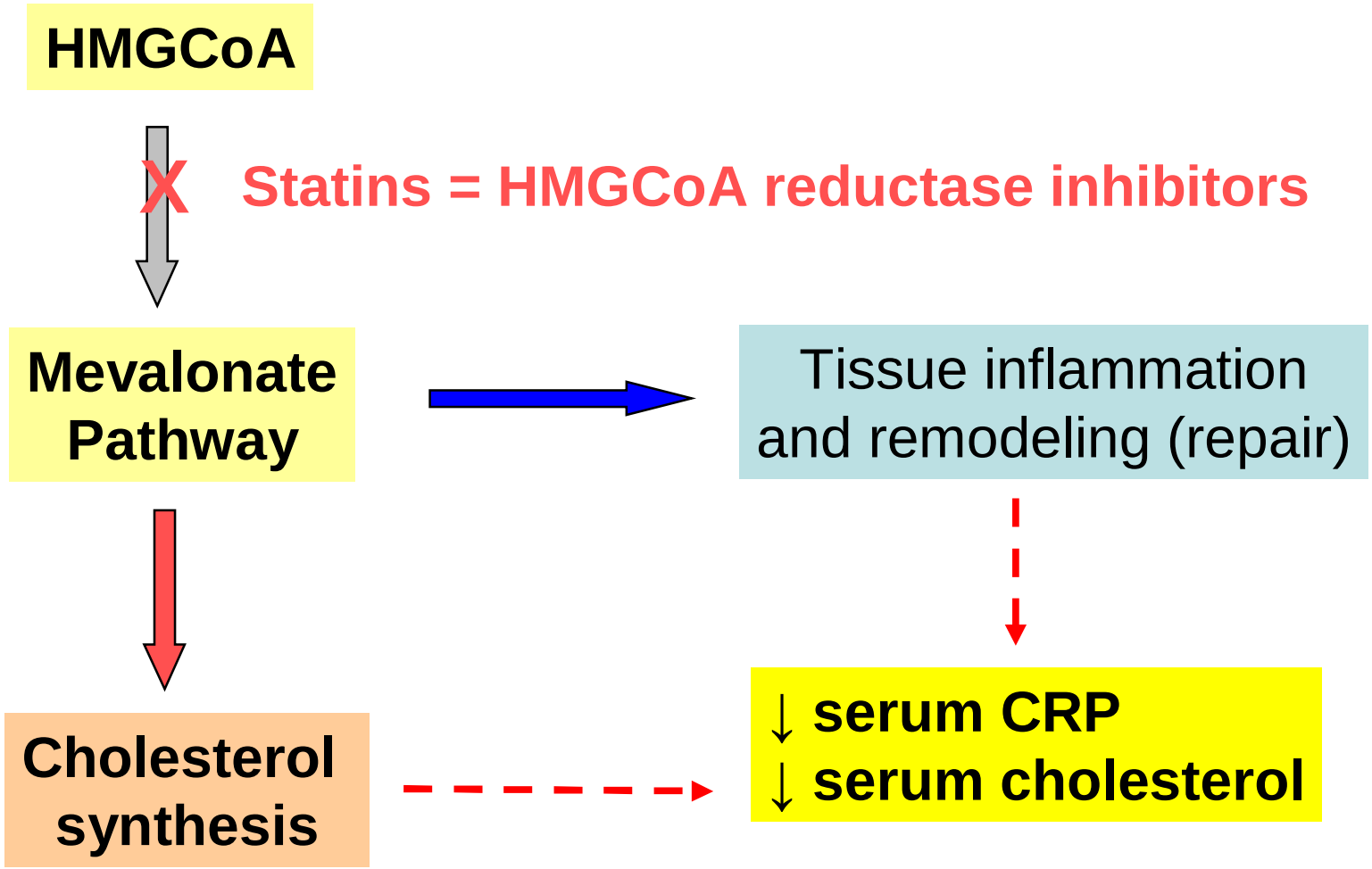
Statins in vascular disease



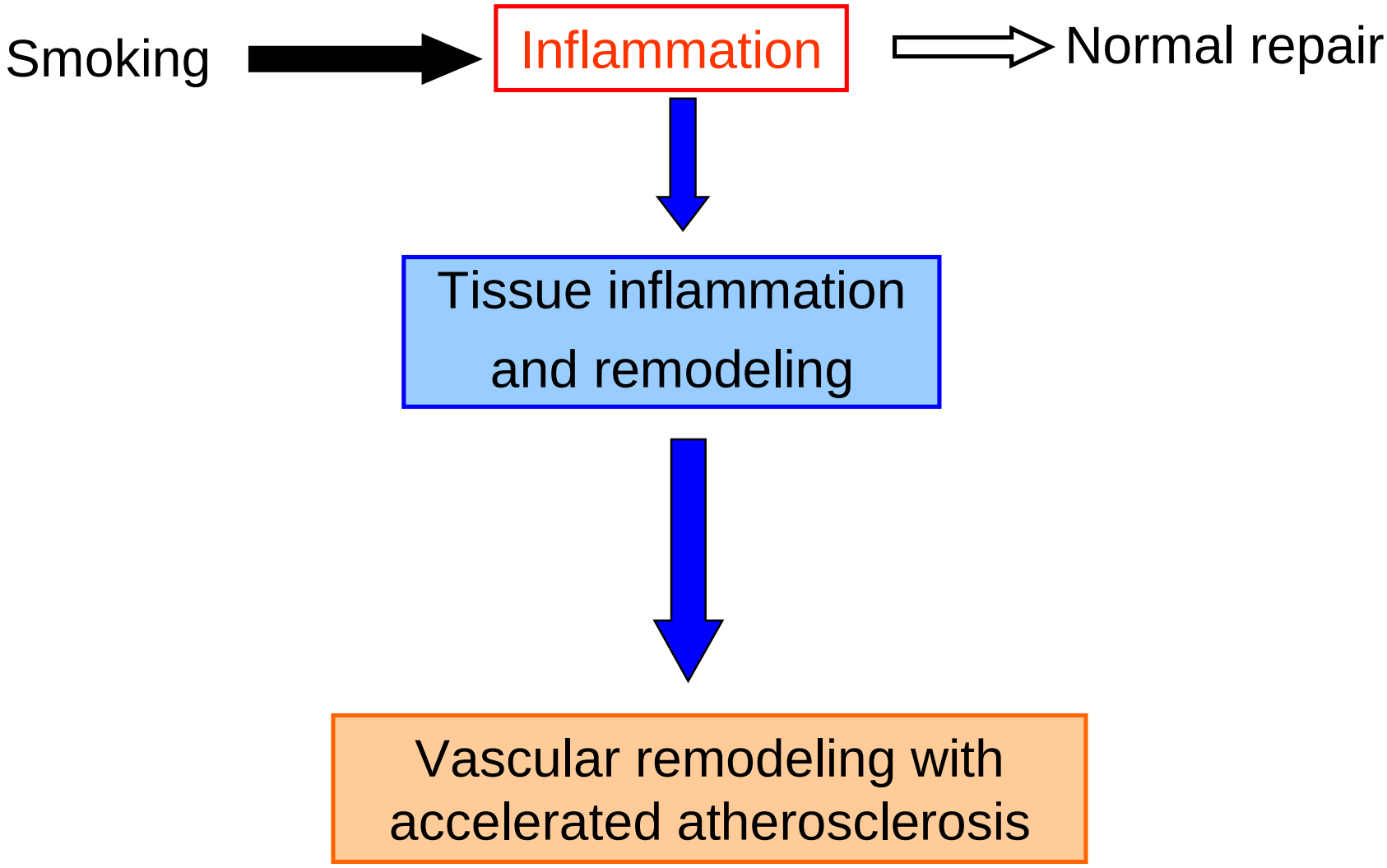
Pharmacological effects of statins



Pharmacological effects of statins



Smoking, inflammation and CAD



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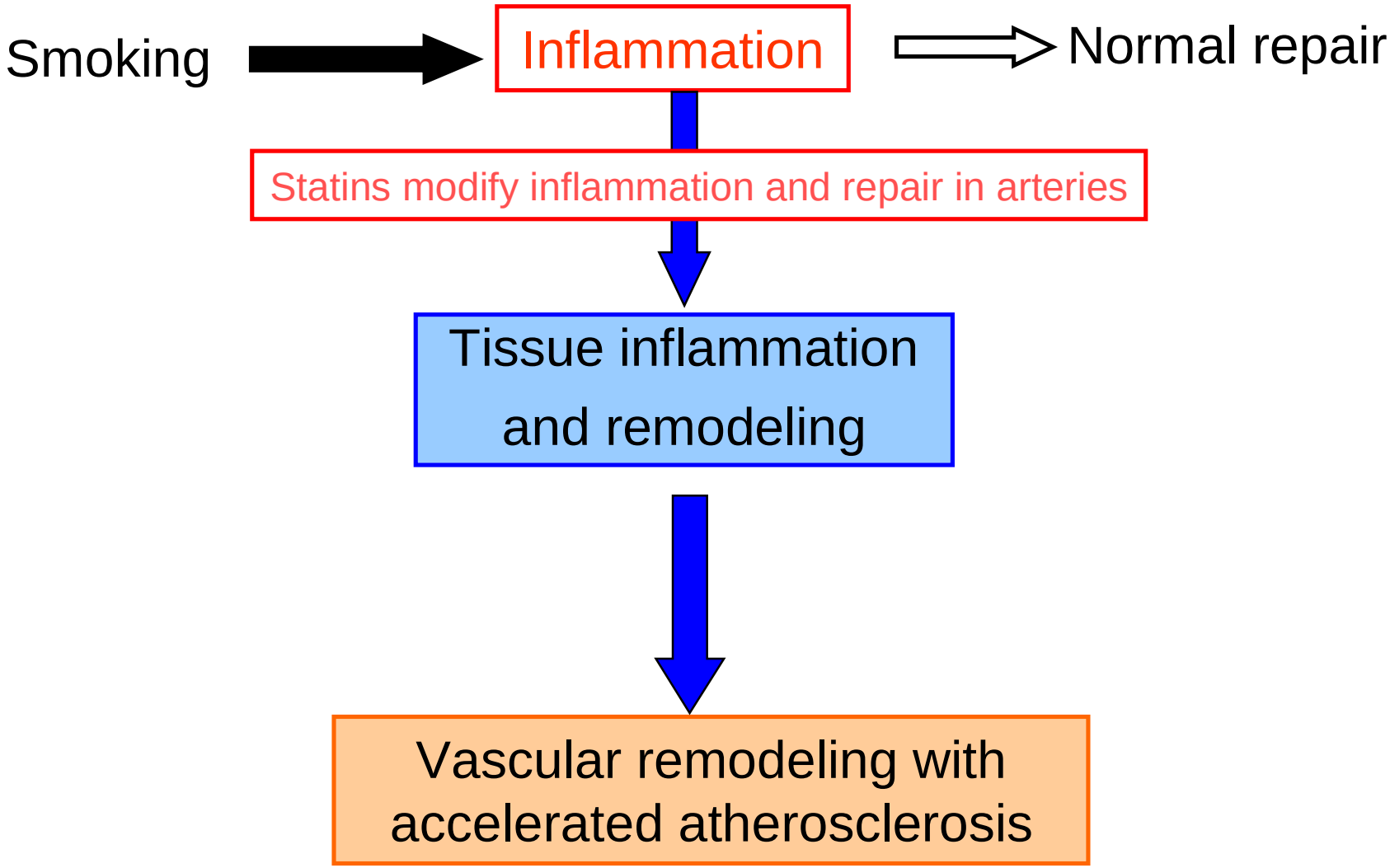
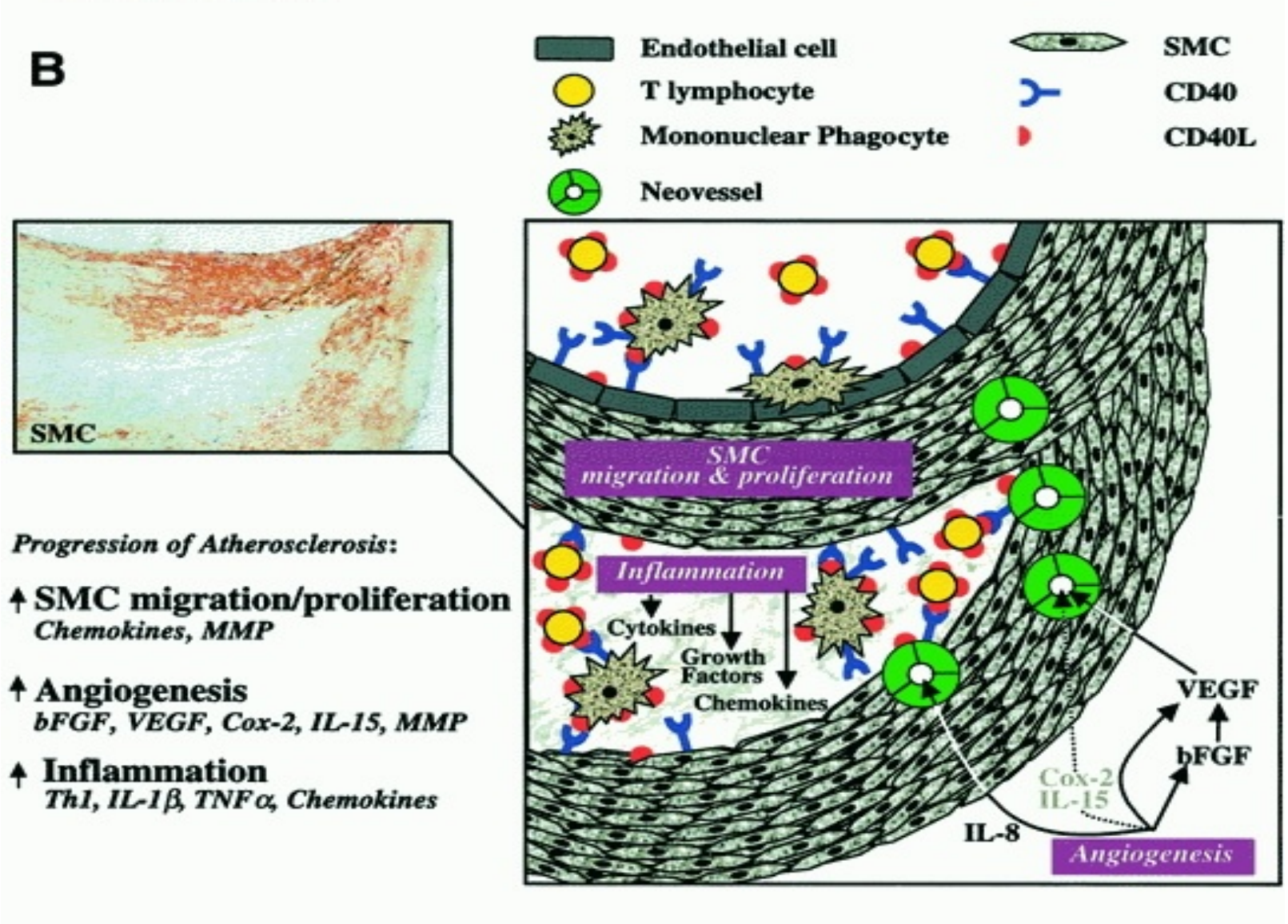
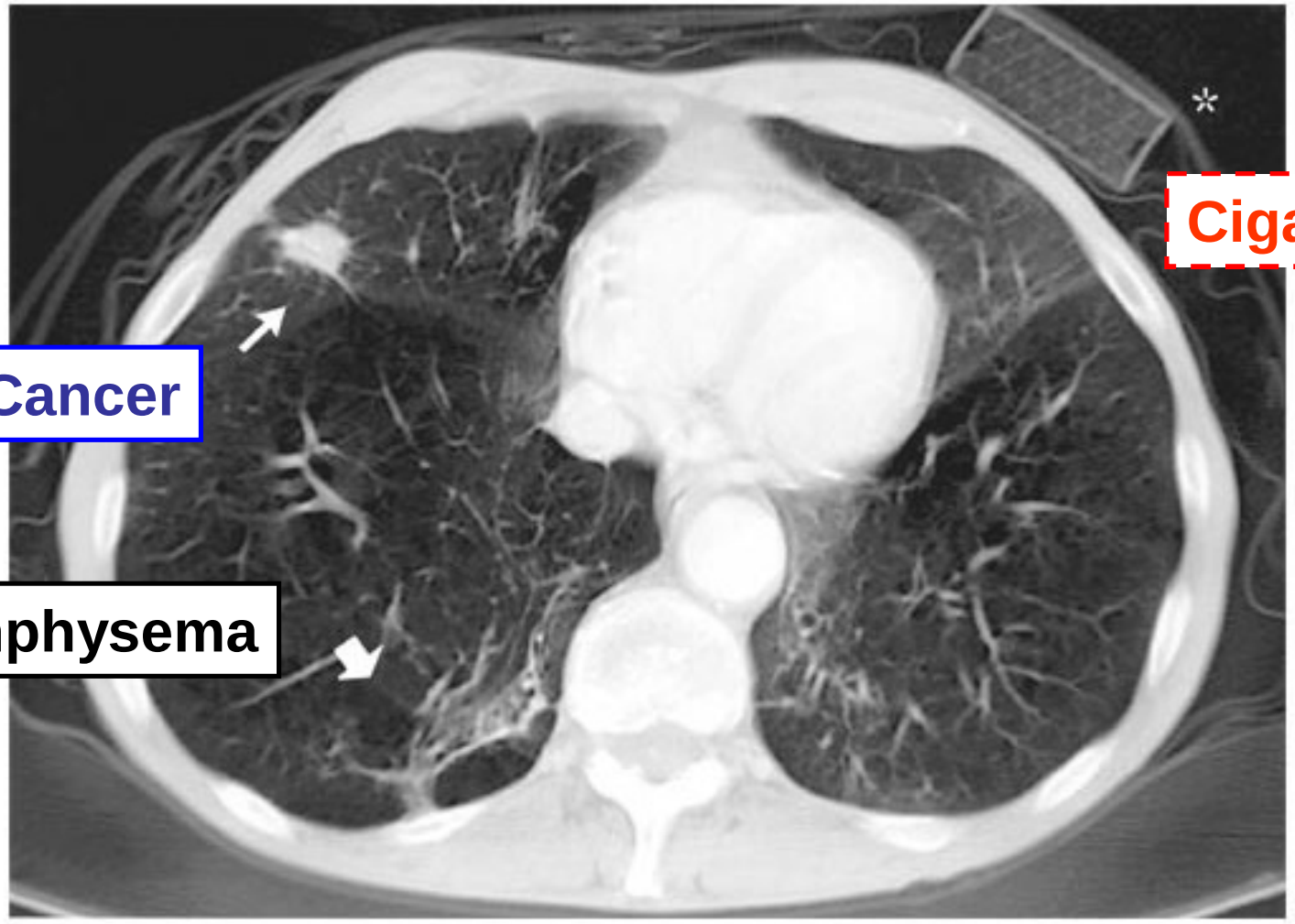


Arterial wall remodelling and unstable coronary plaques - 2

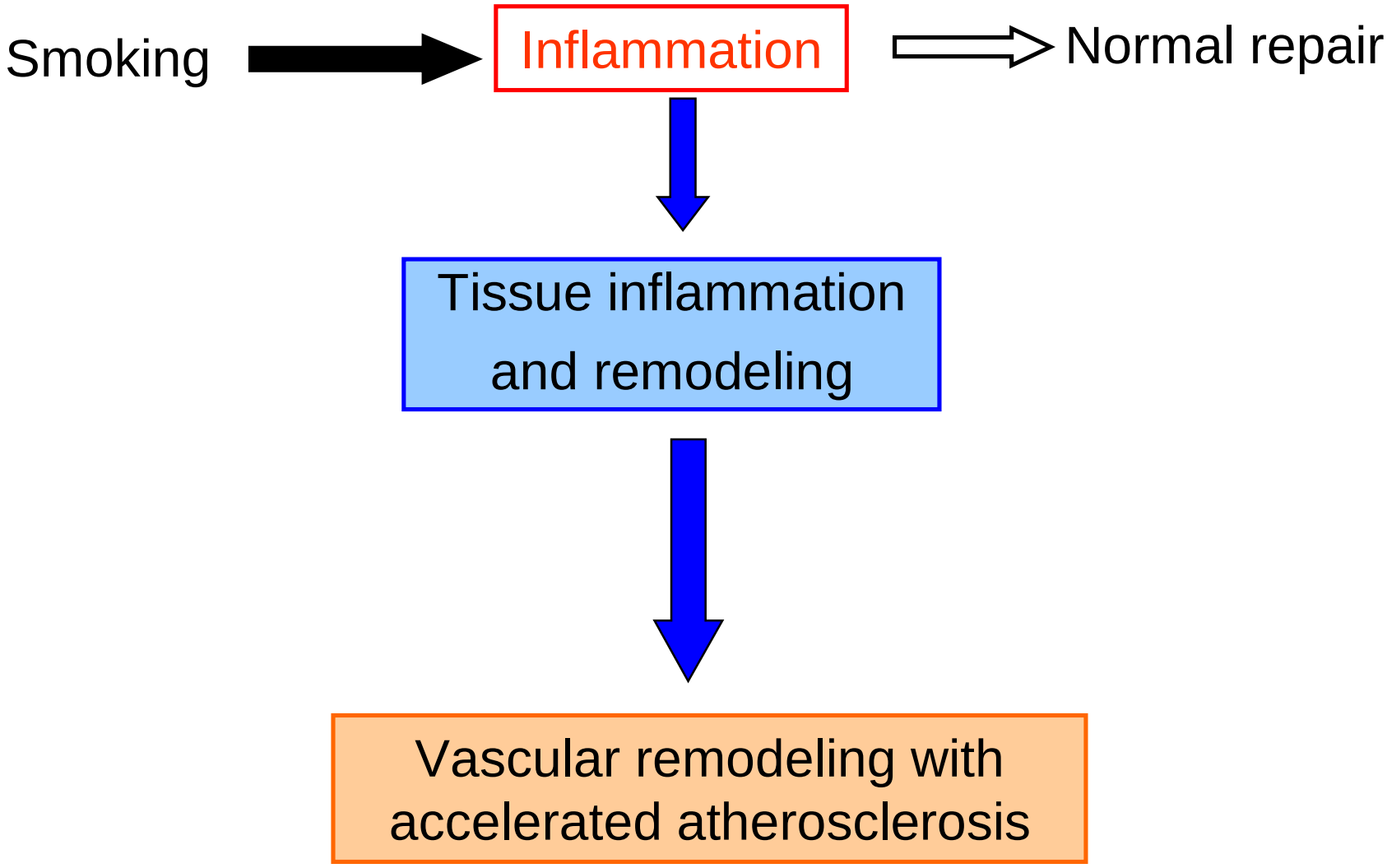
Progression of plaque



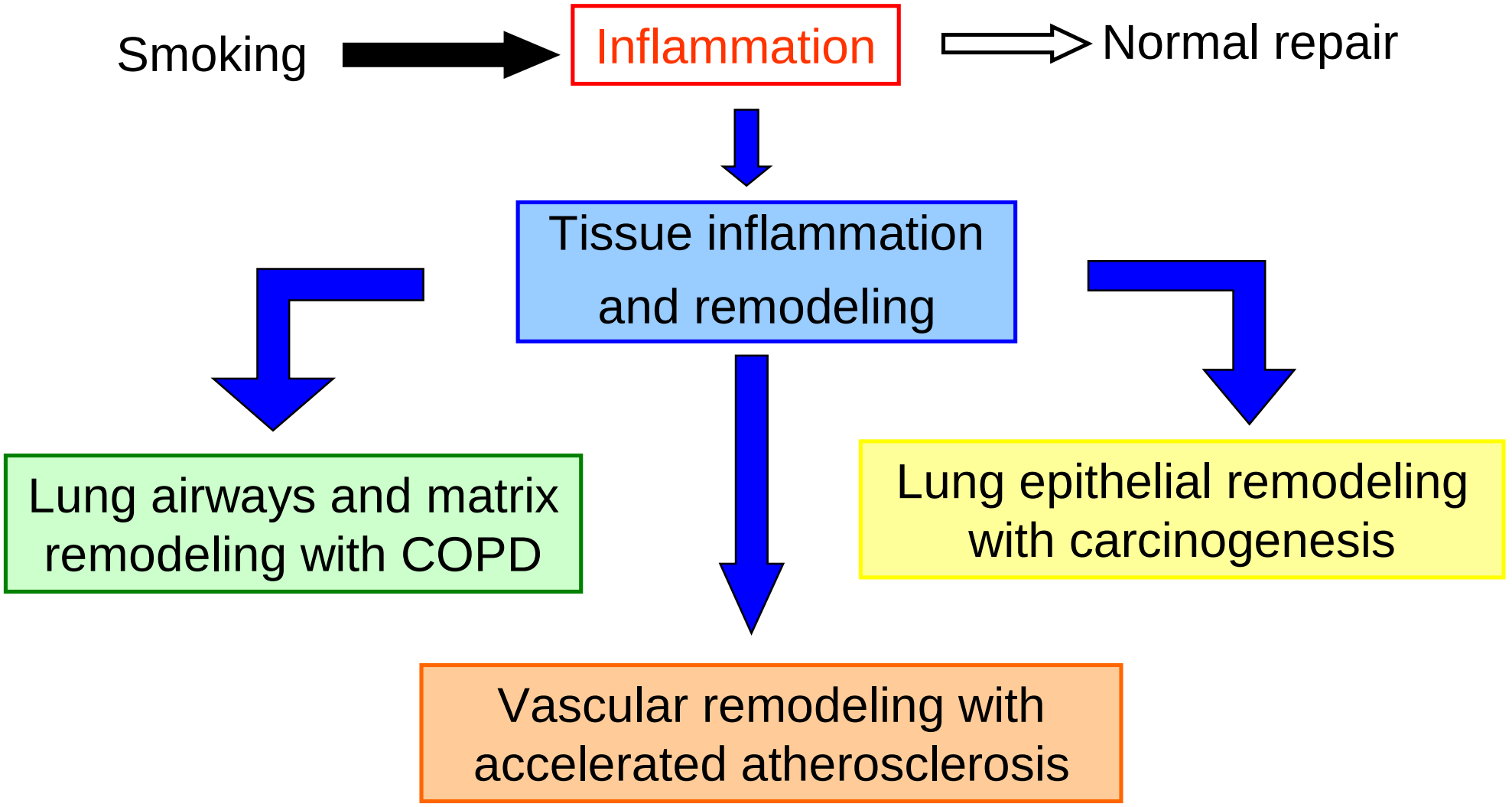
Statins and lung disease



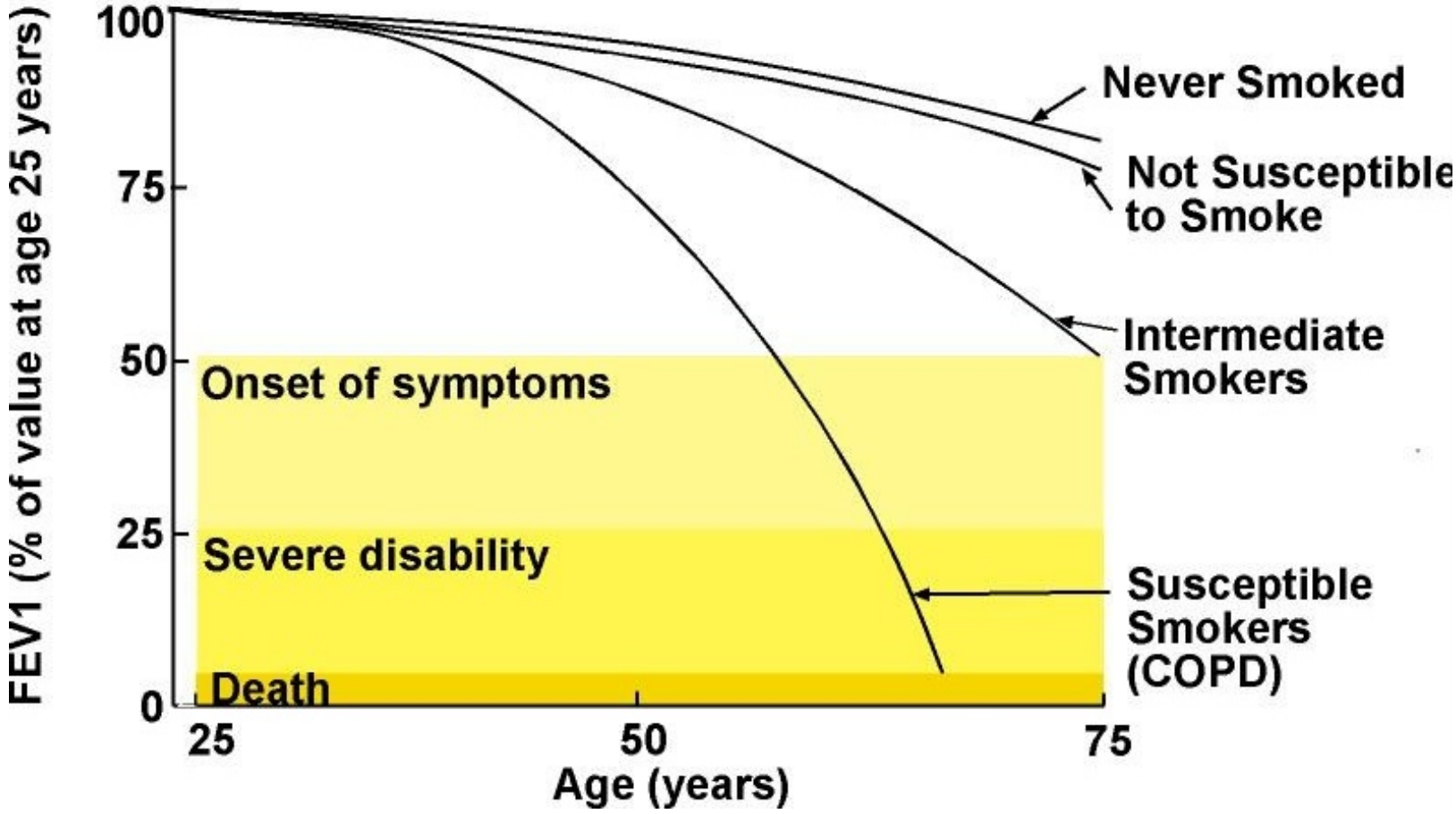
Smoking, inflammation and CAD



Inflammation and cardio-pulmonary disease

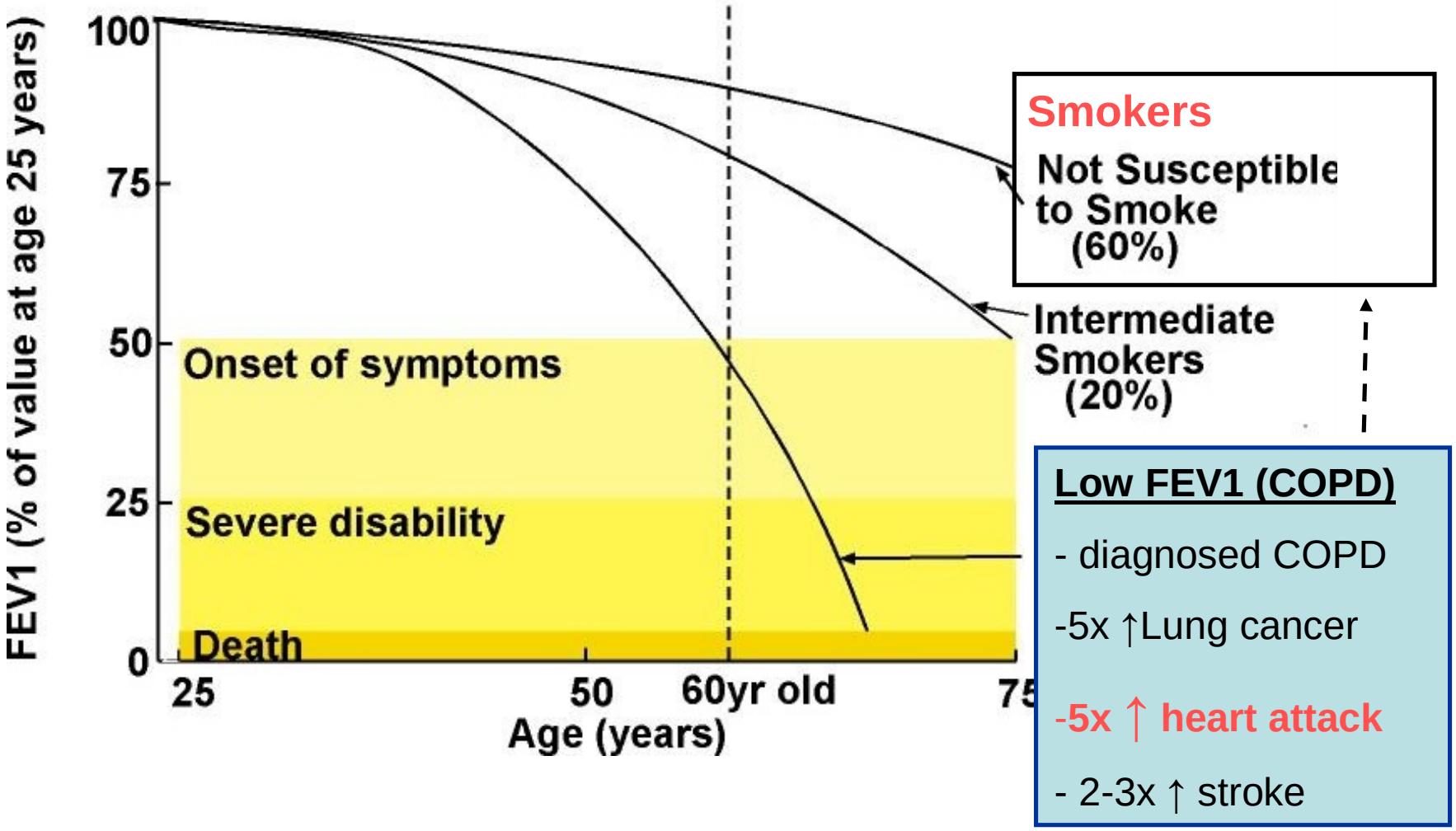


Decline of Lung Function: Not Homogeneous

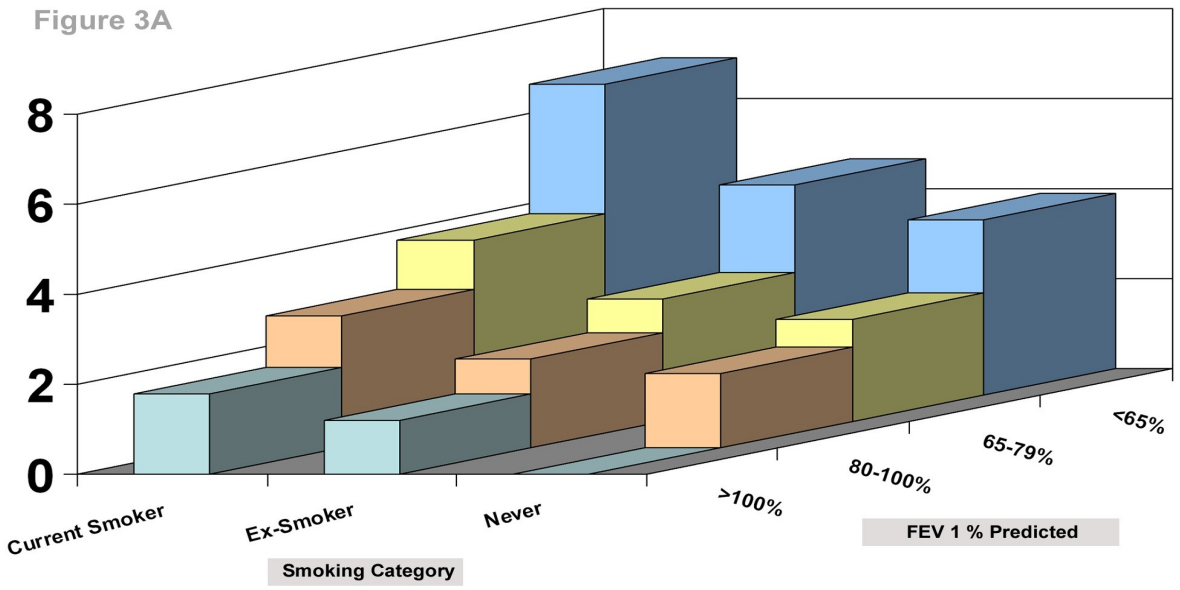


Lung function in smokers who get COPD

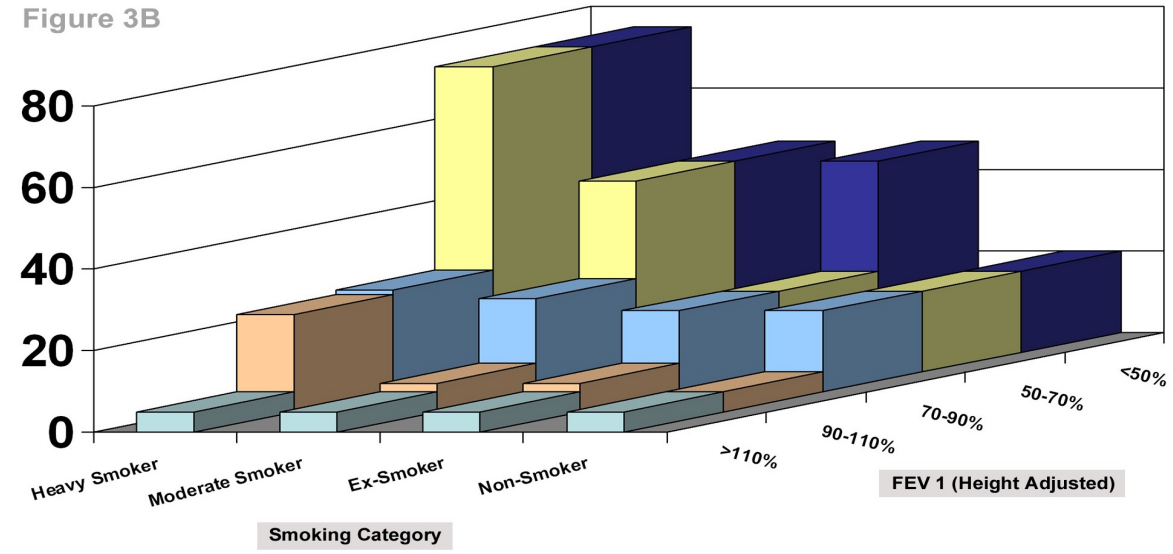
Reduced FEV_1: linked to all cause mortality



CAD mortality



All cause mortality



↓FEV_1 and mortality

- predicts CAD and all cause mortality
- independent of smoking status
- additive with smoking status

Young et al. ERJ 2007

Clinical indication for statins in COPD

- Reduced FEV_1 is an independent risk factor for CAD (marker of susceptibility to smoking)
- Studies show 75% of COPD patients have CAD

Statin therapy might be considered along with other CVS risk factors in primary prevention

Statins in COPD

Evidence for benefit in the lungs?

Eur Respir J 2007; 30: 1–7
DOI: 10.1183/09031936.00021707

PERSPECTIVE

Forced expiratory volume in one second: not just lung function test but a marker of premature death from all causes

R.P. Young*, R. Hopkins# and T.E. Eaton#

ABSTRACT: The clinical utility of spirometric screening of asymptomatic smokers for early signs of air flow limitation has recently come under review. The current authors propose that reduced forced expiratory volume in one second (FEV_1) is more than a measure of airflow limitation, but a marker of premature death with broad utility in assessing baseline risk of chronic obstructive pulmonary disease (COPD), lung cancer, coronary artery disease and stroke, collectively accounting for 70–80% of premature death in smokers.

Reduced FEV_1 identifies undiagnosed COPD, has comparable utility to that of serum cholesterol in assessing cardiovascular risk and defines those smokers at greatest risk of lung cancer. As such, reduced FEV_1 should be considered a marker that identifies smokers at greatest need of medical intervention.

Smoking cessation has been shown to attenuate FEV_1 decline and, if achieved before the age of 45–50 yrs, may not only preserve FEV_1 within normal values but substantially reduce cardiorespiratory complications of smoking.

Recent findings suggest inhaled drugs (bronchodilators and corticosteroids), and possibly statins, may be effective in reducing morbidity and mortality in patients with chronic obstructive pulmonary disease. The current authors propose that spirometry has broad utility in identifying smokers who are at greatest risk of cardiorespiratory complications and greatest benefit from targeted preventive strategies, such as smoking cessation, prioritised screening and effective pharmacotherapy.

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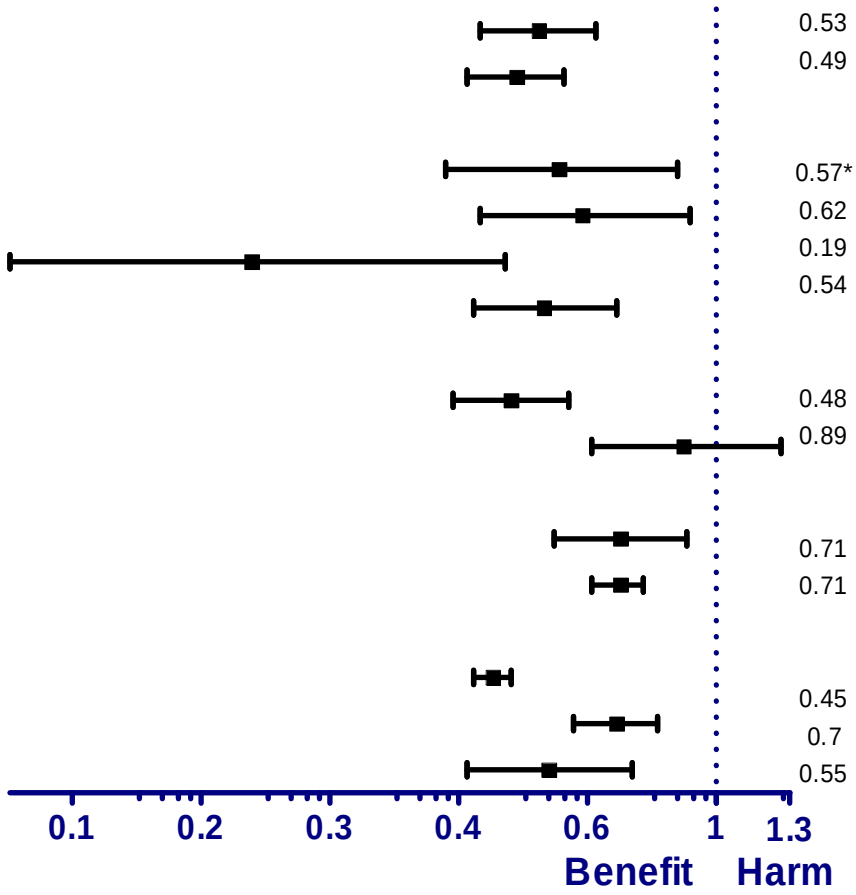
Received:
February 22 2007
Accepted after revision:
July 22 2007

Statins: results from smoking related lung diseases

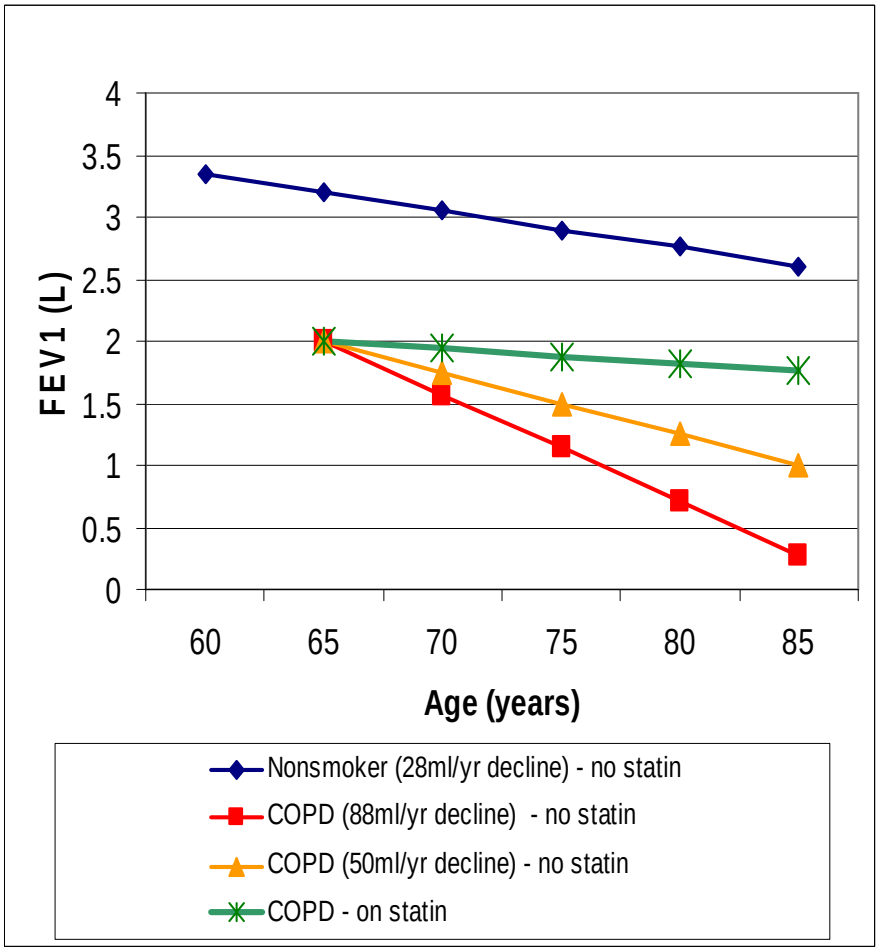
	N	Patients	OR	(95% CI)	Ref
Mortality - All Cause					
High CVS risk (total)	19,720	COPD	0.53	(0.43-0.65)	53
Low CVS risk (total)	103,004	COPD	0.49	(0.41-0.58)	53
Mortality - Chest infection/exacerbation					
Following COPD exacerbation	854	COPD	0.57*	(0.38-0.87)	54
Following pneumonia or influenza	76,232	Population	0.62	(0.43-0.91)	55
Following COPD exacerbation	76,232	COPD	0.19	(0.08-0.47)	55
Following pneumonia	8,652	Population	0.54	(0.42-0.70)	85
MI					
High CVS risk (total)	19,720	COPD	0.48	(0.39-0.59)	53
Low CVS risk (total)	103,004	COPD	0.89	(0.64-1.26)	53
Hospitalisation for COPD					
High CVS risk (total)	19,720	COPD	0.71	(0.56-0.90)	53
Low CVS risk (total)	103,004	COPD	0.71	0.64-0.77	53
Lung Cancer					
Diagnosis of lung cancer	483,733	Population	0.45	(0.42-0.48)	59
Diagnosis of lung cancer	62, 842	Population	0.7	(0.60-0.81)	60
Diagnosis of lung cancer	30,076	Population	0.55	(0.41-0.74)	61



*Hazard Ratio

Young RP, et al. (PMJ in press)

Statin effect on lung function decline: data from 2 observational studies



Young RP, et al. (PMJ in press)

Estimated FEV_1 decline

Non-smokers (no statin therapy)
Estimated decline in FEV_1 is 20-30 ml/year (BLUE)[10,21,74]

Smoker (ex-smoker) with mild COPD on statin therapy
Estimated decline in FEV_1 is 0-12ml/year (**GREEN**)[74,79]

Smoker (ex-smoker) with mild COPD not taking statin therapy
Estimated decline in FEV_1 at 50ml/yr (ORANGE)[75,76] and 88ml/year (RED)[74]

Smoker susceptible to smoking related decline on FEV_1
Estimated decline in FEV_1 is 90-100ml/year[10,24]

Statin use and “healthy user effect”

- “Healthy user effect” = people on statins are “healthier” or undertake other risk reducing activities compared to those not taking statins.

- However, the studies show that those taking statins….
  - are similar to non-users according to age, gender, smoking history and lung function
  - have more CAD, diabetes, hypertension and hyperlipidaemia
  - are not much different with respect to flu vaccinations etc

pj78477 Module 1 Postgraduate Medical Journal 29/4/09 13:42:04 Topics:

Review

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

R P Young,[1] R Hopkins,[1] T E Eaton[2]

[1] Department of Medicine, University of Auckland, Auckland; [2] Respiratory Services, Auckland City Hospital, Auckland, New Zealand

ABSTRACT

Studies show reduced forced expiratory volume in 1 s (FEV_1) in patients with chronic obstructive pulmonary disease (COPD) is an important independent predictor of cardiovascular death and characterised by both pulmonary

LUNG FUNCTION AND CARDIOVASCULAR MORTALITY

Reduced FEV_1 is a powerful marker for CAD[19–20] and mortality from cardiovascular disease[21 22] after controlling for several potential confounders.[23]

Statins and lung disease: results from an RCT

Taiwan study of 123 COPD patients randomised to simvastatin 40 mg od or placebo for 6 months

- Reduced serum CRP and IL-6 levels
- Exercise tolerance increased by 50%

Heart Protection Study (trend only)

- showed a 21% reduction in COPD admissions
- showed a 34% reduction in respiratory deaths

Clinical indication for statins in COPD

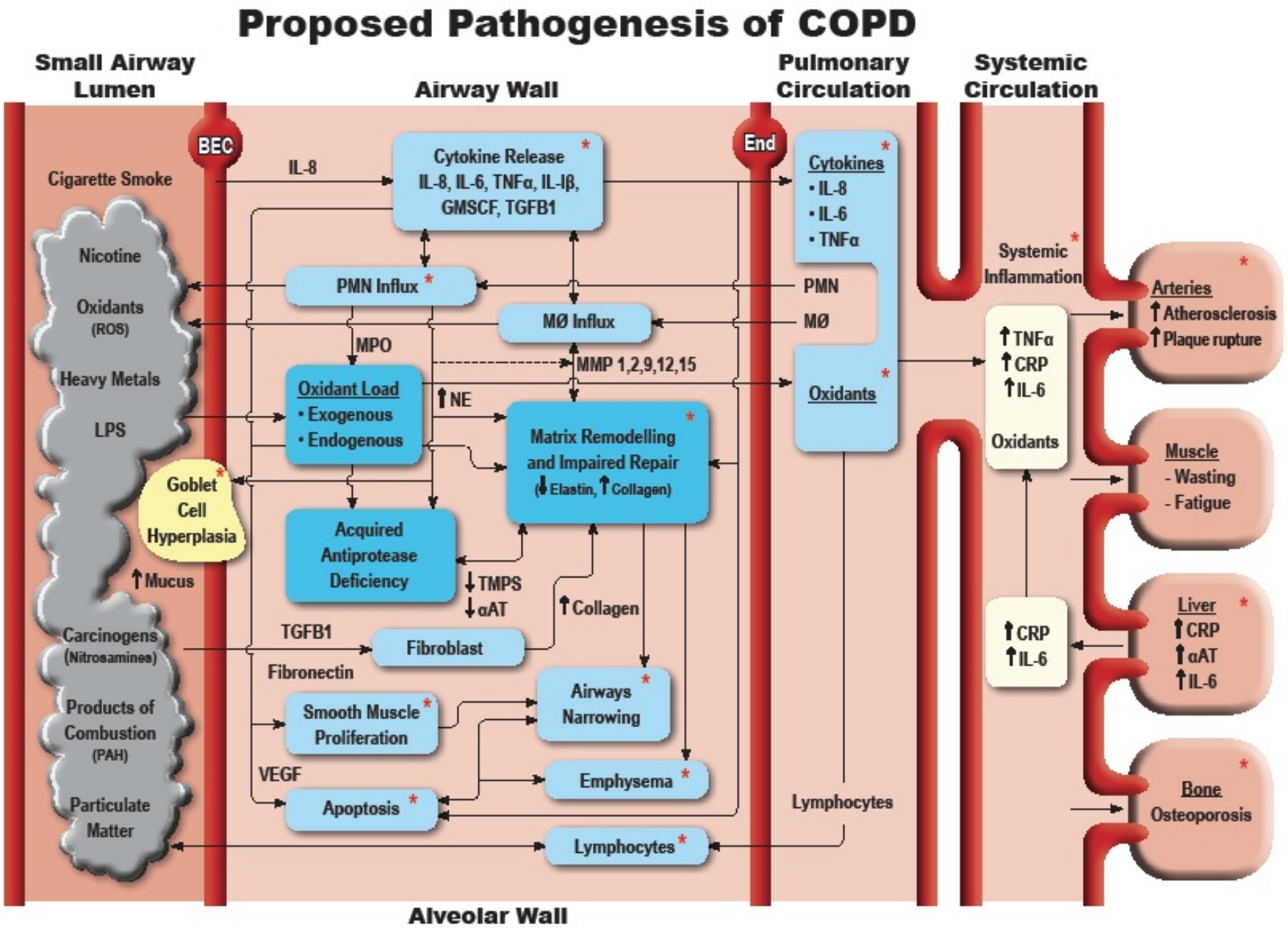
- Reduced FEV_1 is an independent risk factor for CAD (marker of susceptibility to smoking)

- Statins may also
  - Reduce all cause and CAD mortality
  - Reduce COPD exacerbations and mortality from chest infections
  - Reduce lung function decline (first drug to do so)
  - Reduce lung cancer risk and/or progression
  - Improved exercise tolerance

Possible disease modifiers?

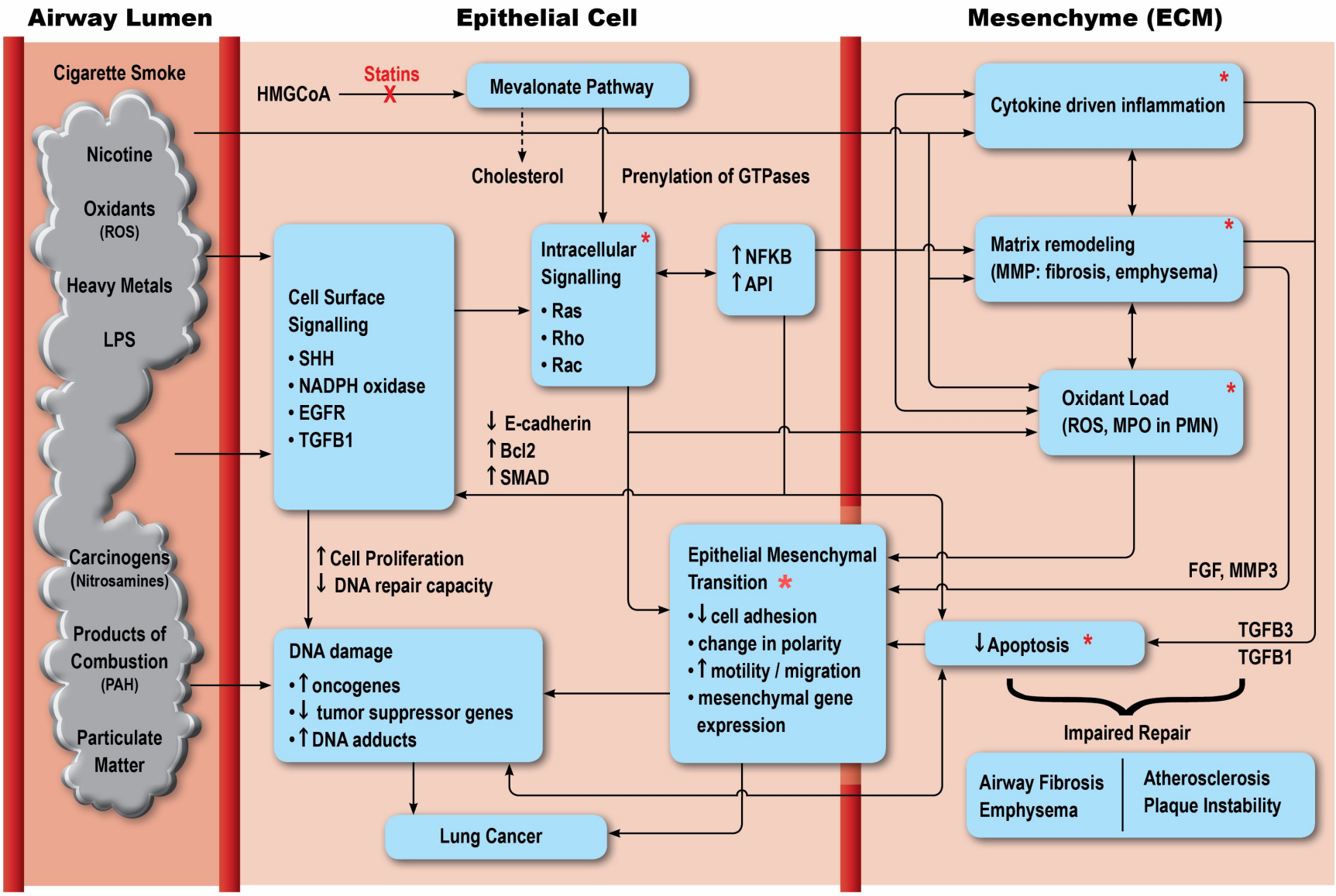
Statins in COPD

Evidence for pharmacological effect of statins in the lungs?



Young RP, et al. (submitted)

Proposed Pathogenesis of Lung Cancer

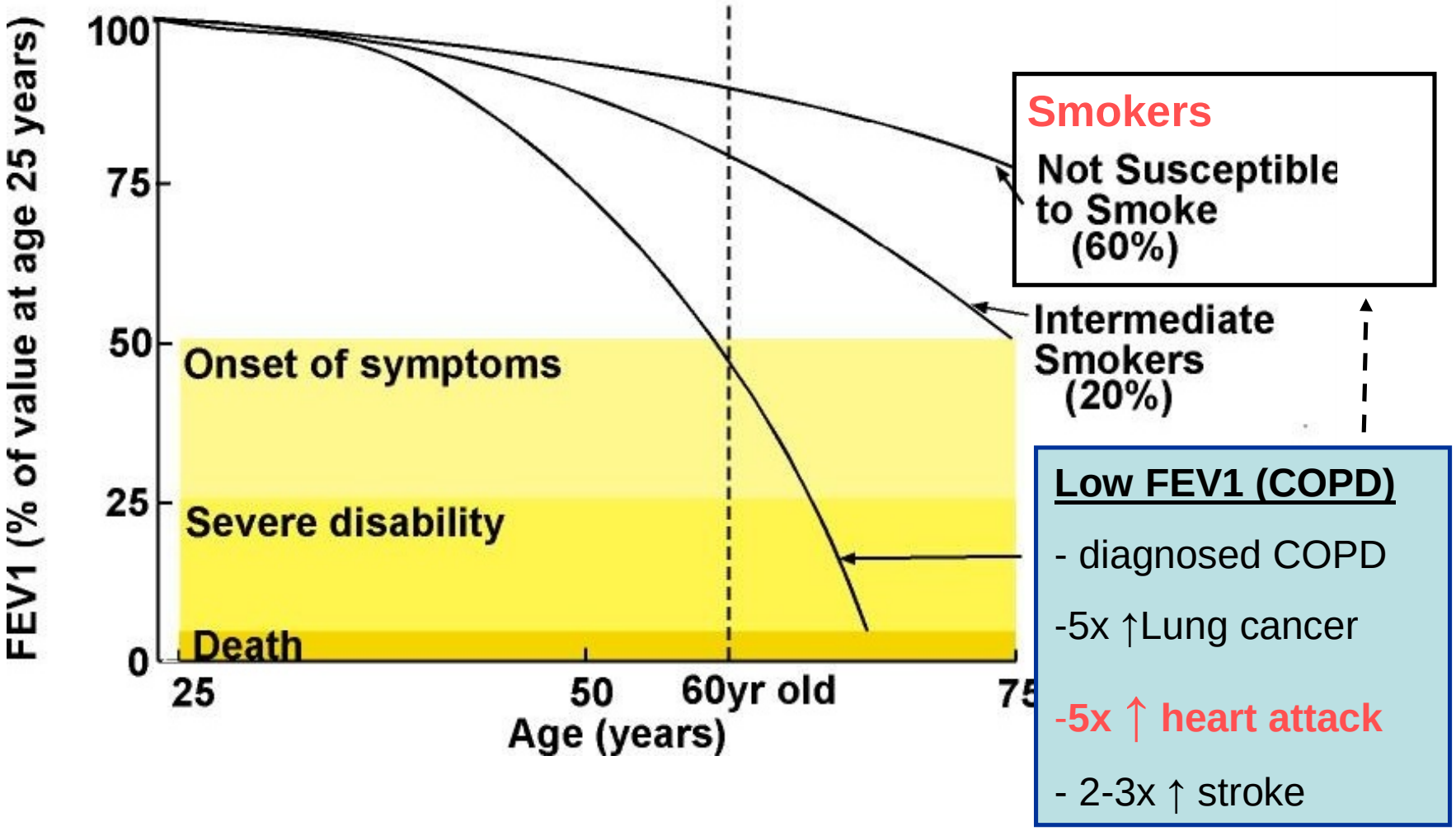


Young RP, et al. (submitted)

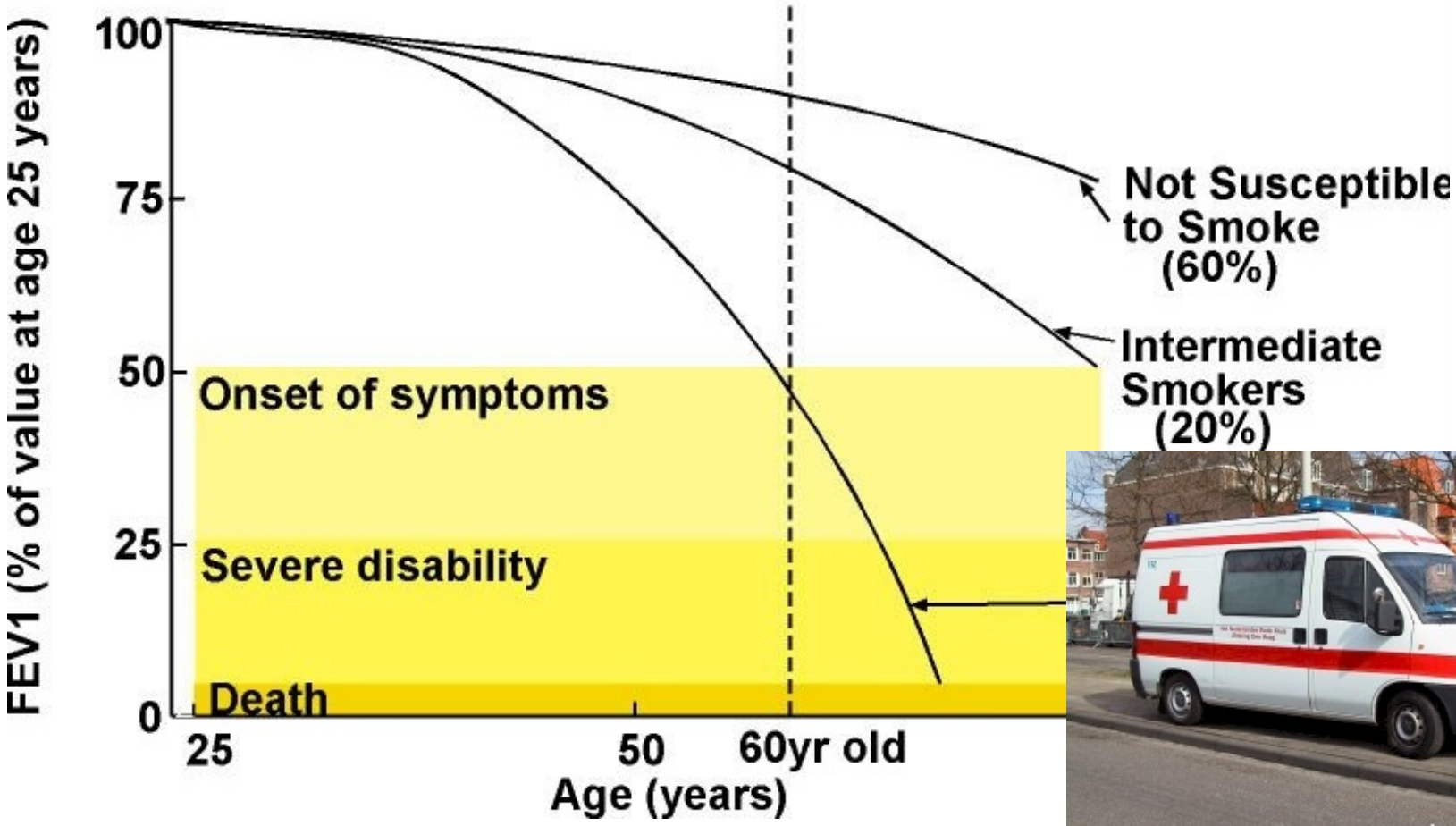
Statin effects in the lungs and beyond

- Inhibit neutrophil infiltration in to the lungs and reduces pro-inflammatory cytokines (IL-8,IL-6, TNFα)
- Inhibits fibrosis reducing small airways fibrosis
- Inhibits (or reverses) epithelial mesenchymal transition (precursor to malignant transformation)
- Inhibits systemic inflammation, reducing atherosclerosis and muscle weakness

COPD: linked to all cause mortality



Decline of Lung Function: Not Homogeneous



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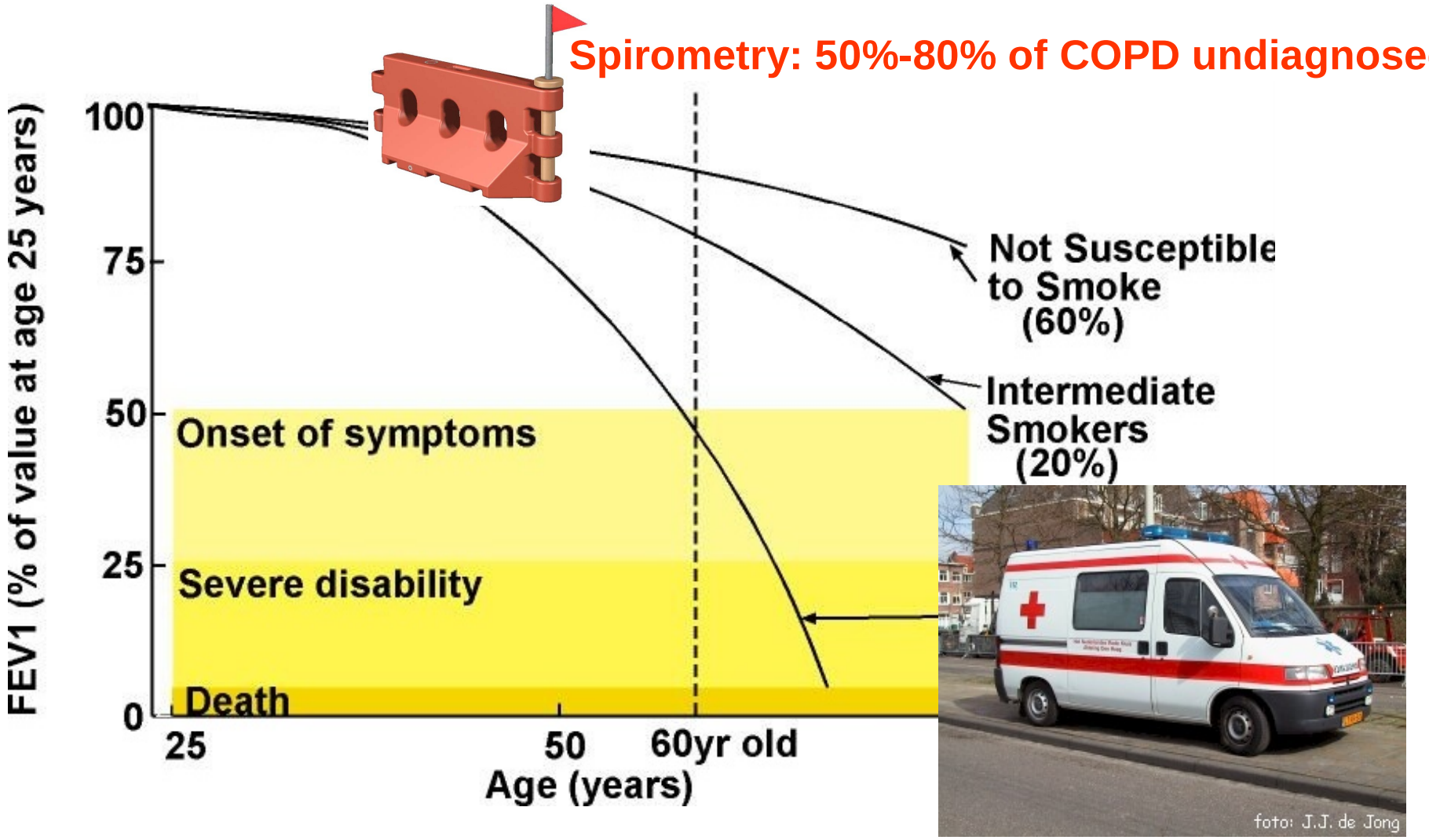

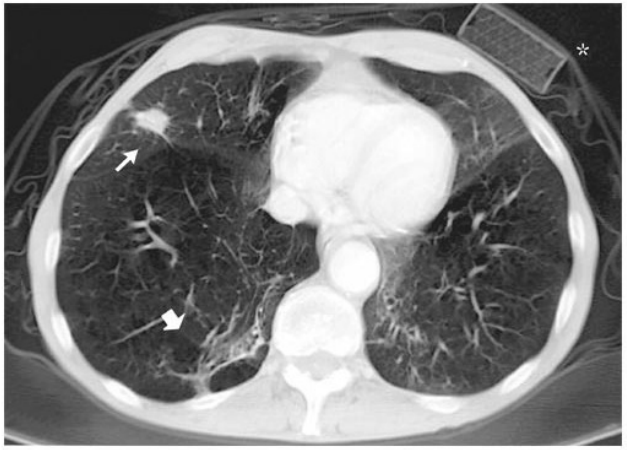

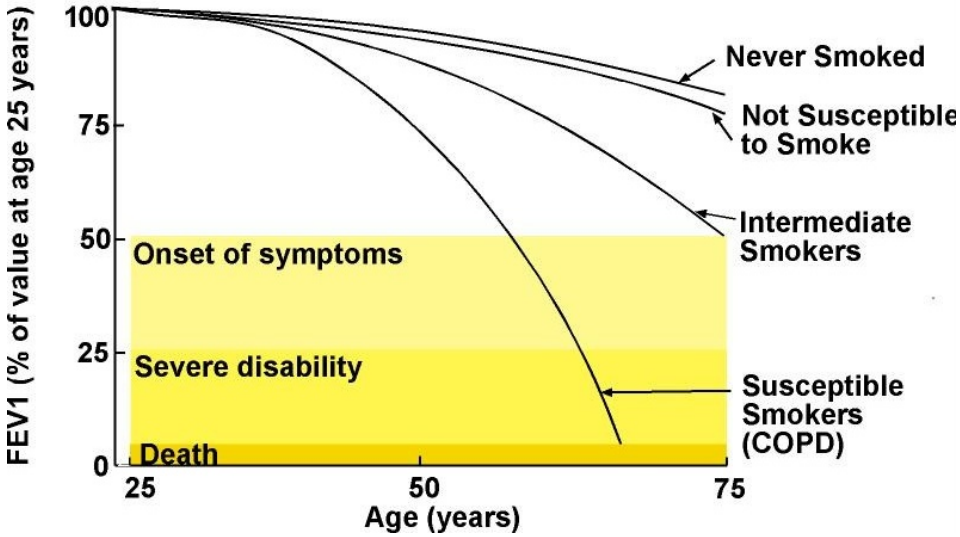

Statins for COPD?