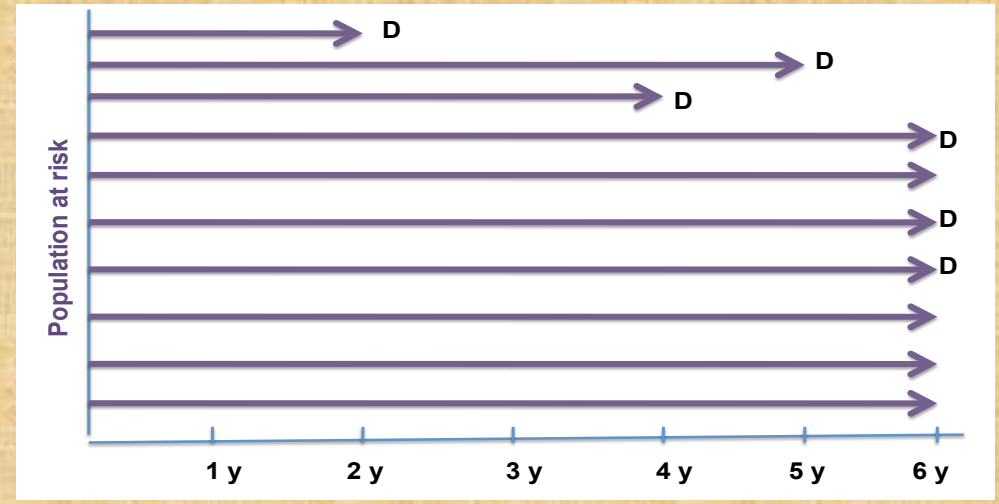

Cohort Studies

Dr. Rufaidah Dabbagh

Most of the content in this presentation has been retrieved from a previous lecture:

Cohort Studies

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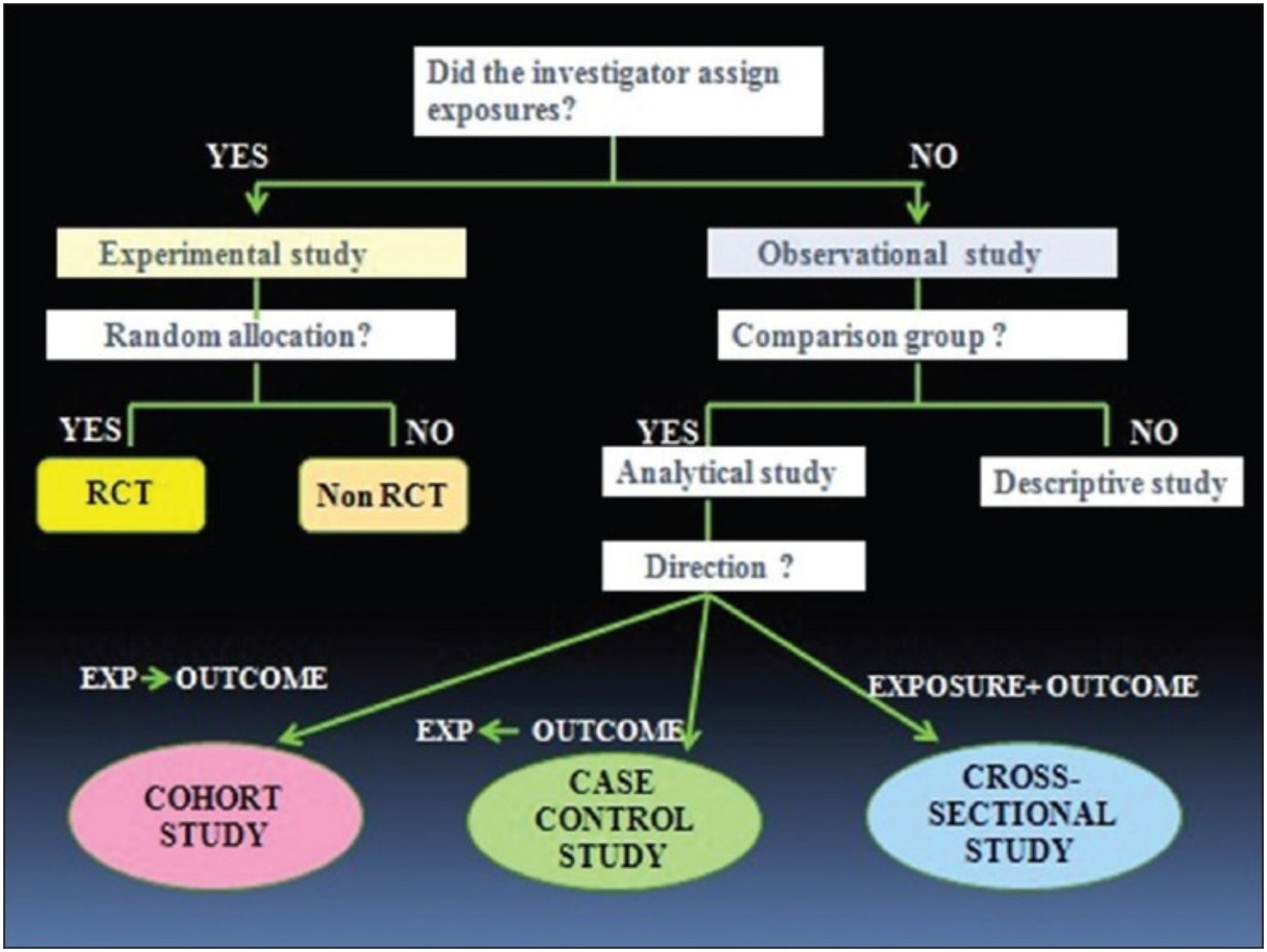
Prof Ashry Gad
Department of Family & Community Medicine

Learning Objectives

- To understand what a cohort design is
- To differentiate between “a cohort” and a “cohort ”study
- To differentiate between types of cohort studies; prospective cohort, retrospective cohort
- To learn the advantages and disadvantages of a cohort study
- To calculate the appropriate measures of disease frequency in cohort studies: incidence, RR, RD



Source: *Avila H, Pandey R, Bolla V, Roa H, Avula JK. Periodontal research: basics and beyond –part 1 (defining .the research problem, study design and levels of evidence). J Indian Soc Periodontol 2013; 17(5): 565-70*

Design of Cohort Studies
? What is a cohort

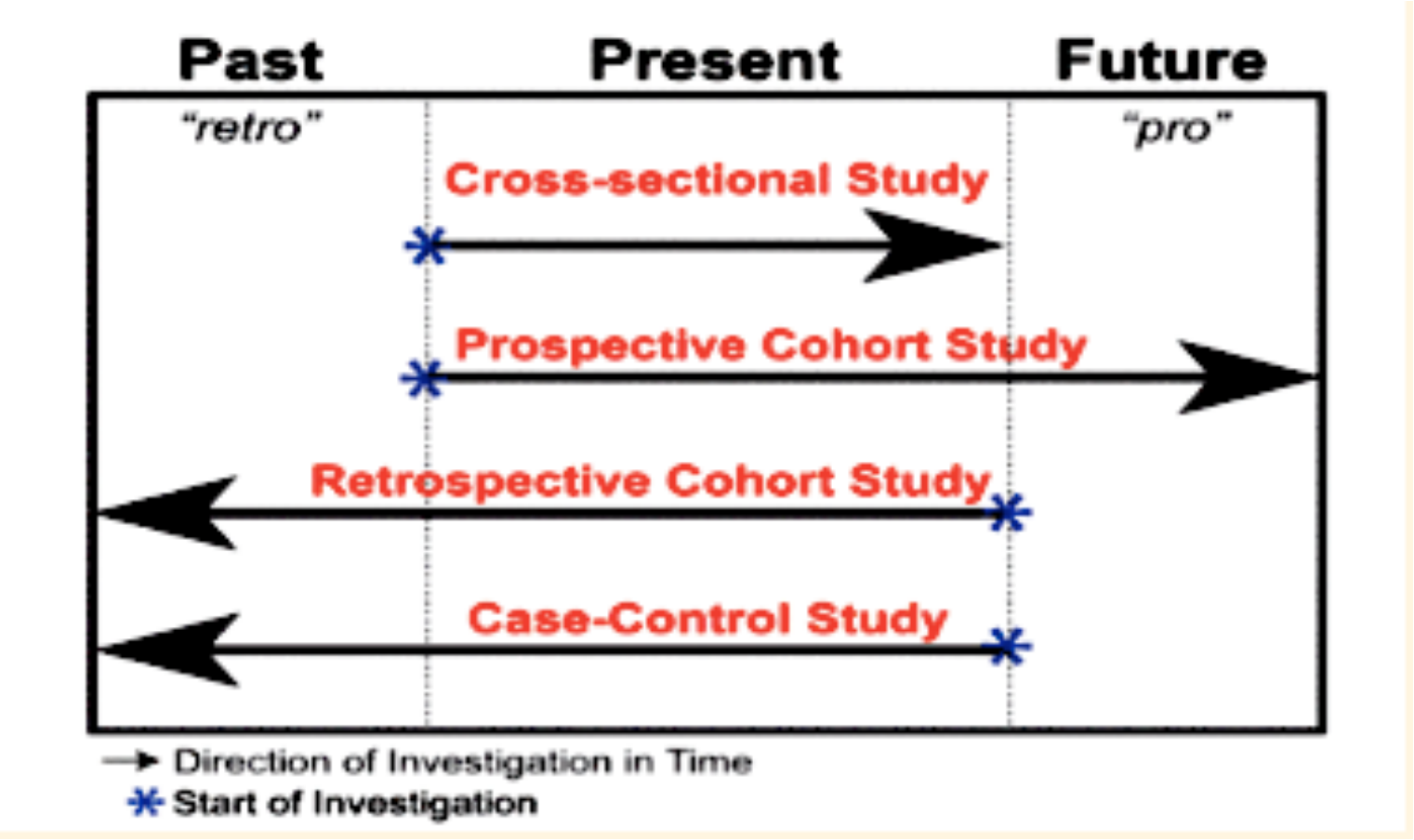
- ***Cohort*:** group of individual with a common characteristic who are followed over a period of time e.g. *A smoker's cohort means all are smokers in that group; birth cohort; class cohort*

- ***Cohort study design*:** selection of cohorts based on exposed and unexposed individuals, and following them over specified time or until development of outcome (disease/death)

.Design of Cohort Studies cont

- And so in a cohort study we select individuals based on their exposure to a specific risk factor (exposed group and non-exposed group)
- It I important that these people are free of the disease at the beginning of the study
- then we follow them over a certain period of time and :record the following measures
  - Total number of people at risk at the beginning (total at risk at baseline)
  - Time until the development of the disease (time at risk)
  - Number of new cases that have developed the disease
  - Number of people who were lost to follow-up

Direction of Investigation Time in Study Designs



Etikan I, Abubakar S, Alkassim R (2017) Frequency Measures of Epidemiological Studies. Biom Biostat Int .J 5(1): 00124

?What is a Risk

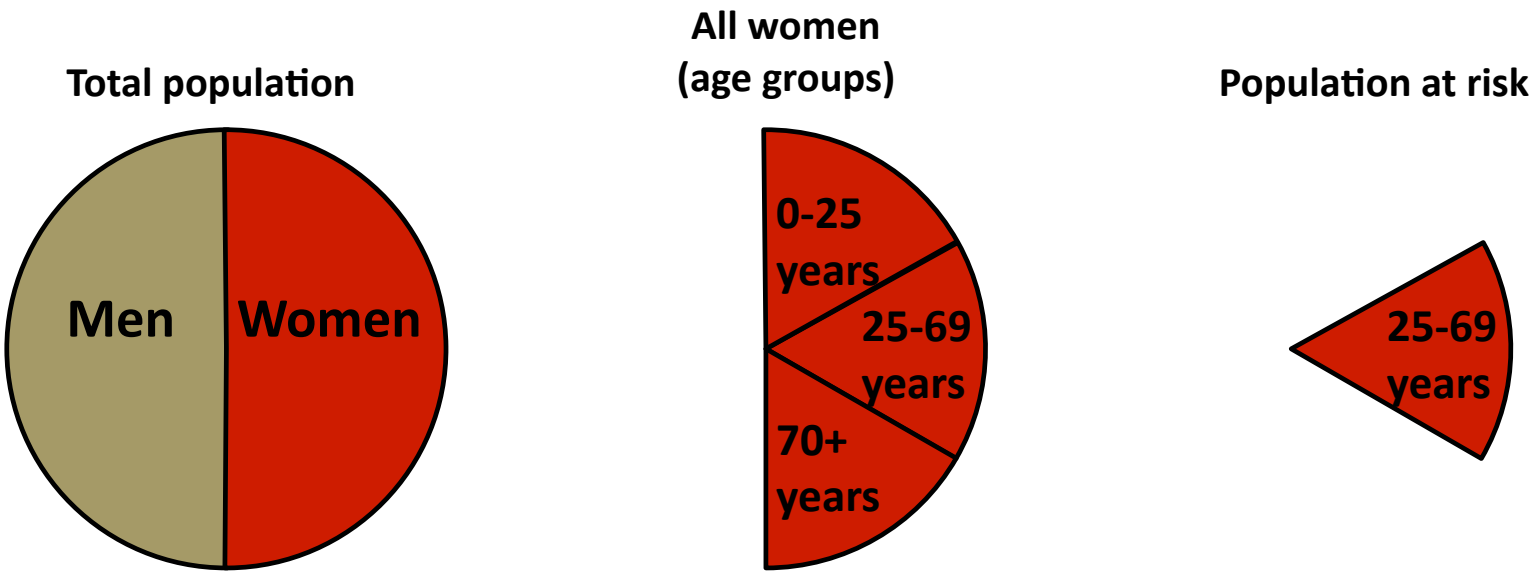
- Risk is the possibility of harm
- In epidemiology risk is the likelihood of an individual in a defined population to develop a disease or other adverse health problem
- It is usually used to refer to the ***incidence proportion***

?What is a Risk Factor

- A **risk factor** is a characteristic associated with .disease
- In cohort studies, we measure the exposure to a certain **risk factor** (exposure or non-exposure), and then we calculate the **risk** for developing the disease based on the exposure
- We then assess the association between **risk factor** exposure and development of disease by comparing the **Risks** in the two groups (exposed and non-exposed); i.e. *compare the incidence proportions*

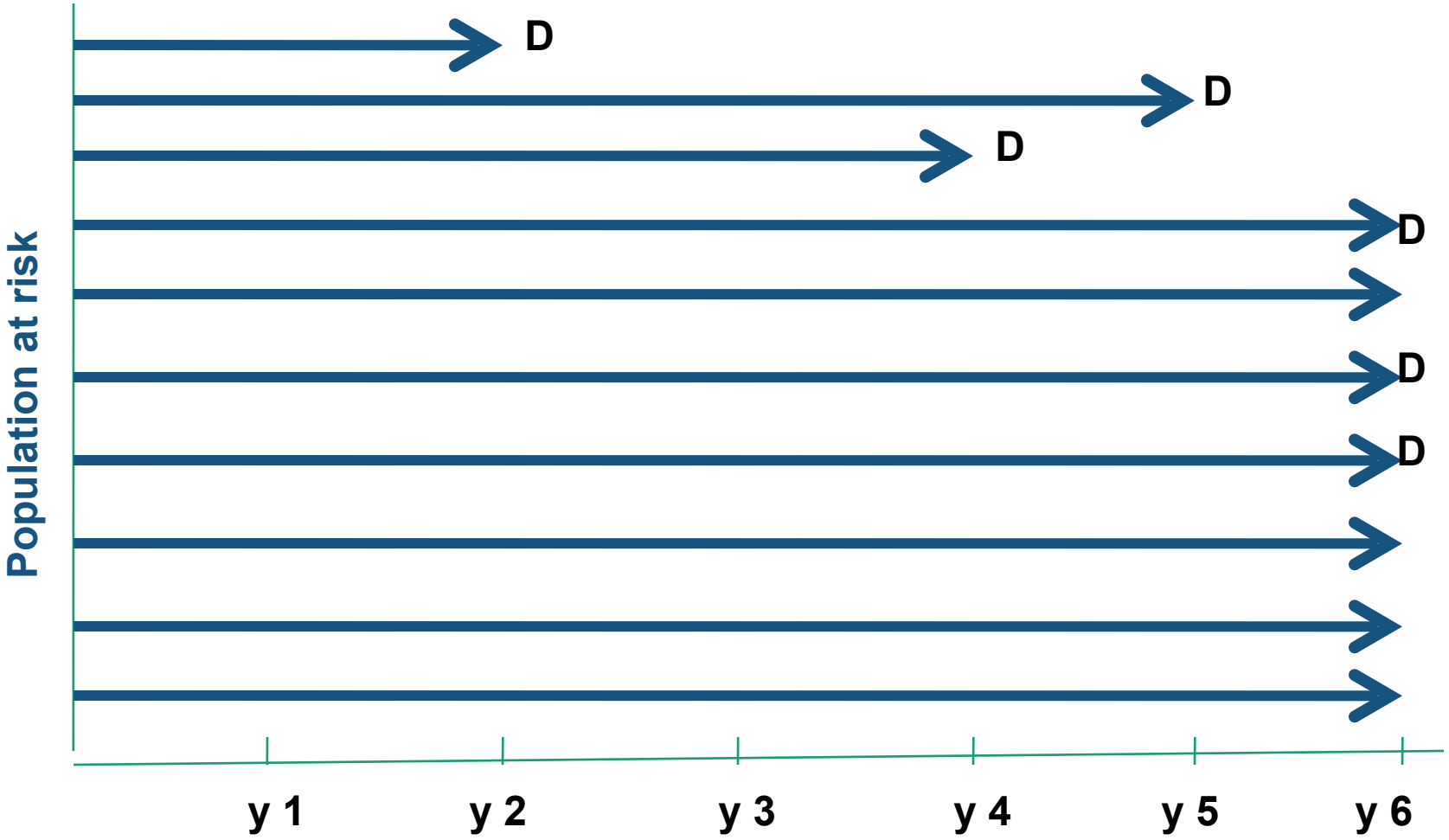
Population at Risk

The population at risk in a cohort study is a well-defined population that is free of the disease at the beginning of the study and has certain characteristics that put them at risk for developing the disease



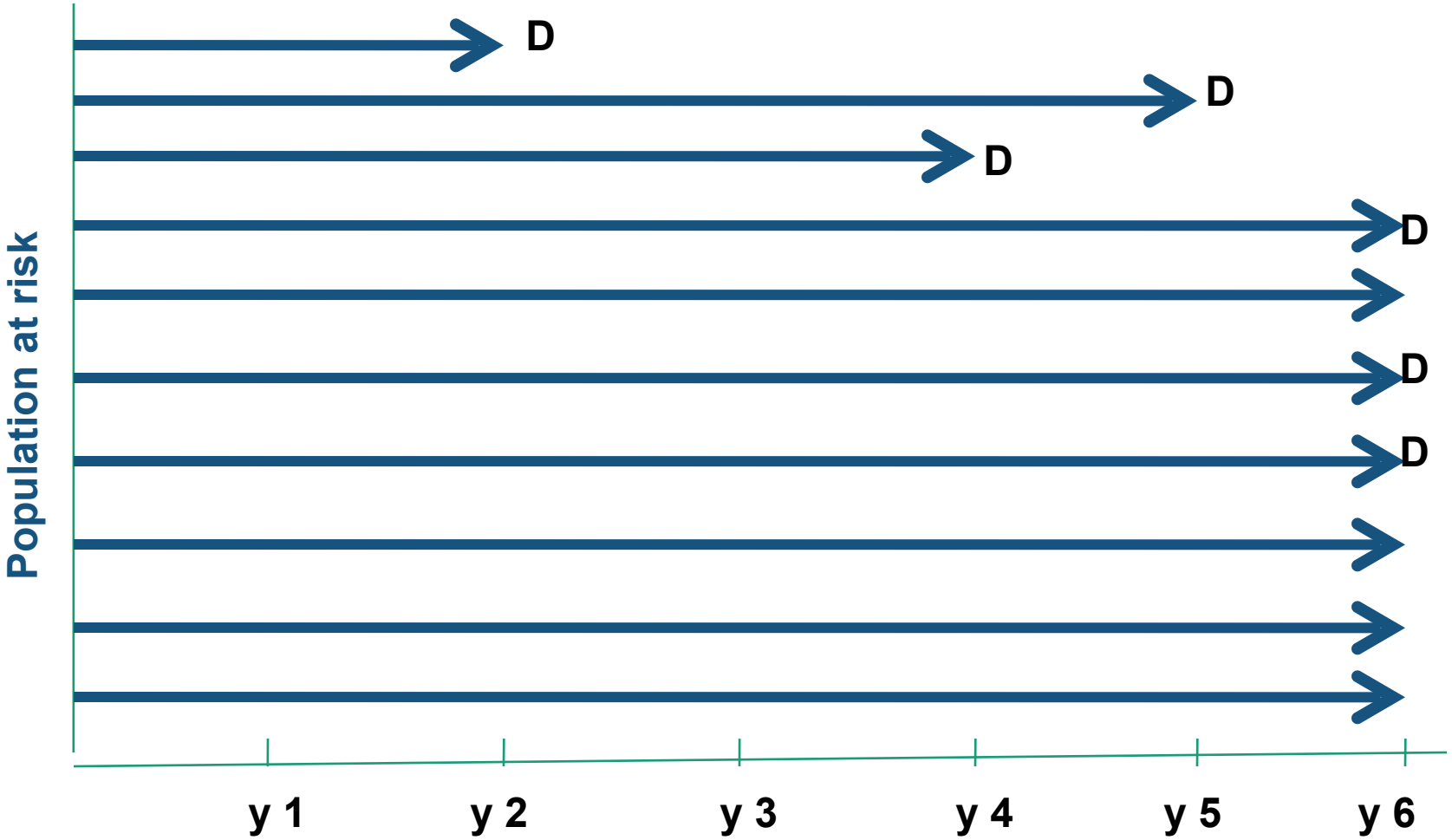
Eg. Population at risk in a study of carcinoma of cervix

Follow-up in a Cohort Study



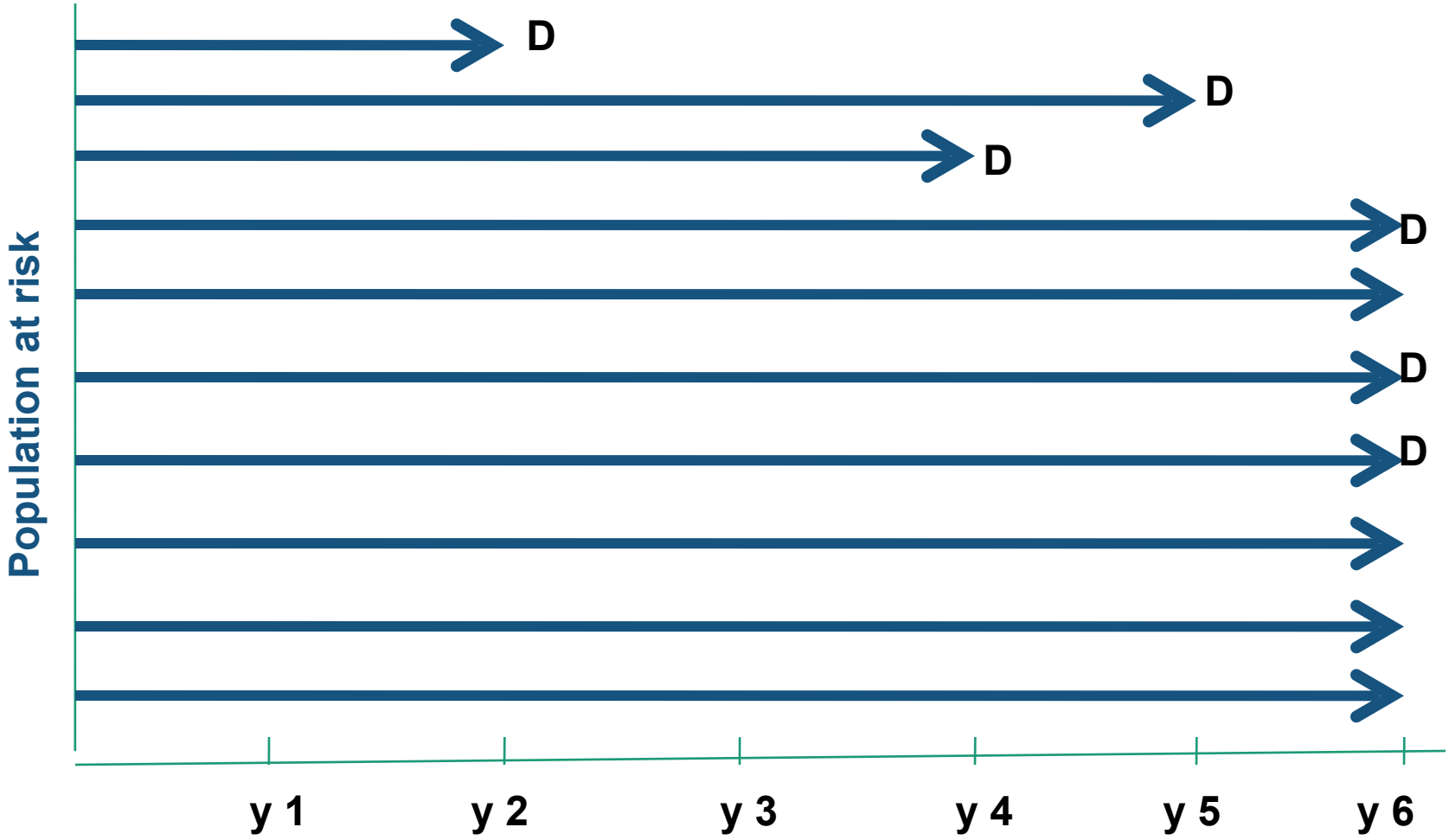
?of people at risk at baseline #
?of cases developed during the 6 year follow-up period #
?Total person-time at risk

Follow-up in a Cohort Study



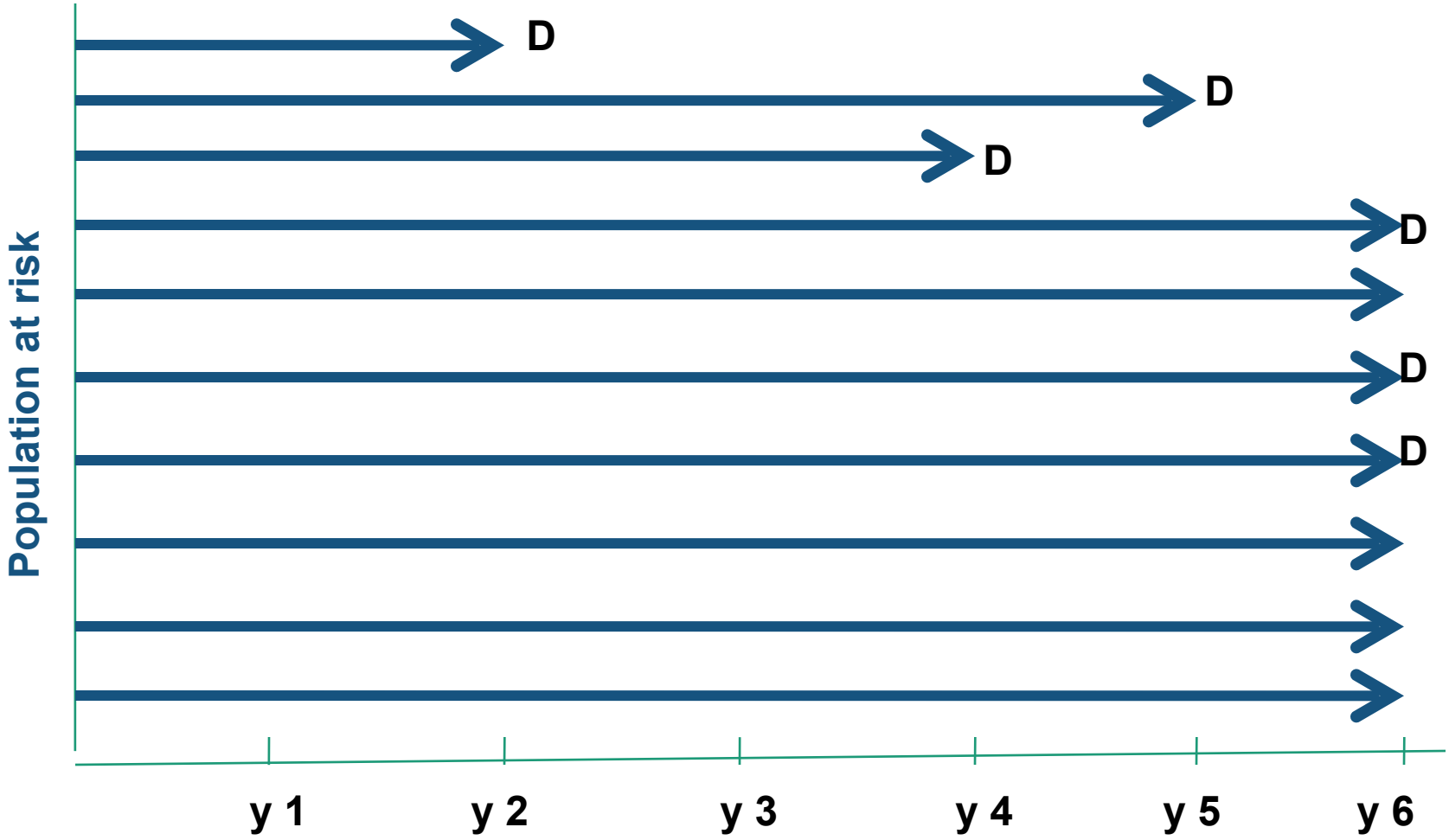
of people at risk at baseline? 10 #
of cases developed during the 6 year follow-up period? 6 cases #
Total person-time at risk? 2+5+4+6+6+6+6+6+6+6= 53 person-years

Follow-up in a Cohort Study



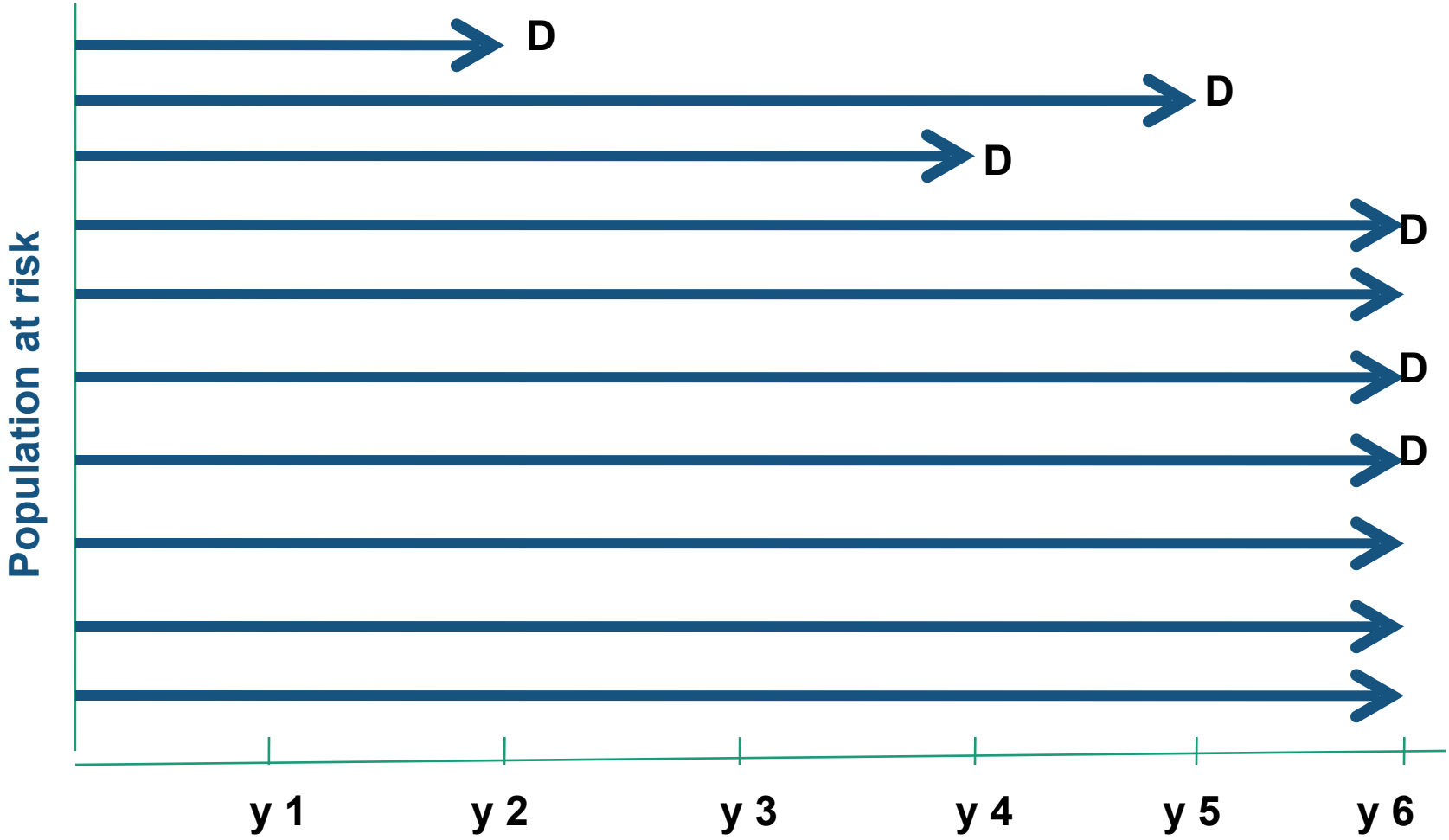
?What is the risk at year 4

Follow-up in a Cohort Study



What is the risk at year 4? 2 / 10 = 0.2

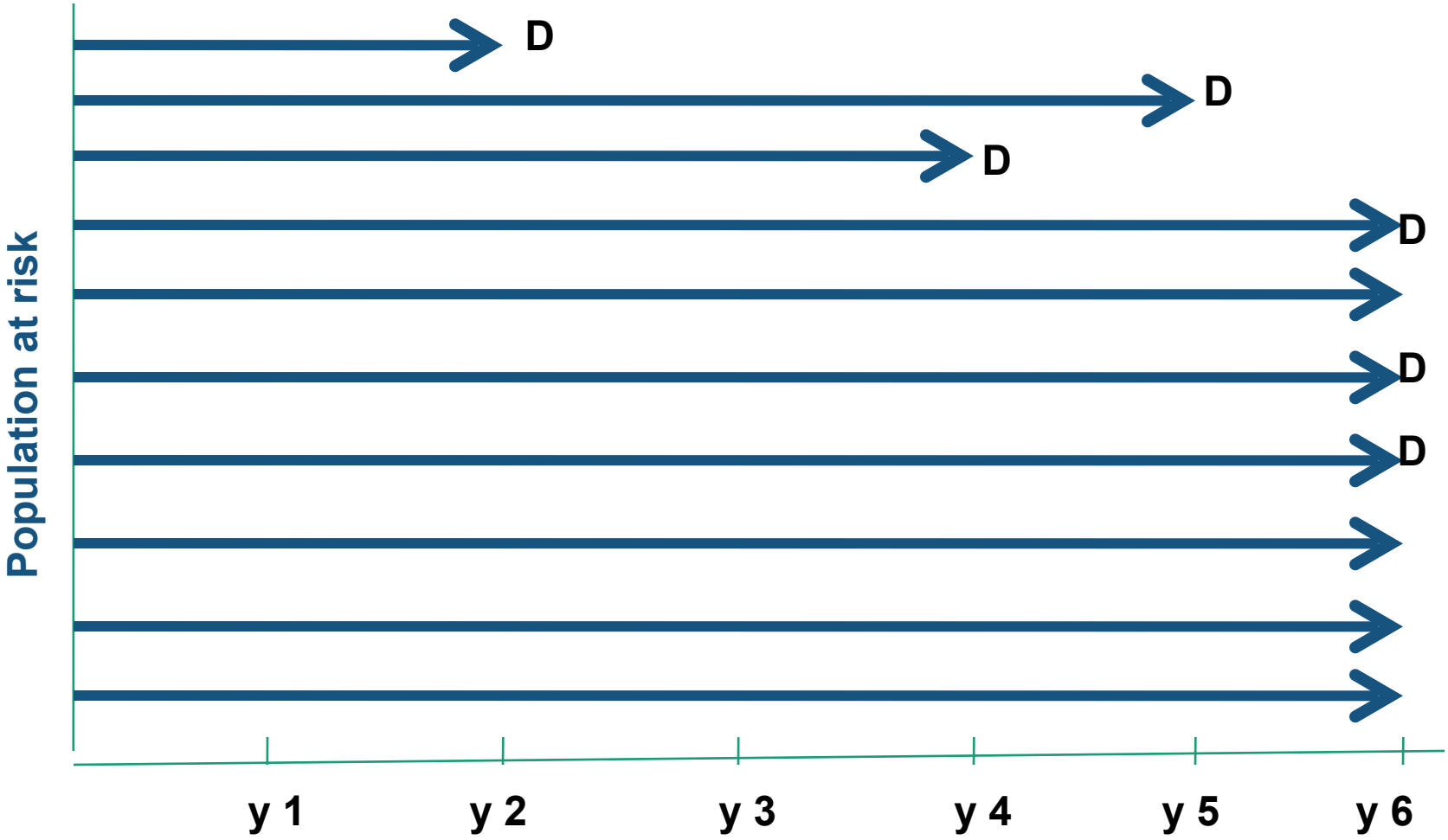
Follow-up in a Cohort Study



?What is the risk between 3y and 5y

?What is the prevalence between 3y and 5y

Follow-up in a Cohort Study



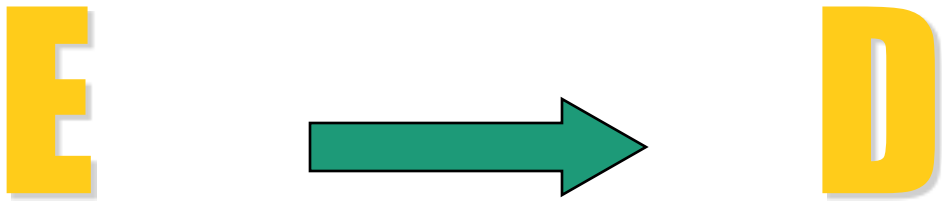
What is the risk between 3y and 5y? 2/ 9 = 0.22

What is the prevalence between 3y and 5y? 3 / 10 = 0.33

?What are we assessing in a Cohort study

?Are exposure and disease linked

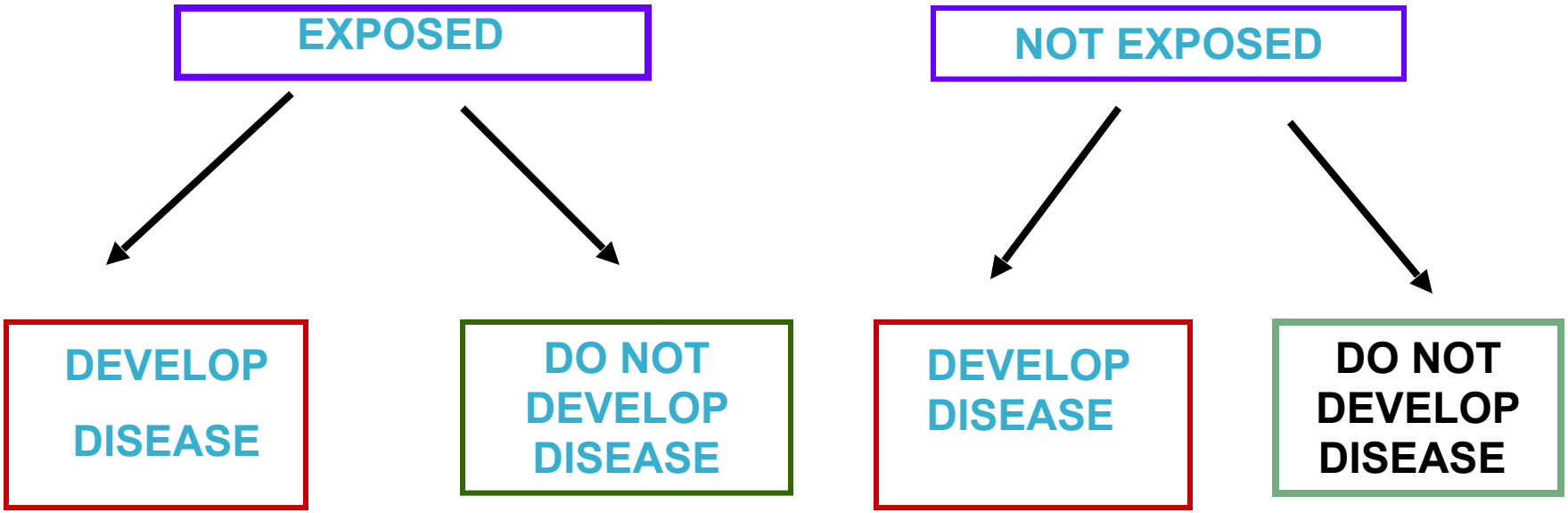
Direction of inquiry in cohort study

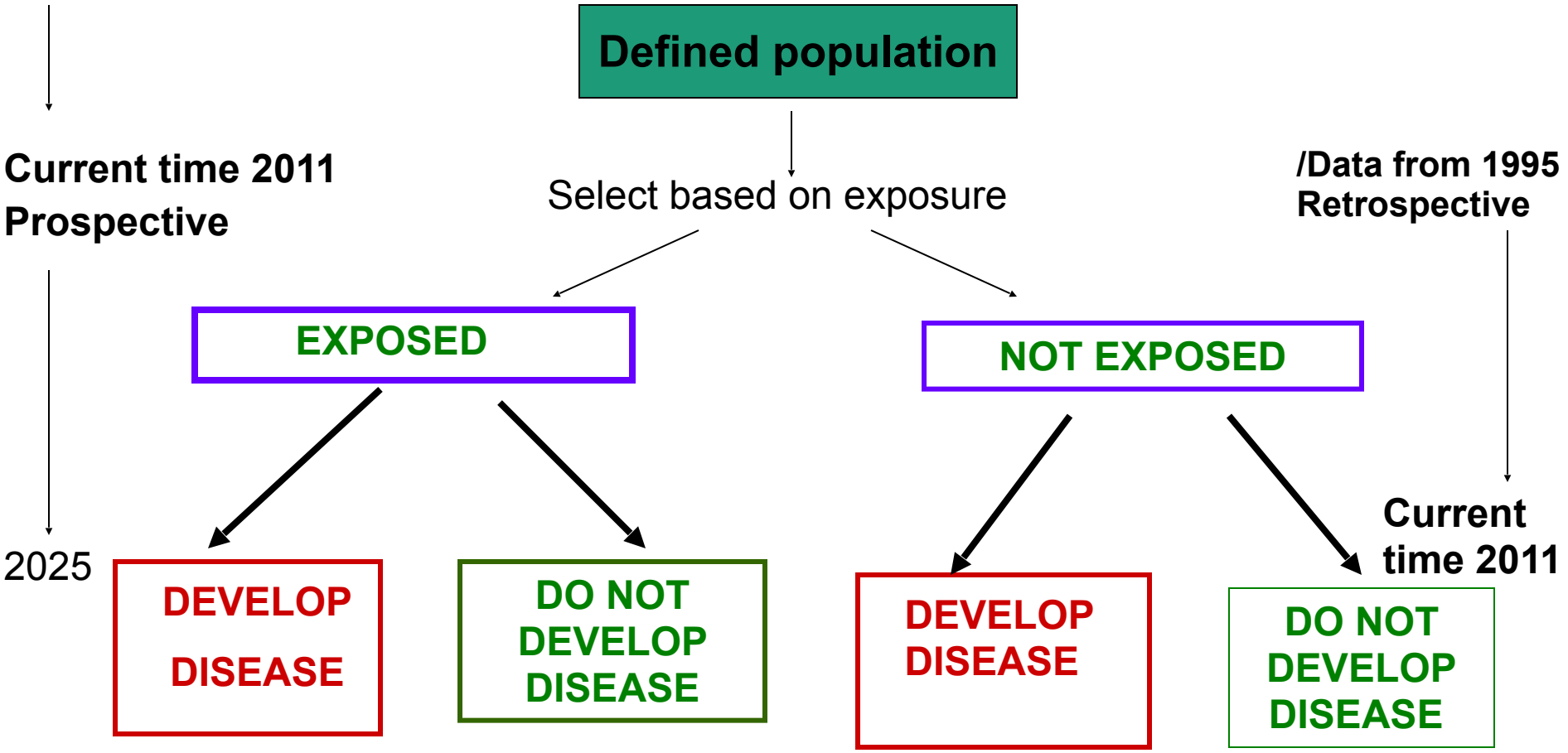


Exposure
.Risk factor e.g
Tobacco chewing

Disease (outcome)
e.g. Myocardial
Infarction (MI)

Design of a Cohort Study



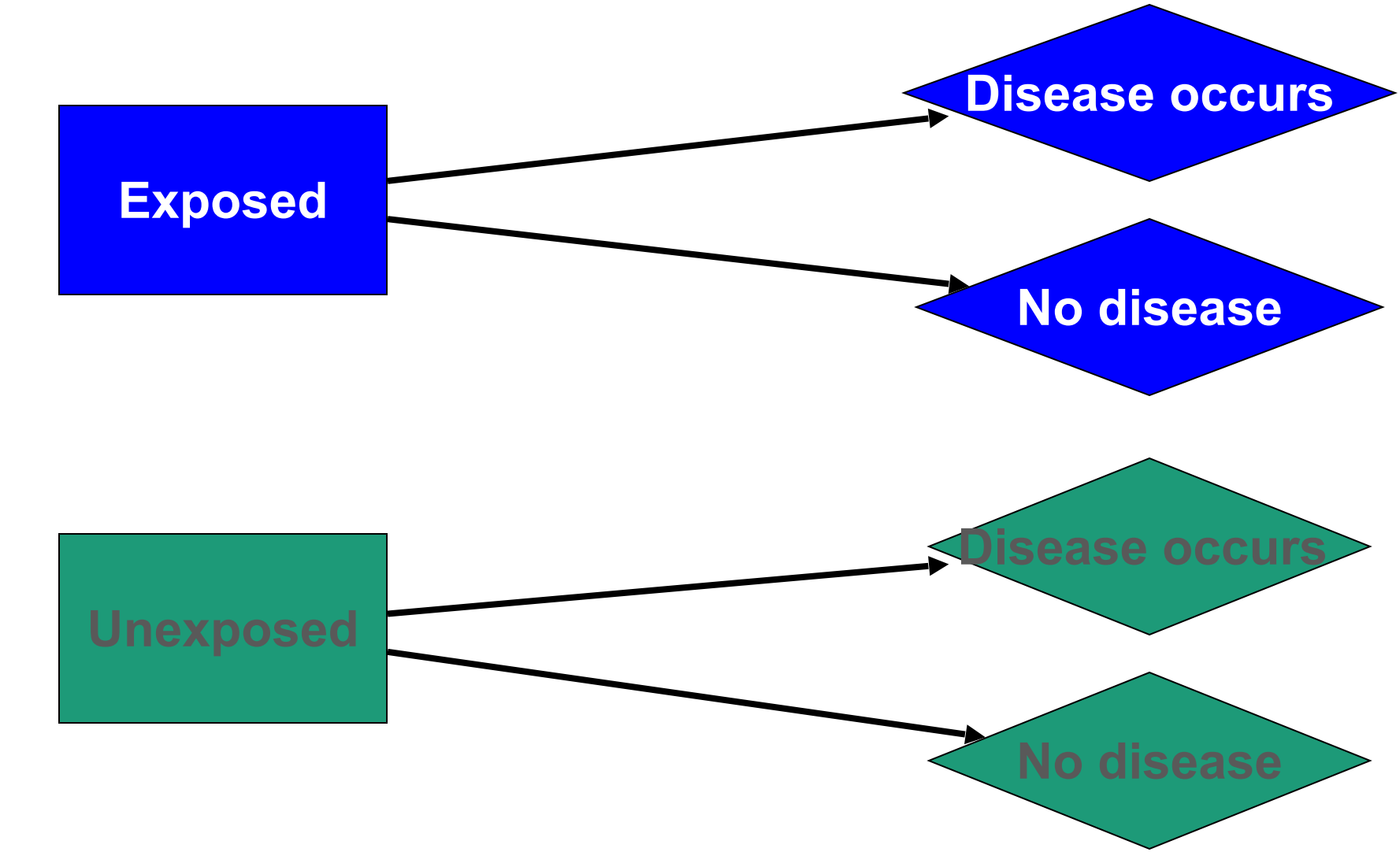


:There are two types of cohort studies

Prospective .1

Retrospective .2

Prospective Cohort Study

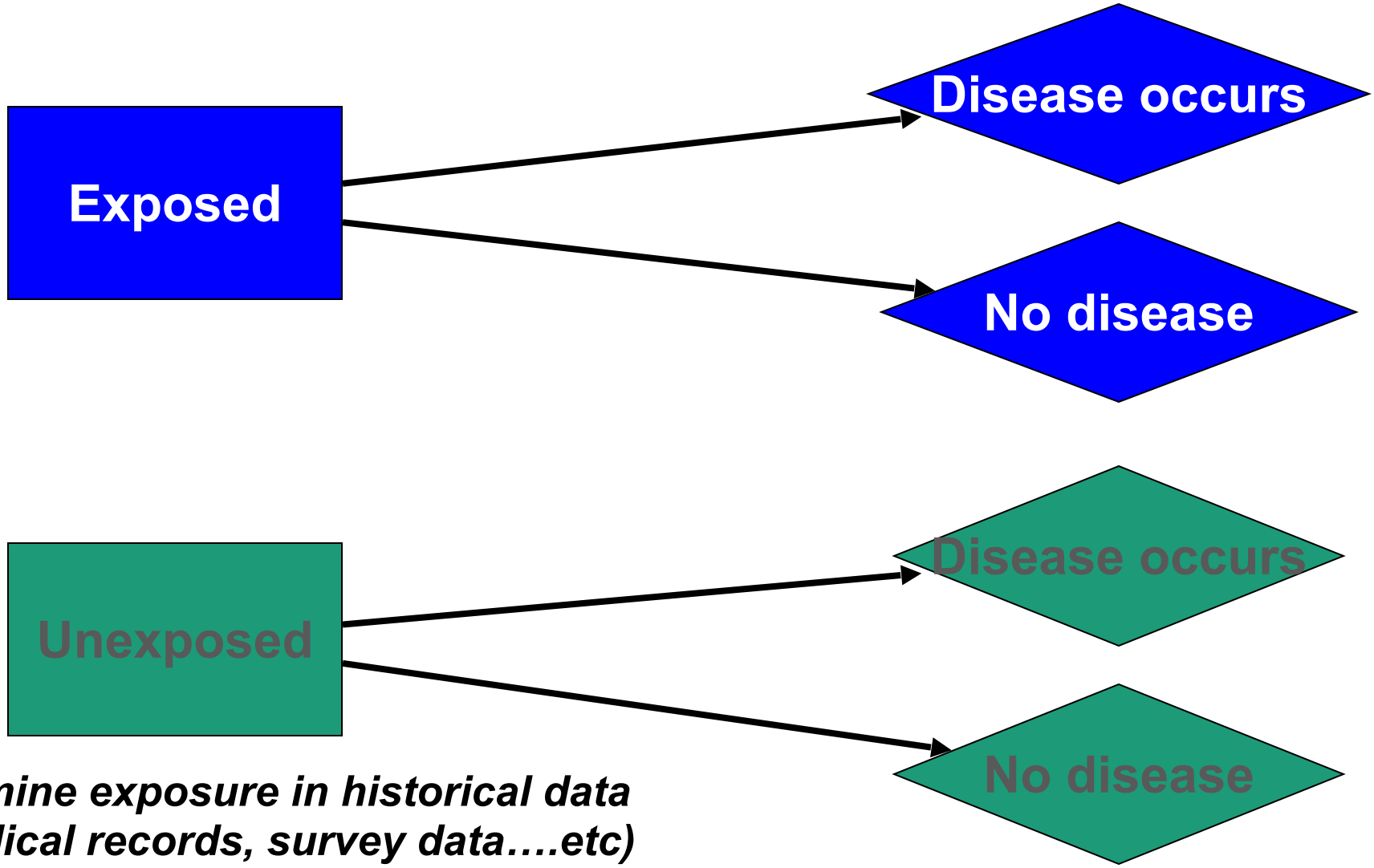


.Prospective Cohort Study cont

- In a prospective cohort the investigator identifies the population at risk at the beginning of the study, and their exposure to the risk factor (determine who is exposed and who is not)

- Then follows them up through a period of time to see who develops the disease and who does not

Retrospective Cohort Study



.Retrospective Cohort Study cont

- In a retrospective cohort, the investigator searches in the medical records (already collected data) to see who had the exposure and who did not and also who developed the disease and who did not

- Note that here the recording of the exposure and the disease all happened in the past, but the records have enough information to determine the timeline of events (that the exposure happened before the disease)

Retrospective Cohort compared to Prospective Cohort

- :Advantages
- In retrospective there is less time consumed for the study (the data is already there)
- Retrospective is cheaper than prospective cohort
- Retrospective is suitable for diseases that take a long time to develop (e.g. cancers, Parkinson's, etc.)

- :Disadvantages
- Some times difficult to determine the accuracy of the historical data in retrospective studies

Examples of Famous Cohort Studies

The Framingham Study

- Began in 1948 for Cardiovascular disease
- A small town 20 miles from Boston in Massachusetts, USA
- Population under 30,000
- ?Participants between 30-62 years of age ..why
- Follow up for 20 years
- Sample size of 5000

,Other famous cohorts include; *British Physicians Cohort UK; Nurses Health Study USA Women Health Initiative (WHI), Study of women across the nation (SWAN) in USA*

Framingham Study

Exposure

- Smoking
- Obesity
- Elevated blood pressure
- Elevated Cholesterol levels
- Physical activity

Outcome

- **New Coronary events determined by**

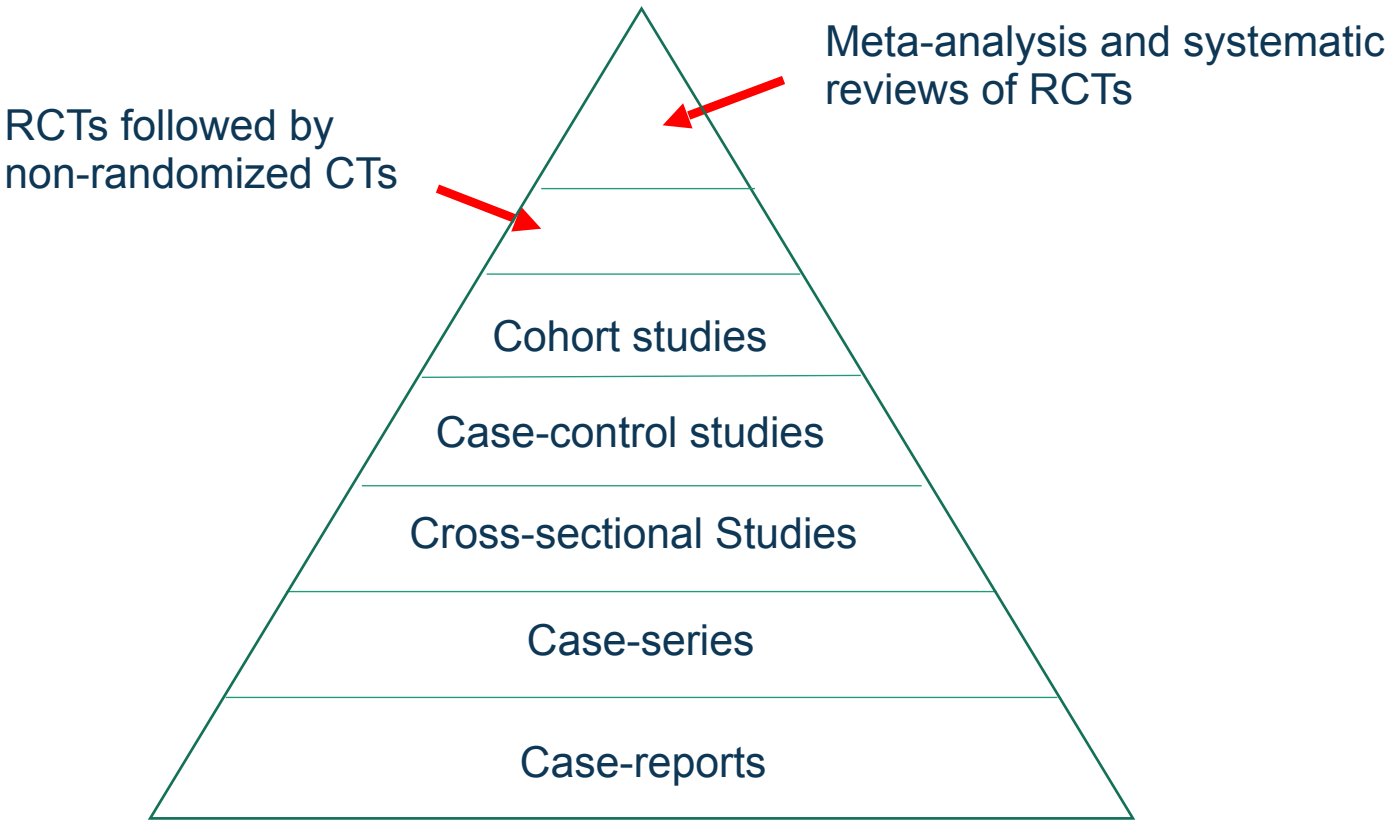
  Daily surveillance-

  Examination / 2 years-

Nurses Health Study

Nurses' Health Study, a large cohort study involving over121,700 women, who enrolled in 1976 from eleven states of USA; using a questionnaire in mail every two years to determine

Exposure	Outcomes in
• Biological	• ,Chronic diseases
• Demographic	• Cancer in general
• Hormonal	• Cancers related to female reproductive tract
• Lifestyle	
• Nutritional and	
• .Other risk factors	



Traditional Evidence-based Medicine Pyramid

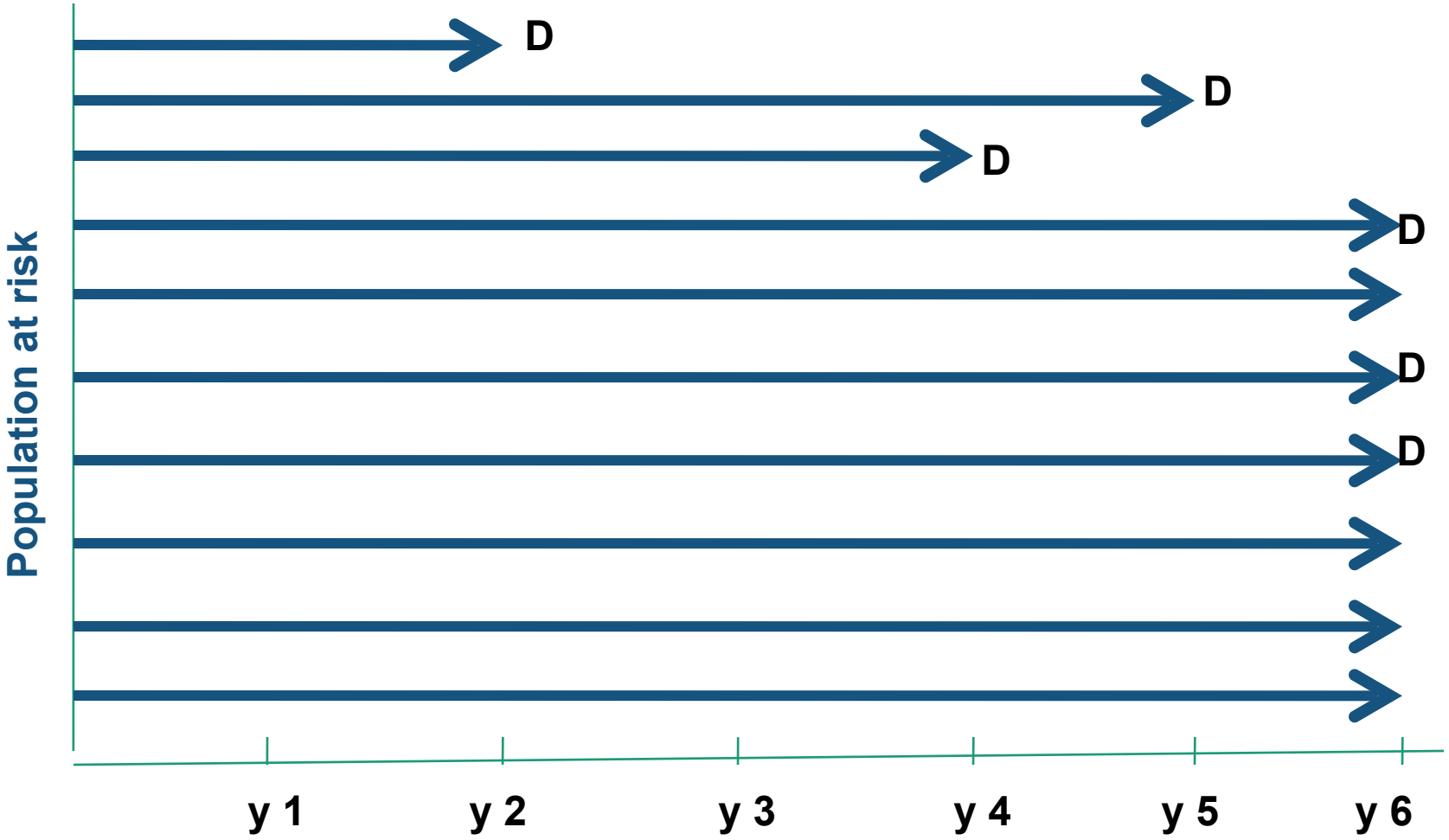
Source: *Murad MH, Asi N, Alsawas M, Alahdab F. New evidence pyramid. Evid Based Med 2016; 21(4): 125-7*

The Cohort study design provides the best evidence compared to other observational studies

?Why

- The temporal relationship between exposure and disease is clear (i.e. we know that the exposure occurred before disease, so it provides stronger evidence for possible causation relationship)

?What can measure in cohort study



of people at risk at baseline #
of cases developed during the 6 year follow-up period #
Total person-time at risk

What can we measure in a ?Cohort study

Risk (incidence proportion)	**.1**
Rate (incidence rate)	**.2**
Prevalence	**.3**
Risk Ratio (relative risk)	**.4**
Risk Difference	**.1**
Attributable Risk Fraction	**.2**

Analysis in Cohort Studies

:The basic analysis involves

- Calculation of incidence proportion among the exposed
- Calculation of incidence proportion among the non-exposed
- Compare the two by calculating the Risk Ratio
- We can also calculate the “incidence rates”, because we measure the time during which individuals were at risk (i.e. person-time at risk)

Risk Ratio (RR)

	Disease	No disease	Total
Exposed	**a**	**b**	**a+b**
Unexposed	**c**	**d**	**c+d**

$$\frac{\text{Incidence in exposed}}{\text{Incidence in unexposed}} = \frac{a/a+b}{c/c+d} \quad RR =$$

? What does RR=1 means

?What does RR > 1 mean? RR < 1

Interpretation of Risk Ratio (RR)

RR=1: No association between exposure and disease

incidence proportions are identical between groups

RR> 1: Positive association (increased risk in exposed)

exposed group has higher incidence than unexposed group

RR< 1: Negative association (decreased risk in exposed)

unexposed group has higher incidence than exposed group. This means the exposure could probably be protective

Example: Risk Ratio Calculation

Cohort study following up individuals for 1 year

	Develop CHD	Not Develop CHD	Total
Smokers	84	2916	3000
Non-smokers	87	4913	5000

$= 84/3000 = 0.028$ Incidence in smokers

Incidence in non-smokers $= 87/5000 = 0.0174$

$= 0.028/0.0174 = 1.61$ Risk ratio

Risk Difference and Attributable Risk Fraction

Risk Difference

- The difference between the Risk of the disease in the exposed to unexposed
- $RD = R_e - R_u$

Attributable Risk Fraction (Excess Fraction)

- The excess proportion of cases that is attributed to exposure
- $ARF = (R_e - R_u) / R_e$

R=Risk. e= exposed, u=unexposed

Attributable Risk Fraction

	Develop CHD	Not Develop CHD	Total
Smokers	84	2916	3000
Non-smokers	87	4913	5000

- What is the excess proportion of CHD cases that is attributed to ?smoking
- ARF= $\frac{(84/3000) - (87/5000)}{(84/5000)} \approx 0.38 = 38\%$

This means that 38% of excess CHD cases are attributed to smoking in this study

Potential Biases in Cohort Studies

Bias refers to any systematic error in the study (design or analysis) that results in a mistake in our estimates

:In a cohort study bias can arise from

- *Non response* => people do not participate
- *Loss to follow up* => people leave
- *Error in measuring exposure or outcome* => mistakes in the classification of the exposure or the disease

In addition to other sources of bias encountered in other study designs

Advantages of Cohort studies

.Useful in rare exposures .1

Can study multiple outcomes of a single exposure / risk .factor .2

Certain about the **temporality** of exposure and disease (disease occurs after exposure) .3

We can calculate incidence proportion and rate .4

Can quantify Risk Ratio and Risk Difference .5

Provides better evidence than case-control study, and cross-sectional study .6

Can establish a natural history of disease when not known .7

Disadvantages of Cohort studies

There is potential for loss to follow up, especially in diseases that take a long time to develop .1

Measurement errors, multiple interviews, tests .2

Not suitable for evaluation of rare diseases .3

Takes a long time (if prospective) .4

More expensive than case-control and cross-sectional studies .5

Provides weaker evidence than RCTs .6

Summary

- Cohort studies are observational in nature (but also analytical) and are useful in comparing risks in subgroups of populations within a specific time frame
- Availability of data from previous years can lead to less expensive estimates for Risk, RR, and RD, using a retrospective cohort study
- Prospective Cohort studies are expensive in time and resources
- When a cohort is conducted accurately, estimates of Risk, RR and AR can help make inferences about a causal link between risk factors and disease/other .outcomes e.g. cancer

References

- Gordis L. Epidemiology. 4th Edition. .Philadelphia, PA: Saunders Elsevier; 2009
- Rothman KJ, Greenland S, Lash TL. Modern Epidemiology. 3rd Edition. Philadelphia, PA: .Lippincott Williams and Wilkins; 2008