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Considering Respiratory Health and the Lifecourse Evolution of Chronic Lung Disease

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Disclosures

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  - GlaxoSmithKline
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  - CVS Caremark
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  - BTG/PneumRx
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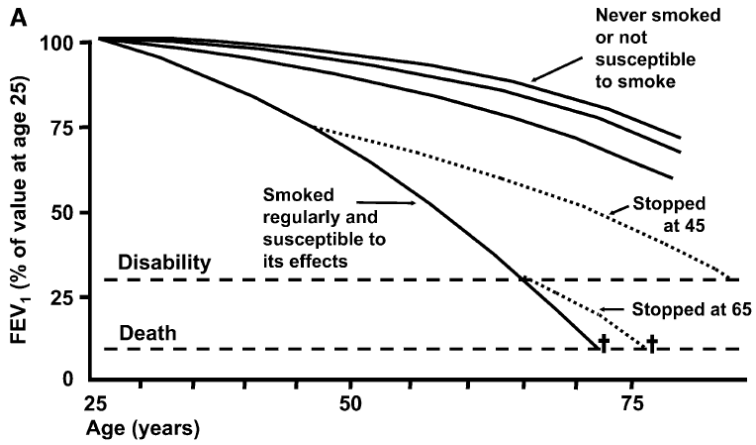
Defining Lung Health

Some facts about the respiratory community's approach to health and disease

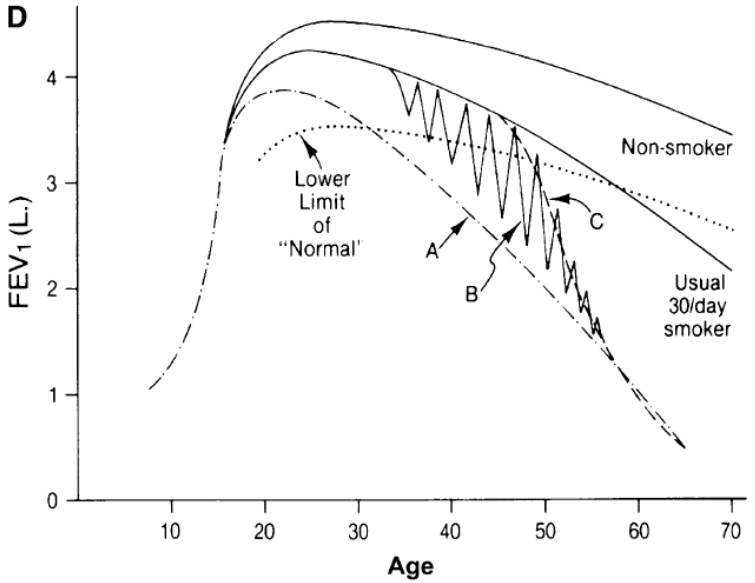
- Lung health in adults has traditionally been defined as the absence of disease
  - "Early disease" then becomes defined as the first appearance of abnormal lung physiology
  - A framework for early disease is critical to test today's therapies
  - A framework for lung health is critical for disease interception
- The trajectory of decline following attainment of peak lung function is variable – we only seem to care, however, if it declines into the "disease range"
- Outside of smoking, there are limited data on factors associated with maintenance versus decline in pulmonary function

Historical Perspectives on Lung Function Decline

Fletcher & Peto 1977



Burrows 1981

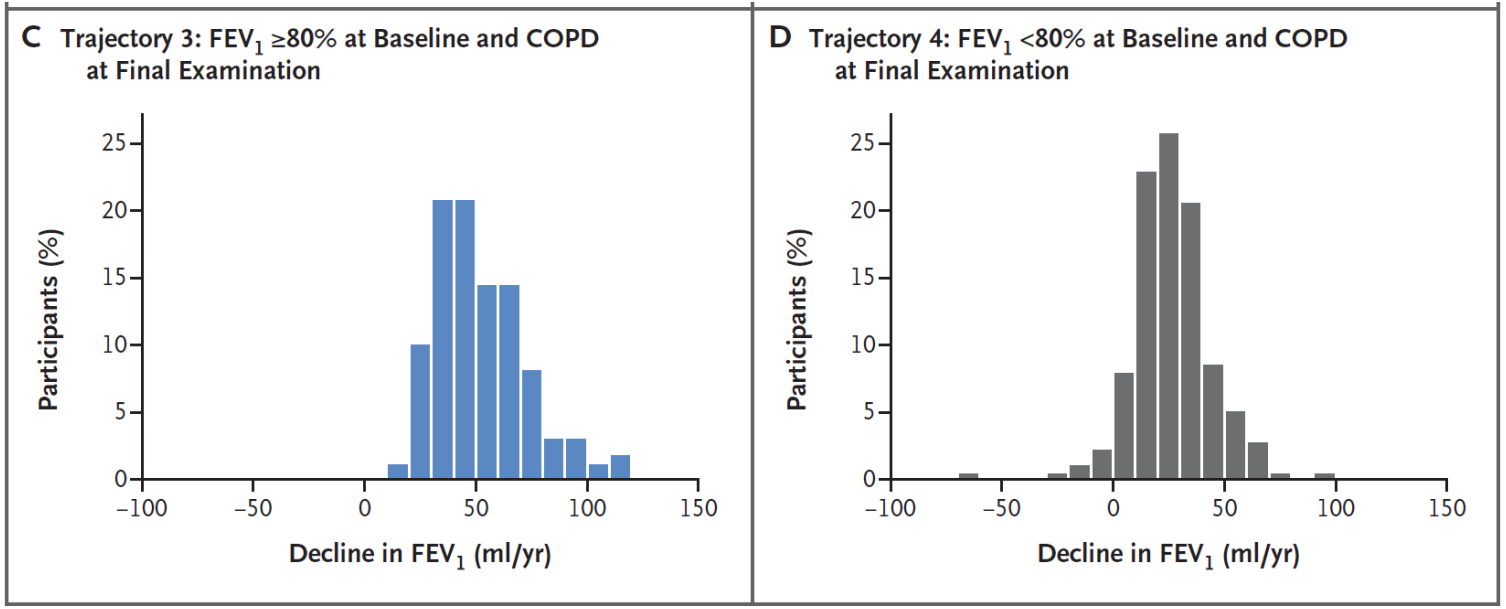


Fletcher & Peto, *BMJ* 1977; 1: 1645-48

Burrows B, *Med Clin N Am* 1981; 65: 455-71

Variable Trajectories from Health to OLD

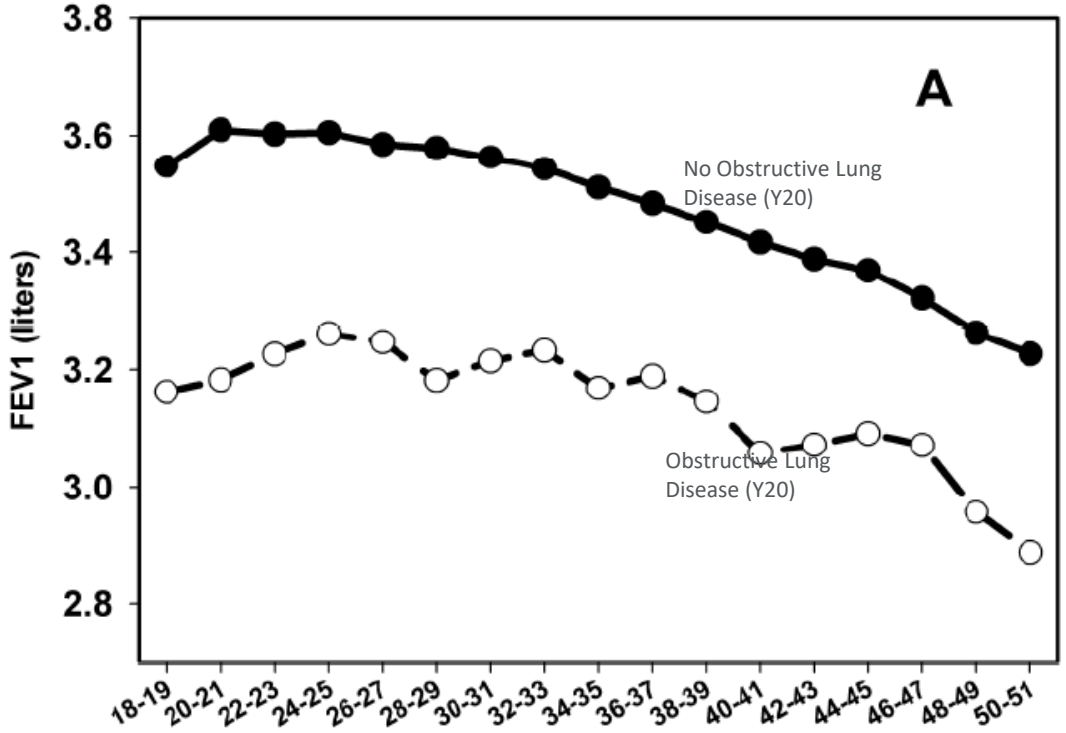
Two distinct pathways to get to COPD



Lange P, et al. *N Engl J Med* 2015; 373: 111-22

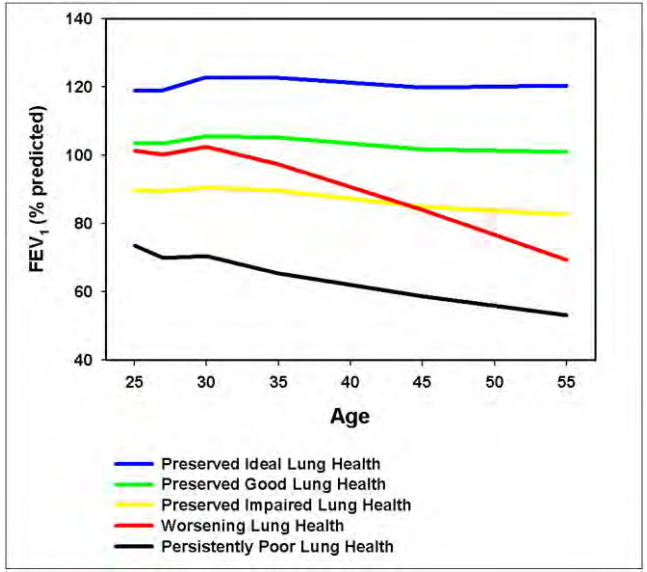
“Early” COPD at age 38-50

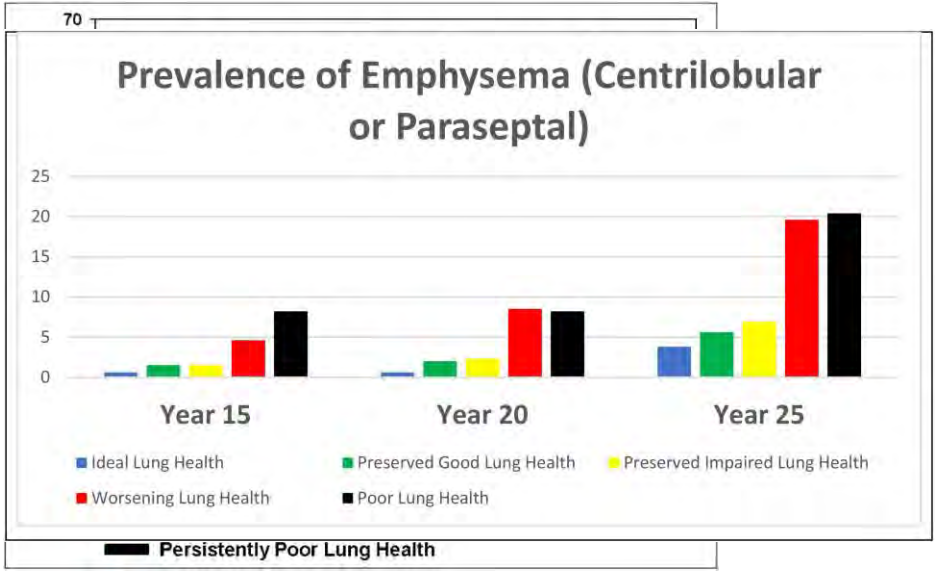
Seems like maybe they always had it……



Kalhan R, et al. *Am J Med* 2010; 123: 468.e1-468.e7

Lung function trajectories as precursors to chronic lung disease





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Washko GR, et al. *Am J Med* 2020; 133: 222-30

Phenotyping Lung Health

Respiratory symptoms at age 25-27 predict future incident lung disease

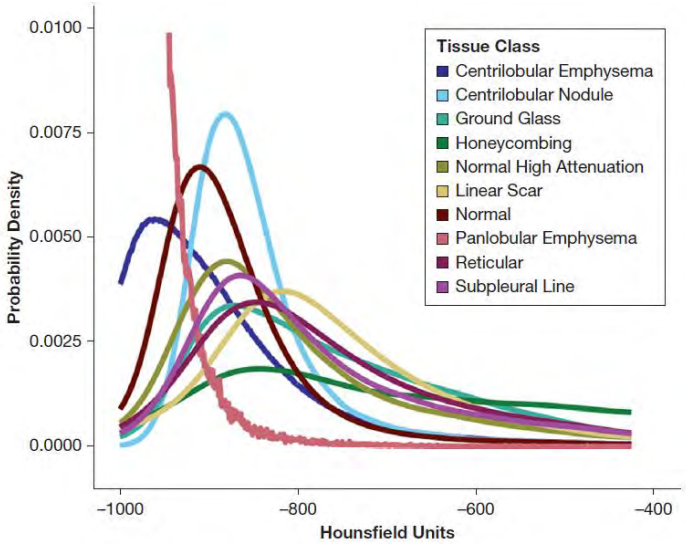
Symptom	Restrictive OR 95% CI	Obstructive OR 95% CI	CT-determined Emphysema
Any symptom	**1.39 (1.10, 1.76)**	**1.83 (1.35, 2.49)**	0.92 (0.70, 1.22)
Cough or Phlegm	1.27 (0.91, 1.77)	**1.47 (1.02, 2.10)**	**1·46 (1.02, 2.07)**
Episodes of bronchitis	1.05 (0.56, 1.98)	1.32 (0.68, 2.54)	**1.95 (1.05, 3.60)**
Wheeze	1.09 (0.84, 1.43)	**2.00 (1.47, 2.71)**	0.93 (0.68, 1.27)
Shortness of breath	**1.85 (1.30, 2.64)**	1.05 (0.63, 1.75)	1.06 (0.60, 1.86)
Chest illnesses	1.04 (0.79, 1.36)	**1.55 (1.13, 2.11)**	1.07 (0.77, 1.48)

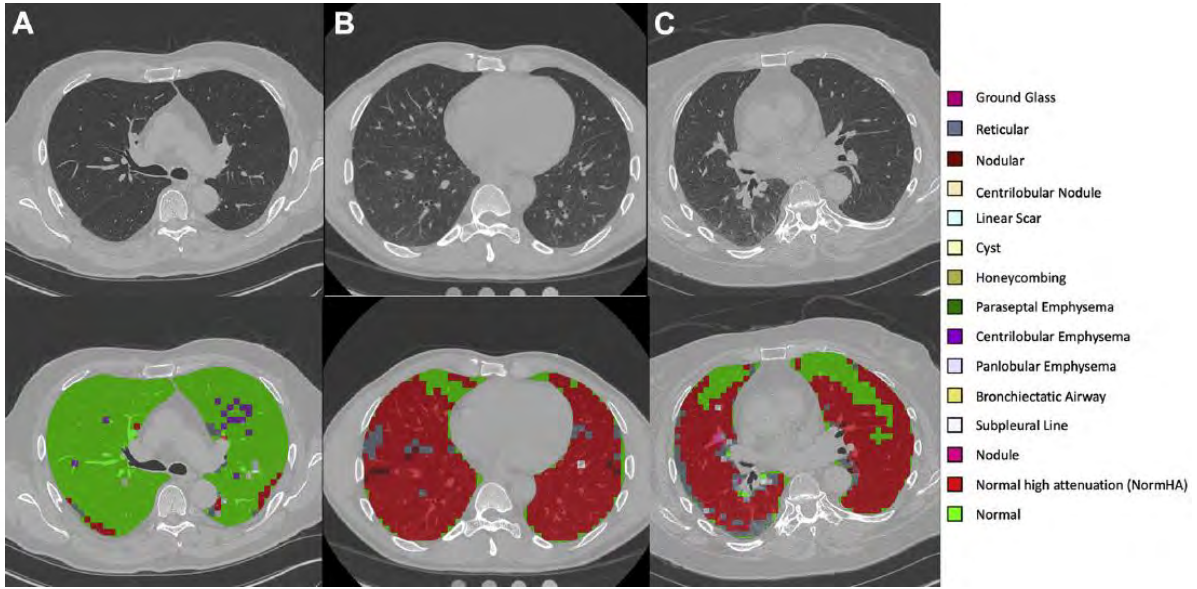
Covariates: age, race-sex group, center, baseline BMI, physician-confirmed asthma, smoking status (never, former current).

Kalhan R, et al. *Am J Resp Crit Care Med* 2018; 197: 1616

Phenotyping Lung Health – Radiographic Imaging

Using the Local Histogram to Create a Lung Health Map





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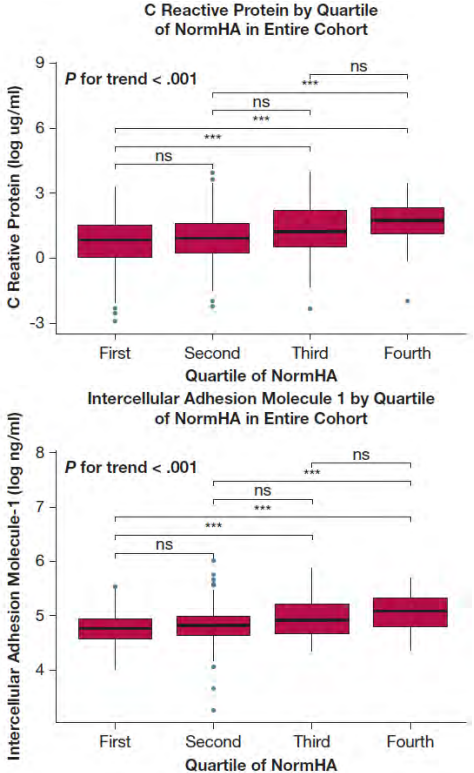
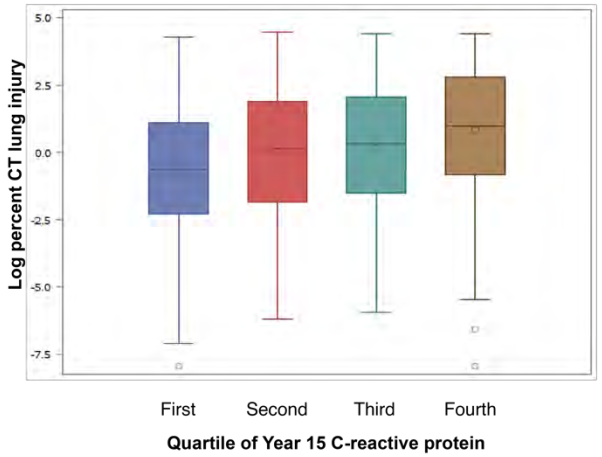
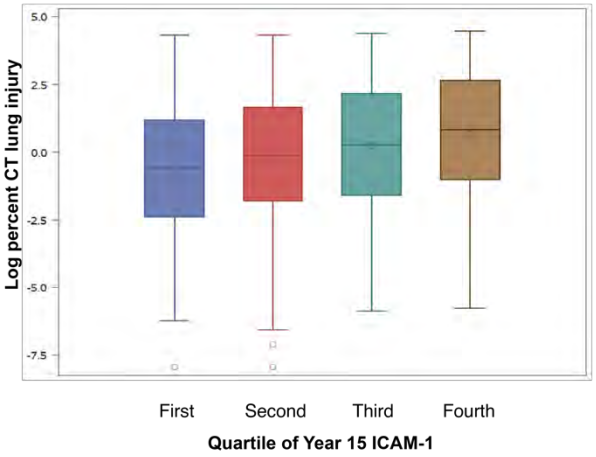
Harmouche R, Ash SY, et al. *Chest* 2019; 156: 1149-59

Phenotyping Lung Health

Blood biomarkers and lung injury







Harmouche R, Ash SY, et al. *Chest* 2019; 156: 1149-59

Liu GY, et al. ATS 2021 – manuscript in preparation

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Lung injury and future disease

CT Abnormality – CARDIA year 25 (mean age 50)	Percentage of Parenchymal Lung Injury (tertiles) – CARDIA year 15 (mean age 40)		
	Tertile 1	Tertile 2	Tertile 3
Centrilobular emphysema, OR (95% CI)	1 (reference)	1.74 (0.97, 3.10)	1.92 (1.08, 3.41)
Paraseptal emphysema, OR (95% CI)	1 (reference)	1.62 (0.95, 2.78)	1.37 (0.79, 2.37)
Interstitial abnormalities, OR (95% CI)	1 (reference)	2.62 (1.67, 4.10)	8.01 (5.24, 12.2)

Liu GY, et al. ATS 2021 – manuscript in preparation

Biomarkers and CT injury and future disease

Association of inflammatory markers with year 25 interstitial features, stratified by year 15 CT lung injury				
	Less Y15 CT lung injury		More Y15 CT lung injury	
	Effect estimate	p-value	Effect estimate	p-value
CRP	-0.003	0.952	0.100	0.011
ICAM-1	0.060	0.782	0.311	0.088

Liu GY, et al. ATS 2021 – manuscript in preparation

Our Paradigm of Lifetime Respiratory Health

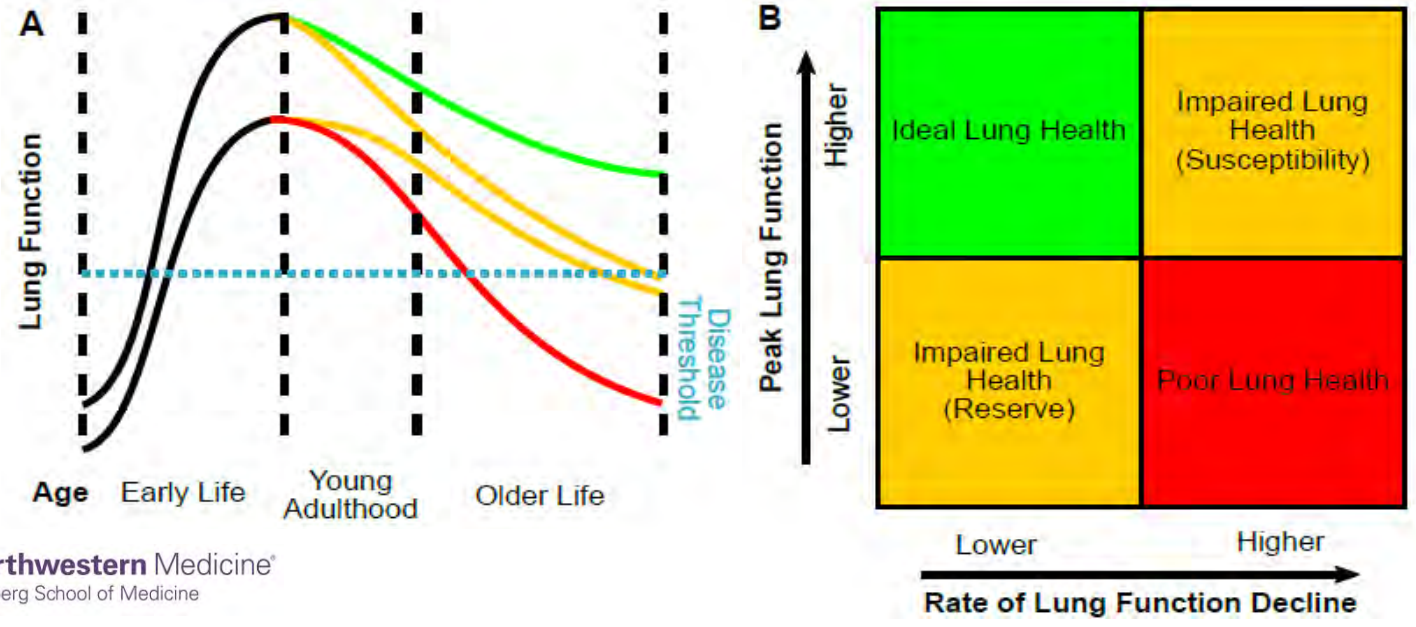
PULMONARY PERSPECTIVE

Defining Impaired Respiratory Health

A Paradigm Shift for Pulmonary Medicine

Paul A. Reyfman[1], George R. Washko[2], Mark T. Dransfield[3], Avrum Spira[4], MeiLan K. Han[5], and Ravi Kalhan[1,6]

American Journal of Respiratory and Critical Care Medicine Volume 198 Number 4 | August 15 2018



Some concluding thoughts

- **Ideal lung health is more than the absence of lung disease**
  - Impaired lung health is associated adverse consequences
  - Disease-focused studies, even when inclusive of early disease, do not inform lung health or prevention strategies nor do they typically enable interception strategies
- **Preservation of lung health is not solely predicated on avoidance of cigarette smoking**
  - The full "exposome" plays a role in loss of lung health and intermediate phenotypes of impaired respiratory health have innumerable adverse health consequences
- **Major gains in cardiovascular disease prevention are attributable to health-promotion**
  - The absence of a disease-agnostic lung health study in the US has hindered our efforts at prevention of lung disease
  - **We lack the cholesterol for the lung – imaging biomarkers are a clear opportunity!**

The American Lung Association Lung Health Cohort

Now recruiting……

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