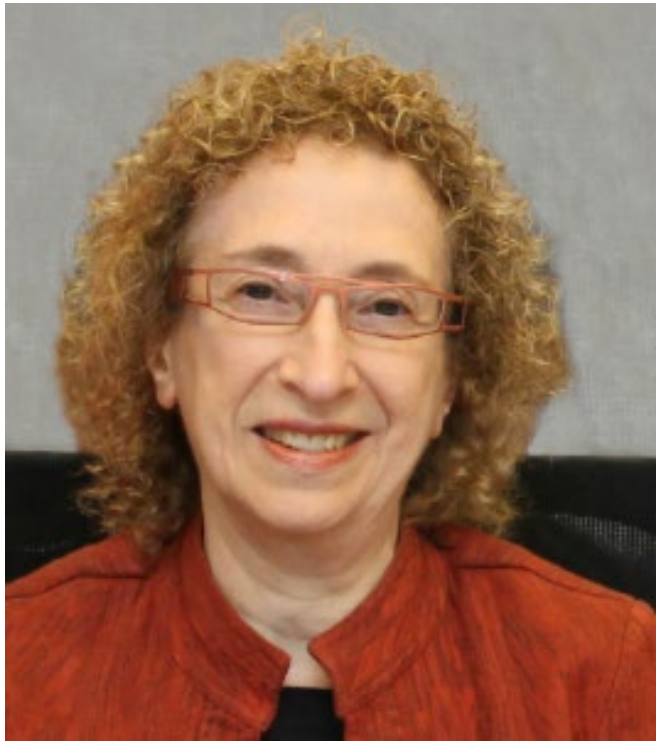
Introduction to Principles of Epidemiology Applicable to Radiation Epidemiology

Martha Linet, M.D., M.P.H.
Senior Investigator
Radiation Epidemiology Branch
Division of Cancer Epidemiology & Genetics (DCEG)
National Cancer Institute
linetm@mail.nih.gov



DCEG Radiation Epidemiology and Dosimetry Course 2019

www.dceg.cancer.gov/RadEpiCourse

Objective

Provide a brief overview of epidemiologic concepts, study design, and study components pertinent to radiation epidemiology

Outline

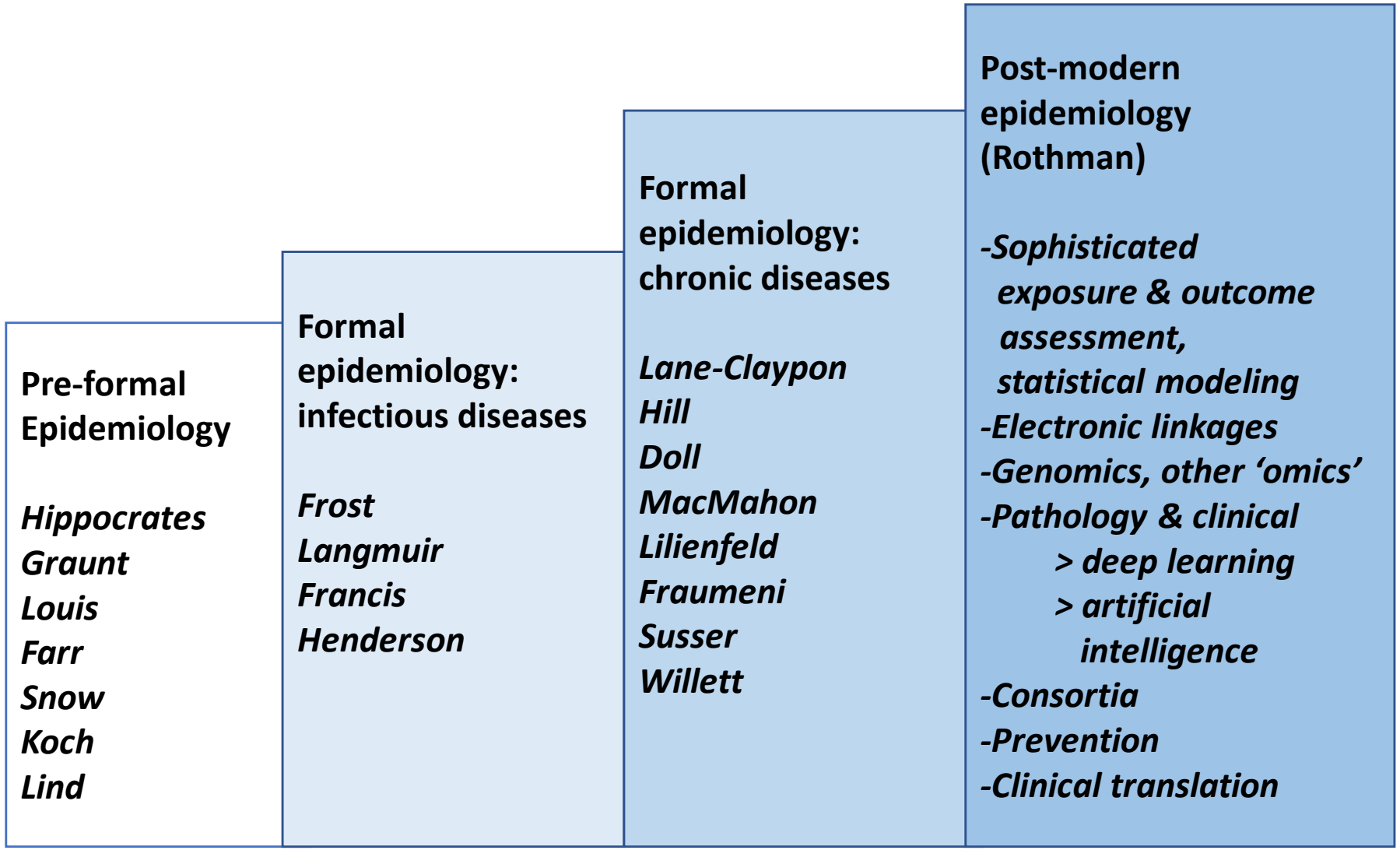
- Epidemiology: history & definitions
- Descriptive patterns
- Disease models and causation
- Exposures & outcomes: sources and assessment methods
- Study designs
- Confounding, effect modification, bias

Epidemiology

A scientific discipline that provides quantitative information about human health risks associated with specific exposures

History and Definitions

History of epidemiology



What is epidemiology?

- **The study of the distribution of a disease or conditions in human populations and the factors that influence the distribution**

Who: Populations

What: Risk factors for disease

When: Temporal aspects

Where: Geographical distribution

How: Methods, mechanisms, biology

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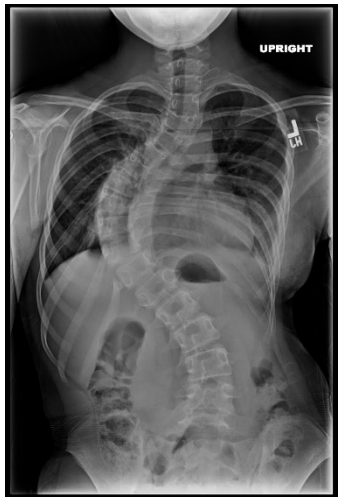
Populations

- **Groups of persons that may be at higher or lower risk of developing a disease(s) or condition(s) due to an agent or substance presumed to be causal**
  - -Cohorts: exposed vs unexposed/ low-level exposure
  - -Cases vs. controls



Examples of radiation-exposed populations

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- The study of the distribution of a disease or conditions in human populations and the factors that influence the distribution

Who: Populations

What: Risk factors for disease
> Exposures
> Outcomes

When: Temporal aspects

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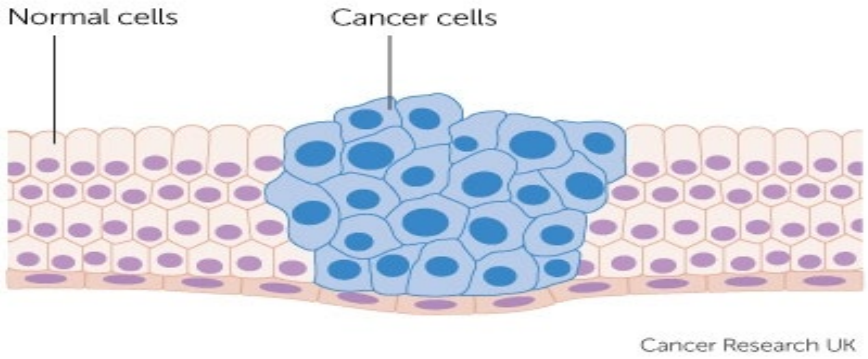
Exposures

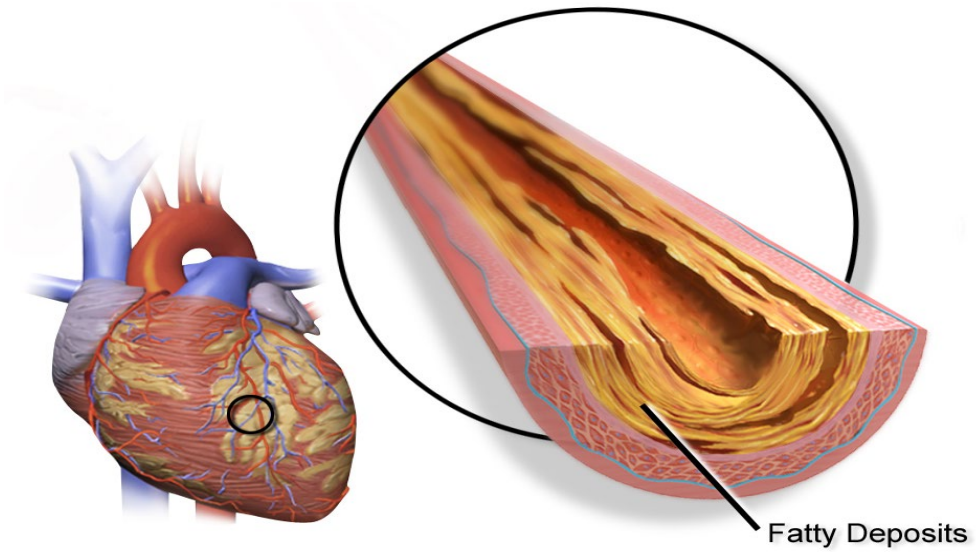
- **Agents or substances presumed to be causal of a disease or event (exposure surrogate is a factor indicating exposure potential, *e.g.*, job title)**

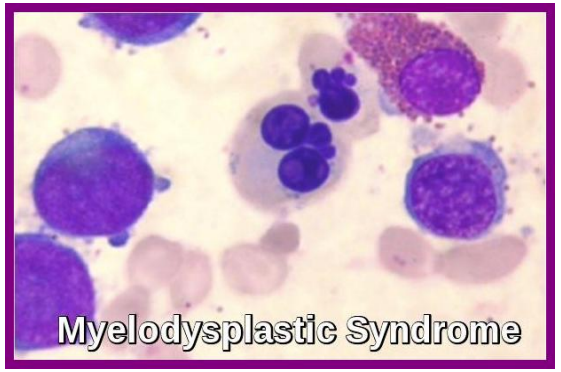
'Exposures' include radiation, pesticides, obesity, cigarettes

Outcomes

- **Diseases, conditions, precursors to diseases or conditions**







Radiation-related adverse outcomes include most cancers, cataracts, heart disease, and probably leukemia precursors such as myelodysplastic syndromes

What is epidemiology?

- The study of the distribution of a disease or conditions in human populations and the factors that influence the distribution

Who: Populations

What: Risk factors for disease
> Risk factor relationships
> Risk measures

When: Temporal aspects

Where: Geographical distribution

How: Methods, mechanisms, biology

Correlation, Association, Causation

- **Correlation:** the degree to which variables change together (no direction assumed)
- **Association:** a disease occurs more (or less) frequently in the presence of an exposure than in its absence & varies by exposure level
- **Causation:** in an individual, an exposure caused a given disease; within a population, at least some cases of the disease would not have occurred in the absence of the exposure

Measures of risk

Definitions

- **Risk:** the probability of disease developing in a population in a specified time interval

- **Relative risk or risk ratio (RR)**: a measure of the risk of a certain event happening in one group compared to the risk of the same event happening in another group; the incidence/mortality of disease in an exposed group divided by the incidence/mortality of disease in a non-exposed group

Examples

- If RR = 1.0, then no difference between the two groups

- If RR >1.0, then being exposed to a certain substance or factor increases the risk of cancer

- If RR <1.0, then being exposed to a substance/factor decreases the risk of cancer

Other measures of risk

- **Attributable risk:** the maximum proportion of a disease attributable to a given exposures
- **Absolute risk:** the observed or calculated probability of occurrence of an event in a population related to a specific exposure
  - Example: Among patients treated with a specific agent at ages 5-10 and followed up through age 75, four percent will develop cardiac insufficiency

Descriptive Patterns & Trends and Disease Classification

Descriptive epidemiology: Rationale for study

Why study disease patterns and trends?

- Explain occurrence (temporal, geographic) and natural history
- Provide guidance for health services: identify susceptible populations
- Suggest hypotheses to elucidate causal inferences and mechanisms

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*Descriptive epidemiology frequently involves factors in addition to temporal aspects

Rates

Rate: a measure of change in a quantity per unit time

- **Incidence:** the total number of new-onset disease events divided by the total person-time at risk during a given period of time
- **Mortality:** the total number of deaths from a disease divided by the total person-time at risk during a given period of time

Disease classification: purpose

What is the purpose of disease classification?

- Group ill persons into categories to distinguish one category from another
- Arrange diseases into groups with common characteristics

Disease classifications internationally used

International Classification of Diseases (ICD)

- Anatomic site
- Periodically modified to reflect ↑knowledge (currently ICD-10)

International Classification of Diseases for Oncology (ICD-O)

- Two major categories: morphology and topography (anatomic site)
- Latest revision includes clinical, immunological, treatment-related and molecular characteristics of some neoplasms (ICD-O-3)

Specialty classifications

- Example: International Classification of Childhood Cancer

International Classification of Childhood Cancer

I. Leukemia

II. Lymphomas and reticuloendothelial neoplasms

III. CNS and other intracranial and intraspinal neoplasms

IV. Sympathetic nervous system tumors

V. Retinoblastoma

VI. Renal tumors

VII. Hepatic tumors

VIII. Malignant bone tumors

IX. Soft tissue sarcomas

X. Germ cell, trophoblastic, & other gonadal neoplasms

XI. Carcinomas & other malignant epithelial neoplasms

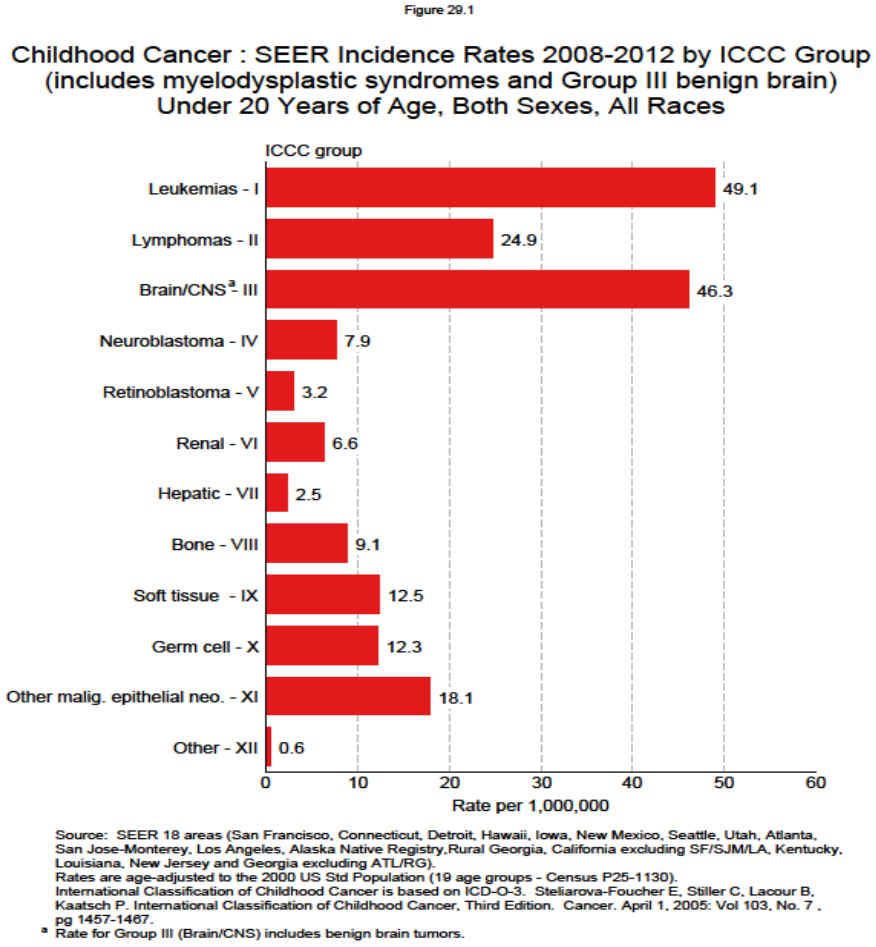
XII. Other and unspecified malignant neoplasms

Childhood Cancer Statistics - USA

Total childhood cancers ages 0-19

- 15,590 estimated annual incident ca
- 1,780 estimated annual deaths
- 5-yr survival 78%

Data shown in figure from NCI SEER program:
Howlader N, Noone AM, Crapcho M et al. SEER Cancer Statistics Review, 1975-2016, National Cancer Institute, Bethesda, MD
https://seer.cancer.gov/csr/1975_2016
based on November 2018 SEER data submission, Posted to the SEER web site, April 2019



Childhood cancer risks vary by type and subgroup

Characteristic	Subgroup	↑ Risks by subgroup & cancer type
- Age	infancy	neuroblastoma, CNS, leukemia, retinoblastoma
	adolescence	Hodgkin lymphoma, germ cell cancers, CNS, leukemia
- Gender	male	lymphoma
- Race	Caucasian	Ewing's sarcoma, acute lymphoblastic leukemia
	African-American	Wilms' tumor, retinoblastoma
	African	endemic Burkitt's lymphoma

Trends in U.S. Childhood Cancer Incidence

- Incidence rose about 0.7% per year for all childhood cancers, 1975-2016
- Rate of increase was lower (e.g., 0.2% per year) during 1990-2006, but rose more rapidly after 2006
- Mortality steadily declined since chemotherapy introduced in 1960s, but decrease has leveled off

Data shown in figure from NCI SEER program:
Howlader N, Noone AM, Crapcho M et al. SEER Cancer Statistics Review, 1975-2016, National Cancer Institute, Bethesda, MD
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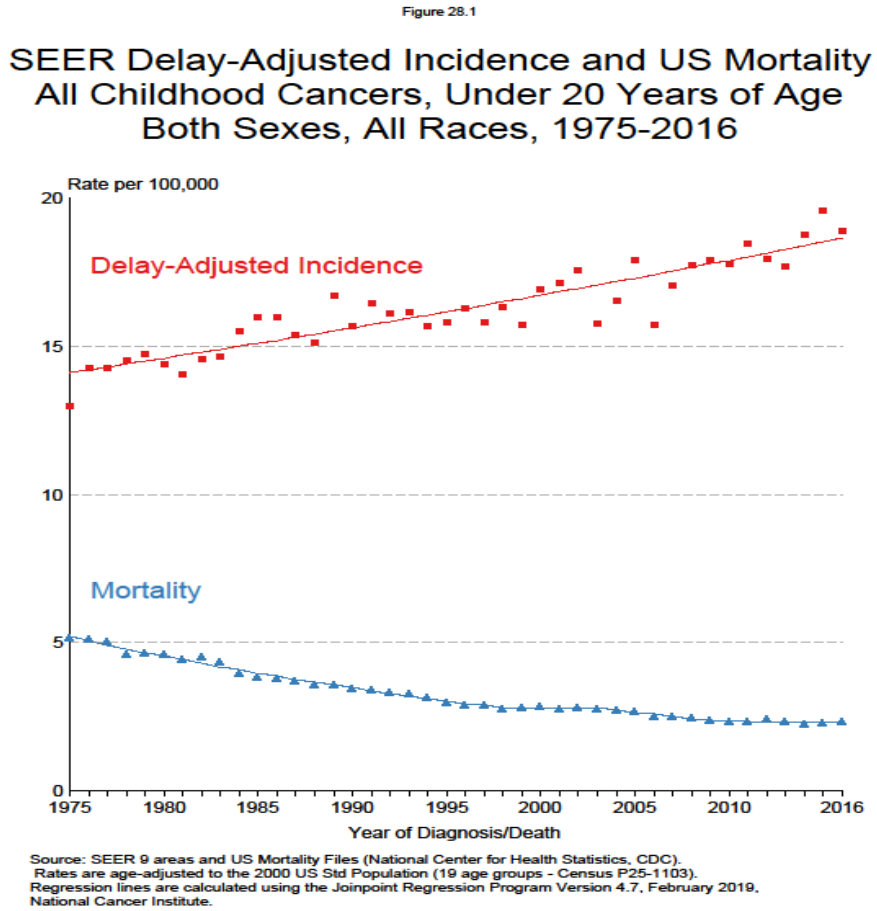

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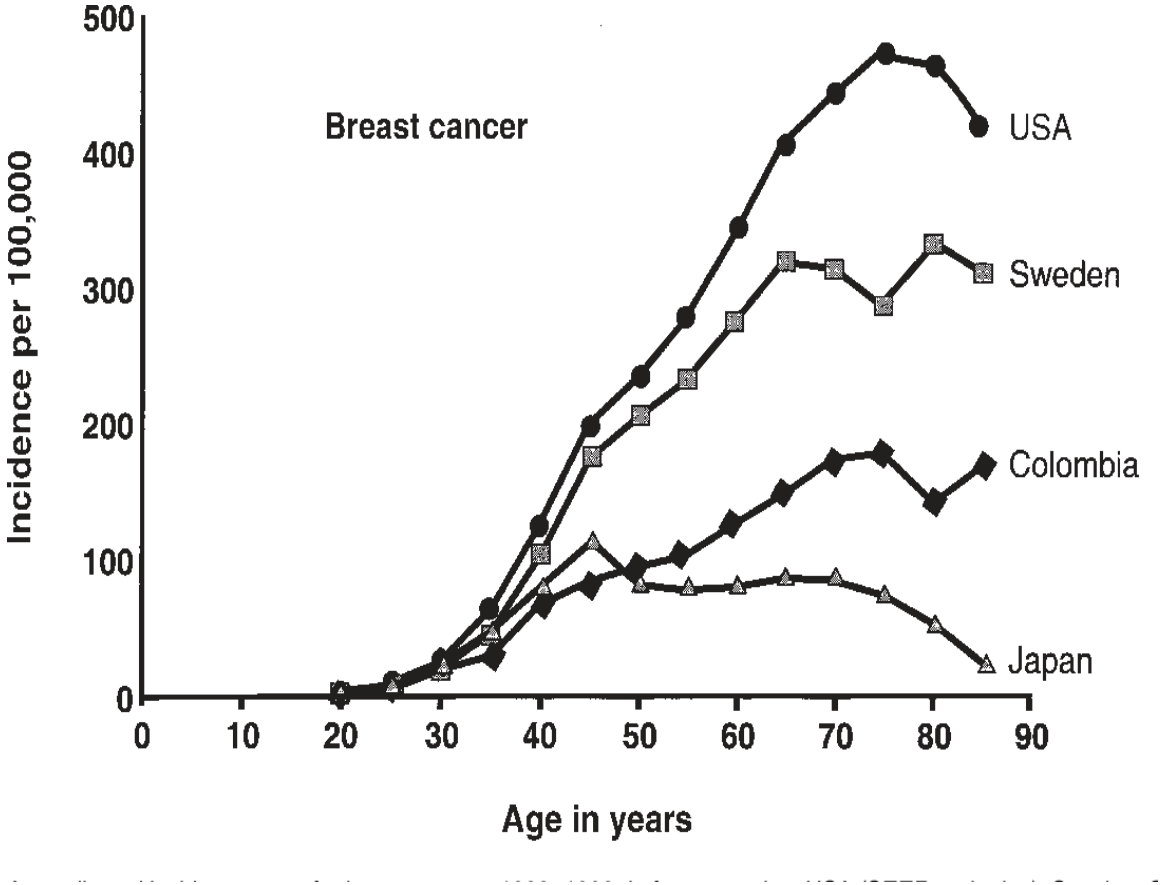
Geographic (and Population) variation in incidence

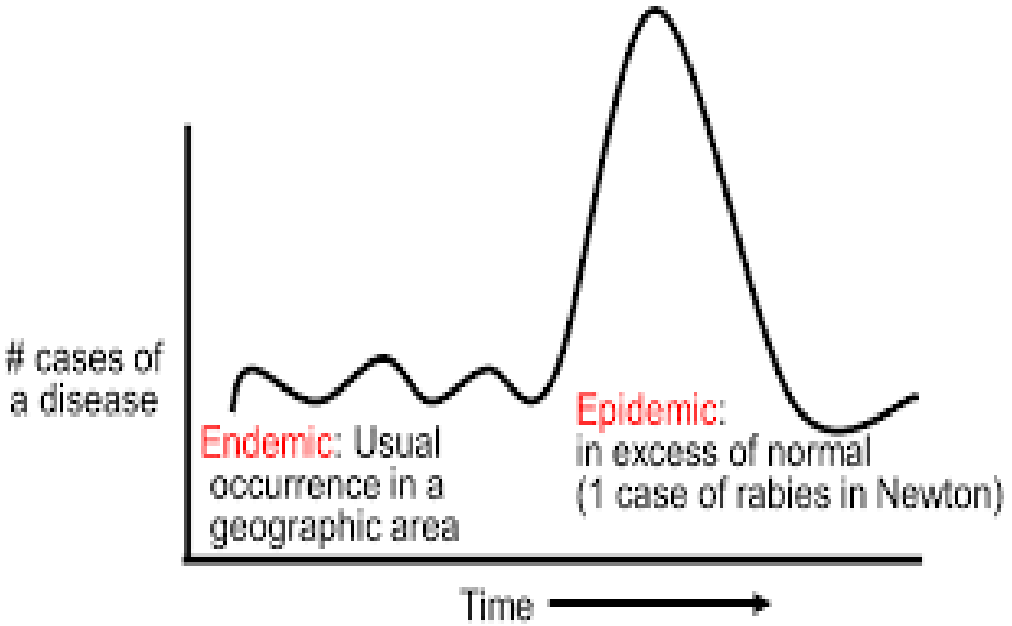
- **Background disease rates** in a geographic area and population are important for interpretation and extrapolation
  - Japanese atomic bomb survivors: low background rates of female breast cancer and chronic lymphocytic leukemia
  - African-Americans: low background rate of childhood leukemia



Age-specific patterns in breast cancer in four countries, 1988-1992. Hulka BS and Moorman PG. Maturitas 2001;38:103-113.

Endemic (background) vs epidemic

- **Endemic or background rates:** usual incidence of a given disease within a defined geographic area
- "**Epidemic:"** excess occurrence of a group of illnesses of a similar nature in a defined area
  - Thyroid cancers in young persons in Belarus after the Chernobyl accident
  - Breast cancer in Hodgkin lymphoma survivors following radiotherapy



Endemic vs. epidemic disease pattern

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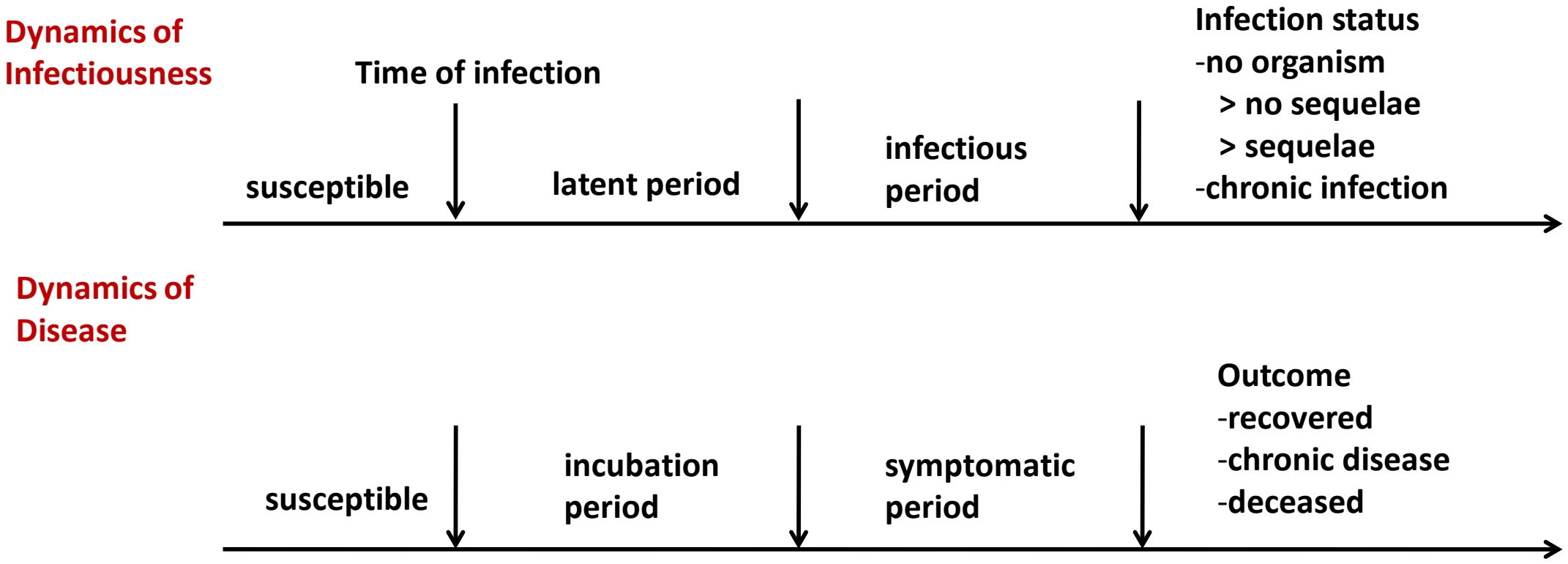
Why: Rationale for methods used
- Disease models
- Natural history
- Association vs. causation

How: Methods, mechanisms, biology

Disease Models

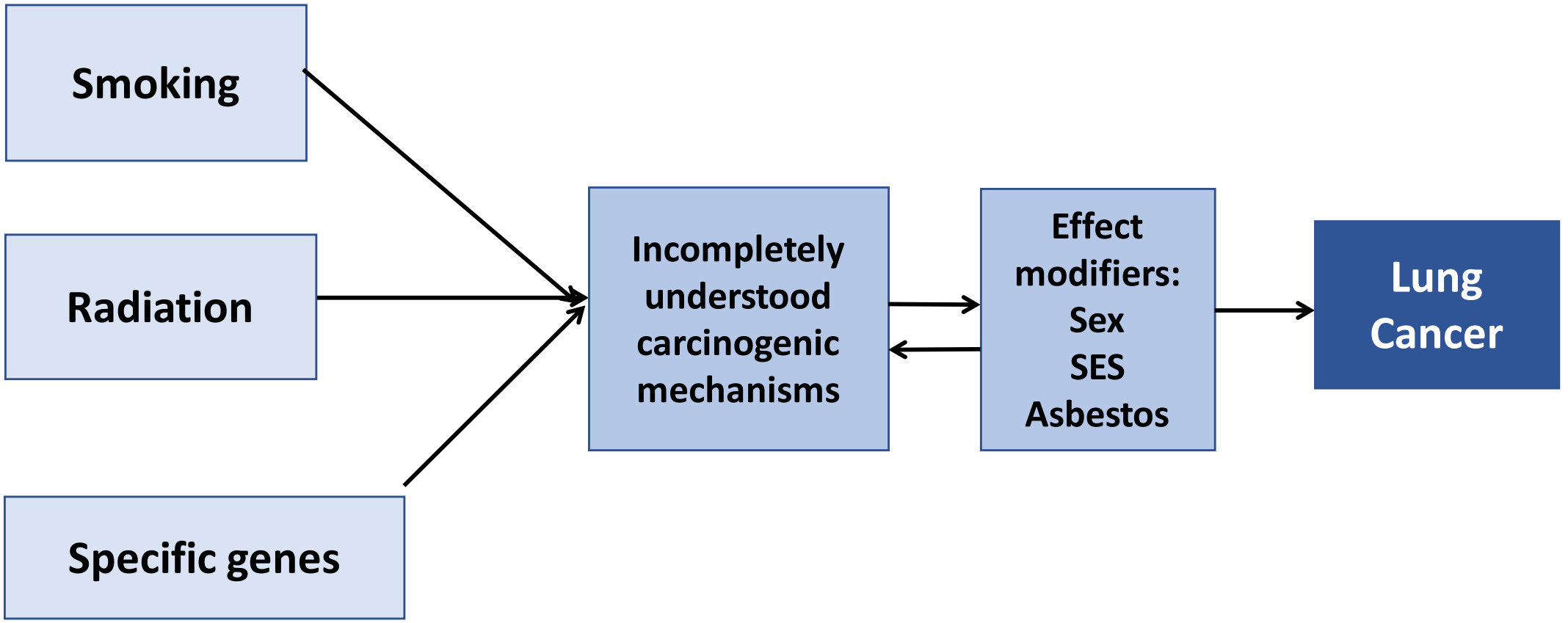
Dynamics of infection and disease



Rothman KJ, Greenland S. Modern Epidemiology, 2nd Edition, 1998

Dynamics of exposure and chronic disease

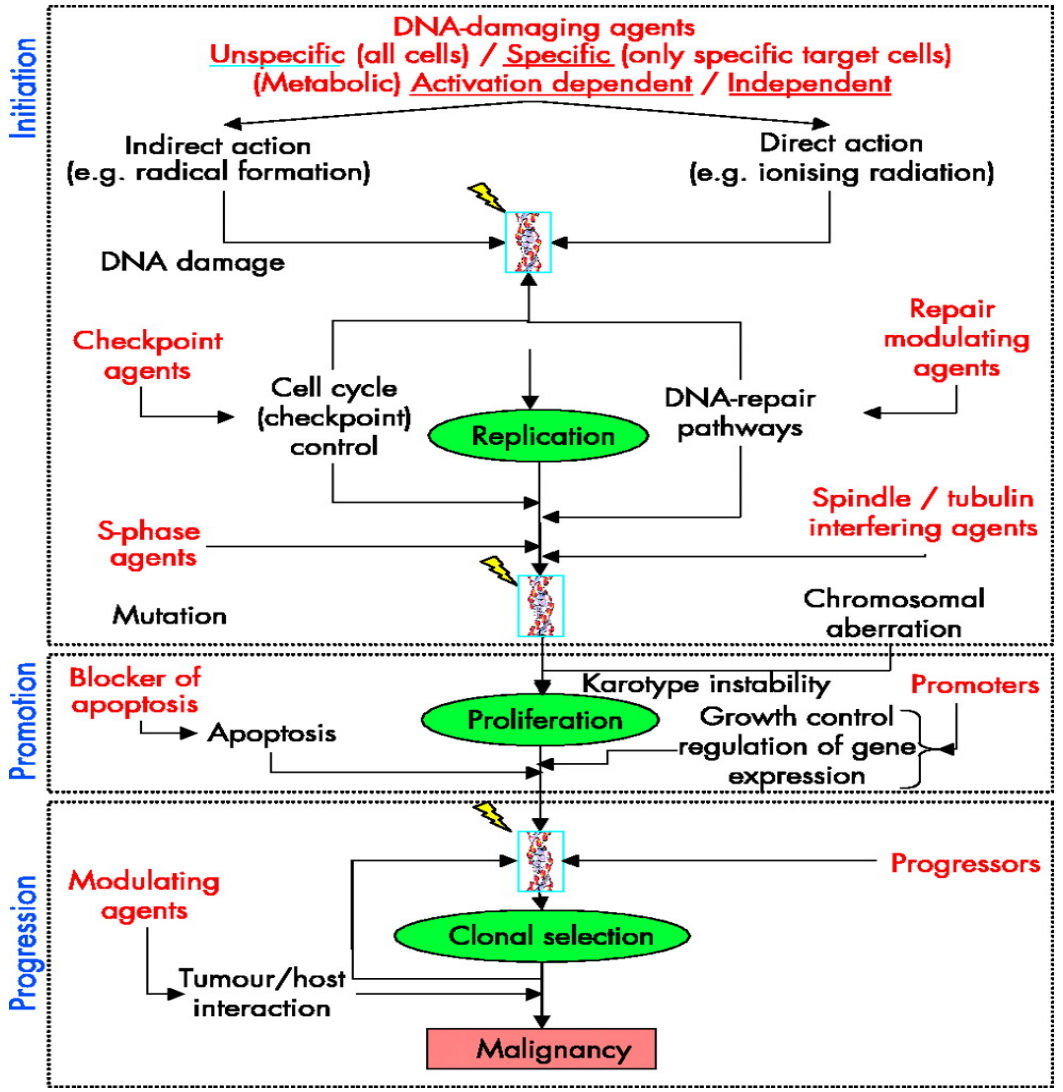
Lung cancer as an example



Natural history

Steps in Malignant Transformation

Figure showing steps in initiation, promotion, and progression for DNA-damaging agents such as radiation



Natural History of Chronic Disease

- **Time periods vary among different steps in process**
- **Time periods may vary for different exposures and different outcomes**

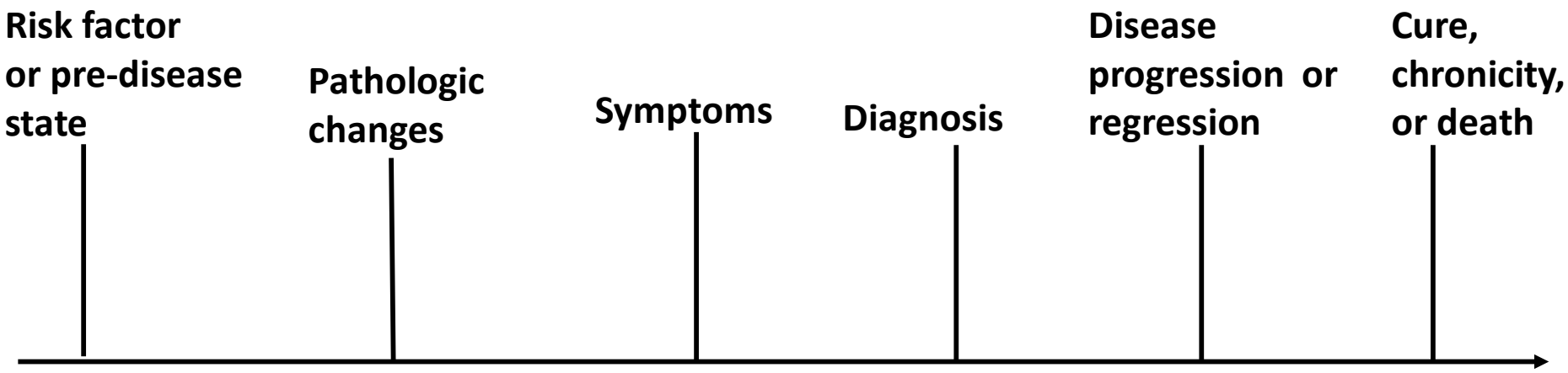
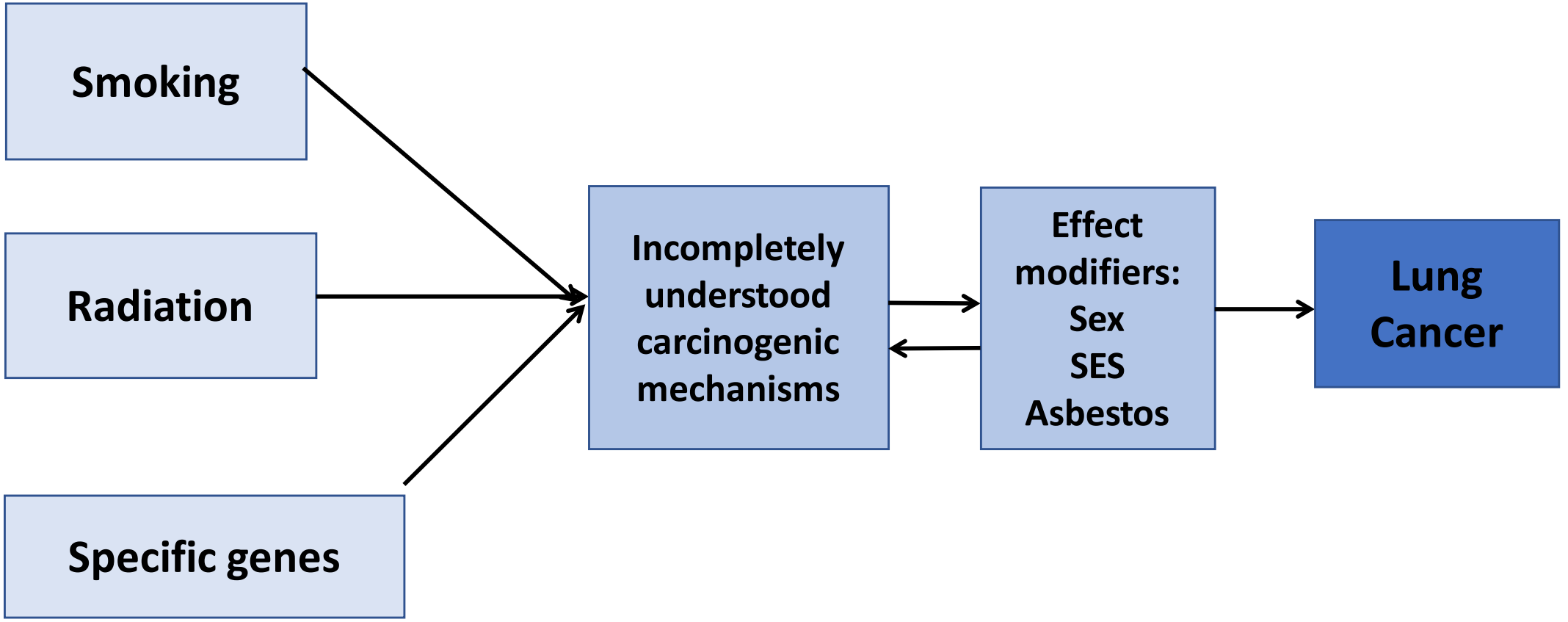


Figure showing steps from pre-disease state through pre-clinical then clinical manifestations to resolution, chronicity or death

Dynamics of exposure and chronic disease

Lung cancer as an example

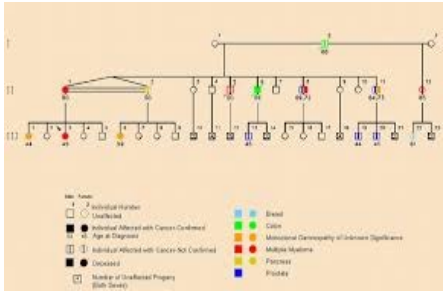


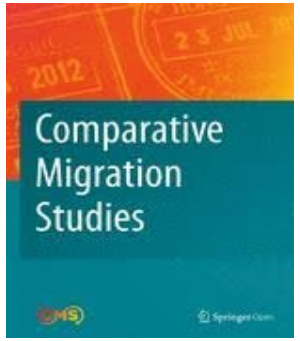
Diseases with Familial Occurrence

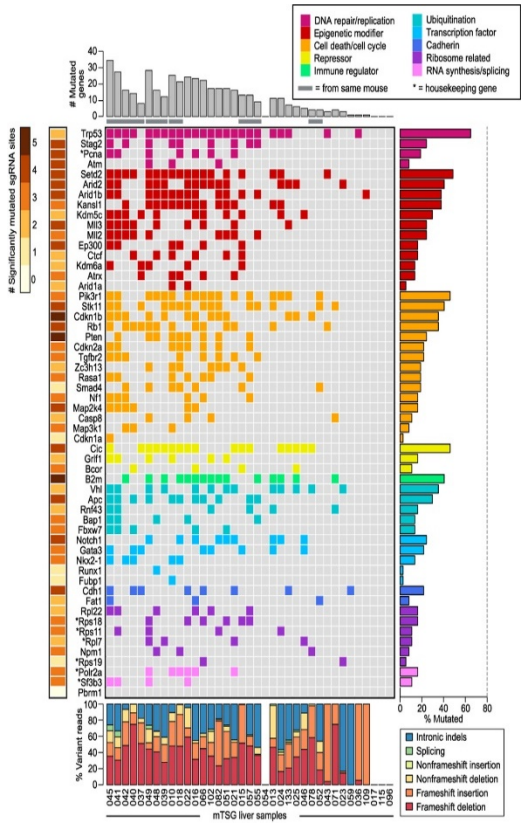
- **Familial occurrence**
  - Rare diseases that are common within affected families (X-linked lymphoproliferative syndrome)
  - Rare genetic syndrome with multiple cases of different phenotypes within affected families (Li-Fraumeni)
  - Small increase in risk within families (sibs with childhood leukemia)
- **Age at onset sometimes notably younger than for sporadic cases**

Genetic vs environmental components of disease

Study goal: to identify	Study type
Familial clustering	Family aggregation
Genetic vs environmental	Twin/adoption/half-sibling/migrant studies
Mode of inheritance	Segregation analysis -single gene -multiple genes
Disease susceptibility loci	Linkage analysis
Disease susceptibility markers	Association studies -population-based -family-based (trios)





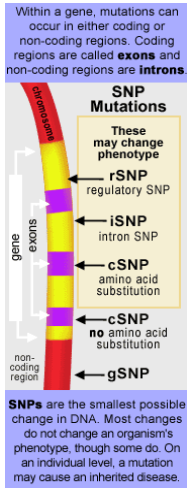


Pictures of pedigree (top left), twins (mid-left), comparative migration (bottom left), and heat map of genes & other (top right)

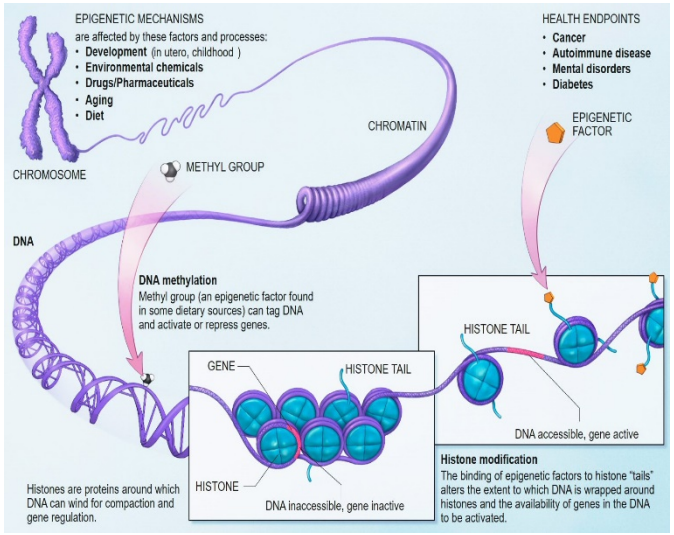
Genetic and other molecular population association studies

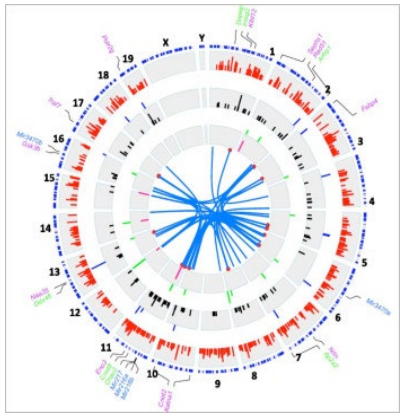
- **Genetic population-based association studies**
  - Genotypes: genome-wide association studies

    (Next Generation Sequencing studies)
    - Germline
    - Somatic
  - Other gene-related
    - RNA
    - Gene expression → metabolic pathways
- **Epigenetics: DNA, RNA methylation**
- **Other molecular studies: O'mics**
  - Proteomics
  - Metabolomics



Pictures of single nucleotide polymorphisms (SNPs) (top left), epigenetics (lower left), and global gene expression regulatory network (lower right)

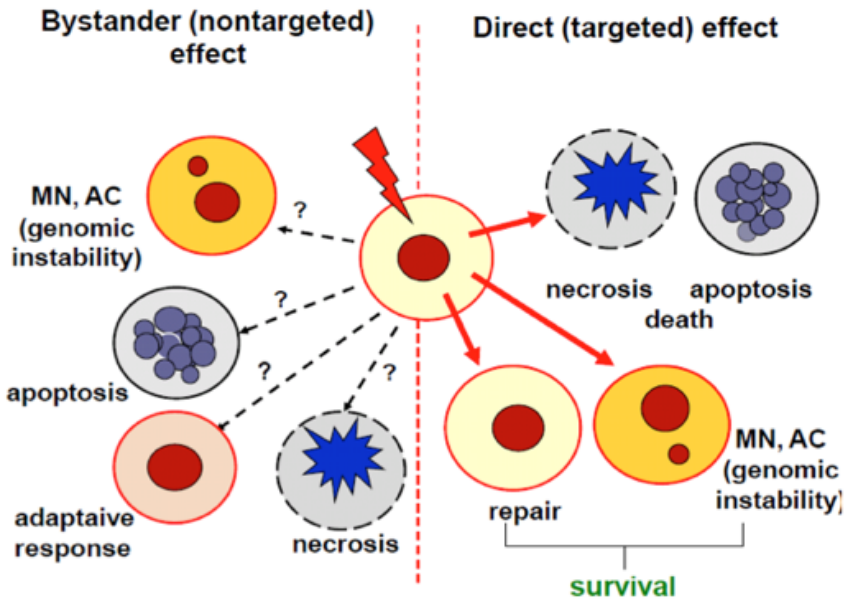




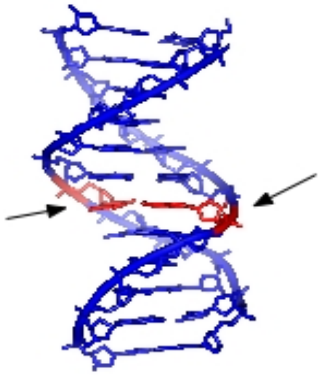
Biology and mechanisms: Radiation carcinogenesis

- **Hallmark of radiation damage**
  - DNA double strand breaks (DSB)
  - Clustered complex lesions
  - DNA repair processes
    - non-homologous end-joining (NHEJ): error prone, can lead to chromosome aberrations
    - homologous recombination (HR): error free

- **Non-targeted effects**
  - Effects in tissues far from 'in-field radiation'
  - Genomic instability: manifests after several generations of cell division



Pictures showing direct (targeted) and bystander (non-targeted) effect (top) and DNA double-strand break (bottom)



Statistical Association versus Disease Causation

Statistical Association

Definition:* Statistical dependence between two or more events, characteristics or other variables. An association is present if the probability of occurrence of an outcome, depends upon the occurrence of one or more exposures or characteristics.

A statistical association does not imply causation

*Modified from Last JM. A Dictionary of Epidemiology, 4th Edition 2001.

Criteria for causation

Criteria	Description
Strength	Level of risk
Consistency	Repeatedly observed in different populations
Specificity	"If…limited to specific workers and to specific types of disease…then clearly that is a strong argument in favor of causation"
Plausibility	"What is biologically plausible depends on the biological knowledge of the day"
Coherence	"…the cause and effect interpretation… should not…conflict with the…known… natural history and biology of the disease"
Experiment	"Occasionally is it possible to appeal to experimental or semi-experimental evidence?"
Analogy	"With the effects of thalidomide and rubella before us we would surely be ready to accept slighter but similar evidence with another drug or another viral disease in pregnancy"

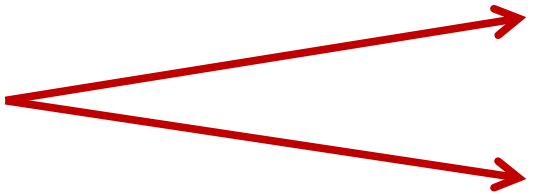
Hill AB. The Environment and Diseases. Association or Causation? Proc R Soc Med 1965:58:295-300

Types of causal associations

Common Cause:

Different outcomes

Radiation



Leukemia

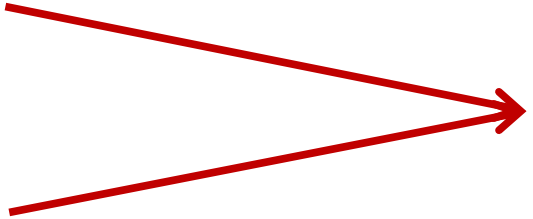
Cataracts

Different Causes

Common outcome

Ultraviolet radiation

Ionizing radiation



Cataracts

Causal model - necessary vs sufficient

- **Necessary: must be present to cause disease**
  (more common with infections: HIV → AIDs)
- **Sufficient: can independently cause disease**
  (acute administration of 20 Gray whole body radiation)

Necessary (+ or -)	Sufficient (S+)	Not sufficient (S-)
Necessary (N+)	**N+S+ (necessary & sufficient)**	**N+S- (necessary but not sufficient)**
Not necessary (N-)	**N-S+ (sufficient but not necessary)**	**N-S- (neither necessary nor sufficient)**

Example: smoking is neither a necessary or sufficient cause of lung cancer

Causal model: Types of non-causal associations

- **Chance association**

- **Bias may result in spurious associations**
  - **Selection bias** (differential selection or participation of exposed vs. unexposed or controls vs. cases)
  - **Recall bias** (differential recall by exposed vs. unexposed or controls vs. cases)
  - **Confounding** (association of disease and an exposure with a third variable may introduce spurious associations)

Multi-factorial disease causation

Individual-level factors

- Sex
- Race/ethnic group
- Lifestyle, behavioral
- Environmental
- Occupational
- Medical
- Genetic predisposition

Societal factors

- Neighborhood
- Cultural
- Economic
- Social
- Environmental

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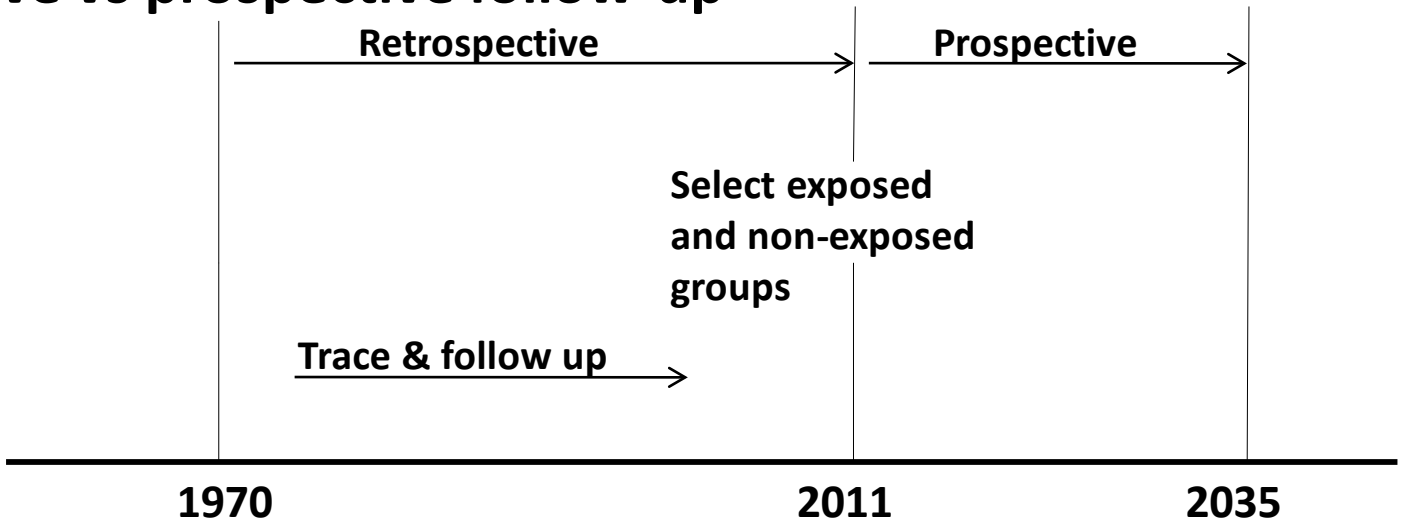
- Natural history
- Association vs. causation

How: Methods, mechanisms, biology

METHODS
Epidemiologic Study Designs

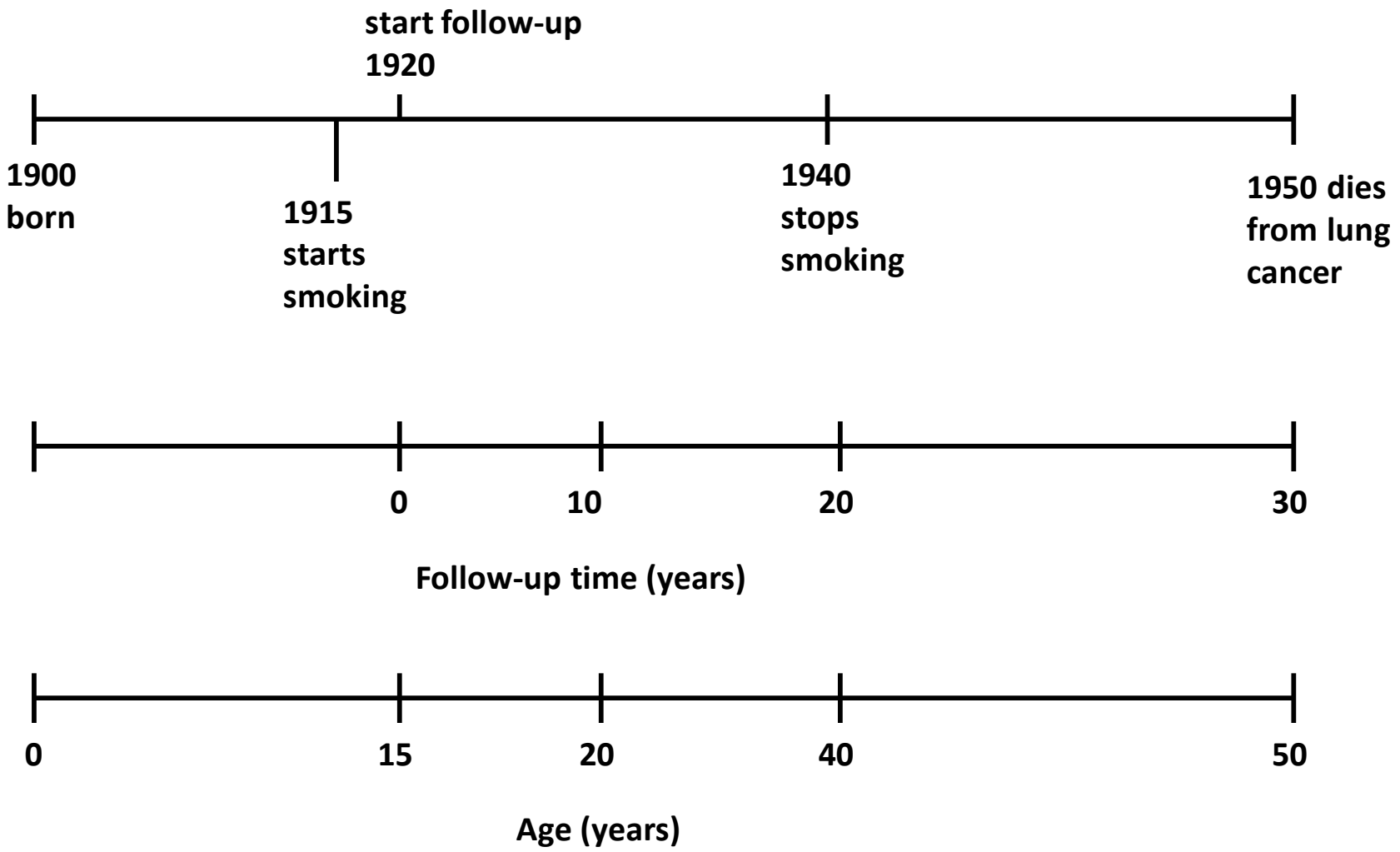
Cohort studies

- **Distinguishing features**
  - population defined by exposures prior to onset of disease
  - population followed over time to estimate disease/death rate
  - compare rates in exposed vs unexposed groups or internal comparison (zero or low-level exposure)
- **Retrospective vs prospective follow-up***



* Retrospective follow-up is by far the most common method used in cohort studies; if high quality methods are used and care is taken, this approach can be just as methodologically sound as a prospective approach

Follow-up: Multiple axes of time



Case-Control Studies

- **Definition:** compare proportion with exposures in diseased cases vs controls
- **Study base:** composed of population at risk of exposure during period of risk of exposure; cases and controls should emerge from same study base & have same exposure opportunity
- **Associations identified from case-control studies:** smoking and lung cancer; DES and vaginal adenocarcinoma; post-menopausal estrogen and endometrial cancer
- **Nested case-control studies**: composed of cases identified from a cohort compared to a random sample or matched controls from the same cohort: Chronic lymphocytic leukemia compared with leukemia excluding chronic lymphocytic leukemia in Chernobyl clean-up workers

Case-Control Studies

- **Distinguishing features**
  - determine exposures prior to diagnosis/referent date using interviews, medical records or other records
  - compare proportion of cases with exposure to proportion of controls with exposure
  - estimate risk using odds ratio = a x d/ b x c
- **Framework**

Characteristics	With disease	Without disease	Total
With exposure	**a**	**b**	**a + b**
Without exposure	**c**	**d**	**c + d**
Total	**a + c**	**b + d**	**a + b + c + d**

Cross-Sectional Studies

- **Not used much in radiation epidemiology except dosimetry studies**
- **Study types**
  - **compare exposures of radiation-exposed groups at a given point in time: problematic without considering earlier exposures, age first exposed, sex, age last exposed, and many other factors**
  - **compare proportion of cases with exposure to proportion of controls with exposure at the time of the study: problematic without considering earlier exposures, age first exposed, sex, age last exposed, and many other factors**

METHODS
Sources of exposure data, strategies for exposure assessment, and types/sources of associated error

Sources of exposure information

- **Measurements**
  - Group: air levels
  - Individual
    - External: badge
    - Internal: blood
- **Questionnaires**
  - Medical history
  - Work history
- **Medical records**
- **Administrative records**
  - birth certificates
  - job records

	Paper-and-pencil	Web-based		
	Mean (SD)	Mean (SD)	ICC (95% CI)	p^a
Mental and psychosocial health				
Vitality index (n = 148)	56.38 (16.42)	56.69 (18.70)	0.79 (0.72–0.84)	0.60
Health behavior				
Number of alcoholic drinks over the whole week (n = 75)	7.85 (7.00)	7.59 (6.21)	0.89 (0.83–0.93)	0.91
Age at start drinking alcohol (n = 131)	17.53 (3.48)	17.32 (3.43)	0.91 (0.88–0.94)	0.14

For each indicator, statistics were calculated among respondents who gave an answer in both modes.

[a] *p* value derived from Wilcoxon signed rank test.

https://doi.org/10.1371/journal.pone.0197434.t004

Pictures of ground radiation monitor (upper left), CT scanner (lower left), radiation badge (upper right) and questionnaire (immediately above)

Strategies for exposure assessment

Strategies for exposure assessment	Component
Definition: Process of estimating magnitude, frequency, and duration of exposure to an agent	- Who is exposed? - Agent location: air, water, skin, other - Intensity, frequency, duration
Exposure pathway	Source to receptor
Exposure route	- Inhalation - Ingestion - Skin
'Direct' measurements	- Personal sampling - Biological sampling
Surrogate measurements	Job title, residence general location

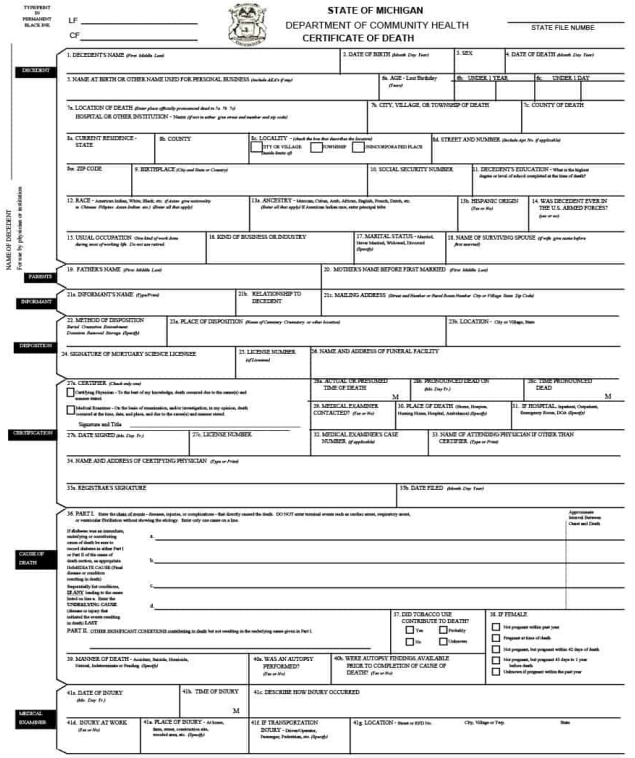
Types and sources of exposure measurement error

Types/sources of error	Description
Classical measurement error	Random error in dose measurement
Berkson measurement error	Error when the mean for a group is substituted for the individual dose
Shared error	Error when incorrect group mean is assigned to all individuals in group
Differential error	Dose estimation error that is not independent of case status
Non-differential error	Dose estimation error independent of case status
Missing dose	Doses of subjects not accounted for in dose-response analyses

METHODS
Sources of outcome data, strategies for ascertaining outcomes, and types/sources of associated error

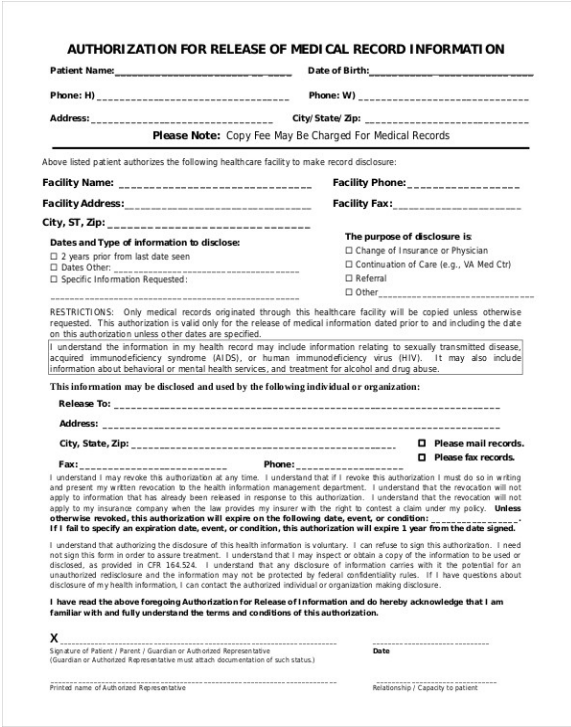
Sources of Outcome Information

- **Vital records**
  - death certificates
  - birth certificates
- **Morbidity surveys**
  - Health Interview Survey
  - Health Examination Survey
- **Disease notification & registration**
  - Cancer registries
  - Infection notification
  - Electronic medical records



STATE OF MICHIGAN
DEPARTMENT OF COMMUNITY HEALTH
CERTIFICATE OF DEATH

STATE FILE NUMBE



AUTHORIZATION FOR RELEASE OF MEDI CAL RECORD INFORMATI ON

Patient Name: _____ Date of Birth: _____

Phone: H) _____ Phone: W) _____

Address: _____ City/ State/ Zip: _____

Please Note: Copy Fee May Be Charged For Medical Records

Above listed patient authorizes the following healthcare facility to make record disclosure:

Facility Name: _____ **Facility Phone:** _____

Facility Address: _____ **Facility Fax:** _____

City, ST, Zip: _____

Dates and Type of information to disclose:

☐ 2 years prior from last date seen
☐ Dates Other: _____
☐ Specific Information Requested:

The purpose of disclosure is:

☐ Change of Insurance or Physician
☐ Continuation of Care (e.g., VA Med Ctr)
☐ Referral
☐ Other _____

RESTRICTIONS: Only medical records originated through this healthcare facility will be copied unless otherwise requested. This authorization is valid only for the release of medical information dated prior to and including the date on this authorization unless other dates are specified.

I understand the information in my health record may include information relating to sexually transmitted disease, acquired immunodeficiency syndrome (AIDS), or human immunodeficiency virus (HIV). It may also include information about behavioral or mental health services, and treatment for alcohol and drug abuse.

This information may be disclosed and used by the following individual or organization:

Release To: _____

Address: _____

City, State, Zip: _____ ☐ **Please mail records.** ☐ **Please fax records.**

Fax: _____ **Phone:** _____

I understand I may revoke this authorization at any time. I understand that if I revoke this authorization I must do so in writing and present my written revocation to the health information management department. I understand that the revocation will not apply to information that has already been released in response to this authorization. I understand that the revocation will not apply to my insurance company when the law provides my insurer with the right to contest a claim under my policy. **Unless otherwise revoked, this authorization will expire on the following date, event, or condition: _____. If I fail to specify an expiration date, event, or condition, this authorization will expire 1 year from the date signed.**

I understand that authorizing the disclosure of this health information is voluntary. I can refuse to sign this authorization. I need not sign this form in order to assure treatment. I understand that I may inspect or obtain a copy of the information to be used or disclosed, as provided in CFR 164.524. I understand that any disclosure of information carries with it the potential for an unauthorized redisclosure and the information may not be protected by federal confidentiality rules. If I have questions about disclosure of my health information, I can contact the authorized individual or organization making disclosure.

I have read the above foregoing Authorization for Release of I nformation and do hereby acknowledge that I am familiar with and fully understand the terms and conditions of this authorization.

X _____ _____

Signature of Patient / Parent / Guardian or Authorized Representative (Guardian or Authorized Representative must attach documentation of such status.) **Date**

_____ _____

Printed name of Authorized Representative Relationship / Capacity to patient

Pictures of death certificate template (left) and medical Record release form (right)

Strategies for outcome assessment

Strategies for outcome assessment	Component
Definition: Process of ascertaining disease outcomes in study populations (e.g., in exposed and comparison cohorts and target population(s) for case-control studies)	- Cohort studies: comprehensive follow-up; linkage with outcome sources, questionnaires, surveys, and other databases to achieve complete ascertainment - Case-control studies: multiple sources of outcomes (hospitals, clinics, national/regional healthcare organizations, health maintenance organizations)
Specific outcome(s) to be evaluated	- Mortality vs. incidence or both - Specific diseases
Disease classification	- International classification of diseases (ICD) revision(s) - International classification of diseases for oncology ICD-O) revision(s) - Special classifications

Types and sources of outcome assessment error

Types/sources of error	Description
Loss to follow-up (LTF)	Usually due to re-location and loss of contact, discontinued participation; date of LTF can be known or unknown
Under-ascertainment	Outcomes not identified or misclassified as another condition
Over-ascertainment	May occur due to screening, or a precursor is identified as the outcome
Misclassification	Incorrect classification
Changes in classification over time	Generally increased specificity of histologic/molecular subtypes

METHODS

Confounding
Selection bias
Recall bias

Confounding, selection bias, recall bias

Sources of potential bias: definitions	Examples
Confounding: comparison groups may differ from exposed groups (cohort studies) or from the cases (case-control studies) by factors related to the disease of interest	A population exposed to occupational radiation may undergo more diagnostic imaging exams than the comparison group; smoking
Selection bias: comparison groups may differ from exposed groups (cohort studies) or from the cases (case-control studies)	Controls may be of higher SES than the case-group in case-control studies
Recall bias: comparison groups may inaccurately recall more or less than comparable exposed groups (cohort studies) or the cases (case-control studies	Mothers of children with pediatric leukemia may have enhanced recall of pesticide exposures in pregnancy than mothers of control children

Radiobiology and mechanisms: Key adjuncts to epidemiology

- **Limits of epidemiology, an observational science**
  - Rare outcomes, population size limits, uncertainties, bias
  - Generally consistent exposure-response at moderate-to-high radiation doses, but inconsistent at low (<100 milligray) doses
  - Need for extrapolation from moderate-to-high to low doses (LNT model)
- **Experimental studies**
  - Control dose, dose-rate, timing, population size, species
  - Evaluate effect modification, risks in susceptible subgroups
  - Lifetime follow-up is shorter in animal models
- **New approach needed**
  - Combined approach: biologically-based dose-response models

- Preston RJ. Integrating basic radiobiological science and epidemiological studies: why and how. Health Phys 2015;103:125-130.
- NCRP SC 1-26. Approaches for integrating radiobiology and radiation epidemiology for enhancing low-dose risk assessment (forthcoming).

Combine radiation epidemiology and radiobiology

- **New combined approach needed: biologically-based dose-response models that incorporate:**
  - Sophisticated exposure assessment with fully validated exposure biomarkers
  - Multiple approaches/data sources for complete follow-up and outcome ascertainment
  - Knowledge of multi-factorial disease causation
  - Efforts to identify effect modifiers and susceptible subgroups
  - Efforts to fully address potential confounders
  - Quantitative mechanistic data into biologically-based disease models
  - Biomathematical disease models
- **Future research is needed to identify:**
  - Adverse outcome pathways
  - Key events on the pathways
- **Objectives: risk protection measures and risk prevention**

Summary - 1

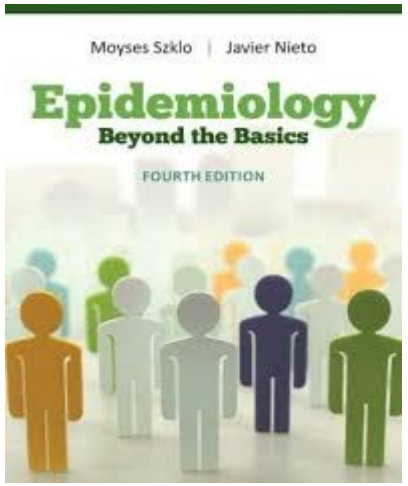
- Epidemiology: history and definitions
- Descriptive patterns and trends
- Disease classifications
- Disease models
- Natural history
- Statistical association vs disease causation

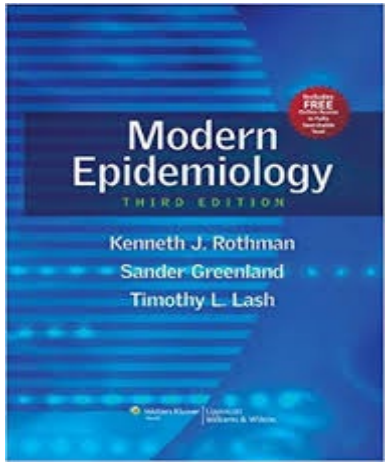
Summary - 2

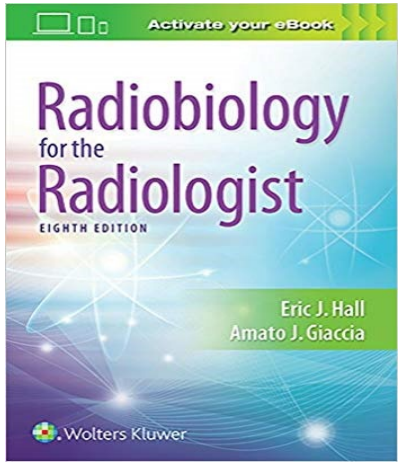
- Epidemiologic study designs: cohort, case-control and cross-sectional studies
- Sources of exposure data, strategies for exposure assessment, and associated errors
- Sources of outcome data, strategies for outcome assessment, and associated errors
- Confounding, selection bias, recall bias
- Radiobiology and mechanisms

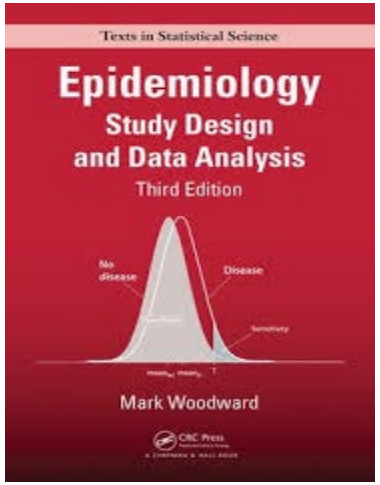
References

- Szklo M and Nieto J. Epidemiology: Beyond the basics. Fourth edition. Jones and Bartlett Learning, Burlington MA, 2019.
- Woodward M. Epidemiology: Study design and data analysis. Third edition. CRC Press, 2013.
- Rothman KJ, Greenland S, Lash TL. Modern epidemiology. Third edition. Wolters Kluwer, 2012.
- Hall EJ, Giaccia AJ. Radiobiology for the radiologist. Eighth edition. Wolters Kluwer, 2018.









NCRP SC 1-26. Approaches for integrating radiobiology and radiation epidemiology for enhancing low-dose risk assessment (forthcoming).

Questions

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2. The risk of a certain event happening in one group compared to the risk of the same event happening in another group
3. The observed or calculated probability of occurrence of an event in a population related to a specific exposure
4. The change in a quantity per unit time

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- Which one is not a criterion for causation?

1. Plausibility
2. Experimental evidence
3. Confounding
4. Strength

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