

# **Identifying Study Designs**

340.721

Epidemiologic Inference in Public Health I

# Learning objectives

- Review and compare epidemiologic study designs
- Contrast different study designs by designing an epidemiologic study
- Name epidemiologic study designs based on information provided in abstracts of published papers
  - Look for clues to the design used



# Summary of Study Designs

## Main Types of Epidemiologic Studies

Study type	Characteristics
Experimental	<ul style="list-style-type: none"><li>Studies prevention and treatment of disease</li><li>Investigator actively manipulates which groups receive the study agent</li></ul>
Observational	<ul style="list-style-type: none"><li>Studies causes, prevention and treatment for diseases</li><li>Investigator watches as nature takes its course</li></ul>
Cohort	<ul style="list-style-type: none"><li>Examines multiple health effects of an exposure</li><li>Subjects defined by exposure levels and follow for disease occurrence</li></ul>
Case-control	<ul style="list-style-type: none"><li>Typically examines multiple exposures in relation to a disease</li><li>Subjects are defined as cases and controls and exposure histories compared</li></ul>
Cross-sectional	<ul style="list-style-type: none"><li>Examine relationship between exposure and disease prevalence in a defined population at one point in time</li></ul>
Ecological	<ul style="list-style-type: none"><li>Examines relationship between exposure and disease with population-level data rather than individual data</li></ul>

# Experimental Study Designs

## Main Types of Epidemiologic Studies

Study type	Characteristics
Experimental	<ul style="list-style-type: none"><li>• Studies prevention and treatment of disease</li><li>• Investigator actively manipulates which groups receive the study agent</li></ul>

= Randomized Trial

# Design of a **Randomized Trial**

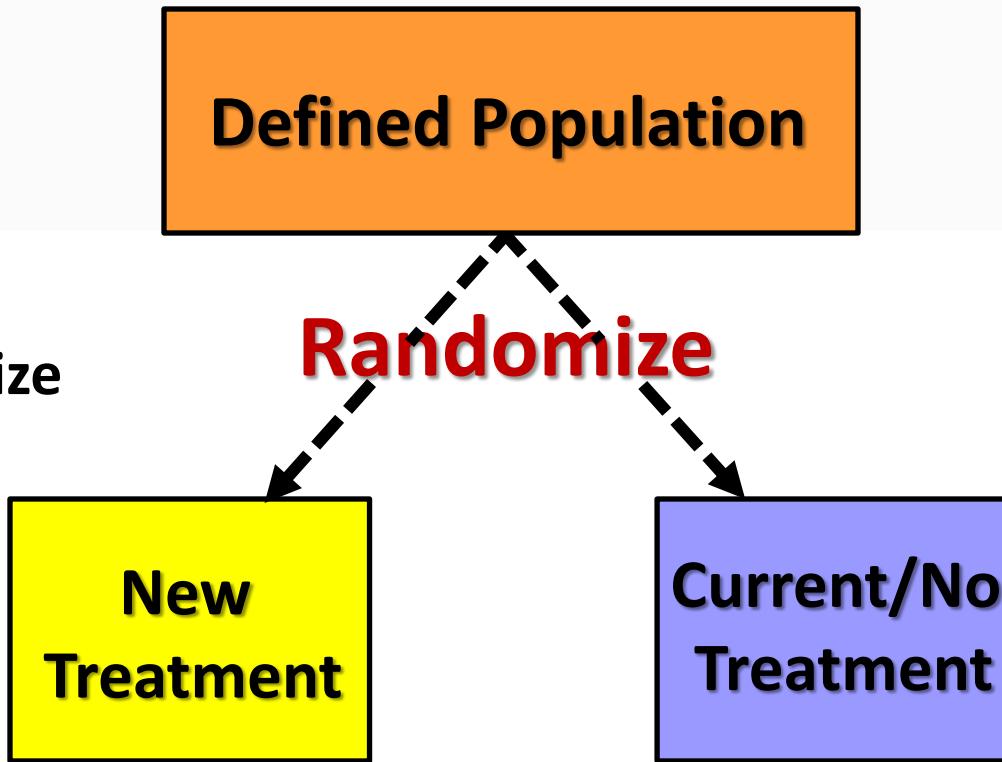
Start  
with:

**Defined Population**

# Design of a **Randomized Trial**

Start  
with:

Then randomize  
to treatment:



# Design of a **Randomized Trial**

Start  
with:

Defined Population

Then randomize  
to treatment:

Randomize

New  
Treatment

Current/No  
Treatment

Then  
follow  
up:

Improve

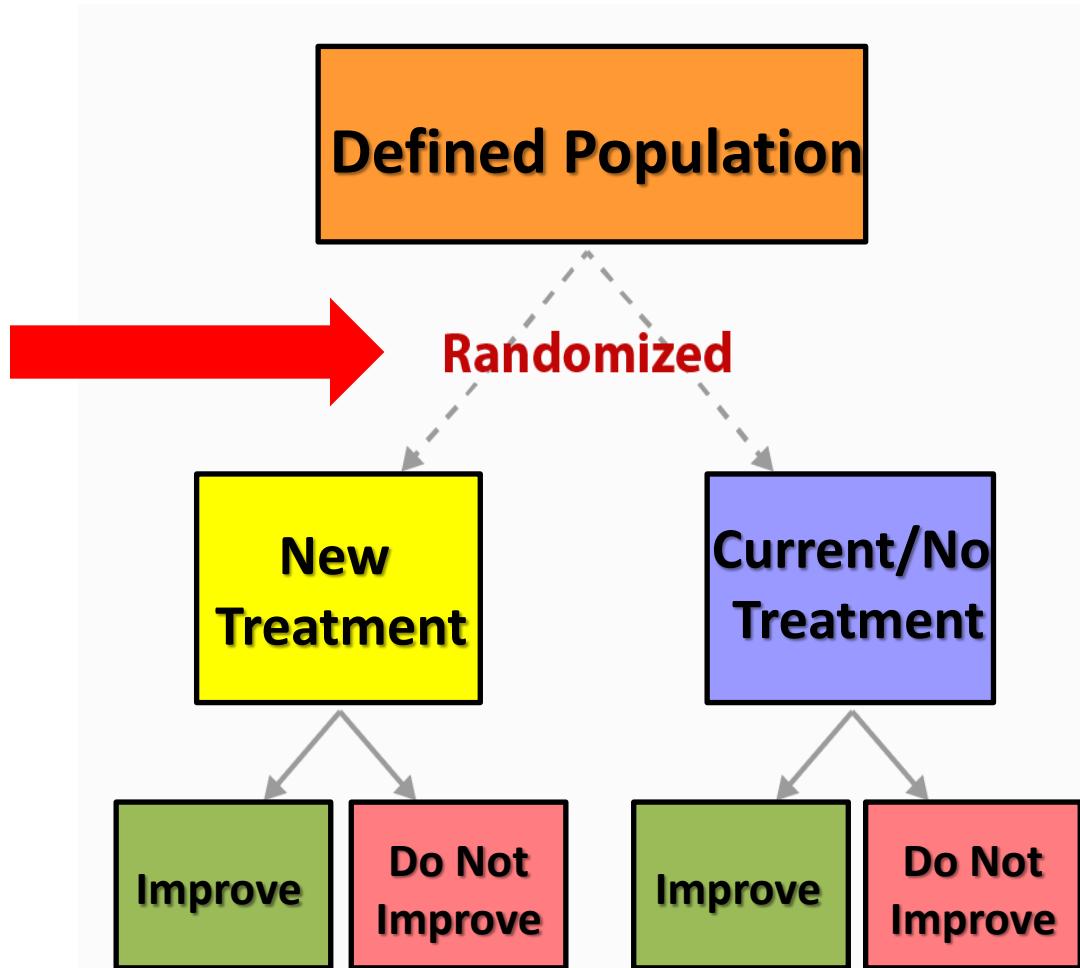
Do Not  
Improve

Improve

Do Not  
Improve

# What is the primary purpose of randomization?

- To prevent bias in the choice of treatment



# Observational Study Designs

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Population-level data

Individual-level data

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**Individual-level data**

# Design of a **Cohort Study**

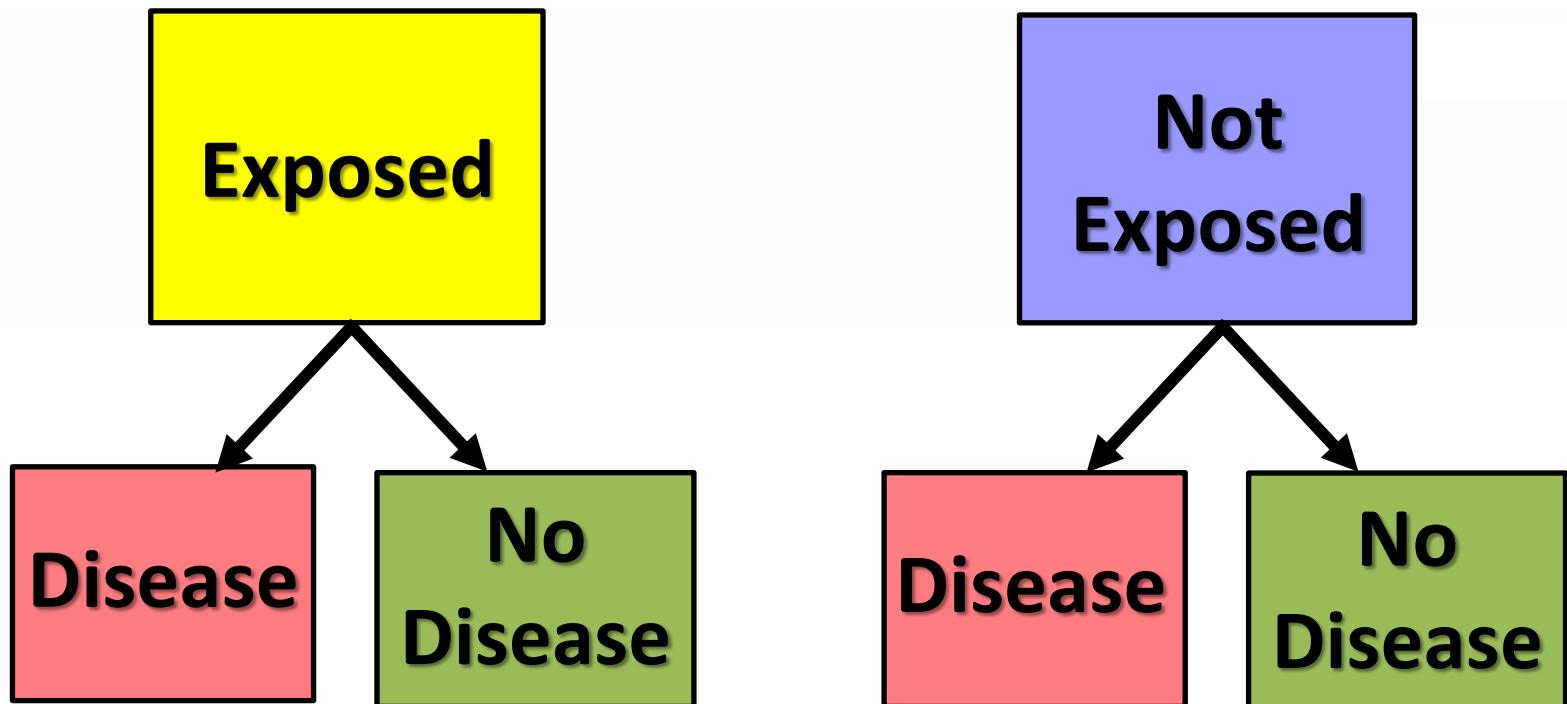
Start  
with:

**Exposed**

**Not  
Exposed**

# Design of a **Cohort Study**

Start  
with:



Then  
follow  
up:

# Alternative Design of a **Cohort Study**

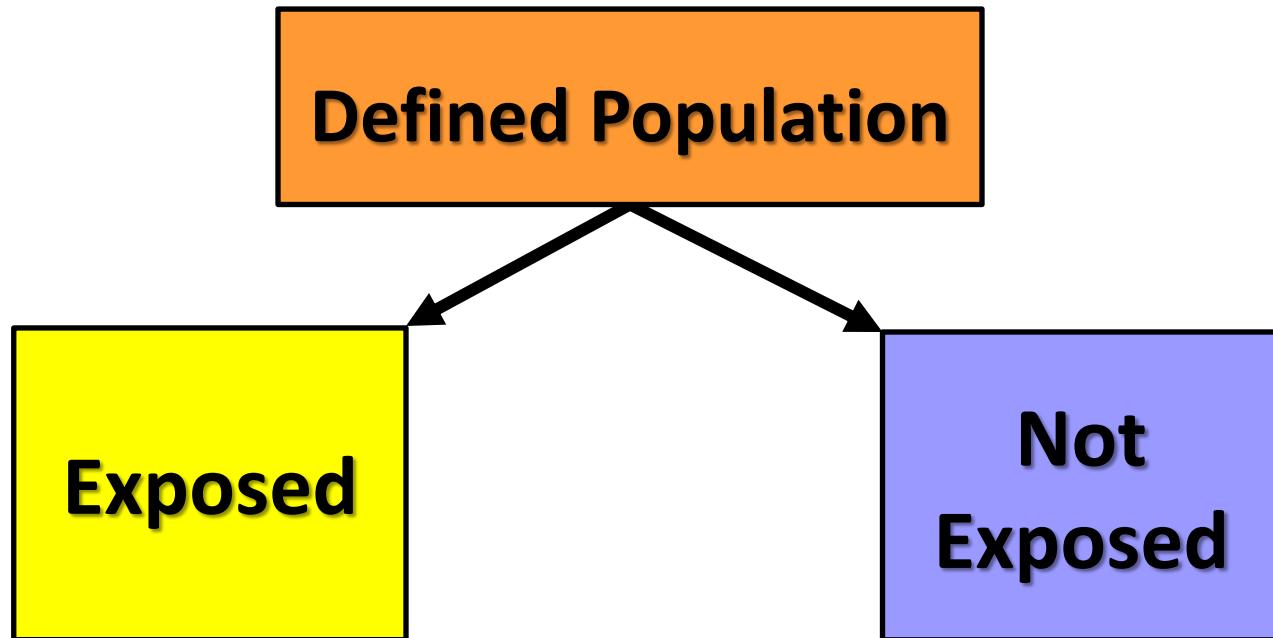
Start  
with:

**Defined Population**

# Alternative Design of a **Cohort Study**

Start  
with:

Then  
measure:

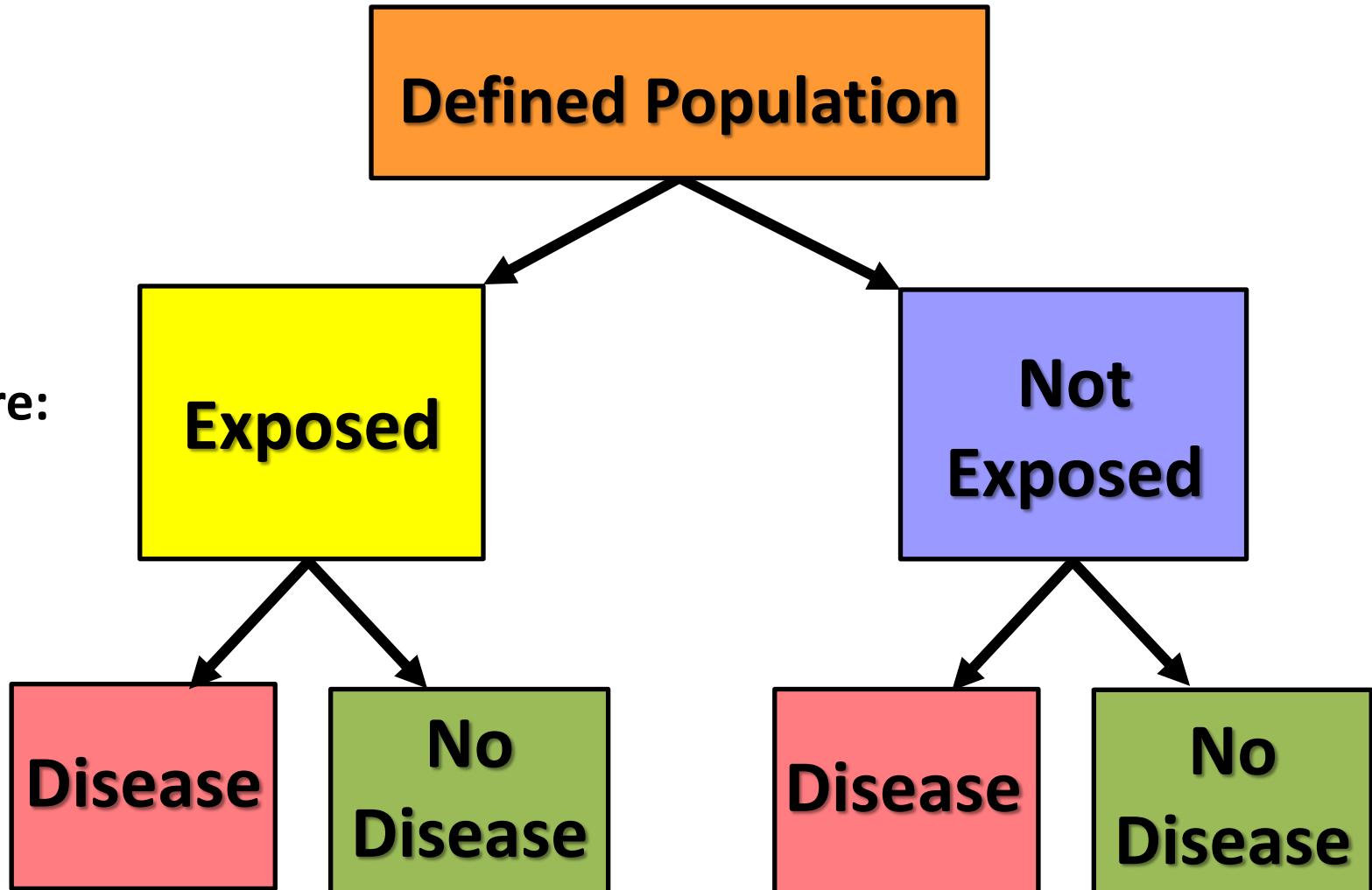


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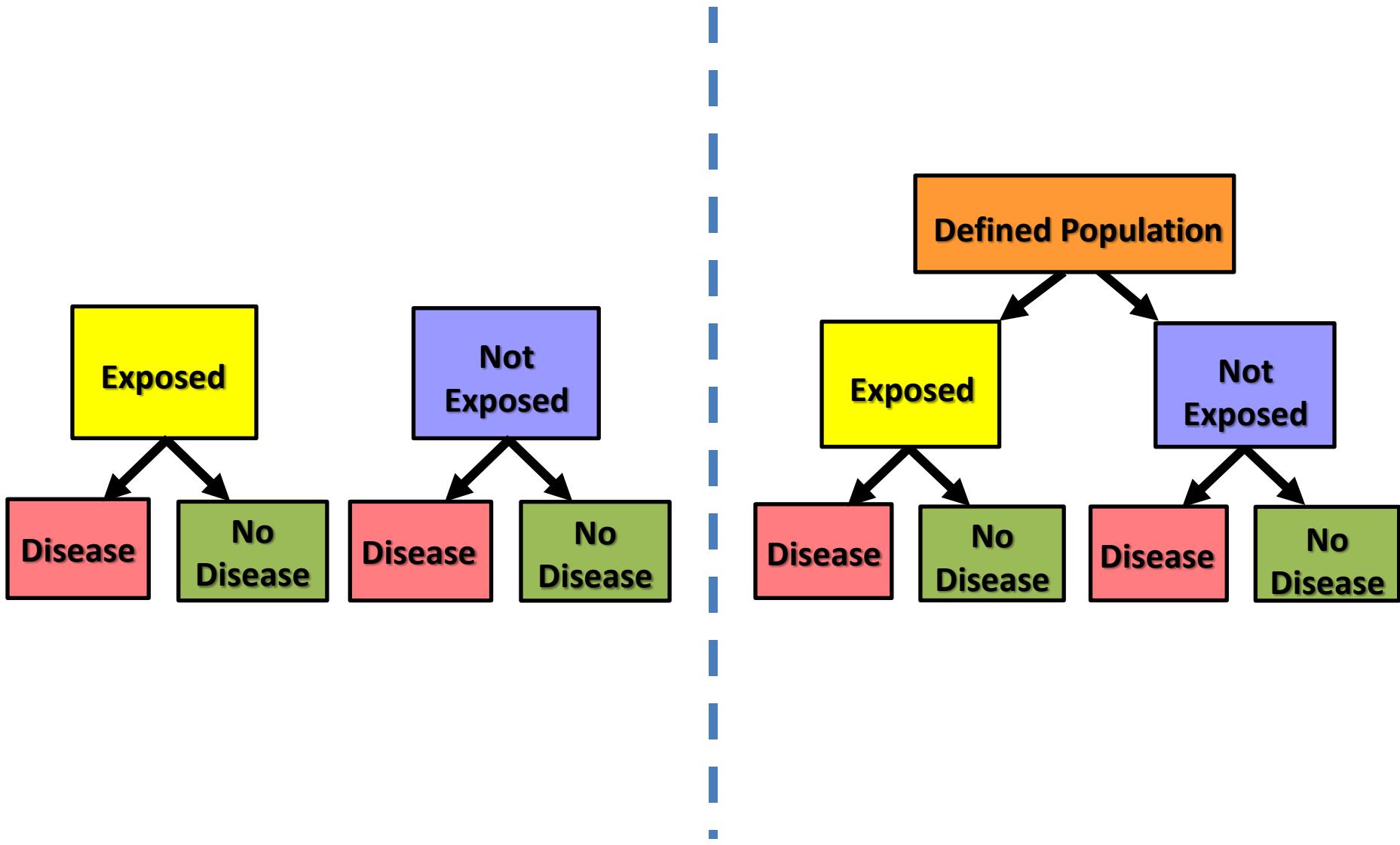
Start  
with:

Then  
measure:

Then  
follow  
up:



# Design of a **Cohort Study**



# Observational Study Designs

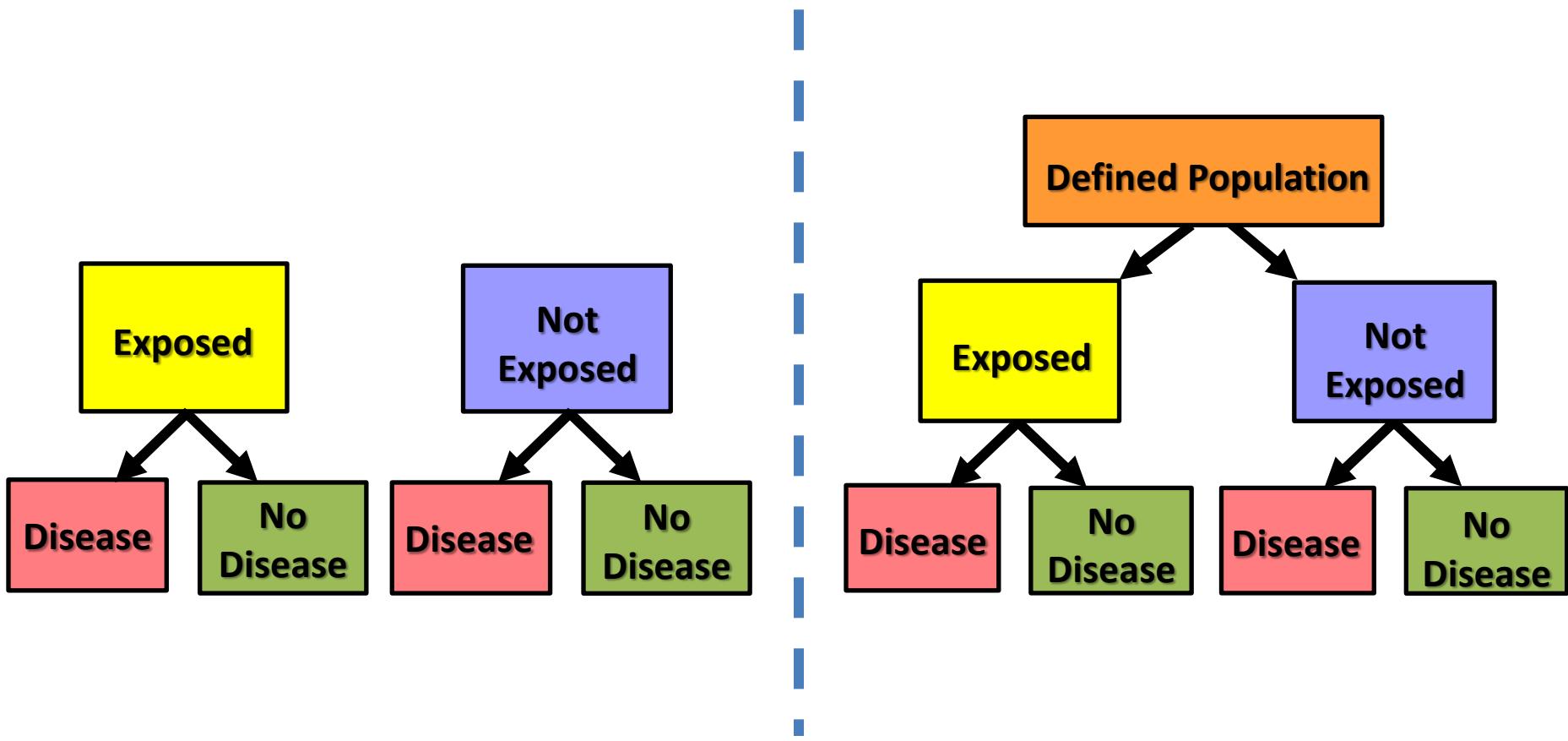
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**Two types of cohort studies:**

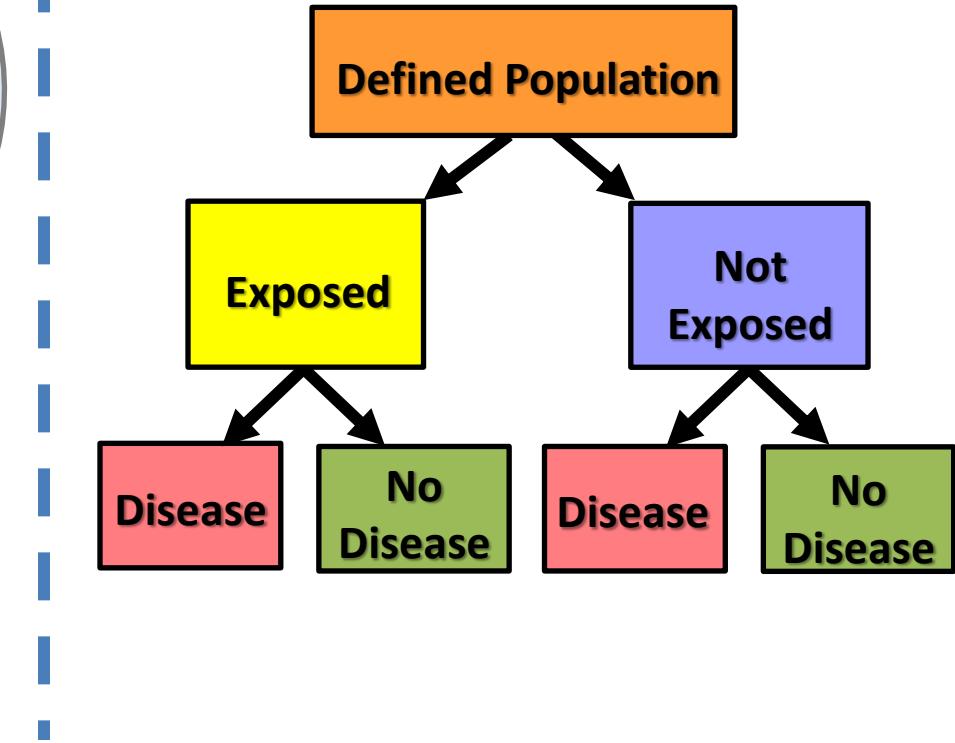
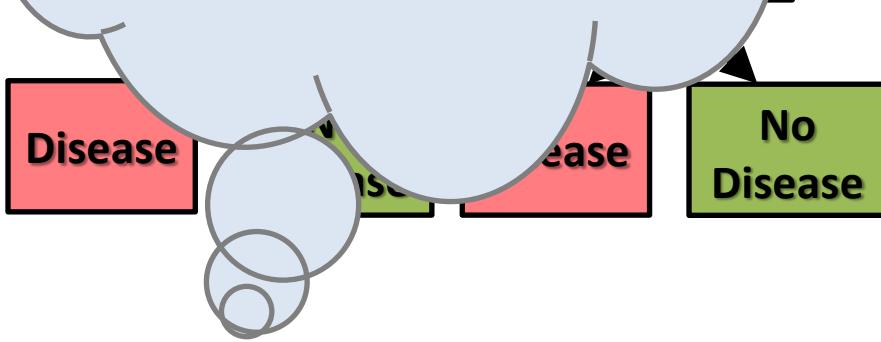
1. Prospective
2. Retrospective

# This design holds for both prospective and retrospective cohort studies!



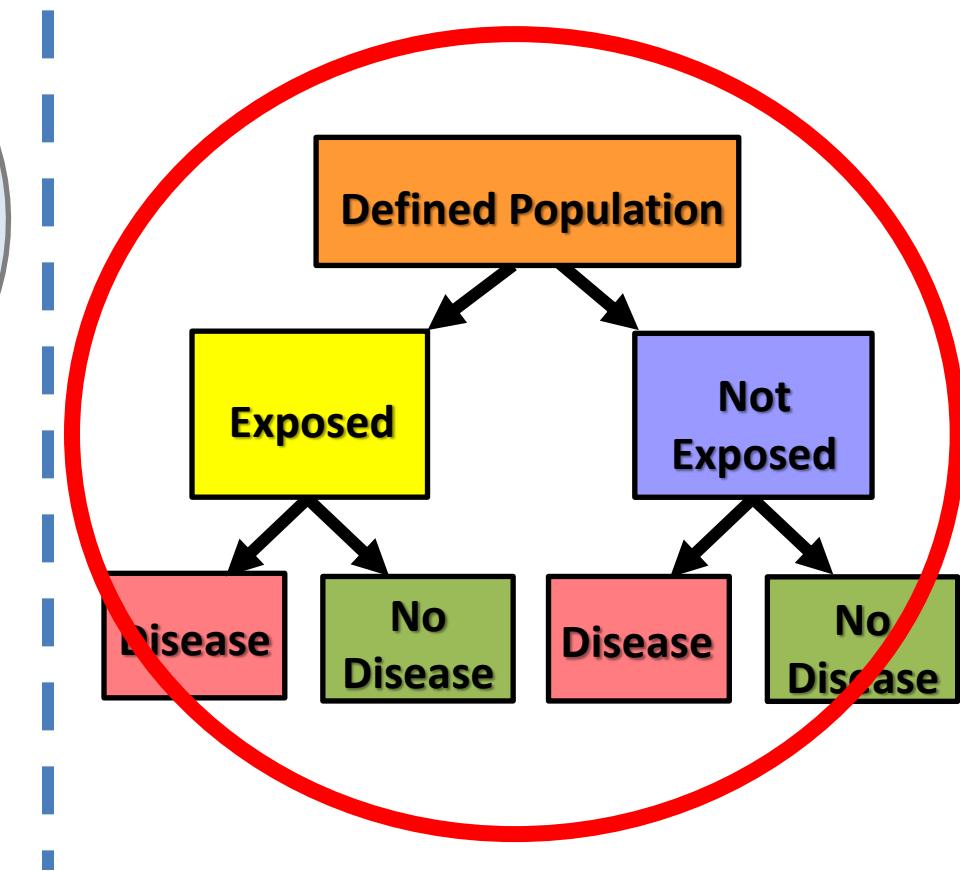
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*So what is the difference between prospective and retrospective cohort studies?*



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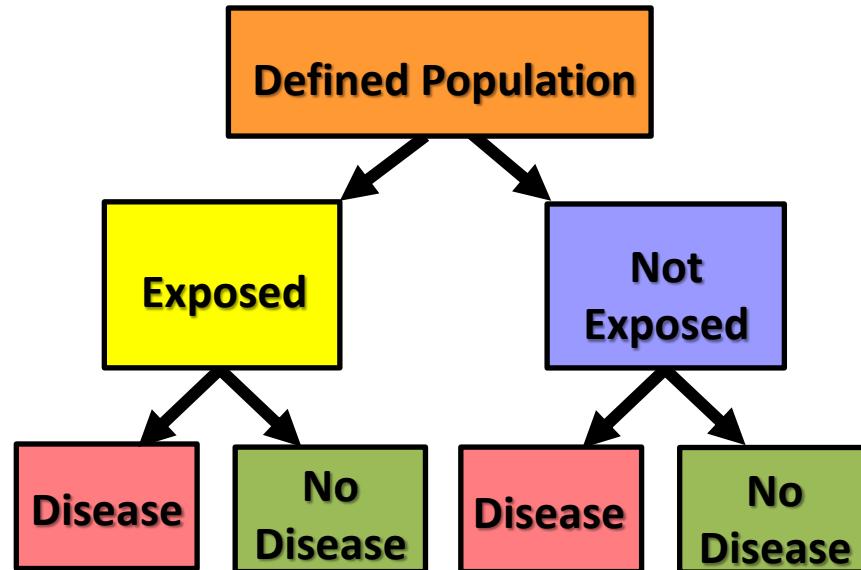


# Design of a *Prospective* Cohort Study

**Today (Feb 2016):**

**Today (Feb 2016):**

**Future  
(for example, Feb 2021):**

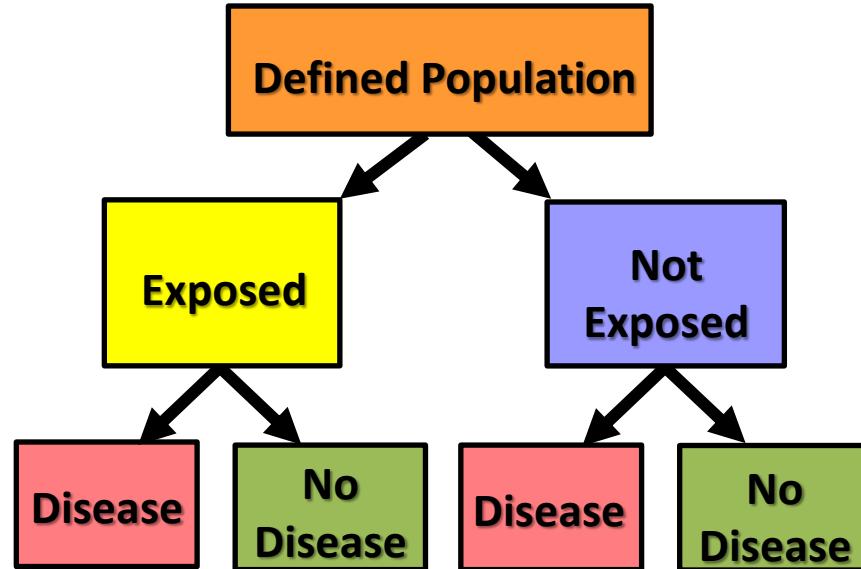


# Design of a *Prospective* Cohort Study

**Today (Feb 2016):**

**Today (Feb 2016):**

**Future  
(for example, Feb 2021):**



Measure **exposure** or  
collect biological  
samples now

**Prospective**

**Endpoint** occurs months  
to years after exposure  
is assessed



**Present (2016)**

**Follow-up**

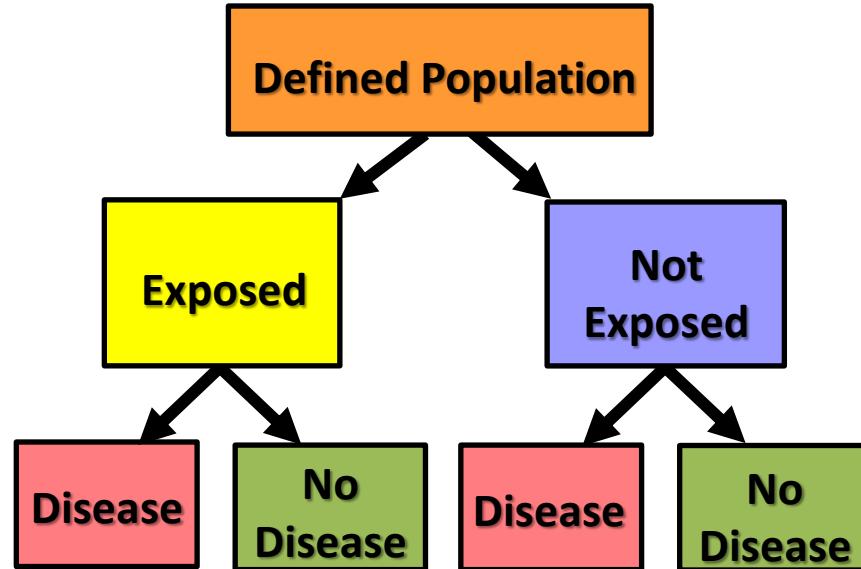
**Future (2021)**

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**Present (2016)**

**Follow-up**

**Future (2021)**



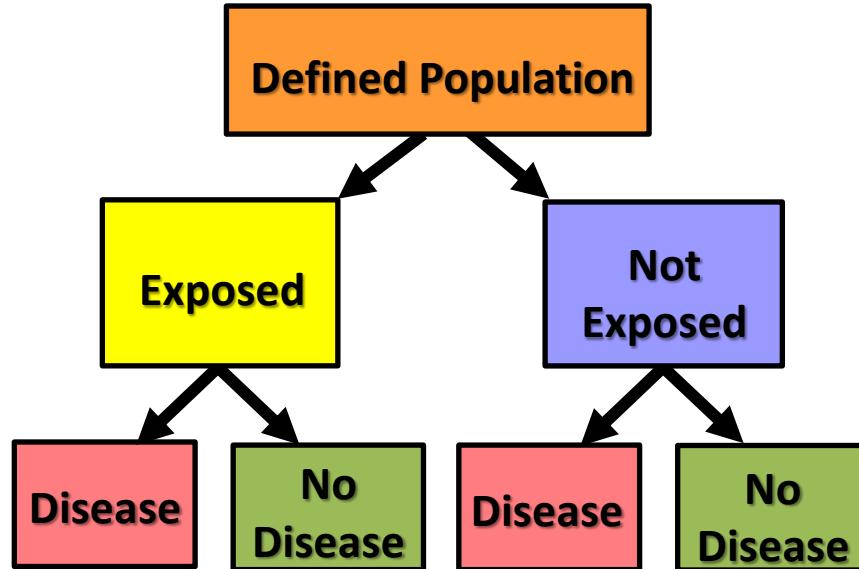
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**Present (2016)**

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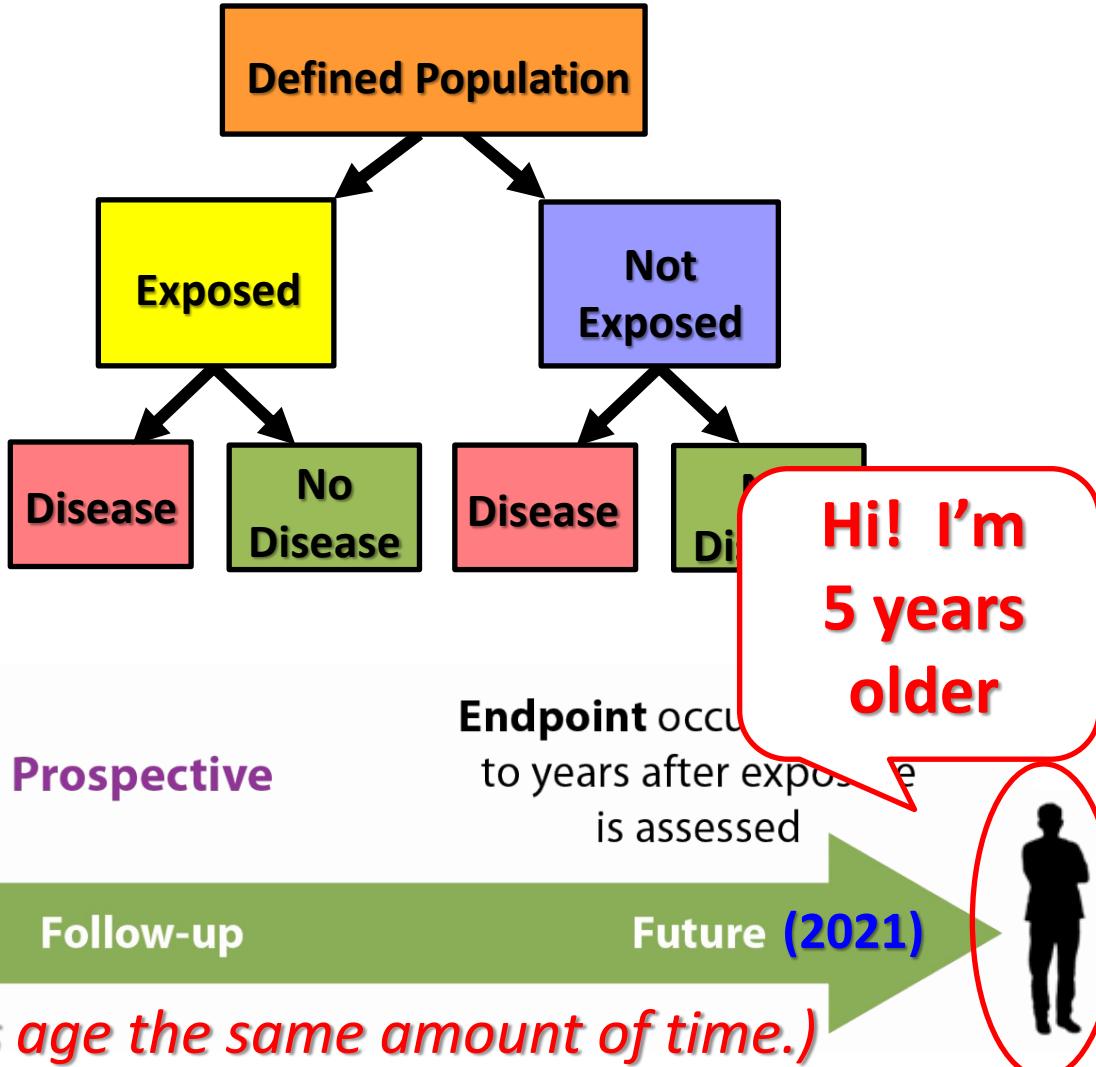
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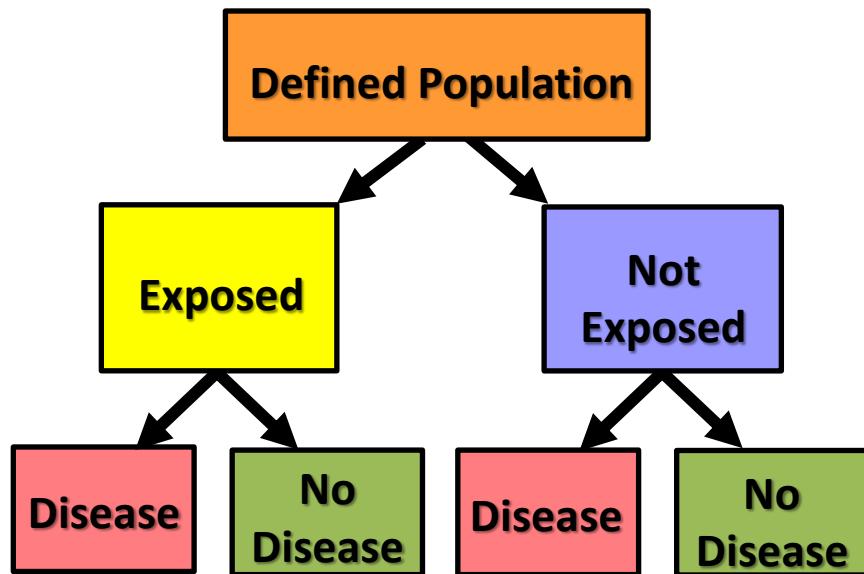


# Design of a *Retrospective* Cohort Study

Past (Feb 2011):

Past (Feb 2011):

Anytime between Feb 2011  
and the Present (Feb 2016):

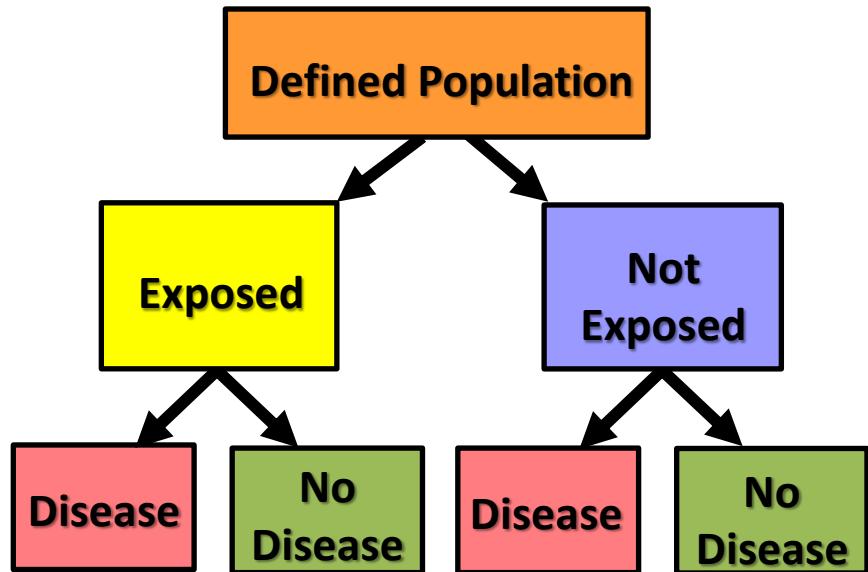


# Design of a *Retrospective* Cohort Study

Past (Feb 2011):

Past (Feb 2011):

Anytime between Feb 2011  
and the Present (Feb 2016):



Exposure  
was measured

Retrospective

Past (2011)

Follow-up

Present (2016)

Identify the cohort  
Endpoint had  
already occurred

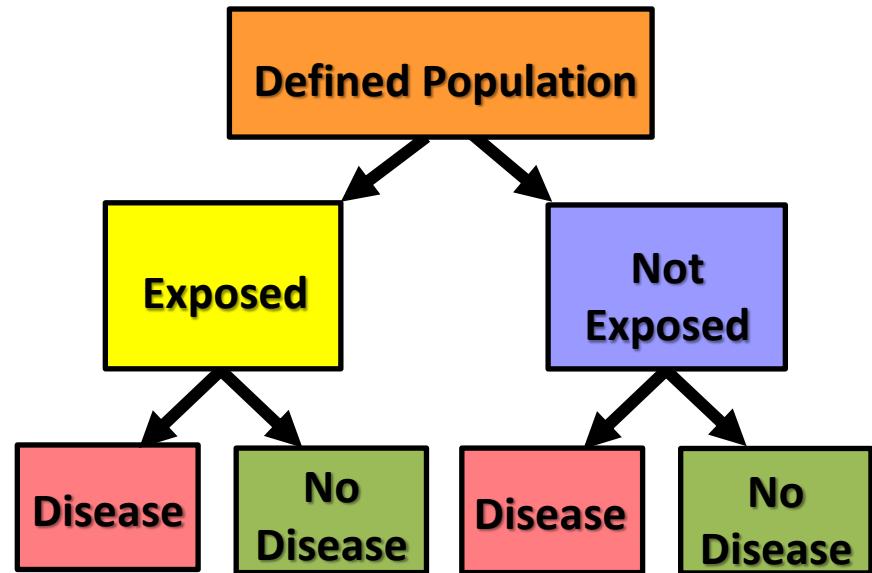


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Retrospective

Past (2011)

Follow-up

Present (2016)

Identify the cohort  
Endpoint had  
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Retrospective

Past (2011)

Follow-up

Present (2016)

Defined Population

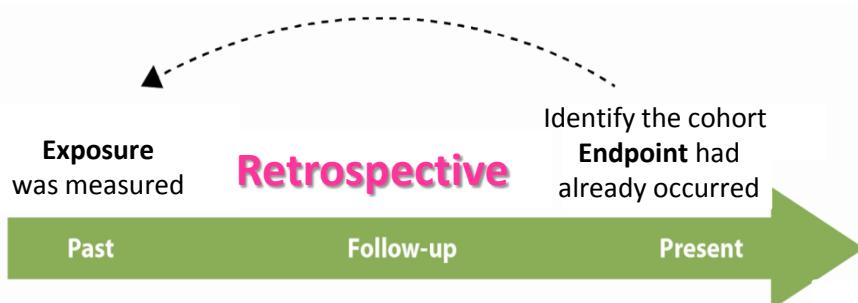
Hi! Materials were collected  
in the past for non-research  
reasons and I'm now finding  
and assembling them.  
e.g., occupations, medical,  
school records

Identify the cohort  
Endpoint had  
already occurred



# Retrospective vs. Prospective Cohort Studies

## RETROSPECTIVE



**Exposure measured**      **Then follow up for the outcome**

## PROSPECTIVE



**Exposure measured**      **Then follow up for the outcome**

# Retrospective vs. Prospective Cohort Studies

## RETROSPECTIVE



**Exposure measured**      **Then follow up for the outcome**



## PROSPECTIVE



**Exposure measured**      **Then follow up for the outcome**



# Is this a prospective or retrospective cohort study?

Measure **exposure** or  
collect biological  
samples now



Present

**Dr. Deal started  
a cohort in 2000**

Follow-up

Future

**Endpoint** occurs months  
to years after exposure  
is assessed

# Is this a prospective or retrospective cohort study?

In 2016, Dr. McKay asks her research question in Dr. Deal's cohort



Measure **exposure** or collect biological samples now



Present

Follow-up

Future

Dr. Deal started a cohort in 2000

**Endpoint** occurs months to years after exposure is assessed

# Is this a prospective or retrospective cohort study?

Prospective

In 2016, Dr. McKay asks her research question in Dr. Deal's cohort



Measure **exposure** or collect biological samples now



Present

Follow-up

Future

Dr. Deal started a cohort in 2000

# Retrospective vs. Prospective Cohort Studies

## RETROSPECTIVE



**Exposure measured**      **Then follow up for the outcome**



## PROSPECTIVE



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**Individual-level data**

# Design of a **Case-control Study**

Start  
with:

Have  
the disease

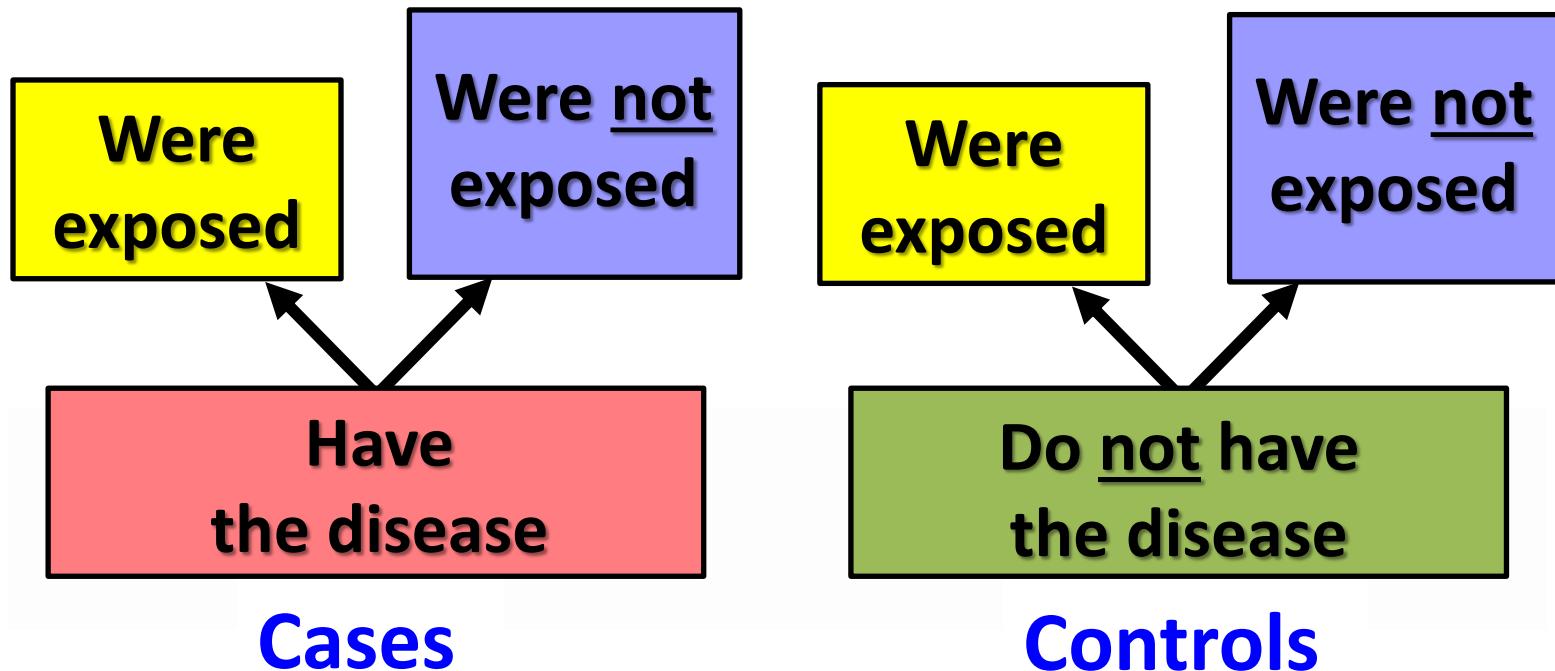
**Cases**

Do not have  
the disease

**Controls**

# Design of a Case-control Study

Then  
determine  
exposure  
history:



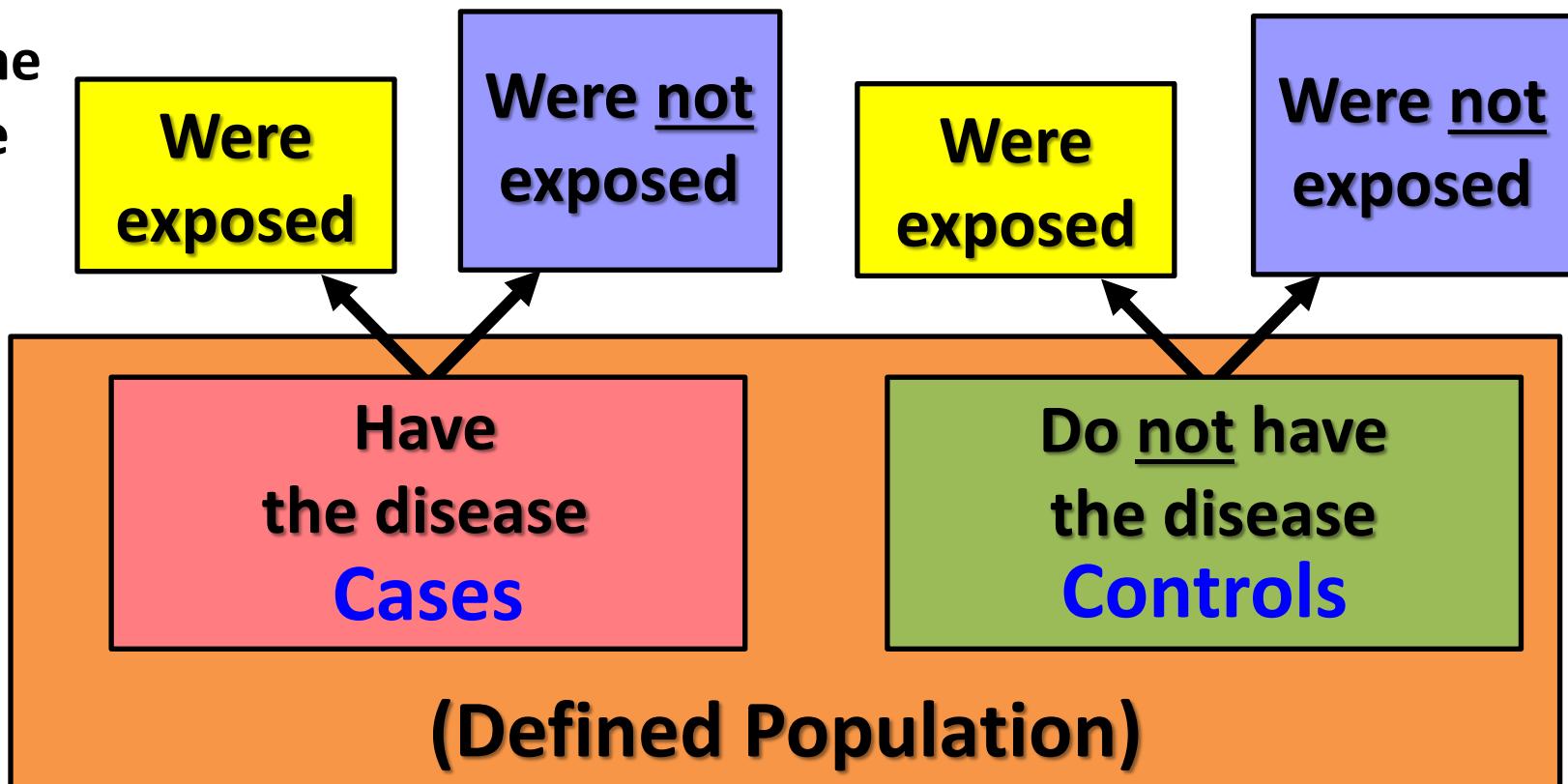
Start  
with:

Cases

Controls

# Design of a Case-control Study

Then  
determine  
exposure  
history:



*(Controls should come from the same source population as the cases – if they don't, inferences may not be valid)*

# Observational Study Designs

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### Types of case-control studies:

1. Traditional
2. Within a defined cohort
  - a. Nested case-control
  - b. Case cohort

# Observational Study Designs

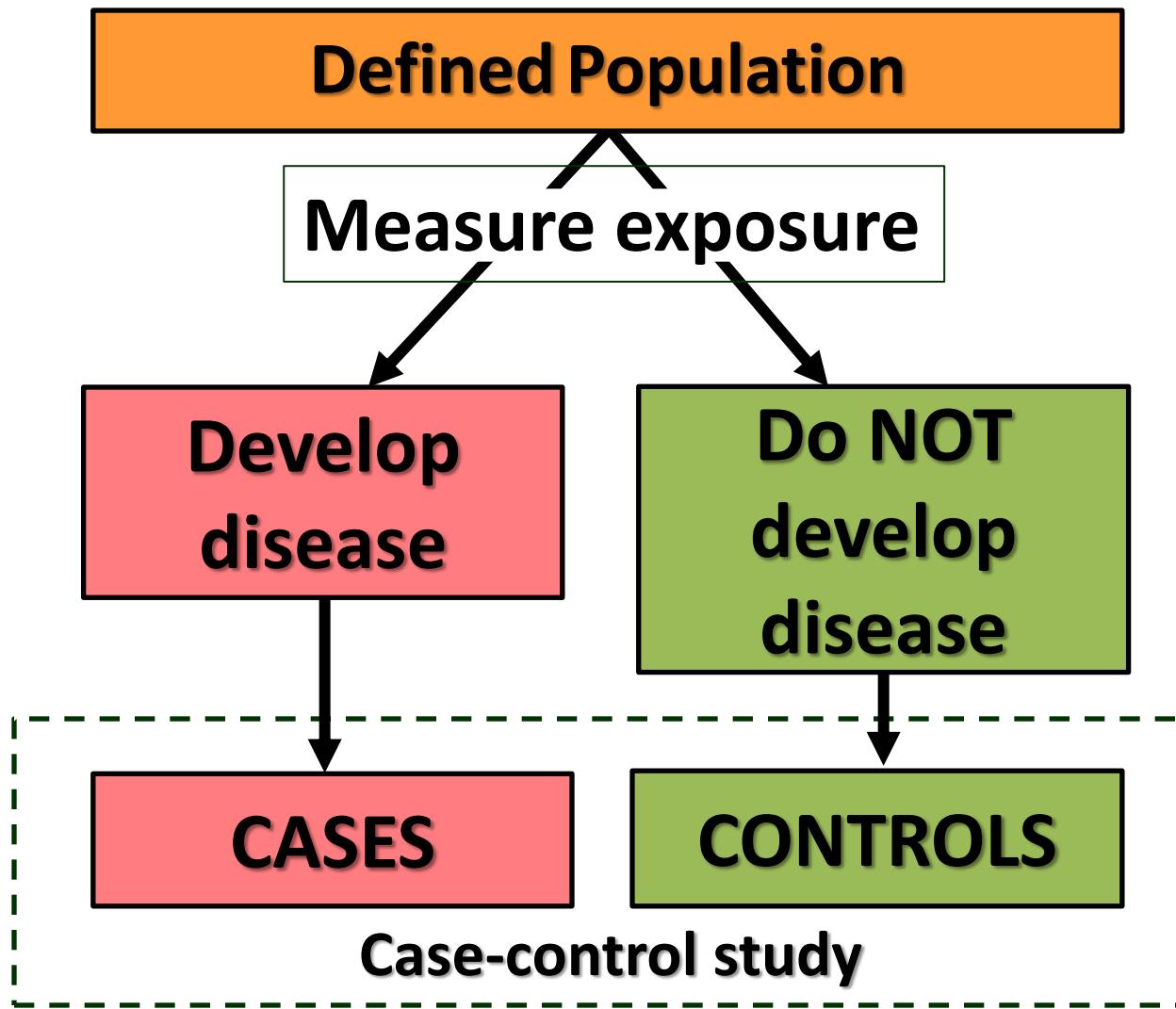
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# Design of a case-control study nested in a cohort



# Observational Study Designs

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Another way to think about this: these are efficient types of cohort studies!

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**Individual-level data**

# Design of a Cross-Sectional Study

**Begin with:**

**Defined Population**

**Gather data on exposure and outcome (or 2 exposures)  
e.g., height and weight**

**Exposed;  
have disease**

**Exposed;  
do not have  
disease**

**Not exposed;  
have disease**

**Not exposed;  
do not have  
disease**

# Types of Outcome Data from Different Study Designs

Study Design	Design	Outcome Data & Measures of Association
Randomized trial	Randomize participants to treatment and then follow up to see who develops the outcome	Incident cases of disease; Incidence (risk); Incidence rate
Cohort	Exposure measured and then participants followed up to see who develops the outcome	Incident cases of disease; Incidence (risk); Incidence rate
Case-control	Participants selected into study based on outcome; then go back and assess previous exposure	Mix of prevalent and incident cases (can design to limit to incident cases); Odds
Cross-sectional	Exposure and outcome measured at the same time	Prevalence

# Types of Outcome Data from Different Study Designs

Measures of disease frequency	Type of study
Incidence (risk)	Randomized trial; Cohort study
Incidence rate	Randomized trial; Cohort study
Prevalence	Cross-sectional
Odds	Case-control

Let's contrast  
different study designs  
by designing an  
epidemiologic study



# Research question

- Is regular physical activity at matriculation into a Master's degree program associated with successful completion of that degree?
  - Exposure = Physical activity (yes vs. no)
  - Outcome = Graduation (yes vs. no)



# Study population

- Scientific considerations
  - *What is the research question?*
  - *Who is at risk of the outcome?*
  - *Person, place, time*
- Practical considerations
  - *Participation*
  - *Feasibility and financial considerations*

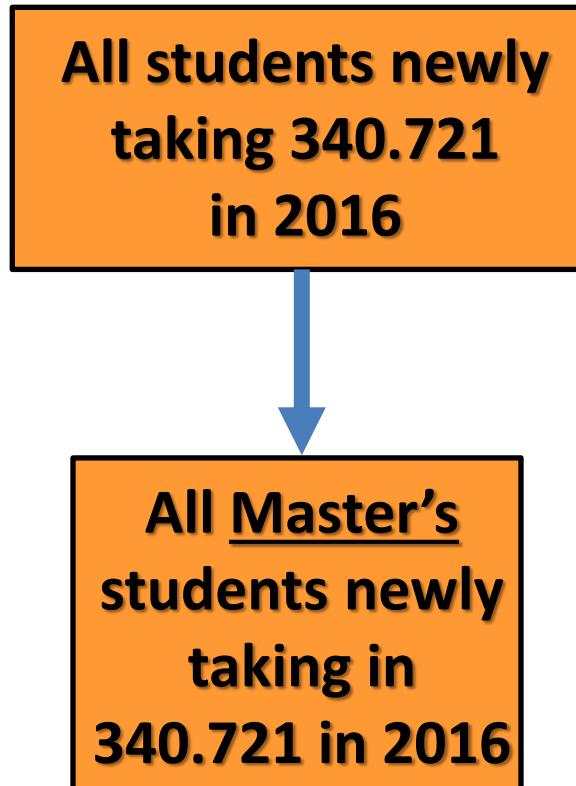
# Study population – students in 340.721

- Limit to students enrolled in a Master's program

**All students newly taking 340.721 in 2016**

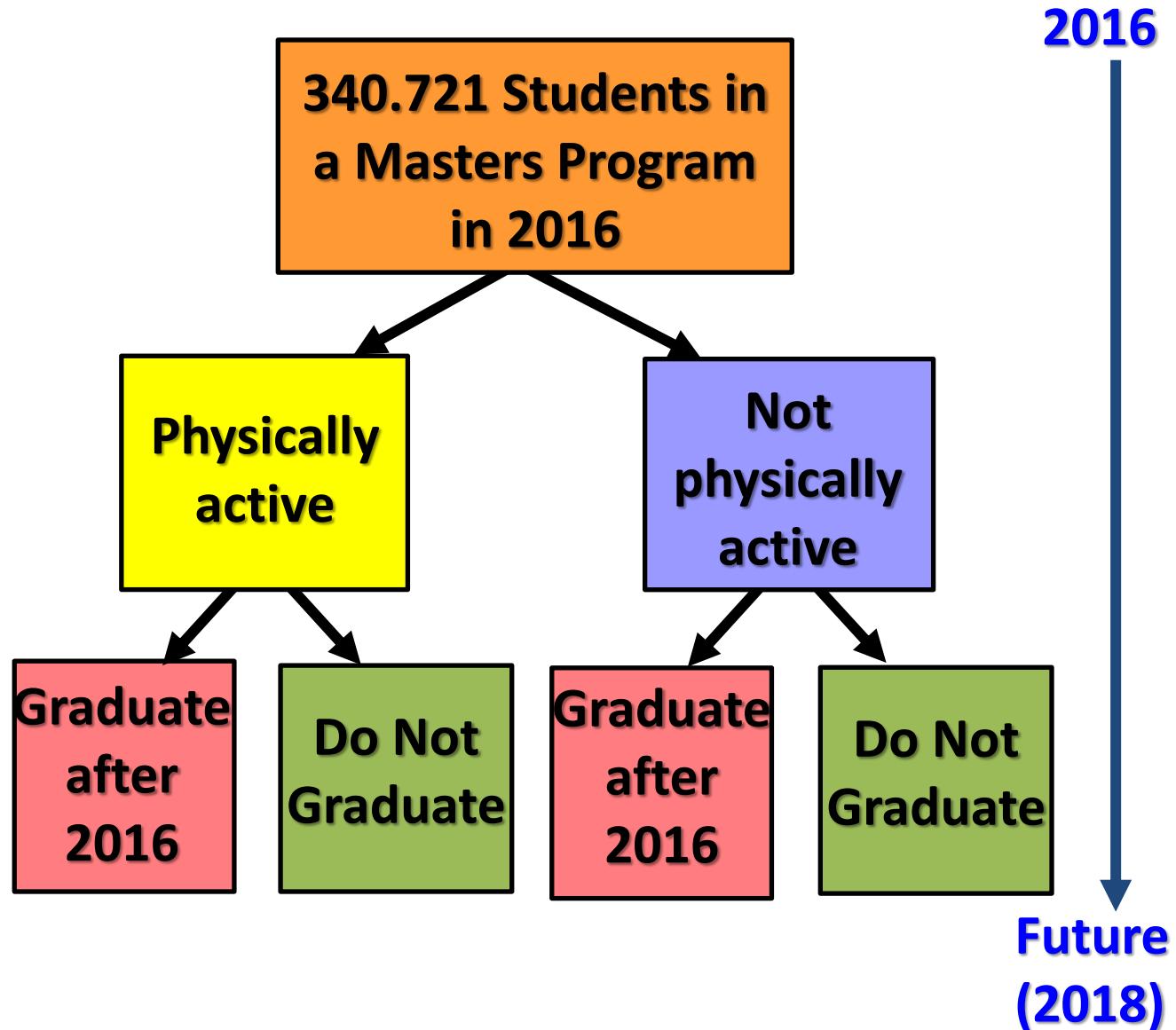
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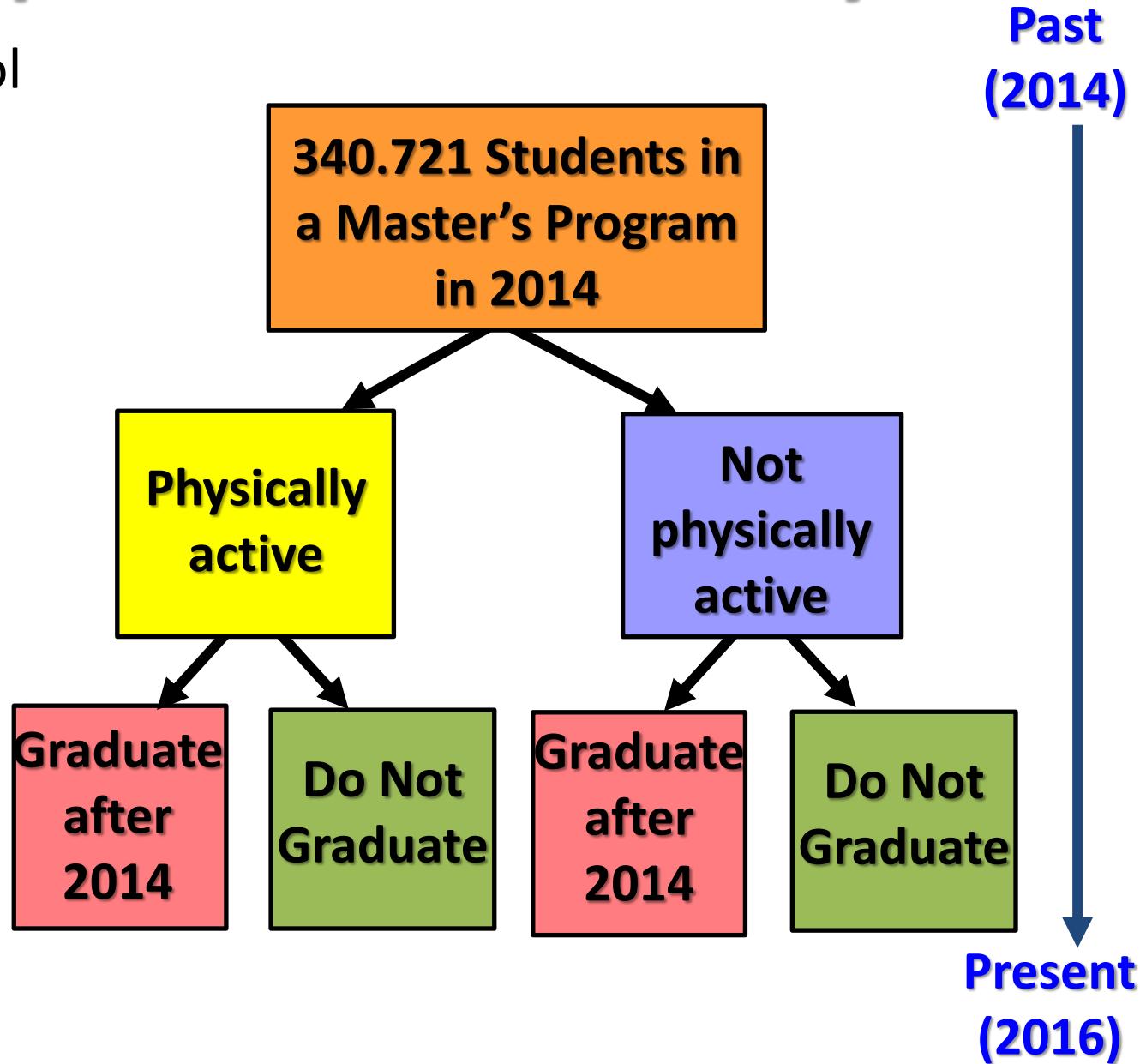
# Prospective Cohort Study

- Enroll students in 2016
- Assess physical activity
- Follow up students to determine who graduates



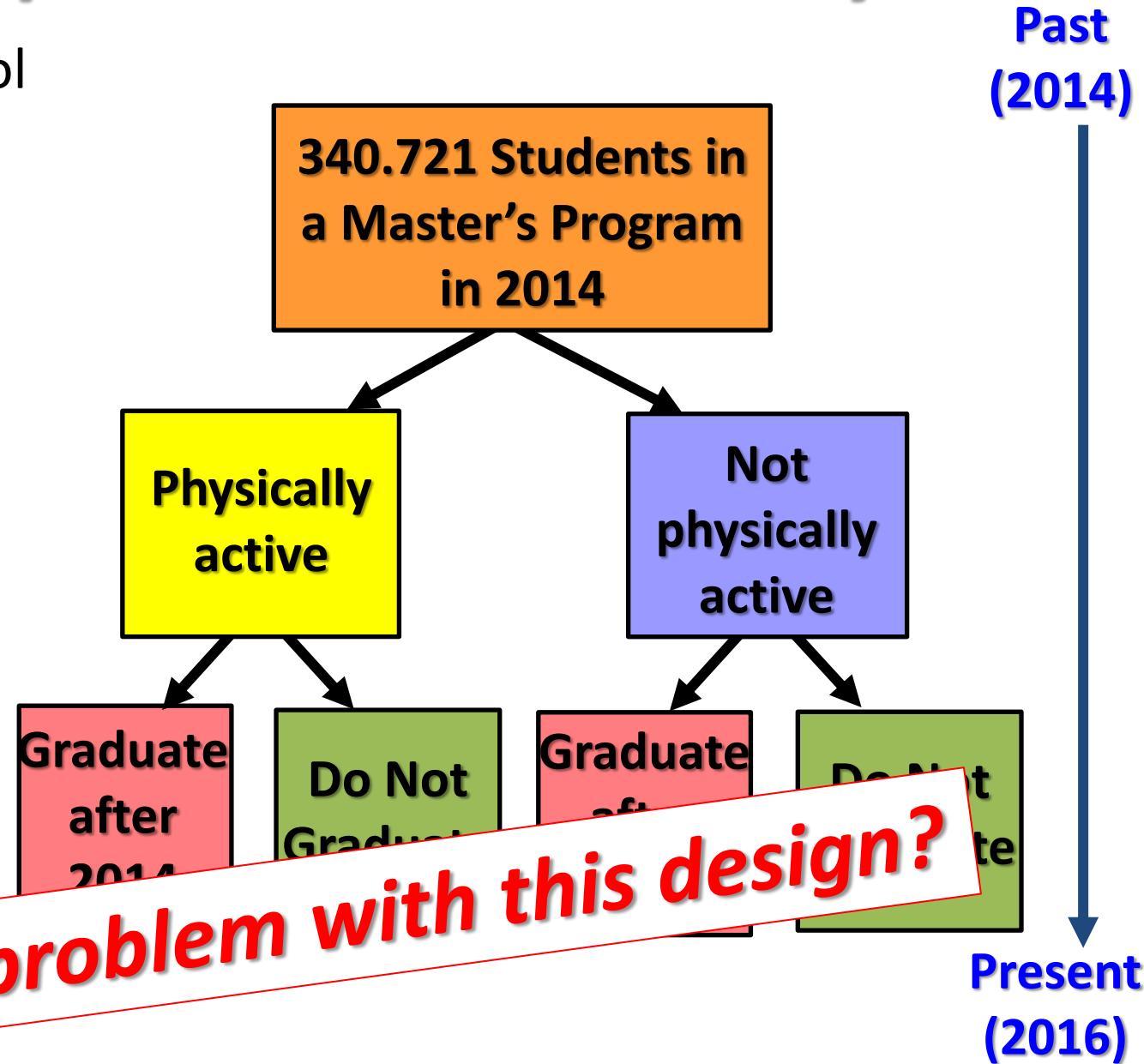
# Retrospective Cohort Study

- Go back to School records to determine who was enrolled in 2014
- Using School records, determine who was physically active in 2014
- Follow up students through 2016 to determine who has graduated



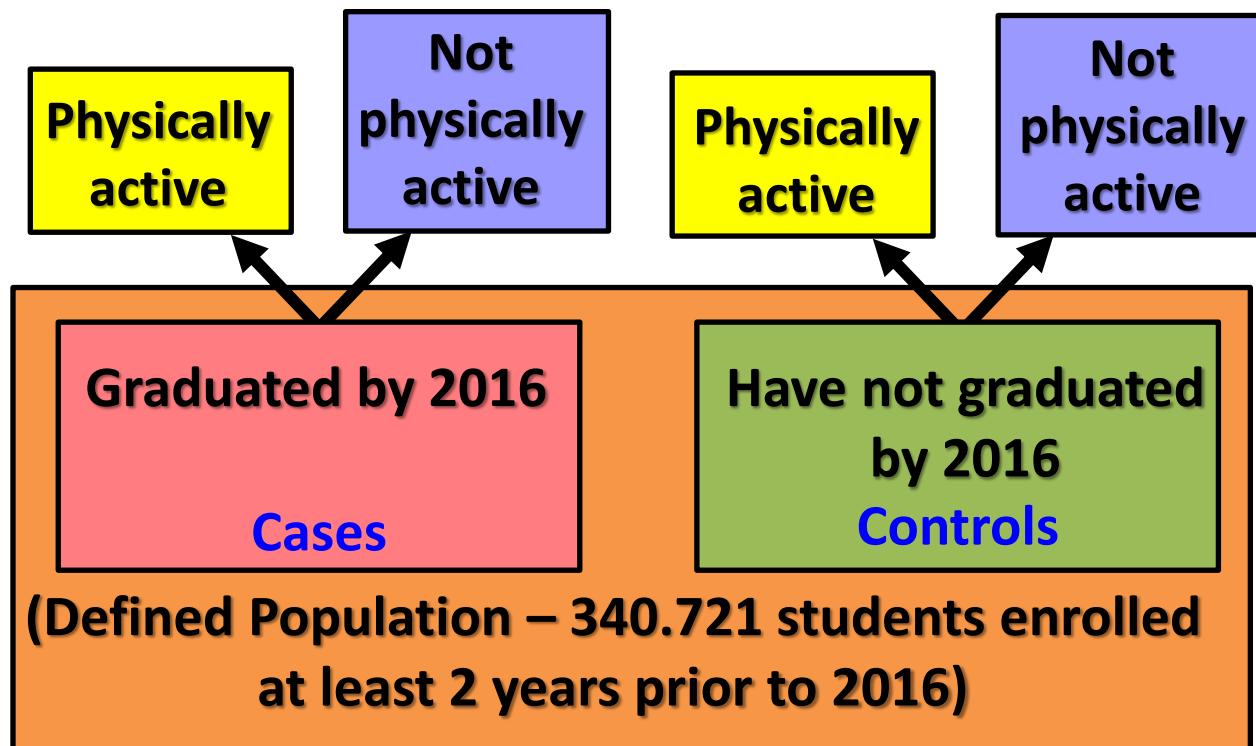
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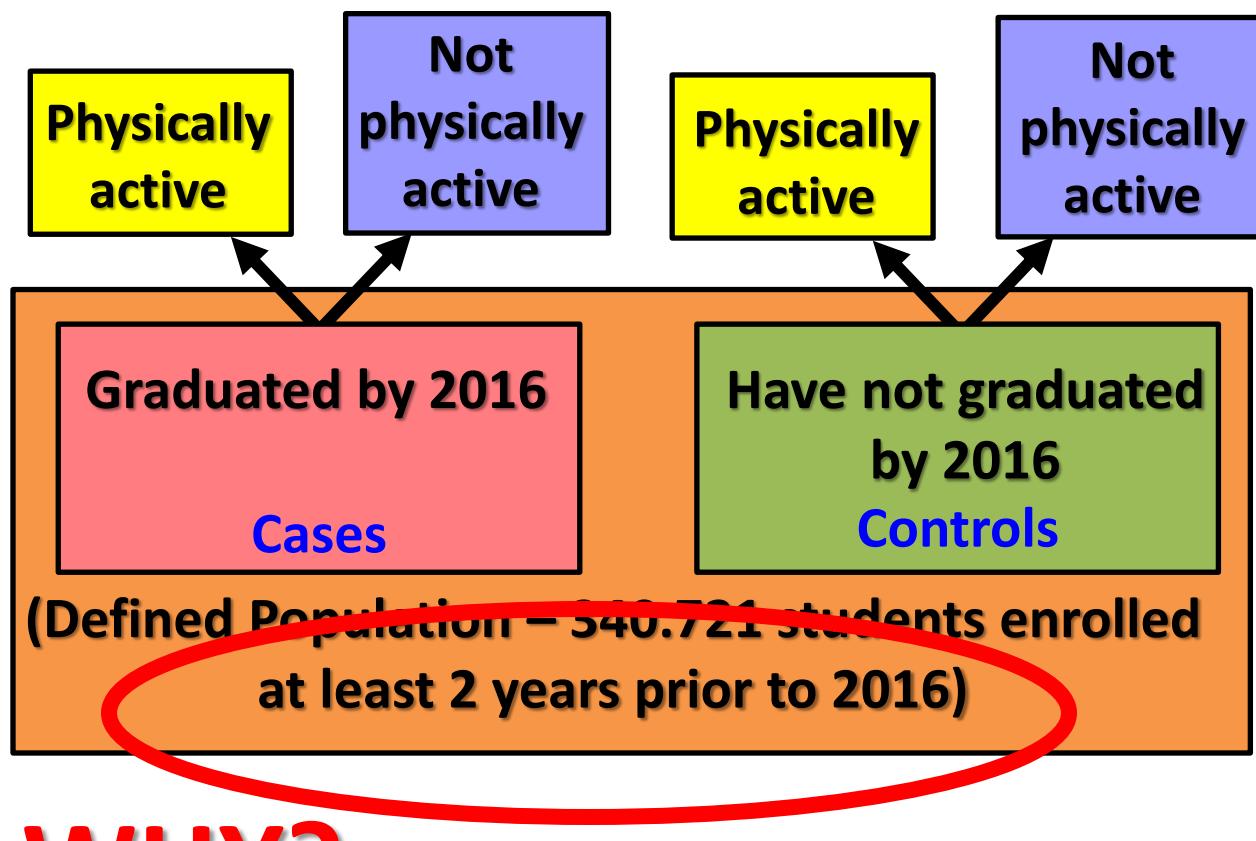
# Case-Control Study

- Identify graduates and non-graduates in 2016
- Ask participants if they were physically active at the time they took 340.721



# Case-Control Study

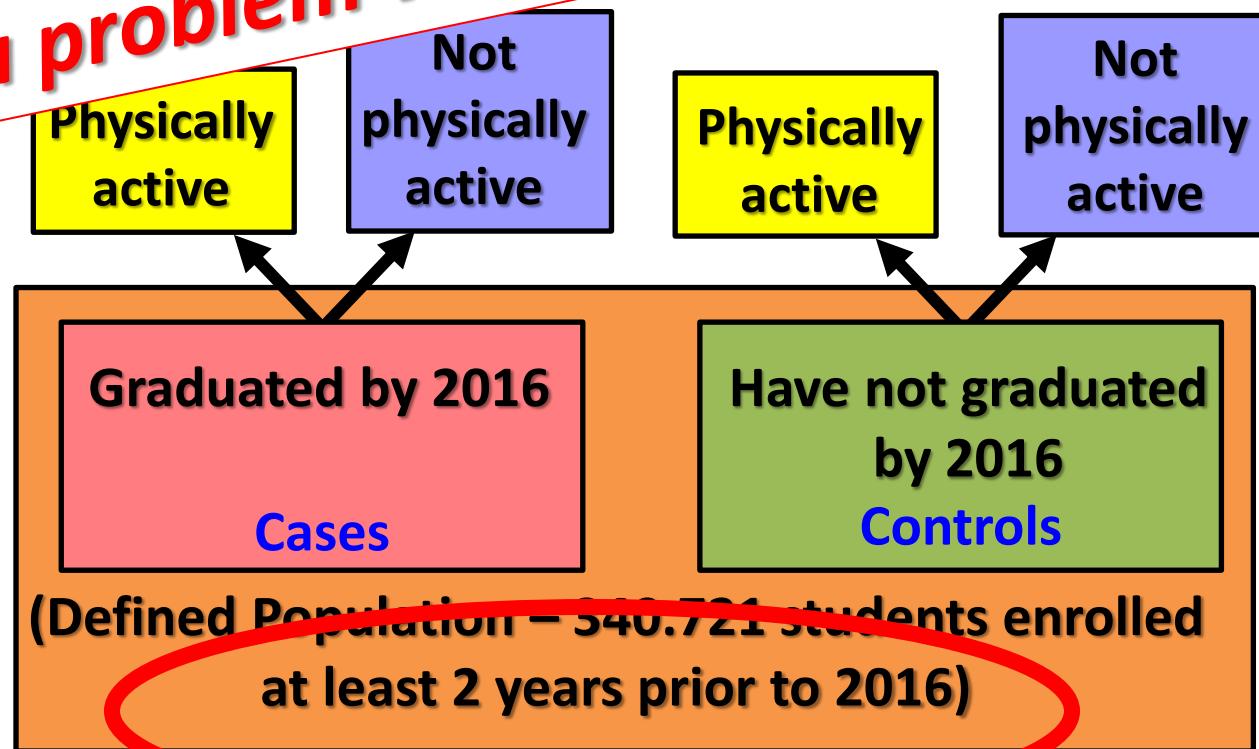
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# Case-Control Study

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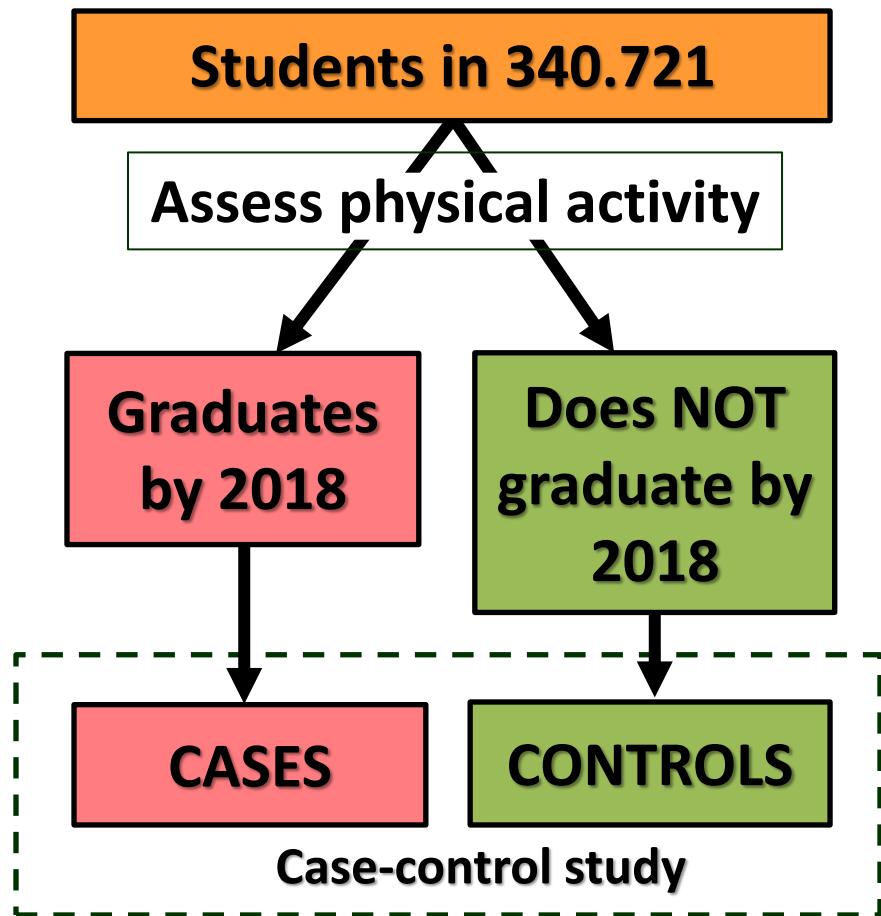
**What is a problem with this design?**



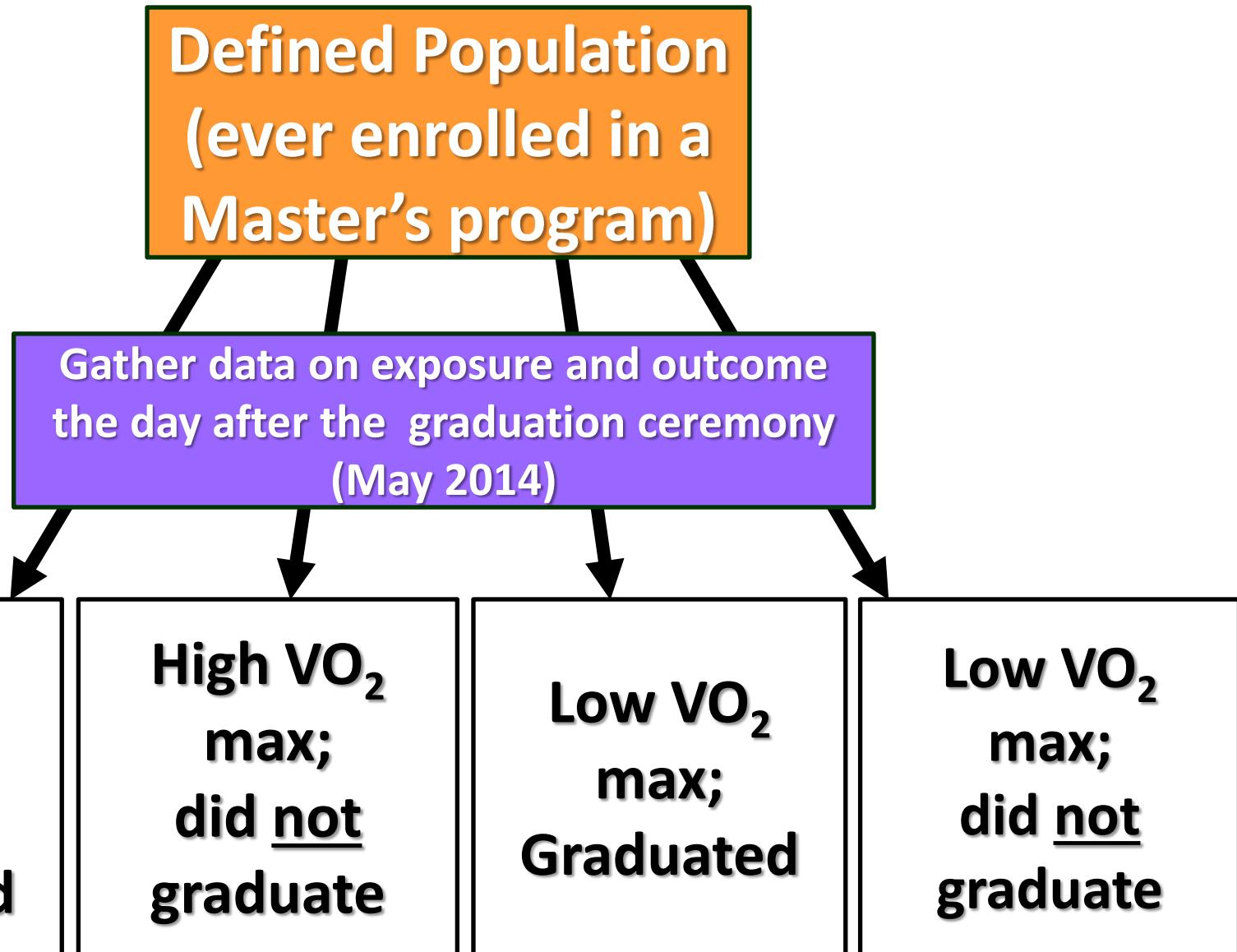
**WHY?**

# Case-Control Study Nested Within a Cohort Study

- Enroll students in 2016
- Assess physical activity (using accelerometry collected 24 hours a day for 7 days)
- Follow up students to determine who graduates
- Select cases (graduates) and a sample of controls (non-graduates) for the study
- Go back and analyze accelerometry data for cases and controls



# Cross-sectional Study



# Cross-sectional Study

Defined Population  
Gathering data at one point in time  
(in a Master's program)

**What is a problem with this design?**

Gather data on exposure and outcome  
the day after the graduation ceremony  
(May 2014)

**High VO<sub>2</sub>  
max;  
Graduated**

**High VO<sub>2</sub>  
max;  
did not  
graduate**

**Low VO<sub>2</sub>  
max;  
Graduated**

**Low VO<sub>2</sub>  
max;  
did not  
graduate**

# Let's Practice!

- Name epidemiologic study designs based on information provided in abstracts of published papers

# Statin Drugs and Risk of Advanced Prostate Cancer

Elizabeth A. Platz, Michael F. Leitzmann, Kala Visvanathan, Eric B. Rimm,  
Meir J. Stampfer, Walter C. Willett, Edward Giovannucci

**Background:** Statins are commonly used cholesterol-lowering drugs that have proapoptotic and antimetastatic activities that could affect cancer risk or progression. Results from previous epidemiologic studies of the association between statin use and cancer have been inconsistent. We investigated the association of statin use with total and advanced prostate cancer, the latter being the most important endpoint to prevent.

**Methods:** We analyzed data from a

study of 34989 US male health professionals who were cancer free in 1990 and were followed to 2002. Participants reported their use of cholesterol-lowering drugs on biennial questionnaires. Prostate cancer diagnosis was confirmed by medical record review. Multivariable-adjusted relative risks (RRs) were estimated from Cox proportional hazards regression models. Statistical tests were two-sided.

**Results:** During 376 939 person-years of follow-up, we ascertained 2579 prostate cancer cases, 316 of which were advanced (regionally invasive, metastatic, or fatal). The age-standardized incidence rates of advanced prostate cancer were 38 and 89 per 100 000 person-years in current statin users and in past or never users, respectively. The multivariable-adjusted relative risk of advanced disease was 0.51 (95% confidence interval [CI] = 0.30 to 0.86) and of metastatic or fatal disease was 0.39 (95% CI = 0.19 to 0.77) for current statin use compared with no current use. The associations remained after adjusting for prostate-specific antigen screening history (advanced disease: RR = 0.57, 95% CI = 0.30 to 1.11; metastatic or fatal disease: RR = 0.35, 95% CI = 0.14 to 0.92). Risk of advanced disease was lower with longer statin use ( $P_{\text{trend}} = .003$ ); compared with never use, the relative risk for less than 5 years of use was 0.60 (95% CI = 0.35 to 1.03) and for 5 or more years of use was 0.26 (95% CI = 0.08 to 0.83). We found no association between statin use and risk of total prostate cancer (RR = 0.96, 95% CI = 0.85 to 1.09). **Conclusions:** In

male health professionals, use of statin drugs was not associated with risk of prostate cancer overall but was associated with a reduced risk of advanced (especially metastatic or fatal) prostate cancer. [J Natl Cancer Inst 2006;98:1819–25]

## Which study design was used?

- Cross-sectional study
- Case-control study
- Nested case-control study
- Prospective cohort study

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## Which study design was used?

- Cross-sectional study
- Case-control study
- Nested case-control study
- Prospective cohort study

# Glycated hemoglobin and cancer incidence and mortality in the Atherosclerosis in Communities (ARIC) Study, 1990–2006

Corinne E. Joshu<sup>1</sup>, Anna E. Prizment<sup>2</sup>, Paul J. Dluzniewski<sup>1</sup>, Andy Menke<sup>1</sup>, Aaron R. Folsom<sup>2,3</sup>, Josef Coresh<sup>1,4</sup>, Hsin C. Yeh<sup>1,4</sup>, Frederick L. Brancati<sup>1,4</sup>, Elizabeth A. Platz<sup>1,5,6</sup> and Elizabeth Selvin<sup>1,4</sup>

Diabetes is a risk factor for many cancers; chronic hyperglycemia is hypothesized to be, in part, explanatory. We evaluated the association between glycated hemoglobin, a time-integrated glycemia measure, and cancer incidence and mortality in nondiabetic and diabetic men and women. We conducted a [redacted] study of 12,792 cancer-free participants attending the second visit (1990–1992) of the Atherosclerosis Risk in Communities (ARIC) Study. We measured glycated hemoglobin in whole-blood samples using HPLC. Incident cancers were ascertained from registries and hospital records through 2006. We estimated multivariable-adjusted hazard ratios (HR) of cancer incidence and mortality for nondiabetic participants with values  $\geq 5.7\%$  (elevated), nondiabetic participants with  $<5.0\%$  (low) and diabetic participants all compared with nondiabetic participants with 5.0–5.6% (normal). We ascertained 2,349 incident cancer cases and 887 cancer deaths. Compared with nondiabetic women with normal glycated hemoglobin, nondiabetic women with elevated values had an increased risk of cancer incidence (HR:1.24; 95% CI:1.07,1.44) and mortality (HR:1.58; 95% CI:1.23,2.05) as did diabetic women (incidence, HR:1.30; 95% CI:1.06,1.60, mortality, HR:1.96; 95% CI:1.40,2.76). Nondiabetic women with low values also had increased risk. Diabetic women with good glycemic control ( $<7.0\%$ ) had a lower cancer risk than those with higher values. Glycated hemoglobin in nondiabetic and diabetic men, and diabetes were not statistically significantly associated with total cancer risk. Our findings support the hypothesis that chronic hyperglycemia, even in the nondiabetic range, increases cancer risk in women. Maintaining normal glycated hemoglobin overall, and good glycemic control among diabetic adults, may reduce the burden of cancer, especially in women.

## Which study design was used?

- Cross-sectional study
- Case-control study
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Diabetes is a risk factor for many cancers; chronic hyperglycemia is hypothesized to be, in part, explanatory. We evaluated the association between glycated hemoglobin, a time-integrated glycemia measure, and cancer incidence and mortality in nondiabetic and diabetic men and women. We conducted a [REDACTED] study of 12,792 cancer-free participants attending the second visit (1990–1992) of the Atherosclerosis Risk in Communities (ARIC) Study. We measured glycated hemoglobin in whole-blood samples using HPLC. Incident cancers were ascertained from registries and hospital records through 2006. We estimated multivariable-adjusted hazard ratios (HR) of cancer incidence and mortality for nondiabetic participants with values  $\geq 5.7\%$  (elevated), nondiabetic participants with  $<5.0\%$  (low) and diabetic participants all compared with nondiabetic participants with 5.0–5.6% (normal). We ascertained 2,349 incident cancer cases and 887 cancer deaths. Compared with nondiabetic women with normal glycated hemoglobin, nondiabetic women with elevated values had an increased risk of cancer incidence (HR:1.24; 95% CI:1.07,1.44) and mortality (HR:1.58; 95% CI:1.23,2.05) as did diabetic women (incidence, HR:1.30; 95% CI:1.06,1.60, mortality, HR:1.96; 95% CI:1.40,2.76). Nondiabetic women with low values also had increased risk. Diabetic women with good glycemic control ( $<7.0\%$ ) had a lower cancer risk than those with higher values. Glycated hemoglobin in nondiabetic and diabetic men, and diabetes were not statistically significantly associated with total cancer risk. Our findings support the hypothesis that chronic hyperglycemia, even in the nondiabetic range, increases cancer risk in women. Maintaining normal glycated hemoglobin overall, and good glycemic control among diabetic adults, may reduce the burden of cancer, especially in women.

Which study design was used?

- Cross-sectional study
- Case-control study
- Nested case-control study
- Prospective cohort study

# A [REDACTED] Study of Obesity, and the Incidence and Progression of Lower Urinary Tract Symptoms

Alison M. Mondul,\* Edward Giovannucci and Elizabeth A. Platz

From the Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health and Brady Urological Institute, Johns Hopkins School of Medicine, Baltimore, Maryland (AMM, EAP), and Departments of Nutrition and Epidemiology, Harvard School of Public Health and Channing Division of Network Medicine, Department of Medicine, Harvard Medical School and Brigham and Women's Hospital, Boston (EG), Massachusetts

**Purpose:** We [REDACTED] evaluated the association between adiposity and the risk of lower urinary tract symptoms incidence and progression in the Health Professionals Followup Study (HPFS).

**Materials and Methods:** At baseline participants reported current height and weight, and weight at age 21 years. A year later they reported waist and hip circumferences, and every 2 years thereafter they reported weight. Participants periodically completed the International Prostate Symptom Score (I-PSS) and reported surgery or medication use for lower urinary tract symptoms. We used Cox proportional hazards regression to estimate the multivariable adjusted association between adiposity and lower urinary tract symptoms incidence and progression. The incidence analytical cohort of 18,055 men had no lower urinary tract symptoms at baseline. A total of 6,461 men entered the progression analytical cohort when they first experienced lower urinary tract symptoms.

**Results:** The risk of lower urinary tract symptoms in 4,088 cases increased with increasing body mass index ( $35 \text{ kg/m}^2$  or greater vs 23 to less than 25 HR 1.61, 95% CI 1.31–1.99), waist circumference (greater than 42 inches vs 33 or less HR 1.39, 95% CI 1.19–1.63) and weight gain since age 21 years (50 pounds or greater vs stable weight HR 1.31, 95% CI 1.17–1.46, each p trend <0.0001). The risk of lower urinary tract symptom progression in 1,691 cases increased with body mass index ( $35 \text{ kg/m}^2$  or greater vs 23 to less than 25 HR 1.44, 95% CI 1.04–2.00, p trend <0.0001), weight gain since age 21 years (50 pounds or greater vs stable weight HR 1.35, 95% CI 1.14–1.60, p trend <0.0001) and waist circumference (greater than 42 inches vs 33 or less HR 1.32, 95% CI 0.95–1.85, p trend 0.005).

**Conclusions:** Men with higher total and abdominal adiposity and those who gained weight were more likely to have lower urinary tract symptoms develop or progress. Our findings support the notion that obesity may be an important target for lower urinary tract symptom prevention and intervention.

Mondul AM et al. J Urol 2014;191:715-21. PMID: 24076306.

## Which study design was used?

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- Case-control study
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## Which study design was used?

- Cross-sectional study
- Case-control study
- Nested case-control study
- Prospective cohort study

# **Association between endogenous sex steroid hormones and inflammatory biomarkers in US men**

Which study design was used?

- Cross-sectional study
- Case-control study
- Nested case-control study
- Prospective cohort study

<sup>1</sup>K. K. Tsilidis, <sup>2</sup>S. Rohrmann, <sup>3</sup>K. A. McGlynn, <sup>3</sup>S. J. Nyante, <sup>4</sup>D. S. Lopez, <sup>5</sup>G. Bradwin, <sup>6</sup>M. Feinleib, <sup>6</sup>C. E. Joshu, <sup>7,8</sup>N. Kanarek, <sup>7,8,9,10</sup>W. G. Nelson, <sup>6,11</sup>E. Selvin and <sup>6,7,9,11</sup>E. A. Platz

<sup>1</sup>Department of Hygiene and Epidemiology, University of Ioannina School of Medicine, Ioannina, Greece, <sup>2</sup>Institute of Social and Preventive Medicine, University of Zurich, Zurich, Switzerland, <sup>3</sup>Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD, <sup>4</sup>Division of Epidemiology, University of Texas School of Public Health, Houston, TX, <sup>5</sup>Department of Laboratory Medicine, Harvard Medical School and Children's Hospital, Boston, MA, <sup>6</sup>Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, <sup>7</sup>Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins Medical Institutions, <sup>8</sup>Department of Environmental Health Sciences, Johns Hopkins Bloomberg School of Public Health, <sup>9</sup>James Buchanan Brady Urological Institute, Johns Hopkins Medical Institutions, <sup>10</sup>Departments of Oncology, Pathology, Pharmacology and Molecular Sciences, Radiation Oncology and Molecular Radiation Sciences, Johns Hopkins Medical Institutions, and <sup>11</sup>Welch Center for Prevention, Epidemiology and Clinical Research, Johns Hopkins Bloomberg

## **SUMMARY**

Sex steroid hormones and inflammatory biomarkers are both associated with the development and progression of chronic diseases, but their interrelationship is relatively uncharacterized. We examined the association of sex hormones and sex hormone-binding globulin (SHBG) with biomarkers of inflammation, C-reactive protein (CRP) and white blood cell (WBC) count. The study included data from 809 adult men in the National Health and Nutrition Examination Survey 1999–2004. Geometric means and 95% confidence intervals were estimated separately for CRP and WBC concentrations by sex steroid hormones and SHBG using weighted linear regression models. Higher concentrations of total (slope per one quintile in concentration,  $-0.18$ ;  $p$ -trend, 0.001) and calculated free (slope,  $-0.13$ ;  $p$ -trend, 0.03) testosterone were statistically significantly associated with lower concentrations of CRP, but not with WBC count. Men in the bottom quintile of total testosterone ( $\leq 3.3$  ng/mL), who might be considered to have clinically low testosterone, were more likely to have elevated CRP ( $\geq 3$  mg/L) compared with men in the top four quintiles (OR, 1.61; 95% CI, 1.00–2.61). Total and calculated free estradiol (E2) were positively associated with both CRP (Total E2: slope, 0.14;  $p$ -trend,  $<0.001$ ; Free E2: slope, 0.15;  $p$ -trend,  $<0.001$ ) and WBC (Total E2: slope, 0.02;  $p$ -trend, 0.08; Free E2: slope, 0.02;  $p$ -trend, 0.02) concentrations. SHBG concentrations were inversely associated with WBC count (slope,  $-0.03$ ;  $p$ -trend, 0.04), but not with CRP. These findings are consistent with the hypothesis that higher androgen and lower oestrogen concentrations may have an anti-inflammatory effect in men.

# **Association between endogenous sex steroid hormones and inflammatory biomarkers in US men**

Which study design was used?

- Cross-sectional study
- Case-control study
- Nested case-control study
- Prospective cohort study

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# Primary Care Providers' Perspectives on Discontinuing Prostate Cancer Screening

Craig E. Pollack, MD, MHS<sup>1,2</sup>; Elizabeth A. Platz, ScD, MPH<sup>2</sup>; Nrupen A. Bhavsar, PhD, MPH<sup>1,2,3</sup>; Gary Noronha, MD<sup>4</sup>; Gene E. Green, MD<sup>4</sup>; Sean Chen, BA<sup>5</sup>; and H. Ballentine Carter, MD<sup>6</sup>

**BACKGROUND:** Clinical guidelines recommend against routine prostate-specific antigen (PSA) screening for older men and for those with lower life expectancies. The authors of this report examined providers' decision-making regarding discontinuing PSA screening.

**METHODS:** A survey of primary providers from a large, university-affiliated primary care practice was administered. Providers were asked about their current screening practices, factors that influenced their decision to discontinue screening, and barriers to discontinuing screening. Bivariate and multivariable logistic regression analyses were used to examine whether taking age and/or life expectancy into account and barriers to discontinuing were associated with clinician characteristics and practice styles. **RESULTS:** One hundred twenty-five of 141 providers (88.7%) participated in the survey. Over half (59.3%) took both age and life expectancy into account, whereas 12.2% did not consider either in their decisions to discontinue PSA screening. Providers varied in the age at which they typically stopped screening patients, and the majority (66.4%) reported difficulty in assessing life expectancy. Taking patient age and life expectancy into account was not associated with provider characteristics or practice styles. The most frequently cited barriers to discontinuing PSA screening were patient expectation (74.4%) and time constraints (66.4%). Black providers were significantly less likely than nonblack providers to endorse barriers related to time constraints and clinical uncertainty, although these results were limited by the small sample size of black providers. **CONCLUSIONS:** Although age and life expectancy often figured prominently in decisions to use screening, providers faced multiple barriers to discontinuing routine PSA screening. *Cancer* 2012;118:5518-24. © 2012 American Cancer Society.

Which study design was used?

- Cross-sectional study
- Case-control study
- Nested case-control study
- Prospective cohort study

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Which study design was used?

- Cross-sectional study
- Case-control study
- Nested case-control study
- Prospective cohort study

## Which study design was used?

# The association between circulating high-sensitivity C-reactive protein concentration and pathologic measures of colonic inflammation

Corinne E. Joshu · Kostantinos K. Tsilidis · Sarah B. Peskoe · Francis M. Giardiello ·  
Paul J. Dluzniewski · William G. Nelson · Christine A. Iacobuzio-Donahue ·  
Elizabeth A. Platz

### Abstract

**Purpose** C-reactive protein (CRP), an inflammation marker, is associated with colorectal cancer (CRC) risk in some prospective studies. Whether increased CRP is indicative of colonic inflammation, a possible CRC cause, or of other sources of inflammation (e.g., adiposity), is unknown. Thus, we evaluated the association between CRP and colonic mucosal measures of inflammation.

**Methods** 151 adults undergoing colonoscopy provided a blood sample and random left- and right-side colonic mucosal biopsies. Height and weight were measured, and lifestyle information was collected. High-sensitivity C-reactive protein (hsCRP) was measured by immunoturbidometric assay. A gastrointestinal pathologist evaluated biopsies for seven colonic inflammation measures. Of 119 participants with complete information, 24 had an inflammatory bowel disease (IBD) history and were analyzed separately. We calculated the number of colonic inflammation measures present in both biopsies, and separately for right and left biopsies. Adjusted geometric mean hsCRP

- Cross-sectional study
- Case-control study
- Nested case-control study
- Prospective cohort study

was calculated using linear regression, overall, by demographic and lifestyle factors, and inflammation measures.

**Results** Most participants had  $\geq 1$  colonic inflammation measure (0: 21 %, 1: 39 %,  $\geq 2$ : 40 %). Adjusted mean hsCRP did not increase with increasing number of inflammation measures (0: 1.67; 1: 1.33;  $\geq 2$ : 1.01 mg/L;  $p$  trend = 0.21). Obese (2.03 mg/L) and overweight (1.61 mg/L) participants had higher adjusted mean hsCRP than normal-weight participants (0.62 mg/L;  $p$  trend <0.0001). Patterns were similar for participants with a history of IBD.

**Conclusions** hsCRP concentration was not associated with colonic inflammation, although hsCRP increased with adiposity. The hsCRP–CRC association may be explained by residual confounding by other risk factors, such as adiposity, rather than by CRP marking colonic inflammation.

**Keywords** C-reactive protein · Inflammation · Colorectal cancer · Obesity

## Which study design was used?

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### Abstract

**Purpose** C-reactive protein (CRP), an inflammation marker, is associated with colorectal cancer (CRC) risk in some prospective studies. Whether increased CRP is indicative of colonic inflammation, a possible CRC cause, or of other sources of inflammation (e.g., adiposity), is unknown. Thus, we evaluated the association between CRP and colonic mucosal measures of inflammation.

**Methods** 151 adults undergoing colonoscopy provided a blood sample and random left- and right-side colonic mucosal biopsies. Height and weight were measured, and lifestyle information was collected. High-sensitivity C-reactive protein (hsCRP) was measured by immunoturbidometric assay. A gastrointestinal pathologist evaluated biopsies for seven colonic inflammation measures. Of 119 participants with complete information, 24 had an inflammatory bowel disease (IBD) history and were analyzed separately. We calculated the number of colonic inflammation measures present in both biopsies, and separately for right and left biopsies. Adjusted geometric mean hsCRP

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was calculated using linear regression, overall, by demographic and lifestyle factors, and inflammation measures.

**Results** Most participants had  $\geq 1$  colonic inflammation measure (0: 21 %, 1: 39 %,  $\geq 2$ : 40 %). Adjusted mean hsCRP did not increase with increasing number of inflammation measures (0: 1.67; 1: 1.33;  $\geq 2$ : 1.01 mg/L;  $p$  trend = 0.21). Obese (2.03 mg/L) and overweight (1.61 mg/L) participants had higher adjusted mean hsCRP than normal-weight participants (0.62 mg/L;  $p$  trend <0.0001). Patterns were similar for participants with a history of IBD.

**Conclusions** hsCRP concentration was not associated with colonic inflammation, although hsCRP increased with adiposity. The hsCRP–CRC association may be explained by residual confounding by other risk factors, such as adiposity, rather than by CRP marking colonic inflammation.

**Keywords** C-reactive protein · Inflammation · Colorectal cancer · Obesity

# Vasectomy and Prostate Cancer: A [REDACTED] Study in India

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Platz E A (Department of Epidemiology, Harvard School of Public Health, Boston, MA, USA), Yeole B B, Cho E, Jussawalla D J, Giovannucci E and Ascherio A. Vasectomy and prostate cancer: A case-control study in India. *International Journal of Epidemiology* 1997; 26: 933-938.

**Background.** The role of vasectomy in the development of prostate cancer remains controversial. In particular, there has been concern about detection bias and confounding in the previously published epidemiological studies examining this hypothesis. With the goal of minimizing detection bias, we have evaluated the relation between vasectomy and prostate cancer in a population without routine prostate cancer screening.

**Methods.** A [REDACTED] study consisting of 175 prostate cancer cases and 978 controls with cancer diagnoses other than prostate cancer was conducted at hospitals covered by the Bombay Cancer Registry in Bombay, India. History of vasectomy, demographic, and lifestyle factors were obtained by structured interview. Multiple logistic regression was used to estimate odds ratios (OR) and 95% confidence intervals (CI).

**Results.** Standardizing by age, 8.7% of cases and 8.3% of controls had had a vasectomy. The OR for prostate cancer comparing men who had had a vasectomy to those who did not was 1.48 (95% CI : 0.80-2.72) controlling for age at diagnosis, smoking status, alcohol drinking, and other demographic and lifestyle factors. Risk of prostate cancer associated with vasectomy appeared to be higher among men who underwent vasectomy at least two decades prior to cancer diagnosis or who were at least 40 years old at vasectomy.

**Conclusions.** Although not statistically significant, the results of this hospital-based [REDACTED] study are consistent with the hypothesis of a positive association between vasectomy and prostate cancer. Because routine prostate cancer screening is not common in this population, detection bias was unlikely to account for this association.

**Keywords:** prostate cancer, vasectomy, case-control study, India

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# Association between plasma cholesterol and prostate cancer in the PSA era

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We previously found that statin users had a lower risk of advanced and possibly high-grade prostate cancer compared with nonusers. We hypothesize that statins' effects on cholesterol synthesis may explain those findings because prostate cancer cells exhibit cholesterol dysregulation. Thus, we investigated whether low plasma cholesterol is associated with prostate cancer overall and by stage and grade. Participants were drawn from the 18,018 members of the Health Professionals Follow-Up Study who provided blood in 1993–1995. We ascertained 698 incident cases through January 2000. Controls were 698 men who had a PSA test and were matched to cases. Plasma cholesterol was measured enzymatically. Conditional logistic regression was used to estimate multivariable ORs and 95% CIs of total, clinically organ-confined ( $n = 518$ ), advanced (T3b or worse;  $n = 61$ ), low-grade (Gleason sum < 7;  $n = 386$ ) and high-grade (Gleason sum  $\geq 7$ ,  $n = 247$ ) disease. Low cholesterol (<25th percentile vs.  $\geq 25$ th percentile) was not associated with total (OR = 0.93, 95% CI: 0.72–1.20), organ-confined (OR = 0.87, 95% CI: 0.64–1.18) or low-grade (OR = 1.06, 95% CI: 0.75–1.51) disease. However, men with low cholesterol had a lower risk of high-grade disease (OR = 0.61, 95% CI: 0.39–0.98), especially if organ-confined (OR = 0.54, 95% CI: 0.29–0.99). The association for advanced disease appeared inverse, but number of cases was small (OR = 0.42, 95% CI: 0.13–1.36). Associations remained after excluding cholesterol-lowering drug users. These results coupled with prior statin findings suggest that mechanistic studies on cholesterol metabolism should be pursued to understand a possible target for preventing poorly differentiated prostate cancers.

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# You should be able to...

- Distinguish between and identify epidemiologic study designs

This discussion is beginning to motivate the idea of bias, which is formally introduced in lectures 15 & 16 (Dr. Platz)