

Smoking and Pulmonary Health Among Women and Girls

Katherine Menson, DO

University of Vermont
Larner College of
Medicine

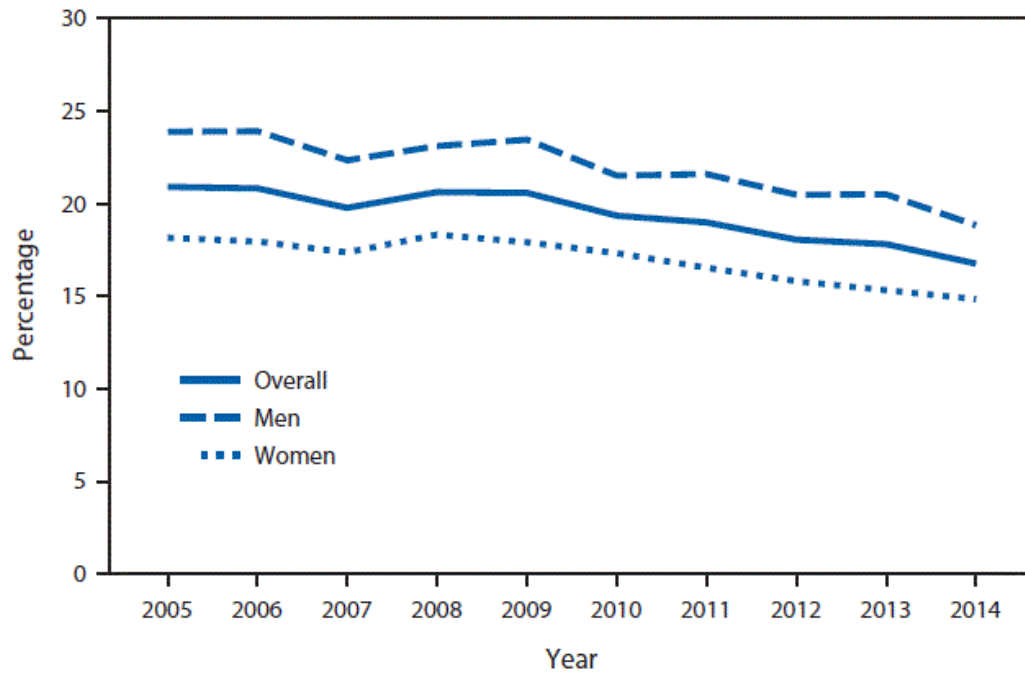


The University of Vermont

Disclosures

- Supported by grants from NIH, FDA, and ALA
- These views are my own and do not reflect the views of these agencies.
- No conflicts to disclose

Rates of Smoking in Women

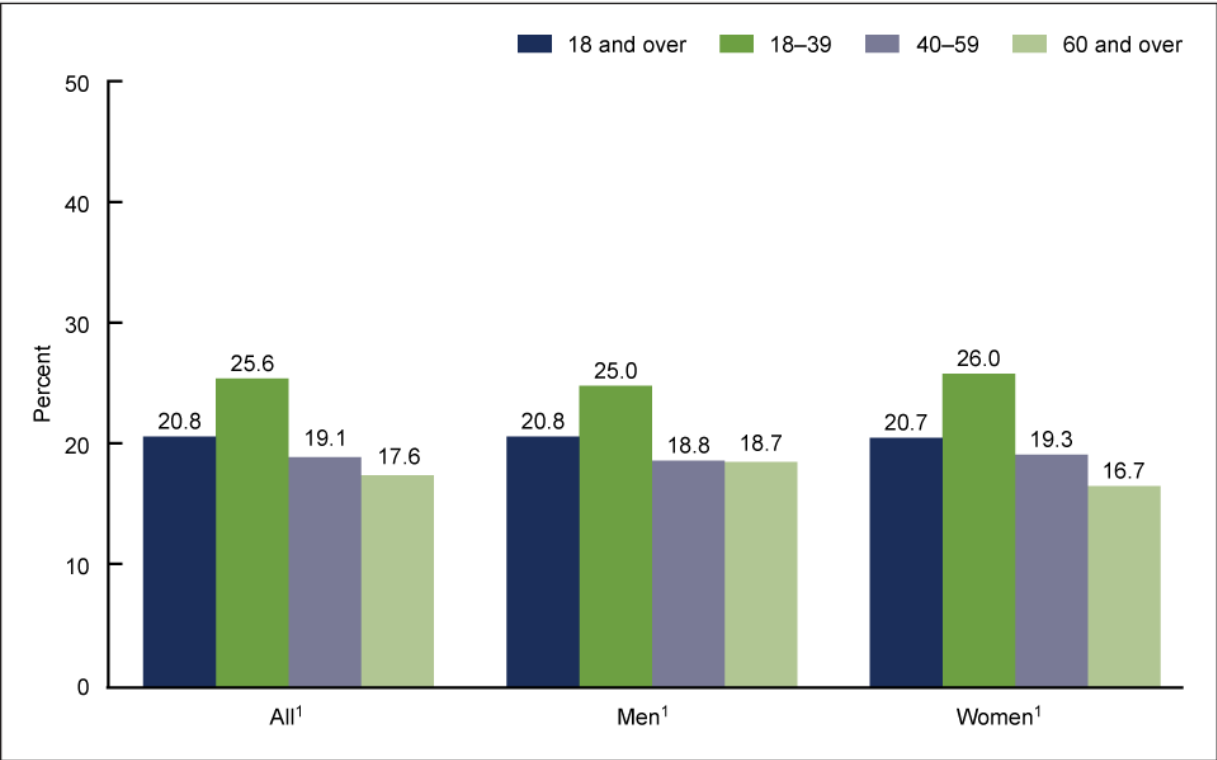


- Largest preventable cause of death in women



Rates of Secondhand Smoke (SHS) Exposure in Women

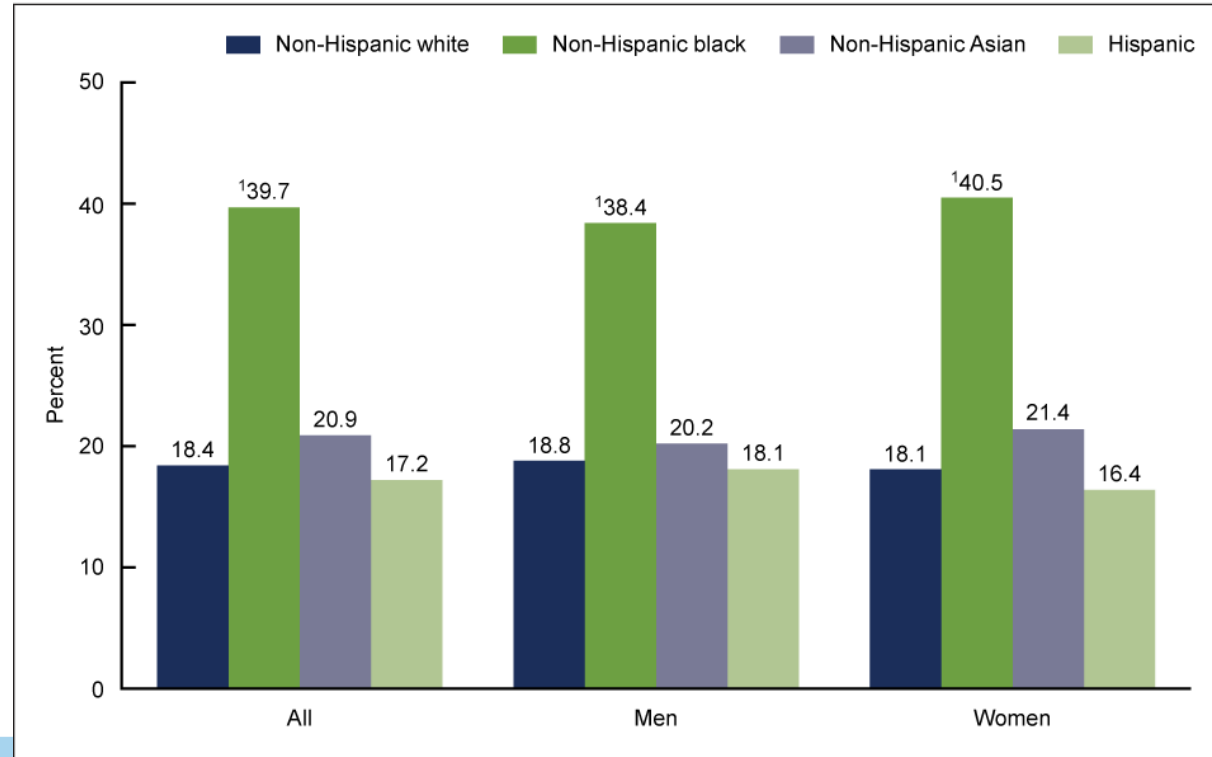
Figure 1. Percentage of secondhand smoke exposure among nonsmoking adults, by sex and age: United States, 2015–2018



¹Significant decreasing linear trend with increasing age.
NOTES: Secondhand smoke is defined as serum cotinine levels of 0.05–10.00 ng/mL. Access data table for Figure 1 at: <https://www.cdc.gov/nchs/data/databriefs/db396-tables-508.pdf#1>.
SOURCE: National Center for Health Statistics, National Health and Nutrition Examination Survey, 2015–2018.

Disproportionately Higher in Non-Hispanic Black Adults

Figure 2. Percentage of secondhand smoke exposure among nonsmoking adults, by sex and race and Hispanic origin: United States, 2015–2018

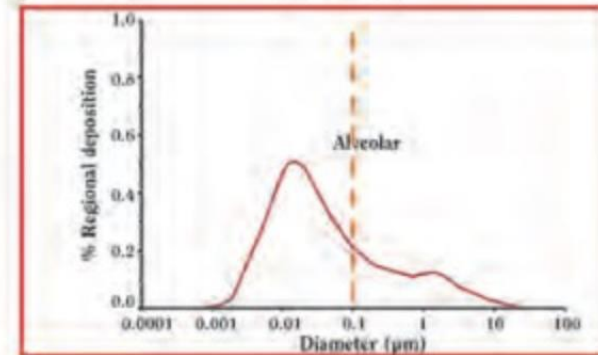
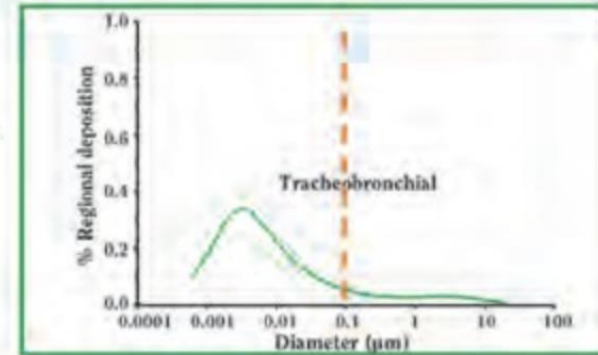
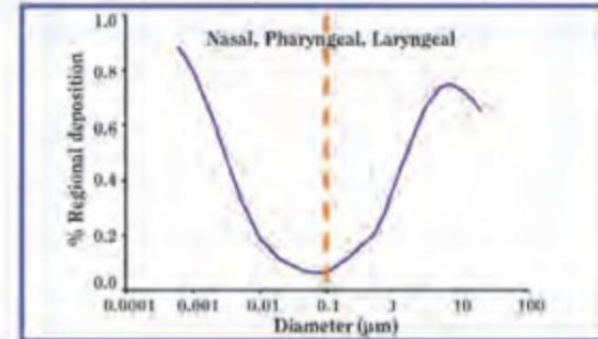
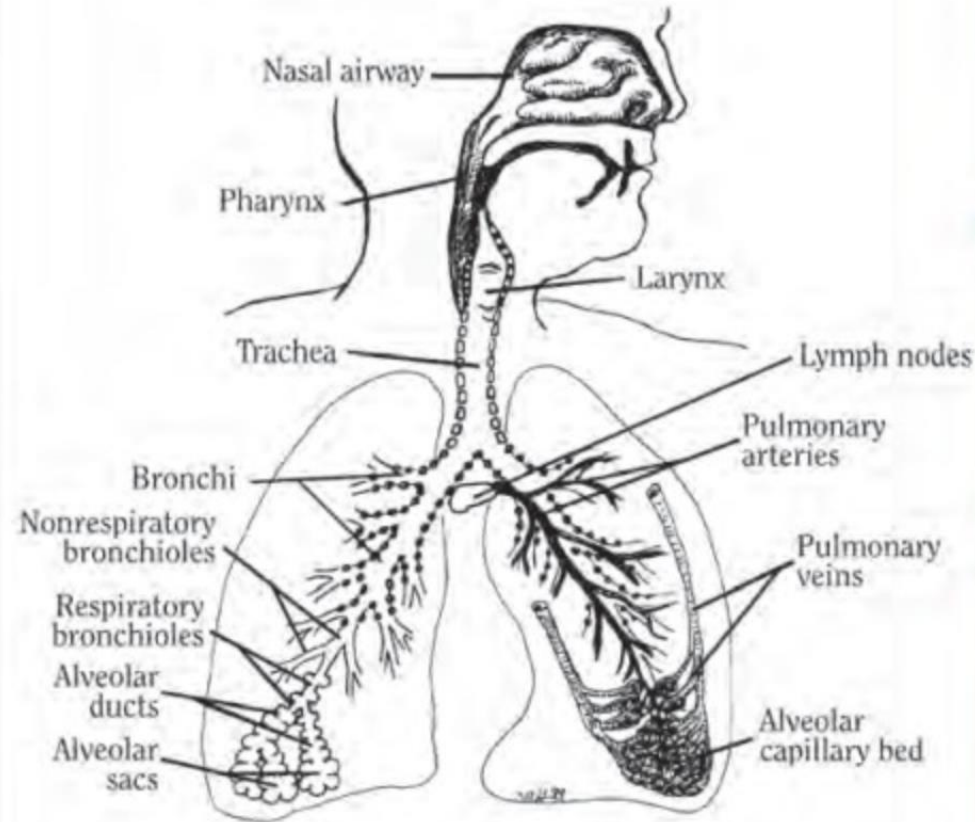


¹Significantly different from all other race and Hispanic-origin groups.

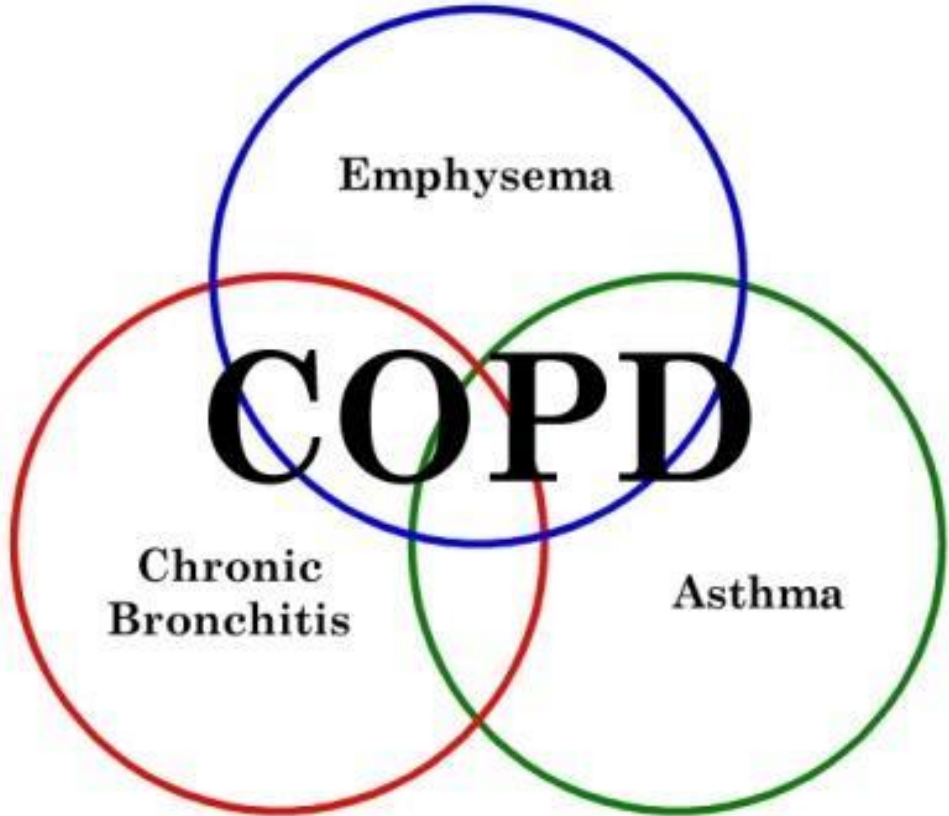
NOTES: Secondhand smoke is defined as serum cotinine levels of 0.05–10.00 ng/mL. Only persons reporting a single race are included. Access data table for Figure 2 at: <https://www.cdc.gov/nchs/data/databriefs/db396-tables-508.pdf#2>.

SOURCE: National Center for Health Statistics, National Health and Nutrition Examination Survey, 2015–2018.

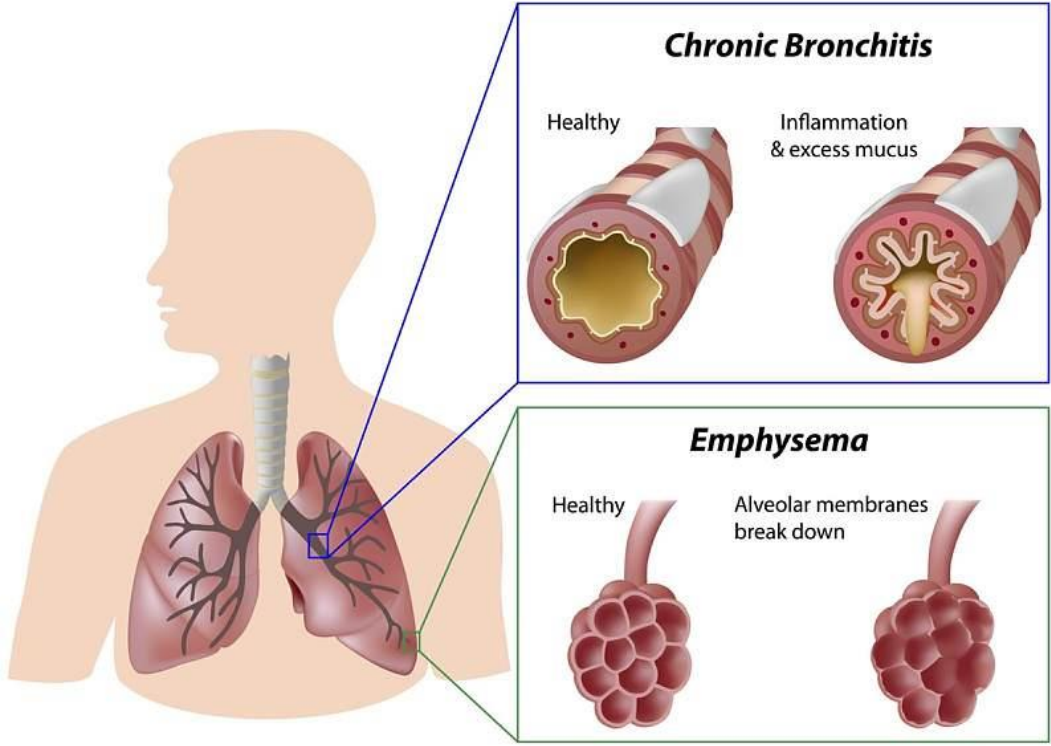
Pulmonary Anatomy



Smoking-Related Lung Disease



Chronic Obstructive Pulmonary Disease (COPD)



Diagnosis of COPD

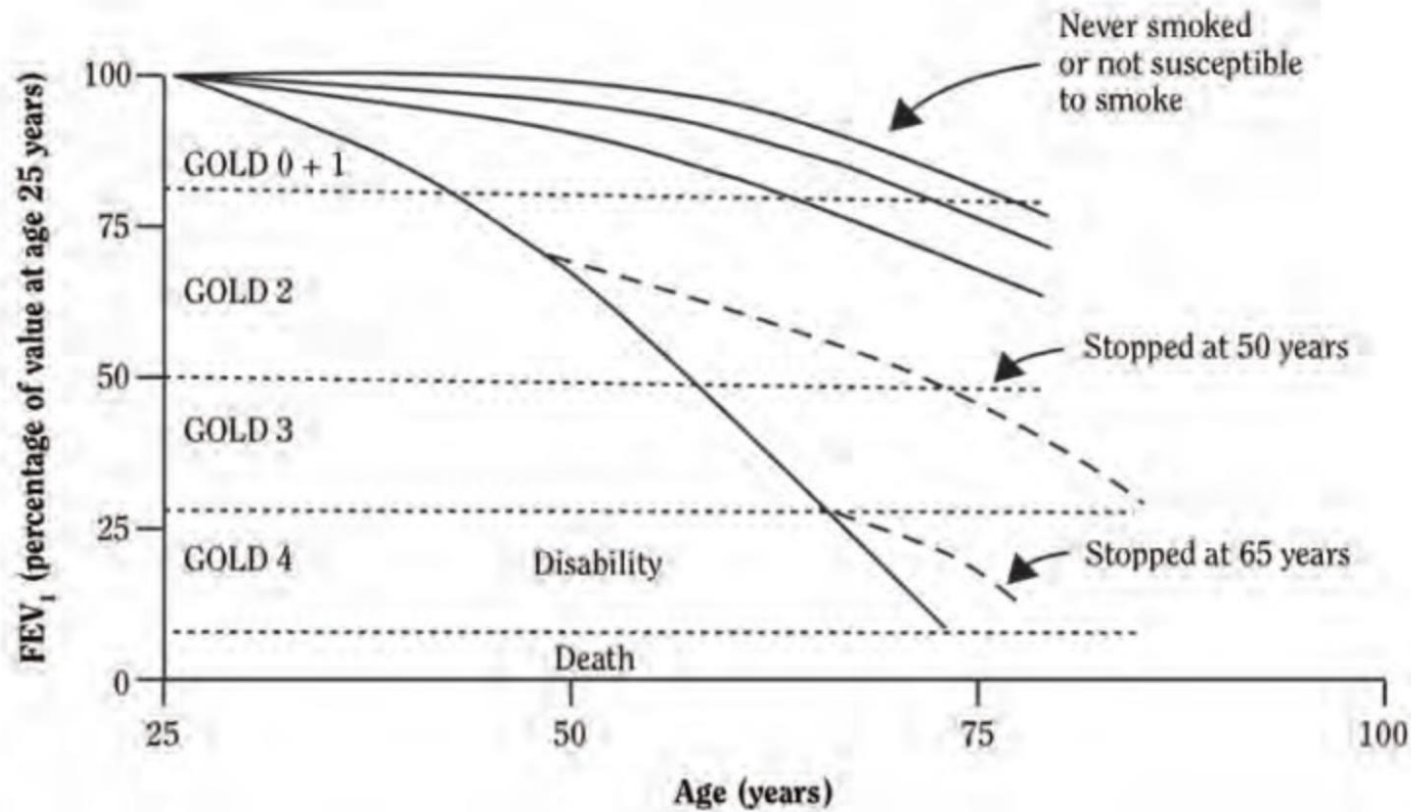
GOLD Grades and Severity of Airflow Obstruction in COPD (based on post-bronchodilator FEV1)

Table 2.6

In COPD patients (FEV1/FVC < 0.7):

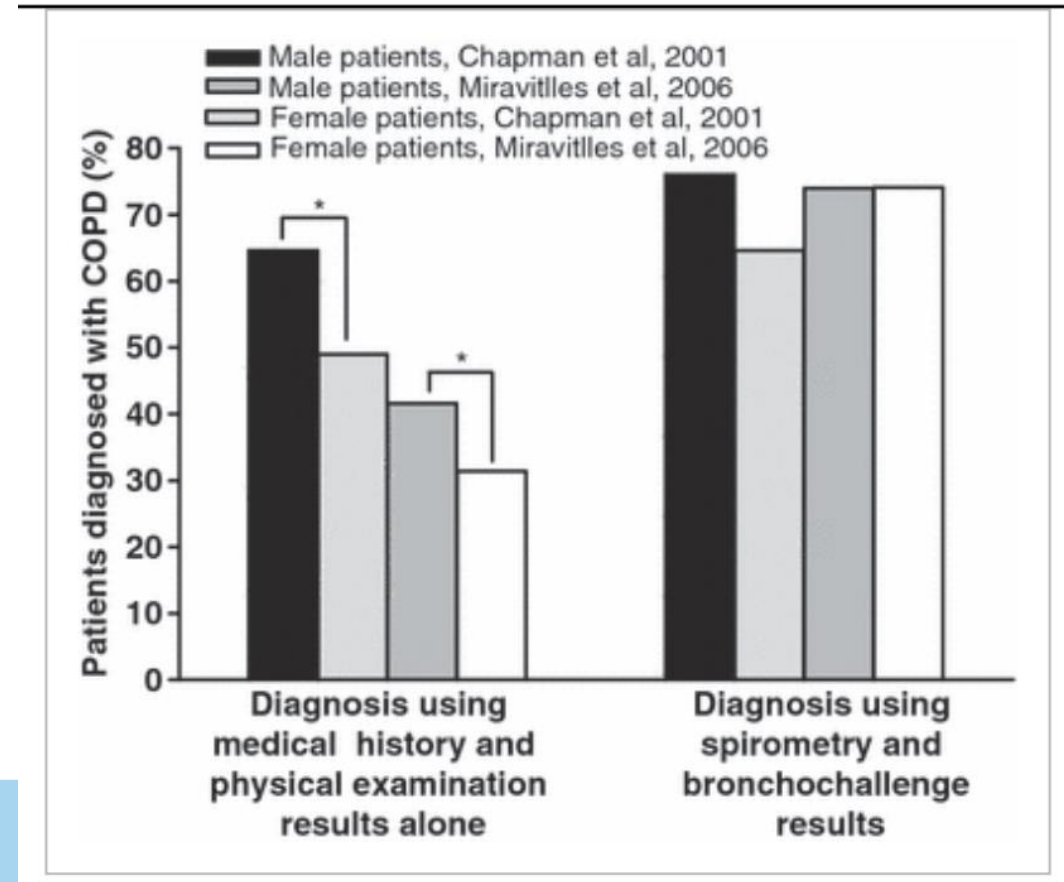
GOLD 1:	Mild	FEV1 ≥ 80% predicted
GOLD 2:	Moderate	50% ≤ FEV1 < 80% predicted
GOLD 3:	Severe	30% ≤ FEV1 < 50% predicted
GOLD 4:	Very Severe	FEV1 < 30% predicted

Lung Function Declines With Age



Women Are Less Likely to be Diagnosed

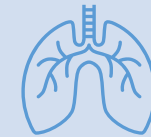
- Disparity in diagnosis based on examination alone
- Only 20-30% of PCPs order PFTs to make the diagnosis



Women with COPD



More likely to have severe symptoms



Worse airway hyperresponsiveness



Depression & anxiety



Worse HRQOL



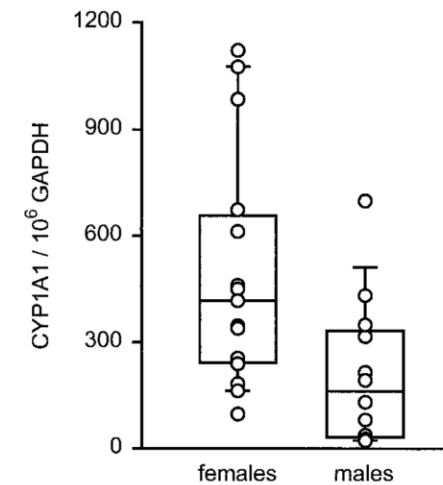
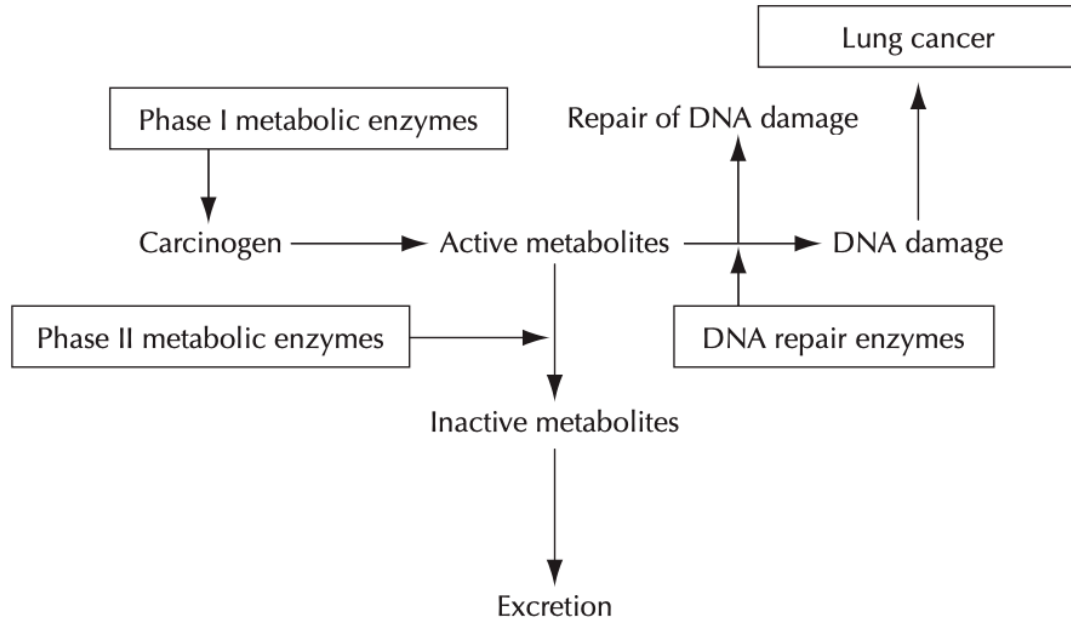
Lung Cancer

- Leading cause of cancer death in women
- 5-year survival rate 27%
- Never-smoking women are **twice** as likely to get lung cancer as never-smoking men

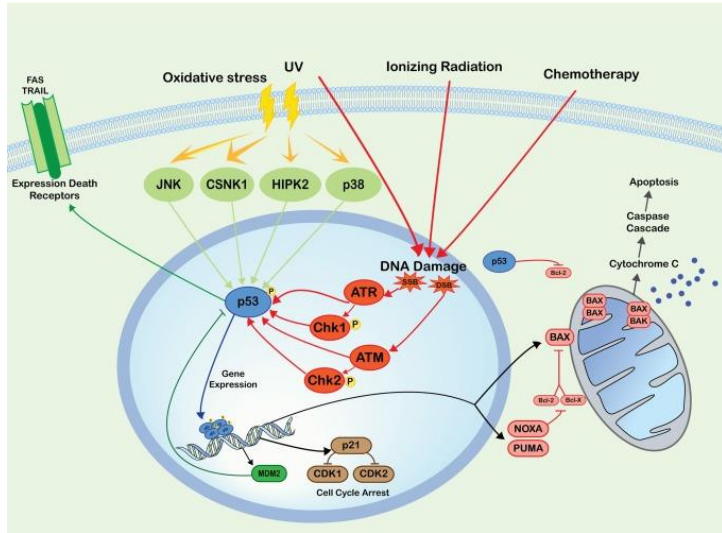


Genetics of Tobacco Detoxification

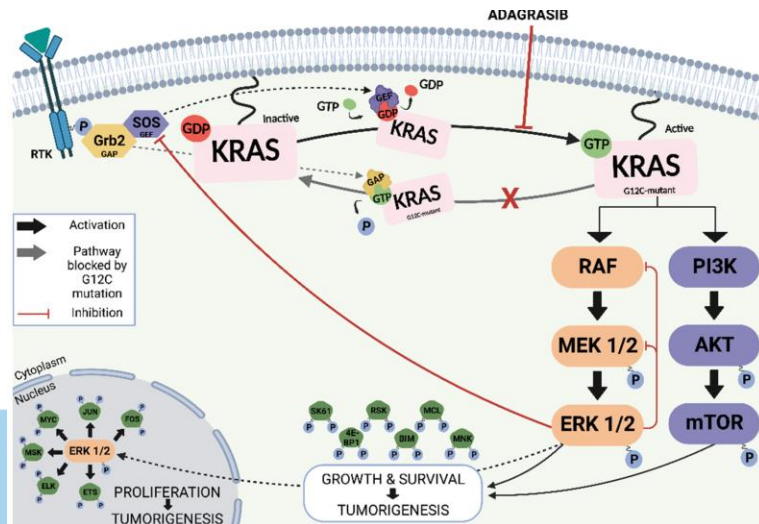
- Estrogen induces Phase 1 enzymes
- Null expression of Phase II Enzymes present in ~50% population



Molecular Factors

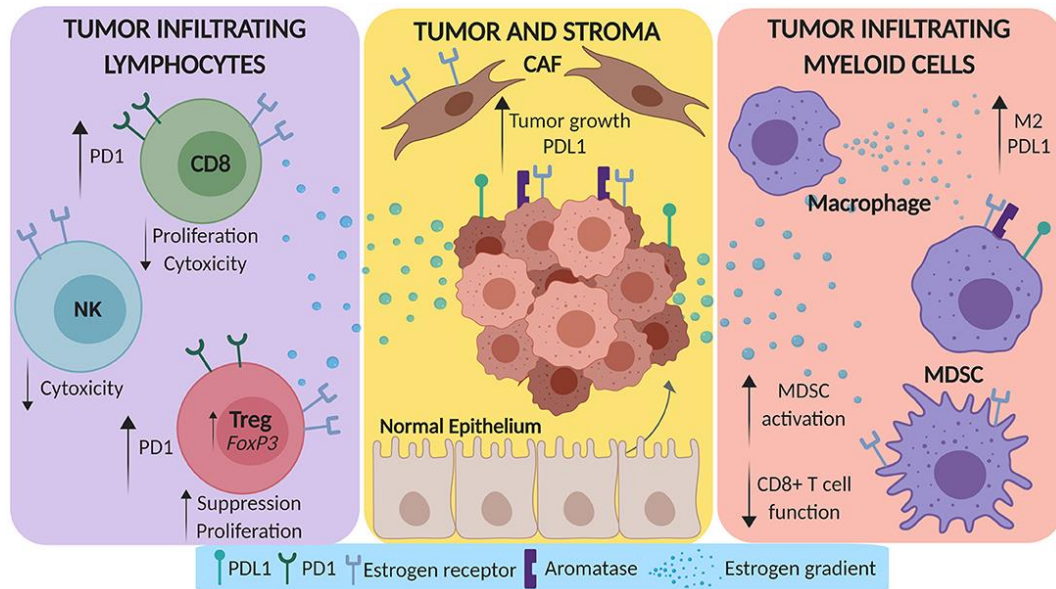


- Higher rate of mutation of p53 (tumor suppressor gene) in females with lung cancer despite lower pack-year history



- K-ras mutation (proto-oncogene) higher in females (26%) vs males (17%)

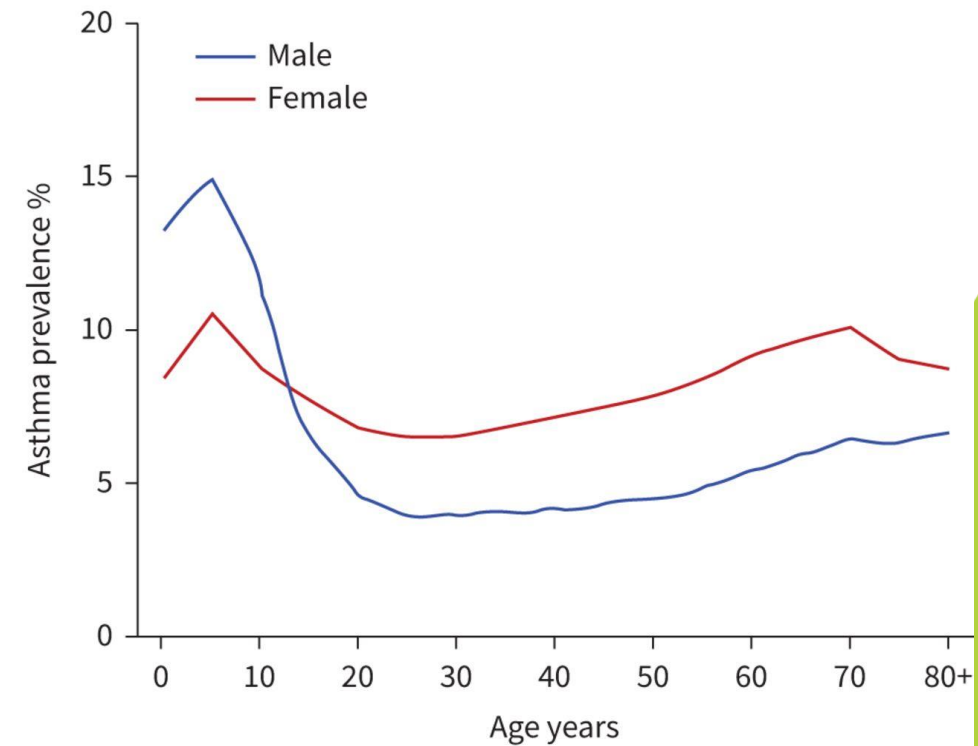
Estrogen Contributes to Lung Maturation



- Estrogen receptors expressed on lung tumor cells
- 17-fold increase in cell proliferation in tumor cells
- Post-menopausal women taking HRT 50% increased risk of lung cancer

Smoking Reduces Asthma Control

- Women who smoke have increased asthma symptoms compared to men
- Prematurity and SHS are risk factors for asthma



Summary

1. Females have more severe manifestations of pulmonary disease likely due to the role of estrogen in lung maturity.
2. Women are less likely to be diagnosed with COPD which may contribute to decline in lung function.
3. Women are more susceptible to carcinogen exposure due to enhanced phase 1 metabolism.

Citations

Oberdörster G. Nanotoxicology: an emerging discipline evolving from studies of ultrafine particles. *Environ Health Perspect.* 2005 Jul;113(7):823-39.

Brody DJ. Secondhand smoke exposure among nonsmoking adults: United States, 2015–2018. NCHS Data Brief, no 396. Hyattsville, MD: National Center for Health Statistics. 2021.

Sun S. Lung cancer in never smokers—a different disease. *Nat Rev Cancer.* 2007 Oct;7(10):778-90.

Wakelee HA. Lung cancer incidence in never smokers. *J Clin Oncol.* 2007 Feb 10;25(5):472-8

Siegel, RL. Cancer statistics, 2023. *CA Cancer J Clin.* 2023; 73(1): 17- 48.

Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database, National Cancer Institute, DCCPS, Surveillance Research Program, released April 2022.

Mollerup S. Sex differences in lung CYP1A1 expression and DNA adduct levels among lung cancer patients. *Cancer Res.* 1999 Jul 15;59(14):3317-20.

Sabile LP. Human non-small-cell lung tumours and cells derived from normal lung express both estrogen receptor α and β and show biological responses to estrogen. *Cancer Res.* 2002; 62: 2141-2150

Nelson HH. Implications and prognostic value of K-ras mutations for early-stage lung cancer in women. *J Natl Cancer Inst.* 1999; 91: 2032-2038

Cote CG, Chapman KR. Diagnosis and treatment considerations for women with COPD. *Int J Clin Pract.* 2009 Mar;63(3):486-93.

O'Sullivan É, Keogh A, Henderson B, Finn SP, Gray SG, Gately K. Treatment Strategies for KRAS-Mutated Non-Small-Cell Lung Cancer. *Cancers.* 2023; 15(6):1635.

Kiyohara C, Ohno Y. Sex differences in lung cancer susceptibility: a review. *Gend Med.* 2010 Oct;7(5):381-401. doi: 10.1016/j.genm.2010.10.002. PMID: 21056866.

Slatore CG. Lung cancer and hormone replacement therapy: association in the vitamins and lifestyle study. *J Clin Oncol.* 2010 Mar 20;28(9):1540-6.

Smida T, Bruno TC, Stabile LP. Influence of Estrogen on the NSCLC Microenvironment: A Comprehensive Picture and Clinical Implications. *Front Oncol.* 2020 Feb 18;10:137..

