



# Lung cancer

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# Objectives:

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- Risk Factors
- Canadian Statistics and SK Statistics
- Signs and Symptoms
- Screening practices in Canada

# Lung cancer risk factors: Causal relationship

- Active smoking of cigarettes and other tobacco products
  - Single most important causal determinant of individual and population risk
  - Risk increases with great number of cigarettes smoking per day and greater number of years of smoking
  - Populations risk increases with the prevalence of current smoker
  - 2,000% increase relative risk in lung cancer compared to non-smoker



# Lung cancer risk factors: Causal relationship



Secondhand smoke exposure (20-30% relative increase in risk)<sup>1</sup>



Ionizing radiation (radon)



Occupational exposure (arsenic, chromium, nickel, asbestos, tar, and soot)



Indoor and outdoor air pollution

1. US Department of Health and Human Services. *The Health Consequences of Involuntary Exposure to Tobacco Smoke: A Report of the Surgeon General*.

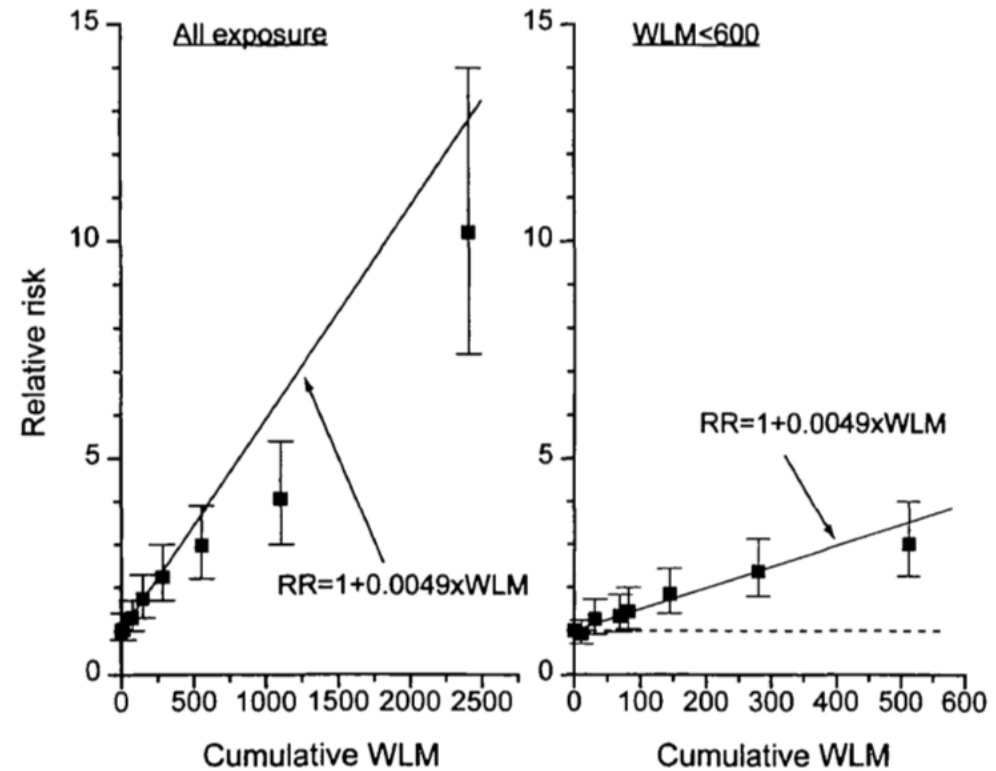


# Lung cancer: Risk associated with Radon exposure in underground miners

## Lung Cancer in Radon-Exposed Miners and Estimation of Risk From Indoor Exposure

Jay H. Lubin, John D. Boice, Jr., Christer Edling, Richard W. Hornung, Geoffrey R. Howe, Emil Kunz, Robert A. Kusiak, Howard I. Morrison, Edward P. Radford, Jonathan M. Samet, Margot Tirmarche, Alistair Woodward, Shu Xiang Yao, Donald A. Pierce\*

Study site (reference No.)	Type of mine	Person-years		Lung cancer deaths		WLM*	No. of years exposed*	ERR/WLM	95% CI
		Exposed	Non-exposed	Exposed	Non-exposed				
Yunnan Province, People's Republic of China (4)	Tin	135 357	39 985	936	44	277.4	12.9	0.0016	0.001-0.002
W. Bohemia, Czech Republic† (5)	Uranium	103 652	4216	656	5	198.7	7.3	0.0034	0.002-0.006
Colorado Plateau‡ (6)	Uranium	73 509	7403	292	2	595.7	4.0	0.0042	0.003-0.007
Ontario, Canada§ (7)	Uranium	319 701	61 017	282	2	30.8	3.0	0.0089	0.005-0.015
Newfoundland, Canada (8)	Fluorspar	35 029	13 713	112	6	367.3	4.8	0.0076	0.004-0.013
Malmberget, Sweden (9)	Iron	32 452	841	79	0	80.6	17.8	0.0095	0.001-0.041
Grants, New Mexico (10)	Uranium	46 797	12 152	68	1	110.3	7.4	0.0172	0.006-0.067
Beaverlodge, Canada (11)	Uranium	68 040	50 345	56	9	17.2	1.9	0.0221	0.009-0.056
Port Radium, Canada (12)	Uranium	30 454	22 222	39	18	242.8	3.2	0.0019	0.001-0.006
Radium Hill, Australia (13)	Uranium	25 549	26 301	32	22	7.6	1.1	0.0506	0.010-0.122
France (14)	Uranium	39 487	4556	45	0	68.7	13.2	0.0036	0.001-0.013
Combined		907 459	242 332	2597	109	158.0	5.7	0.0049	0.002-0.010¶



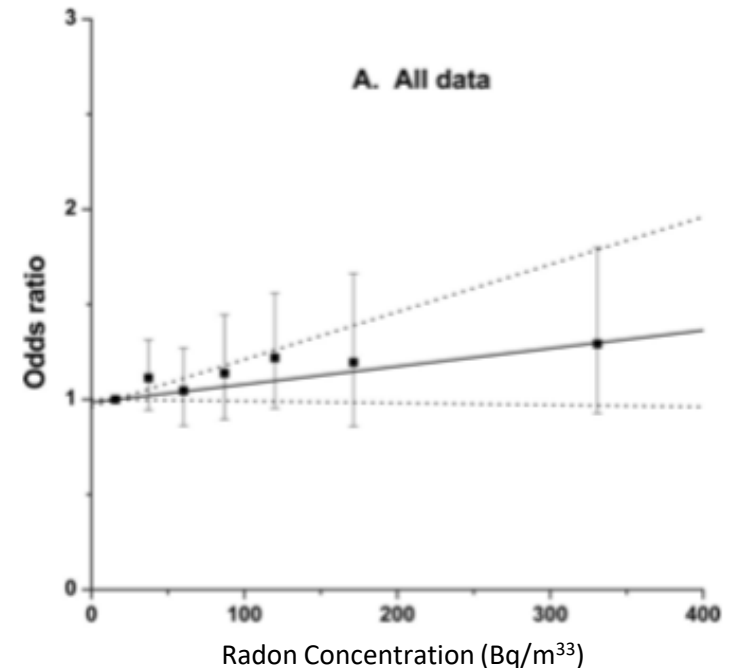
# Lung cancer: Risk with exposure to residential radon

## Residential Radon and Risk of Lung Cancer

### *A Combined Analysis of 7 North American Case-Control Studies*

*Daniel Krewski,<sup>\*</sup> Jay H. Lubin,<sup>†</sup> Jan M. Zielinski,<sup>\*\*</sup> Michael Alavanja,<sup>§</sup> Vanessa S. Catalan,<sup>||</sup>  
 R. William Field,<sup>\*\*\*</sup> Judith B. Klotz,<sup>††</sup> Ernest G. Létourneau,<sup>‡‡</sup> Charles F. Lynch,<sup>§</sup> Joseph I. Lyon,<sup>§§</sup>  
 Dale P. Sandler,<sup>|||</sup> Janet B. Schoenberg,<sup>††</sup> Daniel J. Steck,<sup>¶¶</sup> Jan A. Stolwijk,<sup>\*\*\*</sup> Clarice Weinberg,<sup>†††</sup>  
 and Homer B. Wilcox<sup>††</sup>*

Region	No. of Cases	No. of Controls	Average Radon Concentration (Bq/m <sup>3</sup> ) <sup>a</sup>	Excess Odds Ratio <sup>†</sup> (95% CI)
North America <sup>‡</sup>				
New Jersey (NJ) <sup>9</sup>	480	442	26	0.56 (-0.22-2.97)
Winnipeg (Winn) <sup>10</sup>	738	738	120	0.02 (-0.05-0.25)
Missouri-I (MO-I) <sup>12</sup>	538	1183	63	0.01 (<0.00-0.42)
Missouri-II (MO-II) <sup>13</sup>	512	553	56	0.27 (-0.12-1.53)
Iowa (IA) <sup>14</sup>	413	614	127	0.44 (0.05-1.59)
Connecticut (CT) <sup>16</sup>	963	949	33	0.02 (-0.21-0.51)
Utah-South Idaho (UT-ID) <sup>16</sup>	511	862	57	0.03 (-0.20-0.55)



# Lung cancer risk factor: Associative



Older age



Family history of lung cancer



Acquired lung disease



Acquired immunodeficiency such as HIV infection

# Lung cancer factors: reducing the risk



Reduction with fruit and vegetable (non-starchy) intake<sup>1</sup>

Roughly 20-40% relative risk reduction.



Reduction with physical exercise<sup>2</sup>

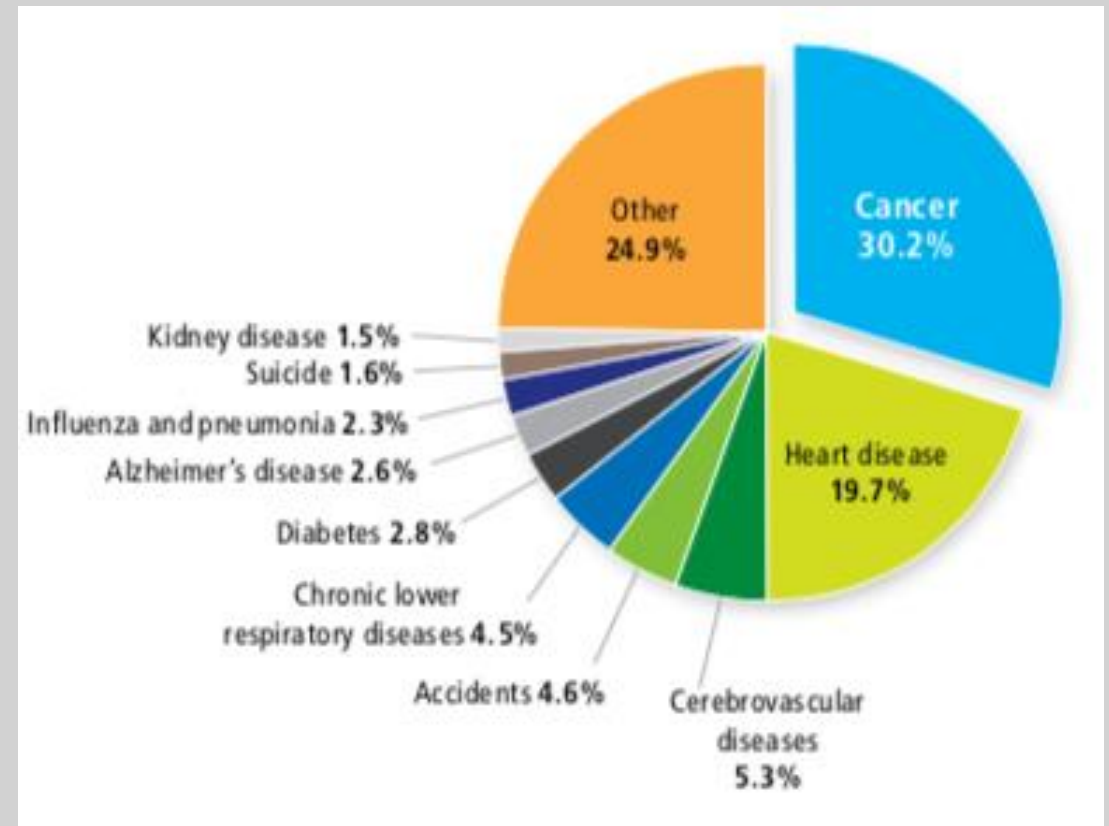
1. World Cancer Research Fund. *Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective*.

2. *Cancer Causes Control*. 2005;16(4): 389-397

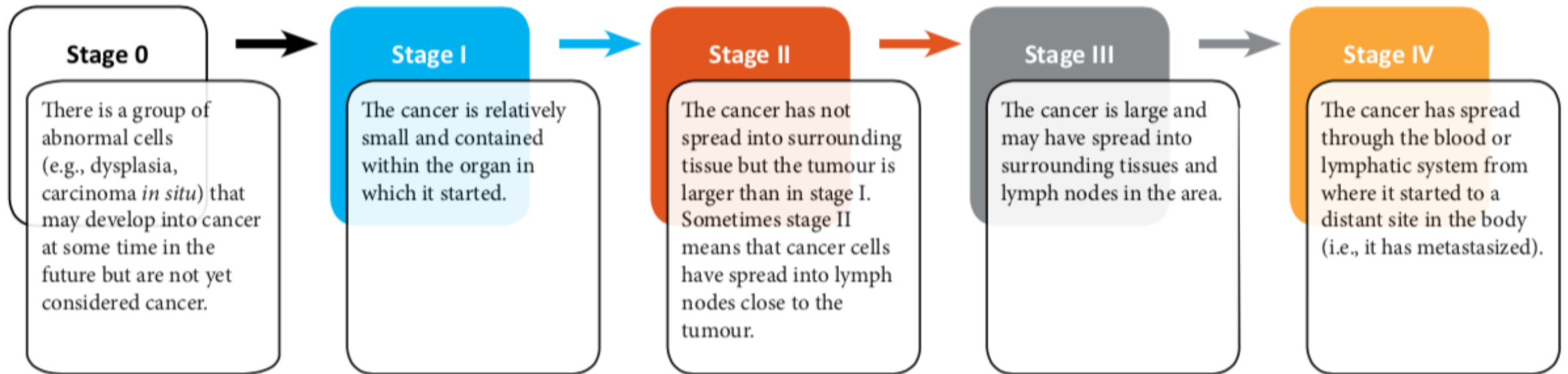


# Lung cancer facts

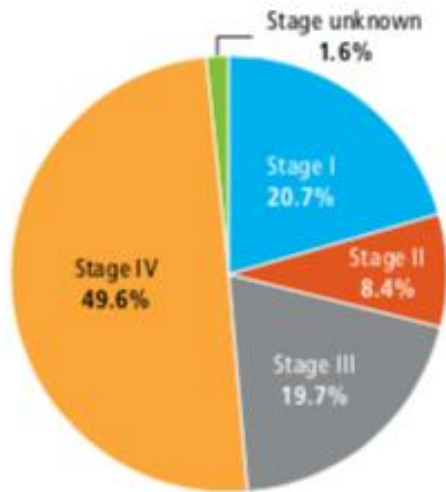
- Most commonly diagnosed cancer among Canadians
- 28,600 new cases in 2017 (14% of all cancers)
- Two major type:
  - Non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC)
  - NSCLC accounts for 80% of all lung cancers



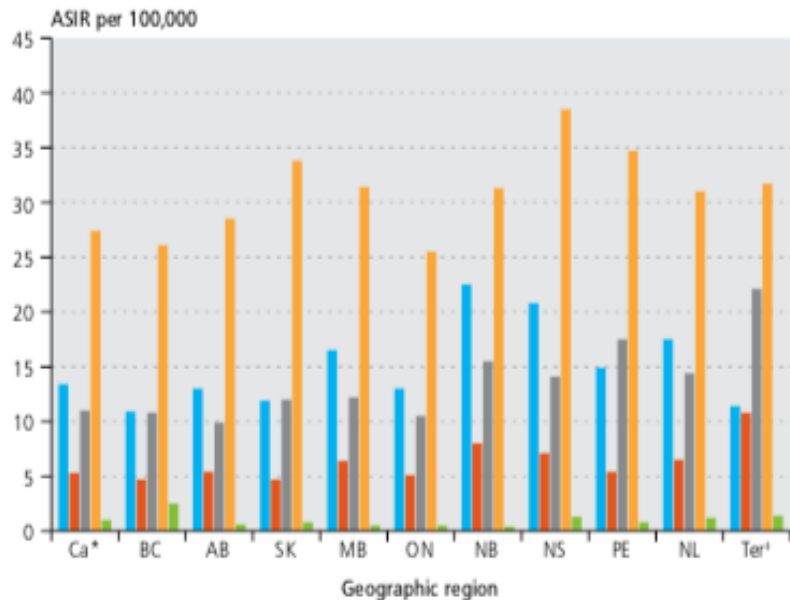
# Lung cancer staging



## Lung and bronchus cancer



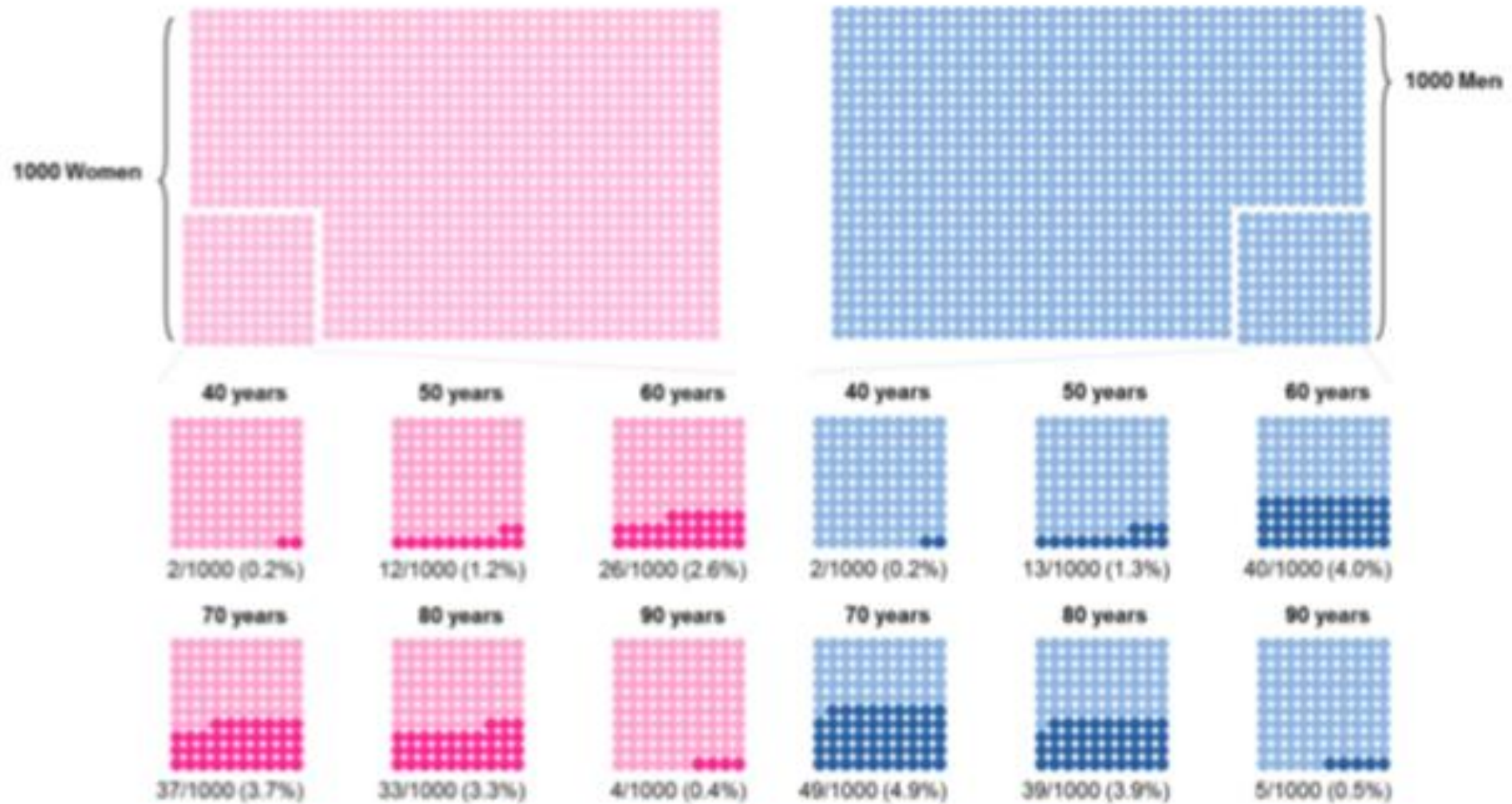
## Non-small cell lung cancer



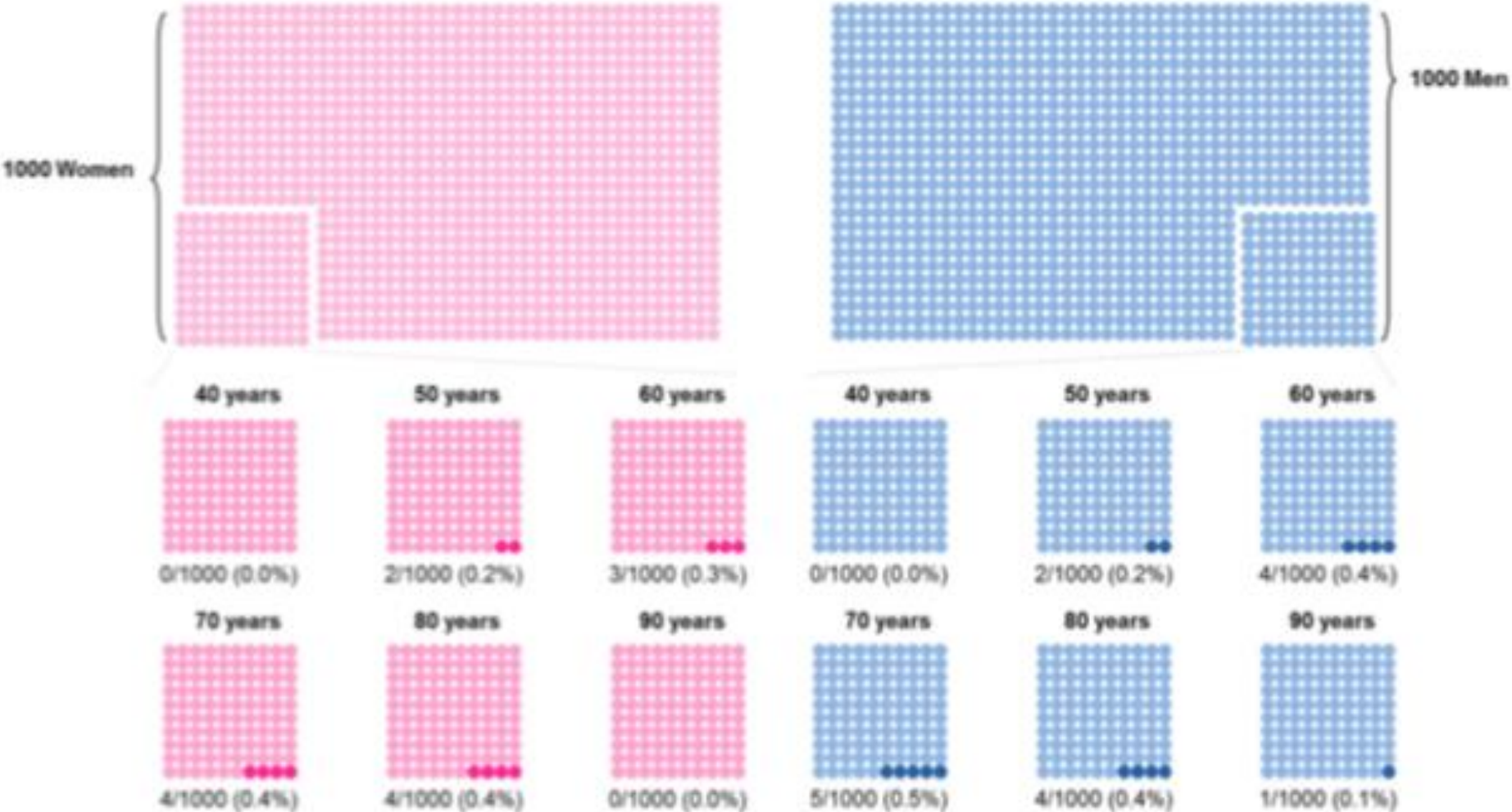
# Lung cancer facts

- Approximately half all lung cancer diagnosed at stage IV
  - Affect survival
- The rate of advanced lung cancer is generally higher in the east\*
- ~800 new cases diagnosed in Saskatchewan during 2017

# Lung cancer: Life time risk for current smoker

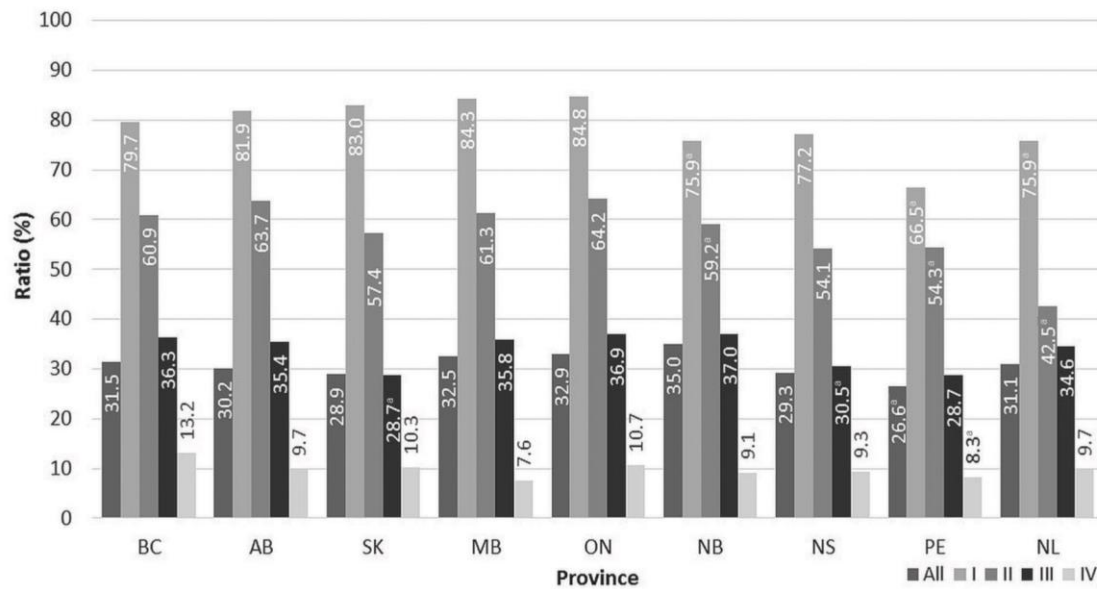


# Lung cancer: Life time risk for never smoker

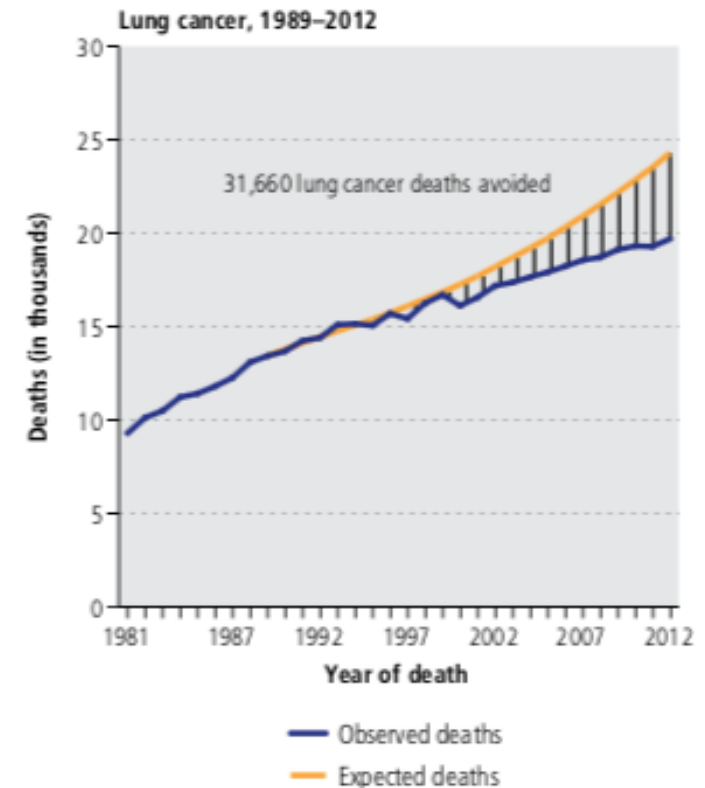




# Lung cancer: survival 2010-2012 Data



*Curr Oncol.* 2016 Apr;23(2):119-124

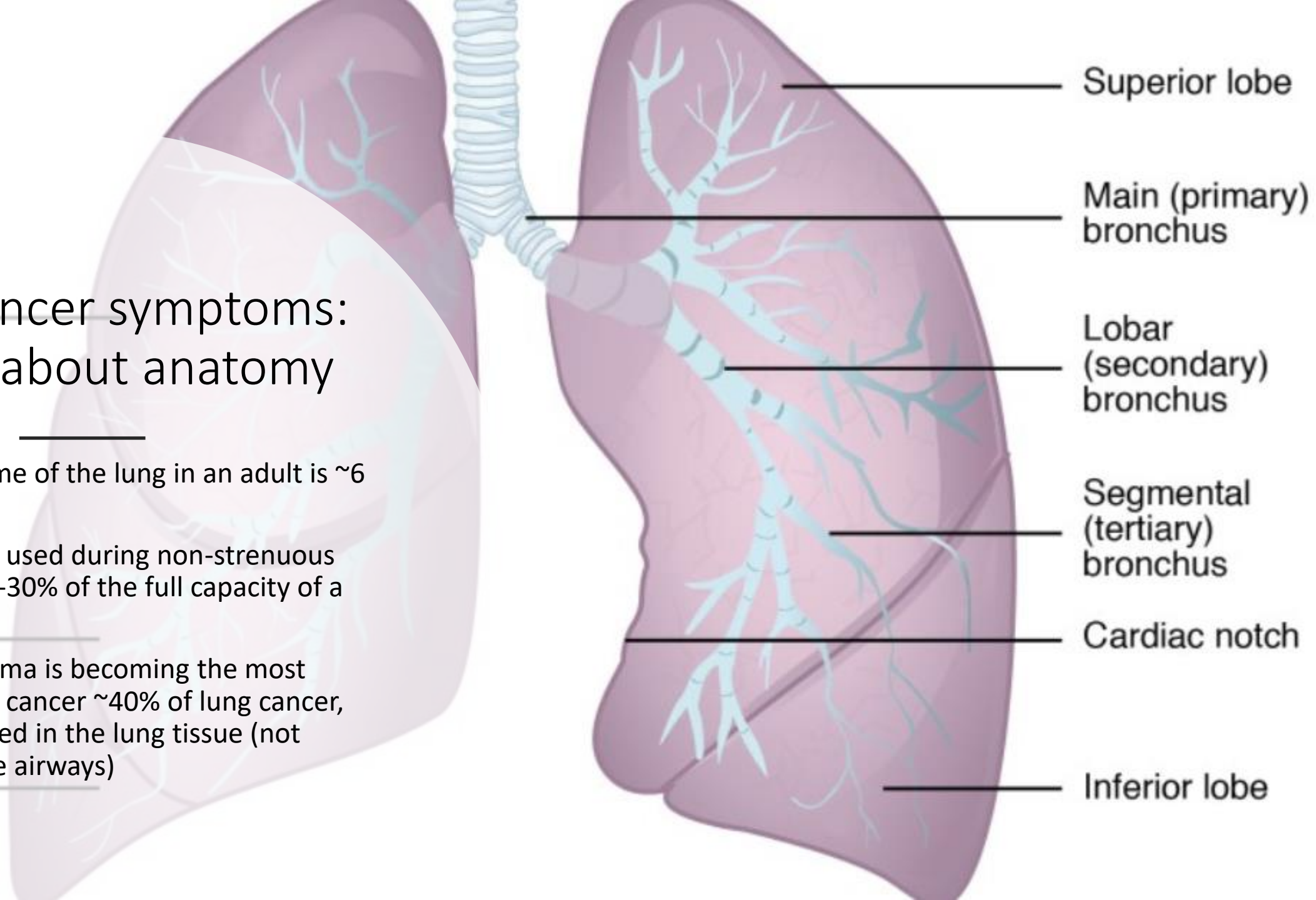


Canadian Cancer Society's Advisory Committee on Cancer Statistics. *Canadian Cancer Statistics 2017*. Toronto, ON: Canadian Cancer Society; 2017.



# Lung cancer symptoms: A little about anatomy

- Average volume of the lung in an adult is ~6 litres
- Lung function used during non-strenuous activity is ~20-30% of the full capacity of a health adult
- Adenocarcinoma is becoming the most common lung cancer ~40% of lung cancer, typically located in the lung tissue (not involving large airways)



# Lung cancer symptoms and signs: Local versus systemic

LOCAL (from lung)	
Symptoms and Signs	Frequency (%)
Cough	8-75
Dyspnea	3-60
Chest pain	20-49
Hemoptysis	6-35
SVC obstruction	0-4
Dysphagia	0-2
Wheezing and stridor	0-2

SYSTEMIC (potentially high stage)	
Symptoms and Signs	Frequency (%)
Weight loss	0-68
Bone pain	6-25
Clubbing	0-20
Fever	0-20
Weakness	0-10

# Lung cancer screening: Chest x-ray (CXR)

## Four large randomized controlled trials in the 1970s-1980s<sup>1-4</sup>

- No significant mortality benefit from CXR screening\*
- Significant difference in 5-year survival of early-stage detected cancers between surgical resection and those who did not<sup>5</sup>

## Prostate, Lung, Colorectal and Ovarian (PLCO) started in 1993<sup>6</sup>

- 155000 smoker and non-smokers aged 55-74 randomized to annual CXR or no screening
- No overall effect on lung cancer diagnosis, stage, histology or mortality

1. J Natl Cancer Inst 2000;92:1308–16 2. Am Rev Respir Dis 1984;130:549–54. 3. Chest 1984;86:44–53. 4. Cancer 1986;57:2427–37. 5. Chest 1992;101:1013–18 6. JAMA 2011;306:1865–73

# Lung cancer screening: National Lung Screening Trial (NLST) 2011

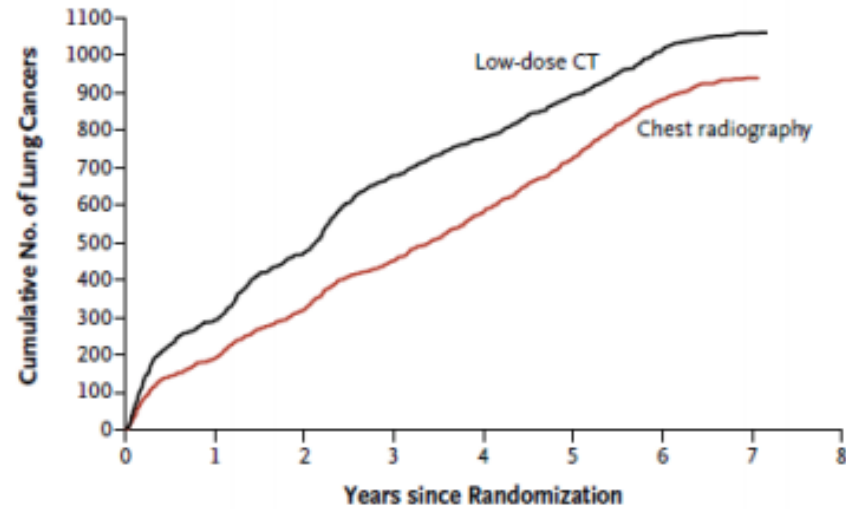
Annual screening by low-dose CT compared to chest radiograph for 3 years

- N = 53,454, 33 US centres and randomized
- Age 55-74, quit smoking within 15 years up to current smoker,  $\geq 30$  PYH

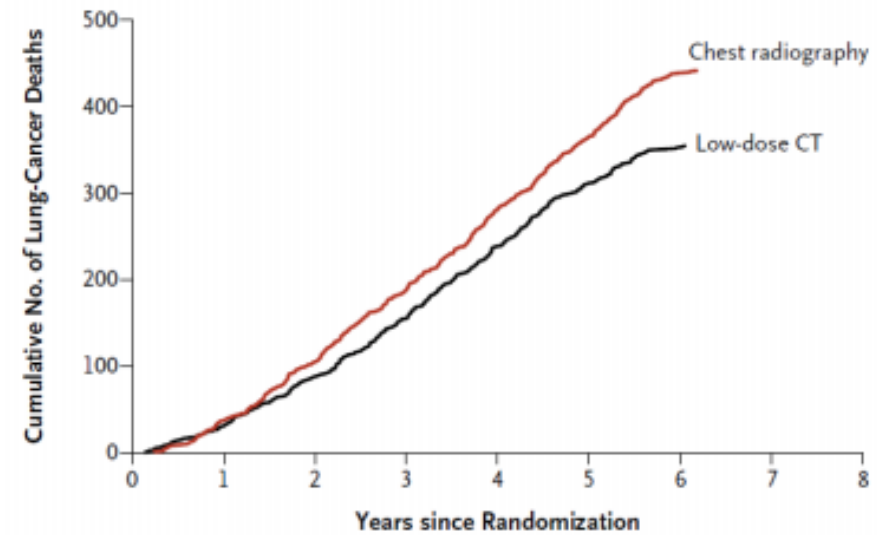
Positive defined as non-calcified nodule  $\geq 4$  mm on LDCT or any non-calcified nodule in CXR

Suggestion for further evaluation was made by the reporting Radiologist

**A Lung Cancer**



**B Death from Lung Cancer**



N Engl J Med 2011;365:395–409.

Lung cancer screening:  
National Lung Screening Trial  
(NLST) 2011

- 20% relative reduction in lung cancer mortality
- 6.7% relative reduction in all-cause mortality
- 79 less mortality in study arm

# Lung cancer screening: National Lung Screening Trial (NLST) 2011

- False-positive 96.4%
  - 90% of the false-positive had additional investigation (mostly imaging)
  - 2.6% had invasive investigation; low complication rate
- Majority of the NLST participants were younger, white, well educated, and affluent



# Recommendation by Canadian Task Force on Preventive Health Care (CTFPHC) for lung cancer screening

- Low-dose CT once each year for 3 years in adults
  - 50-74 years of age
  - Current smokers or former smokers who quit in the last 15 years
  - Smoked 30 pack years
- Any screening program should include smoking cessation program.
- No provincial or territorial screening programs for lung cancer in Canada

Lung cancer  
screening:  
Detection of  
lung cancer  
through low-  
dose  
screening  
(NELSON)

- LDCT versus no screening, 50-75 years, N=15822
- $\geq 15$  cigarette for 25 years or  $\geq 10$  cigarette for 30 years
- Screen group received LDCT at years 1, 2, 4 and 6.5
- **Volumetric** software used to determine baseline nodule volume and doubling time

Lung cancer screening:  
Detection of lung cancer through low-dose screening (NELSON)

Screen arm

- 65% to 70% were stages IA to II

Control arm

- 70% were stage III/IV at diagnosis

CT scanning decreased mortality by 26% in high-risk men and 39% in high-risk women over a 10-year period, 57 less mortality

# Lung cancer screening: The cost of screening

## Health

- Data extrapolated from atomic bomb survivors
- Long term screening by low dose CT may cause 0.05% - 1.8% increase in the development of major cancers<sup>1,2</sup>

## Economic (High risk patients)

- US study: estimates \$81,000 (US dollars) quality adjusted life-year (QALY)<sup>1</sup>
- Canadian study: estimates \$74,000 (CaD dollars) quality adjusted life year<sup>2</sup>

1. *BMJ* 2017;356:j347

2. *Radiology*. 2004 May;231(2):440-5.

1. *N Engl J Med* 2014;371:1793-802.

2. *JAMA Oncol*. 2015;1(6):807-813

	<b>Breast cancer screening with mammograph</b>	<b>Colorectal cancer screening with faecal occult blood test</b>	<b>Lung cancer screening with low-dose CT</b>
Population target and screening type	All women in an age range	All population in an age range	Selective screening: smokers or former smoker fulfilling a number of pack year
Screen interval	Biennial	Annual	Unknown
Cancer risk due to repeated screening tests	Very low	No risk	Moderate
Confirmation of disease after a positive test	Within days by echographic biopsy	Within days by colonoscopy	Dependent on the size of the nodule
Understanding of disease risk factor	Limited	Moderate	Well established: cigarette smoking
Cost of screening test and screening technology	Low to moderate	Low	Moderate to high

# Take home message on lung cancer

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Common cancer with known risk factors    Prevention is the key



Early stage lung cancer can be asymptomatic



Prognosis is heavily affected by stage    More patients are diagnosed at a high stage



Evidence for screening is emerging