Department of Clinical Sciences

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The *Right* Study Design to Answer the Right Research Question

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Asking the Right Question

A Well-built Research Question should:

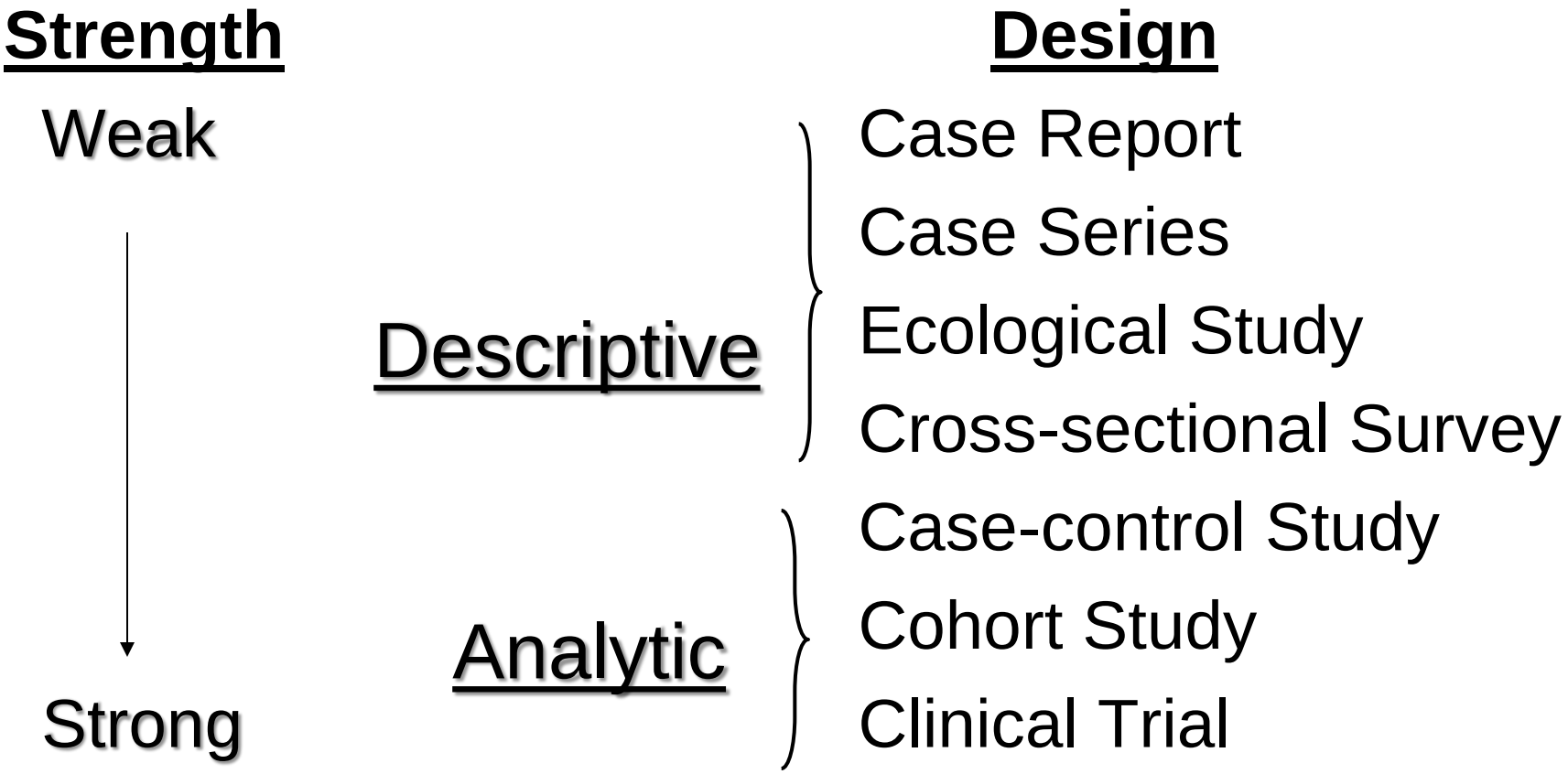
- Be specific with no ambiguity about
  -population,
  -subjects,
  -variables
- Be stated in writing at the outset of the study
- Direct the study design

Asking the Right Question

A Good Research Question is:

- Feasible
- Ethical
- Relevant and interesting
- *Novel…maybe!*

Strength of Evidence



Case Report / Case Series

- Anecdotal Reports of Interesting Observations
  - Unusual cluster of symptoms
  - Departure from a normal pattern of known disease
  - Repetitive disease occurrence among people with a specific exposure

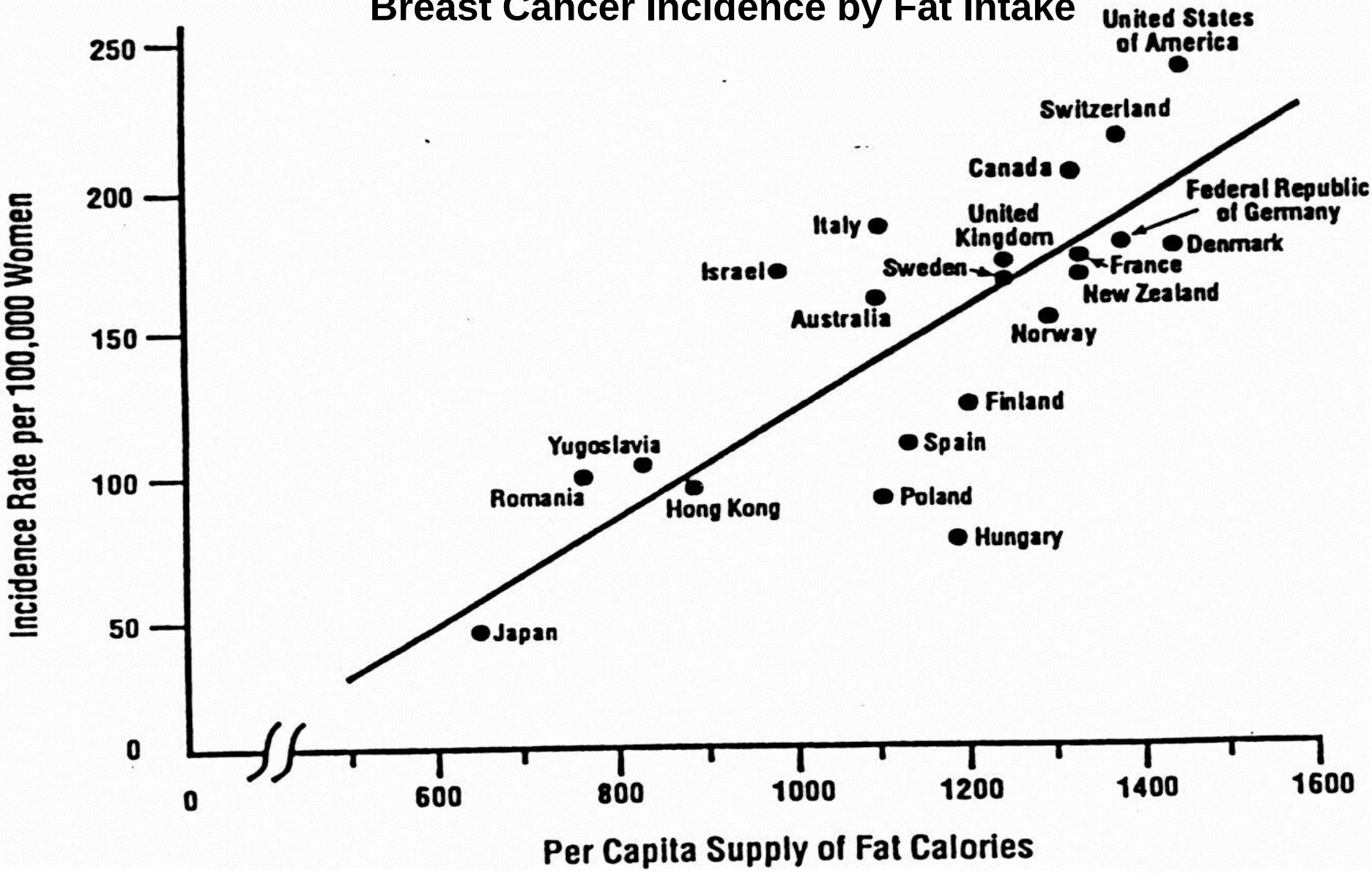
- Cluster of observations in short time period or small geographic area
  - New epidemic of known disease
  - New disease occurrence
  - New cause of existing disease

Ecologic Studies

- Evaluation of associations between exposures and outcomes in populations rather than individuals
- *Ecological Fallacy*

  -results from making causal inferences about individual phenomena based on observations of group

Breast Cancer Incidence by Fat Intake

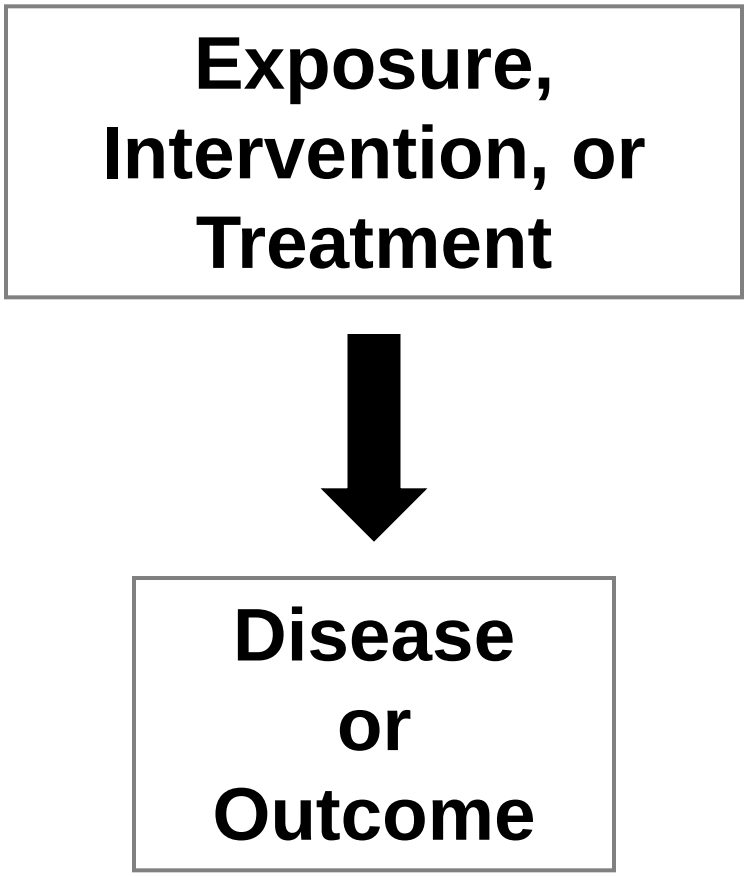


Cross-Sectional Studies

- Provide “snapshots” of the health of a specified population at one moment in time.
- Usually descriptive in nature
- Often used to determine ‘prevalence’ of a condition or correlation between 2 variables
- Temporality cannot be determined → ‘chicken or egg problem’
- Low cost and no loss to follow-up

Analytic (Observational) Studies

- **Case Control study**
- **Cohort Study**



Case Control Study

- Select subjects with outcome/disease of interest (Cases)
- Select similar group of individuals without disease/outcome of interest (Controls)
- Determine exposure status of all subjects

	Cases (With Disease)	Controls (Without Disease)
Exposed	a	b
Not exposed	c	d
Total	a + c	b + d

Case Control Study Advantages

- Quick and easy
- Able to study multiple risk factors simultaneously
- Efficient for rare diseases
- Requires ‘small-ish’ sample sizes

Case Control Study Disadvantages

- Cannot address causality
- Cases may reflect survival benefit
- Only investigates 1 disease outcome
- Can only compare odds of exposure; not incidence of outcome
- High, **HIGH** likelihood of bias

Control Sources

- General population controls
- Hospitalized individuals
- Neighborhood residents
- Spouses / relatives/ friends of case

ODDS RATIOS

In a case control study, we use the **ODDS RATIO** to estimate the odds of a case being exposed versus the odds of a control being exposed.

ODDS RATIO (OR) = AD/BC

	Cases (Disease)	Controls (No Disease)
Exposure	**A**	**B**
No Exposure	**C**	**D**

OR = Odds of case exposed / Odds of control exposed $= \frac{A}{C} \Big/ \frac{B}{D}$ or $= AD/BC$

Interpreting an Odds Ratio

If OR = 1

- Odds of exposure is equal between groups (no association)

If OR > 1

- Odds of exposure is greater in cases than in controls (positive association);

If OR < 1

- Odds of exposure in cases is less than odds of exposure in controls (negative association; possibly protective)

Example of an Odds Ratio

History of Alcohol and Tobacco Exposure Among Males with Advanced Laryngeal Cancer Before Diagnosis

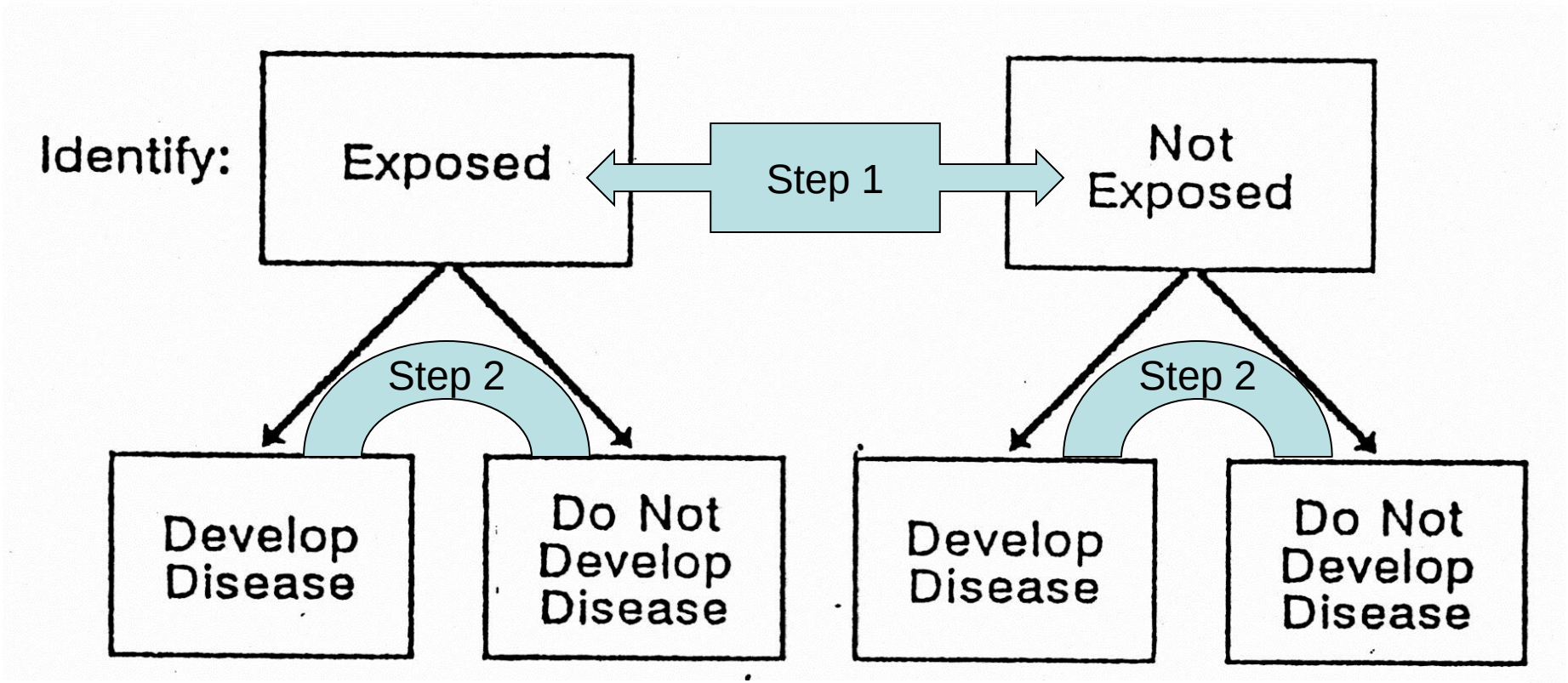
	CASES Laryngeal Cancer	CONTROLS No Cancer Hx
Heavy Alcohol & Tobacco Use	25	10
One or None	50	80
Total	75	90

$$OR = \frac{ad}{bc} = \frac{25*80}{50*10} = \frac{2000}{500} = 4.0$$

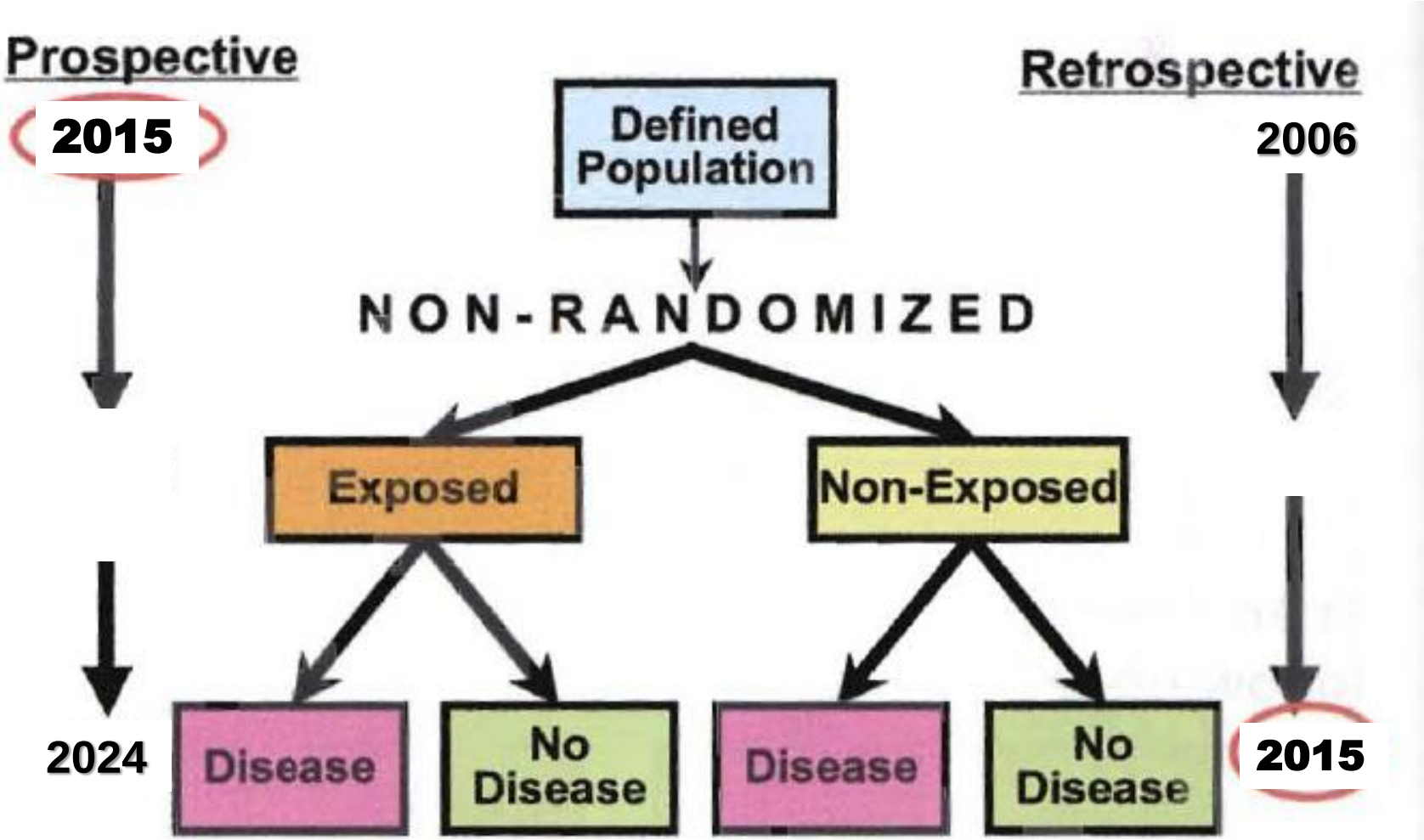
Cohort Studies

- Designed to address a specific hypothesis;
- Select a group of subjects exposed to factor of interest (risk factor/treatment) and a group **not** exposed
- **OR** select a group of subjects and then categorize them by presence or absence of risk / exposure / treatment
- Collect additional data related to other factors that may confound (bias) the association
- Prospectively follow both the exposed and unexposed group to determine occurrence of outcome of interest

Cohort Studies



Prospective & Retrospective Cohort Studies



Concurrent (Prospective) Cohort Study

- Exposure status collected in present time and subjects followed forward in time for outcome of interest;
- Disease has short induction and latency period
- Exposure is current or recent
- Want high-quality data

Non-concurrent (retrospective) Cohort Study

- Past exposure status established from previously collected data; subjects followed **forward** to present time or future to examine outcome
- Disease has long induction and latent period
- Historical exposure data available
- Desirable to save time and money

Calculation of Relative Risk in a Cohort Study

	Outcome		Incidence
	Yes	**No**	
Exposed	a	b	a/(a+b)
Not exposed	c	d	c/(c+d)

Relative Risk (RR) = incidence of disease in exposed divided by incidence of disease in the unexposed

RR = (a/a+b) / c/c+d)

Interpreting the Relative Risk of a Disease

If RR = 1

- Risk in exposed equal to risk in unexposed (no association)

If RR > 1

- Risk in exposed greater than risk in unexposed (positive association);

If RR < 1

- Risk in exposed less than risk in unexposed (negative association; possibly protective)

Table 8–1. Design of a Cohort Study

		Then Follow to See Whether			
		Disease Develops	*Disease Does Not Develop*	Totals	Incidence Rates of Disease
First select	Exposed	a	b	$a + b$	$\frac{a}{a + b}$
	Not exposed	c	d	$c + d$	$\frac{c}{c + d}$

Table 8–2. Results of a Hypothetical Cohort Study of Smoking and Coronary Heart Disease (CHD)

		Then Follow to See Whether			
		Develop CHD	*Do Not Develop CHD*	Totals	Incidence per 1,000 per Year
First select	Smoke cigarettes	84	2,916	3,000	28.0
	Do not smoke cigarettes	87	4,913	5,000	17.4

Advantages of Cohort Studies

- Cases are incident cases and may be more representative of all cases of the disease
- Provides more information on the natural history of a disease
- Incidence rates are available
- Fewer sources of bias
- Temporal relationship between exposure and disease can be established
- Able to study a rare exposure and a common disease

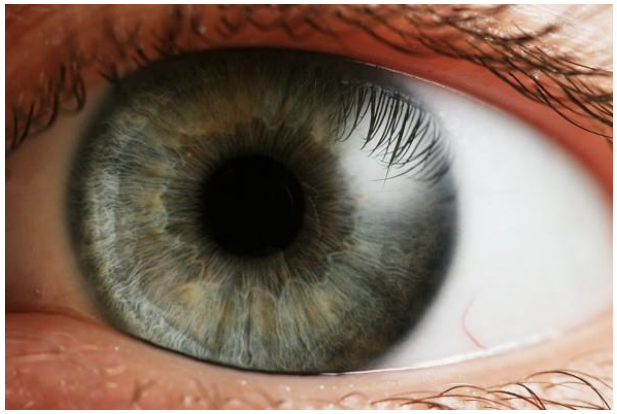
Disadvantages of Cohort Studies

- Duration may be long with difficulty maintaining consistent study methods and staff
- Expensive
- Large population required
- Exposure may not have been measured at baseline or may change
- Rare diseases cannot be studied

When is a Prospective Study the RIGHT Design

- Good evidence of an association between an exposure and a disease exists;
- Attrition of study population can be minimized;
- Ample funds are available;
- The investigator has a long life-expectancy

REMEMBER….



Observational studies may be fraught with bias!

<u>Proceed Cautiously</u>