Lung Cancer, Radon and Screening

Wallace Akerley MD

EPA Region 8 Radon Stakeholder Meeting
September 9, 2025

HUNTSMAN CANCER INSTITUTE
UNIVERSITY OF UTAH

HEALTH
UNIVERSITY OF UTAH

Radon and Lung Cancer

- Lung cancer is the reason we identify + mitigate radon
  - Smoking
  - Avoid asbestos, radiation, heavy metals, etc
- Statistics are real people
- Those involved in Awareness/Mitigation save lives

Outline

1) Dramatic Evolution of Lung Cancer Understanding
   - Precision Medicine, Genetics and Immunology
   - New Diagnosis and Treatment (many types of lung cancer)
   - Smoker and non-smoker

2) Radon-induced Lung Cancer
   - What we do and don't understand – the Gap!

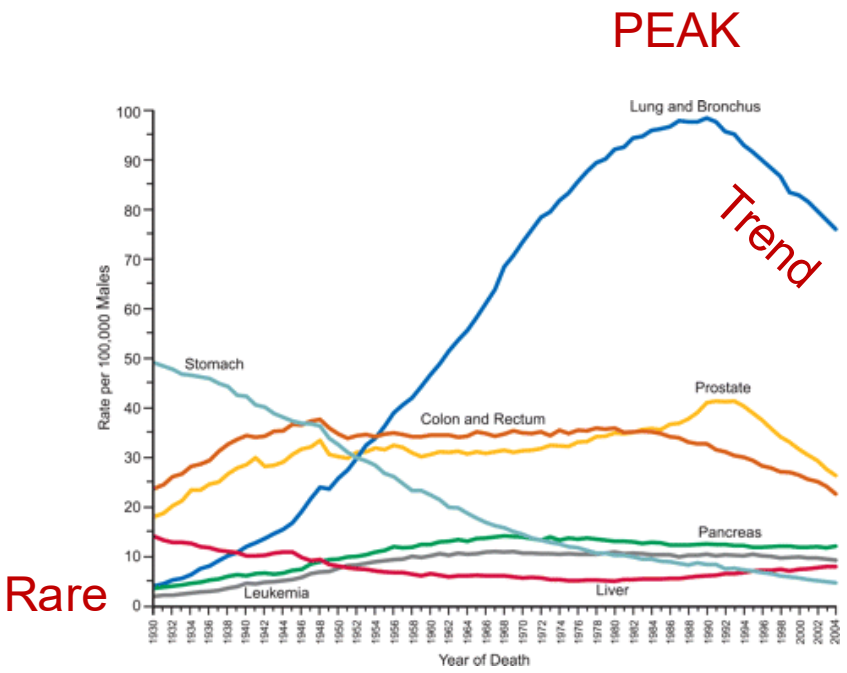
3) Lung Cancer Screening

Invisible Ribbon

- Lung Cancer – Unrecognized
- Invisible Killer
- Number 1 Cancer Mortality in the USA
- Lacks Advocacy (lethality)
- Guilt (Tobacco)

A L C A S E

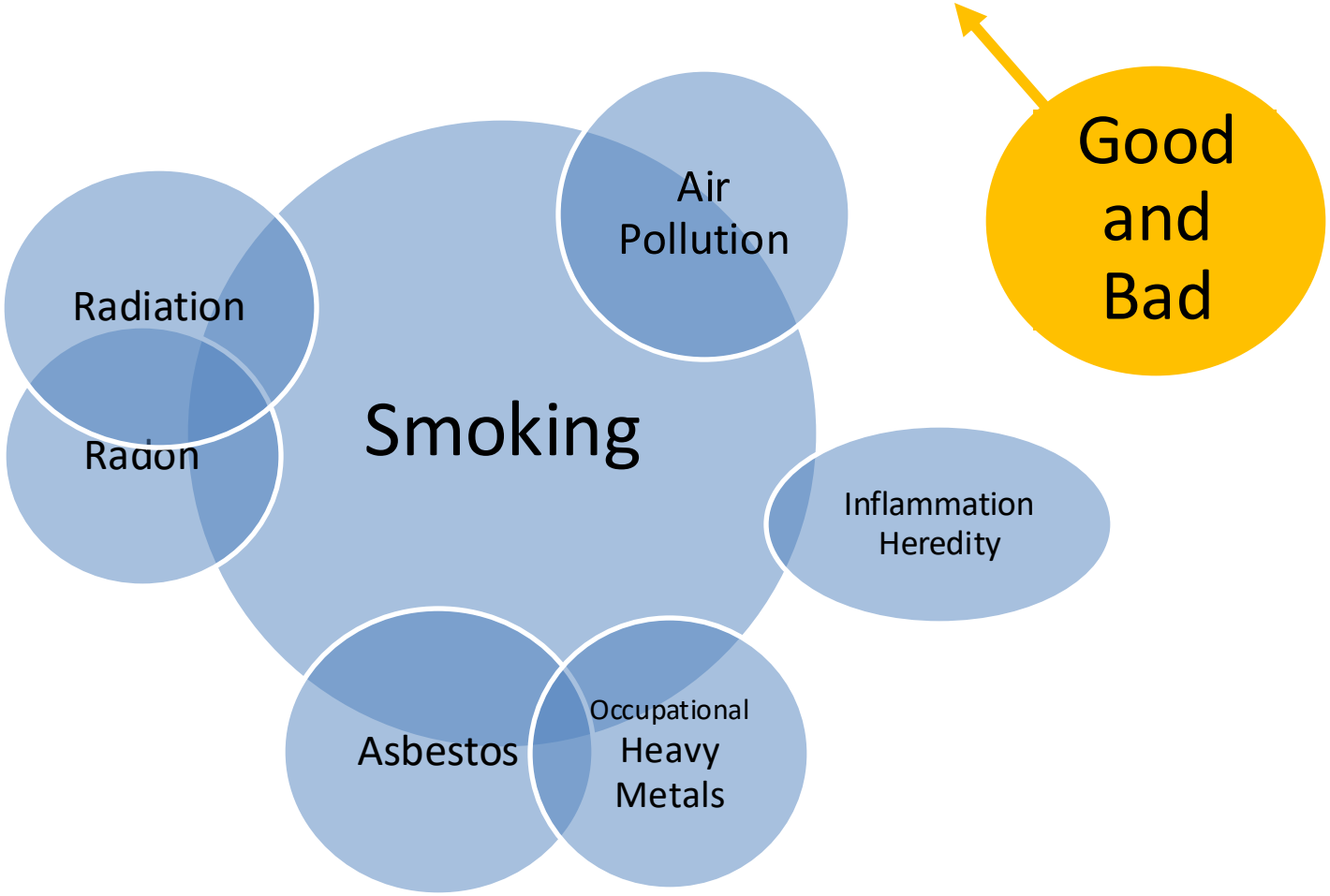
USA Cancer Mortality



– #1 Cause of cancer death (nationally and Utah)
– Improving Mortality Trend
– Has the potential to be a rare cancer again

HUNTSMAN CANCER INSTITUTE UNIVERSITY OF UTAH

Lung Cancer and Synergy (1+1=3)



– Cancer is cumulative DNA damage

– Lung Cancer is NOT one cancer (many subtypes)

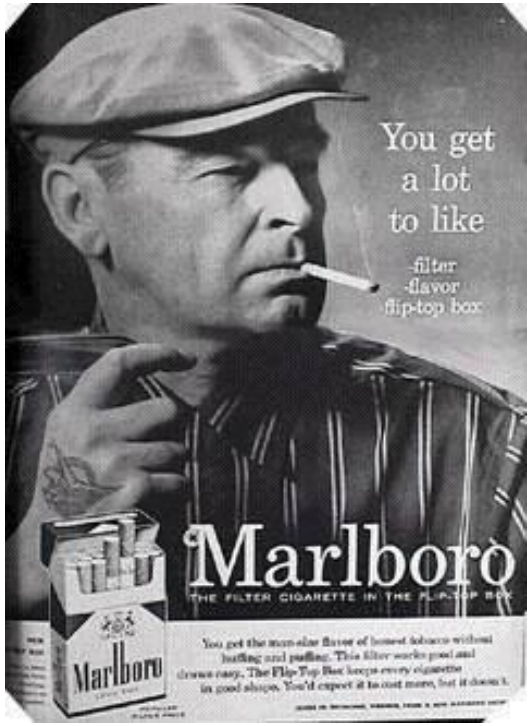
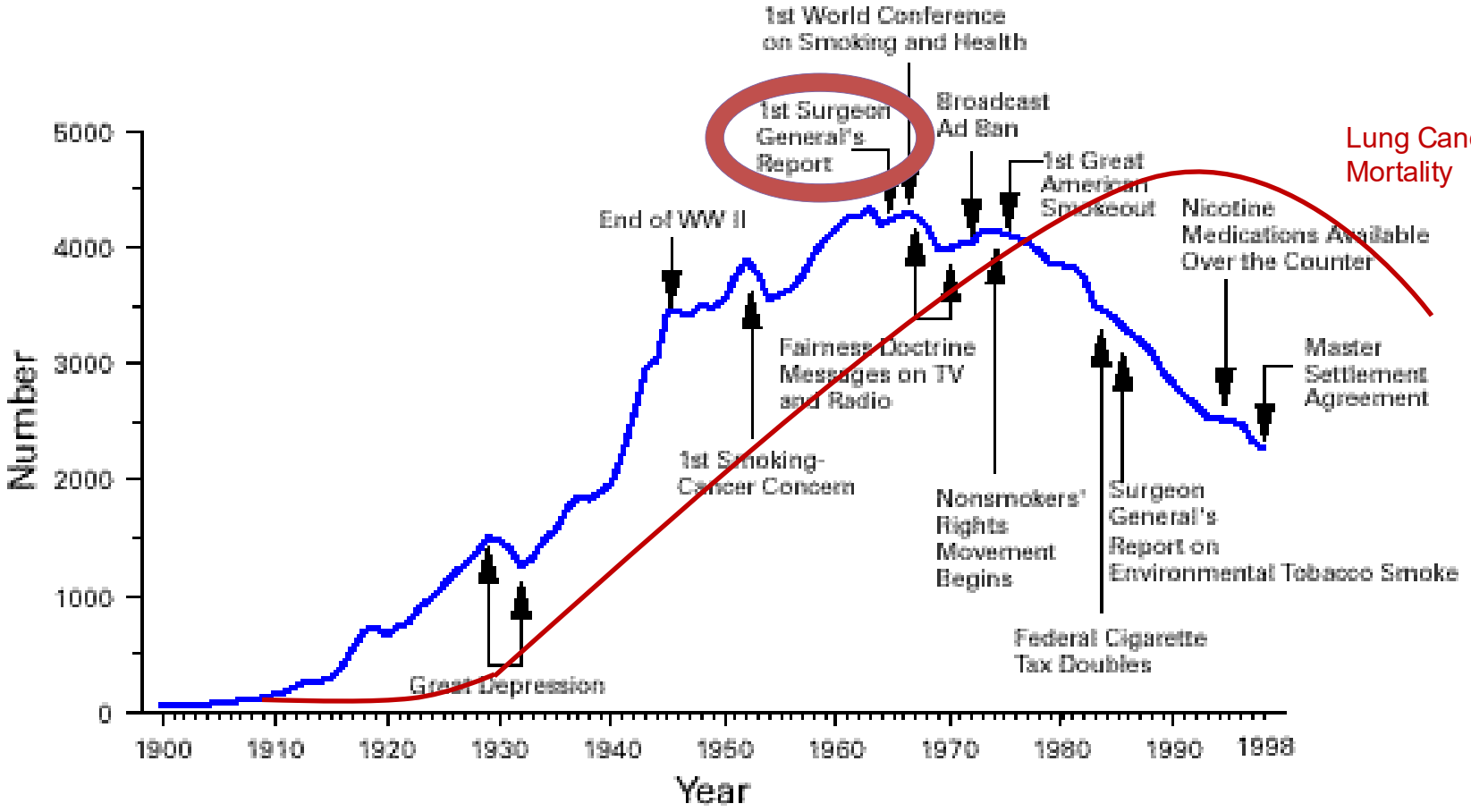
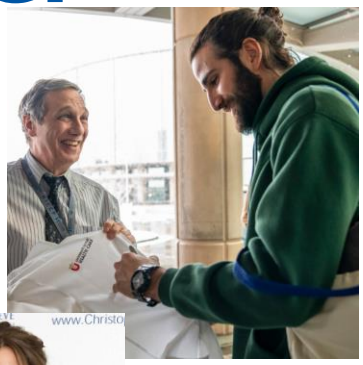


FIGURE 1. Annual adult per capita cigarette consumption and major smoking and health events — United States, 1900–1998



Sources: United States Department of Agriculture; 1986 Surgeon General's Report.

Never-Smoking Lung Cancer



Smoking

Radon

Non-Smoker

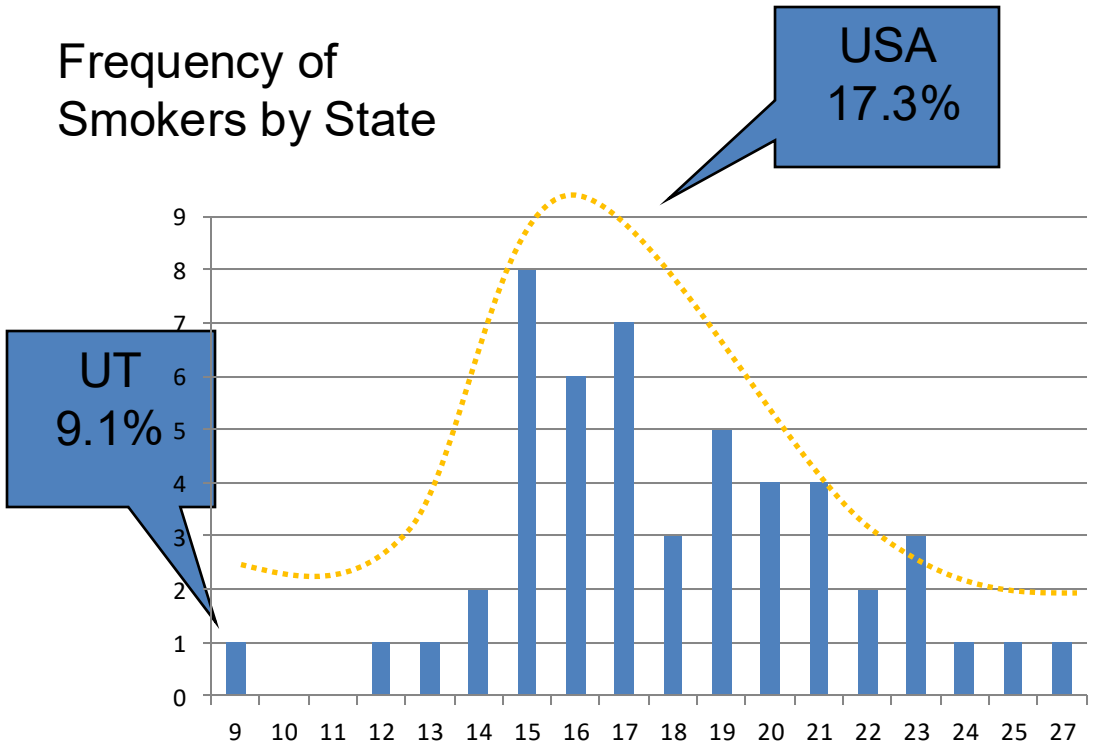
JOAN'S LEGACY

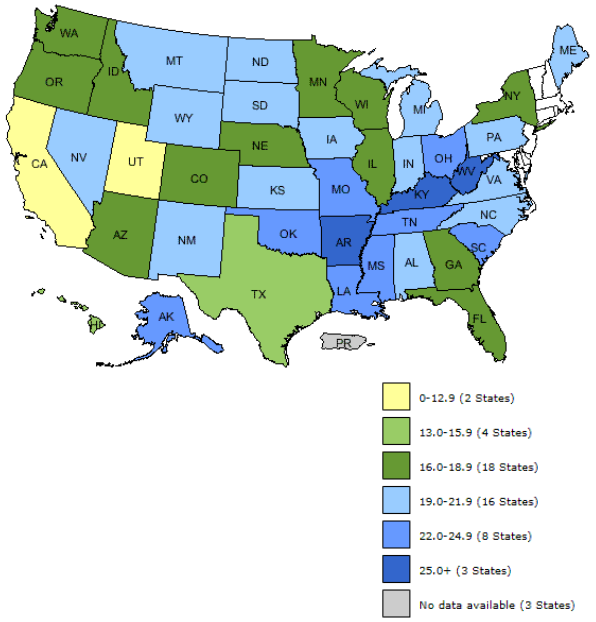
CanSAR™
Cancer Survivors Against Radon

HUNTSMAN CANCER INSTITUTE
UNIVERSITY OF UTAH

Example of Low Smoking State (Utah)

Frequency of Smokers by State



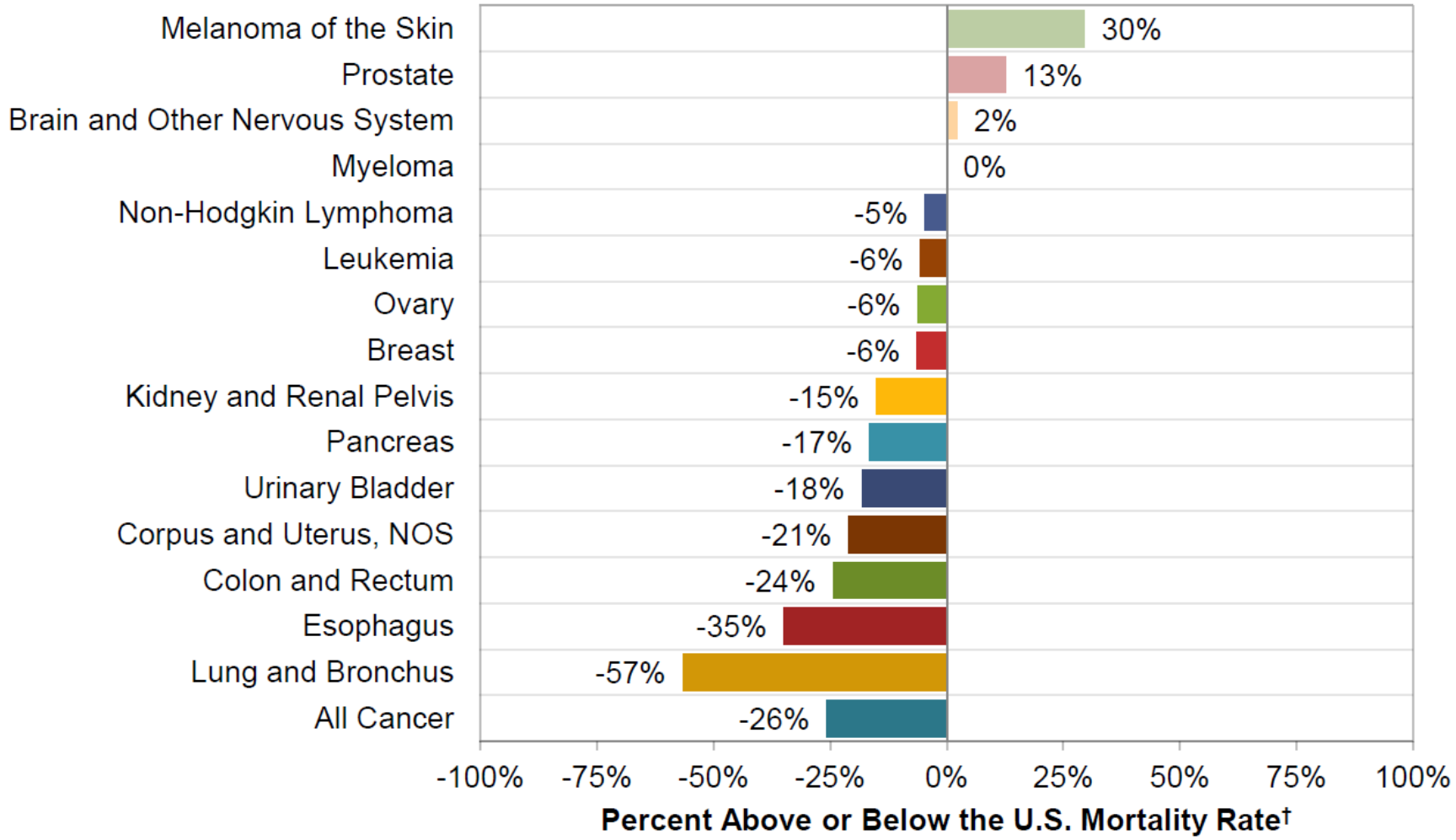


5.8% in Provo-Orem

CDC: BRFSS 2010

MMWR / May 31, 2013 / Vol. 62

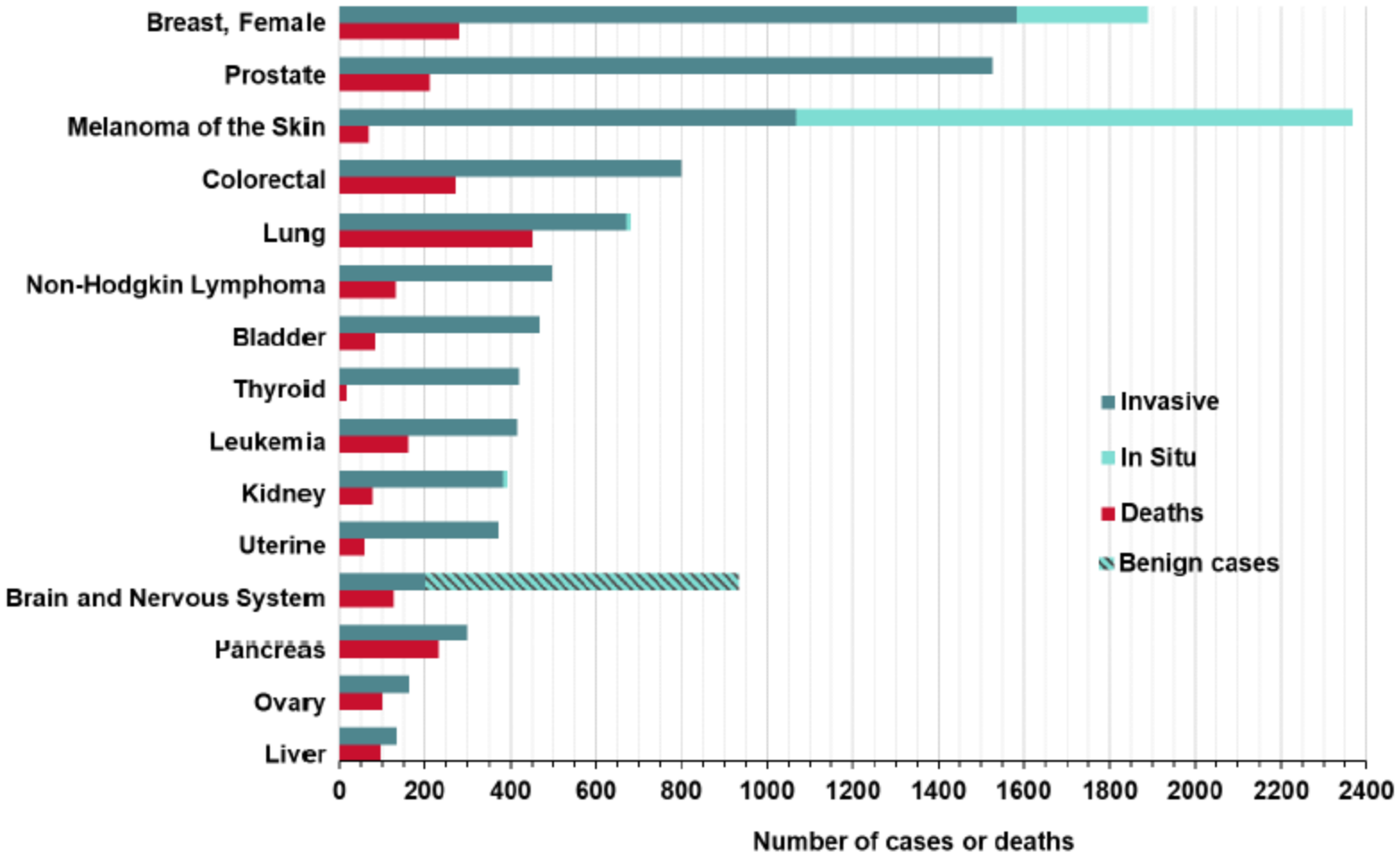
Utah Lung Cancer Mortality compared to USA



Harrell et al. Utah Cancer Registry, 2014.

HUNTSMAN CANCER INSTITUTE UNIVERSITY OF UTAH

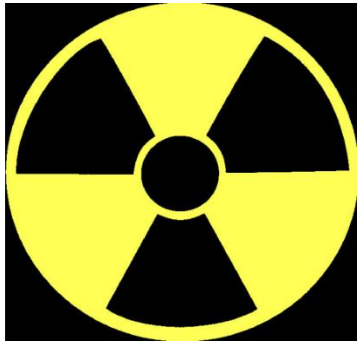
Utah Cancer Incidence and Mortality

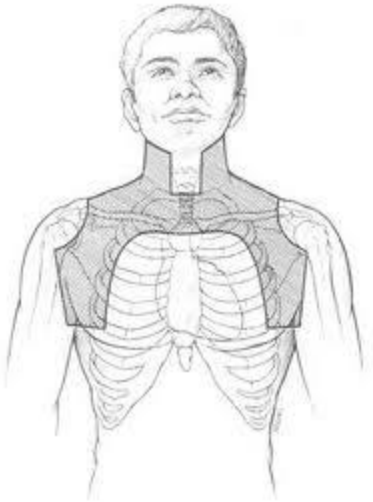


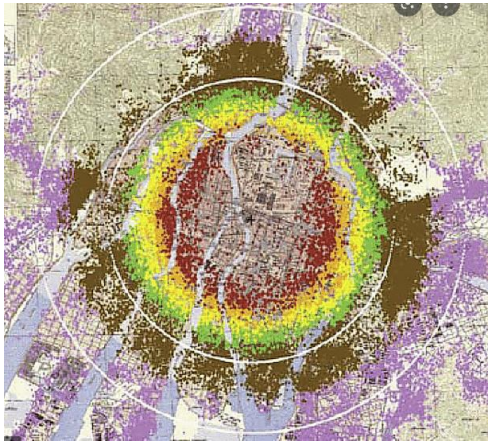
Millar et al. Utah Cancer Registry, 2019.

HUNTSMAN CANCER INSTITUTE UNIVERSITY OF UTAH

Radiation and Cancer

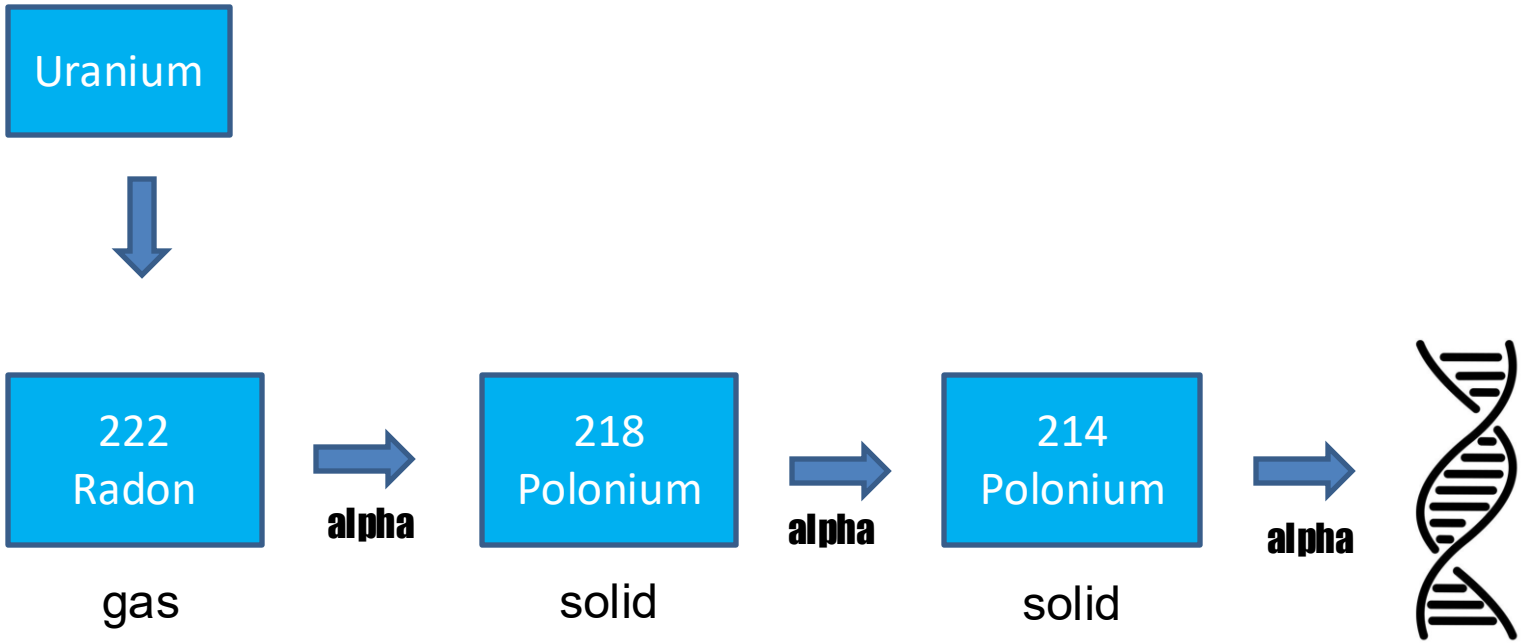






HUNTSMAN
CANCER INSTITUTE
UNIVERSITY OF UTAH

Radon Decay Chain



Cumulative DNA damage
Inflammation
Immune

Radon-Induced Lung Cancer

- 2nd leading cause of Lung Cancer
- Radon is Synergistic with other Carcinogens
  - Tobacco
- Radon-induced cannot be distinguished from other causes by microscopy
  - Potential for gene identification
- Clinical Medicine, Epidemiology, Science Mismatch
  - Radon Signature is missing link (gene or protein)

Cancer Treatment Revolution

Past

- Non-small Cell Lung Cancer – One Group
- Organ based Therapy (chemotherapy)

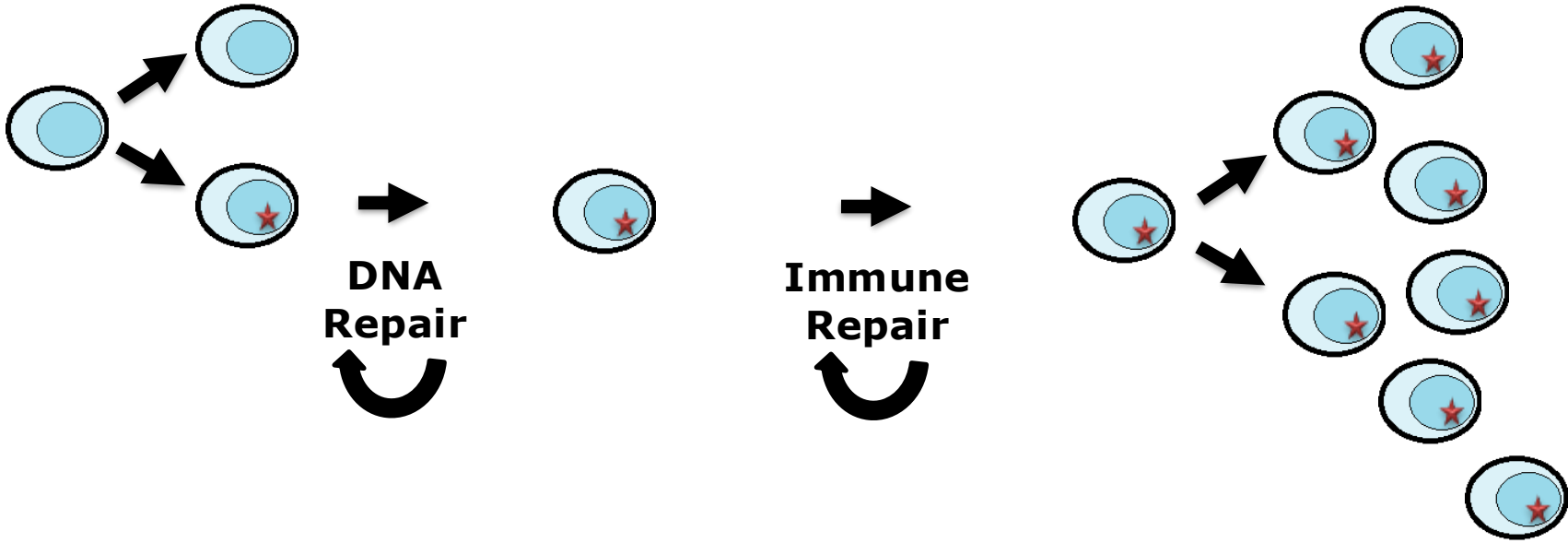
Present (PRECISION MEDICINE)

- NSCLC - Many types
- Defined by Histology, Genetics and Immune Profiles
  - Tissue and Blood Profiling
- Precision Medicine (treat based on cancer weakness)
  - Gene Targeted therapy
  - Immunotherapy

Clinical Carcinogenesis-

Gene Repair and Immune Surveillance

What went wrong can inform therapy?

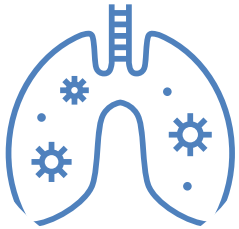


DNA Panel

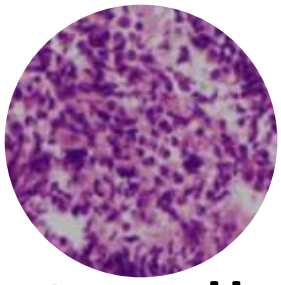
Immune Panel

★ Genetic damage

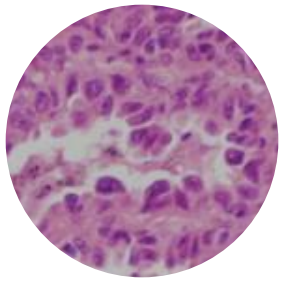
Lung Cancer is diagnosed by microscope
One Problem is broken Genes



Lung Cancer

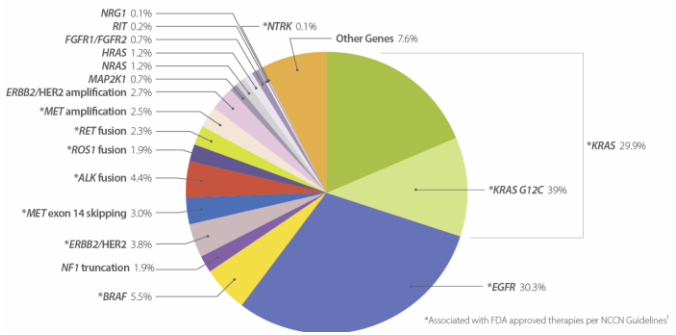


Small Cell



Non-Small Cell

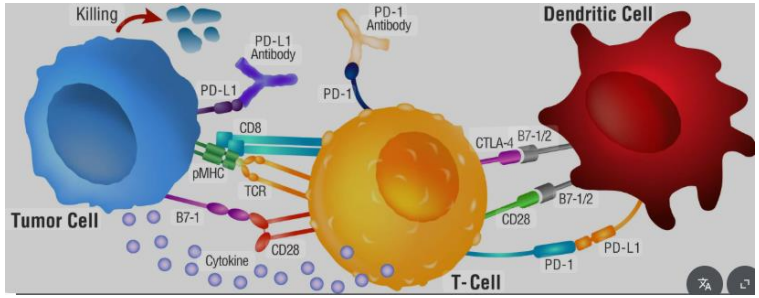
Squamous
Non-Sq

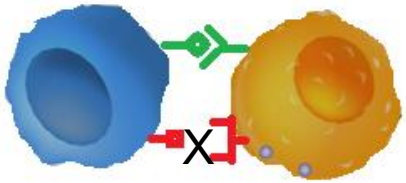


Lung Cancer is Many Cancers
Define Genetically

HUNTSMAN
CANCER INSTITUTE
UNIVERSITY OF UTAH

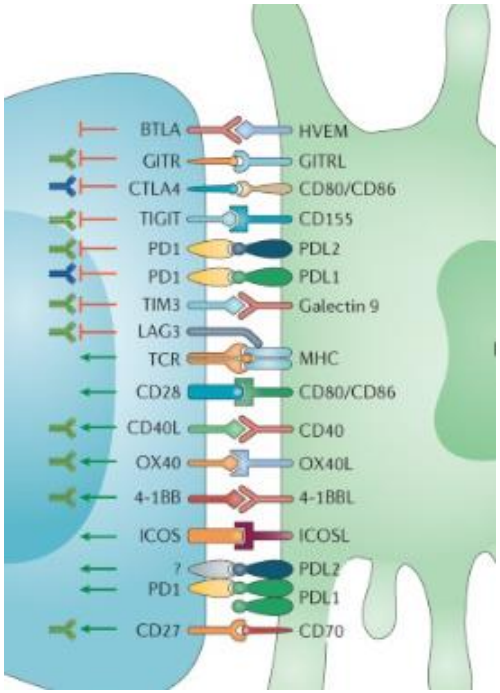
Immune System Mechanics Dysregulation





Activation Regulators

Inhibitory Regulators



Alternate Opportunities

PD1/L1
-Inhibitory Pathway that can be blocked
-Enhanced Kill with Natural Activation
- Measurable: >50%, 1-49%, <1%

Examples: Keytruda, Nivolumab

Immune Oncology at Infancy

NSCLC Treatment

NSCLC

Actionable Gene YES

No

IMMUNE

PDL1>50%

PDL1 1-49%

PDL1<1%

Gene Targeted Therapies

EGFR ALK

9 total

Immunotherapy

ChemoImmunotherapy

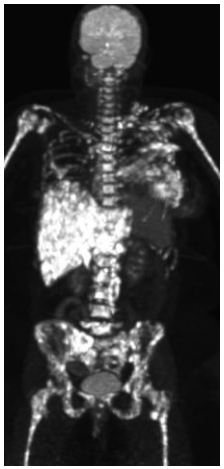
Dual Immunochemo

Precision Medicine: Cancer-type determines Therapy

9 x 3 x 2 x 2 = 108

HUNTSMAN CANCER INSTITUTE UNIVERSITY OF UTAH

NSCLC
How effective are we?

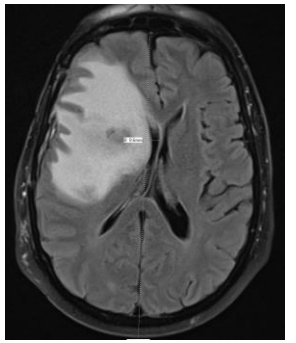


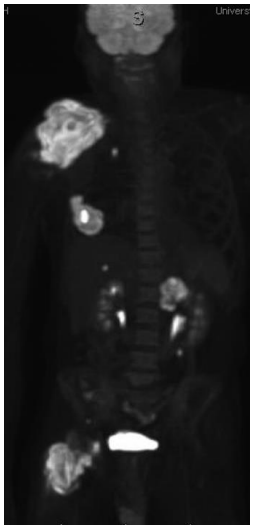
Definitions

Surgery: 5-Year Survival 50%

Metastatic: Response Rate, 1-Year Survival, Median Survival

	Group	Pub Yr	1YS	5YS
Chemo	all	2002	33	0
ALK	Gene	2024	80	>60%
Immuno	PDL1>50%	2021	70	33%
ChemoImmuno	PDL1>1-49%	2020	70	15%
Dual IO	PDL1<1%	2025	60	22%





Schiller NEJM 2002
Solomon JTO 2024
Reck JCO 2021
Gadgeel JCO 2020
Peters JTO 2025

Cure may be Possible?

HUNTSMAN CANCER INSTITUTE
UNIVERSITY OF UTAH

HUNTSMAN CANCER INSTITUTE UNIVERSITY OF UTAH

HEALTH UNIVERSITY OF UTAH

Sophia Deep Lung IV
International Collaboration

Seeking Treatment Strategies Versus another Chemotherapy: A Medical Oncologist's Perspective

Artificial Intelligence

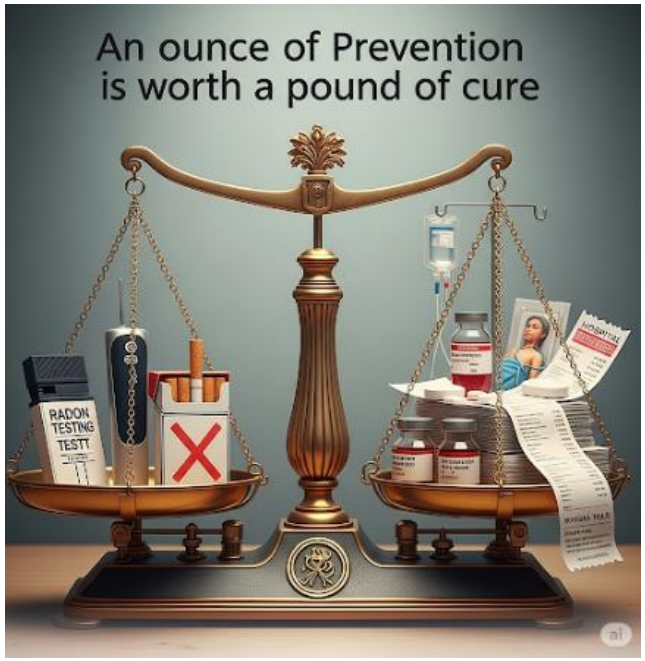
Can AI help us examine further?

- Cancer (genes, immune, scan)
- Host factors
- Treatments

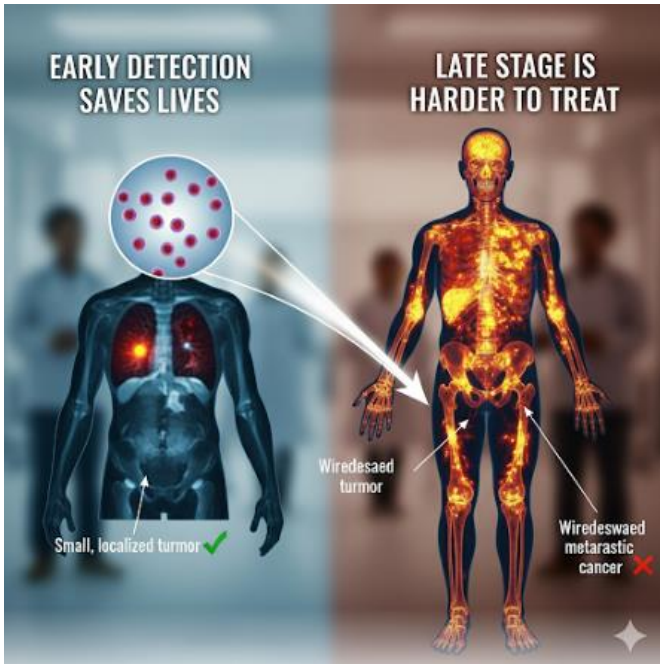
Wallace Akerley, MD, 2019

Huntsman Cancer Institute

Prevention and Screening



Prevention means the cancer never happened



Screening attempts find the cancer before it has spread

https://g.co/gemini/share/7e750152bbc9

Google Gemini AI June 2025

What about Screening those with Radon Exposure?

-Not indicated

-May cause more harm than good

-Dose-response relationship

- How much?
- How long?
- What age?

-High suspicion for any symptom

Gemini AI

1) Risk-Benefit Analysis of Lung Cancer in Never-smoke with Radon
    1) NCCN- Annual CT Screening Guidelines - Smoking 20 pack-years
        (+) Find cancer at curable surgical stage
        (-) Most spots are not Cancer, Biopsy has risk, Anxiety
        (-) Possibility to find Incurable Cancer
        (-) CT scan and radiation exposure
    2) Chinese Studies show benefit for screening in never smokers
        Caveat- More pollution, Heredity Factors
    3) Radon Causes Lung Cancer at lower rate than tobacco
        (-) Limited data, no prospective study
        (-) can't distinguish radon from other causes of lung cancer (statistical model)
        (-) years of exposure before cancer
        (-) when to screen
    4) Evaluate the Risk-Benefit Ratio of Screening Never-Smokers with High Radon Exposure

Gemini AI Report

10 Page Executive Summary

27 references

30 websites used in analyses, innumerable discarded

4 slide presentation with Risk Analyzer https://g.co/gemini/share/7e750152bbc9

Conclusion and suggestions for Future

Excerpts

- Overdiagnosis, perhaps harm with too many surgeries
- In East countries CT screening has become commonplace with high detection rates of early-stage lung cancers in never-smokers but biological and pathological differences exist.

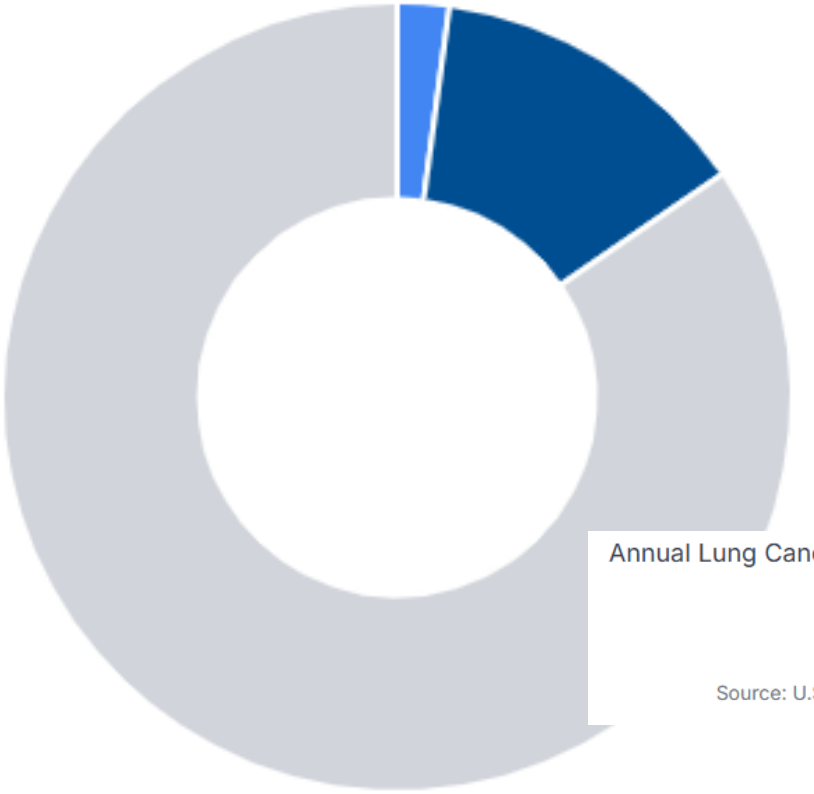
Gemini AI Conclusion

The current standard of lung cancer screening, while successful in its intended population, fails to address a significant public health burden: lung cancer in non-smokers. However, the available evidence on the clinical utility of screening this non-traditional cohort is limited and suggests a potential for significant harm from overdiagnosis.

In light of this analysis, the continued reliance on a singular, smoking-exclusive screening model is a policy that is both scientifically and ethically incomplete. The future of lung cancer screening lies in a more nuanced, risk-stratified paradigm that integrates a broader array of etiological factors. It is a paradigm that will require not only new policy frameworks but also new, dedicated research to prove that the life-saving benefits of screening can be extended safely and effectively to all individuals who bear a high risk of lung cancer, regardless of its cause.

Radon: The Unseen Contributor to Lung Cancer

Radon's Share of Lung Cancer Cases



Annual Lung Cancer Deaths in the U.S. Attributed to Radon

21,000

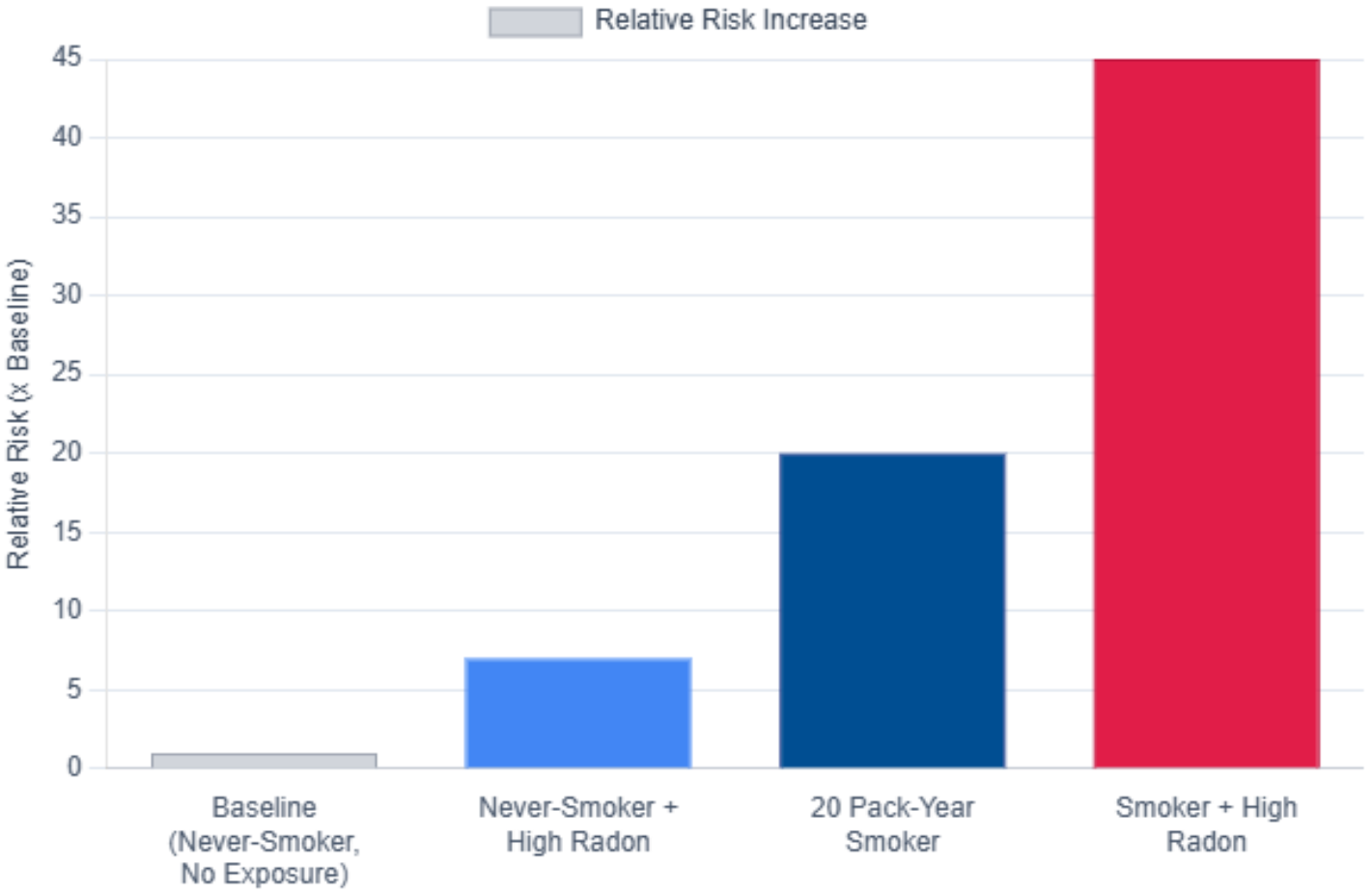
Source: U.S. Environmental Protection Agency (EPA)

Radon-Related (Never-Smokers) Radon-Related (Smokers) Other Causes

Risk Comparison: Radon vs. Smoking

Current screening guidelines are based on a 20 pack-year smoking history. This analysis compares that benchmark against the risk posed by high-level radon exposure to a never-smoker, and the dangerous synergistic effect when both risk factors are present.

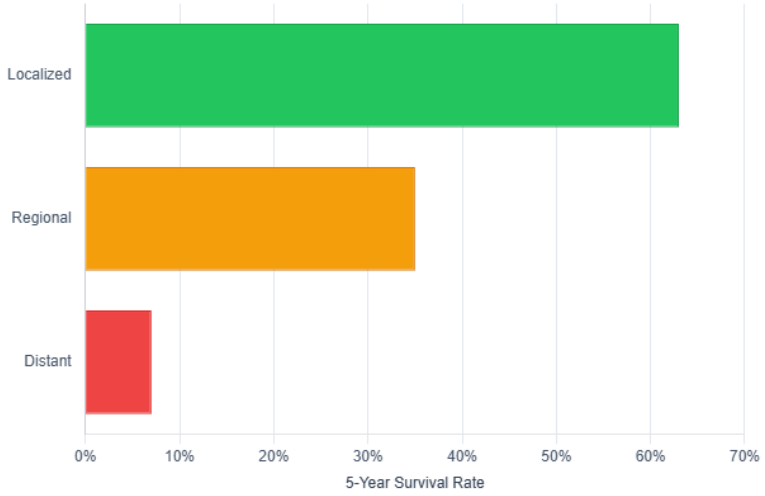
Relative Increase in Lung Cancer Risk



The Screening Dilemma

Benefits of Screening

Early detection dramatically improves outcomes. Screening can find cancers at a more treatable, localized stage.



Harms of Screening

~95% High False Positives
The vast majority of nodules found on LDCT scans are not cancerous, leading to anxiety and unnecessary follow-up procedures.

1 in 4 Invasive Procedures
For every 1,000 people screened, a significant number will undergo invasive procedures like biopsies or surgery for benign nodules.

Radiation Exposure
Annual screening involves cumulative radiation exposure, which carries its own small but non-zero risk of inducing cancer over a lifetime.

The Path Forward: A New Risk Model

The limitations of a smoking-only model highlight the need for a more comprehensive, multi-factor approach to determine screening eligibility.

Current Model

Pack-Years

A limited model based solely on smoking history.

Proposed Future Model

Smoking | Radon | Genetics | History

A holistic risk-stratified model for more precise screening.

Further research is crucial to define the specific risk thresholds at which the benefits of screening outweigh the harms for never-smokers with high radon exposure.

✨Risk Profile Generator✨

Input your radon exposure level (in pCi/L) to see a personalized risk summary. For context, the EPA recommends taking action to reduce radon above 4 pCi/L.

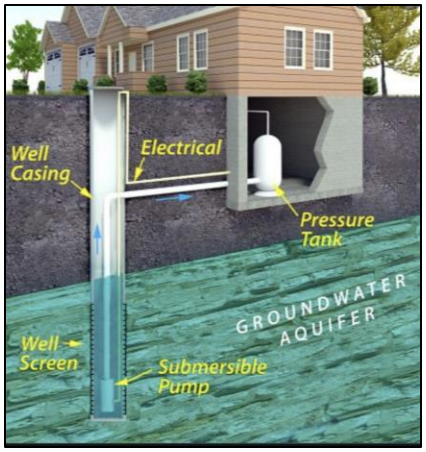
Your Radon Level (pCi/L):

e.g., 5.0

☐ I have a history of smoking.

Generate Profile

UPDB:National Database
HCI is one of the best places in the world to study LCINS



EPA

Zillow

UTAH DEPARTMENT of ENVIRONMENTAL QUALITY

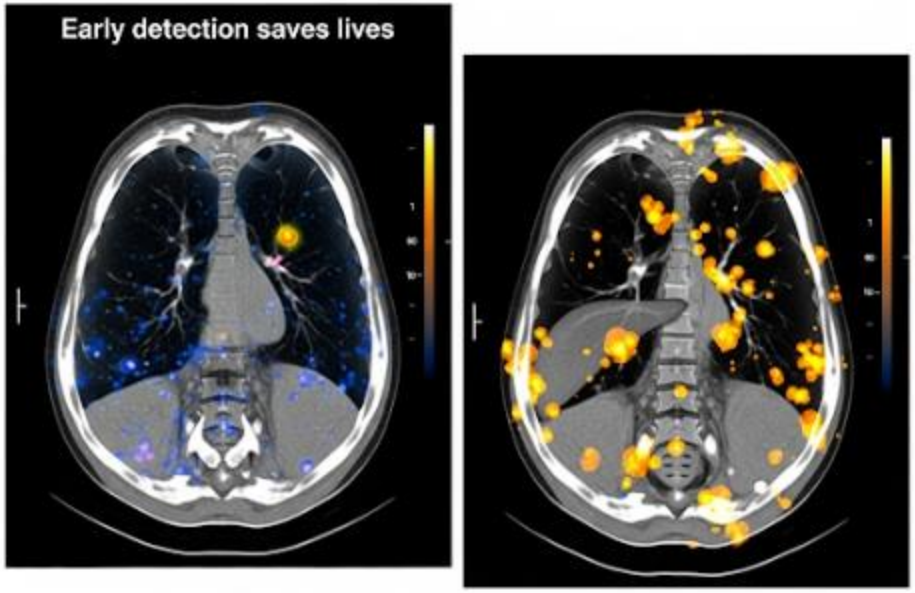
UTAH DNR UTAH GEOLOGICAL SURVEY

Ou et al. Patterns of indoor radon concentrations, radon-hazard potential, and radon testing on a small geographic scale in Utah. Journal of Environment Radioactivity 2022 .
McCarty et al. County-level smoking and radon exposure and lung cancer risk by histotype, sex, race, and ethnicity (manuscript)

Lung Cancer Summary

- Lung cancer is many cancers defined by Genes, their proteins and Immune Dysregulation
  - Long-term survival is possible even with metastatic disease
- Prevention beats Treatment and Screening
  - CT Lung Cancer Screening after Radon exposure is not indicated
  - A nuanced Screening Model is needed
    - Smoke, Radon, Age, Heredity, Dose/Duration
- Radon
  - Causes lung cancer in smokers and never-smokers
  - Most important natural cause of cancer (preventable)
  - Awareness, Testing and Mitigation saves lives

AI Bloopers



Gemini AI 2025