The Second Most Common Cause of Lung Cancer: Radon

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Disclosures

None

Objectives

Understand what radon is and how it is harmful to the body

Review literature and guidelines regarding radon and its link to lung cancer

Apply this knowledge while discussing lung cancer risk factors with your patients

2024 Lung Cancer Statistics

American Cancer Society's Estimates for Lung Cancer in the US for 2024

About 234,580 new cases of lung cancer (116,310 in men and 118,270 in women

About 125,070 deaths from lung cancer (65,790 in men and 59,280 in women)

Lung cancer is the second most common cancer in both men and women in the United States (not counting skin cancers)

Lung cancer is the leading cause of cancer death in the US, accounting for about 1 in 5 of all cancer deaths

https://www.cancer.org/cancer/types/lung-cancer/about/key-statistics.html

5-year relative survival rates for non-small cell lung cancer

These numbers are based on people diagnosed with NSCLC between 2012 and 2018.

SEER stage	5-year relative survival rate
Localized	65%
Regional	37%
Distant	9%
All SEER stages combined	28%

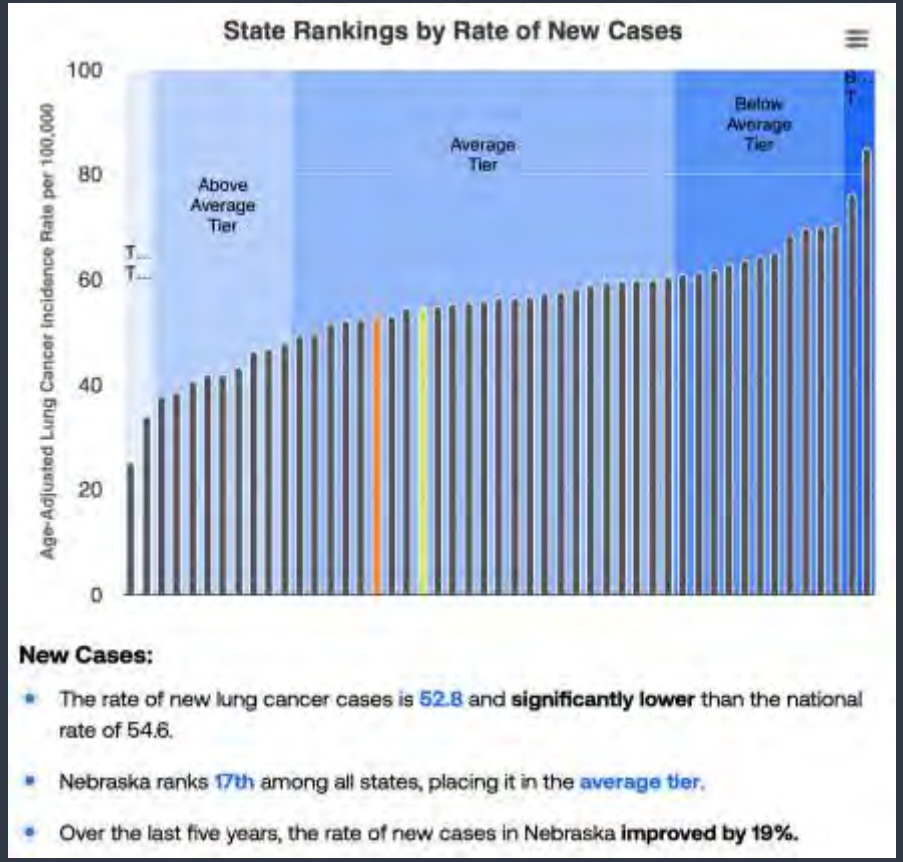
5-year relative survival rates for small cell lung cancer

These numbers are based on people diagnosed with SCLC between 2012 and 2018.

SEER stage	5-year relative survival rate
Localized	30%
Regional	18%
Distant	3%
All SEER stages combined	7%

https://www.cancer.org/cancer/types/lung-cancer/detection-diagnosis-staging/survival-rates.html

Nebraska Lung Cancer Stats

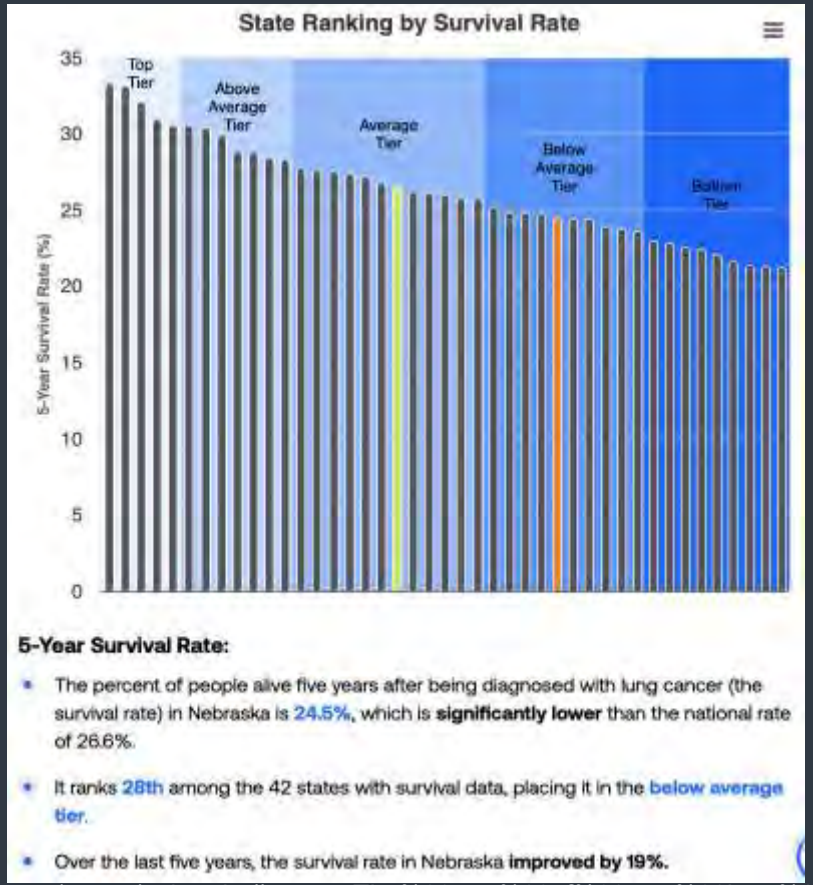


New Cases:

- The rate of new lung cancer cases is 52.8 and **significantly lower** than the national rate of 54.6.
- Nebraska ranks 17th among all states, placing it in the average tier.
- Over the last five years, the rate of new cases in Nebraska **improved by 19%.**

https://www.lung.org/research/state-of-lung-cancer/states/nebraska#:~:text=The%20rate%20of%20new%20lung%20cancer%20cases%20is%2067.6%20per,amo

Nebraska Lung Cancer Stats



5-Year Survival Rate:

- The percent of people alive five years after being diagnosed with lung cancer (the survival rate) in Nebraska is **24.5%**, which is **significantly lower** than the national rate of 26.6%.
- It ranks **28th** among the 42 states with survival data, placing it in the **below average tier**.
- Over the last five years, the survival rate in Nebraska **improved by 19%.**

https://www.lung.org/research/state-of-lung-cancer/states/nebraska#:~:text=The%20rate%20of%20new%20lung%20cancer%20cases%20is%2067.6%20per,amon

Smokers vs Non-smokers

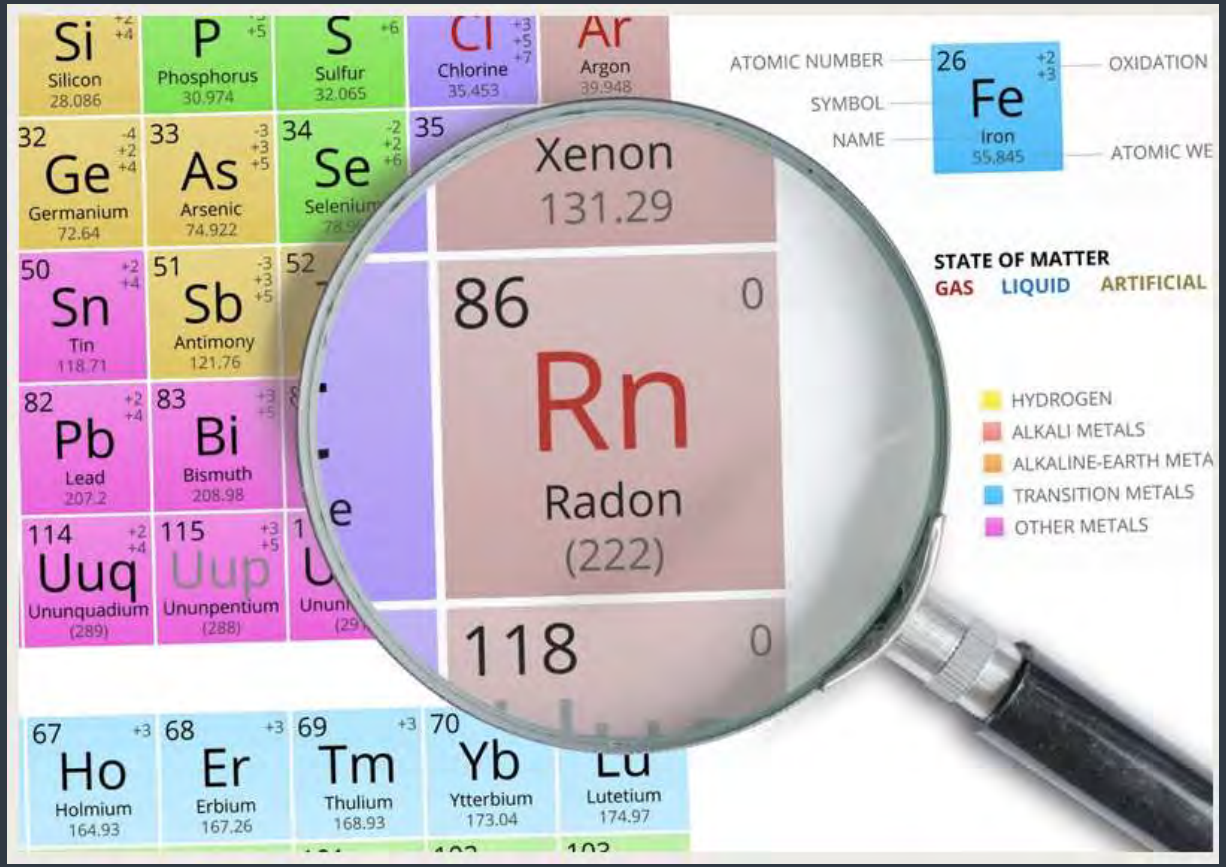
Percent of lung cancers

Smokers 80-90%

Never smokers (smoked less than 100 cigarettes lifetime) 10-20%

Tend to have more adenocarcinomas

Radon



https://health.wyo.gov/is-radon-a-concern-for-your-home/

Radon

Radioactive gas that forms naturally when uranium, thorium, or radium, which are radioactive metals break down in rocks, soil and groundwater

People can be exposed to radon primarily from breathing radon in air that comes through cracks and gaps in buildings and homes

Radon is linked to the formation of lung cancer and possibly some forms of leukemia

https://www.epa.gov/radon/what-radon

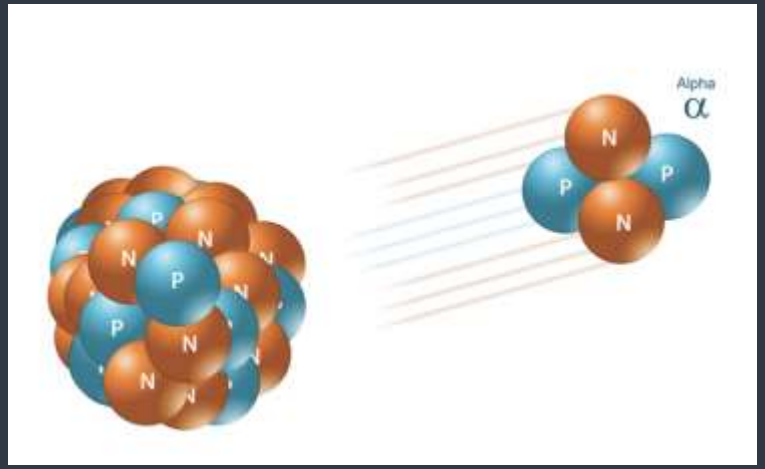
IAEA
International Atomic Energy Agency

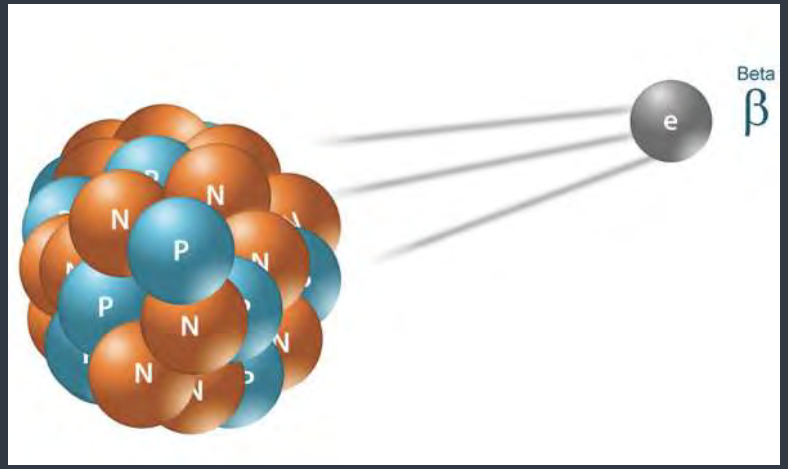
https://www.iaea.org/newscenter/news/what-is-radon-and-how-are-we-exposed-to-it

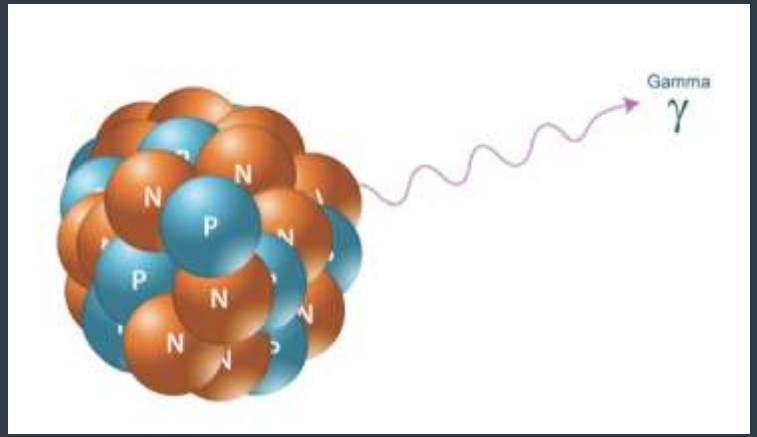
Radioactive Decay

Unstable atoms (too much energy or mass)
Turn into more stable forms by giving off some of the energy or mass

Alpha radiation
  Giving off 2 protons and 2 neutrons
  Cannot penetrate intact skin, can be stopped by a piece of paper
Beta radiation
  Giving off either an electron or positron
  Can penetrate the skin a few centimeters, can be stopped by a thin piece of metal
Gamma radiation
  Giving off no particles, rather gives off a photon of energy
  Can travel far and penetrate deeply into most matter, can be stopped by thick or dense materials like lead

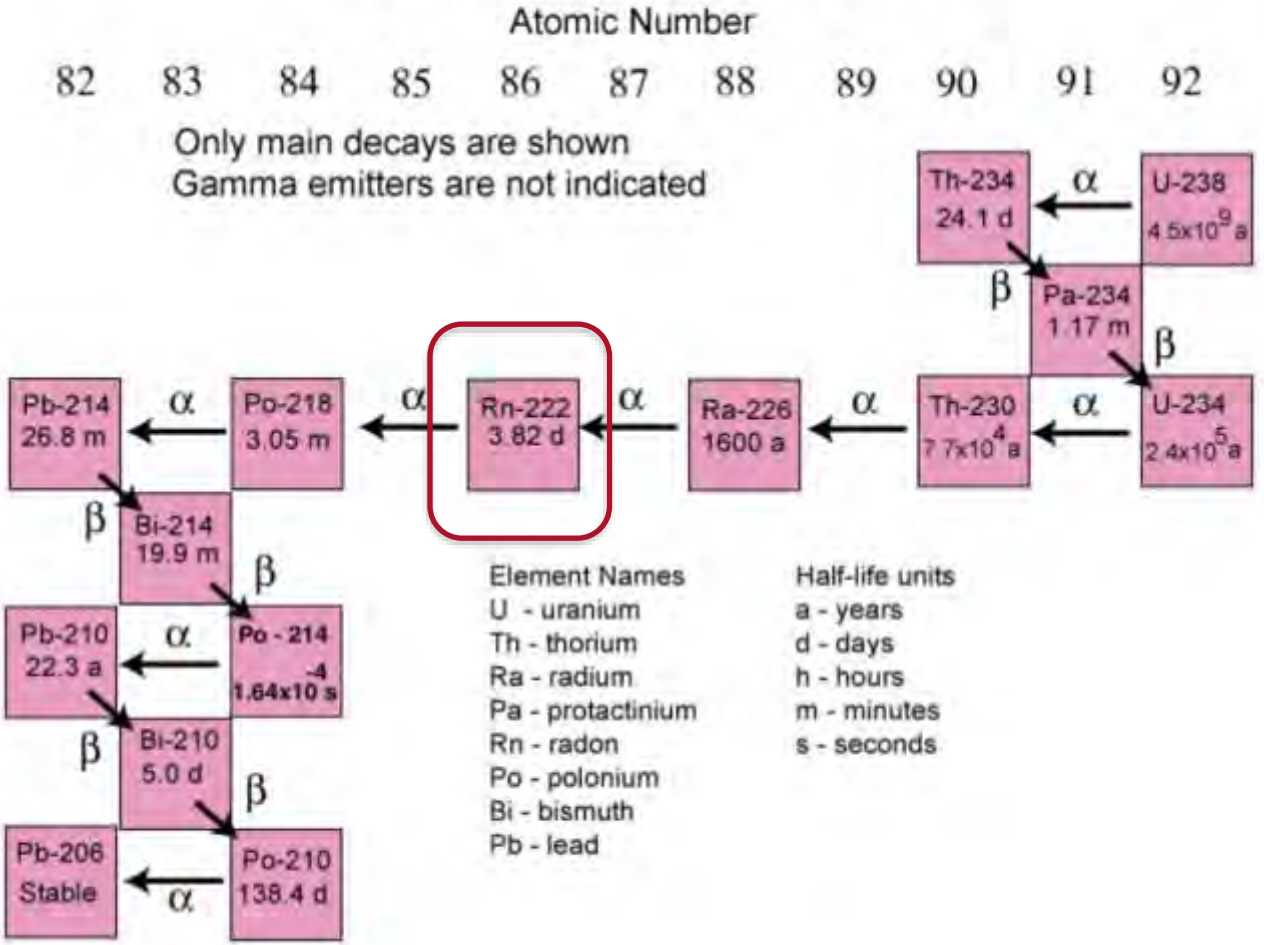






https://www.mirion.com/discover/knowledge-hub/articles/education/types-of-ionizing-radiation

The Uranium-238 Decay Chain



Radon

Radon 222 is the most stable of the three isotopes of radon

Half life 3.8 days

The other two isotopes are Rn 219 (action) and Rn 220 (thoron)

Half lives of 4 sec and 56 sec respectively

Odorless and invisible

Testing is the only way to know of exposure

More Statistics

Environmental protection agency

Estimates

Radon is responsible for 21,000 lung cancer deaths per year

Only about 2900 of them are in patients who had never smoked

Risk Factors for Lung Cancer

National Comprehensive Cancer Network®

NCCN Guidelines Version 11.2024
Non-Small Cell Lung Cancer

NCCN Guidelines Index
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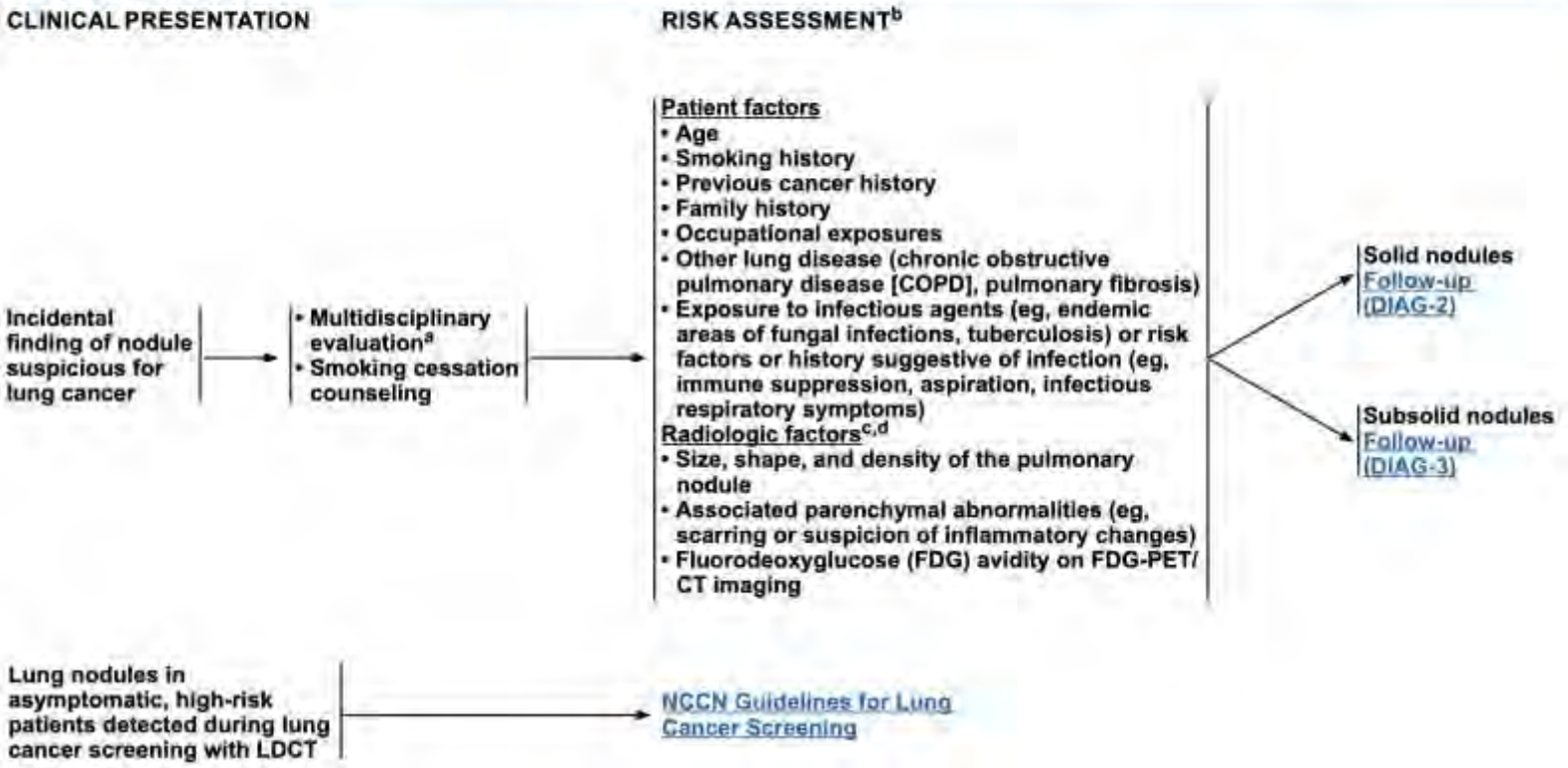
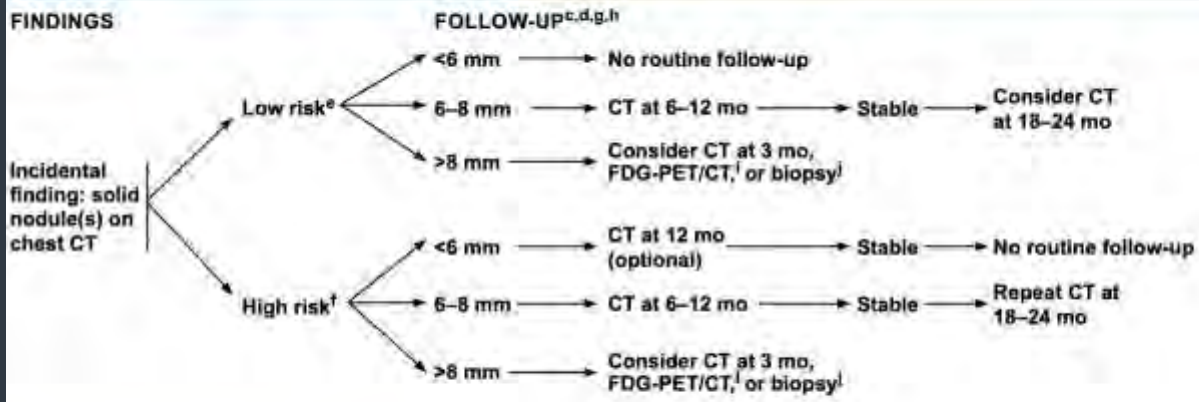
Discussion





[c] Principles of Diagnostic Evaluation (DIAG-A 1 of 3).
[d] The most important radiologic factor is change or stability compared with a previous imaging study.
[e] Low risk = minimal or absent history of smoking or other known risk factors.
[f] High risk = history of smoking or other known risk factors. Known risk factors include history of lung cancer in a first-degree relative or exposure to asbestos, radon, or uranium.
[g] Non-solid (ground-glass) nodules may require longer follow-up to exclude indolent adenocarcinoma.
[h] Adapted from Fleischner Society Guidelines: MacMahon H, Naidich DP, Goo JM, et al. Guidelines for management of incidental pulmonary nodules detected on CT images: From the Fleischner Society 2017. Radiology 2017;284:228-243. ®Radiological Society of North America. Fleischner Society Guidelines do not direct whether or not contrast is necessary or if an LDCT is appropriate. LDCT is preferred unless there is a reason for contrast enhancement for better diagnostic resolution.
[i] FDG-PET/CT performed skull base to mid-thigh. A positive FDG-PET/CT result is defined as a standardized uptake value (SUV) in the lung nodule greater than the baseline mediastinal blood pool. A false-positive FDG-PET/CT scan finding can be caused by infection or inflammation, including absence of lung cancer with localized infection, presence of lung cancer with associated (eg, postobstructive) infection, and presence of lung cancer with related inflammation (eg, nodal, parenchymal, pleural). A false-negative FDG-PET/CT scan can be caused by a small nodule, low cellular density (nonsolid nodule or ground-glass opacity [GGO]), or low tumor avidity for FDG (eg, adenocarcinoma in situ [AIS; previously known as bronchoalveolar carcinoma], carcinoid tumor). If a false-negative FDG-PET/CT is due to low tumor avidity and/or low cellularity is suspected, follow-up CT or biopsy are reasonable options.
[j] Prior to treatment, multidisciplinary evaluation that includes treating physicians and specialists in obtaining tissue diagnosis (thoracic surgery, interventional pulmonology, and interventional radiology) is required to determine the safest and most efficient approach for biopsy, or to provide consensus that a biopsy is too risky or difficult, that a clinical diagnosis of lung cancer is appropriate, and that treatment is warranted.

Note: All recommendations are category 2A unless otherwise indicated.

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2025
Lung Cancer Screening

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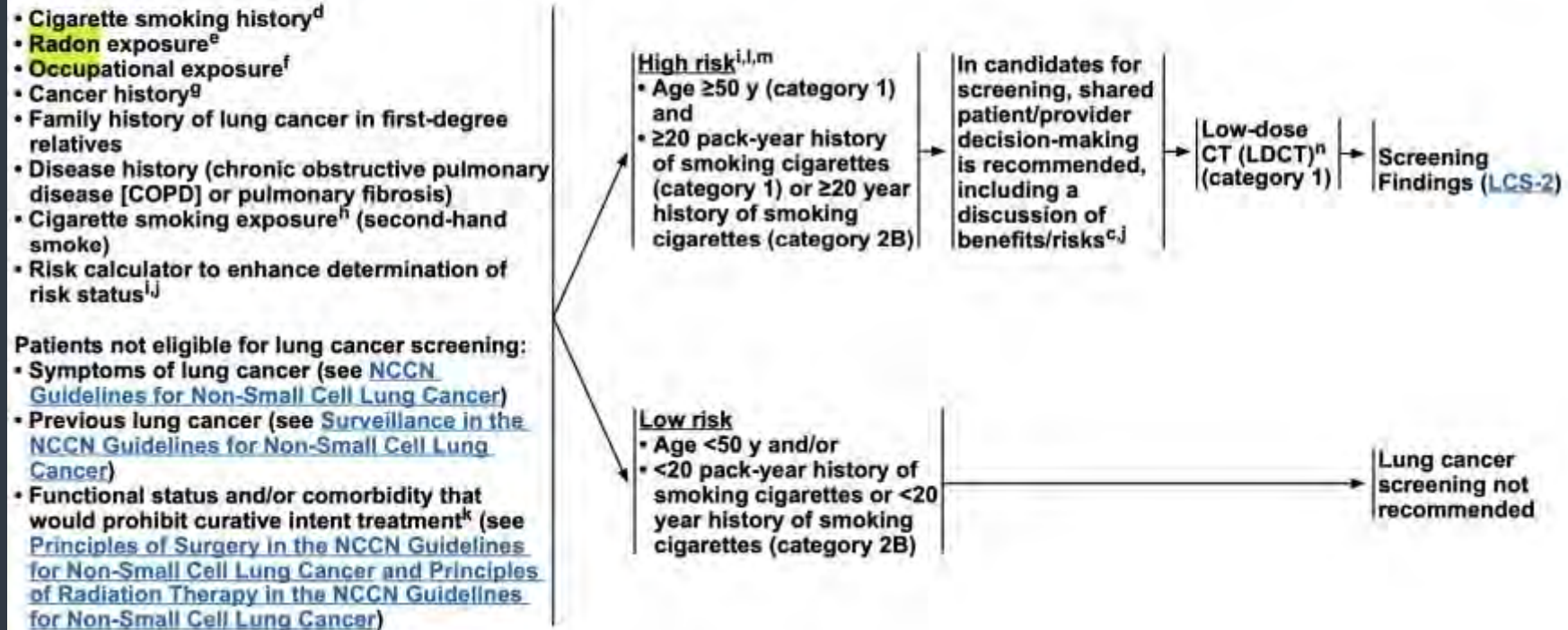
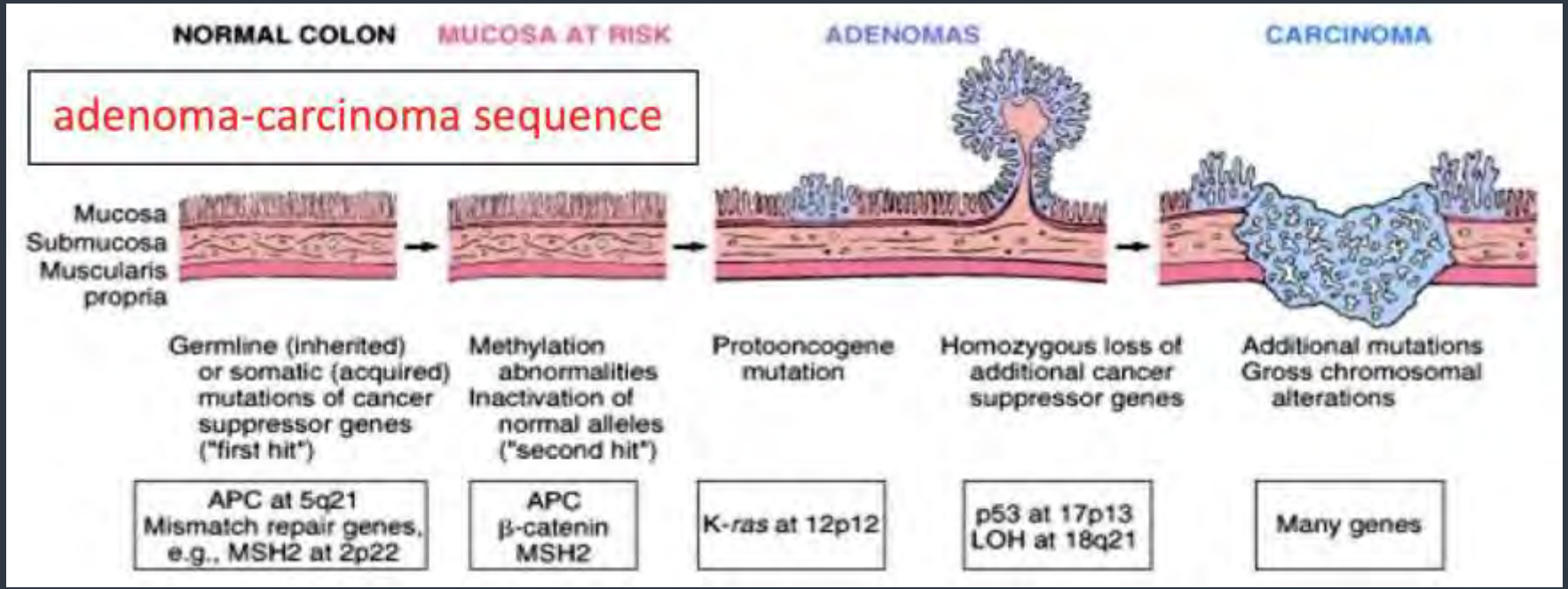


Carcinogenicity


NORMAL COLON
MUCOSA AT RISK
ADENOMAS
CARCINOMA
adenoma-carcinoma sequence
Mucosa
Submucosa
Muscularis propria
Germline (inherited) or somatic (acquired) mutations of cancer suppressor genes ("first hit")
Methylation abnormalities Inactivation of normal alleles ("second hit")
Protooncogene mutation
Homozygous loss of additional cancer suppressor genes
Additional mutations Gross chromosomal alterations
APC at 5q21 Mismatch repair genes, e.g., MSH2 at 2p22
APC β-catenin MSH2
K-ras at 12p12
p53 at 17p13 LOH at 18q21
Many genes

Lung carcinogenesis by tobacco smoke

Stephen S. Hecht

Masonic Cancer Center, University of Minnesota, Minneapolis, MN

Int. J. Cancer: **131,** 2724–2732 (2012) © 2012 UICC

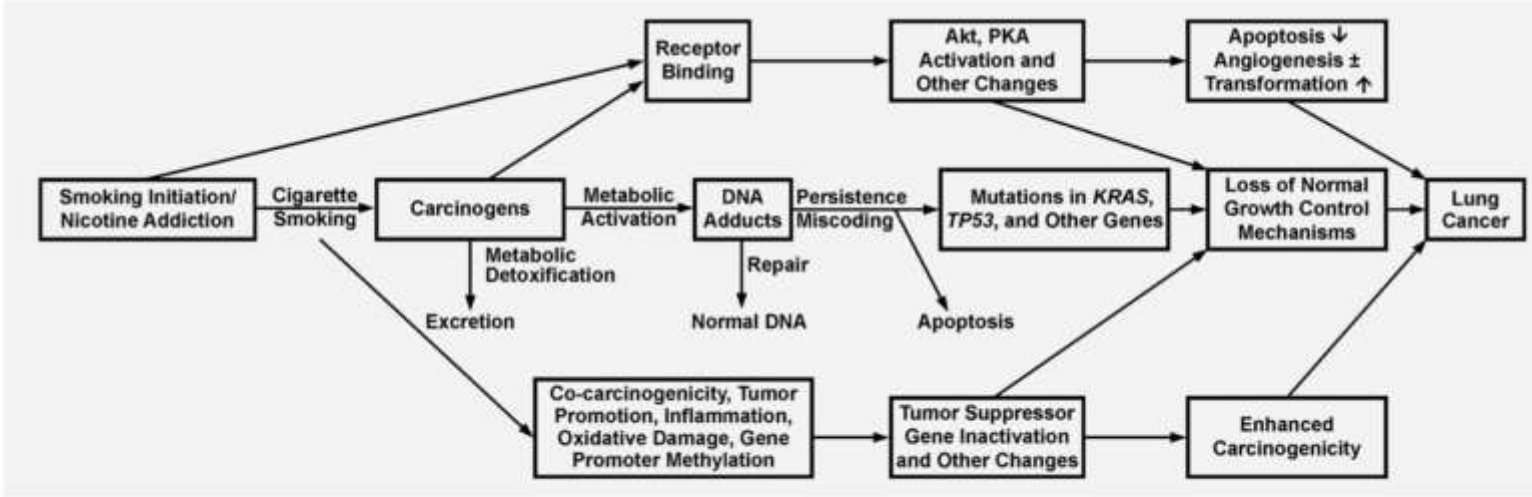
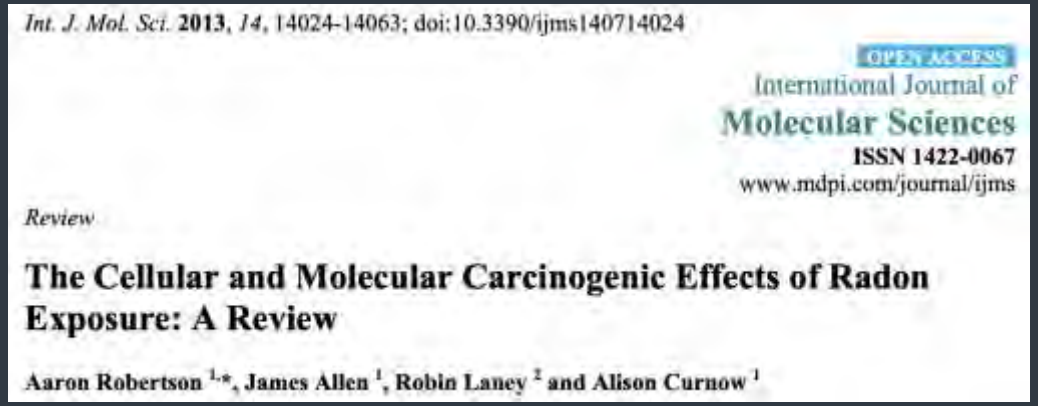


Figure 1. Mechanistic framework for understanding how cigarette smoking causes lung cancer. All events can occur chronically since a smoker typically uses multiple cigarettes per day for many years.



Int. J. Mol. Sci. **2013**, *14*, 14024-14063; doi:10.3390/ijms140714024

OPEN ACCESS

International Journal of

Molecular Sciences

ISSN 1422-0067

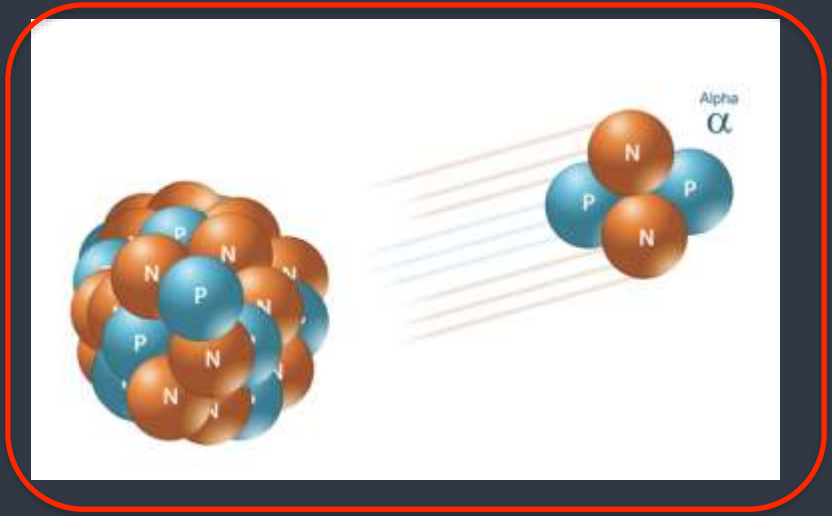
www.mdpi.com/journal/ijms

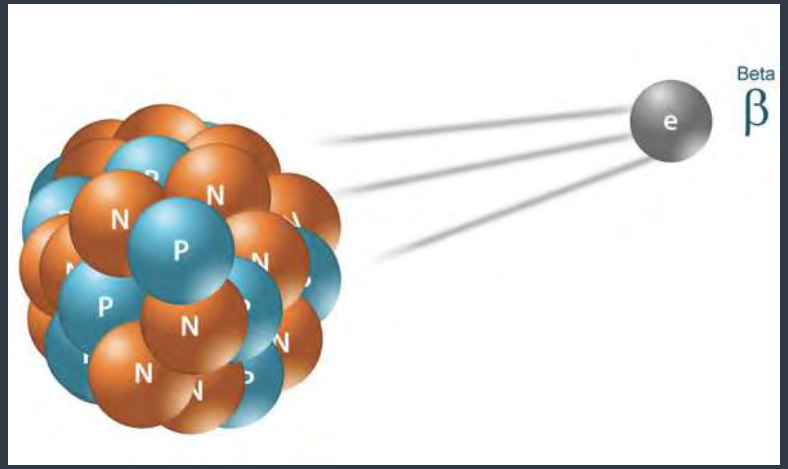
Review

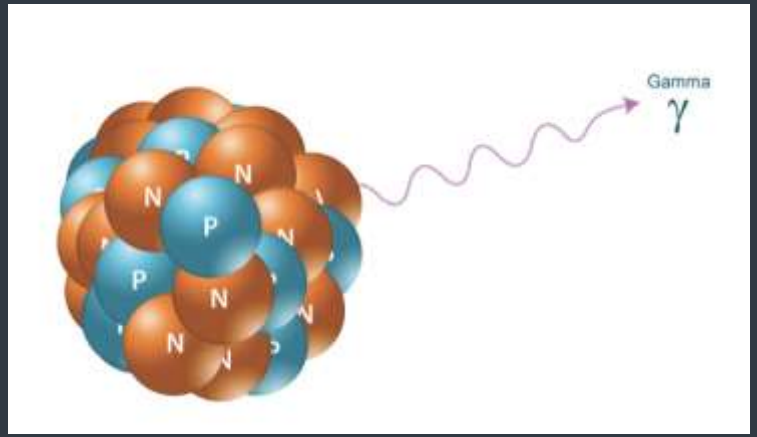
The Cellular and Molecular Carcinogenic Effects of Radon Exposure: A Review

Aaron Robertson [1,*], James Allen [1], Robin Laney [2] and Alison Curnow [1]

“Ionizing radiation in the form of alpha particles can cause DNA damage in the form of chromosomal aberrations, double strand DNA breaks, and generate reactive oxygen species resulting in cell cycle shortening, apoptosis, and an increased potential for carcinogenesis.”







https://www.mirion.com/discover/knowledge-hub/articles/education/types-of-ionizing-radiation

Alpha particle

α - helium nucleus

Does not penetrate deeply into tissue but has a high linear energy transfer

This actually makes it more biologically significant than beta or gamma radiation

Reacts more readily with DNA and generates oxidative stress

Radon progeny

Polonium 218 - 47 micrometers

Polonium 214 - 70 micrometers

Thickness of bronchial epithelium: 13 micrometers

The Uranium-238 Decay Chain

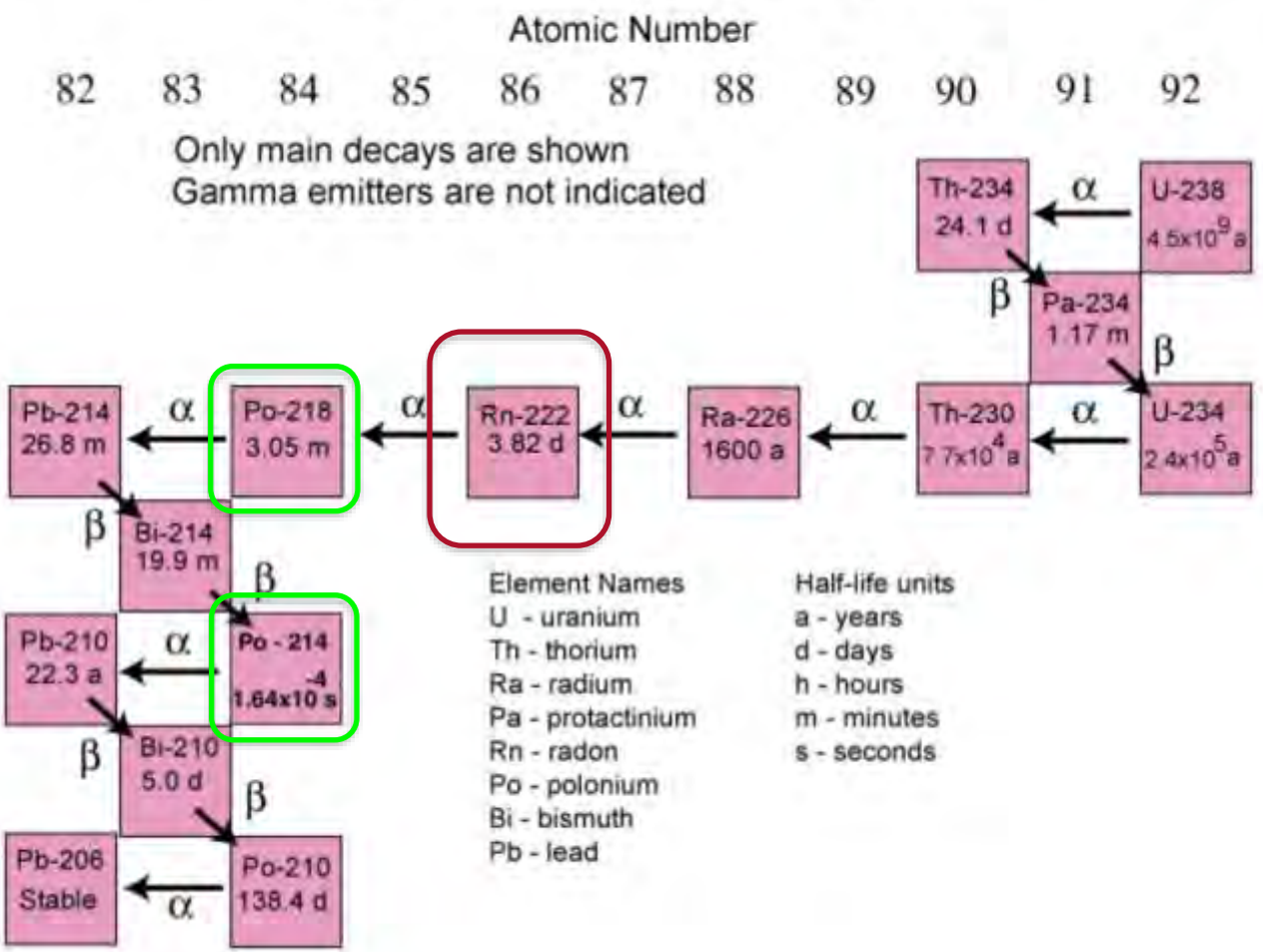


Table 2. Estimated lifetime risk of lung cancer death by radon level for never smokers, current smokers and the general population assuming lifetime exposure (adapted from United States Environmental Protection Agency [55]).

Radon level Bq/m^3	Lifetime risk of lung cancer death from radon exposure in homes (%)		
	Never smokers	Current smokers	General population
740	3.6	26.3	10.5
370	1.8	15	5.6
296	1.5	12	4.5
148	0.7	6.2	2.3
74	0.4	3.2	1.2
46.25	0.2	2	0.7
14.8	0.1	0.6	0.2

Radon Carcinogenicity

Research for specific gene mutations

- TP53 (p53)
  - Chromosome 17p13.1
  - p53 protein integral in the maintenance of the cell cycle
- HPRT
  - X linked hypoxanthine phosphoribosyl transferase
  - Plays a key role in purine salvage pathway

Radon in Uranium Miners

Uranium Mines

Production from mines (tonnes U)

Country	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Kazakhstan	22,451	23,127	23,607	24,689	23,321	21,705	22,808	19,477	21,819	21,227
Canada	9331	9124	13,325	14,039	13,116	7001	6938	3885	4693	7351
Namibia	4323	3255	2993	3654	4224	5525	5476	5413	5753	5613
Australia	6350	5001	5654	6315	5882	6517	6613	6203	4192	4553
Uzbekistan (est.)	2400	2400	2385	3325	3400	3450	3500	3500	3520	3300
Russia	3135	2990	3055	3004	2917	2904	2911	2846	2635	2508
Niger	4518	4057	4116	3479	3449	2911	2983	2991	2248	2020
China (est.)	1500	1500	1616	1616	1692	1885	1885	1885	1600	1700
India (est.)	385	285	385	385	421	423	308	400	600	600
South Africa (est.)	531	573	393	490	308	346	346	250	192	200
Ukraine	922	926	1200	808	707	790	800	744	455	100
USA	1792	1919	1256	1125	940	582	58	6	8	75
Pakistan (est.)	45	45	45	45	45	45	45	45	45	45
Brazil	192	55	40	44	0	0	0	15	29	43
Iran (est.)	0	0	38	0	40	71	71	71	21	20
Czech Republic	215	193	155	138	0	0	0	0	0	0

https://world-nuclear.org/information-library/nuclear-fuel-cycle/mining-of-uranium/world-uranium-mining-production

Uranium

Used for

- Fueling nuclear reactors to produce electricity
- Weapons
- In Medicine
  - Harvesting isotopes for cancer therapy
  - Using depleted uranium as shielding as it is more dense than lead

Published in final edited form as:
Am J Ind Med. 2020 October ; 63(10): 859–867. doi:10.1002/ajim.23167.

Radon and cancer mortality among underground uranium miners in the Příbram region of the Czech Republic

Kaitlin Kelly-Reif, PhD[1], Dale P. Sandler, PhD[2], David Shore, PhD[2], Mary K. Schubauer-Berigan, PhD[3], Melissa A. Troester, PhD[1], Leena Nylander-French, PhD[4], David B. Richardson, PhD[1]

Pribram uranium mine operated between 1946 and 1991

46,000 workers making over 98,500 metric tons of uranium

In the 1960s, over 70% of the world's uranium production was from this mine

Study data was based on digitalized work records

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16,434 men met inclusion criteria

During 16 years of follow up, 4,207 (25.6%) of workers died. For those with a listed cause of death 3770 (89.6%)

705 lung cancer deaths were found which is 18.7 percent of those with a listed cause of death

Also of note 102 stomach cancer deaths, 59 extra thoracic cancer deaths, and 58 hematopoietic cancer deaths

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The researchers claim an identification of a strong association between radon and lung cancer mortality

Also, suggested associations between radon and cancer mortality other than lung

The numbers were confounded by things such as diesel fumes

Residential Radon Exposure

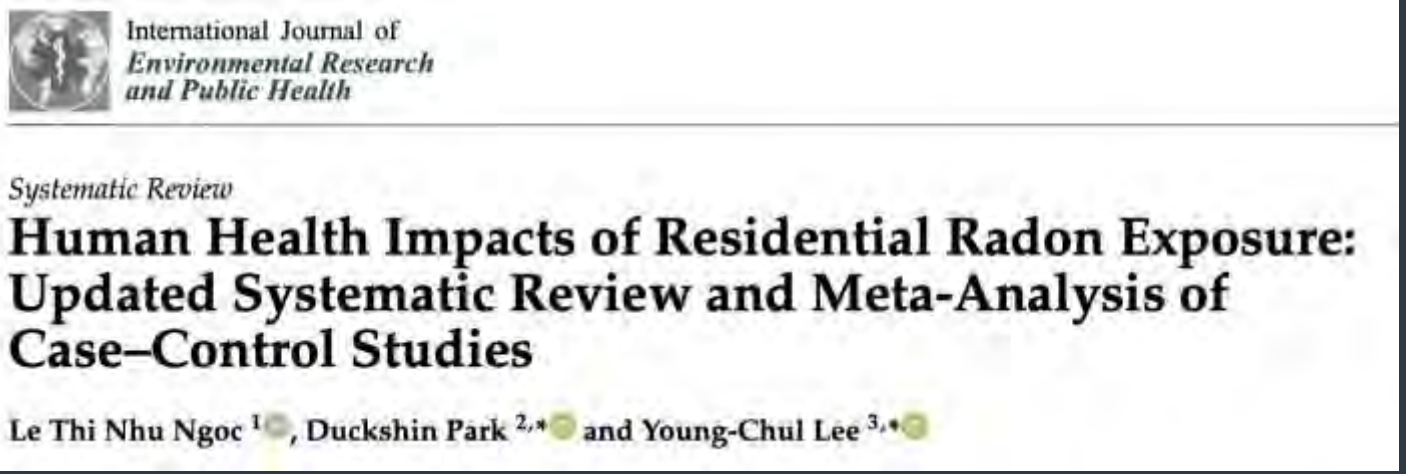
“Residential Radon Exposure” in NCCN Lung Cancer Screening Guidelines

Radon has been implicated in the development of lung cancer/ however, the individual risk associated with residential radon is uncertain

Challenges in using radon exposures as an indication for lung cancer screening include difficulty in measuring individual exposure, and lack of clinical trials

IAEA
International Atomic Energy Agency

https://www.iaea.org/newscenter/news/what-is-radon-and-how-are-we-exposed-to-it



Review out of Korea in 2023

42 Case controlled studies reported the incidence of lung cancer

Int. J. Environ. Res. Public Health **2023**, *20*, 97. https://doi.org/10.3390/ijerph20010097

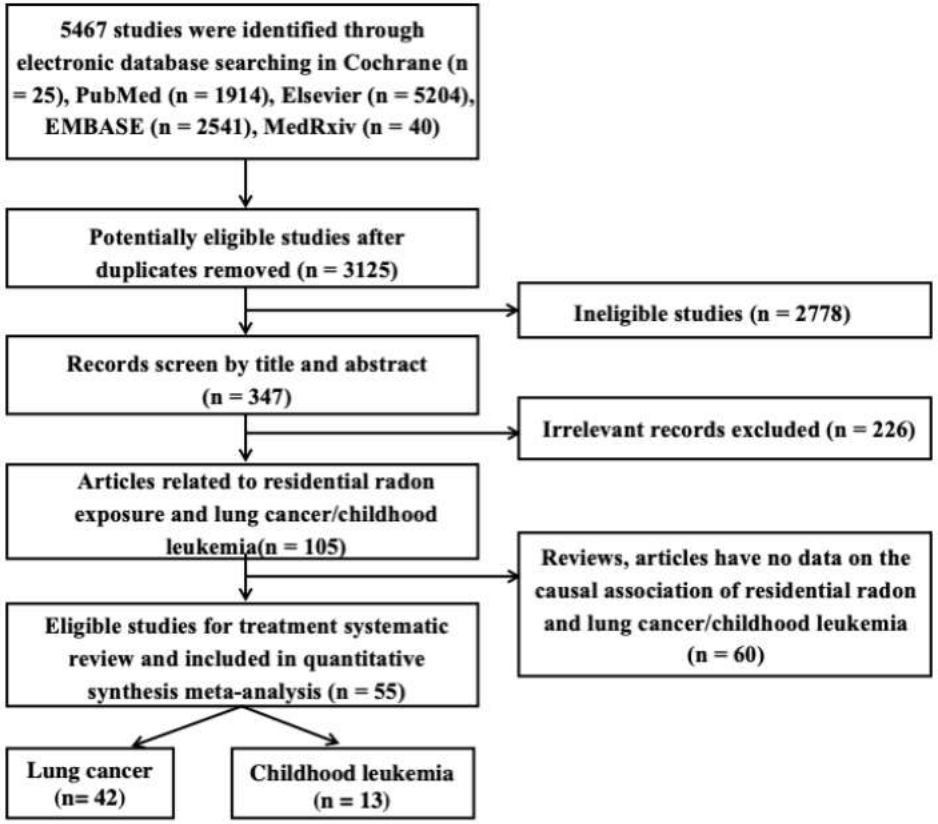
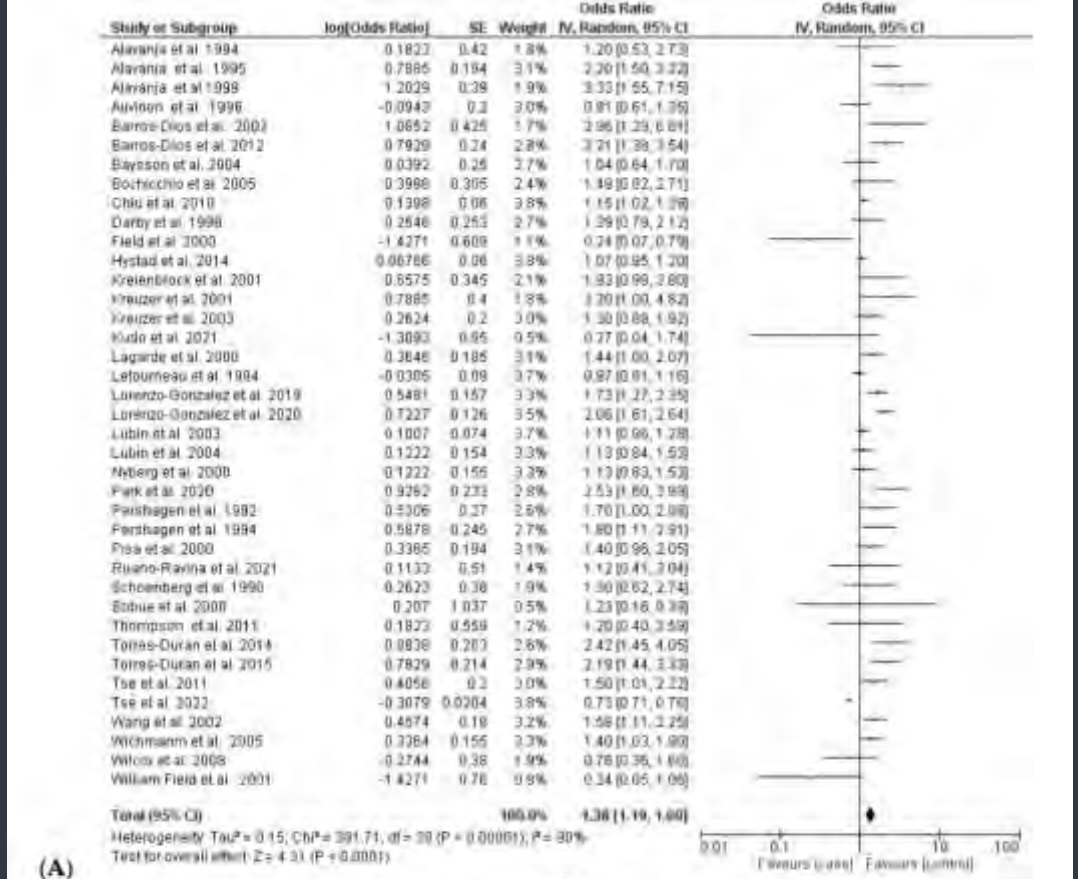


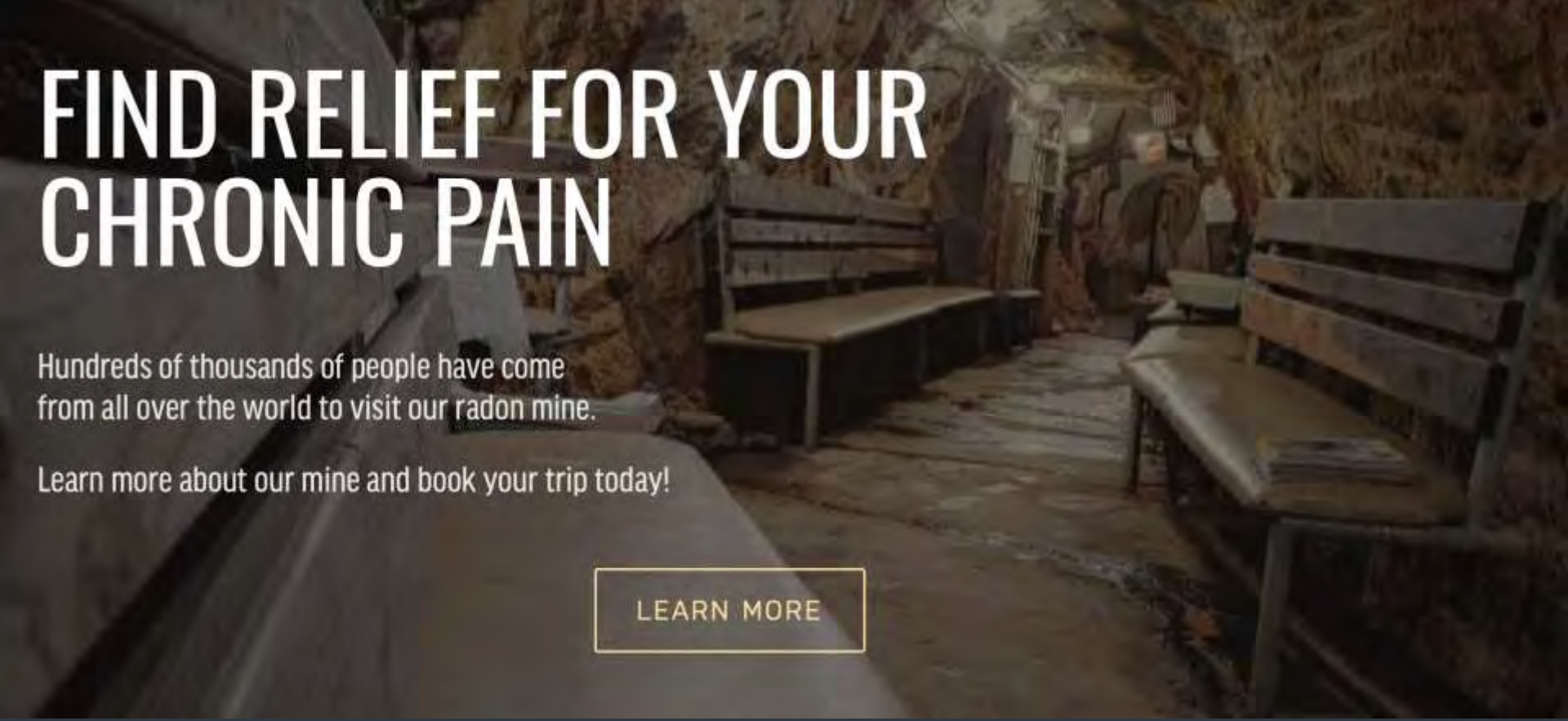
Figure 1. Systematic screening stages of literature review.


Odds Ratio
Odds Ratio
Study or Subgroup log[Odds Ratio] SE Weight IV, Random, 95% CI
IV, Random, 95% CI
Alavanja et al. 1994 0.1823 0.42 1.8% 1.20 [0.53, 2.73]
Alavanja et al. 1995 0.7885 0.184 3.1% 2.20 [1.50, 3.22]
Alavanja et al 1999 1.2029 0.39 1.9% 3.33 [1.55, 7.15]
Auvinen et al. 1996 -0.0943 0.2 3.0% 0.91 [0.61, 1.35]
Barros-Dios et al. 2002 1.0652 0.425 1.7% 2.90 [1.29, 6.81]
Barros-Dios et al. 2012 0.7929 0.24 2.8% 2.21 [1.39, 3.54]
Baysson et al. 2004 0.0392 0.25 2.7% 1.04 [0.64, 1.70]
Bocchicchio et al. 2005 0.3988 0.305 2.4% 1.49 [0.82, 2.71]
Chiu et al. 2010 0.1398 0.06 3.8% 1.15 [1.02, 1.29]
Darby et al. 1998 0.2546 0.253 2.7% 1.29 [0.79, 2.12]
Field et al. 2000 -1.4271 0.609 1.1% 0.24 [0.07, 0.79]
Hystad et al. 2014 0.06786 0.06 3.8% 1.07 [0.95, 1.20]
Kreienbrock et al. 2001 0.6575 0.345 2.1% 1.93 [0.99, 3.80]
Kreuzer et al. 2001 0.7885 0.4 1.8% 2.20 [1.00, 4.82]
Kreuzer et al. 2003 0.2624 0.2 3.0% 1.30 [0.88, 1.92]
Kudo et al. 2021 -1.3893 0.95 0.5% 0.27 [0.04, 1.74]
Lagarde et al. 2000 0.3646 0.185 3.1% 1.44 [1.00, 2.07]
Letourneau et al. 1994 -0.0305 0.09 3.7% 0.97 [0.81, 1.16]
Lorenzo-Gonzalez et al. 2019 0.5481 0.157 3.3% 1.73 [1.27, 2.35]
Lorenzo-Gonzalez et al. 2020 0.7227 0.126 3.5% 2.06 [1.61, 2.64]
Lubin et al. 2003 0.1007 0.074 3.7% 1.11 [0.96, 1.28]
Lubin et al. 2004 0.1222 0.154 3.3% 1.13 [0.84, 1.53]
Nyberg et al. 2000 0.1222 0.155 3.3% 1.13 [0.83, 1.53]
Park et al. 2020 0.9262 0.233 2.8% 2.53 [1.60, 3.99]
Pershagen et al. 1992 0.5306 0.27 2.6% 1.70 [1.00, 2.88]
Pershagen et al. 1994 0.5878 0.246 2.7% 1.80 [1.11, 2.91]
Pisa et al. 2000 0.3365 0.194 3.1% 1.40 [0.96, 2.05]
Ruano-Ravina et al. 2021 0.1133 0.51 1.4% 1.12 [0.41, 3.04]
Schoenberg et al. 1990 0.2623 0.38 1.9% 1.30 [0.62, 2.74]
Stolue et al. 2000 0.207 1.037 0.5% 1.23 [0.16, 9.39]
Thompson et al. 2011 0.1823 0.559 1.2% 1.20 [0.40, 3.59]
Torres-Durán et al. 2014 0.8838 0.203 2.6% 2.42 [1.45, 4.05]
Torres-Durán et al. 2015 0.7829 0.214 2.9% 2.19 [1.44, 3.33]
Tse et al. 2011 0.4055 0.2 3.0% 1.50 [1.01, 2.22]
Tse et al. 2022 -0.3079 0.0204 3.8% 0.73 [0.71, 0.76]
Wang et al. 2002 0.4574 0.19 3.2% 1.58 [1.11, 2.25]
Wichmann et al. 2005 0.3364 0.155 3.3% 1.40 [1.03, 1.90]
Wilcox et al. 2008 0.2744 0.38 1.9% 0.76 [0.35, 1.60]
William Field et al. 2001 -1.4271 0.76 0.9% 0.24 [0.05, 1.06]
Total (95% CI) 100.0% 1.38 [1.19, 1.60]
Heterogeneity: Tau² = 0.15; Chi² = 391.71, df = 38 (P < 0.00001); I² = 90%
Test for overall effect: Z = 4.31 (P < 0.0001)
0.01 0.1 1 10 100
Favours [cases] Favours [controls]
(A)
Risk Ratio
Risk Ratio
Study or Subgroup log[Risk Ratio] SE Weight IV, Random, 95% CI
IV, Random, 95% CI
Lagarde et al. 2002 0.47 0.37 34.7% 1.60 [0.77, 3.30]
Sandler et al. 2007 -2.0099 0.64 27.5% 0.13 [0.04, 0.47]
Svensson et al. 1988 0.588 0.23 37.8% 1.80 [1.15, 2.83]
Total (95% CI) 100.0% 0.85 [0.26, 2.75]
Heterogeneity: Tau² = 0.91; Chi² = 14.77, df = 2 (P = 0.0006); I² = 86%
Test for overall effect: Z = 0.28 (P = 0.78)
0.01 0.1 1 10 100
Favours [cases] Favours [controls]
(B)

Patient Perception of Radon

Often do not know what radon is or that you are supposed to test for it

Usually will get this mixed up with carbon monoxide detectors



https://merrywidowhealthmine.com/

World Health Organization

WHO response

Indoor radon is a preventable risk factor that can be handled through effective national policies and regulations. The *WHO handbook on indoor radon: A public health perspective (4)* provides policy options for reducing health risks from residential radon exposure through:

- providing information on levels of radon indoors and the associated health risks;
- implementing a national radon programme aimed at reducing both the overall population risk and the individual risk for people living with high radon concentrations;
- establishing a national annual average residential radon concentration reference level of 100 Bq/m^3, but if this level cannot be reached under the prevailing country-specific conditions, the reference level should not exceed 300 Bq/m^3;
- developing radon measurement protocols to help ensure quality and consistency in radon testing;
- implementing radon prevention in building codes to reduce radon levels in buildings under construction, and radon programmes to ensure that the levels are below national reference levels;
- promoting education for building professionals and providing financial support to remove radon from existing buildings; and
- considering the inclusion of radon as a risk factor in national strategies related to cancer control, tobacco control, indoor air quality and energy conservation.

EPA United States Environmental Protection Agency

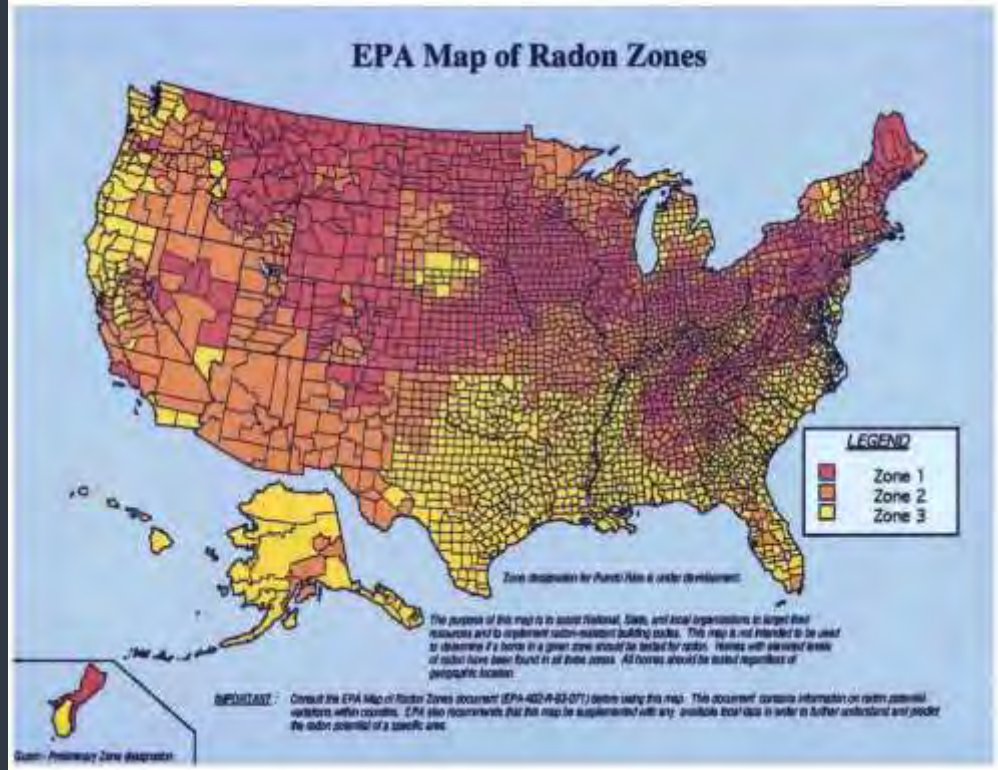
- **Radon** is the number one cause of lung cancer among non-smokers, according to EPA estimates. Overall, radon is the second leading cause of lung cancer. Radon is responsible for about 21,000 lung cancer deaths every year. About 2,900 of these deaths occur among people who have never smoked. On January 13, 2005, Dr. Richard H. Carmona, the U.S. Surgeon General, issued a national health advisory on radon.

World Health Organization

Radon in buildings

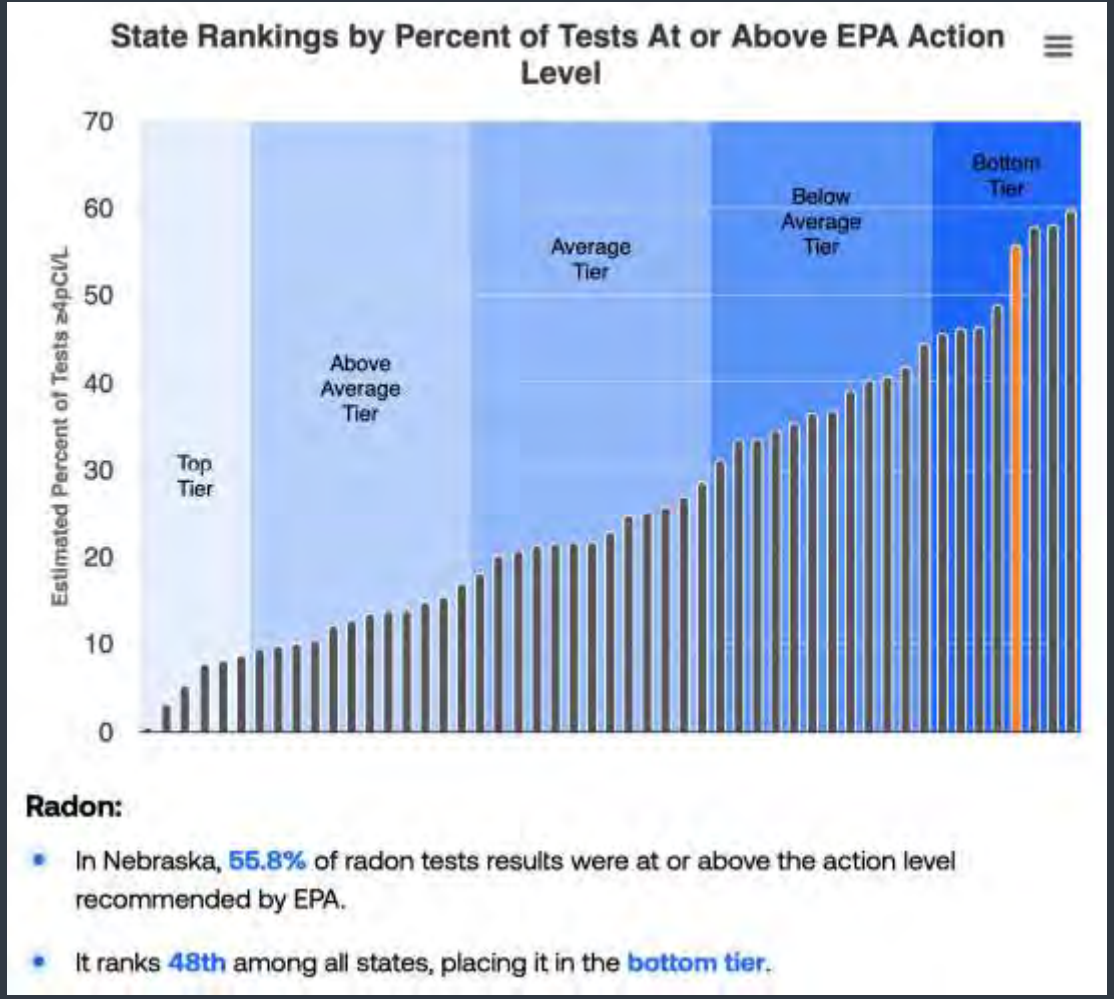
For most people, the greatest exposure to radon occurs in the home where people spend much of their time, though indoor workplaces may also be a source of exposure. The concentration of radon in buildings depends on:

- the local geology, for example the uranium content and permeability of the underlying rocks and soils;
- the routes available for the passage of radon from the soil into the building;
- the radon exhalation from building materials; and
- the rate of exchange between indoor and outdoor air, which depends on the construction of the building, the ventilation habits of the occupants, and the air-tightness of the building.



What do the colors mean?

	Zone 1 (red zones)	Highest potential; average indoor radon levels may be greater than 4 pCi/L (picocuries per liter)
	Zone 2 (orange zones)	Moderate potential; average indoor radon levels may be between 2 and 4 pCi/L
	Zone 3 (yellow zones)	Low potential; average indoor radon levels may be less than 2 pCi/L



Radon:

- In Nebraska, **55.8%** of radon tests results were at or above the action level recommended by EPA.
- It ranks **48th** among all states, placing it in the **bottom tier**.

https://www.lung.org/research/state-of-lung-cancer/states/nebraska#:~:text=The%20rate%20of%20new%20lung%20cancer%20cases%20is%2067.8%20per,a

Radon Test Kits

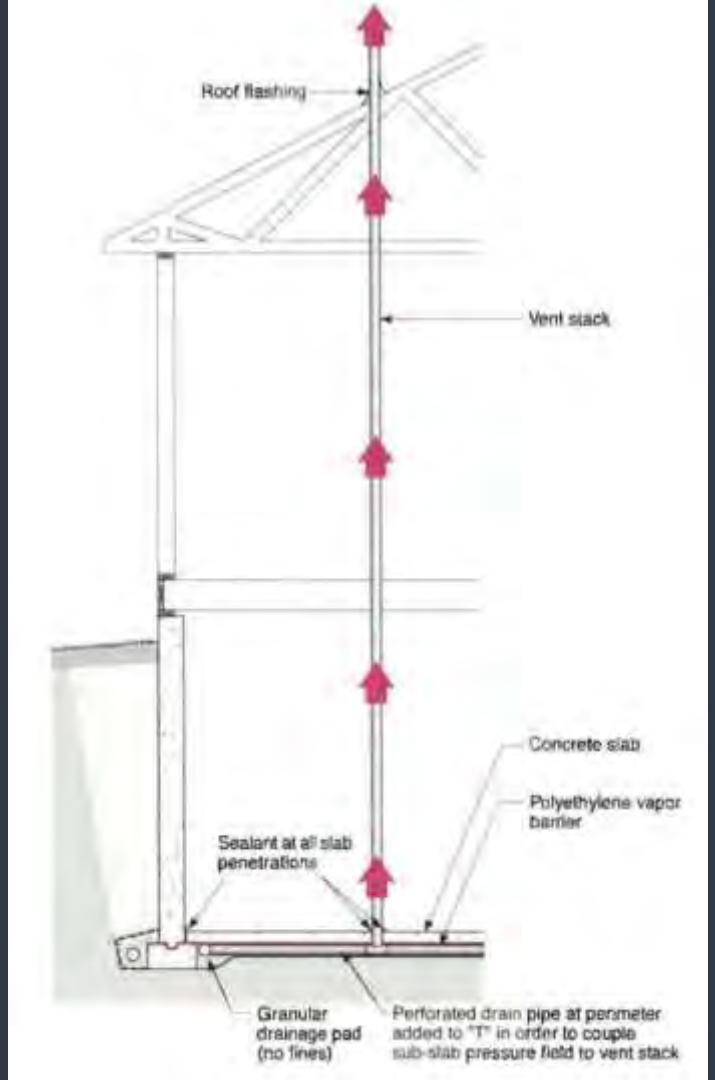
Short term test devices can be purchased many places or there are services which will come place one for you and pick it up and test it.

They should be placed in the lowest level of the house, toward the center of the room, off the ground several feet, and left for the appropriate number of days (3-7 days)

An elevated level of Radon is 2-4 pCi/L and recommended action level is ≥ 4 pCi/L

Recommended action is installation of a radon mitigation system


RADON
REDUCTION SYSTEM


Roof flashing
Vent stack
Concrete slab
Polyethylene vapor barrier
Sealant at all slab penetrations
Granular drainage pad (no fines)
Perforated drain pipe at perimeter added to "T" in order to couple sub-slab pressure field to vent stack

Local Health Department Radon Contacts | 2022-2023

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Name: Melissa Haas
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Loup Basin Public Health Department
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Central District Health Department
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Local Health Departments who are not participating.

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South Heartland District Health Department
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NEBRASKA
Good Life. Great Mission.
DEPT. OF HEALTH AND HUMAN SERVICES
UPDATED 01.17.2023

Nebraska Radon Resistant New Construction (RRNC)

Summary of the Law Effective September 1, 2019

The purpose of the Radon Resistant New Construction Act is to protect public health and welfare from exposure to radon, the second leading cause of lung cancer next to smoking. RRNC utilizes design elements and construction techniques that passively resist radon entry and prepare a building for an active post construction mitigation system.

Summary

Lung cancer is a deadly disease still today and radon is estimated to be the second most common cause overall and the most common cause in non-smokers

Radon is a radioactive gas which can be harmful to the airway epithelium

A large portion of the central part of the country including eastern Nebraska and Iowa are in a high radon zone

We should encourage our patients to understand what radon is, how to test for it, and how to mitigate it

There are several international, federal, and state programs via the internet which can help with the education of our patients

Questions?

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University of Nebraska Medical Center